Abstract Book

Society of Surgical Oncology
69th Annual Cancer Symposium

Boston, Massachusetts
March 2-5, 2016

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An Oncology Journal for Surgeons

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ABSTRACTS

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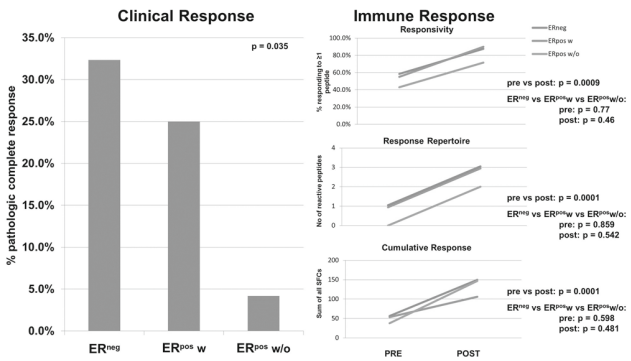
Combination Anti-Estrogen Therapy and Anti-HER2 Dendritic Cell Vaccination Improves Pathologic Complete Response in $ER^+/HER2^+$ DCIS Patients L. Lowenfeld,[1]* S. Zaheer,[1] M. Fracol,[2] J. Datta,[1] S. Xu,[1] E. Fitzpatrick,[1] A. DeMichele,[1] P. Zhang,[1] E. McDonald,[1] B.J. Czerniecki.[1] *1. Surgery, University of Pennsylvania, Philadelphia, PA; 2. Northwestern, Chicago, IL.*

INTRODUCTION: ER signaling has been proposed as an escape pathway in the setting of HER2 inhibition, resulting in resistance to anti-HER2 therapy. In our clinical trials of a neoadjuvant HER2-pulsed dendritic cell (DC) vaccine, we observed higher rates of pathologic complete response (pCR) in hormone independent (ER^-) patients. We investigated the effect of combination anti-estrogen (AE) therapy and anti-HER2 DC vaccination on clinical and $CD4^+$ T-helper type 1 (Th1) immune responses. METHOD: Seventy-eight $HER2^+$ DCIS patients received a neoadjuvant HER2-pulsed DC1 vaccine: ER^- (n=34, 43.6%), ER^+ treated without AE therapy (ER^+w/o AE; n=24, 30.8%), ER^+ treated with concurrent AE therapy (ER^+w AE; n=20; 25.6%). pCR was assessed at surgical resection and patients were followed clinically to detect subsequent breast events. Of available anti-HER2 $CD4^+$ Th1 responses pre and post-vaccination (n=51; 65.4%), reactivity to an individual HER2 peptide was defined as a minimum of 20 SFC/2x10^5 cells after subtracting unstimulated background and at least a two-fold increase over unstimulated background. Three metrics were used to evaluate Th1 responses: (1) responsivity (% of patients reacting to ≥1 peptide), (2) response repertoire (number of reactive peptides), and (3) cumulative response (sum of SFCs across all 6 peptides). RESULTS: Eleven ER^- patients (32.4%) and 5 ER^+w AE patients (25%) achieved pCR (p=0.76); whereas, only 4.2% of ER^+w/o AE patients achieved pCR (p<0.01). Patients were followed for a minimum of 1yr, median follow-up 5yrs. Subsequent breast events (DCIS or IBC) only occurred in ER^+w/o AE patients (n=4; 16.7%). Each cohort mounted a significant Th1 immune response following vaccination (pre vs post; p<0.01). However, there was no significant difference in pre or post immune responses between ER, ER^+w/o AE, or ER^+w AE cohorts. CONCLUSION: Simultaneous neoadjuvant AE therapy and anti-HER2 DC1 vaccination increases the rate of pCR and decreases the rate of subsequent breast events in patients with $ER^+/HER2^+$ breast cancer. Combination AE and anti-HER2 therapy warrants further exploration with randomized controlled trials.



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Neoadjuvant Chemotherapy Increases Complete Cytoreduction Rate but Does Not Improve Final Outcome in Advanced Epithelial Ovarian Cancer H. Medina-Franco,* F. Lambreton, A. Fimbres-Morales, J. Vargas-Siordia. *National Institute of Medical Sciences and Nutrition, Mexico City, Mexico.*

Background. Most epithelial ovarian cancers present in advanced stages. Traditional management is maximum cytoreductive effort followed by platinum-taxane based chemotherapy. We hypothesize that giving all 6 cycles of chemotherapy before surgery will increase the complete cytoreductive rate and improve patient prognosis. Methods. Patients with advanced epithelial ovarian carcinoma (FIGO stages IIIC and IV without parenchymal metastasis) were included in a comparative study. Group A underwent cytoreductive surgery followed by 6 cycles of chemotherapy and Group B completed 6 cycles of preoperative systemic therapy followed by cytoreduction. Demographic, clinical, surgical and pathological variables were recorded and analyzed. Complete cytoreduction (R0) was defined as absence of macroscopic disease at the end of surgical procedure. Main outcome endpoints were: R0 rates, progression free survival (PFS) and overall survival (OS). Kaplan-Meier curves were constructed for survival analysis and univariate and multivariate analysis was performed. Significance was considered at p<0.05. Results. 105 patients were included: 42 in Group A and 63 in Group B. Mean patient age was 56 years old (range 32-85). There were no significant differences between groups regarding demographic, clinical, surgical or pathological variables. Surgical morbidity was low and not different between groups and there was no surgical mortality. R0 cytoreduction was obtained in 35.5% vs. 64.5% in Groups A and B respectively. Median PFS and OS for the entire cohort were 16.2 and 38 months, respectively. Median PFS were 17.52 and 14.71 months for Groups A and B, respectively (p=NS) and OS were 44.2 and 33.6 months for groups A and B, respectively (p=NS). Factors associated with worse prognosis on multivariate analysis for the entire cohort were: anemia (Hb <12 g/dl) (p=0.004) and hypoalbuminemia (<3.5 g/dl)(p=0.007). Low performance status (Kanofski < 70) was of borderline significance (p=0.05). Conclusion. In spite of nearly doubling the rate of complete cytoreduction, preoperative chemotherapy does not improve outcome in advanced epithelial ovarian carcinoma.

3

Probing Compensatory Signaling to MEK Inhibition Uncovers the Vulnerability of Pancreatic Cancer to Dual Therapy with Trametinib Plus Foretinib A. Michaels,* J.M. Lindberg, T. Newhook, S.J. Adair, M.G. Mullen, J. Parsons, T.W. Bauer. *Surgery, University of Virginia, Charlottesville, VA.*

Background: The MEK inhibitor trametinib achieves modest growth inhibition in preclinical models of pancreatic ductal adenocarcinoma (PDAC). We hypothesized that in vivo evaluation of signaling pathways in PDAC tumors during trametinib treatment would reveal suitable targets for combination therapy with trametinib. Methods: Mice were engrafted orthotopically with KRAS-mutant patient-derived xenograft (PDX) PDAC tumors and treated with trametinib for 10 days, then phospho-receptor tyrosine kinase (pRTK) arrays of whole tumor lysates were performed to evaluate activation of compensatory signaling pathways. In subsequent experiments, PDAC PDXs were implanted into mice that were then treated with trametinib plus an inhibitor of compensatory signaling pathways and serial MRI was used to monitor tumor growth. Results: Trametinib treatment of PDAC tumors led to significantly increased activation of Axl (15-fold), VEGFR2 (14-fold), and Tie2 (11-fold) (p<0.01 for all) and a trend toward increased activation of the related receptors PDGFRa (3-fold), Ron (2-fold), and Met (2-fold). Interestingly, these pRTKs were not activated in drug-naïve tumors, but only after MEK inhibition with trametinib. In subsequent experiments, PDAC PDX-bearing mice were treated with control, trametinib, foretinib (inhibitor of Axl, Met, Ron, PDGFRa, VEGFR2 and Tie2), or trametinib + foretinib. Compared to control, trametinib resulted in 63% inhibition in tumor growth (p<0.01), foretinib led to 65% inhibition (p<0.01), and trametinib + foretinib led to 100% growth inhibition (p<0.01; Fig 1), confirming the importance of these compensatory signaling receptors to tumor growth. Conclusions: Combination therapy with trametinib plus an inhibitor of these compensatory signaling pathways achieved complete inhibition of tumor growth in vivo. The combination of trametinib plus foretinib in PDAC warrants further investigation. This in vivo paradigm for discovery of rational combination therapy in cancer is likely to be more successful than searching for targets in drug-naïve tumors.

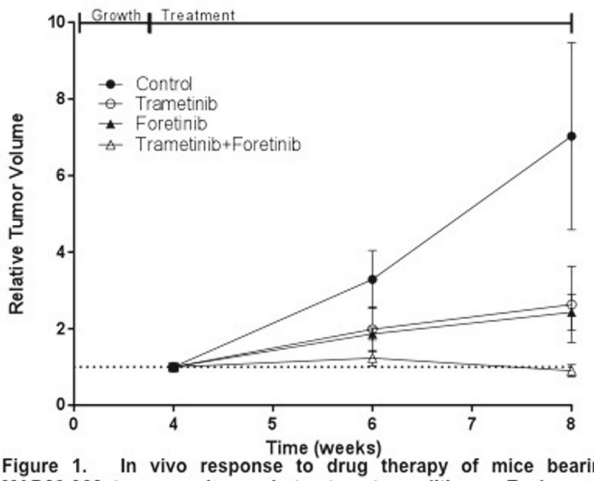

Figure 1. In vivo response to drug therapy of mice bearing MAD09-366 tumor under each treatment condition. Each group contained 5-6 replicates. Presented as the mean relative change in tumor volume.

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The Effect of Event-Free Years on the Risk of 5-Year Local Recurrence in Different Subtypes of Breast Cancer M. Moossdorff,[1]* T. van Nijnatten,[1] R. Bretveld,[2] B. Goorts,[1] E. Heuts,[1] L.J. Strobbe,[3] M. Smidt.[1] *1. Maastricht University Medical Center, Maastricht, Netherlands; 2. Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands; 3. Canisius-Wilhelmina Hospital, Nijmegen, Netherlands.*

Introduction. After treatment for breast cancer, follow-up consists of physical examination and mammography for five years, to detect local and regional recurrence. The chance of getting such a recurrence may decrease after event-free time, perhaps even to the point that follow-up is no longer useful. The aim of this study is to determine the risk of local recurrence (LR) as a first event before 5 years after diagnosis, conditional to being event-free 1, 2, 3, and 4 years. Methods. From the National Cancer Registry, all new epithelial (M0) breast cancers diagnosed in 2005-2008 were analyzed. LR risk was calculated with Kaplan-Meier analysis. Conditional LR (assuming x event-free years) was determined by selecting patients without an event at x years, and calculating the risk of LR within 5 years after diagnosis. Results. Of 51239 breast cancers, 5-year follow-up regarding recurrences was available for 34453 (67.2%). Overall, 5-year local recurrence as a first event occurred in 2.5%. After 1, 2, 3, and 4 event-free years, the risk of LR before the end of regular follow-up (5-years after diagnosis), decreased to 2.0%, 1.4%, 0.9%, and 0.4%. For the approximate subtypes, the risk of LR at diagnosis was highest for triple negative (5.6%) and lowest for ER+PR+Her2- (1.9%) tumors (see Table). In subtypes with the highest baseline risk (ER-, particularly triple negative tumors), risk was highest in the first three years and showed a strong decrease. Finally, it approximated the risk of the other subtypes. After 3 event-free years after diagnosis, the risk of LR in the next two years (i.e. before 5 years after diagnosis/end of regular follow-up) was less than 1% in all subtypes except triple negative (1.2%). Conclusion. The risk of 5-year LR as a first event was low overall. This risk decreased even further with the number of event-free years. After 3 event-free years, the overall risk was less than 1%. This improvement in prognosis is reassuring to patients during follow-up. It also suggests that follow-up beyond 3 years may be of limited value because of the low yield, both for individual follow-up and clinical studies using local recurrence as the primary outcome.

Impact of a number of event-free years on the chance of developing local recurrence as a first event within 5 years after diagnosis

			Risk of local recurrence before 5 years after diagnosis (i.e. before end of regular follow-up) Assuming x event-free years			
	N=	Risk of LR at diagnosis	After 1 event-free year	After 2 event-free years	After 3 event-free years	After 4 event-free years
All patients	34453	2.5% (874/34453)	2.0% (671/32814)	1.4% (433/30477)	0.9% (247/29020)	0.4% (120/26807)
Approximate breast cancer subtypes						
ER+PR+Her2-	17770	1.9% (331/17770)	1.7% (292/17214)	1.2% (203/16463)	0.8% (126/15617)	0.4% (61/14426)
ER+PR-Her2-	3930	2.0% (79/3930)	1.8% (66/3723)	1.2% (43/3507)	0.8% (25/3260)	0.4% (12/2982)
ER+Her2+	2689	2.5% (66/2689)	2.0% (52/2591)	1.4% (34/2461)	0.9% (22/2316)	0.5% (10/2175)
ER-Her2+	1897	4.1% (77/1897)	3.0% (53/1749)	1.9% (29/1566)	0.7% (10/1435)	0.2% (3/1337)
Triple negative	3619	5.6% (203/3416)	3.8% (122/3227)	2.2% (62/2874)	1.2% (31/2641)	0.7% (17/2446)

Subtype unknown for 4548 (13.2%)
ER: estrogen receptor, PR: progesterone receptor, Her2: Her2Neu receptor

5

Cancer Registries: Can We Improve the Quality of Thyroid Cancer Data? C.M. Kiernan,[1]* M. Whiteside,[2] C.C. Solorzano.[1] *1. General Surgery, Vanderbilt University, Nasvhille, TN; 2. Tennessee Department of Health, Nashville, TN.*

Cancer registries are increasingly being used in research and the results are cited in practice guidelines. Studies utilizing the National Cancer Database (NCDB) report that 20% of patients with thyroid lobectomy (TL) also receive radioiodine (RAI). RAI after TL is non-standard care. We hypothesize that many thyroid cancer registry abstracts have the variable surgery of the primary site inaccurately coded. Methods: A retrospective review of the Tennessee Cancer Registry (TCR) thyroid cancer database was performed. The TCR receives case information from TN healthcare providers and facilities that diagnose and/or treat cancer patients. Hospital facilities are classified as Commission-on-Cancer (CoC) accredited or non-CoC accredited. Certified Registrars at the TCR reviewed the abstracted text and/or telephoned the reporting facility staff to confirm that TL was in fact the definitive procedure. A subgroup of records originally coded with TL as the definitive procedure and postoperative receipt of RAI was also reviewed. Results: A total of 918 thyroid cancer cases, diagnosed/treated at TN facilities during 2004-11, were coded with TL. There were 369(40.2%) incorrectly coded. Of these 369 incorrectly coded cases, 242(65.6%) were changed to total thyroidectomy. Of the 242 cases changed from TL to total thyroidectomy, 85% were reported from CoC facilities. A total of 184 (20.0%) abstracts were originally coded with TL and also received postoperative RAI. There were 115(62.5%) incorrectly coded. Thus, after review only 7.5% of TL cases received RAI (before and after review comparison, $p<0.01$). Conclusion: Thyroid cancer registries that include extent of surgical procedure are at risk for inaccurate coding. This study demonstrates that in one state cancer registry approximately 26% of cases originally coded as TL should have been coded as total thyroidectomy. The large majority of incorrectly coded cases were reported from CoC-accredited facilities. These CoC-facilities contribute case information to other large national cancer databases, such as the NCDB. Using text-to-code re-abstraction audits and facility contact where needed, these discrepancies can be corrected to improve data quality.

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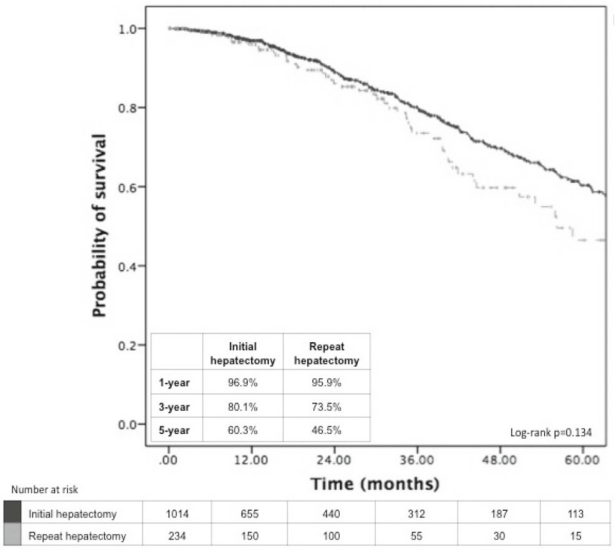
The National Quality Forum Colon Cancer Metrics and Survival: Does Hospital Performance Matter? M.C. Mason,[1]* G. Chang,[2] Y.H. Sada,[3] H.S. Tran Cao,[1] C.Y. Chai,[1] D.H. Berger,[1] N.N. Massarweh.[1] *1. Baylor College of Medicine, Michael E. DeBakey Department of Surgery, Houston, TX; 2. The University of Texas M.D. Anderson Cancer Center, Department of Surgical Oncology, Houston, TX; 3. Baylor College of Medicine, Department of Medicine, Houston, TX.*

INTRODUCTION: We have previously shown hospital performance on the National Quality Forum (NQF) colon cancer quality metrics (adequate lymph node evaluation; adjuvant chemotherapy administered to stage III

patients; timely adjuvant chemotherapy [within 4 months]) is poorly correlated. However, it remains unclear whether hospital performance on these metrics is associated with better patient outcomes. METHODS: A retrospective cohort study of 22,242 surgically resected, stage III colon cancer patients using the National Cancer Data Base (2003-2005). Hospitals were categorized using the proportion of patients achieving each metric individually (very low [0-25%]; low [25-50%]; high [50-75%]; very high [>75%]). Multivariable Cox shared frailty modeling was used to evaluate the association between very high hospital performance for each metric and 5-year overall survival (OS). RESULTS: Less than half (47%) of patients achieved all 3 metrics. Postoperative length of stay >7 days and 30-day readmission rates across hospital performance categories for each metric were either not significantly associated or not clinically meaningful. Very high hospital performance on one or more metrics was associated with a lower risk of death relative to hospitals performing well on no metrics (1 metric—Hazard Ratio [HR] 0.83 [0.74-0.94]; 2 metrics—HR 0.79 [0.72-0.87]; 3 metrics—HR 0.75 [0.66-0.84]). However, this association did not demonstrate a dose-response relationship (very high performance on 1 vs 2—HR 1.06 [0.95-1.18]; 1 vs 3—HR 1.12 [0.98-1.28]; 2 vs 3 metrics—HR 1.06 [0.94-1.19]) and was not dependent on which specific (or combination of) metrics were achieved. CONCLUSIONS: In the context of poor national performance on all 3 NQF metrics, the lack of a dose-response relationship between hospital performance and survival suggests either the minority of patients is receiving optimal colon cancer care or these metrics are weak quality measures. These findings suggest improving hospital metric adherence would be unlikely to improve outcomes and highlight both the challenges facing quality improvement efforts as well as the need for more clinically meaningful quality indicators.



Overall survival from the time of recurrence in patients that recurred following initial hepatectomy compared to following repeat hepatectomy for colorectal liver metastases.

7

Outcomes of Re-hepatectomy for Colorectal Liver Metastases: A Multi-Institutional Analysis J. Hallet,[1]* A. Sa Cunha,[2] R. Adam,[2] D. Goéré,[3] P. Bachellier,[4] D. Azoulay,[5] A. Ayav,[6] E. Grégoire,[7] F. Navarro,[8] P. Pessaux.[9] *1. Surgery, Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada; 2. Hôpital Paul Brousse, Villejuif, France; 3. Institut Gustave Roussy, Villejuif, France; 4. Hôpital Hautepierre, Strasbourg, France; 5. Hôpital Henri Mondor, Créteil, France; 6. Hôpital de Brabois - Centre Régional Hospitalier Universitaire de Nancy, Nancy, France; 7. Hôpital de la Timone, Marseilles, France; 8. Université de Montpellier - Hôpital Saint-Eloi, Montpellier, France; 9. Institut de Recherche sur les Cancers de l'Appareil Digestif (IRCAD), Strasbourg, France.*

Background: Curative intent hepatectomy for colorectal liver metastases (CRLM) is standard of care when feasible. Recurrence remains frequent. We sought to define short and long-term outcomes, and identify pre-hepatectomy factors associated with survival, following re-hepatectomy (RH) for recurrence, with modern multi-modal management of CRLM. Methods: We conducted a retrospective cohort study of hepatectomy for CRLM at 39 institutions (2006-2013). Second-stage resections were excluded. Primary outcomes were overall (OS) and recurrence free survival (RFS) assessed with Kaplan-Meier methods. Secondary outcomes included 30-day overall morbidity and mortality, and survival from recurrence. Outcomes of RH and initial hepatectomy (IH) were compared. Multivariate Cox regression examined the association between RH and survival. Results: Of 2,771 hepatectomies included, 447 were RH with 14 months median time from IH (inter-quartile range: 8-23). Median operative time (235 Vs. 240 min, p=0.25), 30-day morbidity (28.9% Vs. 30.8%, p=0.41), mortality (1.3% Vs. 1.2%, p=0.81), and median length of stay (10 Vs. 11 days, p=0.26) did not differ for RH and IH. 5-year OS did not statistically differ with 56.5% from RH and 67.6% from IH (adjusted hazard ratio – HR 0.9 [0.5-1.7]). 5-year RFS was inferior after RH (18.5% Vs. 28.8%; adjusted HR 1.3 [0.9-1.7]). In patients who eventually recurred, 5-year survival from the time of recurrence did not differ whether it was after RH (46.5%) or IH (60.3%) (adjusted HR 1.1 [0.8-1.8]). In multivariate analysis, rectal primary tumor (HR 1.4 [1.0-2.1]) and a metastasis larger than 3 cm (HR 1.3 [1.1-2.7]) were independently associated with RFS, but not OS, after RH. Conclusion: In a contemporary cohort, short-term outcomes of RH did not differ from IH. While recurrence was more frequent after RH than IH, it may not significantly decrease OS. Moreover, survival from the time of recurrence did not appear impacted whether recurrence occurred after RH or after IH. CRLM recurrence can be treated with curative intent to procure excellent long-term outcomes. This supports pursuing RH for CRLM with similar indications and clinical aggressiveness as for IH.

8

Comparative Analysis of Breast Cancer Phenotypes in African American, White American, and West Versus East African Patients: Correlation Between African Ancestry and Triple Negative Breast Cancer L. Newman,[1]* E. Jiagge,[2] J. Bensenhaver,[2] A. Jibril,[5] B. Awuah,[4] A. Stark.[3] *1. Henry Ford Health System Breast Oncology Program and University of Michigan, Ann Arbor, MI; 2. University of Michigan, Ann Arbor, MI; 3. Henry Ford Health System, Detroit, MI; 4. Komfo Anoyke Teaching Hospital, Kumasi, Ghana; 5. St. Paul's Millenium Hospital, Addis Ababa, Ethiopia.*

Introduction: Population-based incidence rates of triple negative breast cancer (TNBC) are higher for African American (AA) compared to White American (WA) women, but it is unclear whether TNBC risk is genetically associated with African ancestry because AA women represent an ancestrally admixed population. Higher frequencies of TNBC have also been observed in western sub-Saharan African breast cancer (BC) patients, and this study represents a first comparison of AA, WA, West and East African cases. Methods: Formalin-fixed, paraffin-embedded invasive BC tumors diagnosed 1998-2014 in AA, WA, Ghana/East Africa, and Ethiopia/West Africa were compared. All African tumors underwent pathology confirmation and immunohistochemistry for estrogen receptor (ER), progesterone receptor (PR) and HER2/neu expression in the U.S. Statistical analyses were performed in SAS v. 9.0 (Carey, NC). Results: 234 Ghanaian cases (mean age 49 yrs); 271 AA (mean age 60); and 321 WA (mean age 62)(P=0.001) were compared. ER-negative and TNBC were more common among Ghanaian and AA compared to WA cases (frequency ER-negativity 67.5%, 37.1%, and 19.8%, respectively, p<0.0001; frequency TNBC 53.2%, 29.8%, and 15.5%, respectively, p<0.0001). In the age group <50 years, 82 cases (42.5%) were ER+/PR+/HER2-; 65 (33.7%) were TNBC. In this young age group, prevalence of TNBC remained highest among Ghanaian women (50.8%), followed by AA (34.3%) and WA (15.9%); (P=.0006). Highest prevalence of ER+/PR+/HER2+ and ER+/PR+/HER2- phenotypes was observed in WA, followed by AA and Ghanaians. The addition of 33 cases from Ethiopia revealed a different distribution: the majority (55%) were HER2/neu-overexpressing; 42% were triple-positive; and only 15% were TNBC. Conclusions: This study confirms an association between TNBC and West African ancestry, and AA patients have a TNBC frequency that is intermediate between WA and Ghanian/West Africans. East Africans appear to have a low frequency of TNBC but an increased risk of HER2/neu overexpression.

Frequency of TNBC

White Americans	African Americans	West Afr/Ghana	East Afr/Ethiopia	pValue
15.5%	29.8%	53.2%	15%	<0.05

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PET-CT Compared to No PET-CT in the Management of Potentially Resectable Colorectal Cancer Liver Metastases: The Cost Implications of a Randomized Controlled Trial P. Serrano Aybar,[4]* A. Gafni,[3] C. Gu,[1] J. Julian,[1] C. Moulton,[2] S. Gallinger,[2] M.N. Levine.[1] *1. Ontario Clinical Oncology Group, McMaster University, Hamilton, ON, Canada; 2. Department of Surgery, University of Toronto, Toronto, ON, Canada; 3. Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, ON, Canada; 4. Department of Surgery, McMaster University, Hamilton, ON, Canada.*

Introduction PETCAM was a randomized trial evaluating the effect of PET-CT compared to conventional imaging (control) on the surgical management of patients with resectable colorectal cancer liver metastases (CRLM). It concluded that PET-CT did not result in frequent change in surgical management (80%, 21/263) with only 27% (7/263) avoidance of liver resections. In this study we conducted a cost analysis of these two arms up to one year following randomization. Methods Health care utilization was collected for all study participants. Unit costs for hospitalization, physician services, chemotherapy and outpatient radiological and endoscopic procedures were obtained from administrative databases. Cost analysis was undertaken from the perspective of a third-party payer (i.e., Ministry of Health). Mean cost with its 95% credible interval was estimated using a Bayesian approach. Results The estimated mean cost per patient in the PET-CT arm was CAN $45,454 (min-max: 1,340-181,420) and in the control arm, CAN $40,859 (min-max: 279-293,558), with a net difference of CAN $4,327, 95% credible interval -2,207 to 10,614. The primary cost driver was cost of hospitalization for liver surgery (+ $2,997 CAN for the PET-CT arm), mainly due to a longer length of hospital stay for the PET-CT arm compared to control (median 7 days vs. 6 days, P=0034) and a higher rate of postoperative complications (52/255, 20% vs. 13/128, 10%, P = 0014). Baseline characteristics were similar between groups, including a similar number of liver segments involved with cancer, number of segments resected and type of liver resection performed. Conclusion PET-CT does not appear to provide a significant clinical benefit in the surgical management of patients with resectable CRLM and it is not cost saving compared to control.

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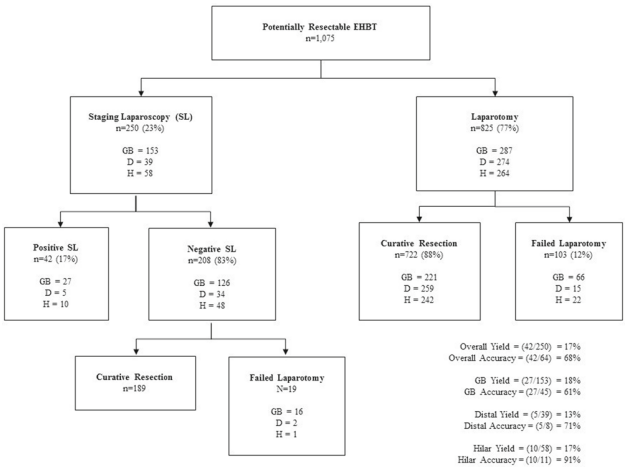
A Reappraisal of Staging Laparoscopy in Three Subtypes of Cholangiocarcinoma: A Multi-Institution Analysis from the U.S. Extrahepatic Biliary Malignancy Consortium J.T. Davidson,[1]* L. Jin,[1] B.A. Krasnick,[1] C.G. Ethun,[2] T.M. Pawlik,[3] G.A. Poultsides,[4] T.B. Tran,[4] K. Idrees,[5] C.A. Isom,[5] S. Weber,[6] A.I. Salem,[6] W. Hawkins,[1] S. Strasberg,[1] R.C. Martin,[7] C. Scoggins,[7] P. Shen,[8] H. Mogal,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] S.K. Maithel,[2] R.C. Fields.[1] *1. Washington University in St. Louis School of Medicine, Saint Louis, MO; 2. Emory University, Atlanta, GA; 3. The Johns Hopkins Hospital, Baltimore, MD; 4. Stanford University Medical Center, Stanford, CA; 5. Vanderbilt University Medical Center, Nashville, TN; 6. University of Wisconsin School of Medicine and Public Health, Madison, WI; 7. University of Louisville, Louisville, KY; 8. Wake Forest University, Winston-Salem, NC; 9. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 10. New York University, New York, NY.*

Introduction: Staging laparoscopy (SL) has been shown to be useful in extraheptic biliary tumors to avoid unnecessary laparotomies in patients with unresectable disease. However, the added value of SL has not been well characterized in the era of modern imaging for patients with (EHBTs). Methods: We reviewed patients from ten institutions who underwent attempted resection of EHBTs between 1998 and 2015, including gallbladder cancer, distal cholangiocarcinoma and hilar cholangiocarcinoma. Yield of laparoscopy = (Number of positive SL / Total number of SL). Accuracy of laparoscopy = (Number of positive SL / Patients with unresectable disease). These data were compared by use of analysis of variance with two-sided Student t test. Significance was $p < .05$. Results: A total of 1,075 patients were taken to the OR for attempted curative resection, of which 250 patients (23%) underwent staging laparoscopy. SL identified unresectable disease in 42 patients (overall yield 17%). Of 208 patients who underwent exploratory laparotomy (EL) after negative SL, 19 were found to be unresectable (false negative rate 9%). Amongst gallbladder, hilar, and distal cholangiocarcinoma pathology types, the yield of SL were 18%, 13%, 17%, respectively (p=0.78). Accuracy of SL was 61%, 71%, and 91% respectively (p=0.17), with an overall accuracy of 68%. A total of 825 patients went directly to EL, of which 103 (13%) failed. The rate of failure for patients going straight to EL was significantly higher for patients with gallbladder cancer (n=66/287, 23%) when compared with hilar (n=15/274, 6%) and distal cholangiocarcinoma (n=22/264, 8%) (p<0.001). Conclusions: Our analysis demonstrates that staging laparoscopy still has added utility in preventing unnecessary laparotomies in unresectable disease for selected patients with EHBTs, although the overall yield is lower than previously reported. Patients with gallbladder cancer had high rates of failed laparotomies, representing a subset of patients who may benefit from more frequent use of staging laparoscopy at the time of resection.

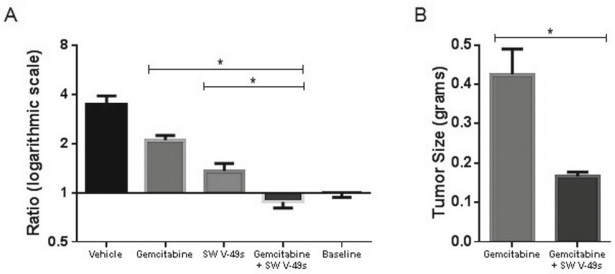


11

Targeted Therapy in Pancreatic Cancer Utilizing the Novel Small Molecule Drug Conjugate SW V-49 in Combination with Standard Chemotherapy K.A. Ohman,* S. Vangveravong, D. Spitzer, W. Hawkins. *Department of General Surgery, Washington University in St. Louis, Saint Louis, MO.*

Introduction: Pancreatic cancer (PDAC) is a devastating disease, and there is a desperate need to invest in novel therapies to improve outcomes. Cancer-selective drug therapy improves treatment efficacy while minimizing toxicity. Sigma-2 (S2) receptors are overexpressed in PDAC and S2 ligands are selectively internalized and can deliver drug cargoes. Conjugation of the S2 ligand SV119 with an Erastin analog formed SW V-49, which is effective in syngeneic and xenograft PDAC mouse models. Since most cancers are or become resistant to single-agent therapy, we combined SW V-49 with standard chemotherapy to further improve treatment outcomes and limit systemic toxicities. Methods: Murine and human PDAC cell lines were treated with SW V-49 and standard chemotherapy in vitro to assess therapeutic killing potential. In vivo treatment efficacy was evaluated using orthotopic and subcutaneous syngeneic models (KP-02 tumor-bearing C57BL/6 mice). Mass spectrometry was utilized to assess drug uptake in vitro and in KPPC spontaneous and orthotopic implantation models. Results: Combination of SW V-49 with Gemcitabine in vitro suggested a beneficial treatment effect in murine and human PDAC cell lines. In vivo experimentation demonstrated combination therapy was superior in subcutaneous and orthotopic KP-02 mouse models. Combination therapy in the subcutaneous model revealed decreased tumor volumes compared to single agent treatment with an additional trend of remaining at or below baseline tumor volume after a short duration of therapy (Fig. 1A). In the KP-02 orthotopic model, addition of SW V-49 further decreased tumor sizes when combined with Gemcitabine (Fig. 1B). Mass spectrometry confirmed rapid and selective uptake of SW V-49 in vitro and also demonstrated selective delivery to pancreatic tumors in KPPC and orthotopic tumor models in vivo. Conclusions: Combination therapy utilizing the targeted therapeutic SW V-49 and systemic Gemcitabine is a novel treatment option for PDAC. Tumor selective

delivery of SW V-49 further decreased tumor size and suggests combination therapy may be clinically useful. Further experimentation is warranted.



Subcutaneous KP-02 tumor-bearing C57BL/6 mice treated for 10 days with SW V-49, Gemcitabine, or both; tumors treated with combination therapy remained at baseline and were significantly smaller than single therapy alone (Fig. 1A). In orthotopic KP-02 tumor bearing C57BL/6 mice, addition of SW V-49 to Gemcitabine caused a significant decrease in tumor burden after only 10 days of treatment (Fig. 1B).

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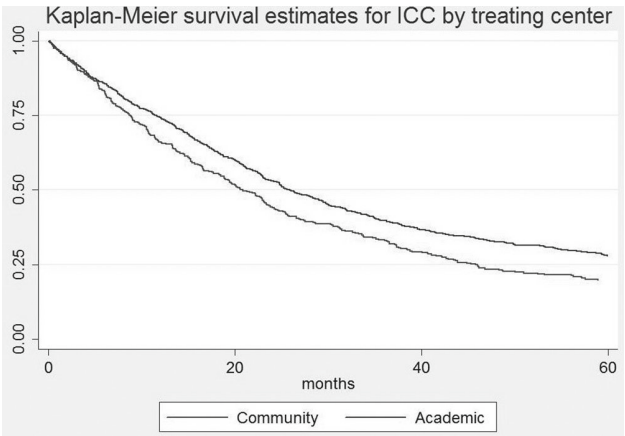
Improved Survival After Hepatectomy for Intrahepatic Cholangiocarcinoma at Academic Cancer Centers N.G. Berger,* A. Hammad, J. Miura, F. Johnston, K. Christians, S. Tsai, K. Turaga, T. Gamblin. *Surgery, Medical College of Wisconsin, Milwaukee, WI.*

Introduction: Margin status is an important prognostic factor of survival following hepatectomy for intrahepatic cholangiocarcinoma (ICC). R0 resection for ICC correlates with improved recurrence-free survival and overall survival (OS). The present study hypothesized that surgical resection margins and survival rates vary between centers. Methods: Patients with ICC undergoing hepatectomy were identified from the National Cancer Database (1998-2011). Treating centers were categorized as Academic Cancer Centers (ACC), and Community Cancer Centers (CCC). Rates of R0 vs. R1/2 resection were examined. OS was analyzed by Kaplan-Meier method, and Cox multivariate modeling identified independent predictors of survival. Results: A total of 2,774 patients were identified. Hepatectomy was most often performed at ACC compared to CCC: 1,928 (69.5%) vs. 846 (30.5%). Hepatectomy at ACC was associated with higher rates of R0 resections compared to CCC (72.5% vs. 68.1%, p=0.018). Higher 30-day readmission rates were seen following hepatectomy at ACC (9.9% vs. 5.7%, p=0.002). Improved median OS was seen for hepatectomy done at ACC across all stages (25.8 months vs. 20.1 months; p<0.001). After adjusting for age, sex, ethnicity, cirrhosis, alpha-feto protein level, comorbidity, disease stage, and margin status, hepatectomy at ACC was independently associated with improved OS (Hazards ratio: 0.79 [95%CI 0.62-0.99, p=0.046]). Conclusion: ACC have higher rates of negative resection margins for ICC, but higher readmission rates following surgery. Overall survival and median survival were improved at ACC compared to CCC, suggesting that site of care plays a role in patient outcomes.



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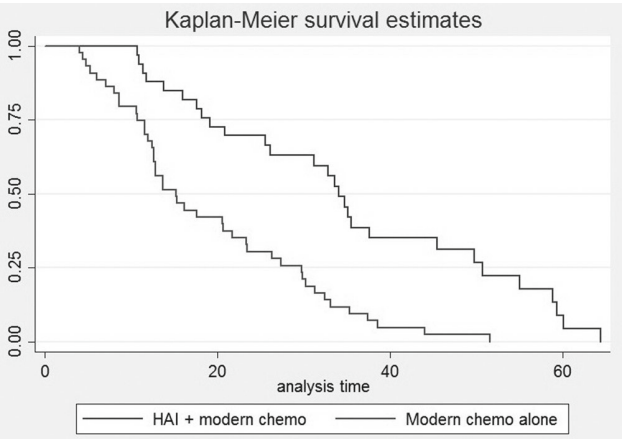
Hepatic Arterial Infusion with Modern Systemic Chemotherapy is Superior to Modern Systemic Chemotherapy Alone in Patients with Isolated Unresectable Colorectal Liver Metastasis: A Retrospective Case Control Study M. Dhir,* H.L. Jones, A.K. Clifford, J. Steve, M. Hogg, M.A. Choudry, M. Holtzman, H. Zeh III, N. Bahary, J.F. Pingpank, D. Bartlett, A. Zureikat. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Isolated unresectable colorectal liver metastases (IU-CRLM) portend a poor prognosis. In the era of effective modern chemotherapy (CT) regimens, the role of HAI-FUDR therapy remains controversial. The aim of this study was to compare overall survival of HAI + modern systemic CT vs modern systemic CT alone in patients with IU- CRLM. Methodology: Patients with IU-CRLM who underwent HAI-FUDR + modern systemic CT from 2004 to 2014 were compared to a contemporaneous case control group of patients who received modern CT alone. Modern systemic CT was defined as use of multidrug regimens containing oxaliplatin and/or irinotecan +/- biologics. To eliminate lead in bias, overall survival was calculated from the time of diagnosis of IU-CRLM. All patients had complete follow-up. Results: Thirty four patients with IU-CRLM underwent HAI + systemic CT. These patients were compared to a control group of 45 patients treated with modern systemic CT alone. The two groups were similar with respect to age (median 58 vs 62 yrs), gender, ECOG (median 1 vs 1), BMI (median 31 vs 27), race, CEA at diagnosis of unresectable disease (median 117 vs 218), use of biologic agents (91% vs 82%), number of lines of systemic chemotherapy (3 vs 2), positive nodal status (72% vs 85%), and other primary tumor characteristics (grade, LVI) (all p >0.05). Additionally, the two groups were comparable with respect to liver tumor burden [median number of lesions (11 vs 14), % liver tumor replacement (30% vs 40%), all p > 0.05]. Median follow up for the entire cohort was 21 (2.1 to 84) months. Median overall survival in the HAI + modern CT group was 34 months compared to 15 months in the CT alone (p < 0.001). Figure 1 Conclusions: In this case control study of patients with IU-CRLM, HAI-FUDR in combination with modern systemic chemotherapy was associated with improved overall survival when compared to modern chemotherapy alone.



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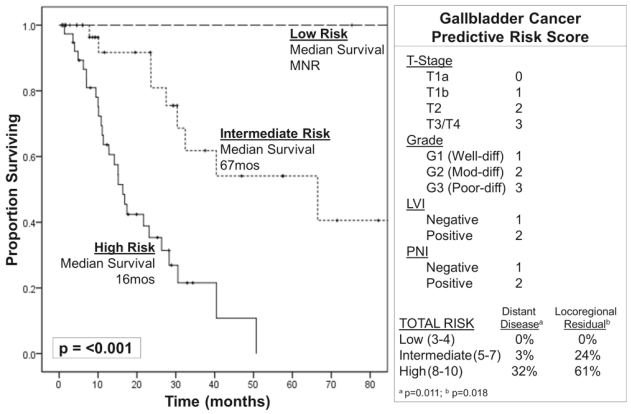
A Novel Pathology-Based Preoperative Risk Score to Predict Distant and Locoregional Residual Disease and Survival for Incidentally Discovered Gallbladder Cancer: A 10-Institution Study from the U.S. Extrahepatic Biliary Malignancy Consortium C.G. Ethun,[1]* L.M. Postlewait,[1] N. Le,[1] T.M. Pawlik,[2] S. Buettner,[2] G.A. Poultsides,[3] T. Tran,[3] K. Idrees,[4] C.A. Isom,[4] R.C. Fields,[5] L. Jin,[5] S. Weber,[6] A.I. Salem,[6] R.C. Martin,[7] C. Scoggins,[7] P. Shen,[8] H. Mogal,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] K. Cardona,[1] S.K. Maithel.[1] *1. Emory University, Atlanta, GA; 2. The Johns Hopkins Hospital, Baltimore, MD; 3. Stanford University Medical Center, Stanford, CA; 4. Vanderbilt University Medical Center, Nashville, TN; 5. Washington University School of Medicine, St. Louis, MO; 6. University of Wisconsin School of Medicine and Public Health, Madison, WI; 7. University of Louisville, Louisville, KY; 8. Wake Forest University, Winston-Salem, NC; 9. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 10. New York University, New York, NY.*

Background: T-stage alone is currently used to guide treatment for incidentally-discovered gallbladder cancer. We aimed to develop a more robust predictive model for discovering distant or locoregional-residual disease at the time of re-resection. Methods: All patients with incidentally-discovered gallbladder cancer who underwent re-resection at 10 institutions from 2000-2015 were included. We utilized routine pathology data from initial cholecystectomy to create a gallbladder cancer predictive risk score (GBRS) for finding distant or locoregional-residual disease at re-resection and predicting overall survival (OS). Results: Of 449pts with gallbladder cancer, 262(58%) were incidentally discovered and underwent attempted re-resection. Advanced T-stage, grade, and presence of lymphovascular (LVI) and perineural (PNI) invasion were all associated with increased rates of distant and locoregional-residual disease, and decreased OS. Each pathologic characteristic was assigned a value (T1a:0, T1b:1, T2:2, T3/4:3; well-diff:1, mod-diff:2, poor-diff:3; LVI-neg:1, LVI-pos:2; PNI-neg:1, PNI-pos:2), which were added for a total GBRS score ranging from 3-10. The scores were then separated into 3 risk-groups (Low:3-4; Intermediate:5-7; High:8-10). Each progressive GBRS group was associated with an increased risk of finding distant and isolated locoregional-residual disease at the time of re-resection, and was associated with reduced OS (Figure). Conclusion: By accounting for subtle pathologic variations within each T-stage, this novel predictive risk-score better stratifies patients with incidentally-discovered gallbladder cancer. Compared to T-stage alone, it more accurately identifies patients at risk for distant and locoregional-residual disease, and predicts long-term survival, as it redistributes T1b, T2, and T3 disease across separate risk-groups based on additional biologic features. This score may help to better optimize treatment strategy for patients with incidentally discovered gallbladder cancer.



Gallbladder Cancer Predictive Risk Score and Survival

15

Pattern of CA19-9 Response to Neoadjuvant Chemotherapy in Locally Advanced, Borderline Resectable Pancreatic Cancer Predicts Progression J. Rose,* A. Edwards, A. Alseidi, T.R. Biehl, B. Lin, V. Picozzi, F.G. Rocha, W.S. Helton. *General Surgery, Virginia Mason Medical Center, Seattle, WA.*

Introduction: As neoadjuvant therapy of locally advanced, borderline resectable pancreatic cancer (BRPC) is becoming more widely utilized; better indicators of progression are needed to help guide therapeutic decisions. The aim of this study is to determine if CA19-9 response during treatment predicts disease progression. Methods: A retrospective review was performed on all patients with BRPC (by AHPBA/SSO consensus criteria) between 2008-2015 who received 24 weeks of neoadjuvant gemcitabine and docetaxel. Patients with medical comorbidities limiting treatment completion were excluded. Serum CA19-9 levels were checked at baseline and every 3 weeks while on therapy. A normal CA19-9 level was defined as < 37.5 units/mL and levels with concomitant biliary obstruction were censored. CA19-9 response was analyzed as a predictor of disease progression, recurrence, and survival. Results: Eighty patients were included with a mean of 11 CA19-9 levels checked per patient during treatment. Thirty-two (40%) progressed on treatment (18 local and 14 distant) and 48 (60%) were resected (79% R0). CA19-9 responses were categorized into 5 groups (fig 1): 1) Always normal [n=13]; 2) Increasing [n=3]; 3) Slow decline [n=7]; 4) Rapid decline with plateau [n=41]: and 5) Rapid decline with late rise [n=16]. Univariate logistic regression analysis found that a final CA19-9 decline >50% of baseline (OR 0.06, p=<.0001), a normal final CA19-9 (OR 0.08, p=<.0001), pattern group 1 (OR 0.16, p=.0001), and group 4 (OR 0.10, p=.0001) were predictive of non-progression. Baseline or maximum CA19-9 levels were not predictive of progression. All patients in group 2 progressed; none were resected. Patients in pattern group 5 that underwent resection had an increased risk of recurrence (HR 12.5, p=.0005). Median overall survival for groups 1-5 were 20.4, 9.3, 20.8, 31.4, and 16.4 months respectively. Conclusion: Patients with measurable CA19-9 levels who do not have rapid decline with sustained low or normal levels should be considered high risk for progression or recurrence and alternative treatment strategies should be entertained prior to curative resection.

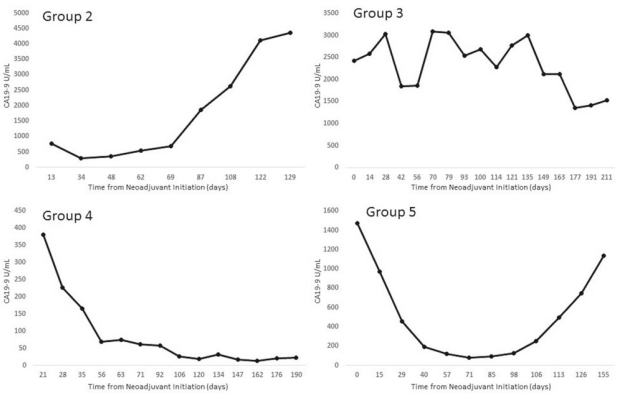


Figure 1: Representative graphs of each pattern group. Always normal (Group 1 not shown), Increasing (Group 2), Slow decline (Group 3), Rapid decline with plateau (Group 4), and Rapid decline with late rise (Group 5).

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Optimal Prognostic Lymph Node Staging System for Gallbladder Adenocarcinoma: A Multi-Institutional Study N. Amini,[1]* Y. Kim,[1] A. Wilson,[1] G.A. Georgios,[1] C.G. Ethun,[2] S.K. Maithel,[2] G.A. Poultsides,[3] T. Tran,[3] K. Idrees,[4] C.A. Isom,[4] R.C. Fields,[5] B.A. Krasnick,[5] S. Weber,[6] A.I. Salem,[6] R.C. Martin,[7] C. Scoggins,[7] P. Shen,[8] H. Mogal,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] T.M. Pawlik.[1] *1. The Johns Hopkins Hospital, Baltimore, MD; 2. Winship Cancer Institute, Emory University, Atlanta, GA; 3. Stanford University Medical Center, Stanford, CA; 4. Vanderbilt University Medical Center, Nashville, TN; 5. Washington University School of Medicine, St. Louis, MO; 6. University of Wisconsin School of Medicine and Public Health, Madison, WI; 7. University of Louisville, Louisville, KY; 8. Wake Forest University, Winston-Salem, NC; 9. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 10. New York University, New York, NY.*

Introduction: The American Joint Committee on Cancer (AJCC) classification is the most universally accepted lymph node (LN) staging system for gallbladder adenocarcinoma (GBA); however, it focuses more on location of LN metastasis than number of LN metastasis. Other lymph node staging systems have been proposed for GBA. We therefore sought to examine the performance of different staging systems including AJCC LN staging system, number of metastatic LN (NMLN), log odds of metastatic LN (LODDS), and LN ratio (LNR). Methods: Patients who underwent curative-intent resection for GBA between 2000 and 2015 and who had lymphadenectomy were identified from a multi-institutional database. The prognostic performance of four staging systems was compared by Harrell's C and Akaike information criterion (AIC). Results: Overall 214 patients with a median age of 66.7 years (IQR 56.5, 73.1) were identified. A total 1,334 LNs were retrieved from 214 patients, with a median of 4 (IQR 2-8) LNs per patient. In the study cohort, 98 (45.5%) patients had LN metastasis with total of 271 positive LNs [median of 1 (IQR 1-3)]. Patients with LN metastasis had an increased risk of death (HR 1.87, 95%CI 1.24-2.82; P=0.003). In addition, risk of death increased by each additional LN metastasis (HR 1.20, 95%CI 1.06-1.37; P=0.005). In the entire cohort, LNR, in either a continuous (C-index: 0.603, AIC: 808.4) or a discrete scale (C-index 0.609, AIC 802.2), provided better discrimination versus LODDS, AJCC LN staging system, and NMLN. The relative performance of all scoring systems was better among patients who had ≥4 LN examined. In the cohort of patients with ≥4 LN examined, LODDS (C-index 0.621, AIC 363.8) had the best performance compared with LNR (C-index 0.615, AIC 368.7), AJCC LN staging system (C-index 0.601, AIC 373.4), and NMLN (C-index 0.613, AIC 369.5) (Table). Conclusions: LODDS and LNR performed better than the AJCC LN staging system. Among those who had more LN examined, LODDS performed better than LNR. LODDS and LNR should be incorporated into the AJCC LN staging system of GBA.

Table. Prognostic Performance of Different Lymph Node Staging Systems

	Overall		TLNE<4		TLNE ≥ 4	
	C-index	AIC	C-index	AIC	C-index	AIC
AJCC LN staging	0.596	808.6	0.596	309.9	0.601	373.4
LNR (continuous)	0.603	808.4	0.606	307.9	0.601	369.5
LODDS (continuous)	0.588	804.5	0.586	310.2	0.605	368.1
NMLN (continuous)	0.595	809.4	0.595	310.1	0.604	371.3
LNR categorical	0.609	802.2	0.602	308.9	0.615	368.7
LODDS (categorical)	0.604	799.0	0.595	307.7	0.621	363.8
NMLN (categorical)	0.599	806.2	0.593	308.1	0.613	369.5

AJCC, The American Join Committee on Cancer; LNR, lymph node ratio; LODDS, log odds of metastatic lymph node; NMLN, number of metastatic lymph node; TNLE, total number of lymph node examined

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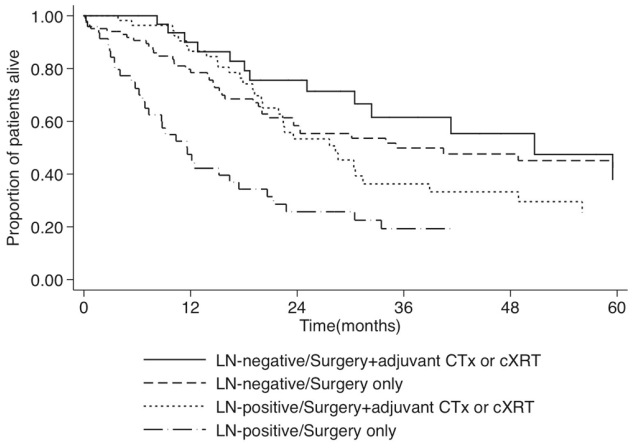
Impact of Chemotherapy and External-Beam Radiation Therapy on Outcomes Among Patients with Resected Gallbladder Cancer: A Multi-Institutional Analysis Y. Kim,[1]* N. Amini,[1] G.A. Georgios,[1] A. Wilson,[1] C.G. Ethun,[2] G.A. Poultsides,[3] T. Tran,[3] K. Idrees,[4] C.A. Isom,[4] R.C. Fields,[5] B.A. Krasnick,[5] S. Weber,[6] A.I. Salem,[6] R.C. Martin,[7] C. Scoggins,[7] P. Shen,[8] H. Mogal,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] K. Cardona,[2] S.K. Maithel,[2] T.M. Pawlik.[1] *1. The Johns Hopkins Hospital, Baltimore, MD; 2. Emory University, Atlanta, GA; 3. Stanford University, Stanford, CA; 4. Vanderbilt University, Nashville, TN; 5. Washington University, Saint Louis, MO; 6. University of Wisconsin, Madison, WI; 7. University of Louisville, Louisville, KY; 8. Wake Forest University, Winston-Salem, NC; 9. The Ohio State University, Columbus, OH; 10. New York University, New York, NY.*

Background: Use of adjuvant chemotherapy (CTx) and chemoradiation therapy (cXRT) in the treatment of resectable gallbladder cancer remains varied. We sought to define the utilization and effect of adjuvant therapy on patients having undergone curative-intent resection for gallbladder cancer. Methods: Using a multi-institutional national database, 291 patients with gallbladder cancer who underwent curative-intent resection between 2000 and 2015. Patients with metastasis or an R2 margin were excluded. The impact of adjuvant therapy on survival was analyzed among patients who received surgery alone versus CTx versus cXRT. Results: Median patient age was 66 years. Most patients had a T2 (41.9%) or T3 (35.1%) lesion and 37.8% of patients had lymph node (LN) metastasis. A total of 186 (63.9%) patients underwent surgery alone, 61 (21.0%) received CTx, whereas the remaining 44 (15.1%) patients received cXRT. Median and 5-year overall survival (OS) was 28.3months and 33.0%, respectively. On multivariable analysis, factors associated with worse OS included AJCC T3/T4 (hazard ratio [HR] 2.97), LN metastasis (HR 1.75) and lymphovascular invasion (HR 1.98; all P<0.05). In contrast, receipt of CTx or cXRT was associated with improved long-term OS (CTx, HR 0.33; cXRT, HR 0.27; P<0.001) compared with surgery alone. Similar results were observed for disease-free survival (DFS)(CTx, HR 0.53; cXRT, HR 0.45; P<0.01). Of note, the OS benefit for CTx or cXRT was observed among patients with high-risk features such as AJCC T3/T4 disease (HR 0.61; HR 0.31), LN-metastasis (HR 0.45; HR 0.46), and R1 disease (HR 0.33; HR 0.11) (all P<0.05). In contrast, the OS benefit of CTx and cXRT was not noted among patients with T1/T2 or N0 disease, or among those with an R0 margin (all P>0.05) (Figure). Conclusions: Adjuvant CTx and cXRT were utilized in 36% of patients undergoing curative-intent resection for gallbladder cancer. After adjusted analysis, CTx and cXRT were independent factors associated with improved long-term outcomes, but the benefit was isolated to only patients with high-risk characteristics.



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Management of Neuroendocrine Tumor Liver Metastases: Long-term Outcomes and Prognostic Factors from a Large Prospective Database M. Fairweather,* R. Swanson, J. Wang, M. Kulke, T. Clancy. *Brigham and Women's Hospital/Harvard Medical School, Boston, MA.*

Objective: Neuroendocrine liver metastases (NELM) display a wide spectrum of clinical behavior. Liver-directed therapies have been used to treat NELM for symptomatic control and potential oncologic benefit. We reviewed our experience with NELM to investigate the outcomes of available treatment modalities and to identify prognostic factors for progression and survival. Methods: We identified all patients with NELM who were managed at our institution from a prospectively collected institutional database. Overall survival (OS) was determined for each treatment modality. Factors influencing survival were analyzed using multivariate Cox regression. Results: Between 2003 and 2010, 649 patients with NELM were identified. The primary tumor site was small intestine in 245 patients (38%) and pancreas in 194 patients (30%). Treatment modalities included hepatic resection with or without ablation (n=58, 9%), radiofrequency ablation (RFA) alone (n=28, 4%), chemoembolization (CE) (n=130, 20%), chemotherapy (n=316, 49%), and no therapy (n=117, 18%). With a median follow up of 44 months, the median, 5-, and 10-year OS for each treatment group were: hepatic resection, 160 months (mos), 90%, 70%; RFA, 123 mos, 84%, 55%; CE, 66 mos, 55%, 28%; chemotherapy, 70 mos, 58%, 31%; no therapy, 38 mos, 38%, 20% (Figure 1). On multivariate analysis, prognostic factors determined to significantly impact OS included age (hazard ratio (HR) 1.0, P<0.001), small bowel primary site (HR 0.5, P<0.001), hepatic resection (HR 0.3, P=0.001), well-differentiated tumors (HR 0.3, P<0.001), alkaline phosphatase (ALP) within normal limit (WNL) (HR 0.4, P<0.001), and chromogranin A (CGA) WNL (HR 0.5, P<0.001). Conclusions: This series represents one of the largest single-institution studies of NELM reported. While this certainly represents a heterogeneous patient population with varying burdens of hepatic disease, an aggressive approach with hepatic resection is associated with significantly improved OS in patients in whom resection is possible. Patient (age), tumor (location, grade, hepatic resection), and biochemical (ALP, CGA) characteristics significantly impact survival.

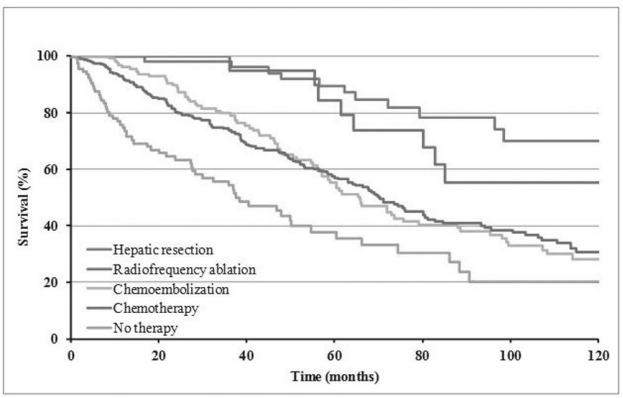

Figure 1. Kaplan-Meier overall survival curve for patients with neuroendocrine tumor liver metastases by treatment modality.

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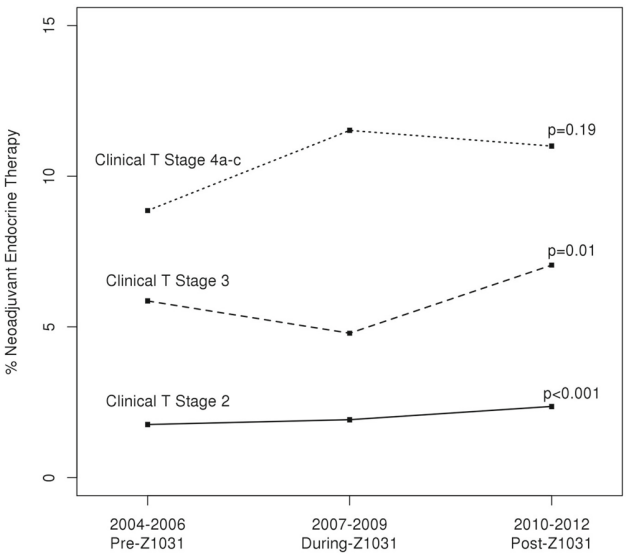
Neoadjuvant Endocrine Therapy Use in the U.S. for Hormone Receptor Positive Breast Cancer: Results from the National Cancer Data Base A. Chiba,[1]* T.L. Hoskin,[1] C.N. Heins,[1] K.K. Hunt,[2] J.C. Boughey.[1] *1. Mayo Clinic, Rochester, MN; 2. MD Anderson Cancer Center, Houston, TX.*

BACKGROUND: The ACOSOG Z1031 study published in 2010 showed neoadjuvant endocrine therapy (NET) increases the rate of breast conservation surgery (BCS) for postmenopausal patients with clinical tumor stage 2-4c estrogen receptor (ER) and progesterone receptor (PR)–positive breast cancer. We evaluated national trends in the use of NET and the impact of NET on rates of BCS. STUDY DESIGN: Using the National Cancer Data Base (NCDB), we identified all cT2-4c ER and PR positive (hormone receptor positive) breast cancer patients age ≥50 from 2004 to 2012. Patients who received neoadjuvant chemotherapy and/or radiation were excluded. Time intervals of pre-Z1031 (2004-2006), during-Z1031 (2007-2009), and post-Z1031 (2010-2012) were examined. Use of NET over time was analyzed using the Cochran-Armitage Trend Test, and the rate of BCS was analyzed using the chi-square test. RESULTS: Of 79,909 patients identified, 2308 (2.9%) received NET. Clinical T stage distribution was 68,538 (85.8%) cT2, 7751 (9.7%) cT3, and 3620 (4.5%) cT4a-c. There were small but statistically significant increases in use of NET from 2.6% pre- and during-Z1031 to 3.2% post-Z1031 (p<0.001). NET use varied by clinical T stage; in cT2 patients, NET use increased from 1.8% pre-Z1031 to 2.4% post-Z1031 (p<0.001). In cT3 patients, NET use was 5.9% pre-Z1031 and increased to 7.1% in the post-Z1031 period (p<0.001). Patients undergoing NET were significantly more likely to undergo BCS compared with patients undergoing upfront surgery (PS) (46.3% vs 43.8%, p=0.02). Within clinical T stage subgroups, the rates of BCS for NET vs PS were as follows: cT2 (58.7% vs 47.8%, p<0.001), cT3 (25.8% vs 14.9%, p<0.001), cT4a-c (24.6% vs 20.0%, p=0.04). CONCLUSION: NET use has increased slowly since Z1031, although the overall rate of NET use remains very low. NET significantly increases rates of BCS in patients with hormone receptor positive clinical T2-4c breast cancer. Clinicians should consider use of NET for patients with hormone receptor positive breast cancer interested in breast conservation.



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National Trends in the Use of Neoadjuvant Chemotherapy and Impact on Breast and Axillary Surgery in Hormone Receptor Negative Breast Cancer: A National Cancer Data Base Study C.A. Puig,* T.L. Hoskin, C.N. Heins, J.C. Boughey. *General Surgery, Mayo Clinic, Rochester, MN.*

Introduction: Neoadjuvant chemotherapy (NAC) is equivalent to adjuvant chemotherapy (AC) in terms of overall survival. In addition to downsizing the breast tumor it can also downstage nodal disease. The goal of this study was to evaluate national practice patterns of use of NAC in ER-/PR- breast cancer and impact on breast and axillary surgery. Methods: From the National Cancer Database (NCDB) we identified all patients (pts) with ER-/PR- invasive breast cancer from 2004 to 2012. Pts not receiving chemotherapy were excluded. Associations were examined using chi-square tests. Results: Of 132,976 pts with invasive ER-/PR- breast cancer, 108,128 (81.3%) had AC and 24,848 (18.7%) NAC. Use of NAC increased from 14.2% in 2004 to 23.7% in 2012 (p<0.001). Pts that received NAC had higher clinical T and N stage compared to those treated with AC (see Table). In pts <50 years old NAC was more commonly used [NAC used in 22.3% of pts <50 and 16.7% of pts ≥50 (p<0.001)]. More pts treated at an academic/research program received NAC (21.2%) compared to comprehensive community cancer program (17.9%, p<0.001). Overall, breast conservation surgery (BCS) rates were lower for NAC (33.2%) vs AC (54.7%, p<0.001). Stratified by clinical T stage, the BCS rate was higher for NAC vs AC only in T3 tumors (26.2% vs 20.2%, p<0.001) while BCS rates were either similar or lower for NAC in other T stages. Mastectomy rates increased over time in the AC group (41.5% in 2004, 48.9% in 2012, p<0.001),

and BCS rates increased in the NAC group (32.5% in 2004, 36.8% in 2012, p<0.001).Of pts with cN1-3 that received NAC, 31.9% converted to pN0. Pts with cN1-3 disease with NAC were more likely to undergo less extensive axillary surgery (1-6 nodes removed) compared to those with AC (20.7% vs15.7%, p<0.001) Conclusion: For ER-/PR- breast cancer in the United States chemotherapy is most commonly given adjuvantly, but NAC use is increasing. NAC is used more frequently in young patients and in academic centers. Patients treated with NAC have less nodal positivity and are more likely to have less extensive axillary surgery.

	AC (N=108128)	NAC (N=24848)	Total (N=132976)	p value
Clinical T Stage				<0.001[1]
cT0	321 (0.3%)	83 (0.3%)	404 (0.3%)	
cT1	36182 (33.5%)	2508 (10.1%)	38690 (29.1%)	
cT2	31003 (28.7%)	9576 (38.5%)	40579 (30.5%)	
cT3	4167 (3.9%)	5317 (21.4%)	9484 (7.1%)	
cT4 a-c	1041 (1.0%)	2485 (10.0%)	3526 (2.7%)	
cT4d	580 (0.5%)	2341 (9.4%)	2921 (2.2%)	
cTX/Missing	34834 (32.2%)	2538 (10.2%)	37372 (28.1%)	
Clinical N Stage				<0.001[1]
cN0	54833 (50.7%)	8120 (32.7%)	62953 (47.3%)	
cN1-3	17295 (16.0%)	13579 (54.6%)	30874 (23.2%)	
cNX/Missing	36000 (33.3%)	3149 (12.7%)	39149 (29.4%)	
Pathologic T Stage				<0.001[1]
pT0	1680 (1.6%)	4127 (16.6%)	5807 (4.4%)	
pT1	49908 (46.2%)	6617 (26.6%)	56525 (42.5%)	
pT2	45112 (41.7%)	4969 (20.0%)	50081 (37.7%)	
pT3	5870 (5.4%)	2225 (9.0%)	8095 (6.1%)	
pT4 a-c	1116 (1.0%)	1085 (4.4%)	2201 (1.7%)	
pT4d	410 (0.4%)	1009 (4.1%)	1419 (1.1%)	
pTX/Missing	4032 (3.7%)	4816 (19.4%)	8848 (6.7%)	
Pathologic N Stage				<0.001[1]
pN0	64533 (59.7%)	11700 (47.1%)	76233 (57.3%)	
pN1-3	39108 (36.2%)	9229 (37.1%)	48337 (36.4%)	
pNX/Missing	4487 (4.1%)	3919 (15.8%)	8406 (6.3%)	
Breast Surgery Type				<0.001[1]
Missing	214	45	259	
Lumpectomy/BCS	58990 (54.7%)	8227 (33.2%)	67217 (50.6%)	
Mastectomy	48924 (45.3%)	16576 (66.8%)	65500 (49.4%)	
Axillary Operation				<0.001[1]
None	1749 (1.6%)	1800 (7.2%)	3549 (2.7%)	
SLN (1-6 nodes)	57647 (53.3%)	8431 (33.9%)	66078 (49.7%)	
ALND (>6 nodes)	48089 (44.5%)	14357 (57.8%)	62446 (47.0%)	
Unknown Type	643 (0.6%)	260 (1.0%)	903 (0.7%)	

[1]Chi-Square

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Combining Clinical and Pathologic Staging Variables with Biologic Factors has Prognostic Value in Predicting Local-Regional Recurrence Following Neoadjuvant Chemotherapy for Breast Cancer

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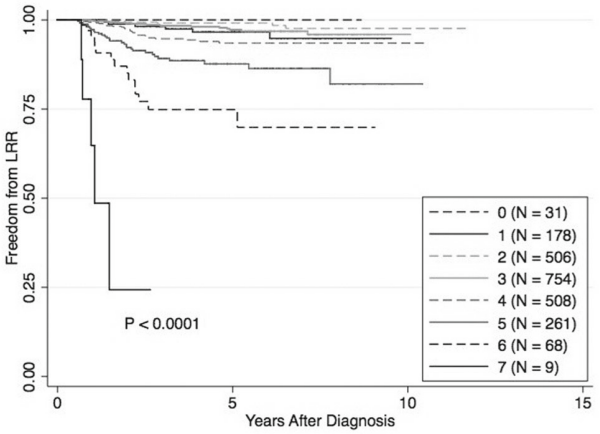
Background: Our group has defined a novel scoring system, the Neo-Bioscore, that incorporates the American Joint Commission on Cancer (AJCC) clinical stage, final AJCC pathologic stage, estrogen receptor status, HER2 status and grade. The Neo-Bioscore is associated with breast cancer specific survival outcomes in patients treated with neoadjuvant chemotherapy (NCT). The current study was undertaken to determine if the Neo-Bioscore could stratify patients with respect to local-regional recurrence (LRR). Methods: Patients receiving NCT between 2005 and 2012 were identified from a prospective database. Clinicopathologic data were used to determine each patient's Neo-Bioscore which ranged from 0-7. The type of local treatment received, breast conserving therapy (BCT), mastectomy alone, or mastectomy followed by postmastectomy radiation therapy (PMRT), was recorded. A multivariate analysis that included Neo-Bioscore and local therapy was performed to evaluate for association with LRR. Results: A total of 2315 patients treated with NCT were identified. BCT was performed in 750 (32.4%), mastectomy in 376 (16.2%) and mastectomy+PMRT in 1189 (51.4%). At a median follow-up of 4.2 years (range 0.5-11.7), the crude incidence of LRR was 4.5%. Freedom from LRR at 5 years ranged from 87.4%-100% by clinical stage, 83.0%-99.2% by pathologic stage and 74.9% - 100% by Neo-Bioscore (Figure). On multivariate analysis, Neo-Bioscore was independently associated with LRR, with decreased risk among patients with Neo-Bioscore of 3 or less (HR 0.47, 95% CI 0.19-1.21). Local therapy was not associated with LRR. Using BCT as baseline, the hazard ratio for patients undergoing mastectomy was 1.18 (95% CI 0.62-2.24) and for those undergoing mastectomy+PMRT was 0.81 (95% CI 0.52-1.25). Conclusion: The Neo-Bioscore better stratifies patients with respect to LRR after NCT than presenting clinical or final pathologic stage confirming the importance of tumor biology in local regional control.



Local-regional recurrence-free survival according to NeoBioscore in breast cancer patients receiving neoadjuvant chemotherapy

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Anti-HER2 Th1 Response is Superior to Breast MRI in Assessing Response to Neoadjuvant Chemotherapy in Patients with HER2 Positive Breast Cancer

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INTRODUCTION: In HER2 positive breast cancer ($HER2^+$BC) neoadjuvant chemotherapy (nCT) achieves complete pathologic response (pCR) ranging from 40–67%. Differentiating those with pCR from non-pCR (<pCR) can help tailor subsequent therapy making it critical to develop a sensitive tool to guide post nCT treatment. Post-treatment breast magnetic resonance imaging (pMRI) is currently considered the gold standard with high specificity (90.7%) but lower sensitivity (63.1%). We have identified that anti-HER2 Th1 response is associated with pathologic response following nCT therapy in patients with $HER2^+$BC. We compared pMRI versus anti-HER2 Th1 response in assessment of pCR in patients with $HER2^+$BC. METHODS: We retrospectively identified 40 patients with $HER2^+$BC and anti-HER2 Th1 analysis at our institution. Original pMRI reports were collected and imaging reviewed by a breast radiologist, blinded to pCR and immune response. Imaging-based tumor response was evaluated based on standard RECIST criteria, modified to include non-mass enhancement evaluated similar to solid lesions. Anti-HER2 Th1 immune response was determined by pulsing unstimulated peripheral blood mononuclear cells with MHC class II derived with six HER-2 peptides and measuring INF-g via ELISPOT assay, deriving cumulative response. Patients were dichotomized to a cutpoint of 50 SFC/10^6 cells ("low"<50, "high">50). MRI and anti-HER2Th1 responses were correlated with pathologic response and standard diagnostic metrics computed. RESULTS: Thirty-three out of 40 (82.5%) patients who received nCT had pMRI, with 16 (48.5%) patients achieving pCR. Mean anti-HER2 Th1 response in pCR was 150.6 + 109.5, and for <pCR was 23.9 + 15.2, the distributions were nearly non-overlapping. Diagnostic metrics are shown for all patients in Table1. Original pMRI had much lower diagnostic outcomes for pCR compared to anti-HER2 Th1 response. In the subset of 28 patients with blinded review pMRI, pCR diagnostic outcomes remained noticeably inferior to anti-HER2 Th1 response (sensitivity 41.7% vs 100.0%, specificity 62.5% vs 94.1%, overall accuracy 53.6% vs 97.0%). Similar findings were observed when patients were stratified by estrogen receptor status. CONCLUSION: Immune response demonstrated strikingly accurate diagnostic metrics compared with MRI. The presence of "high" anti-HER2 Th1 response is superior to the use of post-treatment MRI in the assessment of pCR in $HER2^+$BC. This assay has considerable promise and validation in large-scale study is warranted.

TABLE 1. Diagnostic Metrics

	Sensitivity	Specificity	PPV	NPV	Overall Accuracy
All Patients					
Original pMRI Report	37.50%	64.70%	50.00%	52.40%	51.50%
Blinded Re-review pMRI	41.70%	62.50%	45.50%	58.80%	53.60%
Anti-HER2 Th1 Response +	100.00%	94.10%	94.10%	100.00%	97.00%
ER Negative					
Original pMRI Report	20.00%	66.70%	66.70%	20.00%	30.80%
Blinded Re-review pMRI	28.60%	66.70%	66.70%	28.60%	40.00%
Anti-HER2 Th Response +	100.00%	100.00%	100.00%	100.00%	100.00%
ER Positive					
Original pMRI Report	66.70%	64.30%	44.40%	81.80%	65.00%
Blinded Re-review pMRI	60.00%	61.50%	37.50%	80.00%	61.10%
Anti-HER2 Th1 Response +	100.00%	92.90%	85.70%	100.00%	95.00%

pMRI=Post-treatment MRI, PPV= Positive Predictive Value, NPV= Negative Predictive Value
+ dichotomized by a cut point of 50

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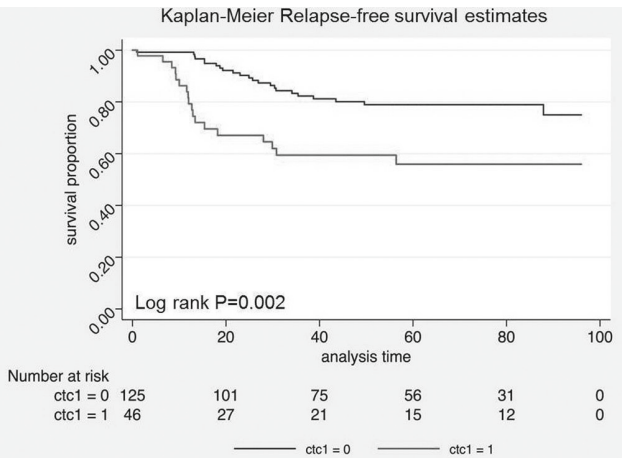
Circulating Tumor Cells After Neoadjuvant Therapy and Relapse in Stage I-III Breast Cancer C. Hall, L. Valad, J. Bauldry, M. Karhade, H.M. Kuerer, S.M. DeSnyder, C.H. Barcenas, A. Lucci.* *Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Circulating tumor cells (CTCs) can be identified in 25% of non-metastatic breast cancer patients, and ≥1 CTC predicts outcome. The aim of this study was to determine if CTCs present after neoadjuvant chemotherapy (NACT) predicted worse outcome in non-metastatic breast cancer patients. Methods: We evaluated 171 patients with stage I - III breast cancer who had a blood sample drawn after the completion of NACT, just prior to resection of the primary tumor. CTCs (per 7.5 ml blood) were identified using the Cell Search® System (Janssen). We correlated the identification of CTCs with standard tumor characteristics and axillary lymph node status using chi-square or Fisher exact tests. Log-rank test and Cox regression analysis was applied to correlate CTCs with relapse-free survival (RFS). Results: Median follow-up was 51 months; mean age was 50 years. Fourteen patients (8%) had T1 tumors, 54 (32%) had T2 tumors, 30 (18%) were T3, and 70 (42%) had T4 tumors. Forty-four (26%) patients were lymph node negative, 57 (34%) were N1, 10 (6%) were N2, and 58 (34%) had three or more positive lymph nodes. One or more CTC was identified in 27% of all patients. CTC presence was not associated with primary tumor size, high grade, hormone and/or HER2/neu status, lymph node positivity, type of NACT administered, or treatment response (pathologic complete response). There were 41 recurrences. Univariate (log-rank P = 0.002, HR = 2.68, 95% CI, 1.45 to 4.97) and multivariate (P = 0.004, HR = 3.03, 95% CI, 1.41 to 6.46) analyses demonstrated that detection of ≥1CTC predicted decreased RFS. Conclusions: One or more CTCs present after NACT predicted decreased RFS in stage I-III breast cancer patients. This information is important for future clinical trial design to identify patients at high risk for relapse who would benefit from additional adjuvant therapies.



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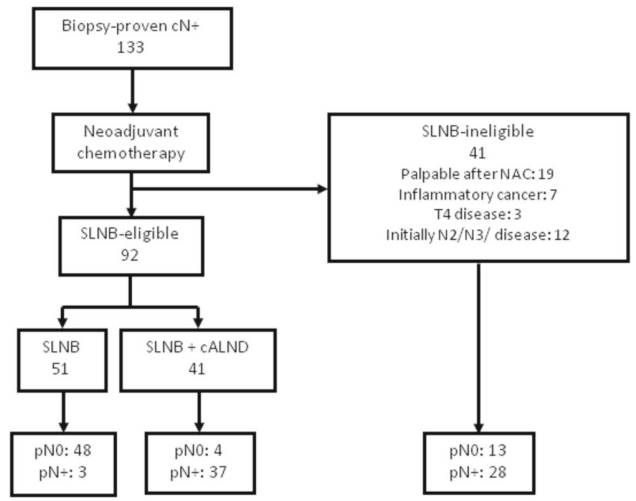
How Often Does Neoadjuvant Chemotherapy Avoid Axillary Dissection in Patients with Histologically Confirmed Nodal Metastases? Results of a Prospective Study A. Mamtani,* A. Barrio, T.A. King, G. Plitas, K.J. Van Zee, M. Pilewskie, M.B. El-Tamer, M.L. Gemignani, A.S. Heerdt, L.M. Sclafani, V. Sacchini, H.S. Cody III, M. Morrow. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Prospective studies have demonstrated false negative rates <10% for sentinel lymph node biopsy (SLNB) in breast cancer patients with confirmed nodal metastases at presentation (cN+) after neoadjuvant chemotherapy (NAC), provided that ≥3 negative sentinel lymph nodes (SLN) are retrieved. The frequency with which axillary dissection (ALND) can be avoided in this population is uncertain. We prospectively evaluated patterns of axillary surgery after NAC in a cohort of cN+ patients. Methods: Consecutive patients with stage I-III cancer receiving NAC were prospectively accrued, and biopsy-proven cN+ cases identified. Those who became node-negative by physical exam after NAC were eligible for SLNB. All patients had dual mapping with Tc-99m sulfur colloid and isosulfan blue. Completion ALND (cALND) was indicated for failed mapping, <3 SLN retrieved, or any positive SLN, including micrometastases and isolated tumor cells. Results: From 11/2013 to 7/2015, 440 patients initiated NAC; 234 (53%) were biopsy-proven cN+. Of these, 133 have completed surgery post-NAC; 92 were eligible for SLNB. Median age was 51 yrs, 51 (55%) were ER+, 14 (15%) ER-/HER2+, 27 (29%) triple negative (TN), and 82 (89%) had palpable nodes initially. At SLNB, ≥3 SLN were retrieved in 79 (88%) patients and 2 failed to map. cALND was done in 41 cases: 31 for positive SLN and 10 for <3 SLN retrieved (Figure 1). Of those with <3 SLN retrieved, 80% had nodal metastases (median 5 positive nodes). cALND was deferred in 3 cases (patient preference or ALLIANCE A011202 trial). 48 (52%) patients had SLNB alone with a nodal pathologic complete response (pCR). pCR occurred in 49% of ER+, 93% of ER-/HER2+, and 52% of TN cases. Of these patients, 42% also had breast pCR. Conclusions: Nearly 70% of biopsy-proven cN+ patients were eligible for SLNB after NAC and the morbidity of ALND was avoided in 52% of these cases, supporting the role of NAC in cN+ patients to downstage the axilla. Longer follow-up will determine rates of regional failure in this cohort. Patients with <3 SLN retrieved have a high rate of persistent nodal disease warranting cALND.



cN+: Confirmed nodal metastases at presentation, SLNB: Sentinel lymph node biopsy, NAC: Neoadjuvant chemotherapy, cALND: Completion axillary lymph node dissection, pN0: Pathologically node-negative, pN+: Pathologically node-positive

Figure 1: Axillary surgery and pathologic findings after NAC among patients presenting as cN+

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How Often is Treatment Effect Identified in Axillary Nodes with a Pathologic Complete Response After Neoadjuvant Chemotherapy?

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Background Sentinel node biopsy (SNB) after neoadjuvant chemotherapy (NAC) in node positive (cN+) breast cancer patients at presentation is accurate, but only when ≥3 negative SNs are obtained. Not all patients have 3 SNs, prompting some to suggest marking the positive node with a clip to ensure removal post NAC. Here we evaluate the frequency with which cN+ patients demonstrate treatment effect in the nodes after a pathologic complete response (pCR) with NAC and determine if treatment effect rates differ after axillary lymph node dissection (ALND) and SNB. Methods Biopsy-proven cN+ patients receiving NAC were identified from a prospectively maintained database. Patients with nodal pCR after ALND or SNB with dual mapping and ≥3 SNs removed were evaluated for treatment effect; ALND patients were compared to SNB patients. Results From 01/09-08/15, 516 cN+ patients received NAC followed by axillary surgery. Of these, 172 were pN0 on final pathology; 124 had an ALND and 48 had SNB. Median age was 49.5yrs, 17% were ER+/HER2 -, 27% triple negative, and 56% HER2+. The median number of nodes removed in ALND patients was 17.5 vs 4 in SNB patients. Treatment effect in nodes was identified in 160 (93%) patients, with a higher frequency of treatment effect in ALND vs SNB patients (97% vs 83%, p=0.004). The median number of nodes with treatment effect in ALND patients was 2 (range 1-19) vs 1 (range 1-5) in SNB patients. Patients with no treatment effect (n=12) were more likely to have residual invasive tumor in the breast (p<0.001) and SNB vs ALND (p=0.004). Other characteristics did not differ (Table 1). Of ALND patients, 5 had a SNB+ALND; only 1 had treatment effect in non-SNs only. Conclusions Following NAC, SNs with treatment effect were retrieved in 83% of patients without marking nodes. Treatment effect was identified more frequently in patients having ALND vs SNB, which may reflect a higher false-negative rate with SN-only. However, the clinical significance of this finding is uncertain. Longer follow-up is needed to determine regional recurrence rates in this cohort, but findings suggest a minority of patients will benefit from nodal clipping.

Table 1. Clinicopathologic characteristics of cN+ patients with and without treatment effect after NAC

Characteristic		Total (n=172)	No treatment effect (n=12)	Treatment effect (n=160)	P-value
Age, years (median, range)		49.5 (25, 85)	52 (28, 83)	49.5 (25, 85)	0.56
Tumor subtype*					0.30
	ER+/HER2-	28 (17%)	4 (33%)	24 (15%)	
	Triple negative	44 (27%)	3 (25%)	41 (27%)	
	HER2+	92 (56%)	5 (42%)	87 (58%)	
cT					0.52
	T0	1 (1%)	0 (0%)	1 (1%)	
	T1	23 (13%)	3 (25%)	20 (12%)	
	T2	71 (41%)	6 (50%)	65 (41%)	
	T3	44 (26%)	2 (17%)	42 (26%)	
	T4	33 (19%)	1 (8%)	32 (20%)	
cN					0.53
	N1	154 (89%)	11 (92%)	143 (89%)	
	N2	8 (5%)	1 (8%)	7 (5%)	
	N3	10 (6%)	0 (0%)	10 (6%)	
Axillary surgery					0.004
	SNB	48 (28%)	8 (67%)	40 (25%)	
	ALND	124 (72%)	4 (33%)	120 (75%)	
LVI#					1.0
	present	37 (25%)	3 (25%)	34 (25%)	
	absent	109 (75%)	9 (75%)	100 (75%)	
pT					<0.001
	T0	54 (32%)	0 (0%)	54 (34%)	
	Tis	21 (12%)	0 (0%)	21 (13%)	
	T1	58 (34%)	9 (75%)	49 (31%)	
	T2	33 (19%)	1 (8%)	32 (20%)	
	T3	6 (3%)	2 (17%)	4 (2%)	

*Unknown, n = 8 for total and ALND; #Unknown, n = 26 for total and ALND; ER, estrogen receptor; cT, clinical tumor stage; cN, clinical nodal stage; LVI, lymphovascular invasion; pT, pathologic tumor stage

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Correlation Between Preexisting Immunity and Clinical Response in a Phase II Trial Using HER2-Based Peptide Vaccines to Prevent Breast Cancer Recurrence

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BACKGROUND We have conducted a prospective, randomized, single blinded phase II trial utilizing two HER2 peptide vaccines, GP2 and AE37, for the prevention of recurrence in breast cancer(BrCa) patients(pts). GP2 is HLA-A2-restricted and stimulates CD8+ T-cells, while AE37 is HLA-unrestricted and stimulates CD4+ T-cells. Local reaction to the first inoculation(LR1) was used to assess pre-existing immunity to the peptides. Here, we examine the relationship between LR1 and clinical outcomes. METHODS Clinically disease-free BrCa pts at high risk of recurrence with any level of HER2 expression were enrolled after completing standard-of-care therapy. HLA-A2+ pts were assigned to the GP2 arms, while HLA-A2- pts were assigned to AE37 arms. Pts were randomized to receive peptide+GMCSF or GMCSF alone. Monthly intradermal inoculations x6 were given as the primary vaccine series(PVS) followed by boosters bi-annually. LRs were recorded 48-72 hours after each inoculation. For this analysis, vaccinated pts who completed the PVS were divided based on LR1 as above or below the median. DFS was analyzed using Kaplan-Meyer survival analysis and demographics with Pearson Chi-square. RESULTS There were 142 pts who completed the AE37 PVS, 71 below(AEL) and 71 above(AEH) the median LR1. For GP2, 82 pts completed the PVS, 40 below(GPL) and 42 above(GPH) the median LR1. All groups were well matched except for more node-positive pts in GPL vs GPH(p=0.033). AEH had improved DFS over AEL(95.3% vs 81.9%,p=0.025). Conversely, GPL had a better DFS than GPH(97.1%vs 89.4%,p=0.354). CONCLUSIONS In this randomized phase II trial of GP2 and AE37, pts with pre-existing immunity to the HER2 peptide, revealed opposing trends with these different vaccines. Pts with pre-existing immunity had better clinical outcomes with AE37; however, pts without pre-existing immunity to GP2 did better. This latter finding is similar to our prior study of E75, another CD8+ eliciting peptide vaccine. Therefore, these findings are likely due to the different T-cell subsets stimulated by these vaccines and the potential for immune tolerance among those effectors.

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Efficacy of Booster Inoculations in a Phase II Trial of GP2, a HER2-Derived Peptide Vaccine, for the Prevention of Breast Cancer Recurrence

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Background: GP2 is an HLA-$A2^{+}$-restricted immunogenic peptide from the HER2 protein (HER2 aa: 654-662). We have previously published the promising effects of booster innoculations with a similar peptide vaccine, E75. Here, we present analysis of the booster inoculations in a prospective, randomized, single-blinded, phase II trial of GP2 for the prevention of breast cancer (BCa) recurrence. Methods: After standard of care therapy, node-positive and high risk, node-negative BCa patients (pts) with HER2 expression of 1-3+ by IHC were enrolled and randomized to receive 6 monthly intradermal inoculations of either GP2+GM-CSF in vaccine group (VG), or GM-CSF alone in the control group (CG) as the primary vaccination series (PVS). Disease-free pts >6 months out from completing their PVS received a series of up to four bi-annual booster inoculations. Pts were followed for recurrence for 60 months. DFS was compared using Kaplan-Meir log-rank analysis. Demographics were compared using Pearson Chi-square and Mann-Whitney test. Results: The trial enrolled 180 pts, 89 pts in VG and 91 in CG. Of the VG, 56 (63%) went on to receive boosters (VB), and 55 (60%) of the CG received boosters (CB). VB pts were

well matched with both CG and CB pts. There were minimal and similar toxicities in all groups. With a median follow-up of 36.2 months, VB had the highest estimated 5 yr DFS at 95.7%. Compared to CG, VB had a decreased relative risk of recurrence (RRR) of 78.4% (DFS 95.7% vs 80.1%, p=0.03). To account for the bias created by early recurrences in CG, we compared VB to CB. Here, the reduction in RRR remained high at 73.7%, though not statistically significant (VB 95.7% vs CB 83.6%, p=.189). Conclusions: The GP2 vaccine with booster is safe, with minimal toxicity attributable to GM-CSF. There is decreased disease recurrence in VB pts when compared to CG and CB pts. Based on this data, a booster regimen appears to be beneficial for sustained immunity and improved disease free survival. Continued research will focus on the optimal booster strategy and schedule to maximize clinical benefit.

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Impact of Boosting in the Phase II Trial of the AE37+GM-CSF Vaccine in High-risk Breast Cancer Patients to Prevent Recurrence
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BACKGROUND We are conducting a randomized, blinded, placebo-controlled phase II clinical trial of the HER2-derived, AE37 vaccine for the prevention of breast cancer (BCa) recurrence in disease-free, node-positive or high-risk node negative patients (pts). The final analysis demonstrated no difference in 5 yr disease-free survival (DFS) in vaccinated pts compared to control pts; however, there was an improved DFS in HER2 1-2+ pts and particularly in triple negative pts. Here, we assess for improved DFS in pts receiving boosters. METHODS Following standard of care therapy, blinded pts with any level of HER2 expression (IHC1-3+) were randomized to receive 6 monthly intradermal inoculations of either AE37+GM-CSF, vaccine group (VG) or GM-CSF alone, control group (CG). A proportion of all pts also received 4 booster inoculations, one every 6 months. Demographic and recurrence data were collected. DFS was compared using Kaplan-Meir log rank analysis. Demographics were compared using Pearson Chi square or Mann-Whitney test as appropriate. RESULTS The trial enrolled 301pts, 154 in VG and 147 in CG. Within VG, 114 pts received boosters (VB) while 88 CG pts were boosted (CB). There were no differences in demographics between groups (all p≥0.1). There were no safety concerns with the boosters, except for an equally distributed 5% incidence of delayed urticarial reactions in each group, as previously reported. 5 yr estimated DFS was 89.1% for VB vs 79.9% for CG, p = 0.051. To adjust for survival bias, we compared VB to CB and found improved DFS in VB pts, though not statistically significant (VB 89.1% vs CB 84.9%, p = 0.76). CONCLUSION Boosting with AE37+GM-CSF in BCa pts at high risk of recurrence produced a non-significant 30% relative improvement in DFS. Intuitively, boosters should help maintain long-term immunity which in turn should help prevent recurrence; however, a larger study will be required to prove this suggested benefit of boosting after vaccination with AE37+GM-CSF.

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Tumor-Targeting microRNA Delivery System in Colorectal Liver Metastases Model
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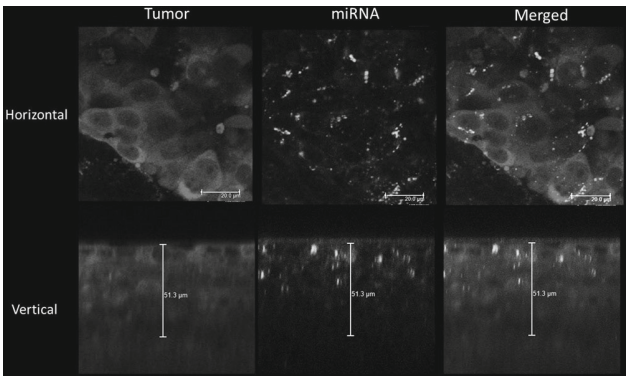
Introduction: Establishment of microRNA (miRNA) delivery system is challenging. Recently we found several miRNAs are associated with the characteristics of an oligometastatic/polymetastatic phenotype in metastatic lesions (1), and established experimental model of xenogenic hepatic metastases of colorectal cancer (2). We hypothesized miRNA delivery therapy combined with conventional cytotoxic agents improve tumor suppressive effect. We demonstrate tumor-targeting miRNA delivery system using nanoscale coordination polymer (NCP) in colorectal liver metastases model. Methods: HCT116 cells stably transfected by luciferase and tdTomato genes were splenically injected to generate liver metastases as described in (2). NCPs carrying oxaliplatin and miRNAs labeled with Alexa647 were assembled as described in (3). NCPs (oxaliplatin 2.0 mg/kg and miRNA mimics 0.5mg/kg) were intraperitoneally injected to evaluate the biodistribution with subsequent IVIS and confocal microscopic imaging. Concentrations of platinum (Pt) in individual organs were quantified with ICP-MS. Results: Ex vivo fluorescent imaging with IVIS system showed miRNA accumulations specifically in liver mesastases at 3, 24 and 72 hours after injection (relative fluorescent intensities of miRNAs were 1, 0.3 and 0.1 respectively). The accumulation of miRNAs was not found in normal liver, kidney, lung and heart. Confocal microscopic imaging demonstrated cytosolic accumulation of miRNAs in tumor cells (image). The miRNAs were preferentially distributed in the perinuclear area. The percent of injected dose per gram tissue (%ID/g) of Pt in liver tumor, liver, kidney, lung and heart were 3.8, 3.8, 1.3, 1.2 and 1.2 at 3 hours after injection, respectively. The Pt %ID/g in liver tumor at 3, 24 and 72 hours after injection were 3.8, 2.6 and 0.9, respectively. Conclusion: Our findings demonstrated that NCP system enhanced the stability of miRNA in vivo, leading to tumor specific accumulation. Our results suggest potential therapeutic miRNA delivery system targeting metastatic diseases. (1) Uppal A, Oncotarget. 28;6(6):3540-52 (2015) (2) Oshima G, Sci Rep. 22;5:10946 (2015) (3) He C, Biomaterials. 36;124-33 (2015)



The confocal microscopic images. Fluorescence of harvested tumors ex vivo. Red; tumors (tdTomato), green; miRNAs (Alexa647).

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Neutrophil-Lymphocyte Ratio Confers Prognostic Significance in MSI-high Colorectal Cancer
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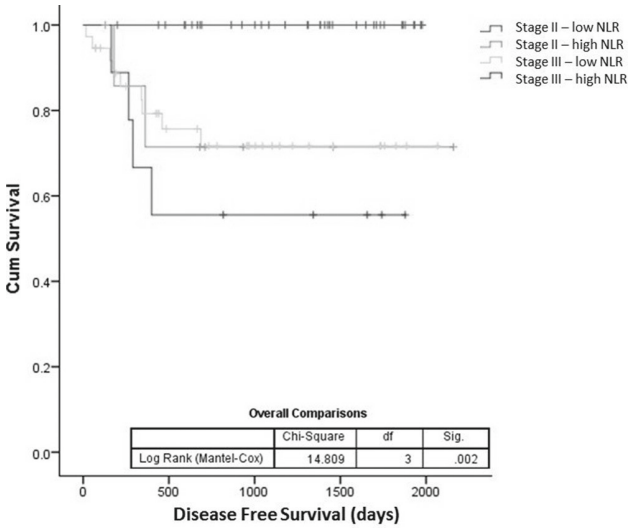
Introduction: Cancer-related inflammation can be a driver of tumor growth and progression in solid tumors. Recent evidence suggests that high circulating neutrophil–lymphocyte ratio (NLR) serves as a surrogate marker for inflammatory tumor microenvironment and is a poor prognosticator in colorectal cancer (CRC). In general, microsatellite instability (MSI-high) is thought to induce robust immune response and confer favorable prognosis. MSI status currently guides the use of adjuvant therapy in early stage CRC. We investigated the prognostic implications of NLR in MSI-high CRCs. Methods: Patients undergoing treatment for MSI-high CRC with curative intent between 2009 - 2015 were retrospectively reviewed. Those who initiated therapy prior to referral were excluded as baseline (treatment-naïve) complete blood counts (CBC) were inconsistently available. Clinicopatholgoic characteristics, TNM stage, and CBC with differential were analyzed. Treatment-naïve NLR was calculated using CBCs obtained as close to diagnosis available but prior to surgery or neoadjuvant therapy. A NLR of ≥ 5 was defined as high. Results: Among 123 patients meeting inclusion criteria, 40 (33%) were MSI-high due to hypermethylation of the MLH1 promotor (MSI-methyl), while the remaining 83 (67%) had germline mutations in either MLH1, MSH2, MSH6, PMS2 (MSI-germline). BRAF mutation was present in 20 (50%) of MSI-methyl CRCs. There was no difference in treatment-naïve NLR between the MSI-methyl and MSI-germline groups. After a median follow-up of 43 months, a high NLR was associated with poor prognosis with worse disease-free sur-

vival (DFS, hazard ratio 3.203; 95% confidence interval: 1.26-8.14; P=0.014) independent of BRAF status. In subgroup analyses, NLR remained prognostic in patients with node-negative (stage II) CRC, but the difference in DFS did not reach statistical difference among patients with node-positive (stage III) disease (Figure). Conclusion: High NLR is an independent marker of poor prognosis among MSI-high CRC. It may provide enhanced prognostic information in early stage MSI-high CRC.



Kaplan Meier curve of disease free survival in stage II and II MSI high patients dichotomized to low and high NLR.

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Impact of Sentinel Lymph Node Mapping on Survival in Colon Cancer Compared to Conventional Surgery: A Prospective Study
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Introduction: Sentinel lymph node (SLN) mapping (M) has been performed for melanoma, breast cancer and other gastrointestinal cancers. In colon cancer (CCa), SLNM has been shown to diagnose micrometastases by ultra-staging of the lymph nodes (LNs) which would have been missed by conventional (conv.) examination. To identify if SLNM impacts survival in CCa patients (Pts), a comparative study was undertaken between SLNM (group A) vs conv. surgery (group B) pts performed in the same institution by two different groups of surgeons. Methods: In pts with CCa, SLNM was done by subserosal and peri-tumoral injection of 1-3 ml of lymphazurin or methylene blue. The first 1-4 blue LNs were tagged as SLNs and were ultra-staged by IHC and H & E. Conv. surgery specimens underwent routine examinations. Data was collected for demographics including recurrence and 5 year overall survival (5yr OS). The Kaplan Meier method was used to estimate survival with p value of significance as < 0.05. Results: Out of a total 833 consecutive pts, 303 pts had SLNM (gp A) with a success rate of 99.3% for identifying a SLN. Average (Avg.) no of SLN/pt was 3. Avg. number of total LNs examined in gp A was 17.5 vs 13.6 in 530 conv. Sx pts (gp B). Demographics of age, sex, grade, mean no. of positive lymph nodes were similar. Overall, the recurrence rate between gp A vs gp B was 7.9% vs 13.4% ($p < 0.05$). The median survival time of gp A vs gp B was 107 months vs 67 months ($p < 0.05$). Five yr OS between gp A vs gp B was 62.6% (95% CI, 57.1-68.6) vs 53.8% (95% CI, 49.6-58.3), respectively ($p = 0.00015$) {Table I}. The most striking difference of 5yr OS was for pts with node negative status— 72.6 vs 63.1% ($p < 0.005$). Conclusion: SLNM allows upstaging of first draining lymph nodes allowing better separation of LN +ve vs LN –ve pts. This allows better treatment stratifications between SLNM gp vs conv. Sx gp. This also leads to detection for more LNs/pt, lower recurrence and higher 5yr OS. A larger multi-institutional trial needs to be done for further confirmation.

Table I: Stage-stratified 5-yr overall survival (KM estimate) with 95% confidence interval for SLNM vs Conventional patients. Median survival comparisons and recurrence data also shown.

		SLNM (gp A)			Conventional (gp B)	
Stage	# of Patients (%)	5-yr OS% (95%CI)	Median Survival (mo)	# of Patients (%)	5-yr OS% (95%CI)	Median Survival (mo)
I	84 (27.7)	78.0 (69.3-87.9)	178	111 (20.9)	72.2 (64.2-81.2)	110
II	86 (28.4)	70.3 (60.9-81.1)	123	166 (31.3)	59.7 (52.5-67.8)	82
III	94 (31.0)	61.5 (51.9-72.9)	92	169 (31.9)	58.0 (50.9-66.1)	84
IV	39 (12.9)	14.4 (6.3-33.0)	19	84 (15.8)	8.8 (4.3-17.7)	13
All Patients	303	62.6 (57.1-68.6)	107	530	53.8 (49.6-58.3)	67
	Recurrence-SLNM (gp A)	Recurrence-Conventional (gp B)				
Stage I	3 (3.6%)	6 (5.4%)				
Stage II	6 (7.0%)	17 (10.2%)				
Stage III	15 (16.0%)	36 (21.3%)				
Stage IV	0 (0%)	12 (14.3%)				
Total	24 (7.9%)	71 (13.4%)				

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KRAS Mutation in Locally Advanced Rectal Cancer is Independently Associated with a Lower Rate of Pathologic Complete Response Following Neoadjuvant Therapy
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Background: KRAS and TP53 mutations have been associated with poor tumor response to neoadjuvant chemoradiation (CRT) in patients with locally advanced rectal cancer. We evaluate whether KRAS and TP53 mutations are independently associated with pathologic complete response (pCR). Methods: Analysis of 217 patients with stage II/III rectal cancer treated with neoadjuvant therapy prior to resection was performed after combining molecular data from 174 patients enrolled in a multicenter phase 2 trial with 43 patients from a single high-volume tertiary cancer center. All patients received CRT. In addition, patients received zero to eight cycles of FOLFOX either before or after CRT, prior to surgical resection. Patient and treatment-related characteristics, along with KRAS and TP53 status, were evaluated for association with pCR. A subset analysis was performed to evaluate concordance between Sanger sequencing of select exons and next-generation sequencing of all exons and select introns of KRAS and TP53. Results: 91 patients (42%) had tumors with KRAS mutation, 146 had TP53 mutation (67%), and 58 (27%) had both. 57 patients (26%) achieved pCR following neoadjuvant therapy. 44 out of the 126 KRAS wild-type tumors (35%) achieved pCR, compared with only 13 of the 91 KRAS mutant tumors (14%). KRAS mutation remained independently associated with a lower pCR rate on multivariable analysis after adjusting for clinical stage, CRT-to-surgery interval, and cycles of FOLFOX administered (OR 0.31, 95% CI: 0.15-0.62, $p < 0.001$). Of 30 patients with either G12V or G13D KRAS mutations, only 2 (7%) achieved pCR. TP53 mutation alone was not associated with pCR, but combined KRAS/TP53 mutation was associated with a particularly low pCR rate (6 of 58, 10%). The concordance between sequencing platforms was high for KRAS (42 of 45, 93%), but low for TP53 (25 of 45, 56%). Conclusions: KRAS mutation is independently associated with a lower pCR rate in locally advanced rectal cancer after adjusting for variations in neoadjuvant regimen. Genomic data can be used to select patients for "watch and wait" strategies.

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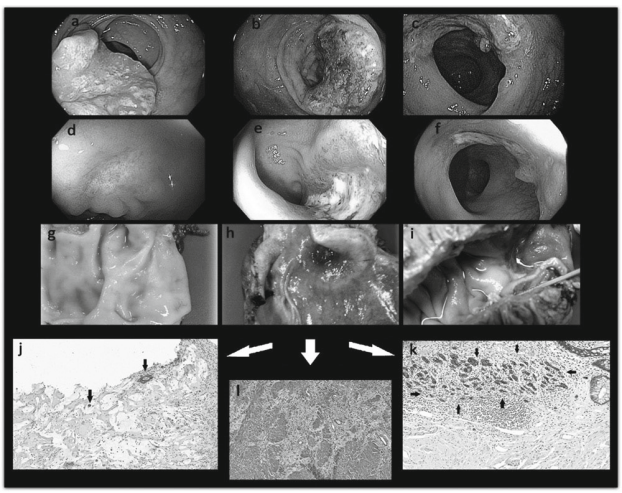
Conventional Histological Analysis is Insufficient to Confirm Complete Pathological Response After Neoadjuvant Chemoradiation for Rectal Cancer M.A. Pereira, A.R. Dias, S.F. Faraj, B.A. Azevedo, E.S. de Mello, C.S. Marques, C. Nahas, A.R. Imperiale, G.C. Cotti, S. Nahas, U. Ribeiro.* *Sao Paulo Cancer Institute -HCFMUSP-ICESP - University of Sao Paulo School of Medicine, Sao Paulo, Brazil.*

Background: Neoadjuvant chemoradiation therapy (nCRT) for colorectal cancer (CRC) may lead to complete response in up to 20% of the cases. Pathological complete response (pCR) may have implications on adjuvant chemotherapy, and may be associated to better overall survival and prognosis. Pathological evaluation protocol includes conventional histological analysis. This method may not be enough to detect if the tumor has been eradicated. Objective: To determine if the current pathological analysis is sufficient to confirm pCR in patients who underwent nCRT for rectal cancer. Methods: A prospective analysis of 130 patients who underwent nCRT for rectal cancer (cT2-T4) followed by radical resection with total mesorectal excision between August 2012 and February 2015 was undertaken. All paraffin blocks from those patients initially confirmed as pCR were assessed at three levels (sections cut separated by 50 μm) and prepared for staining with hematoxilin-eosin and immunostaining with anticytokeratin antibody (CKAE1/AE3) to verify the presence of residual tumor. Results: Twenty five (19.2%) from the 130 patients presented pCR (ypT0N0). Of these 25 patients, 13 were operated due to clinical evidence of disease in their surgical specimen (despite negative biopsies in all 13 cases) and the other 12 had cCR. After reassessment through three levels sections of the tumor site and CK-staining, residual tumor was found in 7 (28%) from 25 patients. Furthermore, 3 of these 7 patients had presented cCR, with no apparent macroscopic lesion in the surgical specimen. Two cases among the remaining 105 had isolated lymph node metastasis (ypT0N1). Therefore, pCR in this population was 13.8% (18 of 130 patients). Conclusion: Routine histological analysis is insufficient to determine complete tumor eradication. Additional sections and CK staining are useful tools that may reveal missed tumor cells and should be added to the routine for those patients initially classified as ypT0. Also, complete response in the rectal wall does not necessarily imply absence of lymph node metastasis.



Colonoscopy imaging of colorectal carcinoma (CRC) patients before neoadjuvant therapy: case 1 (a); case 2 (b); case 3 (c)
Colonoscopy imaging of colorectal carcinoma (CRC) patients after neoadjuvant therapy: case1, (d); case 2 (e); case 3 (f).
Rectosigmoid showing the macroscopic tumor site: case 1 (g), tumor pathologically staged as ypT2N0; case 2 (h), tumor pathologically staged as ypT0N0, with residual tumor after our revaluation by extra sections and immunostaining with anticytokeratin antibody (CKAE1/AE3) (ypT+); case 3 (i), patient with pathological complete response (ypT0N0).
Residual tumor cells in a initially ypT0N0 patient stained with hematoxylin and eosin (l) after extra sections and immunostaining (j, k) with anticytokeratin antibody (CKAE1/AE3) – x200 original magnification

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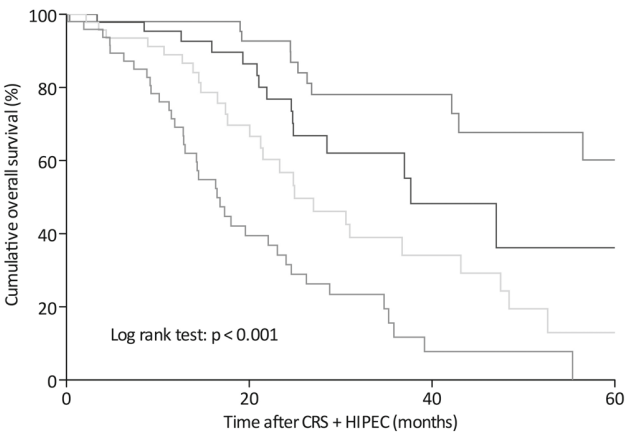
Development of a Prognostic Model for Patients with Peritoneally Metastasized Colorectal Cancer Treated with Cytoreductive Surgery and HIPEC G. Simkens,[1]* T. van Oudheusden,[1] D. Nieboer,[2] E. Steyerberg,[2] H. Rutten,[1] G. Nieuwenhuijzen,[1] M. Luyer,[1] S. Nienhuijs,[1] I. de Hingh.[1] *1. Surgical Oncology, Catharina Hospital Eindhoven, Eindhoven, Noord-Brabant, Netherlands; 2. Erasmus MC - University Medical Center, Rotterdam, Zuid-Holland, Netherlands.*

Introduction: With the introduction of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC), long-term survival in selected patients with colorectal peritoneal metastases (PM) can be achieved. The peritoneal surface disease severity score (PSDSS) was developed to predict overall survival in these patients. The current study aims to validate and adjust this score, thereby providing a useful pre-cytoreduction prediction score for overall survival after CRS + HIPEC in patients with colorectal PM. Methods: Patients with colorectal PM undergoing CRS + HIPEC with (near) complete cytoreduction between 2007 and 2014 in a tertiary referral hospital were included. Statistical analysis, including cox proportional hazard model development and internal validation with bootstrap resampling, were performed with RStudio. Results: Subsequently, 200 patients underwent CRS + HIPEC, with complete macroscopic cytoreduction in 95% of the patients. External validation of the PSDSS showed a Harrell's c and R^2 statistic of 0.62 and 0.08, respectively. The internally validated prognostic nomogram; the Colorectal Peritoneal Metastases Score (CPMS), included four relevant prognostic factors: Age, the PCI score, N2 lymph node metastases, and signet ring cell histology. This nomogram resulted in four prognostic groups with adequate survival differentiation. After internal validation, the CPMS showed a Harrell's c and R^2 statistic of 0.72 and 0.19 respectively. Patients were devided into four categories based on their individual sum scores. Subsequently, these categories differentiated adequately in overall survival (Figure 1). Furthermore, the calibration plot showed good agreement between predicted and observed outcome. Conclusions: This study developed an adjusted version of the PSDSS; the CPMS. This pre-cytoreduction nomogram adequately predicts the overall survival of patients with colorectal PM undergoing cytoreduction and HIPEC. It can be used as tool to assist in the decision of continuing cytoreduction and HIPEC and can provide valuable information for patients and surgeons in the follow-up period after CRS + HIPEC.



Category: Point range	Events / N	MS; months (95% CI)
I: 0 - 51.9	11/50	NR
II: 51.9 - 64.7	15/49	37.7 (28.5 - NR)
III: 64.7 - 82.0	26/49	25.0 (21.3 - 47.5)
IV: ≥ 82.0	37/50	16.5 (13.0 - 24.0)

Figure 3. Overall survival after cytoreductive surgery in peritoneally metastasized colorectal cancer patients stratified for the four categories of the CPMS

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Predicting Incomplete Cytoreduction and Aborted Hyperthermic Intraperitoneal Chemotherapy in Patients with Mucinous Peritoneal Carcinomatosis of Appendiceal Origin V. Milovanov,* A. Sardi, R. MacDonald, C. Nieroda, V. Gushchin. *Surgical Oncology, Mercy Medical Center, Baltimore, MD.*

Background: Selection of patients with peritoneal carcinomatosis (PC) of appendiceal origin for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is challenging. Even in peritoneal malignancy centers, rate of incomplete cytoreduction (IC) and aborted HIPEC (AHIPEC) varies from 17-30%. A risk predictive model (RPM) to identify patients at greatest risk for IC/AHIPEC is needed. Methods: Data from 305 attempted CRS/HIPEC's (including IC and AHIPEC) was used to apply a combination univariate analyses (UA) and multivariate binary logistic regressions (MBLR). Preoperative risk factors for IC/AHIPEC were selected to develop a RPM. Data on all CRS/HIPEC attempts was randomly separated in two subsets. The first subset (n=149) defined the model and the second (n=153) was used to validate it. Results: After UA and MBLR, 5 variables remained: high grade, prior surgical score ≥2 (PSS), CA-125 and CEA x3 the upper limit of normal (ULN), neutrophil-lymphocyte ratio (NLR) >2.6 and C-reactive protein (CRP) >2.5mg/L. Internal validation of RPM on subset 1 showed area under ROC curve (AUROC) 0.88, sensitivity 88% and specificity 76%. External validation of subset 2, AUROC 0.85, sensitivity 88% and specificity 69%. Weights attributed to each variable in the score were obtained from b-coefficients of the whole population MBLR analysis (305 attempts). Weights were high grade (2 points (pt)), PSS (2pt), CA-125 x3 ULN (4pt), CEA x3 ULN (3 pt), NLR >2.6 (3pt) and CRP >2.5 mg/L (6pt). Internal validation of scoring model for the entire sample, AUROC 0.87, sensitivity 88%, and specificity 74% for cutoff of 6 pt. Correlation between score and percentage of IC/AHIPEC is in Table 1. Conclusion: We developed and validated a model predicting IC/AHIPEC procedures for PC. Clinical implications of a high final cumulative score (FCS) may guide clinical decisions to laparoscopy to assess resectability, prevent surgery in patients with major co-morbidities, or to begin neoadjuvant chemotherapy to decrease tumor burden. External validation of the model by other peritoneal surface malignancy centers is needed.

Correlation between Final Cumulative Score and IC/AHIPEC

Final Cumulative Score	IC/AHIPEC
0-5	6%
6-10	44%
11-15	68%
16-20	83%

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Bridging Disparities in Colorectal Cancer Screening in the Indigent Population S. Misra,* J. Allan, N. Ray, S. Trehan, M. Marsh, M. Guzman, D. Gregory, N. Aydin, A. Mishra. *Surgery, TTUHSC, Amarillo, TX.*

Introduction: In the Texas Panhandle, 22 of the 26 counties are medically underserved, and 1 out of 3 people are uninsured with low literacy rate. Colorectal Cancer (CRC) screening rate of 41% here is significantly lower than the national average of 65% and the National Colorectal Cancer Coalition's goal of 80%. Barries to increasing screening are lack of patient awareness, cost, and lack of access. Methods: To address these barriers, we obtained a $1.5 million grant from the Cancer Prevention Research Institute of Texas to provide CRC education, awareness and improve screening rates using Fecal Immunochemical Tests (FIT) and colonoscopies at no cost to the participants. Community public and private partnerships were established for effective outreach. A website: www.cancerscreeningtx.com, Facebook and Twitter accounts were created. Public Service Announcements and interviews aired on television and radio. Education was provided via public sessions conducted by Community Health Workers using flip charts, translation services and FIT demonstrations. Screen eligibility was determined by the criteria in Chart 1. The "navigation" is referral to primary care and high risk indicates colonoscopy without F.I.T. Participant satisfaction surveys were analyzed to evaluate the quality of the session. Results: Outreach has covered 176,000 people. The website shows an upward trend in views, 35% being on mobile devices. In five months 331 participants attended education sessions, 145 have completed FIT screenings. 26 colonoscopies have been booked based off of risk factors. 100% thought the session was a good use of their time and the CHW was knowledgeable about the topic. 98% thought the information was easy to understand and the CHW provided reassurance about the procedures. 97% thought an adequate explanation was provided and 99% are able to make a decision about CRC screening. 95% were not embarrassed by the information. Conclusions: Targeted use of media is effective in bridging gaps in public awareness of CRC. Complex information can be delivered in meaningful ways by tailoring education methods to the target population. Establishing community partnerships has bridged access and cost barriers.

Indication	Outcome
Not 50-75yo nor high risk status; Not TX resident; OR Has health insurance	Education Only
Hx of CRC; OR blood in rectum/stool within last 3 months	Navigation Only
Yes to questions 2 or 3; Yes to question 1 if one immediate or two extended family members	Colonoscopy
No to questions 1, 2, and 3	F.I.T Screening

Yes to any of the below may indicate high risk status:

Question 1: Have any of your parents, siblings, or children been diagnosed with colon cancer before the age of 60? If yes, please provide additional information.

Question 2: Have you ever been told by a doctor that you have ulcerative colitis or Crohn's disease?

Question 3: Have you ever been told by a doctor that you have adenomatous polyps (pre-cancerous)?

Intake eligibility criteria for screening and education.

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Impact of Insurance Expansion on Access to Colorectal Cancer Care A. Loehrer,* D.C. Chang, Z. Song, M.M. Hutter, J.T. Mullen. *Surgery, Massachusetts General Hospital, Boston, MA.*

Introduction Colorectal cancer is the third most common cancer and the third leading cause of cancer deaths in the United States. While earlier diagnosis has led to improved survival, disparities in access to and outcomes of care for colorectal cancer persist across populations. Lack of insurance coverage has been associated with more advanced disease at presentation, more emergent admissions at time of colectomy, and lower overall survival relative to privately-insured patients. The 2006 Massachusetts health reform serves as a unique natural experiment to assess influence of insurance expansion on colorectal cancer outcomes. Methods We used the AHRQ State Inpatient Databases to identify patients with government-subsidized or self-pay (GSSP) or private insurance admitted to a hospital with colorectal cancer between 2001 and 2011 in Massachusetts (n= 19,670) and three control states (n=157,569). Difference-in-difference models were used to show impact of the 2006 Massachusetts health care reform on outcomes, controlling for age, sex, comorbidities, and secular trends. Resection of colorectal cancer was our primary outcome. Results Prior to the 2006 Massachusetts reform, government-subsidized/self-pay patients had significantly lower rates of resection for colorectal cancer compared to privately-insured patients in both Massachusetts and control states. The Massachusetts insurance expansion was associated with a 33% increased rate of resection (IRR 1.33, 95% CI [1.18 to 1.51], P<0.001), an 8.0 percentage-point increased probability of an elective admission (95% CI [2.7 to 13.6], P=0.003) and a 6.4 percentage-point decreased probability of emergent admission (95% CI [-11.1 to -1.7], P=0.008) for government-subsidized/self-pay patients in Massachusetts compared to control states. Conclusion The 2006 Massachusetts health reform – a model for the Affordable Care Act – was associated with a 33% increased rate of resection with a corresponding decreased probability of emergent admission and increased probability of elective admission for government-subsidized/self-pay patients in Massachusetts. Our findings suggest that insurance expansion may help to improve access to care for patients with colorectal cancer.

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Chasing the Proverbial Unicorn of Relative Value Units (RVU) and Block Time R. Rajeev,* F. Johnston, T. Gamblin, K. Turaga. *Surgical Oncology, Medical College of Wisconsin, Milwaukee, WI.*

Introduction: Competitive market forces on healthcare have led to increasing demands on work effort on academic surgical oncologists. This has to be balanced against resource constraints of limited operating room space and

block time availability. We hypothesized that the current work RVU (wRVU) requirements pose an unrealistic expectation of practicing surgical oncologists. Methods: University HealthSystem Consortium (UHC) median wRVUs were utilized to determine the effort expected of a surgical oncologist. Surgical oncology subspecialties were divided into breast, colorectal, melanoma, sarcoma, liver and pancreas. Representative procedures from each specialty were determined using Healthcare Common Procedure Coding System and median wRVUs were obtained per procedure including a single consultation cost without incorporating modifiers and adjustments for multiple procedures. A work year was assumed to include 48 weeks of work time to account for CME, and vacation. Night and weekend call was excluded from the analysis. Results: The median UHC wRVU for a surgical oncologist is 7800 wRVU, which corresponds to a theoretical reimbursement of $383,387-493,459 in a pure Medicare population. In order to meet the wRVU requirements, the number of annual major procedures performed varied from 124-1625 (breast 365-701, colorectal 192- 324, melanoma 677-1625, sarcoma 234-334, liver 124-571, pancreas 139-264). The number of major procedures performed per day varied from 3 procedures/day for a 4 day block time to 12 procedures/day for a single day block time (Table 1). Conclusions: Current wRVU expectations and block time schedules need to be better aligned to account for increasing demands on surgical oncologists. Society driven surveys as recently conducted by the American Society of Breast Surgeons might be effective ways to truly understand workforce demands in the nation.

Annual number of representative procedures required to achieve target Relative Value Units in various block time scenarios classified by surgical oncology subspecialties

Specialty	Representative procedures	Total wRVU	Annual maximum number of procedures required to achieve target wRVU	No. of procedures/day: 1-day block time	No. of procedures/day: 2-day block time	No. of procedures/day: 3-day block time	No. of procedures/day: 4-day block time
Breast	Lumpectomy + sentinel lymph node biopsy	15.8	493	10.3	5.1	3.4	2.6
	Modified radical mastectomy	21.4	364	7.6	3.8	2.5	1.9
Colorectal	Partial colectomy with anastomosis	25.8	302	6.3	3.2	2.1	1.6
	Partial colectomy with cecostomy or colostomy	33.1	235	4.9	2.5	1.6	1.2
	Total abdominal colectomy + ileostomy	33.4	233	4.9	2.4	1.6	1.2
	Abdominoperineal resection + colostomy	33.9	229	4.8	2.4	1.6	1.2
Melanoma	Excision of malignant lesion 2.1 - 3.0 cm + Sentinel lymph node biopsy	8.5	918	19.1	9.6	6.6	4.9
	Excision of malignant lesion over 4.0 cm + Sentinel lymph node biopsy	10.7	729	15.2	7.6	5.1	3.8
Liver	Partial liver resection	42.2	184	3.8	1.9	1.3	0.9
	Radical liver resection	62.6	124	2.6	1.3	0.9	0.6
Pancreas	Distal subtotal pancreatectomy	29.5	264	5.5	2.8	1.8	1.4
	Pancreaticoduodenectomy	51.8	150	3.1	1.6	1.0	0.8
Sarcoma	Excision of abdominal tumor 5 cm or less	23.3	334	6.9	3.5	2.3	1.7
	Excision of abdominal tumor 10 cm or more	33.3	234	4.9	2.4	1.6	1.2

wRBU - work Relative Value Units

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Preclinical Studies of Tumor-Reactive T-Cells Derived from Human Pancreatic Cancer Draining Lymph Nodes for Use in Adoptive T-Cell Therapy K. Choong,* H. Graor, V. Sandoval, M. Zhang, J. Kim, J. Ammori. *Surgery, University Hospitals Case Medical Center, Shaker Heights, OH.*

Background Pancreatic cancer is the 4th leading cause of cancer death with an overall 5-year survival of only 5%. Recent success in immunotherapy using checkpoint inhibitors to treat melanoma and lung cancer suggests that tumor-reactive T-cells exist in vivo. The purpose of our study was to expand tumor-reactive T-cells from pancreatic cancer draining lymph nodes (PDLNs) derived from patients undergoing surgery for pancreatic adenocarcinoma. Our goal is to develop a method of ex vivo expansion of PDLNs as a source of effector T-cells for adoptive immunotherapy (AIT). Methods Between January 2013 and 2015, under an IRB-approved protocol, portions of regional lymph nodes were sampled during pancreatic cancer surgeries in 26 patients. Samples were mechanically separated into single cell suspensions and subsequently activated and expanded using anti-CD3/anti-CD28 coated beads and human recombinant IL2 (100 IU/mL) for 14 days. Phenotypic analysis was performed throughout the culture using flow cytometry. Tumor apoptosis assays and cytokine production assays against multiple cancer cell lines were performed to assess PDLN culture functionality. Results We observed, in 13 patients, an average 162 fold expansion of PDLNs over 14 days. By culture day 14, PDLN cultures were >90% CD3+ T-cells with a CD4 to CD8 ratio of ~2:1. When cell cultures were stimulated with a human pancreatic cancer cell line AsPc-1, an increased proportion of PDLN cells expressed intracellular IL2, IFNγ, and TNFα. Co-culture of activated PDLN cells with various human tumor cell lines (AsPc1, MIA PaCa-2, A375 melanoma, U87 glioblastoma) demonstrated broad killing of all tumor lines. However, when activated PDLN cells were co-cultured using transwell plates, which prohibit direct contact between the cancer cells and PDLN cells, pancreatic cancer-specific killing was demonstrated. This suggests the presence of antigen cross-presentation and pancreatic cancer-specific responses. Conclusions Acquisition, activation and expansion of cells from human PDLNs is feasible and activated PDLN cultures demonstrate reactivity against human tumor cell lines in vitro.

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Th1-type Immune Response in Metastatic Lymph Nodes from Pancreatic Adenocarcinoma is Associated with Improved Prognosis E. Nizri,* S. Bar David, G. Weiner, G. Lahat, J. Klausner. *General Surgery, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel.*

Background: Tumor-immune interactions have been the subject of intense research recently, culminating in the approval of immune modifying agents in anti-cancer therapy. However, not much is known about tumor-immune interactions in the metastatic lymph node (LN), in spite of the natural occurrence of immune cells in this environment and the prognostic implication of LN involvement by tumor. Our aim was to study tumor-immune interactions in the LN and determine whether such interactions have prognostic implications. Methods: Histological sections from metastatic LNs of 55 patients with pancreatic adenocarcinoma patients were retrospectively evaluated for architectural and morphological parameters. Then specific lymphocytes subsets in tumor vicinity were determined ($CD4^+$, $CD8^+$ and $CD20^+$). Finally, determination of T-helper (Th) type immune response was done by the expression of specific transcription factors, T-bet (Th1) and GATA-3(Th2). Data was correlated with overall survival (OS) and disease free survival (DFS), both expressed in months. Results: The number of metastatic LN affected OS: patients with less than 7 affected LN survived 21.5±2.1 months whereas those with >7 survived only 7.9±1.7 ($p<0.01$). Preservation of overall LN histology was associated with 32.4±6.4 months of OS vs. 18.7±0.7 with tumor replacement of LN ($p<0.05$). Similar to what was described for primary tumor regarding tumor-infiltrating lymphocytes, peritumoral $CD8^+$ number was higher among long term survivors (46.8 vs. 18.5 per 3 HPF) ($p<0.05$) whereas $CD4^+$ number was not. Long term survivors had also a higher number of peritumoral $CD20^+$ cells in metastatic LN; 101.9 vs. 30.2 ($p<0.05$). Finally, longer survival was associated with Th1-immune response, with a T-bet/GATA-3 ratio of 1.4 vs. 0.06 for short term survivors ($p<0.05$). Conclusions: $CD8^+$ tumor-infiltrating cells and Th1-deviated immune response in metastatic LN is associated with improved OS. T-bet may serve as a novel marker for increased survival. The elucidation of a protective immune response in LN may affect the selection of specific adjuvant protocol.

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A Novel Nomogram Predicts Survival in Patients with Nonfunctional Pancreatic Neuroendocrine Tumors M.V. Beems,[2]* Y. Ma,[2] R.C. Martin,[1] D.A. Kooby,[3] S.K. Maithel,[3] C. Scoggins,[1] A. Parikh,[4] N. Merchant,[5] H.J. Kim,[6] E.R. Winslow,[2] S. Weber,[2] C.S. Cho.[2] *1. University of Louisville, Louisville, KY; 2. University of Wisconsin, Madison, WI; 3. Emory University, Atlanta, GA; 4. Vanderbilt University, Nashville, TN; 5. University of Miami, Miami, FL; 6. University of North Carolina, Chapel Hill, NC.*

Introduction: A nonfunctional pancreatic neuroendocrine tumor (NF-PanNET) is a rare but increasingly prevalent pancreatic neoplasm without symptoms of hormone hypersecretion. Over the last decade, several classification systems have been proposed for grading and staging, and these have marginally correlated with patient prognosis. To better predict individual patient survival, we propose a novel nomogram that includes both grade and stage

criteria. Methods: Prospectively maintained data pertaining to demographics, pathology, treatment, and follow-up were collected for 394 patients with NF-PanNETs who underwent surgical resection at 5 academic institutions between 2000 and 2013. Cox regression analysis was performed for overall survival and recurrence-free survival. Regression models were used to impute missing values. Bootstrapping with 200 samples allowed calculation of the optimism-corrected concordance index (c-index) for the predictive models. Results: Of 394 patients available for analysis, 38 patients (9.6%) had died and 111 patients (28.2%) had developed recurrent disease by the end of follow-up. The median follow-up time was 22 months. A prognostic nomogram incorporating WHO 2010 tumor grade, presence of extrapancreatic metastases, largest tumor diameter, and gender best predicted overall survival at 36 and 60 months with a c-index of 0.82 (Figure 1). These four variables, in addition to lymph node metastases, best predicted recurrence-free survival at 36 and 60 months with a c-index of 0.73. Conclusions: Two novel nomograms can be used to predict overall survival and recurrence-free survival and may be more accurate than current classification systems.

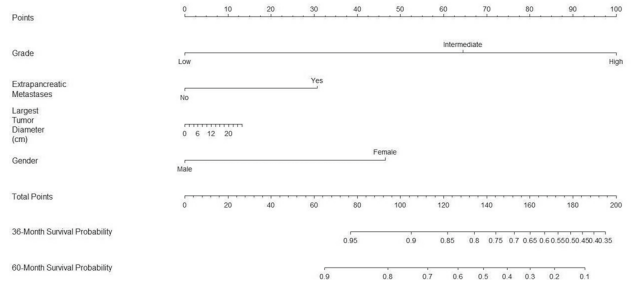

Figure 1 - Nomogram for predicting 36- and 60-month overall survival probabilities.

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Multi-Institution Review of the Role of Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy in Metastatic Gastric Adenocarcinoma in the U.S L.M. Enomoto,[1]* M.A. Choudry,[2] S. Pakrafter,[2] D. Magge,[2] K. Votanopoulos,[3] E.A. Levine,[3] K. Turaga,[4] C. Pameijer,[1] J. Wong.[1] *1. Surgery, Penn State Hershey Medical Center, Hummelstown, PA; 2. University of Pittsburgh Medical Center, Pittsburgh, PA; 3. Wake Forest Medical Center, Winston-Salem, NC; 4. Medical College of Wisconsin, Milwaukee, WI.*

Introduction. Cytoreductive surgery (CRS) followed by heated intraperitoneal chemotherapy (HIPEC) is an established treatment in patients with peritoneal malignancies, and has been proposed as an aggressive treatment for gastric cancer. Methods. A multi-institutional database of patients undergoing CRS, HIPEC, and gastrectomy for cancer from 4 US tertiary centers was reviewed. Demographic and perioperative data from 7/1995–10/2014 was analyzed. Results. 62 patients were included, with median age of 52.6 years (range 26-79) and a slight male predominance (N=34, 55%). 39 (63%) patients received neoadjuvant chemotherapy; 22 (36%) had at least 6 months between diagnosis and CRS/HIPEC and 12 (19.4%) had at least 1 year. Median time for receipt of chemotherapy was 7 months. Signet ring cells were present in most (N=42, 70%). The median peritoneal cancer index (PCI) was 10.5 (range 0-29), with the majority having a PCI ≥ 13 (N=40, 65%). Following HIPEC, most patients had a completeness of cytoreduction (CC) score of 0 or 1 (N=46, 85%). The median survival from diagnosis to death was 16 months (range 1-118 months), and the median survival from surgery to death was 7 months (range 0.4-78 months). Patients who received neoadjuvant chemotherapy and had at least 6 months between diagnosis and surgery survived longer than those who did not receive neoadjuvant therapy or had a shorter time between diagnosis and surgery (p=0.02, median survival 24.7 months versus 9.5 months). Patients with a CC of 0 had significantly better survival than those with CC > 0 (p=0.05, median survival 20.3 months versus 16.5 months). Presence of signet ring cells or PCI ≥ 13 was not significantly associated with decreased survival (p=0.29 and p=0.52, respectively). Conclusions. CRS and HIPEC is a potentially promising treatment modality for metastatic gastric cancer in low volume disease patients who have received at least 6 months of neoadjuvant chemotherapy and achieved complete CRS. Further study is needed to understand the best application and role of CRS and HIPEC in gastric cancer treatment in the US.

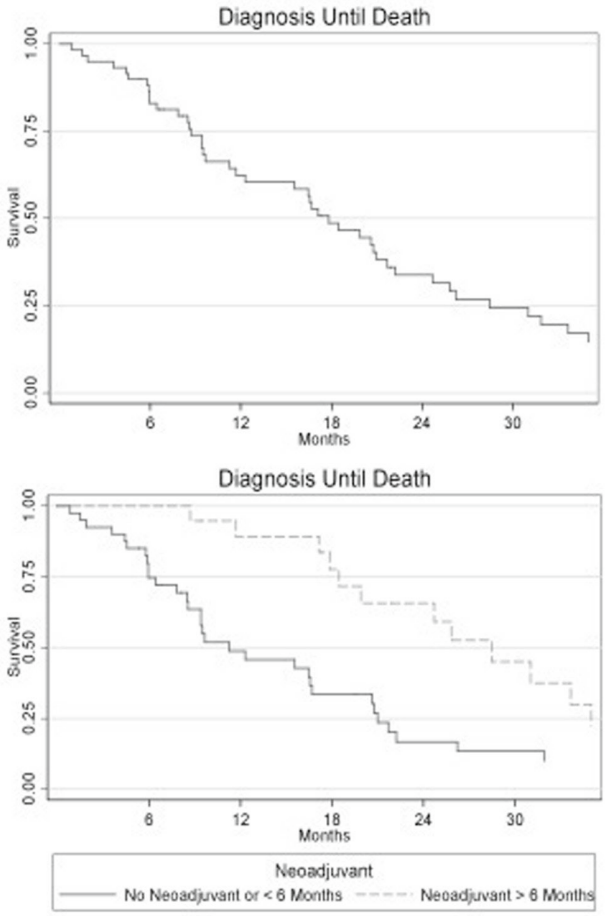

Figure 1. Kaplan Meier survival curves. Log rank p = 0.007.

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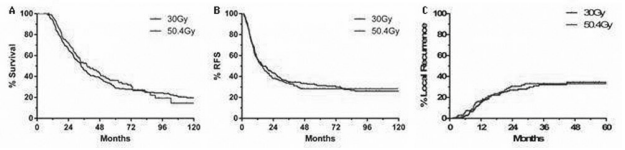
Influence of Preoperative Radiation Dose on Pathological Features, Local Control and Overall Survival Following Pancreatoduodenectomy for Pancreatic Ductal Adenocarcinoma J. Cloyd,* C.H. Crane, E. Koay, R.A. Snyder, P. Das, S. Krishnan, H.M. Wang, M. Kim, J.E. Lee, V. Gauri, M. Javle, R. Shroff, R.A. Wolff, D. Fogelman, J.B. Fleming, K.H. Matthew. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: We have previously demonstrated that preoperative chemoradiation is associated with an improved margin negative resection rate and local tumor control among patients who undergo pancreatoduodenectomy (PD) for pancreatic ductal adenocarcinoma (PDAC). However, the optimal preoperative regimen has not been established. Methods: Consecutive patients with PDAC who received both preoperative chemoradiation and PD between 1999-2015 were retrospectively reviewed. The effects of two external-beam radiation therapy (RT) regimens were compared: a hypofractionated course of 30Gy/10 fractions and a standard course of 50.4Gy/28 fractions. Differences in clinicopathologic characteristics, superior mesenteric artery (SMA) margin distance, local recurrence (LR), recurrence free survival (RFS) and overall survival (OS) were assessed. Results: 443 patients received either 30Gy (n=224) or 50.4Gy (n=219) of RT with concurrent gemcitabine or capecitabine followed by PD. Patients who received 50.4Gy were more likely to have received induction chemotherapy (43.3.% vs 61.6%, p<0.001), received capecitabine as a sensitizing agent (40.6% vs 56.6%, p<0.001), required vascular resection (33.9% vs 46.1%, p<0.05) and received treatment later in the study period (17.4% vs 50.7%, p<0.0001). There was no difference in the R1 margin status (tumor

cells ≤1mm from any margin: 25.4% vs 22.8%), SMA margin length (6.1 ± 5.9mm vs 6.7 ± 6.2mm), or treatment effect (complete pathologic response 3.1% vs 3.7%). 50.4Gy was associated with a lower frequency of positive lymph nodes (58.9% vs 46.6%, p<0.01) and a lower lymph node ratio (0.09 ± 0.12 vs 0.06 ± 0.1, p<0.01). There was no difference in LR, RFS or OS (Figure). On multivariate Cox proportional hazards analysis, 50.4Gy was not associated with improved survival (HR 0.93, 95% CI 0.71-1.22). Conclusion: Notwithstanding potential differences in pre-treatment tumor size and disease stage, preoperative hypofractionated chemoradiation for PDAC was associated with similar pathologic and survival outcomes following PD compared to standard fractionated radiation.



Overall survival (A), recurrence free survival (B), and local recurrence (C) for patients receiving 30Gy vs 50.4Gy.

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Treatment of Borderline Resectable (BR) and Locally Advanced (LA) Pancreatic Cancer in the Era of FOLFIRINOX and Gemcitabine + Nab-Paclitaxel: A Multi-Institutional Study K. Idrees,[1]* A. Parikh,[1] L.M. Postlewait,[2] S. Weber,[3] C.S. Cho,[3] A.I. Salem,[3] R.C. Martin,[4] C. Scoggins,[4] H.J. Kim,[5] J. Carr,[5] B. Xia,[6] S. Ahmad,[6] D. Abbott,[6] S. Maithel,[2] D.A. Kooby,[2] N. Merchant.[7] *1. Surgery, Vanderbilt University, Nashville, TN; 2. Emory University, Atlanta, GA; 3. University of Wisconsin, Madison, WI; 4. University of Louisville, Louisville, KY; 5. University of North Carolina, Chapel Hill, NC; 6. University of Cincinnati, Cincinnati, OH; 7. University of Miami, Miami, FL.*

Introduction: FOLFIRINOX or Gemcitabine + nab-Paclitaxel (Gem/nPac) has superior overall survival (OS) compared with gemcitabine alone in pts with Stage 4 pancreatic cancer (PC). Based on these results, FOLFIRINOX or Gem/nPac therapy has been utilized in neoadjuvant (NA) setting for BR and LA PC. This report describes our experience with NA treatment with FOLFIRINOX or Gem/nPac followed by surgical resection. Methods: Pts with BR and LA PC who received NA FOLFIRINOX or Gem/nPac and underwent surgical resection between January 2011 and August 2015 at 7 high volume centers were reviewed. Pre-operative chemoradiation therapy (pCXRT) was administered selectively based on radiographic response (RR). Demographic data including clinico-pathological, treatment toxicities and survival were collected. Results: 78 pts received either NA FOLFIRINOX or Gem/nPac therapy for BR (n=56, 72%), LA (n=22, n=22%) PC. pCXRT was administered in 74% of pts. Pts received a median of 4 cycles of FOLFIRINOX and 3 cycles of Gem/nPac with no grade 4-5 toxicities. The majority of pts underwent pancreaticoduodenectomy (85%) and vascular resection was performed in 58% - 39 with venous resection and 6 with arterial resection. R0 resection rate was 88% with no difference between two treatment groups (p=0.9). Reduction in CA 19-9 or RR did not correlate with pathological response (p=0.8). A complete pathologic response was seen in 6 pts – 5.6% vs. 12% for FOLFIRINOX and Gem/nPac, respectively (p=0.3). Adjuvant chemotherapy or CXRT was administered in 40% of pts. With a median follow up of 18 months, OS was 30 months and disease-free survival (DFS) was 27 months with FOLFIRINOX and 30 months with Gem/nPac (p=0.9). Recurrence was noted in 38 (49%) patients – 47% had distant recurrence, 24% had local recurrence and 29% had both. Conclusions: Neoadjuvant FOLFIRINOX or Gem/nPac therapy are equally effective in patients with BR and select LA PC in achieving R0 resection and lead to impressive OS and DFS. Further, optimization of treatment protocols in the neoadjuvant and adjuvant setting is warranted since recurrence rates are high.

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Liquid Biopsy Reveals High Prevalence of Circulating Mutant KRAS from Exosome-derived DNA in Patients with Early Stage Pancreatic Cancer K. Allenson,* V. Bernard Pagan, A. San Lucas, D. Li, J. Castillo, E. Ellis, K.H. Matthew, A. Maitra, H. Alvarez. *The University of Texas MD Anderson, Houston, TX.*

Introduction: Pancreatic ductal adenocarcinoma is predicted to become the second leading cause of cancer related death in the United States in the coming generation. Neoadjuvant strategies and newer chemotherapeutic regimens have reached clinical acceptance, but their efficacy is yet to be fully elucidated and clinical outcomes remain poor. Diagnosis of the disease at early stage while still amenable to surgical resection affords the best chance of long term survival. In the absence of early symptomatic manifestations, peripheral-blood-based liquid biopsy for tumor markers has emerged as an early diagnosis strategy. Methods: Exosomes were obtained by serial gradient ultracentrifugation of biobanked plasma samples from 51 patients with pancreatic ductal adenocarcinoma at various clinical stage. Presence and purity of exosome isolation was confirmed with scanning and transmission electron microscopy as well as western blot and flow cytometry analysis for exosomal markers. Exosome count and size were characterized using Zetaview nanoparticle tracking analysis. Droplet digital PCR was used to identify KRAS gene mutations in exosome derived DNA. Results: KRAS gene mutations found in exosome-derived DNA, were identified in 59.2%, 72.7% and 76.9% of localized, locally advanced, and metastatic patients, respectively. KRAS mutant allele frequency was associated with disease free and overall survival in patients with localized disease. Higher concentration of exosomes was associated with unresectability. Conclusions: Exosomes are a potential source of circulating tumor DNA that may be complementary to other blood based liquid biopsies including plasma cell free DNA and circulating tumor cells. A higher percentage of patients with localized disease exhibited detectable KRAS mutations than that previously reported. Exosome mutant KRAS allele frequency, as well as exosome size and count may be of utility in terms of therapeutic stratification.

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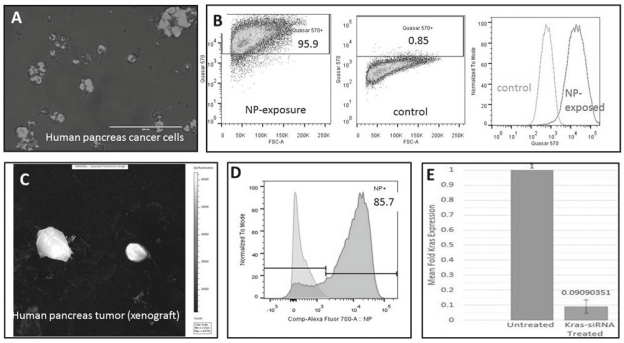
Precision Cancer Therapy through Nanoparticle Delivery of siRNA Against KRAS M. Strand,[2]* H. Pan,[1] J. Grossman,[2] P. Goedegebuure,[2] T. Fleming,[2] S.A. Wickline,[1] R.C. Fields.[2] *1. Department of Medicine, Washington University in St. Louis, Saint Louis, MO; 2. Department of Surgery, Washington University in St. Louis, Saint Louis, MO.*

Introduction Small interfering RNA (siRNA) has potential for highly specific gene manipulation, making it attractive for delivering precision therapy to cancer patients. However, efforts to employ siRNA therapeutically have been limited by its short half-life in circulation, low target tissue specificity, and cellular entrapment within endosomes. We utilized serum-stable, cell-penetrating, and endosomolytic peptide-based nanoparticles (NPs) to overcome these obstacles and deliver siRNA against KRAS to KRAS-mutant human and mouse pancreas and colorectal cancers. Methods Human and mouse pancreas and colorectal cancer cell lines were tested for NP uptake in vitro utilizing fluorescent siRNAs. Uptake was assessed via fluorescent microscopy and flow cytometry (FC). Mice bearing subcutaneous tumors from these cells were injected IV with the same NP, and uptake was assessed with an in vivo imaging system (IVIS), and FC. Cell lines were treated with KRAS-siRNA NP and KRAS knockdown was assessed by real-time PCR. Results Mouse and human pancreas and colorectal cancer cell lines took up NP in vitro, with signal detected within >93% of cells at 24 hours. Tumors from these cells grown in mice were strongly fluorescent after IV injection of fluorescent NP within 2 hours, and until at least 30 hours. FC of a tumor treated with fluorescent NP showed that 86% of tumor cells expressed fluorescent signal 24 hours post-injection. IVIS revealed signal in mouse liver and kidneys, but when assessed by FC, only 17.8% and 13.5% of cells from these tissues were fluorescent, respectively. The brain, heart, lungs, spleen, and pancreas of mice receiving injections were negative. Cancer cell lines exposed to KRAS-siRNA NP for 48 hours express KRAS at levels that are 4.5 to 15.1% of untreated cells. Conclusions Human and mouse pancreas and colorectal cancers efficiently and specifically take up NP in vitro and in vivo. Selected limitations of siRNA are overcome with this NP delivery system, and NP-packaged siRNA effectively inhibits KRAS. This platform represents a highly specific approach to targeting tumor genes of interest, which may ultimately enable selective knockdown of putative drivers of tumor progression.



A.Fluorescence microscopy of human pancreas cancer cells showing nanoparticle uptake at 24 hours post-exposure
B.At 24 hours post-exposure, greater than 95% of these cells are positive for nanoparticle by flow cytometry
C.In vivo imaging system fluorescence detection of a human pancreas tumor grown in a NOD-SCID mouse shows nanoparticle uptake within 2 hours of intravenous injection. Signal is detectable within the tumor for at least 30 hours after injection.
D.Flow cytometry of tumors from control mice (no nanoparticle, blue) and experimental (nanoparticle-injected, red) 20 hours post-injection demonstrates a striking difference, with >85% of human cancer cells (human EpCAM+) positive for nanoparticle, compared to <1% in tumors of control mice.
E.In vitro treatment of cancer cells with Nanoparticle-packaged Kras siRNA shows knockdown of Kras after 48 hours of exposure, with Kras levels reduced to 9.1% of expected expression (on average) compared to untreated cells.

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Differential Expression of microRNA in Human Pancreatic Fibroblasts and Pancreatic Cancer-Associated Stellate Cells M. Kitano,[1]* J.L. Chen,[1] T.A. Mace,[1] M.R. Farren,[1] H.M. Komar,[1] T. Bekaii-Saab,[1] C.R. Schmidt,[1] M. Bloomston,[2] G.B. Lesinski.[1] *1. Division of Surgical Oncology, The Ohio State University Wexner Medical Center, Columbus, OH; 2. 21st Century Oncology, Fort Myers, FL.*

Introduction: Pancreatic cancer-associated stellate cells (PSCs) are prominent in the tumor microenvironment of pancreatic ductal adenocarcinoma (PDA). They promote fibrosis by deposition of stromal components and secrete immunosuppressive factors yet their exact contribution in pancreatic cancer progression is unclear. We hypothesized that there are differentially expressed miRNAs in normal pancreatic fibroblasts and PSCs, which may play a role in PSC activation, PDA progression, metastasis, or immune suppression. Methods: RNA was extracted from human fetal primary pancreatic fibroblasts (HPPFC) and from primary human PSC cultures established from PDA tumors of 11 individual patients. The expression of 800 human miRNAs were profiled using the NanoString microRNA expression assay version 2.1. Differential expression of miR-21 and -410 were validated using quantitative real time-PCR (qRT-PCR) on HPPFC and PSC. miRNA RNA target analysis was performed using miRBase. Results: A total of 185 miRNAs were differentially expressed in PSC as compared to HPPFC by 1.5 fold change. Of these miRNAs, 125 were downregulated and 60 were upregulated. 30 miRNAs were differentially expressed in PSC as compared to HPPFC by greater than 10 fold change. miR-21 expression was significantly higher than of miR-410 in both HPPFC and PSC using qRT-PCR. Using miRBase, STAT-3 was identified as a potential target of miR-20a-5p, -20b-5p, -1244, -4516, and -21-5p. Conclusion: Pancreatic cancer-associated stellate cells harbor a characteristic miRNA signature that is distinct from normal pancreatic fibroblasts, which may play a role in PDA progression, metastasis and immune suppression. This study represents one of the few unique and comprehensive analyses of miRNA expression in patient samples. These differentially expressed miRNAs may impact tumor microenvironment, function as regulators of PSC biology related to PDA, and may provide insight into novel targets for therapeutic intervention.

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A Molecular Biomarker Targeted Approach to Adjuvant Therapy for Resected Pancreatic Adenocarcinoma: Results of a Phase II Prospective Trial L.M. Postlewait,[1]* C.G. Ethun,[1] D.A. Kooby,[1] J.M. Sarmiento,[4] C.A. Staley,[1] E. Brutcher,[2] V. Adsay,[3] B. El-Rayes,[2] S.K. Maithel.[1] *1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Medical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; 3. Department of Pathology, Winship Cancer Institute, Emory University, Atlanta, GA; 4. Division of General Surgery, Department of Surgery, Emory University, Atlanta, GA.*

Background: Standard adjuvant treatment for resected pancreatic adenocarcinoma is gemcitabine (Gem) (CONKO-001 trial: Gem vs placebo DFS 13.4vs6.7mo;p<0.001; OS 22.8vs20.2mo;p=0.01). Adding cisplatin (Cis) to Gem has shown increased response rates in the metastatic setting. This benefit may be inhibited by high expression of excision repair cross-complementing gene–1 (ERCC1), the key enzyme in nucleotide excision repair. This Phase II prospective trial assesses outcomes of patients treated with adjuvant Gem/Cis chemotherapy, stratifying results by tumor ERCC1 expression. Methods: Patients with resected pancreatic adenocarcinoma at a single institution were enrolled from 2010-2013. Initially, patients received Gem(1000mg/m^2)/Cis-(50mg/m^2) Day 1/8/15, Q28d for 6 cycles. After enrolling 5pts, this was modified to Day 1/15 due to toxicity. Two dose reductions were permitted. Intent to treat analyses were conducted. Tumor ERCC1 expression was evaluated by immunohistochemistry and dichotomized into low and high expression groups. Primary outcomes were RFS and OS stratified by ERCC1 expression. Results: Of 22pts, 16 (73%) had Stage IIB disease, 5 (23%) Stage IIA, and 1 (4%) Stage IA. Thirteen (59%) completed all 6 cycles of therapy, of whom 9 required dose reduction. Of the remaining 9pts, 4 completed >68% of intended therapy. Grade 3 and 4 toxicity occurred in 13pts (59%); neutropenia was most common (n=9;41%). Median follow-up was 37.5mo. Median RFS was 16.7mo, and OS was 35.5mo. ERCC1 tumor expression data were available for 20pts: 15 low (75%) and 5 high (25%). Low compared to high ERCC1 was not associated with improved RFS (12.4vs16.7mo;p=0.68) or OS (Median not reached vs21.6mo;p=0.22). Conclusions: Adjuvant gemcitabine/cisplatin is tolerated by patients with resected pancreatic adenocarcinoma. RFS and OS for Gem/Cis appear promising compared to historic control. Tumor ERCC1 expression can be reliably evaluated, and low expression is present in the majority of patients. Further prospective trials evaluating Gem/Cis as an adjuvant regimen and ERCC-1 as a biomarker in resected pancreatic adenocarcinoma are warranted.

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Sphingosine-1-phosphate Signaling Targeted by FTY720 Suppress Obesity-related Breast Cancer Progression, Metastasis, and Improve Survival K. Takabe,[1]* M. Nagahashi,[2] S. Spiegel.[1] *1. Surgical Oncology, Virginia Commonwealth University, Richmond, VA; 2. Niigata University, Niigata, Japan.*

INTRODUCTION Obesity, which induces low-grade inflammation, is a known risk factor for worse prognosis in many cancers, including breast cancer. We have previously published that sphingosine-1-phosphate (S1P), a bioactive lipid mediator produced by sphingosine kinases (SphKs) and signal through S1P specific receptors (S1PRs), links inflammation and cancer progression. Objective of this study is to elucidate the role of S1P in obesity-related breast cancer progression and evaluate the effect of S1P signaling targeted therapy using FTY720. METHOD E0771 murine syngeneic orthotopic implantation model as well as in the MMTV-PyMT transgenic breast cancer model were used. Sphingolipids were measured by liquid chromatography-electrospray ionization tandem mass spectrometry (LC-ESI-MS/MS). RESULTS Diet-induced obesity significantly worsened cancer progression, with higher expressions of SphK1 and S1PR1, and inflammatory cytokines including IL-6 and TNF-α. These were all dramatically decreased by targeting S1P signaling with FTY720, a functional antagonist of S1PRs. Obesity increased levels of S1P in the tumor microenvironment, determined by analysis of tumor interstitial fluid, as well as in the primary tumor, and even in the systemic circulation and in the lungs. FTY720 suppressed not only primary tumor growth, but also lung metastasis in obese animals. In a tumor conditioned media treatment assay, SphK1-overexpressed tumor conditioned media promoted cancer metastasis in the lung with more infiltration of macrophages. In this assay, high fat diet-induced obesity increased macrophage infiltration in the lung and FTY720 inhibited both macrophage infiltration and breast cancer metastasis.

Moreover, FTY720 significantly prolonged survival of the obese orthotopic implantation model compared to the non-treatment group. CONCLUSION Our results suggest that S1P signaling play a key role in obesity-related breast cancer progression and metastasis. S1P signaling is a promising target for treatment of metastatic breast cancer in the setting of obesity-related inflammation.

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Breast Density and Contralateral Breast Cancer Risk M. O'Donnell,[1]* M.X. Chowdhury,[2] P. Choudhary,[2] S. Biswas,[2] D. Euhus.[1]
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Background: Increased mammographic density is a significant risk factor for breast cancer. It is not clear if increased density is also a risk factor for the development of contralateral breast cancer (CBC). Methods: The study population was derived from the Breast Cancer Surveillance Consortium and included women ages 18-89 undergoing screening mammography between 1998-2009. Each case of CBC was matched with three controls on the basis of year of first breast cancer diagnosis, race, and length of follow-up. A total of 1921 cases and 5763 controls met eligibility criteria. The risk factors included in the study were mammographic density recorded prior to diagnosis, age of first breast cancer, anti-estrogen treatment, hormone replacement therapy, menopausal status, and ER status. Both univariate and multivariate conditional logistic regression analysis were performed. Results: In the univariate analysis, breast density, age, anti-estrogen treatment, and ER status were found to be significant with p-values <0.05. Increasing breast density had a dose dependent effect on the risk of CBC. Relative to 'almost entirely fat' category, the odds ratios (ORs) (and p-values) for 'scattered density', 'heterogeneously dense', and 'extremely dense' categories of breast density were 1.54 (0.071), 1.77 (0.016), and 2.13 (0.004), respectively. Relative to the 50-plus category of age, the ORs (and p-values) for 'under 30','30-40',and '40-50' age group were 2.27 (0.009), 1.38 (0.005) and 0.95 (0.44), respectively. Anti-estrogen therapy was a negative risk factor with OR 0.73 (p-value <0.001). The OR for ER-negative group is 1.23 (p-value=0.006) relative to ER-positive group. In multivariate analysis, breast density, age, and anti-estrogen treatment remained significant with p-values less that 0.05. The ORs (and p-values) for breast density after adjusting for age and anti-estrogen treatment remain essentially the same as in univariate analysis, with respective values: 1.55 (0.068), 1.78 (0.015), and 2.14 (0.004). Conclusion: Increased mammographic density is a significant risk factor for contralateral breast cancer.

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Association Between Mammographic Breast Density (BD) and the Development of a Second Contralateral Breast Cancer (CBC): A Nested Case-control Study A. Raghavendra,* A.K. Sinha, N. Garg, L. Hsu, M. Patangan Jr, T. Bevers, B. Arun, H. Le-Petross, D. Tripathy, I. Bedrosian, C. Barcenas. *MD Anderson, Houston, TX.*

Background: Women with increased BD have a 4- to 6-fold increased risk of primary breast cancer (BC). It is unclear if mammographic BD is associated with the development of a metachronous CBC. Methods: From a cohort of female patients treated at MD Anderson for sporadic, non-metastatic BC between January/1997 and December/2012, we selected cases who developed CBC and matched controls, using a 1:2 case-control incidence density sampling method. Controls were matched year at diagnosis and tumor hormonal receptor status of the primary BC. Demographic, clinical, pathologic and treatment information were obtained from an institutional database. We excluded patients who underwent bilateral mastectomy, BRCA-positive patients, and those with unknown tumor characteristics. The primary endpoint was the development of CBC. Mammographic BD was derived from images obtained at time of diagnosis of the index malignancy and categorized by combining the American College of Radiology breast composition categories of fatty and scattered density as type I, and heterogeneously dense and extremely dense as type II. Multivariable conditional logistic regression models were used to adjust by demographic, tumor characteristics and treatment factors. Results: We evaluated 680 patients (229 cases and 451 controls). In those who developed CBC, 39% had a mammographic BD type I, and 61% had a type II. This distribution was different for controls. After adjusting for race/ethnicity, tumor histology and stage, chemotherapy and hormonal therapy, patients who had type II mammographic BD had a 52% increased risk of developing a CBC (OR=1.52, 95% CI: 1.05, 2.2, p value= 0.026). Patients who received endocrine therapy and Hispanic women had lower risk of CBC. Compared to women who received an anthracycline-taxane regimen, those who did not receive chemotherapy had a higher risk of CBC. Conclusions: Patients with mammographically dense breasts appear more likely to develop a second CBC compared to those with fatty breast tissue. Mammographic BD may be considered as a risk factor in models predicting CBC risk.

Distribution of One to Two Matched Patients

	Cases(n=229) N	Cases %	Control (n=451) N	Controls %
Age at Diagnosis, Years				
20 - <39	18	7.9	21	4.7
40 - <50	54	23.6	267	59.2
51 and above	157	68.6	163	36.1
Diagnosis of year				
1997 - 2000	80	35.0	155	34.4
2001-2006	96	42.0	191	42.3
2007-2012	53	23.2	105	23.2
Race/Ethnicity				
White	176	76.9	318	70.5
Black	28	12.2	49	10.9
Spanish/Hispanic	18	7.9	58	12.9
Others	7	3.1	26	5.8
Breast Density				
Type I	90	39.3	218	48.3
Type II	139	60.7	233	51.7
Menopausal Status				
Post	159	69.4	317	70.3
Pre	64	27.9	120	26.6
Peri/Unknown	6	2.6	14	3.1
Chemotherapy Agents				
Not received	102	44.5	144	31.9
Anthracycline + Taxane	78	34.1	225	49.9
Anthracycline	41	17.9	68	15.1
Others	8	3.5	14	3.1
Hormone Therapy				
Yes	153	66.8	352	78
No	76	33.2	99	22

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Do LORIS Trial Eligibility Criteria Identify a Ductal Carcinoma In Situ (DCIS) Patient Population at Low-risk of Upgrade to Invasive Carcinoma? M. Pilewskie,* M. Stempel, H. Rosenfeld, A. Eaton, K.J. Van Zee, M. Morrow. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction The LORIS (Surgery vs Active Monitoring for Low-Risk DCIS) trial is studying the safety of monitoring low-risk DCIS without excision; however, identifying patients with undiagnosed synchronous invasive carcinoma is essential in assessing the safety of observation alone. Non-high grade DCIS diagnosed by core biopsy carries an overall 20% risk of upgrade at surgical excision, but the upgrade rate for women meeting all LORIS trial eligibility criteria is unknown. Methods Women meeting LORIS eligibility criteria (age ≥46 years, screen-detected calcifications, non-high grade DCIS diagnosed by core biopsy, absence of nipple discharge or strong family history of breast cancer) who underwent surgical excision from 2009–2012 were identified. Final pathology details from surgical excision were collected. Clinicopathologic features were compared between women with and without invasive carcinoma at surgical excision. Results 325 cases were identified; 67 (21%) had invasive carcinoma on final pathology (90% invasive ductal, 24% high grade, 94% estrogen receptor positive, 8% HER2 overexpressing). Tumor staging for upgrades were 14 (21%) T1mic, 33 (49%) T1a, 16 (24%) T1b, 3 (5%) T1c, 1 (2%) T2. Five women had axillary nodal metastases. Table 1 shows clinicopathologic characteristics for the overall cohort and by upgrade to invasive carcinoma. Women upgraded to invasive carcinoma at surgical excision were more likely to have solid-type or mixed DCIS histology or intermediate grade DCIS on core biopsy. Conclusions LORIS eligibility criteria did not identify women with DCIS at lower risk for upgrade to invasive carcinoma at surgical excision. Interestingly, the invasive carcinomas identified in this cohort of women with non-high grade DCIS on core biopsy were heterogeneous in grade, size, and receptor status. Information gained from final pathology in these women would alter treatment recommendations, and therefore surgical excision is warranted until additional risk stratification is available to identify a cohort of DCIS patients at lower risk for synchronous invasive carcinoma.

Table 1: Patient clinicopathologic characteristics overall and by upgrade to invasive carcinoma

	Overall (n=325)	Ductal carcinoma in situ only (n=258)	Invasive carcinoma on final pathology (n=67)	p-value
Age, years, median (range)	57.2 (46-86)	57.3 (46-84)	56.9 (46-86)	0.52
Menopausal Status				0.88
Postmenopausal	212 (67.9%)	168 (68.3%)	44 (66.7%)	
Pre/perimenopausal	100 (30.8%)	78 (30.2%)	22 (32.8%)	
Missing	13	12	1	
Family history of breast cancer*	143 (44.0%)	109 (42.2%)	34 (50.7%)	0.22
DCIS histology core biopsy				0.024
Micropapillary	2 (0.6%)	2 (0.8%)	0 (0)	
Papillary	1 (0.3%)	0 (0)	1 (1.5%)	
Cribriform	25 (7.8%)	24 (9.4%)	1 (1.5%)	
Solid	14 (4.3%)	9 (3.5%)	5 (7.5%)	
Mixed	266 (82.6%)	207 (81.2%)	59 (88.1%)	
Non specified	14 (4.3%)	13 (5.1%)	1 (1.5%)	
Missing	3	3	0	
DCIS grade core biopsy				0.018
Low	57 (17.5%)	52 (20.2%)	5 (7.5%)	
Intermediate	268 (82.5%)	206 (79.8%)	62 (92.5%)	
Breast Surgery				<0.001
Wide local excision	235 (72.3%)	200 (77.5%)	35 (52.2%)	
Mastectomy	90 (27.7%)	58 (22.5%)	32 (47.8%)	

*Family history of breast cancer in only one first- or second-degree relative; patients with 2 family members with breast cancer were excluded for having a strong family history. DCIS, ductal carcinoma in situ

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Age and Recurrence Risk in 2,996 Women with DCIS Treated with Breast-Conserving Surgery (BCS) P.A. Cronin,* C. Olcese, S. Patil, M. Morrow, K.J. Van Zee. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Age is a risk factor for local recurrence (LR) for women with DCIS treated with BCS. However, little is known about the pattern of risk over the spectrum of ages. We sought to assess the effect of age on LR rates across 6 age categories and to examine the relationship between age and development of distant disease. Methods: We reviewed a prospectively maintained database of DCIS patients undergoing BCS from 1978 to 2010. Kaplan–Meier LR estimates by age were calculated. Multivariable analysis (MVA) and competing risk MVA (CRMVA) were used to assess the relationship between age and LR and invasive LR. Results: 2996 cases were identified. Median follow-up for those without LR was 75 mos and 732 had ≥10 years follow up. 363 (12%) had LR; 192 (53%) as DCIS, 160 (44%) as invasive, 11 (3%) unknown. On MVA, age ≤40y was a significant risk factor for LR even after controlling for family history, clinical presentation, necrosis, number of excisions, margins, treatment year, radiation (RT) and endocrine therapy. Risk of LR progressively decreased with age (hazard ratios [HR] with ≤40y as reference: 41-50y [0.82, p=0.36], 51-60y [0.46, p<0.001], 61-70y [0.50, p<0.003], 71-80y [0.56, p=0.02] and >80y [0.21, p<0.002]). For subsets with and without RT, MVA showed the same effect of age on LR. Using CRMVA for invasive LR, only age and RT were significant. The effect of age on invasive LR was stronger than on overall LR, with ≤40y being at much higher risk than all other ages (HR=0.43-0.14, p<0.01). For women ≤40y, 10yr invasive LR was 16% vs 6.5% in women >40y. Only 0.6% of the population ultimately developed distant disease; those ≤40y constituted 4.7% (n=141) of the population but 21% (4 of 19) of those developing distant disease. Conclusions: Risk of LR decreases with age; this effect is particularly strong at the extremes of age, and is independent of other clinicopathologic and treatment factors. DCIS in the youngest patients has a higher overall and invasive LR rate, although mortality remains low. These findings should inform our discussions with patients presenting with DCIS, and be incorporated into risk/benefit considerations for various treatment options.

		Overall 10-yr LR	10-yr LR with RT	10-yr LR no RT
		(N=2996)	(N=1588)	(N=1374)
Age	N	% (95% CI)	% (95% CI)	% (95% CI)
≤40	141	27 (19-38)	20 (11-33)	38 (24-55)
41-50	704	19 (16-23)	17 (13-23)	22 (17-29)
51-60	887	13 (10-16)	9 (7-13)	17 (12-23)
61-70	727	15 (12-19)	7 (4-12)	24 (19-31)
71-80	426	14 (10-19)	8 (4-17)	18 (12-24)
≥81	111	8 (4-15)	0	9 (4-18)

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Disparities in Tamoxifen Recommendation and Compliance for Young Women with Ductal Carcinoma In Situ A.E. Voci,* B.C. Bandera, J. Lee, M. Goldfarb, M.L. DiNome. *Breast Oncology Surgery, John Wayne Cancer Institute, Santa Monica, CA.*

INTRODUCTION: NCCN guidelines were updated in 2000 to include Tamoxifen (TAM) therapy as adjuvant treatment for DCIS. TAM therapy has side effects that can be complicated for the reproductive-aged female. We examined whether there were notable disparities in physician recommendations and patient compliance regarding TAM use for early stage, non-invasive disease in this specific patient cohort. METHODS: The NCDB was used to query female patients aged 15-39 with DCIS treated between the years 2000-2013. Patient demographic, socioeconomic, and treatment data were collected. Chi-squared test and multivariate analysis was used for statistical assessment. RESULTS: 3988 women were identified. 1795 (45%) were recommended for TAM therapy for DCIS. 2193 (55%) were not recommended. Of those recommended, 311 (17%) did not receive treatment. In total, only 37.2% (1484/3988) of women in this age cohort received TAM for treatment of DCIS. Women of Asian or Black race were more likely than White to be recommended, OR 1.43 (1.081-1.888 CI 95%, p=0.01) and OR 1.40 (1.164- 1.687 CI 95%, p=0.0004). Patients treated at an NCI-designated versus Community Center, OR 0.712 (0.556- 0.913 CI 95% p=0.007) and patients treated in the Mountain regions of the US were less likely to be recommended. The women who were recommended but did not take it were of higher income bracket. Those treated in Southern Central regions of the US and of Hispanic race appeared to be more compliant with treatment recommendations (Table 1). CONCLUSION: In this study just over a third (37.2%) of the patients in this young patient population were found to be treated with TAM therapy for DCIS despite the expanded NCCN guidelines. Disparities in both physician recommendation and patient compliance were identified and centered on race, socioeconomic factors and type and location of treating facility. The benefit and side effect profile of this type of therapy in reproductive aged women may have a large impact on the notable disparities identified. This study suggests that factors exist other than medical that impact whether younger women of reproductive age receive adjuvant TAM for treatment of DCIS.

Variables significant for disparities in Tamoxifen treatment among young patients with DCIS

Variable	Odds Ratio	95% Confidence Interval	p-value
Recommended vs Not Recommended			
Asian vs White	1.428	1.081-1.888	0.0122
Black vs White	1.401	1.164-1.687	0.0004
NCI Center vs Community Center	0.712	0.556-0.913	0.0073
East North Central vs Mountain	2.224	1.559-3.173	<0.0001
Middle Atlantic vs Mountain	2.020	1.399-2.918	0.0002
New England vs Mountain	2.566	1.667-3.951	<0.0001
West North Central vs Mountain	1.976	1.314-2.970	0.0011
Recommended and Taken			
Income > 63,000/yr vs < 38,000/yr	0.582	0.380-0.892	0.0129
Hispanic vs White	2.074	1.093-3.935	0.0256
East South Central vs Mountain	3.394	1.211-9.511	0.0201
West South Central vs Mountain	2.545	1.088-5.953	0.0311

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Omitting a Re-excision for a Focally Positive Surgical Margin After Primary Breast Conserving Surgery is Safe E. Vos,[1]* S. Siesling,[2] C. Verhoef,[1] A. Voogd,[2] L. Koppert.[1] *1. Erasmus MC Cancer Institute, Rotterdam, Netherlands; 2. Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands.*

Background: In 2014, SSO/ASTRO published a guideline recommending no ink on tumour as an adequate surgical margin after breast conserving surgery (BCS) for invasive breast cancer thus advising reexcision for (focally) positive margin. In contrast, since 2002, the Dutch guideline considers focally positive as an adequate margin and advises reexcision only in case of more than focally positive margin. Our aim was to retrospectively study the impact of omitting a reexcision for focally positive margin on the occurrence of ipsilateral breast tumour recurrence (IBTR), disease-free and overall survival. Methods: All women ≤75 years, without prior malignancy, diagnosed with invasive breast cancer between 2003-2008 and treated by BCS and radiotherapy were selected from the Netherlands Cancer Registry, a nationwide population-based cancer registry. Patients were excluded if surgical margin status or 5-year follow-up information was missing. Results: The availability of margin status

was not associated with the occurrence of IBTR (OR 1.10 95%CI 0.93-1.29). From the total of 10087 patients, negative margin was found in 7753 (76.9%), focally positive margin in 962 (9.5%), and more than focally positive margin in 1372 (13.6%). IBTR occurred in 165 (2.1%), 17 (1.8%), and 39 (2.8%) of the patients respectively (P=0.137). In patients with a focally positive margin, re-excision was omitted - in accordance to the Dutch guideline - in 472 (49.1%) which was not associated with IBTR (unadjusted HR 0.51 95%CI 0.19-1.38, adjusted HR 0.58 95%CI 0.25-1.30), nor with disease free survival (unadjusted HR 0.99 95%CI 0.87-1.14) and overall survival (unadjusted HR 0.8495%CI 0.60-1.17). In patients <50 years and focal positive margin, 6/156 (3.7%) with primary BCS only had IBTR and 2/225 (0.9%) with a reexcision had IBTR (P=0.078). Conclusion: Omitting a re-excision for focally positive margin after primary BCS does not seem to be associated with 5-year IBTR, disease free survival, and overall survival in invasive breast cancer. These data supports the Dutch guideline that considers omitting a re-excision for a focally positive margin after BCS safe in patients >50 years of age.

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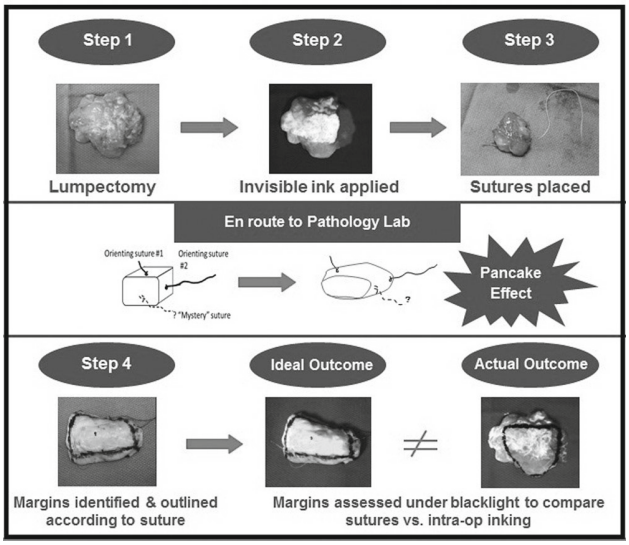
The Specimen Margin Assessment Technique (SMART) Trial: A Novel 3-D Method of Identifying the Most Accurate Method of Breast Specimen Orientation A. Arnaout,[1]* S. Robertson,[2] D. Gravel,[2] G. Rockwell,[2] Y. Ayroud.[2] *1. Surgery, Ottawa Hospital Research Institute, Ottawa, ON, Canada; 2. Ottawa Hospital, Ottawa, ON, Canada.*

BACKGROUND: Achieving negative margins remains one of the most important determinants for local recurrence following breast-conserving therapy. Re-excision of a positive margin is recommended in order to reduce recurrence. Inaccuracies in margin labeling or orientation during surgery translates into additional unnecessary surgery or wrong margin re-excision. We report the results of the world's first prospective clinical trial that evaluates the accuracy of intra-operative specimen inking versus suturing on the same lumpectomy specimen, in a blinded fashion, using a novel 3 D technique. METHODS: A prospective clinical trial was performed using sham lumpectomies within the prophylactic mastectomy or breast reduction tissue. The specimen was inked using special phospholuminescent inks that dry clear but glow under black light. In addition, specimen suturing using two labeled sutures was performed by the surgeon as per usual. A third "mystery" suture was placed; the location of which is known only to the surgeon but blinded to the pathologist. RESULTS: 72 patients were accrued for the study. There was a 42% discordance between the pathologist and surgeon in identification of the "mystery" suture and a 76% discordance in identification of surface area of each margin. A median of 3 additional "surgeon identified" margins were included in the "pathologist identified" anterior margin. Using 3D imaging, we demonstrated how the specimen center of gravity and volume changes en-route to the pathology department. CONCLUSION: This is the first trial of its kind comparing the two methods of specimen orientation in a blinded fashion on the same lumpectomy specimen. Discordance between the surgeon and the pathologist in margin orientation would influence the accuracy of margin identification and the subsequent directed re-excisions, as well as subject patients to unnecessary surgeries or prevent them from having re-excisions they need. Intra-operative specimen inking by the surgeon is a more accurate method of margin assessment. Results of this trial can be extended to other cancers in which a negative margin is prognostic.



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Preoperative Axillary Ultrasound in Early Stage Breast Cancer is Associated with More Axillary Surgery B.E. Splittgerber,* A.R. Thawani, J. Liao, S.L. Sugg, C. Scott-Conner, R. Weigel, I. Lizarraga. *University of Iowa Hospitals and Clinics, Iowa City, IA.*

Introduction: The role of preoperative axillary ultrasound (AUS) in breast cancer patients with non palpable axillary lymph nodes (cN0) is controversial. The purpose of this study was to determine the differences in clinical management in cN0 patient who underwent AUS or not, after institutional adoption of selective axillary dissection (ALND) based on criteria from the ACOSOG Z0011 trial. Methods: A single institution, retrospective review was performed of Stage I and II breast cancer patients without clinically palpable nodes (cN0) treated from 2011 to 2014. AUS was done at clinician discretion initially and became routine for patients receiving imaging at our institution in mid-2013. Correlation with final pathology was done. Patients who received staging AUS were compared to those who did not. Multivariate analysis was performed to control for confounding variables. Results: 463 patients were identified. Of the 261 who received AUS (56.4%), 106 (40.3%) had abnormal results, and 97 underwent fine needle aspiration (FNA). Overall, lymph node metastases were found in 115 /463 (24.8%) patients with 37 identified on AUS+FNA and 78 identified at axillary surgery. The false negative (FN) rate of AUS was 11% and of AUS+FNA was 5%. The AUS and no AUS groups were compared by year of diagnosis, age, histology, clinical T stage, receptor status, and type of breast surgery (Table 1). On multivariate analysis, the patients with FNA detected nodal metastasis (FNA+) were more likely to have neoadjuvant chemotherapy (NAC) (OR=16.7,p <0.001) and ALND (OR=6.7,p=0.001) than those identified at surgery, even when controlled for age, T stage, receptor status and type of surgery. There was no significant difference in rates of adjuvant chemotherapy, reconstruction, or whole breast and post mastectomy radiation. Conclusion: In this study, patients with clinically occult nodal metastasis diagnosed on AUS were more likely to receive NAC and also ALND than those diagnosed at surgery. AUS may be a useful tool to identify candidates for NAC, but is associated with more axillary surgery.

Table 1: Univariate analysis of characteristics and treatment for breast cancer patients compared by AUS group and method of diagnosis of lymph node metastasis.

Variable	All patients			Node positive patients		
	AUS done	AUS not done	P	Diagnosed on AUS/FNA	Diagnosed at surgery	P
Total	261(56.3%)	202 (43.7%)		37 (32.2%)	78 (67.8%)	
Age at diagnosis	58.5	58.2	0.958	53.7	55.6	0.394
Clinical T stage T1 T2 T3	---------- 179 (68.5%) 75 (28.7%) 7 (2.68%)	---------- 159 (78.7%) 40 (19.8%) 3 (1.49%)	0.046	---------- 19 (51.3%) 18 (48.6%) 0 (0%)	---------- 49 (62.8) 25 (32.0%) 4 (5.13 %)	0.138
ER positive	206 (78.9%)	177 (87.6%)	0.014	25 (67.5%)	74 (94.8%)	<0.001
HER2 positive	36 (13.9%)	23 (11.6%)	0.473	5 (13.5%)	10 (13.1%)	0.958
Imaging at our institution	182 (69.7%)	60 (29.7%)	<0.001	24 (64.8%)	34 (43.5%)	0.033
Biopsy at our institution	205 (78.5%)	75 (37.1%)	<0.001	28 (75.6%)	39 (50.0%)	0.009
Treatment						
BCT	153 (58.6%)	127 (62.8%)	0.354	16 (43.24%)	39 (50.0%)	0.498
Neoadjuvant chemotherapy	42 (16.0%)	11 (6.44%)	0.001	19 (51.35%)	5 (6.41%)	<0.001
SLNB	234 (89.6%)	197 (97.5%)	0.001	25 (67.5%)	77 (98.7%)	<0.001
ALND	35 (13.4%)	8 (3.96%)	0.001	23 (62.1%)	20 (25.6%)	<0.001

AUS: Axillary Ultrasound, ALND: Axillary Lymph Node Dissection, BCT: Breast Conservation Therapy, ER: Estrogen Receptor, FNA: Fine needle Aspiration of Lymph Node, Her2: Her-2-neu Receptor, SLN: Sentinel Lymph Node Biopsy

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Survival Benefit of Bilateral Mastectomy for Young Women with Early Stage Breast Cancer O. Kantor,[1]* C. Wang,[2] C. Pesce,[2] K. Yao,[2] D. Winchester.[2] *1. Department of Surgery, University of Chicago, Chicago, IL; 2. Northshore University HealthSystem, Evanston, IL.*

Introduction: The use of contralateral prophylactic mastectomy is controversial. Proper selection should include patients at increased risk for a second primary tumor with a low risk of competing comorbidities and high cure rates for treated disease. We used the National Cancer Data Base (NCDB) to examine the overall survival of bilateral vs unilateral mastectomy (UM) in young women with unilateral breast cancer. Methods: The NCDB was queried to identify women ≤45yrs treated for unilateral breast cancer with greater than 10 years of follow up data. Women with >1 cancer diagnosis or those treated with radiation were excluded. Chi-square tests and Cox-regression were used for analysis. Results: 24,038 women ≤45yrs underwent mastectomy between 1998-2002: 20,619 (85.8%) with unilateral and 3,409 (14.2%) with bilateral mastectomy (BM). Women treated with BM were more likely to be Caucasian (87.9% vs 74.1%, p<0.01), have high socioeconomic status (64.4% vs 53.1%, p<0.01), and have pathologic stage I tumors (43.5% vs 31.6%, p<0.01). Rates of chemotherapy and hormone therapy were similar between groups. Cox survival analysis adjusted for race, socioeconomic status, pathologic stage, number of positive nodes, tumor grade, chemotherapy, hormone therapy, and facility type was used to identify patient subgroups with an overall survival (OS) benefit for BM as compared to UM. A survival benefit was seen in patients with tumors ≤2cm (10yr OS 92.7% vs 89.6%, p<0.01), in patients with negative nodes (10yr OS 91.5% vs 89.4%, p<0.01) or 1-2 positive nodes (82.4% vs 79.0%, p=0.02). Patients with 3 or more positive nodes or with tumors 2-4 cm or >4cm did not have significant survival differences between UM and BM (p=0.07,0.22, 0.07 respectively). Conclusion: BM in young women with early stage breast cancer is associated with a modest decrease in overall mortality as compared to unilateral mastectomy, suggesting that with proper selection in patients with increased risk of a second primary tumor and with a good life expectancy, bilateral mastectomy reduces the risk of a second, potentially lethal primary tumor. Additional long term data is necessary to validate this observation.

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Long-term Prospective Assessment of Quality of Life and Lymphedema After Inguinal or Inguinal and Pelvic Lymphadenectomy for Recurrent Melanoma in the Groin M.A. Henderson,[1]* R. Fisher,[1] J. Di Iulio,[1] D. Gyorki,[1] J. Spillane,[1] D. Speakman,[1] B. Burmeister,[2] B. Smithers,[2] A. Hong,[3] K. Shannon,[3] J. Ainslie,[1] R. Scolyer,[3] S. Carruthers,[4] B. Coventry,[4] S. Babington,[5] J. Duprat,[6] H. Hoekstra,[7] J. Thompson.[3] *1. Cancer Surgery, Peter MacCallum Cancer Center, East Melbourne, VIC, Australia; 2. Princess Alexandra Hospital, Brisbane, QLD, Australia; 3. Melanoma Institute of Australia, Sydney, NSW, Australia; 4. Royal Adelaide Hospital, Adelaide, SA, Australia; 5. Christchurch Hospital, Christchurch, New Zealand; 6. Hospital Do Cancer, Sao Paulo, Brazil; 7. University Medical Centre, Groningen, Netherlands.*

Background: The extent of surgery for patients with a palpable inguinal recurrence of melanoma is controversial. Data from the recent ANZMTG/TROG trial of adjuvant RT after lymphadenectomy for patients at elevated risk of lymph node field (LNF) relapse was reviewed to investigate differences in morbidity and QOL between inguinal (IL) and inguinal pelvic lymphadenectomy (IPL) (Henderson MA, Lancet Oncology,16(9),1009, 2015). Methods: The Trial randomised patients with a palpable LNF recurrence to adjuvant radiotherapy (ART) or observation (OBS) after lymphadenectomy (groin procedure was determined by the clinician). Patients were followed 3 monthly for 2 years and 6 monthly to 5 years with clinical examination, assessment of treatment toxicity and QOL measures, (FACT-G and Regional Symptoms Questionnaire (RSQ), a purpose-designed tool) and limb girth measurements. Results: 69 patients with a first isolated inguinal LNF relapse were randomised to OBS (35) or ART (34). 46 patients had an IL (ART n=21) and 25 an IPL (ART n=13). There were no differences in sex, age, lymph node size or use of RT however IPL patients were more likely to have ≥4 positive nodes (14/46 (30%) and 14/23 (61%), p= 0.016) and choice of surgery type was strongly related to institution (P=0.004). Average limb volume ratios (affected : normal leg) increased over the period of the study (0 to 60 months) 9.9% IL, 13.4% IPL; p=0.35. FACT-G and RSQ scores improved from baseline at randomisation but no differences were noted (AUC P=0.68, P=0.65, respectively). Limited differences in surgical toxicity were noted. No difference in overall survival was found between IL and IPL. IPL had fewer LNF relapses (HR(IL:IPL)=2.18) and longer relapse free survival (HR=1.99. P=0.024). Discussion: This study is the first to prospectively and objectively compare the morbidity of IL and IPL. No evidence for a difference in lymphoedema or QOL was found although the numbers are relatively small. No difference in survival was found despite more patients with ≥4 positive nodes in the IPL group: results from a randomised trial of IL v IPL (ANZMTG EAGLEFM) are awaited.

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Preoperative Risk Factors Associated with Secondary Lymphedema Following Limb Lymphadenectomy for Melanoma D.J. Mercante,[1]* R.J. Strobel,[1] R.D. Kramer,[1] S.J. Diljak,[1] B. Sunkara,[1] J.F. Friedman,[1] J.S. Jehnsen,[1] A.B. Durham,[2] T.M. Johnson,[2] M. Cohen.[3] *1. University of Michigan Medical School, Ann Arbor, MI; 2. University of Michigan, Department of Dermatology, Ann Arbor, MI; 3. University of Michigan, Department of Surgery, Ann Arbor, MI.*

Introduction: Secondary lymphedema (SLE) is a significant complication following complete lymphadenectomy (CL) in melanoma patients, with a reported incidence between 9-25% for axillary dissection (ALND) and as high as 24-44% for inguinal dissections (ILND). Using a prospectively collected database to look at outcomes for melanoma patients following ALND and ILND, we identified pre-operative (pre-op) risk factors for SLE using the largest cohort reported to date. Methods: From a prospectively collected, IRB-approved database, we identified 688 melanoma patients who underwent CL between June 2005 and June 2015. Included in the final analysis were 554 patients who had either ALND or ILND. Exclusion criteria included: patients who had iliac or bilateral dissections, or pre-op chemotherapy. A p<0.25 threshold in univariate analysis was employed for considering variables to be included in multivariable analysis. Logistic regression was utilized to estimate the occurrence of lymphedema, and the model's discrimination was assessed (i.e. AUROC). Results: Of the 554 patients included [ALND=321(58%);ILND=233(42%)], 118 (21.3%) developed SLE (10.9% of ALND and 35.6% of ILND). On multivariable logistic regression [Table], ILND (OR=4.70; CI:2.95-7.37), PVD (OR=2.64 CI:0.99-7.00), and BMI 25-30

(OR=1.26 CI:1.25-3.21) or males with BMI>30 (OR: 2.59 CI:1.38-4.85) were each significantly associated with increased odds of developing SLE. Patients who had not smoked at the time of surgery had reduced odds of SLE (OR=0.63 CI:0.38-1.05). The average postoperative (post-op) time to report SLE was 103±126 days. Average follow-up was 1.9±2.2 years. The model also demonstrated fair discriminatory ability (ROC:0.73). Conclusion: This is the largest study to date evaluating pre-op risk factors for SLE in melanoma patients after ALND or ILND. Pre-op factors significantly increasing the risk of SLE include ILND, being overweight (BMI 25-30), and suffering from PVD. Not smoking peri-operatively was protective. This data, combined with future evaluation of intra-op and post-op risk factors, will provide a more thorough risk assessment for SLE and guide clinical discussion with patients.

Table. Multivariable preoperative risk model for lymphedema following melanoma LND

Characteristic	OR (CI)	P-Value
ILND	4.61 (2.94-7.24)	<0.001
PVD	2.64 (0.99-7.06)	0.052
BMI, 25-30	2.07 (1.29-3.32)	0.002
Not currently Smoking	0.63 (0.38-1.05)	0.082
BMI > 30, Male patients only	2.59 (1.38-4.85)	0.003

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Improvement, and Persistent Disparities, in Completion Lymph Node Dissection: Lessons from the National Cancer Data Base

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Introduction: Completion lymph node dissection (CLND) is currently recommended following a positive sentinel lymph node biopsy (SLNBx), though studies have demonstrated that up to 50% of patients with a positive sentinel node do not undergo CLND. We sought to determine trends in CLND over time, and whether certain patient-specific factors contribute to disparities in CLND. Method: The National Cancer Database (NCDB) was queried for patients with pathologic stage I-III melanoma undergoing wide local excision (WLE), with or without SLNBx, with or without CLND. Subsets were created based on demographic, socioeconomic and era of treatment (2003-07 and 2008-12). Univariate and multivariate analyses were used to determine if any patient, pathologic or treatment specific variables were associated with performance of, or trends in, CLND. Results: 146,378 patients underwent WLE with SLNBx. Of those, 29,094 (19.9%) patients had a positive SLNBx, with 15,661 (53.8%) continuing to CLND. CLND was more common during the second study period (54.6% vs. 52.9%; p <0.001). Certain subsets of patients demonstrated a disproportionate increase in CLND utilization (minority populations, in particular), while uninsured patients were less likely to undergo CLND over time (Table 1). On multivariate analysis, patients with head/neck lesions (OR 0.71, 95% CI [0.7-0.8], p<0.001) and lower extremity lesions (OR 0.75, [0.7-0.8], p<0.001) were less likely to undergo CLND. A number of demographic and socioeconomic factors were also associated with failure to undergo CLND, namely black race (OR 0.57, [0.4-0.7], p<0.001), patients with Medicaid (OR 0.83, [0.7-0.9], p=0.003) or Medicare insurance (OR 0.90, [0.8-0.9] p=0.004), being uninsured (OR 0.78, [0.7-0.9], p<0.001) and being treated at non-academic cancer programs (OR 0.75, [0.7-0.8], p<0.001). Conclusion: Increased utilization of CLND across most patient cohorts is encouraging, but racial and socioeconomic disparities persist. Until results of the MSLT-2 trial inform the melanoma community about the utility of CLND, continued focus on understanding these discrepancies and on improving rates of CLND is necessary.

Table 1. Patient and tumor-specific factors associated with undergoing CLND, over time.

Patient and Tumor-Specific Factors	2003-07		2008-12		% Change (Relative)
	N	%	N	%	
Race					
White	6697	53.3	8572	54.9	3.0
Black	48	31.0	72	38.5	24.1
Asian	24	51.1	42	59.2	15.9
Insurance status					
Private	4133	56.2	4861	57.6	2.7
Medicaid	289	50.4	434	51.9	3.0
Medicare	1967	49.7	2835	52.5	5.6
Not insured	307	51.9	408	50.1	-3.5
Location of primary tumor					
Trunk	2669	57.0	3404	58.8	3.2
Head/neck	1073	49.5	1398	49.0	-1.0
Lower extremity	1639	50.5	2064	53.0	5.0
Upper extremity	1421	54.8	1854	56.9	3.8
Facility type					
Academic	3523	56.1	4822	57.8	3.0
Comm. Cancer Program	407	46.0	516	49.6	7.8
Comp. Comm. Cancer Program	2831	50.2	3369	51.4	2.4

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Patterns and Timing of First Relapse in Pathologic Stage II Melanoma Patients N. Droppelmann,* A.Y. Lee, K. Panageas, C.E. Ariyan, M.S. Brady, S. Balakrishna, D.G. Coit. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Stage II melanoma patients have highly variable outcomes when divided by substage. We hypothesized that differences in time, site, and method of detection of initial relapse by substage could be used to inform evidence-based guidelines for follow-up. Methods: We performed a retrospective review of a prospective, single-institution database and identified 754 patients with pathologic stage II cutaneous melanoma (AJCC 7th ed.) treated for primary melanoma at Memorial Sloan Kettering Cancer Center between January 1993 and December 2013. Clinical records were reviewed to determine time from initial treatment to first relapse, location and method of detection. Results: Of the 754 patients, 220 (29%) relapsed. Patients with less than 12 month of follow up were excluded. Median follow-up for non-relapsing patients was 55 months. Median time to relapse for stage IIA, IIB, and IIC patients was 28.5, 22.6, and 14.6 months, respectively. Five-year relapse-free survival for stage IIA, IIB, and IIC was 77%, 64%, and 53%, respectively. Relapses in IIA and IIB patients were most commonly local/in-transit (41% and 45%, respectively), while relapses in IIC patients were most commonly systemic (52%) ($P < 0.05$). Relapses were most commonly detected by the patient (57%), and less commonly by a physician (20%) or by routine radiographic test in asymptomatic patients (19.2%). The 5-year cumulative incidence for patient detected relapse was 13% for IIA, 18% for IIB, and 23% for IIC, and for image detected relapse was 3% for IIA, 7% for IIB, and 16% for IIC. The cumulative incidence of relapse for each substage by method of detection is shown in Table 1. Conclusions: Pattern and method of detection of first relapse for patients with stage II melanoma differed by substage. Relapses were detected most frequently by patients in all stage II substages, highlighting the importance of patient education and self-examination. The highest yield for detecting relapses by routine imaging is in stage IIC patients during the first 5 years. Physical examination by a physician is unlikely to detect additional relapses beyond 3 years for stage IIA, and 2 years for stage IIB and IIC patients.

Table: Cumulative incidence (95% confidence interval) of recurrence by each method of detection and death at 5 years

	Overall	Stage IIA	Stage IIB	Stage IIC
Recurrence detected by patient	16 (13-19)	13 (10-17)	18 (12-23)	23 (15-31)
Recurrence detected by image	7 (5-9)	3 (2-6)	7 (4-12)	16 (10-24)
Recurrence detected by MD	6 (4-8)	4 (3-7)	8 (5-12)	5 (2-11)
Died without recurrence	6 (4-8)	5 (3-9)	6 (4-10)	9 (4-16)

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Prospective Randomized Clinical Trial for the Evaluation of a Stage Adjusted Reduced Follow-up Schedule in Cutaneous Melanoma Patients: Results After One Year S. Damude,[1]* J.E. Hoekstra-Weebers,[5] A. Francken,[2] S. ter Meulen,[3] E. Bastiaannet,[4] H. Hoekstra.[1] *1. Department of Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands; 2. Department of Surgical Oncology, Isala, Zwolle, Netherlands; 3. Netherlands Cancer Institute/Antoni van Leeuwenhoek, Amsterdam, Netherlands; 4. Department of Surgical Oncology, Leiden University Medical Center, Leiden, Netherlands; 5. Wenckebach Institute, UMCG, Groningen, Netherlands.*

Introduction. Evidence-based guidelines for the adequate frequency of follow-up in Stage IB-II melanoma patients are currently not available. The aim of this phase-III study was to determine whether a reduced follow-up schedule affects (1) Patient-Reported Outcome Measures (PROMs), (2) detection of recurrences, and (3) total yearly follow-up costs. Methods. A multicenter trial with 180 patients treated for AJCC stage IB-II cutaneous melanoma, randomized in conventional (CSG, 4 visits yearly, n=93) and experimental (ESG, 1-3 visits yearly, n=87) follow-up schedule groups, stratified for AJCC stage. Four PROMs were collected every six months; State-Trait Anxiety Inventory (STAI-S), Cancer Worry Scale, Impact of Event Scale (IES), and Health Related Quality of Life (HRQoL, RAND-36). All visits were registered by physician reports. Results. Socio-demographic and illness-related characteristics were equal for both groups, as well as the number of patients lost to follow-up (CSG 18.3%, ESG 16.1%, p=0.6) and schedule satisfaction (CSG 84.5%, ESG 92.6%, p=0.1). PROMs at inclusion were compared to one year later (Table 1). The STAI-S and Cancer Worry Scale show less anxiety in the ESG (p=0.57), with a significant decrease in cancer related worry over time in both groups (p<0.001). The ESG reports significantly less cancer-related stress (total-IES, p=0.01). The CSG scores significantly better on physical HRQoL (p=0.01), mental HRQoL is equal for both groups, and total HRQoL in both groups increases significantly over time (p<0.001). Total recurrence rate was 9.7% in the CSG and 9.2% in the ESG, mostly patient-detected instead of physician-detected (CS 66.7%, ES 50%, p=0.5). Total costs of one year follow-up, including recurrences and all visits, was reduced by 50% in the ESG compared to the CSG (€ 15871 and € 31240 respectively). Conclusions. The preliminary results of this study show no negative effect of a stage adjusted reduced follow-up schedule on (1) patient's well-being and (2) the detection of recurrences, and (3) contributed to a significant overall cost reduction of 50% during one year follow-up.

Table 1. Results of the Patient-Reported Outcome Measures from baseline to one year (T1-T3) across time and study group (n=148).

Questionnaire	Study group	T1 Mean (SD)	T3 Mean (SD)	ANOVA
STAI-S	Conventional Experimental	31.4 (8.8) 31.4 (8.0)	31.2 (9.8) 29.6 (8.9)	F=2.8; p=0.09 (time) F=0.3; p=0.57 (group) F=1.8; p=0.18 (interaction)
Cancer Worry Scale	Conventional Experimental	4.6 (1.5) 4.5 (1.6)	4.2 (1.4) 3.7 (1.1)	F=14.7; p<0.001 (time) F=2.5; p=0.12 (group) F=2.2; p=0.14 (interaction)
Total-IES	Conventional Experimental	21.7 (13.8) 14.8 (13.5)	14.4 (13.1) 10.0 (12.1)	F=33.7; p<0.001 (time) F=6.4; p=0.01 (group) F=1.4; p=0.24 (interaction)
RAND-36 Physical Component Score	Conventional Experimental	49.1 (8.5) 44.9 (10.8)	52.5 (7.8) 49.7 (9.4)	F=33.5; p<0.001 (time) F=6.8; p=0.01 (group) F=1.0; p=0.32 (interaction)
RAND-36 Mental Component Score	Conventional Experimental	49.7 (11.4) 49.1 (10.9)	52.5 (8.8) 54.3 (7.6)	F=24.7; p<0.001 (time) F=0.18; p=0.67 (group) F=2.3; p=0.13 (interaction)

Abbreviations: T1; at inclusion, T3; after one year follow-up, STAI-S; State-Trait Anxiety Inventory, IES; Impact of Event Scale, RAND-36; RAND health-related quality of life questionnaire. Level of significance: p<0.05.

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The Impact of Smoking on Melanoma Sentinel Node Metastases: Analysis of Two Multicenter Clinical Trials M.S. Jones,* P.C. Jones, S.L. Stern, M.B. Faries. *Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA.*

Introduction The association of smoking with adverse outcomes in melanoma is not well studied. We hypothesized that smoking increases the metastatic potential of a primary cutaneous melanoma and the incidence of sentinel node (SN) metastasis. Methods Data from the Multicenter Selective Lymphadenectomy Trial (MSLT) –I and the screening phase of MSLT-II were analyzed regarding the association of smoking to clincopathologic variables and sentinel node metastasis. Subjects with incomplete smoking history data were excluded. These deidentified analyses were independently determined to be exempt from Institutional Review Board review. Results Among the 4231 patients (1024 MSLT-I and 3207 MSLT-II), current or former smoking was independently associated with ulceration (p=0.0002 and p=0.0005, respectively). Never smoking was also independently associated with decreased Breslow thickness in multivariate analysis (p=0.0017) and with a 0.251-mm predicted decrease in thickness for never vs. current smokers. Current smoking was also strongly associated with SN metastasis, even after adjusting for other predictors of metastasis (see Table). Conclusions Smoking is directly correlated with a significantly increased risk of SN metastasis in patients with primary cutaneous melanoma, which appears independent of its adverse effect on tumor thickness and ulceration. We speculate that these combined effects might promote regional metastasis via hypoxia-induced cytochemical alterations. Smoking cessation should be strongly encouraged among patients with melanoma.

Logistic Regression for SN Positivity in MSLT-I and II Patients

	Univariable			Multivariable		
Variable	p-value	OR	95% CI	p-value	OR	95% CI
Smoking: Current vs. Never	<.0001	1.64	(1.35-1.99)	0.0041	1.35	(1.10-1.65)
Smoking: Former vs. Never	0.5938	1.05	(0.88-1.26)	0.4526	1.08	(0.89-1.30)
Age (continuous)	<.0001	0.98	(0.98-0.99)	<.0001	0.98	(0.98-0.99)
Male vs. Female	0.0740	1.15	(0.99-1.34)	0.5344	1.06	(0.89-1.25)
Ulceration: Present vs. Absent	<.0001	2.27	(1.94-2.66)	<.0001	1.83	(1.55-2.17)
Breslow (continuous)	<.0001	1.25	(1.20-1.30)	<.0001	1.20	(1.15-1.25)
Extremity vs. Head/Neck	0.5357	0.93	(0.74-1.17)	0.6087	0.94	(0.74-1.20)
Trunk vs. Head/Neck	0.0007	1.47	(1.18-1.84)	0.0100	1.36	(1.08-1.71)

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A Novel Gene Signature that Predicts the Survival of Patients Undergoing Surgical Resection for Metastatic Melanoma J.J. Hong,[1]* K. Gong,[2] D. Kaufman,[1] N. Deng,[1] R. Essner.[1] *1. Surgical Oncology, Cedars-Sinai Medical Center, Los Angeles, CA; 2. UCLA, Los Angeles, CA.*

Background: The survival for patients with metastatic melanoma is poor despite the development of several immunotherapies. The traditional approach to patients with limited metastases is surgical resection yet the role of surgery is becoming more controversial. We evaluated a molecular gene profile to determine if a particular profile could serve as a guide to determine which patients to consider for potentially curative resection. Methods: We prospectively collected melanoma tissue specimens from patients undergoing surgical resection for advanced stage disease. RNA was extracted from specimens to generate cDNA for microarray analyses. Patients were followed for recurrence or melanoma-specific death. Results: Ninety patients underwent surgical resection: 40 with primary tumors (PT), 15 with lymph node metastases (LT), and 35 with distant metastases (MT). Most patients were men (60%), and the median age was 57 years. Primary tumors were most commonly on the extremities (45%) and trunk (25%) whereas the metastases were most commonly subcutaneous (29%), small bowel (14.3%) or lung (14.3%). From the 17,000 genes evaluated in the microarray, we identified six unique genes: PPP2RC, S100A7A, CNFN, ONECUT, PMAL1 and TENC that had significantly (p=0.035) different expression in PT vs LT and MT. When the six gene profile was examined, the 5-year survival of patients with resected metastases was 83+/-8% vs. 8+/7% (p<0.0001) for patients with tumors lacking the profile. Age, gender and site of metastases were not predictive of survival. Conclusion: We identified a 6-gene molecular signature from resected melanoma metastases that strongly predicts patient outcome. This gene signature may be an important first step to accurately identify patients as candidates for resection of metastatic melanoma.

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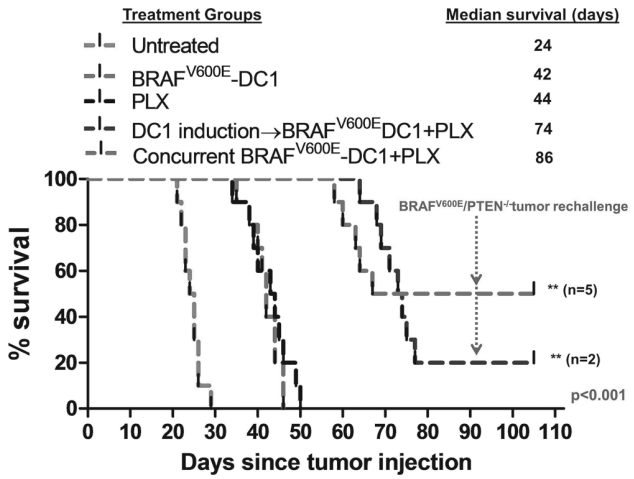
A Novel Dendritic Cell Vaccine Targeting Mutated BRAF Overcomes Vemurafenib Resistance and Synergistically Improves Survival in BRAF-Mutant Murine Melanoma J. Datta,[1]* J.A. Cintolo-Gonzalez,[3] C. Ellingsworth,[2] S. Xu,[1] L. Lowenfeld,[1] E. Berk,[1] R. Somasundaram,[2] B.J. Czerniecki.[1] *1. Surgery, University of Pennsylvania, Philadelphia, PA; 2. Wistar Institute, Philadelphia, PA; 3. Dana Farber Cancer Institute/Harvard Medical School, Boston, MA.*

INTRODUCTION: BRAF inhibitor vemurafenib (PLX) improves survival in BRAF-mutant ($BRAF^{V600E}$) melanoma, but resistance is common. We have shown that a $BRAF^{V600E}$-pulsed type1-polarized dendritic cell vaccine ($BRAF^{V600E}$-DC1) induces antigen-specific $CD8^+$ T-cells that impact murine $BRAF^{V600E}$ melanoma. We investigated if combinations of $BRAF^{V600E}$-DC1 and PLX elicit a synergistic clinical response. METHODS: A transplantable $BRAF^{V600E}PTEN^{-/-}$ melanoma model was developed in the C57Bl/6 background. DC1 were generated from bone marrow precursors using Flt3, IL-6, GM-CSF, IL-4, CpG and LPS, and pulsed with class I $BRAF^{V600E}$ peptide. In addition to untreated and ovalbumin-DC1 controls, $BRAF^{V600E}$-DC1 (2x weekly injections) and PLX were administered alone or in designated combinations to tumor-bearing mice (n=10 each). Tumor growth and survival were determined. Induction of $BRAF^{V600E}$-specific $CD8^+$ T-cell responses from splenocytes were assessed by IFN-γ ELISA. Cytokine mRNA quantification in tumor microenvironments (TME) was performed by RT-qPCR. RESULTS: Mice receiving $BRAF^{V600E}$-DC1+PLX combinations, either initiated concurrently or after $BRAF^{V600E}$-DC1 induction, demonstrated dramatically delayed tumor growth ($P<0.001$) and improved median survival (86d and 74d respectively) vs $BRAF^{V600E}$-DC1 (42d), PLX (44d), ovalbumin-DC1 (28d), or untreated (24d) cohorts ($P<0.001$); 35% were rendered disease-free following $BRAF^{V600E}$-DC1+PLX therapy, and remained immune to $BRAF^{V600E}$ tumor rechallenge. $BRAF^{V600E}$-DC1+PLX, compared with individual, treatments induced synergistically improved systemic $CD8^+$ T-cell recognition of $BRAF^{V600E}$-pulsed antigen-presenting cells and $BRAF^{V600E}$ tumor cells ($P<0.01$) measured by IFN-γ release in vitro. In TME, $BRAF^{V600E}$-DC1+PLX generated higher mRNA levels of Th1 (IFN-γ/TNF-α) and T-cell homing (CXCL9/CCL5) cytokines, while attenuating PD-L1 expression; $CD8^+$ TIL trafficking was augmented by $BRAF^{V600E}$-DC1+PLX. CONCLUSIONS: $BRAF^{V600E}$-DC1 vaccines overcome vemurafenib resistance in $BRAF^{V600E}$ melanoma, synergistically improving immune and clinical responses. Such combinations warrant investigation in human trials.



Kaplan-Meier survival estimates by treatment group; ** mice rendered disease-free and immune to tumor rechallenge

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Local Excision has Comparable Survival to Abdominoperineal Resection in Patients with Anal Melanoma: An Analysis of 760 Patients from the National Cancer Data Base L. Youngwirth,* M. Adam, Z. Sun, E. Benrashid, C. Mantyh, J. Migaly, R. Scheri. *Duke University Medical Center, Durham, NC.*

Introduction: Anal melanoma is a rare, yet highly aggressive cancer. Data on the presentation, oncologic profile, and survival are primarily limited to small, institutional studies. Methods: The National Cancer Data Base (1998-2012) was queried for all adult patients with a diagnosis of anal melanoma. Inclusion was limited to patients who underwent local excision or abdominoperineal resection (APR). Patient demographic, clinical, and pathologic characteristics at the time of diagnosis were determined. A Cox proportional hazards model was developed to identify factors associated with survival. A subgroup analysis was performed for patients with tumors less than 2.0 mm. Results: Of the patients who met inclusion criteria, 488 underwent local excision and 272 underwent APR. Patients who underwent APR were younger (64 years vs 68 years, $p<0.01$) and had larger tumors (5.2 mm vs 3.7 mm, $p<0.01$) when compared to patients who underwent local excision. The two groups were similar with regards to sex, race, insurance status, income, comorbidity status, facility type, presence of distant metastases, and treatment with chemotherapy and radiation therapy. Median survival for patients who underwent local excision was 22.5 months compared to 18.4 months for patients who underwent APR ($p=0.55$). After adjustment for demographic, clinical, and pathologic factors, including chemotherapy and radiation therapy, there was no difference in survival for patients undergoing local excision compared to APR ($p=0.07$). However, when limiting the analysis to tumors less than 2.0 mm, APR was associated with compromised survival (HR=1.3, $p=0.04$). Conclusion: Local excision has comparable survival to APR for patients with anal melanoma of all stages and avoids the morbidity associated with this complex procedure.

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Durable Complete Responses (CRs) in Patients (pts) with Stage IIIB-IV Melanoma Treated with Talimogene Laherparepvec (T-VEC) in OPTiM R. Andtbacka,[1]* H. Kaufman,[2] F. Collichio,[3] T. Amatruda,[4] J. Nemunaitis,[5] J. Chesney,[6] I. Puzanov,[7] K. Harrington,[8] Y. Zhang,[9] L. Chen,[9] M. Shilkrut,[9] M. Ross.[10] *1. Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; 2. Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; 3. The University of North Carolina at Chapel Hill, Chapel Hill, NC; 4. Minnesota Oncology, Fridley, MN; 5. Mary Crowley Cancer Research Center, Dallas, TX; 6. University of Louisville, Louisville, KY; 7. Vanderbilt University Medical Center, Nashville, TN; 8. The Institute of Cancer Research/The Royal Marsden Hospital, London, England, United Kingdom; 9. Amgen Inc., Thousand Oaks, CA; 10. MD Anderson Cancer Center, Houston, TX.*

Background: T-VEC is a herpes simplex virus type 1-derived injectable oncolytic virus. In OPTiM, a phase 3 trial in 436 pts with unresected stage IIIB-IV melanoma, intralesional T-VEC improved durable response rate (continuous partial response [PR] or CR ≥6 mo; primary endpoint) from 2% to 16% vs subcutaneous GM-CSF. Overall response rates for T-VEC and GM-CSF were 26% and 6%, respectively. Median overall survival (OS; secondary endpoint) was 23.3 mo with T-VEC and 18.9 mo with GM-CSF (hazard ratio [HR] = 0.79, 95% CI: 0.62–1.00, P = 0.051). Here we report on pts who achieved CR with T-VEC in OPTiM. Methods: A retrospective analysis of OPTiM final OS data (cutoff Aug 2014; included pts who continued treatment after tumor response analysis at Dec 2012) was conducted to identify pts who achieved a CR (investigator assessment by modified WHO criteria) with T-VEC. The Kaplan-Meier method was used to estimate CR duration, recurrence-free survival (RFS; from CR to recurrence, death due to disease progression, or subsequent anti-cancer therapy), and OS. Results: Of 287 evaluable pts treated with T-VEC, 50 (17%) achieved CR. Among pts with CR compared with PR, more pts were older, had lower total tumor burden, had a higher proportion of pts with stage IIIB, IIIC, and IVM1a melanoma without elevated LDH, and received T-VEC as a 1st-line therapy (Table). Median (Q1–Q3) time to achieve a CR was 8.6 (6.0–13.6) mo. Median CR duration was not reached, with 78% (95% CI: 59-89) of pts estimated to have a CR lasting ≥12 mo. Median RFS was not reached, with 84% (95% CI: 70–92) and 72% (95% CI: 57–83) of pts estimated to be recurrence-free at 1- and 3-y after achieving CR, respectively. Median OS for pts with CR was not reached, with 96% (95% CI: 85–99) and

89% (95% CI: 74–95) being alive at 3- and 5-y, respectively. Conclusion: Treatment with T-VEC resulted in CR in 17% of pts seen in all stages of melanoma but most commonly in pts with earlier stages and lower tumor disease burden. Most pts with durable CR achieved prolonged OS without recurrence. T-VEC is a potential new treatment option for patients with unresectable stage IIIB-IV melanoma.

Table

		CR, N = 50	PR, N = 43	No response, N = 194	P-value
Median age (Q1-Q3), years		70 (60-78)	64 (53-77)	62 (53-71)	0.021
ECOG PS, n (%)	0	42 (84)	31 (72)	135 (70)	0.13
	1	8 (16)	12 (28)	59 (30)	
Disease stage, n (%)	Stage IIIB	12 (24)	3 (7)	7 (4)	<0.0001
	Stage IIIC	19 (38)	12 (28)	35 (18)	
	Stage IVM1a	15 (30)	14 (33)	45 (23)	
	Stage IVM1b	2 (4)	7 (16)	54 (28)	
	Stage IVM1c	2 (4)	7 (16)	53 (27)	
Elevated LDH, n (%)		0	0	13 (7)	0.041
Median baseline total tumor burden* (min-max), sqcm		4.6 (0.3-38.3)	10.9 (0.6-280.6)	20.4 (0.6-350.0)	<0.0001
Line of therapy, n (%)	1st	33 (66)	27 (63)	78 (40)	<0.0001
	≥ 2nd	17 (34)	16 (37)	116 (60)	

*Sum of the products of the 2 largest perpendicular diameters of index lesions at baseline.
CR = complete response; ECOG PS = Eastern Cooperative Oncology Group performance status; PR = partial response; sqcm = square centimeter

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Survival Impact of Lymph Node Dissection in Patients with Microscopic Medullary Thyroid Cancer T.A. Moo-Young,* C. Wang, R. Prinz, D. Winchester. *NorthShore University HealthSystems, Glenview, IL.*

Background: Growing evidence supports a more tailored approach to the management of subclinical thyroid cancers. Little is known about the impact of surgical extent for medullary thyroid microcarcinomas measuring less than 1 cm (mMTC). We conducted a population level analysis to determine if total thyroidectomy with regional lymph node surgery is necessary for patients with mMTC. Methods: 1023 patients with a histologic diagnosis of mMTC were identified in the National Cancer Data Base from 1998-2011. Median follow-up was 77 months. Demographic, clinicopathologic features, surgical treatment, and vital status information was analyzed. Because familial MTC is more likely to present at a younger age, we also evaluated whether there were differences in the clinicopathologic features for patients above and below the age of 30. Differences in overall survival between surgical treatment groups were compared using Kaplan-Meier method with log rank statistics. Risk adjusted multivariable analysis was conducted using Cox proportional hazard regression in SAS 9.4 (Cary, NC). Results: The median tumor size was 6 mm and extracapsular extension was present in 5% of patients. Total thyroidectomy with regional node dissection was performed in 70%. Of those undergoing lymph node dissection 34% had lymph node involvement. There was no difference in tumor size, extracapsular extension, lymph node metastases, or type of surgical procedure in patients greater or less than 30 years of age (all $P<0.05$). After adjustment for age, race, socioeconomic factors, and aggressive clinicopathologic features there was no difference in survival between patients who were treated with total thyroidectomy with regional lymph node dissection vs. those treated with thyroidectomy alone ($p=0.1686$). Conclusion: The routine use of regional lymph node dissection may not be necessary for medullary thyroid microcarcinomas that do not present with evidence of locoregional or distant disease. More studies are needed to better understand the behavior of these subclinical tumors in order to individualize treatment strategies.

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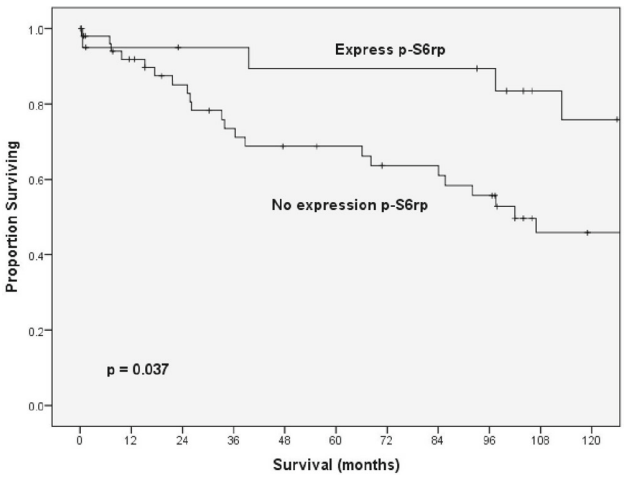
Loss of PTEN and Expression of p-S6rp in Pancreatic Neuroendocrine Tumors Predicts Survival M. Dillhoff,* M. Bloomston, W.L. Frankel, C.R. Schmidt. *Surgery, Ohio State University, Columbus, OH.*

Background: Mammalian target of rapamycin (mTOR), functions in the regulation of apoptosis and stimulates cell growth and proliferation. Inhibitors of mTOR have been shown to improve outcome in patients with metastatic pancreatic neuroendocrine tumors. We sought to determine the expression pattern for PTEN, p-AKT, p-mTOR, and p-S6rp (a target of mTOR activation) in pancreatic neuroendocrine tumors (PNET) and their association with clinicopathologic characteristics. Methods: 78 resected PNETs were microdissected and tissue microarrays (TMA) were constructed from formalin-fixed, paraffin-embedded blocks. TMA's were stained for PTEN, p-Akt, p-mTOR and p-S6rp. Expression intensity was scored as 0 (absent), 1+ (modest), or 2+ (strong). Islets from 7 normal pancreas served as controls. Kaplan-Meier survival curves were constructed and compared by log-rank analysis. Results: PTEN expression was lost or low in 19 (24%) and strong in 59 (76%). Eighteen tumors (23%) expressed modest (1+) p-Akt. Modest to high expression of mTOR was found in 57 (73%) (1+ in 32 and 2+ in 25. Twenty-six (33%) had modest to strong expression of p-S6rp (1+ in 23 and 2+ in 3). Normal islets (controls) expressed PTEN (2+ in 4, 1+ in 3) and no expression of p-Akt, p-mTOR or p-S6rp. Lost or low expression of PTEN was predictive of worse overall survival (median 5.7 years vs. 14.1 years $p=.008$) as was expression of pS6rp (median 16 years vs. 8.5 years, $p=0.037$) on multivariable analysis. Nodal status and differentiation was also predictive of overall survival. mTOR expression was not associated with survival. Low expression of PTEN, and expression of p-S65p were not correlated with tumor size, differentiation, Ki-67, nodal status or T stage. Conclusions: Aberrant activation of the PI3K/Akt/mTOR pathway was detected in the majority of PNETs. Loss of PTEN and expression of p-S6rp was predictive of improved outcome in patients with resected pancreatic neuroendocrine tumors. Expression of p-S6rp and not mTOR emphasizes the multifactorial pathway involved in the tumorigenesis of PNETs.



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The Role of Preoperative Imaging and Double Balloon Enteroscopy in the Surgical Management of Small Bowel Neuroendocrine Tumors: Is it Necessary? N. Manguso,[1]* A. Gangi,[2] J. Johnson,[1] N. Nissen,[1] A. Wachsman,[1] J. Mirocha,[1] A. Hendifar,[1] F. Amersi.[1] *1. Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, CA; 2. Moffitt Cancer Center, Tampa, FL.*

Background: Small bowel (SB) neuroendocrine tumors (NET) account for 54% of gastrointestinal NET. Pre-operative localization of disease improves outcomes. The aim of this study is to determine the effectiveness of pre-operative imaging and double balloon enteroscopy (DBE) in identifying extent of disease. Methods: IRB approved database review identified 178 patients with primary SB NET diagnosed between 2006 and 2013. Final analysis included only patients who underwent imaging, endoscopy and surgery at our institu-

tion. Statistical analysis was performed to identify effectiveness of localization modalities. Results: 107 patients (pts) met study criteria. Average age was 61.0 years and 48% were male. 66 (61.7%) pts had a primary NET in the ileum, 20 (18.7%) pts had mid SB NET, and 21 (19.6%) pts had duodenal NET. 77 pts (67.3%) underwent CT scan, 50 (46.7%) pts had an MRI, 50 (46.7%) pts had an octreotide scan, and 42 (39.3%)pts had a DBE. When compared to outcomes after surgical resection, sensitivity of each of the modalities in identifying the primary NET was 59.7% for CT, 54% for MRI, 56% for octreotide scans and 88.1% for DBE. Moreover, CT scan identified only 7.3% of additional SB lesions and 74% of liver lesions, MRI identified 22% of additional SB lesions and 93% of liver lesions, octreotide scan identified 65% of additional metastatic lesions, and DBE identified 54% of additional SB lesions. There were no significant differences noted in the sensitivity of MRI, CT scan or octreotide scan in identifying the primary NET. DBE was significantly better at identifying the primary NET than CT scan, MRI or octreotide scan ($p = 0.004$, 0.007, & 0.012 respectively). For pts with metastatic disease found at surgical resection, MRI was better at identifying the extent of metastatic disease compared to CT scan or octreotide. Conclusions: DBE is significantly better than other imaging modalities at identifying primary and multifocal SB NET. MRI is better at detecting metastatic disease. Both DBE and MRI should be considered in the pre-operative work up of pts undergoing surgical resection for SB NET.

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Hashimoto's Disease Increases Risk of Cancer in Indeterminate Thyroid Nodules with Suspicious Molecular Testing J.H. Terhune,* C. Willis, C. Kvasnovsky, J. Ferlitch, J. Olson. *General Surgery, University of Maryland Medical Center, Baltimore, MD.*

Patients with thyroid nodules having indeterminate fine needle aspiration (FNA) cytology results (Bethesda III/IV) are often referred for thyroidectomy. Genetic testing of indeterminate thyroid nodules (ITN) provides an additional assessment of malignancy risk and may better identify patients for surgery. The AFIRMA gene expression classifier (GEC) test has been advocated as an assay to inform initial choice of surgery (lobectomy versus total thyroidectomy) for patients with a suspicious GEC. We sought to assess results of thyroidectomy performed for AFIRMA-suspicious nodules to identify clinical factors that are associated with a higher risk of malignancy. We performed a retrospective analysis of consecutive patients undergoing thyroid lobectomy or total thyroidectomy for an ITN with suspicious AFIRMA GEC at a tertiary referral center from June 2012 through July 2015. An ITN was defined as an FNA biopsy showing Bethesda 3 (atypia of undetermined significance/follicular lesion of undetermined significance) or 4 (suspicious for follicular neoplasm) cytology. We examined routinely available preoperative clinical variables and compared patients with final diagnosis of cancer to patients without a cancer diagnosis. A total of 58 patients were studied; 50 were female with median age 54 (43-62). Thirty-nine (62%) had a diagnosis of thyroid disorder, including 13 (22%) with Hashimoto's thyroiditis. Overall, 20 patients (35%) had thyroid cancer. On multivariate logistic regression, a clinical history Hashimoto's disease was the only characteristic predictive of cancer (odds ratio 5.5, P=0.025), with a 62% risk of cancer. Gender, age, nodule size, and Bethesda 3 vs. 4 classification were not associated with an increased risk of thyroid cancer in patients with AFIRMA suspicious ITN. A personal history of Hashimoto's disease is associated with a 5-fold (62%) risk of cancer in AFIRMA GEC suspicious, Bethesda 3 or 4 nodules. When considering operative management of patients with an AFIRMA suspicious ITN, a clinical history of Hashimoto's disease may identify patients at higher risk of harboring thyroid cancer for whom total thyroidectomy is the best initial surgery.

Selected patient & nodule characteristics and associated cancer risk

	Odds ratio	95% CI (lower)	95% CI (higher)	P value
Male gender	1.442	0.221	9.417	0.7019
Nodule size (cm)	1.26	0.743	2.136	0.3909
Age	0.959	0.914	1.005	0.0816
Hashimoto's disease	5.544	1.24	24.794	0.025
Bethesda 3 vs Bethesda 4 classification	1.337	0.339	5.274	0.6784

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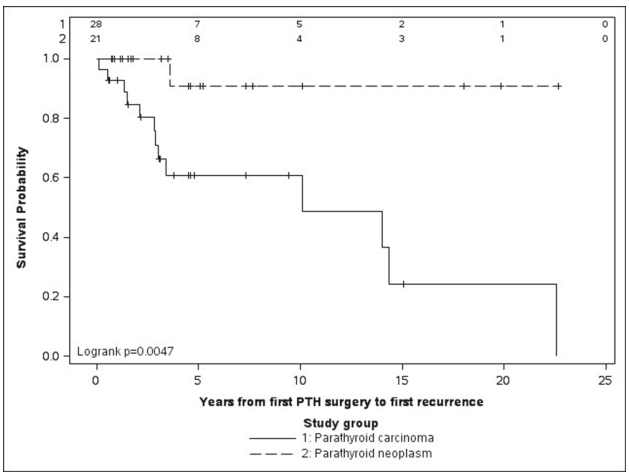
Differentiating Atypical Parathyroid Neoplasm from Parathyroid Cancer I. Christakis,* N. Bussaidy, C.N. Clarke, L. Kwatampora, C.L. Warneke, A. Silva, M.D. Williams, E. Grubbs, J.E. Lee, N.D. Perrier. *MD Anderson Cancer Center, Houston, TX.*

Introduction The differentiation of benign parathyroid gland atypia and true parathyroid carcinoma (PC) can be challenging. An accurate diagnosis involves the combination of histopathologic criteria together with clinical factors such as operative findings. In some instances patients may be classified as having "atypical parathyroid neoplasms" (APN), explicitly acknowledging that the distinction between benign and malignant disease appears impossible to determine. This "grey area" diagnosis makes rendering an accurate prognosis difficult, and clouds clinical management and treatment planning. Methods We performed a retrospective chart review of all adult patients undergoing surgery for primary hyperparathyroidism in our institution (2000-2014). Patients with a histopathological diagnosis of PC or APN were included. Demographics, clinical characteristics and survival rates were analyzed. PC and APN groups were compared using Fisher's exact test or Wilcoxon rank sums test, and the Kaplan-Meier method was used for time-to-event analysis Results There were 54 adult patients, 31 (57.41%) with PC and 23 (42.59%) with APN. PC versus APN was associated with higher parathyroid (PTH) hormone, ionized calcium, and serum calcium levels and with males ($p<0.05$). Five-year overall survival from diagnosis was 82.64% (95% CI 59.82% to 93.17%) for the PC group and 93.33% (95% CI 61.26 to 99.03%) for the APN group. Time from first parathyroid surgery to first recurrence was significantly shorter for those in the PC group (median 10 months, 95% CI 2.9 to 22.6) versus APN group (median not reached) ($p=0.0047$). Five-year recurrence-free survival rate was 60.80% (95% CI 37.49% to 77.70%) in the PC group and 90.91% (95% CI 50.81% to 98.67%) in the APN group. Conclusion PC and APN are distinct clinical entities with demonstrable differences in tumor biology reflected in overall recurrence rates, time to recurrence, disease-free survival and overall survival. APNs present with a less accentuated biochemical profile and demonstrate an indolent clinical course compared to PCs. Efforts to improve categorization and staging through molecular phenotyping of PC and APN is needed.



Kaplan-Meier plot of time from surgery to recurrence stratified by diagnostic group (n = 45).

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Understanding a Rare Disease's Impact on Health Systems: A Population-Based Economic Analysis of Neuroendocrine Tumors Costs J. Hallet,[1]* C. Law,[1] M. Cheung,[1] H. Fischer,[2] N. Liu,[2] N. Mittmann,[3] S. Singh.[1] *1. Surgery, Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada; 2. Institute of Clinical Evaluative Sciences, Toronto, ON, Canada; 3. Sunnybrook Research Institute, Toronto, ON, Canada.*

Background: While rare, neuroendocrine tumors (NET) are increasing in prevalence. Little is known on resource utilization and health care costs in NET care. We sought to define patterns of costs in NET management and compare them to a more common malignancy, colon cancer (CC). Methods:

We identified adults with NET in a universal healthcare system, using a provincial cancer registry (2004-2012). Colon cancer (CC) patients were matched (1:3) on age, gender, comorbidity, diagnosis year, income, and rurality. 2012 CND$ costs were obtained for 4 phases of care around date of diagnosis: pre-diagnostic (PrDx: -2 years to -181 days), diagnostic (Dx: -180 days to +180 days), post-diagnostic (PDx: +181 days to +3 years) and prolonged post-diagnostic (PPDx: +181 days to +9 years). Mean costs per patient were compared between NET and CC. Costs predictors were analyzed with quantile regression. Results: We included 3355 NET and 9320 matched CC. Mean NET cost was higher than CC in PrDx phase ($5877 Vs $5368; p=0.05), driven by higher non-drug costs including physician encounters, emergency room visits. Mean NET costs were lower in Dx and PDx phases (both p<0.01). In PPDx, drug costs were significantly higher in NET ($26788 Vs $7827; p<0.01), accounting for 41% of costs compared to 16% for CC. CC had a high initial increase in costs between PrDx and Dx, decrease by PDx, and gradual increase by PPDx. NET had steady increases between each phase, more pronounced in PrDx and PPDx. Older age, lower income, and comorbidities were predictors of higher NET costs in the 4 phases. Gastro-enteric primary site was associated with higher costs in PrDx (parameter estimate – PE $62), and lower costs in Dx (PE $13644). Pancreatic site was associated with higher costs in PDx (PE $3348) and PPDx (PE $1548). Conclusion: While rare, NETs are a potential significant societal burden. NET cost pattern differed from CC, with maximal costs during PrDx and PPDx phases. Primary NET site affected costs differently at different time points. Defining these cost patterns now allow for tailoring the use of healthcare resources to tumor type and timing in the patient journey.

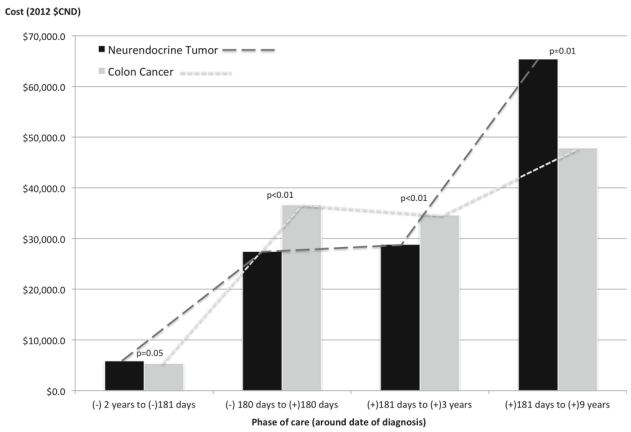

Figure 1. Overall mean healthcare costs per patient according to phase of care for neuroendocrine tumor and colon cancer.

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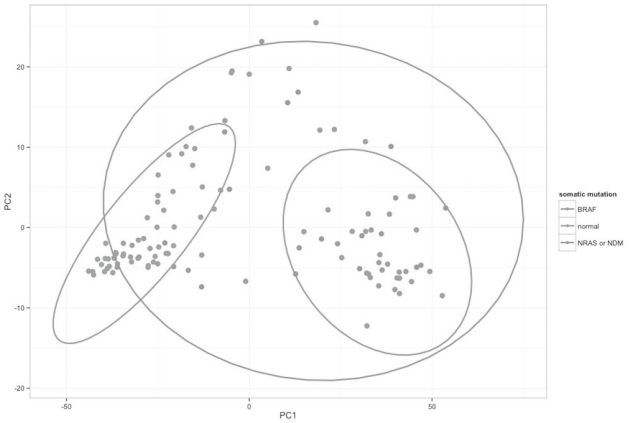
Epigenetic Alterations and Canonical Pathway Disruption in Papillary Thyroid Cancer: A Genome Wide Methylation Analysis M.G. White,[1]* S. Nagar,[1] B. Aschebrook-Kilfoy,[2] F. Jasmine,[2] M.G. Kibriya,[2] H. Ahsan,[2] P. Angelos,[1] E. Kaplan,[1] R.H. Grogan.[1]
1. Surgery, University of Chicago, Pritzker School of Medicine, Chicago, IL; 2. University of Chicago, Department of Public Health Sciences, Chicago, IL.

Introduction: Alterations in DNA methylation have been demonstrated in a variety of malignancies, including papillary thyroid cancer (PTC). The full extent of dysregulation in PTC and the downstream pathways effected remains unclear. Here we report a genome wide analysis of PTC methylation and the dysregulation of various canonical pathways. Materials/Methods: A discovery set utilized data from The Cancer Genome Atlas (TCGA) and a replication set was performed on resected human PTC specimens at our tertiary medical center. Forty-nine PTCs and matched normal controls were described from the TCGA, 16 PTCs and 13 controls were used as a replication set. Genome wide methylation was described using Illumina 450k methylation chips. Differentially methylated sites were identified by comparing PTC and matched normal tissues. Differential methylation was defined as FDR $p < 0.05$ and absolute $\Delta\beta \geq 0.2$. Differentially methylated genetic regions were then analyzed for pathway and disease commonalities. Results: Of 485,577 CpG sites analyzed 1,226 probes were differentially methylated in our discovery and replication setss, 1,061 (86.5%) probes showed hypomethylation when comparing tumor with normal tissue while 165 (13.5%) showed hypermethylation. Unsupervised cluster analysis was able to differentiate tumor with normal tissue in 117 of 127 samples (92.1%). Statistically significant associations with 64 canonical pathways ($p<0.05$) including PTEN, PI3K, molecular mechanisms of cancer, and p53. There were no differentially methylated regions when comparing tumors with and without lymph node metastases ($\alpha=0.46$), or extra-thyroidal extension ($\alpha=0.53$). Conclusion: Epigenetic dysregulation of multiple canonical pathways, including PTEN, PI3K, Molecular Mechanisms of Cancer and p53 are associated with the development of PTC. Dysregulation of does differentiate tumor from normal tissue.



Principal component analysis of the final replicated CIMP depicting tumore versus normal by somatic mutation

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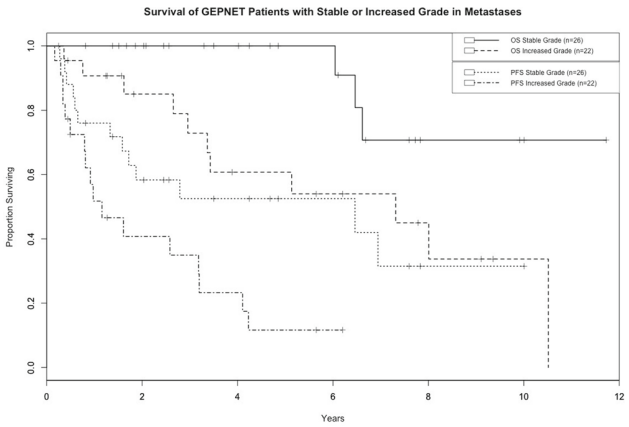
Higher Tumor Grade in Neuroendocrine Tumor Metastases Negatively Impacts Survival K.J. Keck,* J.E. Maxwell, A. Choi, G. Li, T.M. O'Dorisio, A.M. Bellizzi, J.R. Howe. *University of Iowa Carver College of Medicine, Iowa City, IA.*

Background: Tumor grade is an important predictor of survival in gastroenteropancreatic (GEP) neuroendocrine tumors (NETs), as determined by the percentage of cells expressing Ki-67 and mitotic rate. NETs generally grow indolently, but some cells may acquire traits facilitating metastasis. It is currently unclear how frequently metastases differ in grade from their primary tumors, and whether increasing grade in metastases affects prognosis. Methods: Ki-67 immunohistochemistry was performed on GEP NETs; data from 269 resected patients were reviewed to identify cases with Ki-67 results for both primary tumors and concurrent metastases. Grade was determined using the WHO classification (G1 Ki-67 0-2%; G2 >2-20%; G3 >20%). Clinicopathologic factors were examined using the Chi-square test, and survival calculated with the Kaplan-Meier method and log-rank test. Results: Fifty-one patients had Ki-67 performed on both their primary and metastases (43 with lymph nodes, 27 with liver). Tumor grade was higher in metastases from 22 (43%) patients, 21 from G1 to G2, and 1 from G1 to G3; 26 (51%) patients had no change in grade and 3 (6%) decreased from G2 to G1. The mean change in Ki-67 was 5.9% for the increased group (2.5% for all patients). No clinicopathologic factors were predictive of higher grade in metastases. The median progression free survival (PFS) was significantly improved for patients with stable versus increased grade (6.5 years vs. 1.2 years, p = 0.02); 5 year PFS was 52.5 % for patients with stable grade vs. 11.6% with increased grade. There were 3 deaths (12%) in the group with stable grade and 11 (50%) in those with increased grade (p= 0.02); median overall survival (OS) was not reached vs. 7.3 years, respectively (p=0.01; Figure). Conclusions: The Ki-67 grade of GEP NETs is an important prognostic tool. Nearly half of patients had a metastasis with a different grade than their primary, and when grade increased, both PFS and OS significantly decreased. These results suggest the importance of determining grade in both primaries and metastases for improved prognostication and to potentially guide future therapy.



Survival plot of Overal Survival (OS) and Progression Free Survival (PFS) for Increased Grade and Stable Grade groups.

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Association of Survival, Postoperative Morbidity and Mortality Following Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy Using Quality of Life Assessments R.M. Dodson,* H. Mogal, G. Russell, K.E. Duckworth, K. Votanopoulos, P. Shen, E.A. Levine, R.P. McQuellon. *Surgical Oncology, Wake Forest Baptist Health, Winston-Salem, NC.*

BACKGROUND: Cytoreductive surgery with hyperthermic intraperitoneal hyperthermic chemotherapy (CS+HIPEC) for peritoneal carcinomatosis can alleviate symptoms and prolong survival at the expense of morbidity and quality of life. The purpose of this study was to monitor health-related quality of life (HRQoL) and outcomes before and after CR+HIPEC. METHODS: This is the largest prospective HRQoL trial for patients that underwent CS+HIPEC for peritoneal cancers and participated in a HRQoL program from 2000-2015. Surveys consisted of the Short Form-36 (SF-36), Functional Assessment of Cancer + colon subscale (FACT-C), Brief Pain Inventory (BPI), Center for Epidemiologic Studies Depression Scale (CESD), and ECOG performance status rating before and after surgery at 3, 6, 12, and 24 months. The trial outcome index (TOI), a combination of physical (PWB) and functional well-being subscales + the colon-specific subscale of the FACT-C, was analyzed. Proportional hazards were used to model the effect of baseline HRQoL on overall survival. RESULTS: There were 598 patients (53.8% female) with a mean age of 53.3 years (SD 12.1; range18-81). Overall 1 yr survival was 76.8%; median survival was 2.9 years. 30-day minor morbidity was 29.3 %, major morbidity was 21.7% and mortality was 3.5%. BPI ($p<0.0001$), worst pain ($p=0.004$), and CESD ($p<0.0001$) increased at 3 months but returned to baseline at 6 months. FACT Emotional well-being, SF-36 Mental component score, and Emotional health improved after CS+HIPEC (all $p<0.001$). Higher baseline FACT (HR 0.92 for 5 unit change, CI 0.09-0.96), FACT-C (0.73, CI 0.65-0.83), PWB (HR 0.71, CI 0.64-0.78), TOI (HR 0.87, CI 0.84-0.91), and SF-36 vitality (HR 0.88, CI 0.83-0.92) were associated with improved survival (all $p<0.001$). Higher baseline BPI (HR 1.1 for 1 unit, CI 1.05-1.14; $p<0.0001$) was associated with worse survival. CONCLUSIONS: Although CS+HIPEC is associated with perioperative morbidity and detriments to HRQoL, recovery occurs at or before 6 months. In addition to ECOG and patient related factors, HRQoL is associated with mortality following CS+HIPEC.

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A Picture is Worth a Thousand Words: Intraoperative Photography as a Quality Metric for Axillary Dissection B.L. Murphy,* J.C. Boughey, A.C. Degnim, T.J. Hieken, W.S. Harmsen, J.W. Jakub. *General Surgery, Mayo Clinic, Rochester, MN.*

Introduction The adequacy of axillary lymph node dissection (ALND) is frequently measured by the number of LNs pathologically identified. This metric may not equate to the quality of surgical technique, since many other factors contribute to the LN count. We hypothesized that intraoperative photos are an objective measure of the adequacy of ALND and can be reproducibly assessed by independent observers. Methods Intraoperative photos of the axilla were prospectively obtained after ALND. An objective scoring system was created based on anatomic landmarks, with a maximum score of 8. Photos of each case were scored by 3 independent surgeons. Factors that may influence the number of LNs and the ALND score were evaluated for correlation. Inter-rater variability was calculated between raters and for each anatomic landmark. Results 96 cases were evaluated, 84 breast and 12 melanoma. Mean LN count was 24.5(IQR 17-31). 88.5% of cases had a LN count > 15. Factors associated with higher number of LNs were melanoma($p<0.001$), male sex($p=0.015$), visualization of the axillary vein($p=0.04$) and subscapularis muscle ($p=0.02$). Visualization of the latissimus did not reach significance($p=0.06$). No significant difference was associated with patient age, BMI, number of positive LNs, or matted LNs. The mean ALND score was 5.6 (SD1.4). For a change of 1 point in the total score, there was a mean increase of 2.3 LNs identified ($p=0.003$). Intra-class correlations for inter-rater reliability between pairs of surgeons varied from 0.46 to 0.52. The mean ALND photo score was 5.6(SD 1.4) in cases with >15 LNs compared to 4.9(SD 0.9) in cases with <15 LNs($p=0.07$). Conclusion Photographic visualization of axillary anatomic structures correlated with the number of LNs pathologically identified. Photo documentation of ALND should provide a simple quality indicator. Reproducibility of visual assessment varies across features and some anatomic landmarks better correlate with LN yield; thus certain features may be better to include as quality indicators. These findings support pursuing a larger study with greater variability in LN count in order to define optimal photo metrics of adequate ALND.

Variable	Number of additional nodes identified for each variable	p-value
Melanoma	12.71	0.0001
Male gender	8.90	0.015
BMI, per 1 point	0.07	0.69
Age, per 10 years	-0.86	0.27
# of positive lymph nodes	0.009	0.96
Matted lymph nodes	-3.49	0.54
Neoadjuvant chemotherapy	-3.11	0.16
Subscapularis muscle visualized	5.18	0.02
Axillary vein visualized	8.26	0.04
Latissimus dorsi muscle visualized	4.23	0.06
Lateral border of pectoralis major visualized	2.15	0.45
Dissection deep to pectoralis minor visualized	3.39	0.13
Long thoracic nerve visualized	3.33	0.17
Serratus anterior muscle visualized	2.89	0.44
Thoracodorsal bundle visualized	0.00	N/A

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Improving Hospital Level Quality Assessment in Rectal Cancer Surgery S. Patel,[1]* C. Hu,[1] N. Massarweh,[2] Y. You,[1] B. Bednarski,[1] C.A. Messick,[1] M. Rodriguez-Bigas,[1] J.M. Skibber,[1] B. Feig,[1] G. Chang.[1] *1. MD Anderson Cancer Center, Houston, TX; 2. Michael E. Debakey Department of Surgery, Baylor College of Medicine, Houston, TX.*

Background: Surgical margin positivity(MP) after rectal cancer surgery is associated with poor outcomes. Our group previously showed hospital risk-adjusted margin positivity rate(RAMP) was an important potential quality metric. However, circumferential radial margin(CRM) status has only recently become available within the National Cancer Data Base(NCDB). We sought to improve RAMP performance as a quality metric with incorporation of quantitative CRM into a more robust measure of margin status. Methods: This was a cohort study of NCDB patients with rectal cancer(2010-2012). Composite resection margin(RM) indicator was defined as CRM(≤1 mm) or surgical MP. Hospital performance categorized as low outlier(better than expected) and high outlier(worse than expected) using observed to expected ratio methods. The RM indicator and surgical MP were compared at the hospital level and kappa coefficient was used to determine agreement with <1.0 indicating potentially improved sensitivity. Results: 32,663 patients with rectal cancer treated at 1,302 hospitals met inclusion criteria. Surgical MP was 6.1%, CRM(≤1mm) +ve in 13.9%, and composite RM(MP or CRM ≤1mm) +ve in 15.8%. By O:E using MP, 5.3% of hospitals were high outliers and 1.8% were low outliers. Using the composite RM indicator, 9.8% of hospitals were high and 6.3% were low outliers. Kappa coefficient between the surgical MP group and RM indicator was 0.84. 13.3%(n=162) of MP non-outlier hospitals became either high(n=93, 57.4%) or low(n=69, 42.6%) outliers using the composite RM indicator. Facility type, hospital volume, neoadjuvant radiation use, sphincter preservation, and 30d readmission rates were significantly associated with composite RM outlier status. Conclusion: The composite RM indicator is a

more robust quality measure with improved sensitivity for detecting both high/low outliers. Correlation of the RM indicator with previously demonstrated structure, process, and outcome factor supports its role in assessing hospital based quality measures. However, upcoming U.S. quality improvement initiatives for rectal cancer will need to focus on ensuring high quality data collection to accurately identify at-risk and high performing hospitals.

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Cancer Specialists' Attitudes and Practices Regarding Disclosure, Feedback and Reporting of Pre-Referral Medical Errors L. Dossett,* M.C. Lee, R.J. Gonzalez, G. Quinn. *Complex General Surgical Oncology, Moffitt Cancer Center, Tampa, FL.*

Background. Recent emphasis on the quality of cancer care highlights the identification, avoidance, and mitigation of medical errors. Physicians are encouraged to disclose their own errors and confidential institutional peer-review processes facilitate quality improvement, but no mechanisms exist for disclosure, reporting or feedback when care spans institutions or health systems. We sought to describe attitudes and practices regarding disclosure, reporting, and feedback of pre-referral errors discovered by cancer specialists. Methods. We conducted face-to-face qualitative interviews with cancer specialists at a single NCI-designated cancer center, using a semi-structured interview guide. Interviews (30-60 minutes) were audiotaped, transcribed verbatim, and independently coded for a priori and emergent themes using the constant comparative method. Open and axial coding were applied using content analysis. Results. All participants were fellowship-trained cancer specialists of various disciplines (n=20, 35% female). The median years of post-graduate training was 8 (range 6-10); median years of independent practice was 9 (range 2-35). Subjects encountered pre-referral errors of diagnosis (incorrect/delayed), incorrect treatment, and under/over-treatment. Participants described adverse events ranging from decreased quality of life to premature death after disease progression. Specialists had varying practices of disclosure (Table 1); they rarely, if ever, reported errors, and differed in the frequency and methods of feedback to referring physicians. Participants were nearly unanimous in describing medico-legal implications, damage to referral relationships, and avoiding a superiority image as barriers to disclosure, reporting, and providing feedback. Conclusions. Cancer specialists encounter pre-referral errors, but consensus practices regarding disclosure of errors to patients and providing feedback to referring physicians is lacking.

Table 1. Summary of Key Themes Related to Pre-Referral Error Disclosure, Feedback and Reporting

	Key Theme	Statement
Disclosure	No disclosure	"You have a vulnerable person and family, and to go in and stir the pot so to speak—you can't change the past. I don't see that rehashing it is appropriate. Is it serving them to know that someone made an error?"
	Vague disclosure	"I try not to label it as an error. I try not to use comments to the patient like 'standard of care'."
	Explicit disclosure	"In that case where the mass was there and was totally missed and the patient presented with stage IV disease, I definitely showed that image to the patient and the patient was aware."
Reporting	No reporting	"There was one case where I said to my colleague, 'I should report this to the Board of Medicine.' That's how strongly I felt. It was so botched. Would I do that? No. Obviously I thought about, but would I ever execute it? I don't know, I don't think so."
Feedback	No feedback	"We are obligated to call our referring physicians and to communicate with them, but certainly there is no rule about telling them that they screwed up, so I think most people are not doing that—even when it's clear they did."
	Passive feedback	"Most of the cases will simply get our clinic notes that will generally describe the facts and how we interpret them."
	Limited feedback	"I do give feedback to people in my specialty, people in other specialties I do not. I don't call a surgeon to ask him why he left a positive margin or why he would do surgery in a patient with lung mets."
	Emphasize feedback	"Feedback is very important. Most people are not out there trying to do harm, it's just a lack of education or knowledge, so I try to provide that."
Barriers	Medico-legal implications	"The last thing any of us wants is to get bogged down in some malpractice suit based on what you said. It's a nightmare that no one wants because they know how the justice system works, and it's terrible."
	Avoiding a superiority image	"The barrier I have in providing feedback is trying to not come off as being on a different level from that individual. I don't want to make that provider feel as if I am better than them, or that they are inferior."
	Concern for referral patterns	"You don't want to say that this provider down the road did something wrong because that provider might be a big referral base for you. You might put that in jeopardy."

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Postoperative Complications and Long-term Survival After Complex Cancer Resection H. Nathan,* H. Yin, S.L. Wong. *University of Michigan, Ann Arbor, MI.*

Introduction: Recent attention has focused on the ability to "rescue" patients from post-operative complications and prevent short-term mortality. However, few studies have examined whether "rescued" patients have similar long-term outcomes as those with uncomplicated cancer resections. Methods: From 2005-2009 SEER-Medicare data, we identified patients (pts ≥65 years old who underwent resection for cancers of the esophagus, lung (lobectomy), or pancreas. Pts admitted ≥2 days before surgery were excluded. Complications were ascertained using standard codes derived from the Complications Screening Project. Serious complications were defined as complications associated with LOS >75th %ile. Cox proportional hazards models were used to risk-adjust survival for age, gender, comorbidity, stage, and resection subtype. Results: The study included 965 esophagus, 12,395 lung, and 1966 pancreas cases. Rates of 30-day mortality were 6.2%, 3.3%, and 3.9%. Serious complication rates were 17%, 10%, and 12%. Pts with serious complications had lower 5-year survival than those with no complications even if they were "rescued" and survived 30 days: 20% vs 43% for esophagus, 29% vs 54% for lung, and 10% vs 21% for pancreas. In fact, a decrement in risk-adjusted long-term survival was observed even among pts with serious complications who survived 180 days after surgery (Table). Infectious complications constituted 47% of all complications for esophagus, 22% for lung, and 45% for pancreas. Pts with infectious versus non-infectious complications had decreased 5-year survival for lung (26% vs 32%, P<0.0001) and pancreas (9% vs 15% P<0.01). In stage-specific and age-specific analyses, receipt of chemotherapy was significantly decreased among pts with serious complications (e.g., 53% vs 19% for uncomplicated vs seriously complicated stage II lung cancer resection, P<0.0001). Conclusions: Pts who undergo complex cancer resection and experience serious complications have diminished long-term survival even if they are "rescued" and survive >6 months past their surgery. Metrics of surgical success should consider terms beyond 30 and even 90 days and consider the long-term consequences of surgical complications.

Risk-Adjusted* Long-Term Survival for Patients with Complications after Complex Cancer Resection

	Adjusted Hazard Ratio [95% Confidence Interval]		
Esophagus	Survived 30+ days	Survived 90+ days	Survived 180+ days
No complication	*Ref.*	*Ref.*	*Ref.*
Mild complication	1.11 [0.88, 1.41]	1.08 [0.84, 1.38]	0.98 [0.75, 1.28]
Serious complication	2.55 [2.05, 3.16]	1.97 [1.53, 2.53]	1.63 [1.22, 2.17]
Lung			
No complication	*Ref.*	*Ref.*	*Ref.*
Mild complication	1.23 [1.11, 1.36]	1.25 [1.12, 1.39]	1.26 [1.13, 1.40]
Serious complication	2.13 [1.96, 2.32]	1.74 [1.59, 1.91]	1.60 [1.45, 1.77]
Pancreas			
No complication	*Ref.*	*Ref.*	*Ref.*
Mild complication	1.06 [0.88, 1.28]	1.04 [0.86, 1.26]	0.99 [0.80, 1.22]
Serious complication	1.57 [1.34, 1.84]	1.44 [1.22, 1.70]	1.31 [1.09, 1.58]

*Adjusted for age, gender, comorbidity, stage, and resection subtype.

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Hypophosphatemia as a Novel Early Predictor of Intra-Abdominal Infections in 7,423 Patients Undergoing Colorectal Surgery E. Sadot,* G. Nash, J.J. Smith, J.G. Guillem, P.B. Paty, L.K. Temple, J. Garcia-Aguilar, M. Weiser. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Early indicators of intra-abdominal infections (IAI) could help identify those patients eligible for early discharge as part of Enhanced Recovery After Surgery (ERAS) protocols. Hypophosphatemia has been identified as one such indicator and our goal was to evaluate hypophosphatemia after colorectal resection as an early predictor of IAI. Methods: Consecutive patients who underwent their first colon or rectal resection at a single institution were included. IAI were defined as anastomotic leakage or intra-abdominal infection or abscess. Postoperative serum phosphate levels and other IAI risk factors were analyzed and logistic regression was used to construct a risk prediction model. Results: From 2005 through 2015, 7423 patients were included, the median age was 61 years (IQR: 51-70), and the most common indications for surgery were colon cancer (43%) and rectal cancer (26%). The IAI rate was 5%. Compared to normophosphatemic patients, hypophosphatemia on postoperative day 3 (POD3) was associated with a 50% increased risk of IAI (p=0.001, Figure 1A). In a multivariable model, POD3 hypophosphatemia (p=0.03, OR=1.4, CI 1.1-2.0), combined liver resection (p<0.001, OR=1.9, CI 1.3-2.6), BMI >30 kg/m^2 (p=0.04, OR=0.7, CI 0.5-0.9), abnormal WBC on POD3 (p<0.001, OR=1.9, CI 1.3-2.6), and estimated blood loss >400cc

(p=0.01; OR=1.7; CI 1.1-2.5) were independently associated with IAI and used to construct an IAI risk prediction tool, which had a negative predictive value of 95%. Compared to the low risk group, moderate and high-risk cohorts had double and triple the rates of IAI (5%, 10%, and 17%, respectively, p<0.001). The c-index of the model was 0.66 (Figure 1B). Conclusions: The association between hypophosphatemia and IAI after colorectal resection is a novel finding, and early postoperative hypophosphatemia was an independent predictor of IAI. The IAI risk prediction model that includes this variable accurately identified low-risk patients, which are ideal candidates for early discharge. This model may be used in conjunction with an ERAS pathway to safely reduce hospital length of stay.

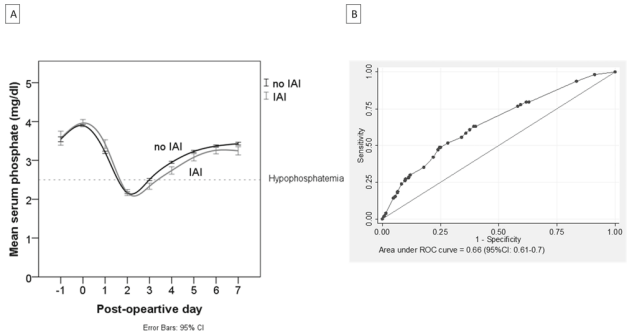

Figure 1.
Colorectal resection (n=7423) and perioperative serum phosphate level (A).
ROC curve of the prediction model (B).

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Race-Based Socioeconomic and Treatment Disparities in Adolescent and Young Adults with Stage II-III Rectal Cancer D. Lee,[1]* A. Teng,[2] R.C. Pedersen,[3] F.R. Tavangari,[3] V. Attaluri,[3] M.C. Elisabeth,[3] S.L. Stern,[3] A.J. Bilchik,[3] M. Goldfarb.[3] *1. John Wayne Cancer Institute, Los Angeles, CA; 2. Mount Sinai St. Lukes Roosevelt Hospital Center, New York, NY; 3. Kaiser Permanente, Los Angeles, CA.*

Introduction: Stage II-III rectal cancer (CA) requires a multidisciplinary approach to optimize outcomes. This study explores whether treatment disparities account for racial differences in outcomes of AYA (ages 15-39) patients. Methods: AYAs with clinical stage II-III rectal CA were identified in the National Cancer Database. Demographic, clinical, and pathologic features predictive of receipt of adjuvant and surgical therapies were examined as well as factors associated with overall survival (OS). Results: Most of the 3,295 patients were white (72.0%), male (57.5%) and free of comorbidities (93.8%). Income, education levels, and rates of health insurance coverage were higher for whites than for blacks or Hispanics. Clinical stage was balanced by race, but more blacks and Hispanics did not receive radiation (24.5% and 27.1%, respectively, vs 16.5% for whites), surgery (22.4% and 15.3%, vs 12.3%), or chemotherapy (21.5% and 24.1%, vs 16.7%; p<0.05). Additionally, the average number of days before treatment was 34.0 for blacks and 33.3 for Hispanics, versus 27.5 for whites (p<0.05). Multivariate analysis showed that receipt of neoadjuvant chemoradiation was less likely when patients were black (OR 0.7, 95%CI 0.5-0.9, p=0.014), Hispanic (OR 0.6, 95%CI 0.4-0.9, p=0.012), female (OR 0.8, 95% CI 0.63-0.94, p=0.011), without insurance (OR 0.5, 95%CI 0.36-0.69, p<0.001), or treated at a community cancer center (OR 0.5, 95%CI 0.36- 0.74, p<0.05). Race significantly influenced treatment, regardless of disease stage. Although 5-year OS was lower (p<0.05) in blacks (59.8±3.3%) and Hispanics (65.9±3.5%) compared to whites (74.9±1.1%), race did not impact mortality on Cox regression. Instead, mortality was associated with male sex (HR 1.5, 95%CI 1.1-2.0, p=0.009), nodal positivity (HR 2.6, 95%CI 1.9-3.6, p<0.001), nonsurgical therapy (HR 7.1, 95%CI 2.8-18.2, p<0.001), no chemotherapy (HR 1.9, 95%CI 1.03-3.6, p=0.04), poorly differentiated histology (HR 3.0, 95%CI 1.3-6.5, p=0.007), and no insurance (HR 1.7, 95%CI 1.1-2.7, p=0.022). Conclusions: Race-based socioeconomic and treatment disparities may contribute to survival differences among AYAs with rectal cancer.

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Modified Frailty Index (mFI) to Predict Morbidity and Mortality After Pancreatectomy R. Shah,* E. Gabriel, A. Visioni, K. Attwood, S. Nurkin, S. Hochwald, M. Kukar. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Background: Pancreatic surgery is associated with significant morbidity and mortality. This retrospective study examined use of a modified frailty index (mFI) as a potential predictor of morbidity and mortality in patients undergoing pancreatic surgery. Methods: National Surgical Quality Improvement Program (NSQIP) Participant Use Files were reviewed from 2005 through 2010. Patients undergoing pancreatectomy were selected based on CPT codes. A modified frailty index (mFI) with 15 variables (functional status, diabetes, COPD, h/o pneumonia, CHF, MI, PCI, angina, hypertension, impaired sensorium, TIA, neurological deficit, PVD, rest pain and pre-operative albumin < 2.5) based on mapping the Canadian Study of Health and Aging Frailty Index to NSQIP comorbidities was used. Statistical analysis was performed using Kruskal-Wallis and Pearson's chi-square tests. A multivariate logistic regression model was used to evaluate association between 30-day mortality and modified frailty index (mFI) while adjusting for demographic characteristics. Results: A total of 11,327 patients were included in the analysis. Morbidity and mortality uniformly increased as the mFI increased. 5.2% of patients with mFI of 0 had a Clavien Grade 4 complication, compared with 29.7% of patients with mFI of 0.27 (p < 0.001). The complication rates between patients with a mFI of 0 & mFI of 0.27 was 3.4% vs 8% for post- operative pneumonia, 2.7% vs 13% for reintubation, 2.9% vs 20.3% for prolonged ventilation, 0.2 % vs 1.4% for MI and 2.5 % vs 14.5% for shock respectively (p < 0.001). An mFI of 0 was associated with a mortality rate of 1.6% compared with 10.4% for an mFI of 0.27 (p < 0.001). When using multivariate logistic regression to predict 30-day mortality age, race, ASA and mFI were significant; with mFI being the single most important factor with an odds ratio of 1.36 (p < 0.001) for every 0.067 unit increase. Conclusions: Using NSQIP dataset, mFI correlates well with post- pancreatectomy morbidity and as a standalone, the most significant predictor of 30-day mortality. It can be used as a simple tool to predict post operative outcomes.

Patient outcomes by modified Frailty Index (mFI)

	mFI=0	mFI=0.067	mFI=0.13	mFI=0.20	mFI=0.27	mFI=0.33	mFI≥0.4	P-value
Overall	4,514 (39.9)	4,312 (38.1)	1,764 (15.6)	549 (4.8)	138 (1.2)	38 (0.3)	12 (0.1)	
Clavien Grade 4	236 (5.2%)	368 (8.5%)	196 (11.1%)	99 (18.0%)	41 (29.7%)	13 (34.2%)	5 (41.7%)	<.001
Post-op Pneumonia	153 (3.4%)	227 (5.3%)	114 (6.5%)	59 (10.7%)	11 (8.0%)	5 (13.2%)	2 (16.7%)	<.001
Reintubation	120 (2.7%)	204 (4.7%)	100 (5.7%)	51 (9.3%)	18 (13.0%)	6 (15.8%)	3 (25.0%)	<.001
Prolonged Ventilation	133 (2.9%)	217 (5.0%)	122 (6.9%)	65 (11.8%)	28 (20.3%)	10 (26.3%)	5 (41.7%)	<.001
Myocardial Infarction	7 (0.2%)	24 (0.6%)	18 (1.0%)	8 (1.5%)	2 (1.4%)	1 (2.6%)	2 (16.7%)	<.001
Shock	112 (2.5%)	164 (3.8%)	81 (4.6%)	45 (8.2%)	20 (14.5%)	9 (23.7%)	2 (16.7%)	<.001
30-day Mortality	58 (1.6%)	109 (3.1%)	65 (4.4%)	33 (7.0%)	12 (10.4%)	6 (20.0%)	6 (54.5%)	<.001

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Aberrant Expression of Epigenetic Modifiers in Dedifferentiated Liposarcoma (DDLS) and the Effects of Dual Inhibition of DNA and Histone Methylation in DDLS Cell Lines A.M. Velez,* T. Okada, S. Singer. *Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

INTRODUCTION: Dedifferentiated liposarcoma (DDLS) is largely resistant to conventional chemotherapy, making it crucial to identify new therapeutic strategies. Aberrant DNA methylation has been identified as a potential epigenetic target in DDLS; however, little is known of the role of histone modifications. We assessed expression of chromatin modifier genes in DDLS patient samples and tested dual inhibition of DNA methylation and the histone methyltransferase EZH2 in cell lines. METHODS: U133A microarrays were used to analyze 79 well-differentiated liposarcoma (WDLS), 84 DDLS, and 23 normal fat tissue samples. In cell lines, quantitative rtPCR was used to assess mRNA levels and western blots were used to assess levels of proteins and histone methylation. Cell lines were treated with vehicle, 5-aza-2′-deoxycytidine (5-aza-dC) or GSK126. Cell proliferation was analyzed by CyQuant

and apoptosis by annexin V staining. RESULTS: Microarray analysis revealed EZH2 and other members of polycomb repressive complex 2 (PRC2) to be significantly overexpressed in WDLS and DDLS (Table 1). For EZH2, both mRNA and protein were elevated in DDLS cells compared to adipose-derived cell lines, with the mRNA elevated up to 8 fold and correlated with global H3K27me3 levels. Combined treatment with a selective EZH2 inhibitor, GSK126, and DNA methyltransferase inhibitor, 5-aza-dC, decreased cell proliferation and increased apoptosis in DDLS cells; adipocyte-derived stem cells were less sensitive. The combination also induced expression of adipocytic differentiation genes more than either drug alone. CONCLUSIONS: DDLS tumors and cell lines overexpress EZH2 and other PRC2 complex genes and have associated global elevation of H3K27me3. Dual targeting of epigenetic silencing mechanisms via inhibition of DNA methylation and H3K27me3 results in reactivation of differentiation pathway genes and has anti-proliferative and pro-apoptotic effects on DDLS cells. Our results suggest the potential value of combining targeted epigenetic blockades as a differentiation-based therapy for patients with liposarcoma.

Table 1. mRNA expression of PRC2 complex genes in tumor compared to normal fat (NF)

Gene	DDLS/NF		WDLS/NF		DDLS/WDLS	
	FC	FDR	FC	FDR	FC	FDR
EZH2	4.7	$4 \bullet 10^{-9}$	—		4.0	$2 \bullet 10^{-8}$
SUZ12	1.8	0.000004	1.6	0.000007	—	
EED	1.8	$4 \bullet 10^{-7}$	1.6	0.00002	—	
RBBP7	1.9	0.00003	1.4	0.000008	—	
RBBP4	1.7	0.005	—		—	

FC, fold change; FDR, false discovery rate. FDR<0.05 was considered significant. Fold changes that were not significantly different from 1 are indicated with a dash.

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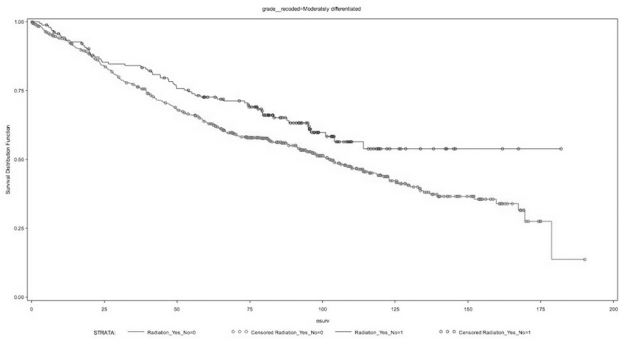
Impact of Radiation Therapy on Retroperitoneal Sarcoma D. Lee,[1]* L. Lim,[2] K.T. Huynh,[1] R.C. Wollman,[1] S.L. Stern,[1] L.J. Foshag,[1] A.J. Bilchik,[1] M.B. Faries,[1] M. Goldfarb.[1] *1. John Wayne Cancer Institute, Los Angeles, CA; 2. Kaiser Permanente, Los Angeles, CA.*

Introduction: The role of external beam radiation therapy (EBRT) for resectable retroperitoneal sarcoma (RPS) remains unclear due to the tumor's infrequency and heterogeneous histology. Methods: 11,964 patients who underwent resection for RPS were identified in the National Cancer Database; those that received EBRT (adjuvant n=2558, neoadjuvant n=727) were compared to those that did not (n= 8679). The effect of EBRT on overall survival (OS) in relation to margin status, histology and tumor grade was studied. Results: Factors associated with receipt of EBRT were male gender (OR 1.2, CI: 1.1-1.3, p=0.002), positive microscopic margin (OR 1.4, CI: 1.3-17, p<0.001), histology other than well-differentiated liposarcoma (LPS) (OR 1.6, CI: 1.3-2.0, p <0.001), and tumor size ≥ 5 cm but < 20 cm (1.4 CI: 1.2-1.6, p<0.001). Overall, patients receiving EBRT had improved 5-year OS (61.0% vs. 57.1%, p=0.005); this improvement was modest (64.8% vs. 61.0%, p=0.043) in patients with negative margins but larger for patients with microscopic (55.0% vs. 47.7%, p=0.014) or macroscopic (39.8% vs. 23.4%, p=0.042) positive margins. Although EBRT did not improve 5-year OS for patients with well-differentiated LPS (90.6% vs 80.1%, p=0.065), it improved OS for leiomyosarcoma (55.5% vs 39.1%, p=0.054), malignant fibrous histiocytoma (57.4% vs 45.6%, p<0.001), and dedifferentiated LPS (55.0% vs 45.7%, p = 0.040). Moreover, EBRT did not improve 5-year OS for patients with well-differentiated tumors, (82.8% vs 79.0%, p=0.202), but did improve OS for higher-grade tumors (Figure). After controlling for tumor features, positive macroscopic margins was the strongest predictor of mortality (HR 3.07, CI 2.62-3.60, p <0.001), followed by high tumor grade (HR 2.82, CI 2.39-3.33 <0.001); comorbidities, government insurance, larger tumor size, and non-well-differentiated LPS histology also increased risk of death. However, EBRT remained an independent predictor of improved OS (HR 0.68, CI 0.62-0.76) and the timing of EBRT had no effect. Conclusions: EBRT improved OS in patients with RPS who had surgical resection. The benefit of EBRT was most evident in those with positive margins and higher grade tumors.

Tumor grade = Moderately differentiated

Radiation	Event / Total N	Median OS (mos)	Estimated Overall Survival Rate ± SE (%)	
			5-year	10-year
No	285 / 577	103.0	63.6 ± 2.1	44.3 ± 2.5
Yes	62 / 167	NA	72.6 ± 3.5	53.9 ± 5.1
	347 / 744			

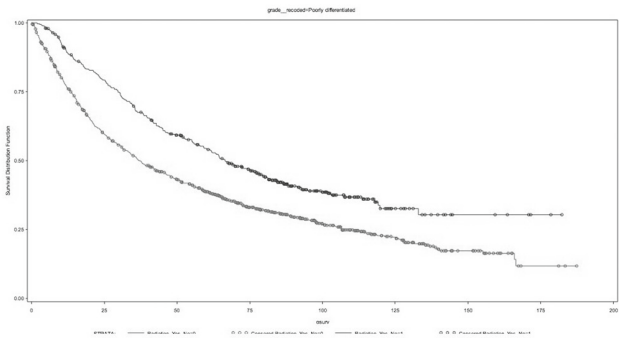
P=0.0167



Tumor grade = Poorly differentiated

Radiation	Event / Total N	Median OS (mos)	Estimated Overall Survival Rate ± SE (%)	
			5-year	10-year
No	741 / 1051	37.1	38.7 ± 1.6	22.7 ± 1.6
Yes	255 / 436	66.6	54.6 ± 2.4	32.6 ± 3.1
	996 / 1487			

P<0.0001



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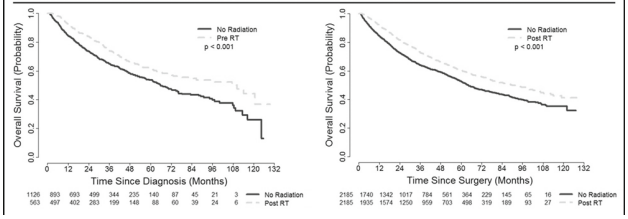
Radiation Therapy is Associated with Improved Survival for Retroperitoneal Sarcoma: A Contemporary Analysis of 9,068 Patients D.P. Nussbaum,[2]* C.N. Rushing,[1] W.O. Lane,[2] D.M. Cardona,[3] D.G. Kirsch,[4] B.L. Peterson,[1] D. Blazer.[2] *1. Duke University School of Medicine Department of Biostatistics & Bioinformatics, Durham, NC; 2. Duke University School of Medicine Department of Surgery, Durham, NC; 3. Duke University School of Medicine Department of Pathology, Durham, NC; 4. Duke University School of Medicine Department of Radiation Oncology; Department of Pharmacology and Cancer Biology, Durham, NC.*

Introduction: Recruitment into clinical trials for retroperitoneal sarcoma (RPS) has been challenging, resulting in termination of the only U.S. randomized trial investigating radiation therapy (RT). Nonetheless, use of RT has increased over the past decade, substantiated primarily by its established role in extremity sarcoma. Methods: Patients in the 2003-2011 NCDB that underwent resection of RPS were classified by use of RT: preoperative RT (preRT), postoperative RT (postRT), and no RT (noRT). Logistic regression was used to determine factors associated with preRT and postRT. Variables retained in these models were used to develop propensity scores, on which preRT and postRT patients were separately matched to noRT patients. Overall survival (OS) between matched groups was estimated using the Kaplan-Meier method. Adjusted OS was evaluated with Cox proportional hazards. Results: In total, 9,068 patients were included: 563 preRT, 2,215 postRT, and 6,290

noRT. Compared to community hospitals, treatment at academic centers was associated with increased use of preRT (OR 7.98, p<0.001) and decreased use of postRT (OR 0.57, p<0.001). Other independent predictors of preRT and postRT were identified (data not shown) and incorporated into propensity scores. Matching resulted in two comparison groups (preRT vs. noRT and postRT vs. noRT) with negligible differences in histologic diagnosis as well as all demographic, clinicopathologic, and treatment-level variables (all std. diff. <0.10). Compared to noRT patients, median OS was 110.2 vs. 65.8 months for preRT and 89.9 vs. 64.2 months for postRT (both p<0.001; Figure 1). Following further adjustment, both preRT (HR 0.67, p<0.001) and postRT (HR 0.77, p<0.001) remained independently associated with improved OS. Conclusions: In this largest study to date, RT is associated with improved OS when delivered as either preRT or postRT. As we await results from the ongoing EORTC trial investigating preRT for RPS, these data support the increasing use of RT in this disease. Future studies must identify patients most likely to benefit from RT and define optimal strategies for the delivery of perioperative RT.

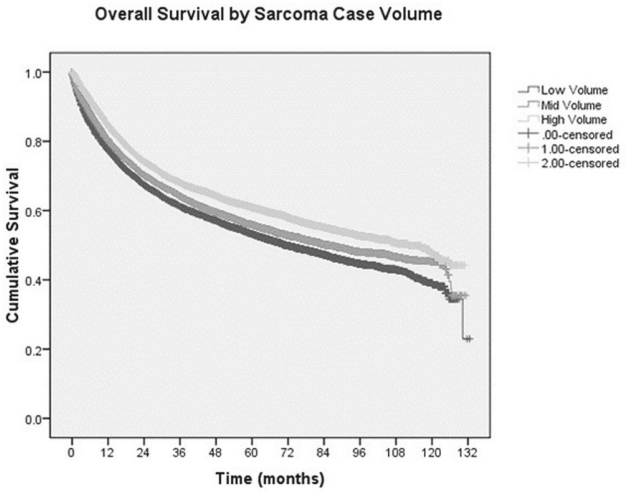
Figure 1. Estimated survival of propensity-matched groups for preoperative RT (left) and postoperative RT (right), respectively, versus no perioperative RT



88

Is there a Volume-Outcome Relationship for Short and Long-term Outcomes in Soft Tissue Sarcoma? Results from Analysis of the U.S. National Cancer Data Base S. Bagaria,* R.J. Gray, S. Attia, J. Ashman, N. Wasif. *Surgery, Mayo Clinic, Jacksonville, FL.*

Introduction Soft tissue sarcoma (STS) is a group of over 50 rare malignancies requiring expert multi-disciplinary care and coordination for optimal treatment. Although a volume-outcome relationship has been shown for other cancers, such a relationship has not been established for STS. We sought to study the association between STS volume seen by a hospital with short and long term outcomes. Methods The US National Cancer Database was queried for soft tissue sarcomas diagnosed between 2003 and 2006. Clinical, pathological, and hospital data were collected. Outcomes measured included R0 margin status, 30-day surgical mortality, and overall survival (OS) defined as time from diagnosis to last follow up or death. Risk-adjusted regression analyses were performed to identify predictors of these outcomes. Mean annual volume for STS surgery and total STS cases were calculated for all hospitals and divided into terciles of low, medium and high volume. Results Our study cohort included 21,608 patients with STS. Median age was 57 years and median tumor size was 7.5 cm. Surgery was performed in 70% of patients with an R0 resection rate of 78% and a 30-day mortality of 1.2%. OS was 54% at 5 years, with a median follow up of 52 months. Hospitals performing high volume surgery (>11.6 operations/year) were more like to achieve an R0 resection (83.5% vs. 73.4%, adjusted OR=1.73; p<0.001) and have a lower 30-day mortality (0.6% vs. 1.7%, adjusted OR=0.61; p=0.047) than hospitals performing low volume surgery (<3.6 operations/year). Patients treated at hospitals with a high volume of STS patients (>14.1 patients/year) had better long term OS (58% vs. 50% 5-year OS, adjusted HR=0.92; p=0.006) than those treated at low volume sarcoma hospitals (<3 patient/year). Conclusion Hospitals that treat a high volume of STS patients have a higher rate of R0 resection, lower 30-day mortality, and improved long term OS than those that manage a low volume of sarcoma patients. We demonstrate the existence of a volume-outcome relationship for sarcoma at the national level and provide benchmark data for cancer care delivery systems and policy makers.



Overall Survival by Sarcoma Case Volume According to the NCDB

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Novel Calculators for Esophageal Adenocarcinoma Accurately Predict which Patients Benefit from Neoadjuvant Chemoradiation and Estimate Overall Survival E. Gabriel,* K. Attwood, R. Shah, S. Hochwald, S. Nurkin, M. Kukar. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction Our group recently published that patients with clinically node negative (cN-) esophageal adenocarcinoma do not derive an overall survival (OS) benefit from neoadjuvant chemoradiation (nCRT) compared to node positive (cN+) patients. The aim of this study was to develop calculators which could 1.) precisely identify which patients derive OS benefit from nCRT and 2.) estimate the individualized 3-year OS from multimodal therapy. Methods The first calculator (E-CALC 1) incorporated pre-operative factors to predict which patients would benefit from nCRT, while the second (E-CALC 2) incorporated both pre- and post-operative factors to estimate individualized 3-year OS. Using the National Cancer Data Base (NCDB) from 1998-2006, patients with clinical stage T1b, N1-N3 or T2-T4a, N-/+, M0 adenocarcinoma of the middle/lower esophagus were selected. Of this cohort, 80% was used to create prediction models using Cox regression. The remaining 20% was used to calibrate and validate the models through receiver operating characteristic (ROC) curves and the associated area under the curve (AUC). Results A total of 1,309 patients were identified. E-CALC 1 incorporated age, grade, clinical T/N stage and nCRT (Figure 1A). Patients who derived OS benefit from nCRT included: age > 57, any cN+ patient, age > 23 with grade 3/4 tumors, age > 37 with T3/T4 tumors, and grade 3/4, T3/T4 tumors of any age. E-CALC 1 model performance was good (Figure 1B, AUC = 0.685). In addition to the above factors, E-CALC 2 identified other variables as independently predictive of OS. These included gender, Charlson-Deyo comorbidity score (CD), tumor size/location, number of positive and examined nodes, type of surgery (partial/total esophagectomy or esophagectomy with gastrectomy), post-operative length of stay, unplanned readmission, and adjuvant CRT (Figure 1C). E-CALC 2 model performance was very good (Figure 1D, AUC = 0.746). Conclusions E-CALC 1 accurately predicts which patient subsets are expected to derive OS benefit from nCRT, while E-CALC 2 accurately estimates individualized 3-year OS for patients who complete multimodal therapy.

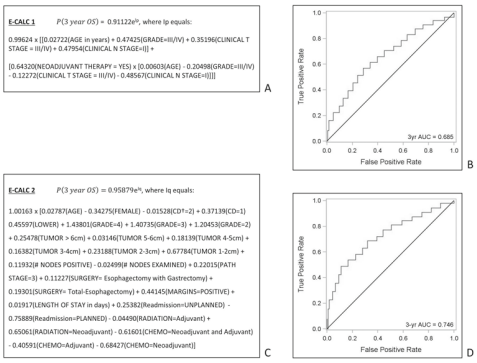

Figure 1. Top panel shows the model for E-CALC 1 (A) and its associated ROC curve (B). Bottom panel shows the model for E-CALC 2 (C) and its associated ROC curve (D). Both provide a good level of accuracy.
† CD – Charlson-Deyo comorbidity score.

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Patterns and Predictors of Locoregional Recurrence Following Neoadjuvant Chemoradiation for Esophageal Cancer A. Blackham,* W. Jin, K. Almhanna, J. Fontaine, S. Hoffe, J. Frakes, P. Venkat, J.M. Pimiento. *Surgical Oncology, Moffitt Cancer Center, Lutz, FL.*

Introduction: Despite neoadjuvant chemoradiation (nCRT) followed by radical resection for locally advanced esophageal cancer, esophageal and regional lymph node recurrences are common. Specific risk factors for locoregional recurrence (LRR) have yet to be identified. Methods: Patients with esophageal cancer who were treated with nCRT and esophagectomy were identified from a single institution, prospectively maintained database (1996-2013). Timing and locations of known recurrences were described and predicting factors of LRR were analyzed. Results: Out of 456 patients treated with nCRT for esophageal cancer, 167 patients developed known recurrence. Locoregional and distant recurrences were observed in 69 (15.1%) and 140 (30.9%) patients, respectively. Median recurrence-free survival was 38.5 months with a median follow-up of 30.4 months. Sixty-eight patients (40.7%) developed recurrence at multiple sites. The median time to recurrence was 13.5 months and survival following recurrence was only 8.0 months in the 27 patients (16.2%) with solitary LRR. Overall survival in patients with solitary LLR was 23.6 months, compared to 20.8 months in all patients who developed distant recurrence. Univariate analysis identified lymph node ratio >0.5 (OR 2.42, p=0.030), non-complete pathologic response (OR 1.90, p=0.022), positive margins (OR 3.58, p= 0.028) and lymphovascular invasion (OR 2.82, p=0.001) as significant predicting factors for LRR. While perineural invasion (p=0.055), nodal stage (0.053) and use of adjuvant therapy (p=0.060) approached significance, other factors such as tumor stage, type of surgery (Ivor-Lewis vs transhiatal), radiation dose and use of IMRT were not significant predictors of LRR. Only lymphovascular invasion was an independent predictor of LRR on multivariate analysis. Conclusions: Prognosis following LRR in patients with esophageal cancer treated with nCRT is poor but is better than in patients who develop distant recurrence. High lymph node ratio, positive margin status, non-complete pathologic response and the presence of lymphovascular invasion are predictive of LRR following nCRT for esophageal cancer.

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The Prognostic Significance of Programmed Death-Ligand 1 and it's Relationship to Pathological Subtypes of Lung Adenocarcinoma in Patients with Resected Lung Adenocarcinoma J. Hung,* Y. Wu, T. Chou, W. Hsu. *Taipei Veterans General Hospital, Taipei, Taiwan.*

Introduction: The programmed death-ligand 1 (PD-L1) pathway plays an important role in maintaining immune homeostasis. PD-L1 pathway may also protect tumor from attack of cytotoxic T cells. Lung adenocarcinoma was classified into five invasive subtypes (lepidic, acinar, papillary, micropapillary, and solid) according to 2015 WHO Classification of Lung Adenocarcinoma. The relationship between PD-L1 expression and the new classification of lung adenocarcinoma has not been well demonstrated. Methods: A total of 112 patients with resected lung adenocarcinoma were included in the study. The pathological subtypes of these tumors were classified according to 2015 WHO Classification of Lung Adenocarcinoma. PD-L1 expression was determined by immunohistochemistry in tumor specimens. Relationship between PD-L1 expression and clinicopathological variables was investigated. The prognostic value of PD-L1 expression in overall survival and disease-free survival was also demonstrated in the study. Results: Overexpression of PD-L1 was identified in 18 (16.1%) of the 112 patients. PD-L1 overexpression was significantly associated with solid predominant subtypes (P = 0.046). PD-L1 overexpression was not significantly associated with age (P = 0.960), sex (P = 0.158), stage (P = 0.940), and visceral pleural invasion (P = 0.665). PD-L1 overexpression (HR, 3.867; 95% CI, 0.865 to 17.292; P = 0.077) tended to be a significant prognostic factor for worse overall survival in univariate analysis. However, it was not a significant prognostic factor in multivariate analysis (P = 0.374). For disease-free survival, PD-L1 overexpression (HR, 4.197; 95% CI, 1.599 to 11.015; P = 0.004) was a significantly poor prognostic factor in multivariate analysis. Conclusions: There was significant relationship between PD-L1 overexpression and pathological subtypes (solid predominant subtype) of lung adenocarcinoma. PD-L1 overexpression was a significant prognostic factor for worse disease-free survival in patients of lung adenocarcinoma. Solid predominant adenocarcinoma might be considered to be a predictor for adjuvant immunotherapy.

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Enhancing CAR T-Cell Efficacy and Functional Persistence in Solid Tumors L. Cherkassky,* A. Morello, J. Villena-Vargas, M. Sadelain, P. Adusumilli. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Following successful translation of our chimeric antigen receptor (CAR) T-cell therapy (Sci Transl Med 2014, NCT02414269), we next address tumor-mediated immunosuppression in mesothelin-expressing solid tumors (mesothelioma, lung, pancreatic, and breast cancers). We hypothesized that genetic strategies to counteract inhibitory signaling would a) potentiate therapy, and b) overcome obstacles limiting checkpoint antibody therapy such as need for repeated administration. Methods: Human T cells were transduced with mesothelin-targeted CARs activating CD3zeta alone (Mz) or with CD28 costimulation (M28z). T cells were cotransduced with PD-1 targeting shRNAs or PD-1 dominant negative receptor (PD-1 DNR). Efficacy was evaluated in vitro and in vivo using a solid tumor mouse model (median survival, tumor burden by bioluminescent imaging). Results: Compared to Mz T cells, M28z T cells exhibit enhanced cytotoxicity and cytokine secretion. In an orthotopic model of pleural mesothelioma, a single low dose of M28z T cells enhance persistence (2010vs.225 CAR+ T cells/spleen) and prolong median survival compared to Mz (64vs29 days). However, mice died from tumor relapse and tumor-infiltrating T cells antigen-challenged ex-vivo demonstrated reduced cytotoxicity (25vs.10%) and cytokine secretion (8217vs.88 pg/mL IL-2, 55954 vs.4075 pg/ml IFN-g) compared to pre-infusion cells. Tumor harvest analysis demonstrated PD-1 and PD-ligand upregulation by T cells and tumor cells, respectively. We confirmed in vitro that PD-L1 overexpression inhibits M28z CAR T cells. M28z CAR T cells coexpressing shRNAs targeting PD-1 (to knockdown PD-1 receptor expression) or a PD1-DNR (functions as a decoy receptor, binding PD-ligands without inhibitory signaling) retained T-cell effector function in vitro. M28z PD1-DNR even at a single low dose (1 CAR T-cell to 12,000 tumor cells) enhanced tumor burden control, prolonged median survival (M28z vs M28z PD1-DNR, 56vs82 days) and resisted tumor rechallenge for >100 days. All $p<0.05$. Conclusion: Genetic strategies engineered within CAR T cells counteract tumor mediated immunoinhibition. These strategies are immediately translatable to solid tumor cellular therapy.

ABSTRACTS

Accepted for
VIDEO PRESENTATIONS

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Society of Surgical Oncology
March 2–5, 2016
Boston, Massachusetts

V1

Posterior Retroperitoneoscopic Approach for Extra-Adrenal Tumors J. St. Julien,* E. Grubbs, J.E. Lee. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Background Patients with small retroperitoneal masses unable to be assessed by minimally invasive methods are often subjected to open procedures. The anterior laparoscopic approach can be very technically challenging, and the open approach is marked by significant morbidity. The posterior retroperitoneoscopic approach has been shown to be safe and effective with good outcomes after adrenalectomy. We have assessed our own experience with this approach for extra-adrenal pathology. Methods We performed a retrospective analysis of all patients who underwent a posterior retroperitoneoscopic approach for extra-adrenal pathology between 2005 and 2015. Outcome measures included success of procedure, perioperative complications, length of hospital stay, and overall survival. Descriptive statistics were compared by chi square and the Student's t-test as appropriate. Overall survival was estimated using the Kaplan–Meier method. Results A total of 28 operations between 2005 and 2015 were included in the analysis. The mean age was 49 (SD 13.6). Sixty-eight percent of patients were male, with 86% white, 7% black, and 7% Hispanic. Mean BMI was 31 (SD 7.2), with 42% of patients having a BMI ≥30. Laterality was evenly split between the right and left side, and 61% of patients had a prior abdominal operation. Mean tumor size was 2.9cm (SD 1.4), mean operative time was 123 minutes (SD 58.4), and median estimated blood loss was 25mL (range 5-1000). Median length of stay was 1 day, with 20 patients staying 1 day, 7 patients staying less than 7 days, and 1 patient who stayed 16 days. There was one complication (3.6%), and two conversions to open (7.1%). Median overall survival was 2,960 days, or 8 years. No patients died within 30 days. Conclusion The posterior retroperitoneoscopic approach is a safe, feasible option in select patients with extra-adrenal tumors of the retroperitoneum. Operative time, complication rates, and conversion rates were all similar to published data for retroperitoneoscopic adrenalectomy. Surgeon experience and careful preoperative planning are paramount to procedural success. This technique should be incorporated into the armamentarium of surgical oncologists managing retroperitoneal pathology.

V2

Novel Use of Tumor Bed Sizers for Intraoperative Radiation Therapy A. Gbegnon,* S.L. Sugg, C. Scott-Conner, R. Weigel, L. Erdahl, W. Sun, T. Waldron, I. Lizarraga. *University of Iowa Hospitals & Clinics, Iowa City, IA.*

Intraoperative radiation therapy (IORT) is a form of partial breast irradiation in which the radiation is delivered directly to the tumor bed at the time of lumpectomy for breast cancer. One common form of IORT utilizes the Zeiss Intrabeam device which provides a point source of low energy x-rays delivered through the center of a spherical tumor bed applicator. The correct size applicator must be used to facilitate proper irradiation to reduce the risk of local recurrence and to prevent radiation injury to the skin. The applicators come in a range of sizes up to 5.0cm.Therefore selection of the appropriate size of tumor bed applicator is essential. Using the applicators themselves as a sizing tool is not cost-effective, as one must test several different applicators prior to obtaining the correct size for the tumor bed. This leads to increased operative costs because the applicators can only withstand a limited number of sterilizations. To solve this problem, we created a cavity sizing tool that enables unlimited fitting to the surgical cavity without consumption of applicator lifetimes. The sizers are made of anodized aluminum handles threaded into spheres of high density plastic in order to facilitate sterilization and match the size, weight and 'feel' of the tumor bed applicators. They have a similar contrasting echogenicity as the applicators under examination with ultrasound, which is used to confirm the safe distance to skin. The sizers are sterilized and packaged as a set of five, and the diameter of the corresponding applicator is stamped into the end of the handle, allowing easy comparison between the cavity sizing tool and the applicator. This video demonstrates how we use the sizers to facilitate intraoperative radiation delivery during lumpectomy for breast cancer.

V3

Colostomy Prolapse Treated with Total Prolapsed Bowel Resection with Manual Anastomosis C.A. Quadros,[1]* M.N. Andrade.[2] *1. Aristides Maltez Cancer Hospital, Salvador, Bahia, Brazil; 2. Medical School, State University of Bahia - UNEB, Salvador, Bahia, Brazil.*

Introduction: Colostomy prolapse is a late surgical complication consisting of an intestinal protrusion in which the colon telescopes into itself. The best treatment is closing the colostomy but it is not possible in some cases, mostly in advanced oncological disease or poor clinical conditions. The prolapsed bulge causes patient discomfort, makes colostomy appliance fitting difficult, requiring surgical correction. Colostomy prolapse can cause block of blood flow and fluid drainage, edema, pain and ischemia, requesting urgent surgical treatment. It is more frequent with loop colostomies with an incidence as high as 22%. Surgical techniques have been suggested for prolapse reduction laparoscopically or through bowel incision using the Délorme technique. Prolapse resection has been suggested using stapler devices. Objective: Describe the surgical technique of total prolapsed bowel resection with manual anastomosis for correction of colostomy prolapse. Method: This video shows an effective surgical technique of treating colostomy prolapse that has not been described previously in PubMed and MEDLINE indexation centrals. Results: Under spinal or epidural anesthesia, incision is performed in the base of the colostomy, in the healthy colon mucosa, cutting through the entire bowel wall of the two prolapsed colon segments. The colon mesentery is transected and ligated. The prolapsed bowel segment is totally resected. The healthy ends of the two colon segments are manually sutured without the need of staplers. The final result is excellent, with early patient feeding and hospital discharge within twelve hours. The surgical technique maintains the colostomy without the need of laparotomy, laparoscopy or skin incisions. It is easy, safe, efficient and economic as it does not require staplers. The procedure has been used in over ten years in more than 100 patients with no surgical related complications and no prolapse recurrence. Conclusion: This technique features advantages such as minimal use of surgical equipment, hospital discharge within twelve hours and expected low prolapse recurrence.

V4

Laparoscopic Intra-Gastric Resection for Proximal Sub-Mucosal Gastric Tumors C. Boulanger-Gobeil,[2]* J. Gagné,[3] S. Ashamalla,[1] F. Julien,[3] J. Hallet.[1] *1. Surgery, Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada; 2. University of Toronto, Toronto, ON, Canada; 3. CHU de Québec, Québec, QC, Canada.*

Introduction: Treatment of confirmed or suspected sub-mucosal gastric malignancies relies on clear margin resection, for which minimally invasive surgery has become widely accepted. However, resection of lesions of the proximal third of the stomach, including the gastro-esophageal junction (GEJ), remains challenging, whereby extensive resection with potential compromise of gastrointestinal function and significant morbidity is often required for small lesions. Methods: This video presents the use of laparoscopic intra-gastric surgery (LIGS) for proximal sub-mucosal gastric tumors, to allow for complete resection while minimizing the extent, invasiveness, and morbidity of the procedure. Results: We focus on a 60 year-old gentleman with a 5 cm sub-mucosal lesion siting 0.5 cm below the GEJ on the lesser curve. Biopsy reported a CD117/CD34/DOG1-positive spindle cell tumor. A LIGS approach was chosen to allow for minimally invasive resection and avoid a total gastrectomy. The video begins with presentation of patient positioning and technique for placement of cuffed gastric ports that approximate the anterior gastric wall to the abdominal wall. A 15 mmHg pneumogastrum is created. Concomitant endoscopy is performed and the endoscope is used to identify and protect the GEJ. The tumor is resected using the cautery. The deficit is closed with intra-gastric suturing. The specimen is extracted through one of the gastric port sites. For each step, alternative techniques are also presented throughout the video. This patient underwent an uneventful post-operative course and was discharged on post-operative day 5. Final pathology revealed R0 resection of a leiomyoma with hyperplasia of cells of Cajal. Conclusion: We herein illustrate the steps for a novel, feasible, and safe minimally invasive approach to proximal sub-mucosal gastric tumors. LIGS is a valuable alternative to resect challenging gastric tumors while limiting surgical invasiveness and preserving gastrointestinal function. LIGS could be added the surgical oncologist's armamentarium for the minimally invasive management of sub-mucosal gastric tumors.

V5

Robotic Liver Resection of Left Lateral Section in a Cirrhotic Patient with Hepatocellular Carcinoma P. Polanco,* R. Pastorek, T. El-Ahmadieh, S. Kukreja. *University of Texas Southwestern, Dallas, TX.*

Introduction:Minimally invasive liver resections have shown to be safe and feasible with outcomes comparable with the open approach. Liver resections of hepatocellular carcinomas (HCC) in cirrhotic patients could be challenging cases but in selected cases these patients can benefit from the robotic assisted approach. Our objective is to present a video that describes our Robotic Left Lateral Sectionectomy technique. Methods: We present the case of a 72 yo male patient with Non Alcoholic Steatohepatitis – Child A cirrhosis with an unremarkable physical exam. Screening ultrasound followed by MRI confirmed findings of cirrhosis, portal hypertension and a 4x3 cm lesion in the left lateral segment. His bloodwork revealed platelet count of 177 cell/mm3, INR of 1.1 and AFP levels of 17 ng/dl. CT guided of this lesion confirmed HCC. Results: The patient was placed in supine, reverse trendelenburg position on a split leg table. The Operating Room set up and trocar placement is depicted in the video.After laparoscopic inspection, the robotic arms were docked (Da Vinci Si, Intuitive Surgical, Sunnyvale, CA, USA). Systematic robotic ultrasound of the liver was performed to map out the lesion as well as the vascular pedicle of the left segments of the liver. The coronary ligament and superior aspect of the liver was mobilized using the robotic hook cautery. Under US-guidance line of transection was defined scoring the liver capsule with robotic hook cautery. Traction stitches with an O Vycril suture towards the right and left side of the line of transection. Transection of the liver is performed with combination of hook cautery, PK bipolar dissector and vessel sealer. Larger vascular pedicles were clipped or stapled with GIA vascular load. Laparoscopic bipolar device was used for hemostasis of transected surface followed by application of hemostatic matrix. A 19 French blake drain is placed and specimen is extracted through the utility port. Patient recovered well from surgery and was discharged to home in postoperative day 4.Conclusions: Robotic liver left lateral sectionectomy can be performed safely in cirrhotic patients with HCC.

V6

Laparoscopic Total Pancreatectomy for a Main Duct IPMN B.C. Chapman,* A. Paniccia, R. Schulick, B.H. Edil. *General Surgery, University of Colorado Denver, Denver, CO.*

Introduction: Main duct intraductal papillary mucinous neoplasms of the pancreas (M-IPMN) are potentially malignant cystic neoplasms of the pancreas that can degenerate into carcinoma in situ in 70% and invasive malignancy in 43% of cases. Although laparoscopic pancreaticoduodenectomy and distal pancreatectomy have been previously described for management of pancreatic neoplasms, laparoscopic total pancreatectomy is rarely described. We present a video demonstrating a laparoscopic spleen sparing total pancreatectomy in a patient with M-IPMN. Case Presentation: A previously healthy 66-year old male was diagnosed with recurrent pancreatitis. Ultrasound (US) showed an 8 mm pancreatic duct and magnetic resonance imaging showed a 10 mm pancreatic duct in the pancreatic head. Endoscopic retrograde cholangiopancreatography demonstrated a "fish mouth" appearance at the major papilla with an extensive villous mass (15 mm) in the pancreatic head. Biopsy was consistent with main duct IPMN. A computed tomography of the abdomen demonstrated a diffusely dilated pancreatic duct and a 5 mm mural nodule in the neck of the pancreas. Tumor markers were normal. A spleen sparing laparoscopic total pancreatectomy was performed. Pathology was consistent with M-IPMN. Results: The patient underwent a spleen sparing laparoscopic total pancreatectomy without complications and was admitted to the intensive care unit for a continuous insulin infusion. The operation took 270 minutes, and estimated blood loss was 150 cc. There were no intraoperative complications. He was transferred to the floor and his nasogastric tube was discontinued on postoperative day (POD) one with subcutaneous insulin injections. His diet was advanced and he transitioned to a diabetic diet on POD#4. His surgical drain had minimal output with no evidence of a bile leak and was discontinued on POD#5. The patient's hospital course was uncomplicated and he was discharged to home on POD#7. Conclusion: Laparoscopic total pancreatectomy can be safely performed in patients with main duct IPMN and this video presentation describes our technique.

V7

Evolving Trends Towards Minimally Invasive Surgery for Solid Pseudopapillary Neoplasms C.L. Stewart,* C. Meguid, B.C. Chapman, R. Schulick, B.H. Edil. *Surgery, University of Colorado School of Medicine, Aurora, CO.*

Introduction: Solid pseudopapillary neoplasms are rare pancreatic tumors with low malignant potential that predominantly arise in young women, lending themselves to minimally invasive surgery. Here we sought to characterize this population, and the evolving trend towards laparoscopic management. Methods: We retrospectively identified all patients at our primary institution and affiliated children's hospital surgically treated for solid pseudopapillary neoplasms from 2008-2015. Demographic and clinical information were queried from the medical record, and descriptive statistics were performed. Student's t-test and chi-square analysis were used for comparison where appropriate. Results: We identified ten women (14-48 years old, average 23 years) surgically treated for solid pseudopapillary neoplasms; four with distal pancreatectomy (three open with splenectomy, one laparoscopic spleen sparing) and six with pancreaticoduodenectomy (three open, three laparoscopic). From 2008-2013, 6/7 (85%) procedures were performed open. Since 2014 3/3 (100%) procedures have successfully been completed laparoscopically (video). Length of stay was similar for patients who had laparoscopic versus open procedures (9 vs 9 days, p=0.95). Two-thirds of patients (4/6) who had open procedures experienced post-operative complications, compared to 25% (1/4) of patients who had laparoscopic procedures (p=0.20). There have been no recurrences. Initial quality of life surveys after laparoscopic surgery are promising, showing rapid recovery of physical and functional well-being. Conclusions: Minimally invasive surgical management of solid pseudopapillary neoplasms is becoming more popular, can be done safely, and has comparable outcomes to an open approach. Quality of life is an important metric for this relatively young population, and may be improved with a laparoscopic approach, warranting further investigation.

V8

Laparoscopic-Assisted Central Pancreatectomy for Solid Pseudopapillary Epithelial Neoplasm J. Hallet,* M.E. Tsang, P. Karanicolas. *Surgery, Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada.*

Introduction: While laparoscopic distal pancreatectomy is being increasingly used, more advanced minimally invasive pancreatic resections remain uncommon. Central pancreatectomy represents an alternative to extended cephalic or tail resection for benign or low-grade malignant tumors of the pancreatic isthmus. Methods: This video highlights a laparoscopic assisted central pancreatectomy with pancreaticogastrostomy reconstruction. Results: We herein present the case of a 44 year-old lady who underwent central pancreatectomy for a two centimeters solid pseudo-papillary epithelial neoplasm sitting in the pancreatic neck. The video begins with presentation of the preoperative anatomy and rationale to proceed with central pancreatectomy. Patient positioning and placement of the five trocars is detailed. Initial surgical steps include division of the gastro-colic ligament, gastric retraction, dissection of the inferior pancreatic edge and identification of the superior mesenteric vein, creation of a retro-pancreatic tunnel, and elevation of the pancreatic isthmus from the splenic vein and retroperitoneum. Proximal pancreatic transection is performed with a stapling device buttressed with a bioabsorbable mesh. Distal transection and pancreaticogastrostomy are performed through a left upper quadrant transverse extraction site. Each step of the pancreaticogastric anastomosis is depicted. The procedure was well tolerated. The patient presented a grade A pancreatic fistula (International Study Group on Pancreatic Fistula classification), likely from the cephalic staple line. The abdominal drain was pulled on day four and she was discharged on day five. Pathology confirmed the resection of a solid pseudo-papillary epithelial neoplasm with negative margins. Conclusion: This video illustrates the technique of laparoscopic assisted central pancreatectomy and steps to pancreaticogastrostomy. It highlights the feasibility of the technique for selected cases. Laparoscopic assisted central pancreatectomy allows for preservation of pancreatic function while minimizing surgical morbidity by providing the patient with the benefits of a minimally invasive approach.

LBV1

Laparobotic DP-2 Radical Pancreatosplenectomy with Left Adrenalectomy for a Primary Pancreatic Sarcoma S. Jones,* A. Yiengpruksawan. *Valley Hospital, Ridgewood, NJ.*

Introduction: This video showed a radical distal pancreatectomy using the robotic surgical system for a rare primary pancreatic sarcoma. For strategic planning and data organizing purposes, the author divided distal pancreatectomy (DP) into 4 types based on the radicality of surgery as follow: DP-0 denotes simple DP with or without splenectomy for a benign or low malignant potential lesion DP-1 is subdivided into 2 types and is indicated for a malignant tumor =< 2cm which is confined within the pancreas - DP-1a: DP with lymphadenectomy and en bloc resection of adrenal fascia, without splenectomy for a proximal lesion, DP-1b: with splenectomy for a tail lesion. DP-2 denotes DP with lymphadenectomy and en bloc resection of left adrenal gland for a malignant tumor > 2cm with posterior fascia invasion. DP-3 denotes DP with lymphadenectomy and en bloc resection of adjacent involved organ(s) for a lesion involving adjacent organ(s). Method: In this video, DP-2 radical resection was employed. The patient was a 67 year-old woman who was found to have a complex 10 cm distal pancreatic mass involving spleen, left adrenal gland, and mesocolon. The splenic vein was occluded and there was a large thrombus in the distal inferior vena cava. After transjugular placement of IVC filter, she underwent surgery. The video illustrated technical steps to complete the DP-2 resection. The operating time was 360 min. and estimated blood loss was 200 ml. The pathology report showed a primary pancreatic sarcoma. All margins and lymph nodes were negative. She was discharged on the 4th postoperative day. She did not receive any adjuvant treatment and has remained without evidence of recurrence 2 years after surgery. Conclusion: Complex robotic pancreatectomy can be done safely with no compromise on oncological outcomes. The robotic surgical system offers better visualization and instrumental dexterity that allow for better tissue dissection and manipulation.

LBV2

Lateral Laparoscopic Distal Pancreatectomy and Splenectomy for Pancreatic Cystic Neoplasm M.E. Tsang,* C. Law, P. Karanicolas, J. Hallet. *Surgery, Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada.*

Introduction: Laparoscopic distal pancreatectomy is now commonly performed for benign and malignant disease. The traditional approach involves creation of a tunnel under the pancreas and dissection from medial to lateral. Alternative approaches may enhance surgical efficiency and results. Methods: This video highlights the lateral approach to laparoscopic distal pancreatectomy and splenectomy. Results: We herein present the case of a 61 year-old patient presenting with a growing cystic lesion in the distal pancreatic tail. Due to the localization in the splenic hilum, a lateral laparoscopic approach was chosen. The patient is positioned in the right lateral decubitus. The procedure begins with mobilization of the splenic flexure. The inferior border of the pancreas is then dissected, followed by the superior pancreatic edge. At this point, the lesser sac is entered and short gastric vessels are divided. Inferior and lateral splenic attachments are divided to achieve full mobilization. Elevation of the pancreatic gland from the retroperitoneum is then carried out in a lateral to medial fashion, posterior to the splenic vessels. After division of the splenic artery and vein, the pancreas is divided with a linear stapler. The specimen is protected in an endobag and extracted through the optical port. Post-operative course was uneventful and the patient was discharged on post-operative day two. Pathology revealed a mucinous cystic neoplasm without dysplasia. Conclusion: Lateral laparoscopic distal pancreatectomy represents a safe and feasible alternative to the traditional medial approach. It presents potential advantages over the medial approach, including retraction of the stomach by gravity, easier and wider access to the distal pancreatic tail, easier access to splenic mobilization, and preservation of pancreatic parenchyma by more lateral transection. With easier and quicker dissection, this technique can eventually further reduce operative time, blood loss, and morbidity following minimally invasive distal pancreatectomy for selected patients.

LBV3

Laparoscopic, Spleen-Sparing, Distal Pancreatectomy for a Symptomatic Pro-Insulinoma C. Contreras.* *Surgery, University of Alabama at Birmingham, Birmingham, AL.*

INTRODUCTION: Proinsulinoma is a rare neuroendocrine tumor which can manifest with hypoglycemia. METHODS: A 47 year old otherwise healthy woman presents with symptomatic hypoglycemia. A thorough evaluation is undertaken. RESULTS: An inpatient fast revealed symptomatic hypoglycemia with a blood glucose of 41 mg/dL, a normal C-peptide, and a pro-insulin level greater than 10 times the upper limit of normal. A cortisol stimulation test and sulfonylurea screen are negative. A triple phase contrasted CT of the chest, abdomen, and pelvis with 2.5 mm axial slices revealed a normal pancreas and no other areas concerning for neoplasm. An endoscopic ultrasound (EUS) demonstrated an 8 x 7 mm hypoechoic mass in the tail of the pancreas; fine needle aspirate showed a neuroendocrine neoplasm. To facilitate intraoperative localization, 3 gold fiducial markers were placed via EUS, and the patient was taken to the operating room for laparoscopic distal pancreatectomy. Intraoperative fluoroscopy and ultrasound was instrumental in confirming the location of the tumor and establishing the level of pancreatic dissection. Fluroscopy of the excised specimen confirms excision of the fiducials bounding the pancreatic tail pro-insulinoma. She was discharged home on postoperative day #4. She remains euglycemic and has had normal surveillance CT scans more than 2 years postoperatively. CONCLUSIONS: Endoscopic ultrasound is an important imaging modality, especially for small pancreatic tumors not visualized on cross-sectional imaging. Preoperative placement of fiducials can reduce the operative duration and improve surgeon confidence.

LBV4

Total Laparoscopic Management of Multi-Stage Surgery for Stage IV Colorectal Cancer C. Conrad,* H. Shiozaki, T.A. Aloia, C. Eng, G. Chang, J. Vauthey, Y. You. *Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX.*

Background: Total laparoscopic complete metastectomy and primary cancer resection of patients with stage IV colorectal cancer may allow for optimal oncologic outcome with possibly shortened inter-treatment intervals in addition to the decreased morbidity of minimally invasive surgery. However, complete and coordinated minimally-invasive multi-stage surgical resection for patients presenting with synchronous metastases from CRC requiring multivisceral resection has not been well described. Patient: A 66 year-old woman presents with a symptomatic descending colon cancer and synchronous metastases involving liver-segments 4a, 4B and 8 and left adrenal gland. After neoadjuvant chemotherapy, surgical resection was completed in two stages combining subtotal colectomy with left transperitoneal adrenalectomy during the first stage. The second stage was an extended left hepatectomy. Technique: The patient was placed in Modified French Position. Coordinated port placement during the combined subtotal colectomy with adrenalectomy and with the planned second stage extended left hepatectomy allowed minimizing access trauma. The first stage begun with splenic flexure take-down and transperitoneal adrenalectomy for overlapping dissection planes. The second stage of extended left hepatectomy was facilitated due to minimial adhesions. Hospital stays were 4 and 3 days respectively and return to adjuvant therapy was 21 days. Conclusion: For patients with stage 4 CRC with multivisceral metastases amendable to surgical resection, a complete minimally-invasive multi-stage surgical resection allows for safe and complete oncologic resection with minimal morbidity and shortened inter-treatment time intervals. Coordination of treatment sequencing, port placement and dissection planes is crucial for maximizing the benefits of the minimally invasive approach and optimizing oncologic outcomes.

LBV5

Feasibility of Robotic Hepatic Segmentectomy: Resection of Segment of 6 and 7 F. Tozzi,* B. Goldner, S. Warner, Y. Woo, Y. Fong, G. Singh. *City of Hope, Duarte, CA.*

Purpose: Robot-assisted liver surgery is gradually making its way into mainstream surgery. Endowrist instruments and a high definition 3-dimensional camera offer precision and versatility beyond the laparoscopic counterpart. This video exemplifies the application of robot-assisted surgery for single lesions situated in the posterior section of the liver under the rib cage. Methods: This is a 61-year-old female with a primary intrahepatic cholangiocarcinoma

located at the border of segment 6 and 7. The patient was positioned tilted with the right side up. A total of 4 robotic trocars and a 10-12 mm SurgiQuest™ port for assistance and extraction of the specimen were placed. The intrahepatic position of the tumor was confirmed with a drop-in probe. The margin was defined by the scoring capsule. The transection of the liver parenchyma was achieved using the robotic sealing vessels device in an antero-posterior direction in a circumferential fashion. The key of the operation is leaving the specimen attached to the lateral abdominal wall which helps pull away the normal parenchyma from the tumor. The final step entails the detachment of the specimen from the lateral abdominal wall. The specimen is retrieved through an Endo catch bag inserted through the SurgiQuest™ site. Conclusion: Robot-assisted resection of posteriorinferior liver segments is technically safe and feasible in selected patients.

LBV6

LigaSure™-Assisted Laparoscopic Left Lateral Sectionectomy for HCC F. Tozzi,* A. Lewis, M. Guye, B. Lee, G. Singh. *City of Hope, Duarte, CA.*

Purpose: Delineating the feasibility of laparoscopic left sectionectomy by the use of Ligasure™ device with gradual compression of the parenchyma and division of the inflow and outflow by stapler device. Methods: This is a 72-year-old female with progressive history of malaise and weight loss. Clinical work up and imaging lead to the identification of a multifocal HCC localized at the left lateral segment. Most of the liver parenchyma of the 2&3 segments was replaced by the mass. The patient was positioned supine and with a reverse 30* Trendelenburg. The laparoscopic procedure progressed in a stepwise fashion: 1) placement of 3 laparoscopic ports (5mm/10mm), 2) Intrahepatic position of the tumor confirmed with drop-in ultrasound probe, 3) Mobilization of the lobe of the liver, 4) Transection of the parenchyma with LigaSure™ sealing device, 5) Division of the vascular pedicle with stapler device. Conclusion: Laparoscopic assisted liver resection of left liver is technically safe and feasible in selected patients.

ABSTRACTS

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P1

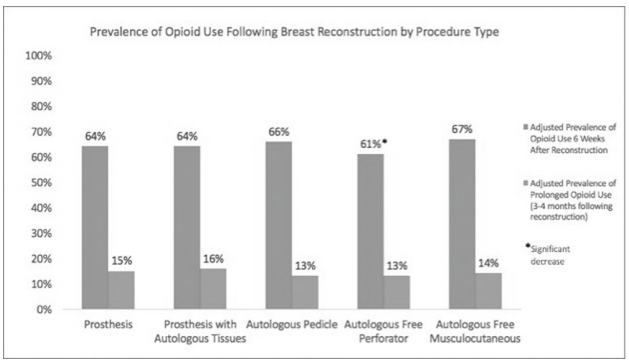
Hospital Level Adjusted Sentinel Lymph Node Positivity Rates in Breast Cancer E.R. Berger,[1]* C.V. Kinnier,[3] C.A. Minami,[2] D.P. Winchester,[4] A.D. Yang,[2] K. Bilimoria.[2] *1. Division of Research and Optimal Patient Care, American College of Surgeons, Chicago, IL; 2. Surgical Outcomes and Quality Improvement Center, Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL; 3. Department of Surgery, Massachusetts General Hospital, Boston, MA; 4. Department of Surgery, Northshore University HealthSystem, Evanston, IL.*

Background:Variation in how a sentinel lymph node biopsy (SLNB) is performed may influence institutional sentinel lymph node (SLN) positivity rates and affect treatment decisions. Hospital-level SLNB positivity rates may reflect a surgeon's resection or a pathologist's identification of positive SLNs. Our objectives were to examine variation in hospitals' SLNB positivity rates, assess patient- and hospital-level characteristics associated with positivity-rate variation, and examine associations between hospital positivity rates and survival. Methods:Stage I-III breast cancer patients who undewent a SLNB were identified from the National Cancer Data Base(2004-2012). Hospital-level SLNB positivity rates were adjusted for patient and tumor factors. Hospitals were divided into adjusted SLNB positivity rate terciles(lower-than, as-expected, and higher-than-expected). Hospital characteristics and survival were examined across terciles. Results: Of 601,062 patients identified from 1,380 hospitals, 132,146 had at least one positive SLN(21.9%). At the patient level, SLN positivity was significantly associated with age < 50 years old, black or Hispanic race, Medicaid or uninsured, hormone receptor positivity, advanced T category, and higher grade($p<0.001$). The median adjusted SLNB positive rate across hospitals was 22.1%. Hospitals with lower- and higher-than-expected SLNB positivity rates were significantly more likely to be low-volume hospitals(low-tercile:OR 2.10,95% CI 1.42-3.11; high tercile:OR 1.69,95% CI 1.15-2.49) compared to as-expected positivity rate hospitals. Stage I and II patients treated at low tercile hospitals had slightly but significantly worse 5-year survival than those treated at as-expected positivity rate hospitals(Stage I-low-tercile:93.3% vs. 93.8%,HR 1.06,95%CI 1.01-1.12; Stage II-low-tercile:87.5% vs 88.5%,HR 1.08,95%CI 1.03-1.14). Conclusion:Low-volume hospitals were more likely to have lower-than-expected SLNB positivity rates. Low tercile hospital SLNB positivity rates were associated with worse survival. A hospital-level SLNB positivity rate may be a novel quality indicator in breast cancer care and could be reported to hospitals for quality improvement purposes.

P2

Risk of Prolonged Postoperative Opioid Use Among Patients Undergoing Breast Reconstruction A.K. Rzepecki,[2]* B. Fillinger,[2] D.C. Cron,[2] D. Marcusa,[2] R. Mann,[2] L. Zhong,[1] J. Waljee.[1] *1. University of Michigan, Section of Plastic Surgery, Ann Arbor, MI; 2. University of Michigan Medical School, Ann Arbor, MI.*

Introduction: Morbidity and mortality related to opioid medications are a major public health concern. There are no guidelines regarding the appropriate use of opioid analgesics following surgery, and the risk factors associated with inappropriate use are not well described. We sought to examine differences in opioid utilization among women undergoing breast reconstruction. Methods: We examined insurance claims from 24,275 women who underwent immediate breast reconstruction between 2010 and 2013 using the Truven Marketscan® Databases. We classified breast reconstruction into the following groups: prosthetic (84%), prosthetic + autologous (6%), autologous pedicle (5%), autologous free perforator (5%), and autologous free musculocutaneous reconstruction (0.2%). We used multivariable logistic regression to determine the correlation between reconstruction groups, adjusting for clinical and sociodemographic factors, and the probability of filling an opioid prescription a) within 6 weeks following surgery, and b) within 3-4 months following surgery. Results: In this cohort, 66% patients filled opioid prescriptions postoperatively, and 28% filled opioid prescriptions 3 months following surgery (Figure 1). Patients undergoing autologous free perforator reconstruction were less likely to fill opioid prescriptions following surgery compared with patients who underwent prosthesis-based reconstruction (OR=0.86, P=0.025). Of patients who received opioids postoperatively, patients undergoing autologous pedicle and autologous free perforator groups were less likely to maintain opioid use beyond 90 days compared to patients undergoing prosthesis-based reconstruction (autologous pedicle: OR=0.79, P=0.022; autologous free perforator: OR=0.79, P=0.029). Conclusion: Opioid use is common following breast reconstruction, and up to 17% of all patients continue to use opioids beyond 90 days following surgery. Patients undergoing autologous reconstruction fill fewer prescriptions compared with patients who undergo prosthesis-based techniques. Future strategies to mitigate prolonged opioid use should focus on alternative analgesics among women who undergo prosthesis-based reconstruction techniques.



P4

Assessing Re-excision Rates Following Implementation of the Society of Surgical Oncology (SSO)/American Society of Radiation Oncology (ASTRO) Consensus Guideline K. Pawloski,* T. Kearney, F. Eladoumikdachi, L. Kirstein. *Rutgers Cancer Institute of New Jersey, New Brunswick, NJ.*

Introduction. Historically, no formal guidelines existed to define optimal margin width in breast-conserving surgery for early-stage invasive breast cancer. In February 2014, the SSO/ASTRO consensus guideline was published supporting no tumor on inked margin as the standard of care. We sought to assess the effect on re-excision rates after implementation of the guideline. Methods. An IRB approved retrospective chart review of patients who underwent lumpectomy plus re-excision for close and positive margins for early-stage invasive breast cancer from September 2012 to July 2015 was performed. Patient and tumor characteristics were recorded including number of margins re-excised, reason for re-excision, pathology of final margin and specimen volumes. Patients with pure DCIS, excisional biopsies for diagnosis, and with initial surgeries at outside institutions were excluded. Results. Of 400 lumpectomy patients, 129 (32%) were excluded for pure DCIS (n=95), for initial surgery at an outside hospital (n=22), for no needle biopsy or excisional biopsy only (n=14), and for re-excision for phyllodes tumor (n=1). Of the remaining 271 lumpectomies, 76 patients (28%) had re-excisions for close and/or positive margins. 42 patients underwent surgery in the pre-guideline period and 34 in the post-guideline period. Results are shown in Table 1. In the pre- and post-guideline periods, there was a statistically significant difference in the margin re-excision rate and no significant difference in specimen volume. Conclusions. The 2014 SSO/ASTRO guideline provided evidence for use of no tumor on inked margin as the standard in breast-conserving therapy. This study identified a statistically significant decrease in re-excisions for close margins following implementation of the guideline at our institution. Interestingly, approximately 2/3 of patients undergoing re-excision for close margins in the pre-guideline period had negative pathology on re-excision. Follow-up studies should be performed to determine local recurrence rates, but this study supports the implementation of current guidelines.

Table 1

	Pre-guideline	Post-guideline	*p value*
Lumpectomies	123	148	
Re-excisions	42	34	0.04
Margins	98	56	
Positive	70 (71%)	52 (93%)	
Close	28 (29%)	4 (7%)	0.02
Pathology at margin			
Invasive	67 (69%)	40 (71%)	
In situ	31 (31%)	16 (29%)	
Pathology of re-excision for close margins			
Invasive	5 (18%)	2 (50%)	
In situ	5 (18%)	0	
Negative	18 (64%)	2 (50%)	
Mean specimen volume (cm^3)	30.04	32.06	*p*=ns
Median specimen volume (cm^3)	19.32	18.48	*p*=ns

P5

Translating a 2-D Mammogram into a 3-D Breast in the Operating Room K. Park,* K. Rosso, S. Nathanson. *Henry Ford Health System, Detroit, MI.*

Introduction: Image-guided wire placement helps surgeons find breast lesions during surgical excision. We hypothesized that the direction of wire placement and other physical variables could alter the mammographically 2 D measured distances from skin to lesion versus 3 D measurements while lying supine in the OR. Methods: Distances from skin to metal clip (placed during needle biopsy) and to wire hook measured mammographically (n=50) were compared to those in excised specimen radiographs. Analyzed variables were: Clip segment location, breast size, density, breast thickness in compression and direction of wire placement (chi-square test; Spearman correlation). Results: There were significant ($\chi^2 = 8.92$, p=0.01) differences between wire placement direction and hook distance. 10 out of 13 (76.9%) of medially placed wires showed the hook had migrated further into the breast. 11 out of 14 (78.5%) of superiorly placed wires had migrated out of the breast. Thickness of breast in compression at the time of localization and breast size had strong associations with wire displacement in superior wires (p=0.07 and p=0.06, respectively) but not in medial wires (p=0.66 and p=0.52, respectively). There were no differences in the distance from skin to clip between the mammogram and the specimen radiograph. Conclusion: The direction in which the guiding wire was placed had the greatest impact on wire migration. Wires exiting superiorly moved out of the breast while wires exiting medially migrated into the breast between mammographic placement and surgical excision. Compressed breast thickness at the time of the wire placement and overall breast size also impacted wire migration.

P7

A Matched Pair Cohort Study of the Effect of Neoadjuvant Chemotherapy in Stage I-III Breast Cancer J. Sprunt,[2]* D. Barrak,[2] E. Morocco,[2] E. Pan,[2] G. Wu,[2] L. Tung,[2] J. Wecsler,[2] A. Raghavendra,[1] O. Ragab,[2] E. Chung,[2] D. Tripathy,[1] M. Bhasin,[2] C. Russell,[2] S. Sener,[2] J. Lang.[2] *1. MD Anderson, Houston, TX; 2. USC Norris Cancer Center, Los Angeles, CA.*

Introduction The primary aim of this study was to evaluate whether neoadjuvant chemotherapy (NAC) was associated with use of breast conserving surgery (BCS) using a matched pair cohort design. We also sought to evaluate survival outcomes in the NAC versus surgery first cohort after controlling for relevant covariates. Methods We performed a retrospective matched pair cohort analysis, matching NAC and surgery first cases based on tumor stage, estrogen receptor (ER) and HER2 status. We included newly diagnosed stage I-III breast cancer patients treated at our institution between 2006-2013. For univariate analysis we used Chi squared and the Kaplan Meier method. For multivariate analysis we used the Cox proportional hazards model to evaluate association with overall survival (OS). Results Although the cohorts were generally well matched, the NAC cohort had a significantly larger proportion of node positive, PR negative, high grade, and triple negative cases. In patients who had surgery first (n = 110), 83 (75.5%) had a mastectomy and 27 (24.5%) had BCS. In patients who received NAC (n=141), 80 (56.7%) had a mastectomy and 63 (44.7%) had BCS. The mean OS in the NAC cohort was 73.3 months (versus 61.2 months for surgery first); median follow up was 79 months in NAC cohort (versus 69 months for surgery first). Of the patients who received NAC, 46.2% had a pathologic complete response (pCR). HER2 status correlated with pCR (OR 0.64, p=0.048, CI 0.54-0.88). On multivariable analysis, the variables associated with overall survival were use of NAC (HR 0.71, p= 0.035, CI 0.69-0.99), grade (HR 3.06, p=0.021, CI 2.69-4.13), stage (HR 2.8, p=0.006, CI 1.8-3.1), ER status (HR 0.58, p=0.032, CI 0.35-0.95), HER2 status (HR 3.0, p<0.0001, CI 2.82-4.77), and nodal status (HR 2.7, p=0.037, CI 1.51-5.98). pCR nor PR status nor use of adjuvant chemotherapy were associated with OS. Discussion The use of NAC was associated with higher rates of BCS in this matched cohort analysis. Use of NAC was independently associated with improved OS, even after controlling for rates of pCR, patient, tumor and treatment variables.

P8

Down Regulation of the c2orf40 Gene Encoding the ECRG4 Chemokine in Human Breast Cancer Correlates with Disease Progression E. Ward,* A. Baird, B. Eliceiri, S. Blair. *General Surgery, UCSD, San Diego, CA.*

Background The human c2orf40 gene encodes ECRG4, a chemokine precursor that sheds a chemotactic peptide for monocytes/macrophages from the surface of epithelial cells and neutrophils, in a thrombin-dependent mechanism. Down-regulation of c2orf40 in melanoma and glioma is associated with a decrease in tumor-associated monocytes/macrophages (TAMs) that is reversed by re-expression of ECRG4. We evaluated changes in c2orf40 expression in 40 human breast cancer samples to correlate ECRG4 with breast cancer disease progression and outcomes. Methods Quantitative reverse transcriptase–polymerase chain reaction was used to evaluate c2orf40 expression in 5 normal, 11 stage I, 8 stage IIA, 6 stage IIB, 8 stage IIIA, 2 stage IIIB, 4 stage IIIC, and 4 stage IV breast cancer samples. Changes in gene expression were between the stage of tumor and the molecular tumor subtypes including Her2, luminal a, luminal b, and triple negative breast cancers. Results Gene expression analyses revealed significant down-regulation in Stage II and III breast cancer compared to normal breast tissue ($P < 0.05$), with Stage IV trending toward significance ($P<0.06$). In this small sample set, we also observed differences between normal and more advanced tumor grades. No differences were detected in gene expression between normal breast and triple negative tumors, while the most significant reductions were between normal breast and Her2+ tumors. Conclusions: This data confirms that the down-regulation of c2orf40 correlates with an overall progression of breast cancer and we report differences in c2orf40 expression between Her2+ and triple negative tumors. The greater loss in ECRG4 in Her2+ breast cancer that results from the decrease in c2orf40 expression may differentially alter the recruitment and/or activation state of TAMs in Her2+ tumors and contribute to the severity of subsequent disease. This ECRG4-mediated regulation of TAMs may validate targeting c2orf40 expression as an adjunct therapeutic in Her2+ tumors.

P9

Contralateral Prophylactic Mastectomy: Becoming the New Norm Despite a Paucity of Evidence Indicating Survival Benefit? S.M. Wong,[1]* R.A. Freedman,[2] Y. Sagara,[3] F. Aydogan,[3] W.T. Barry,[2] M. Golshan.[3] *1. Harvard School of Public Health, Boston, MA; 2. Dana-Farber Cancer Institute, Boston, MA; 3. Brigham and Women's Hospital/Dana-Farber Cancer Institute, Boston, MA.*

Background: A decade ago, a Surveillance, Epidemiology, and End Results (SEER) study revealed a doubling of prophylactic mastectomies in the United States for women with unilateral breast cancers. We sought to update and examine national temporal trends in contralateral prophylactic mastectomy (CPM) and determine whether survival differed for breast cancer patients based on hormone receptor (HR) status and age. Methods: We identified women diagnosed with Stage I-III invasive breast cancer between 1998-2012 within the SEER registry. We compared patients undergoing breast conserving surgery (BCS), unilateral mastectomy (UM), and CPM. We then performed a Cox proportional hazards model to examine disease specific survival (DSS) in women diagnosed between 1998-2007 who underwent BCS with radiation (BCT), UM, or CPM, after stratifying by HR status and age. Results: Of 496,488 women diagnosed with unilateral invasive breast cancer during 1998-2012, 59.6% underwent BCS, 33.4% underwent UM, and 7.0% underwent CPM. For patients with invasive ductal carcinoma, the proportion undergoing CPM increased from 3.3% in 2002 to 12.4% in 2012 (p<0.001). Rising rates of CPM were noted across all age groups and geographic regions (p<0.001). Overall, reconstructive surgery was performed in 48.0% of CPM patients compared to 16.8% of unilateral mastectomy patients, with rates of reconstruction with

CPM rising from 35.3% in 2002 to 55.4% in 2012 (p<0.001). Despite rising rates of CPM, when compared to women undergoing BCT, we found no significant improvement in 10-year DSS for women undergoing CPM regardless of HR status or age (<55 years/HR+, HR=1.30 [95% CI, 0.96-1.24]; <55 years/HR-, HR=1.04 [95% CI, 0.91-1.20]; >55 years/HR+, HR=1.09 [95% CI, 0.95-1.25]; >55 years/HR-, HR=1.08 [95% CI 0.90-1.29]). Conclusion: The use of CPM tripled during the study period despite evidence suggesting no DSS benefit over breast conservation, irrespective of HR status and age. The concomitant increase in reconstruction suggests that women may be making this surgical choice due to availability of breast reconstruction as part of a complex multi-disciplinary decision-making process.

P10

Changes in Margin Re-excision Rates: A Single Institution's Experience Incorporating the "No Ink on Tumor" Guideline into Practice C.R. Patten,* K.K. Walsh, T. Sarantou, L. Hadzikadic-Gusic, M. Forster, M. Robinson, R.L. White. *General Surgery, Carolinas Medical Center, Charlotte, NC.*

Introduction: Prior to the "no ink on tumor" SSO/ASTRO consensus guideline, approximately 20% of women with stage I and II breast cancers undergoing breast conservation surgery at our institution underwent margin re-excision. On 5/20/2013, our institution changed the definition of negative margins from 2 mm to "no ink on tumor". Commensurate with the aim to minimize burden on patients and procedural costs, we investigated margin re-excision rates at our institution before and after the implementation of the new guidelines. Methods: A retrospective review was conducted of patients who had surgery at our institution with clinical stage I and II breast cancers between 6/1/2011 and 5/1/2015. Patients undergoing surgery prior to 5/20/2013 were included in the pre-guideline cohort (PRE), while the rest were included in the post-guideline cohort (POST). In the PRE and POST cohorts, negative margins were 2 mm and "no ink on tumor", respectively. Chi-square tests and nonparametric rank tests were used. Results: Of the 954 patients evaluated, 402 and 552 patients comprised the PRE and POST cohorts. The median age between the PRE and POST cohorts was 62 vs 62.5 years (p=0.691). Median pathologic tumor size was 14 vs 12 mm (p=0.107). Implementation of the guideline resulted in a significant decrease in the positive/close margin rates (29.6% PRE vs 9.6% POST; p<.001) and re-excision rate (20.9% PRE vs 15.9% POST; p = .049). No significant difference was found in local recurrence between the cohorts (1.2% PRE vs 1.5% POST; p=.787); however, follow up was limited (median: 2.9 years PRE vs 1 year POST). Conclusion: The implementation of the "no ink on tumor" guideline resulted in a significant decrease in margin re-excision rates. In the PRE cohort, positive/close margins rates (29.6%) were higher than re-excision rates (20.9%) due to close margins at the skin or chest wall. In the POST cohort positive margins rates (9.6%) decreased more than re-excision rates (15.9%), as our surgeons used clinical judgment to re-excise tumors with close margins and an extensive intra-ductal component present on final pathology.

P11

Omission of Sentinel Node Biopsy in Older Patients with Clinically Node-Negative Invasive Breast Cancer J. Bao,* J. Johnson, C. Donovan, F. Amersi, Q. Li, A. Giuliano, A. Chung. *Surgery, Cedars-Sinai Medical Center, Los Angeles, CA.*

Introduction Sentinel node biopsy (SNB) in patients age 70 and older may contribute to postoperative morbidity and may not affect recurrence rates. We compared regional recurrence (RR) and survival rates in patients who did not have SNB to those who did. Methods Retrospective review of our institution's prospectively maintained database identified 550 patients age 70 and older with clinical T1-2 N0 invasive breast cancer treated with breast conserving surgery from January 1, 2000 through December 31, 2013. One hundred and eleven patients who did not have SNB were compared to 439 patients who did. Analysis included patient and tumor characteristics, RR, disease-free survival (DFS), cancer-specific survival (CSS) and overall survival (OS). Results Of 550 patients, mean age was 77.7 years with a mean follow-up of 4.4 years. Those who did not have SNB were significantly older, had higher American Society of Anesthesiologists (ASA) scores, and had smaller tumors than those who had SNB. The SNB group was more likely to undergo adjuvant systemic therapy and irradiation (Table 1). The two groups did not differ significantly in tumor grade, histology, hormone receptor status, and HER2 status. The incidence of RR in the group without SNB was 1.8% (2/111) vs. 3.0% (13/439) in the group with SNB (p=0.75). The 5-year DFS was 96.4% without SNB vs. 94.7% with SNB (p=0.27). The 5-year CSS was 98.2% vs. 97.5% (p=1.00). The 5-year OS was 72.1% vs. 90.7% (p<0.01). Conclusions Patients age 70 and older with clinical T1-2 N0 breast cancer who did not receive SNB were older, had higher ASA scores, and were less likely to receive adjuvant therapy compared to those who had SNB. Despite this, they had similar RR, DFS, and CSS to those who had SNB. SNB may be safely omitted in some patients age 70 and older with early invasive breast cancer.

Table 1. Patient and tumor characteristics in patients 70 years and older with early invasive breast cancer who did (SNB) and did not receive sentinel node biopsy (No SNB)

Characteristic	SNB	No SNB	p-value
Mean age (years)	76.5	82.3	<0.01
Mean ASA*	2.4	2.6	<0.01
Mean tumor size (mm)	19.0	16.8	0.05
Adjuvant therapy (number of patients who received therapy/total number)			
Chemotherapy	66/421 (15.7%)	6/103 (5.8%)	<0.01
Radiation	333/409 (81.4%)	31/100 (31.0%)	<0.01
Hormonal therapy	324/418 (77.5%)	66/103 (64.1%)	<0.01

*ASA=American Society of Anesthesiologists

P12

Bracketed Radioactive Seed Localization Reduces Re-excision Rates in Comparison to Bracketed Wire Localization M.S. Da Silva,[1]* J.H. Porembka,[2] S.J. Seiler,[2] A.M. Leitch,[1] J. Huth,[1] A.K. Rivers,[1] R. Wooldridge,[1] A. Chu,[2] E. Brown,[2] A. Mokdad,[1] J. Bao,[1] M. Hansen,[1] R. Rao.[1] *1. Division of Surgical Oncology, Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX; 2. Department of Radiology, University of Texas Southwestern Medical Center, Dallas, TX.*

Background. Localization excision of breast lesions using a single Iodine-125 radioactive seed offers several advantages over single wire localization excision, including improved operating room efficiency, decreased excision volume, and lower re-excision rates. Wire bracketing allows accurate excision of more expansive lesions, and has been used to offer breast conserving therapy for large areas of ductal carcinoma in situ. Seed-localized bracketing is also now utilized in a similar capacity. This study aims to compare re-excision rates of bracketed seed-localized excisional biopsies/partial mastectomies to bracketed wire-localized excisional biopsies/partial mastectomies. Methods. Retrospective review was performed of patients undergoing localization of breast lesions using two or more localizers in a bracketed approach at an academic medical center from 2004-2014. Data collected included demographics, histology, tumor size, re-excision rates, neoadjuvant and adjuvant therapy. Student's t-test and Pearson's chi-square test were used to compare continuous and categorical data. A multivariable logistic regression model was used to evaluate the association between re-excision and localization technique after adjusting for clinically relevant variables. Results. 172 bracketed localization excisions were performed. 163 (95%) of excisions were performed for a cancer diagnosis. Median age was 58 years for both groups. The pre-treatment tumor sizes were not different between the two groups. 22/98 (22%) of patients in the seed localization group and 40/74 (54%) in the wire localization group required a second operative procedure to clear the margins (p<0.001). After adjusting for demographic and clinicopathological variables including the utilization of neoadjuvant chemotherapy, patients who underwent wire localization were 3.1 times more likely to undergo re-excision of margins compared to patients in the seed localization group (OR = 3.1, 95% CI 1.5 – 6.6). Conclusions. Bracketed radioactive seed localization of breast lesions is not only feasible but reduces the return to the operating room for re-excision when compared to bracketed wire localization.

Comparison of Bracketed Localization Techniques

	Total	Seed Localization	Wire localization	p-value
Total	172	98 (57%)	74 (43%)	
Age (median)	58	58	58	0.75
Race				0.53
Caucasian	83/172 (48%)	49/98 (50%)	34/74 (46%)	
African American	48/172 (28%)	24/98 (24%)	24/74 (32%)	
Hispanic	29/172 (17%)	19/98 (19%)	10/74 (14%)	
Other	12/172 (7%)	6/98 (6%)	6/74 (8%)	
Tumor Size (mean)	3.6	3.9	3.2	0.053
Tumor Type				0.11
In-situ	67/171 (39%)	32/98 (33%)	35/73 (48%)	
IDC	82/171 (48%)	51/98 (52%)	31/73 (42%)	
ILC	11/171 (6%)	6/98 (6%)	5/73 (7%)	
Other	11/171 (6%)	9/98 (9%)	2/73 (3%)	
Shave Margins	70/172 (41%)	58/98 (59%)	12/74 (16%)	<0.001
Additional Margins	49/172 (28%)	22/98 (22%)	27/74 (36%)	0.043
Neoadjuvant	32/168 (19%)	58/98 (59%)	12/74 (16%)	<0.001
Re-excision Rate	62/172 (36%)	22/98 (22%)	40/74 (54%)	<0.001

Invasive ductal carcinoma (IDC); Invasive lobular carcinoma (ILC)

P13

Defining the Incidence of Imaging and Biopsy After Mastectomy: It's Not Zero S. Ahn,* B. Elnekaveh, C. Weltz, H. Schmidt, E. Port. *Mount Sinai Medical Center/Dubin Breast Center, New York, NY.*

Introduction: Despite equivalent survival rates between BCT and mastectomy, mastectomy rates are increasing. Patient decision making toward bilateral mastectomy (BM) is often driven by factors including the desire to eliminate future imaging and/or biopsy of the remaining breast(s). We investigated the incidence of post-mastectomy imaging and biopsy driven by palpable findings. Methods: Retrospective review and follow up of all unilateral mastectomy (UM) and BM cases performed at a single institution was undertaken. Imaging studies and biopsies driven by physical examination findings by either patient or physician were identified. Results: From 2009-2015, 203 and 191 BM and UM cases respectively were identified. Mean follow up was 26 months. Of BM patients 31/203 (15%) required imaging, including 29 ultrasounds and 2 MRIs. The majority of studies (24/31,77%) were performed for findings on the previous cancer (ipsilateral) side. 16/203 (8%) of BM patients and more than half who underwent imaging also had subsequent biopsy with 11/16 (69%) on the ipsilateral side. Mean time from BM to biopsy was 17 months. 3/16 (19%) biopsies demonstrated malignancy, all on the ipsilateral side, for an overall recurrence rate of 3/203 (1.5%) for BM patients. For UM patients 19/191 (10%) underwent imaging on the ipsilateral side, all ultrasounds. As expected, UM patients also underwent routine contralateral surveillance and thus more biopsies overall were generated with 32/191 (17%) of UM patients requiring biopsy for a suspicious finding: 11/32 (34%) on the UM side and 21/32 (66%) on the contralateral side. 3/32 (9%) of biopsies were malignant: 2/3 ipsilateral and 1 contralateral. Conclusions: BM patients had a 15% rate of requiring subsequent imaging, with 8% requiring biopsy. UM was associated with higher rate of requiring future biopsy (17%), predominantly on the contralateral breast. Risk of recurrence or new contralateral primary was low for both BM and UM patients. Following both BM and UM the possible need for subsequent imaging and biopsy can never be completely eliminated, and this information is critical for patient understanding and expectation related to surgical decision making.

P14

Physician Preference and Patient Satisfaction with Radioactive Seed Versus Wire Localization A. Romanoff,* H. Schmidt, A. Burnett, A. Condren, E. Port. *Mount Sinai Medical Center/Dubin Breast Center, New York, NY.*

Introduction: Radioactive seed localization (SL) is a newer alternative to needle localization (NL) for identifying non-palpable breast lesions. SL offers potential scheduling advantages by uncoupling it from the surgical procedure. Currently there are no standards or recommendations regarding selection of SL vs. NL, with some facilities offering only one or the other. We investigated factors influencing the selection of SL vs. NL at our institution where both are offered, and compared patient satisfaction. Methods: Patients undergoing localizations from 5/14-8/15 were included. Physicians were surveyed upon surgical scheduling to evaluate factors influencing selection of SL or NL. Patient satisfaction was evaluated with a survey at the post-operative visit. Retrospective chart review was completed in order to document patient, disease-related, and operative factors. Results: 341 patients were identified, including 104 (30%) who underwent SL, and 237 (70%) with NL for benign or malignant lesions. There was no difference in age, benign vs. malignant disease, or need for concomitant axillary surgery between the two groups (see Table 1). From 260 physician surveys completed, 48 (18%) patients were deemed candidates for NL only, with the most common reasons cited being the need for multiple/bracketing localizations within the same breast (31, 65%), and radiologist preference (12, 25%). Of 212 patients eligible for both NL and SL, 87 (41%) and 125 (59%) underwent SL and NL respectively. The most commonly cited reason for selection of method was physician preference (129, 61%), followed by patient preference/avoiding a second visit for seed placement (71, 33%). 255 patient surveys were completed. There was no significant difference in self-reported pre-operative anxiety level, inconvenience or pain related to the localization procedure, post-operative pain or medication requirement, or overall patient satisfaction comparing SL and NL. Conclusions: SL and NL offer patients similar satisfaction, and this is the first time these procedures have been compared in this fashion. Factors influencing selection of one modality over the other include both logistic and clinical considerations.

	Seed Localization N=104	Needle Localization N=237	P value
Patient Age (mean, range)	55 (26-87)	56 (20-86)	0.40
Benign	47 (45%)	102 (43%)	0.77
Malignant	57 (55%)	135 (57%)	
No Axillary Surgery	69 (66%)	158 (67%)	0.71
Axillary Surgery	35 (34%)	79 (33%)	

P15

The Use of One Step Nucleic Acid Amplification and Tumor-Related Risk Factors in the Treatment of Axillary Breast Cancer: A Predictive Model S. Banerjee.* *Royal Free London NHS Trust, London, England, United Kingdom.*

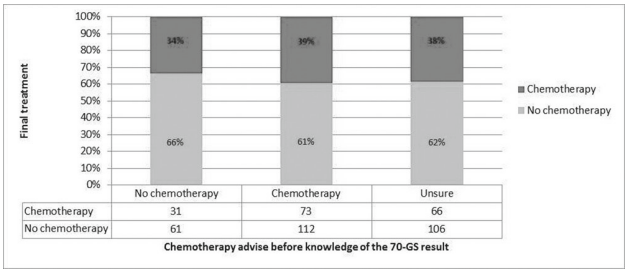
Background: The effectiveness of CK 19 m RNA copy number and tumour related factors in predicting non-sentinel axillary nodal involvement was investigated, in order to facilitate the formulation of local treatment guidelines for axillary clearance (ANC) following intra-operative analysis of the sentinel node biopsy (SNB) using one-step nucleic acid amplification (OSNA). Methodology: Patients due to have (SNB) for breast cancer as well as patients with high-grade ductal carcinoma in situ with pre-operative negative assessment of the axilla were included. Alternate slices of each node were sent for assessment by either OSNA or Histopathology. Immediate ANC was performed if OSNA was positive. The CK19 m RNA nodal copy number, the total tumour load (TTL) measured by summation of m RNA copy numbers of all positive nodes, the total nodal status at ANC and tumour characteristics for each patient was recorded. A model of risk probability was constructed using TTL and tumour related factors. Results: 664 nodes were analysed from 425 patients who had SNB performed. 105 ANC were performed. The concordance was 91.4%, positive predictive value, negative predictive value was 77% and 97% respectively. TTL ($p<0.01$), and presence of LVI ($p<0.05$) were predictive for additional nodal involvement.Patients with TTL less than 1400 did not have additional non sentinel lymph node involvement and were not selected by the model. All patients with 2 or more positive nodes were identified by the risk model. CONCLUSION: In the future only patients deemed high risk may be offered ANC using risk model while axillary surgery in other groups may be omitted or a decision based on risk stratification.

P16

Impact of the 70-Gene Signature on Adjuvant Systemic Therapy Decisions in Early Breast Cancer Patients: Preliminary Results of a Prospective Multicenter Observational Study A. Kuijer,[1]* M. Straver,[1] S.G. Elias,[2] C. Smorenburg,[3] J. Wesseling,[3] S.C. Linn,[3] E. Rutgers,[3] S. Siesling,[4] T. van Dalen.[1] *1. Surgery, Diakonessenhuis Utrecht, Utrecht, Netherlands; 2. University Medical Center Utrecht, Utrecht, Netherlands; 3. Netherlands Cancer Institute, Amsterdam, Netherlands; 4. Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands.*

Background: gene-expression profiles, such as the 70-gene signature (70-GS), were developed for optimizing outcome prediction in breast cancer patients and are increasingly used as adjunct to conventional clinic-pathological prognostic factors to guide adjuvant chemotherapy (CT) decisions. The Dutch guideline suggest the use of a validated gene-expression profile in

early stage breast cancer patients suffering from an oestrogen receptor (ER)+ invasive ductal carcinoma in whom controversy exists, based on conventional prognostic factors, regarding the benefit of adjuvant CT. Patients and methods: In this prospective observational multicentre study the impact of the 70-GS on adjuvant CT decisions in Dutch early stage breast cancer ER+ patients is assessed. Patients within the guideline-intended indication area who received the 70-GS were included. Adjuvant CT advice was stated by the treating physician before and after obtaining the 70-GS result. Results: Until date 450 patients, treated in 31 hospitals, were enrolled. The 70-GS influenced the treatment decision in 307 (68%) of the patients. In 92 patients adjuvant CT would initially be omitted, in 31 (34%) of these patients adjuvant CT was nevertheless advised after obtaining the 70-GS result. In 185 patients adjuvant CT would have been administered without knowledge of the 70-GS, in 112 (61%) of these patients adjuvant CT could be withheld after obtaining the 70-GS result. In 172 patients the treating physician stated to be unsure about the CT decision. In 95% of these patients the treating physician adhered to the 70-GS result and in 106 (62%) adjuvant CT was omitted. Conclusion: use of the 70-GS in Dutch ER+ early breast cancer patients influenced CT treatment decision in 68% of the patients in whom based on conventional prognostic factors controversy exists regarding the benefit of adjuvant CT. 70-GS use was associated with high adherence rates to the test result and led to a decreased administration of adjuvant CT.



P17

Preoperative MRI Exhibits Limited Utility in Axillary Staging for Breast Cancer J. Kuckelman,* J. Bingham, M. Barron, A. Mosier, V. Sohn. *General Surgery, Madigan Army Medical Center, Tacoma, WA.*

Introduction: Magnetic resonance imaging (MRI) is a commonly utilized modality obtained for breast cancer patients. While axillary lymph node findings are routinely reported in these studies, the sensitivity and specificity of these findings remains unclear. We sought to evaluate the utility and clinical impact of axillary findings in patients undergoing routine preoperative MRI for newly diagnosed breast cancer. Methods: In this retrospective study, women diagnosed with infiltrating ductal and lobular carcinoma not undergoing neoadjuvant therapy between 2008-2014 were reviewed. MRI characteristics of the primary tumor and features of the axillary findings, were then compared to the final pathologic results. Results: 219 of 338 female patients met inclusion criteria and comprised our patient cohort. The average age of patients was 54. Sixty five patients (29%) had preoperative imaging concerning for axillary involvement. One hundred forty three (65.5%) underwent breast conservation therapy versus a mastectomy. Of those with confirmed metastasis, 8 (1.2%) had lymph nodes with micrometastasis or isolated tumor cells. MRI was found to have a sensitivity and specificity of 46.9% and 81%, respectively. The negative predictive value was 78.5% with an accuracy of 71% and a false negative rate of 13.8%. Regression analysis was performed and displayed that positive axillary findings on MRI finding did not correlate to age (R^2=.023) tumor size (R^2=.057), hormone status (R^2=.038), or number of positive nodes on final pathology (R^2=.137). Conclusion: Breast MRI exhibits limited utility for axillary staging in women with breast cancer. Staging MRI demonstrated poor sensitivity for detection of axillary metastasis in patients with infiltrating ductal and lobular breast cancer. Additionally specificity and overall accuracy did not rise to a level which would justify routine use.

P18

Prospective Evaluation of Skin and Nipple-Areola Sensation After Nipple-Sparing Mastectomy L. Dossett,* J. Lowe, W. Sun, M.C. Lee, P. Smith, C. Laronga. *Complex General Surgical Oncology, Moffitt Cancer Center, Tampa, FL.*

Background. Nipple sensation before and after mastectomy is poorly understood, despite being an important component of postoperative satisfaction and quality of life (QOL). We sought to prospectively quantify skin and nipple sensation after NSM compared to NSM-eligible patients electing skin sparing mastectomy without nipple-sparing (SSM). Methods. Women electing bilateral mastectomy with immediate reconstruction and eligible for NSM were prospectively offered inclusion in an IRB-approved nipple sensation and body image/QOL cohort study. Eligibility criteria: unifocal, small (<3cm) or no tumor (prophylactic indication), tumor >2cm from the nipple-areolar complex (NAC), clinically lymph node negative, body mass index (BMI) less than 30, no or grade 1 ptosis, and estimated breast volume <700g. After signing informed consent, the women self-selected the control arm (SSM) or investigational arm (NSM). Sensation testing was performed using Semmes Weinstein monofilaments (range: 2.83-6.65mm) at 4 points on the nipple, areola, and breast skin respectively. For SSM patients, skin located in the vicinity of the native nipple was used for nipple/areola sensation postoperatively. Semmes Weinstein monofilaments were converted into categorical values (0=no sensation, 5=sensitive to most fine filament). Descriptive statistics were performed. Results. 53 patients were enrolled; 38 (72%) chose NSM and 15 (28%) chose SSM. Patients choosing NSM were older, more likely to have cancer as the indication for surgery, had a lower BMI, and smaller breasts by weight. There was a trend towards improved preoperative skin sensation for women choosing NSM, but this was not statistically significant in most tested quadrants. Both groups had significant reduction in postoperative skin sensation (Table 1). In the NSM group, measurable NAC sensation was preserved in both NAC for 26% of patients and in at least one NAC for 66%. Conclusion. Patients undergoing SSM and NSM have considerable loss in skin and NAC sensation following surgery, but up to 26% of patients retain some NAC sensation after NSM.

Table 1. Median Sensation by Study Group

	Preoperative Sensation SSM (n=15)	Preoperative Sensation NSM (n=38)	p-value	Postoperative Sensation SSM (n=15)	Postoperative Sensation NSM (n=38)	p-value
Right Skin Sensation	3.25	4.00	0.04	0.00	0.75	0.16
Right Areola Sensation	3.00	3.25	0.15	0.00	0.25	0.01
Right Nipple Sensation	3.00	3.25	0.85	0.00	0.13	0.04
Left Skin Sensation	3.50	4.00	0.21	0.75	0.25	0.92
Left Areola Sensation	2.75	3.13	0.10	0.00	0.00	0.61
Left Nipple Sensation	3.50	3.00	0.33	0.00	0.00	0.31

Filaments sizes converted to categorical values where 0=no sensation, 1=6.65, 2=4.5, 3=4.3, 4=3.8 and 5=2.8

P19

Evaluating the Risk of Underlying Malignancy in Patients with Pathologic Nipple Discharge G. Li,* S.M. Wong, F. Nakhlis, S. Lester. *Brigham and Women's Hospital, Boston, MA.*

Background: Pathologic nipple discharge (PND) is a common constellation of symptoms seen by surgeons. While most PND is due to a benign cause (i.e. an intraductal papilloma), duct excision has been advised to rule out an underlying malignancy. We reviewed our experience to identify factors associated with malignancy in patients with PND. Methods: With IRB approval, we conducted a retrospective record review of patients who presented to our institution with PND (defined as unilateral, spontaneous, clear or bloody nipple discharge) between January 1, 2004 and December 31, 2014. We compared clinical and histopathologic data between patients found to have benign vs. malignant disease on excision, and used multivariable logistic regression to assess factors independently associated with malignancy on final pathology. Results: We identified 280 patients with PND: 45% were postmenopausal, 8% had a personal history of breast cancer, and 50% had a family history of breast cancer. Invasive or in situ malignancy was identified in 49 (18%) cases. Of these, 32 (65%) had extensive DCIS (n=26, 69% of which had invasive or microinvasive component) or solid papillary carcinoma (n=6). Patients diagnosed with

malignancy had a higher rate of suspicious clinical findings, such as a palpable mass and/or nipple inversion (34% vs. 13%, p<0.001), and of abnormal breast imaging (94% vs. 75%, p= 0.004). On multivariable analysis, older age, the presence of a palpable mass and/or nipple inversion, and abnormal imaging were significantly associated with malignancy. The rate of malignancy was 38% for PND with suspicious clinical findings and abnormal imaging, but only 2% for PND without clinical or imaging abnormalities. Conclusions: Patients presenting with PND without associated clinical or imaging abnormalities had a low rate of underlying malignancy, while those with abnormal clinical and imaging findings had substantially higher rates of malignancy. Based on this, for patients with PND without suspicious clinical or imaging findings, close surveillance may be a reasonable alternative to surgery. Prospective data to further address the management of PND would be helpful.

P20

The Effect of Radiation Therapy on Immediate Autologous Flap Reconstruction for Breast Cancer Patients P.N. Thomas,* S. Higgins, S. Fusi, A. Au, M. Young, S. Evans, A. Chagpar, D. Lannin, N. Horowitz, B. Killelea. *Yale, New Haven, CT.*

Introduction: Reconstruction after mastectomy for breast cancer is an integral part of breast cancer treatment. For patients who will likely require post mastectomy radiation therapy (PMRT), decision-making regarding type of reconstruction is complex. Potential complications of PMRT after implant/tissue expander reconstruction have been well described. However, data regarding outcomes after immediate free flap reconstruction (IFFR) and PMRT are sparse. The purpose of this study was to evaluate complications after PMRT for patients who underwent IFFR. Methods: We performed a retrospective review of our database of patients who underwent IFFR after mastectomy followed by PMRT from 2011-2015. Primary outcome measures were flap loss, fat necrosis and wound complications. Results: The series included 75 patients. The average age at mastectomy was 54.5 years (range 31-66). The stage at diagnosis was: Stage 0 (1), Stage 1 (1), Stage 2 (41), Stage 3 (31), Stage 4 (1). The average BMI for all patients was 29.4. There were 33 patients who underwent ms-TRAM reconstruction and 43 who had DIEPs. PMRT was delivered to the ipsilateral chest wall (all patients) and axilla (16 patients). The median time to the beginning of PMRT was 175 days (range 38-396 days). Fat necrosis occurred in 5 patients prior to the start of PMRT and 6 patients following the completion of PMRT. Wound complications occurred in 11/75 patients (14%). Flap loss occurred in one patient that had a DIEP reconstruction (prior to radiation treatment) which equates to an autologous flap loss rate of 1%. Conclusions: Our single-institutional review of 75 patients who underwent IFFR reconstruction followed by PMRT reveals a low overall complication rate, demonstrating the safety and efficacy of this approach for select patients. The risk of complications, most notably flap loss, is minimal after radiation and should not be a deterrent when deciding on immediate breast reconstruction.

Complications Prior to PMRT

	Fat Necrosis	Wound complications	Flap loss
Patients undergoing IFFR followed by PMRT	11/75 (14.6%)	11/75 (14.6%)	1/75 (1.3%)

P21

Nativity Status Negatively Impacts Quality of Breast Cancer Care for Latinos in the U.S D.C. Acosta,* A. Loehrer, D.C. Chang. *Codman Center for Clinical Effectiveness in Surgery, Massachusetts General Hospital, Boston, MA.*

Introduction: Although previous studies have examined disparities across different racial and ethnic groups, few have investigated the effect of nativity status on the quality of care received within a minority group. Stage at diagnosis served as a surrogate to evaluate the quality of primary care, and receipt of radiation served as a surrogate to evaluate quality of specialty care in oncology. Methods: An analysis was performed using the SEER (Surveillance, Epidemiology, and End Results) database linked with the AHRF (Area Health Resources File) and the U.S. Census Bureau's ACS (American Community Survey) databases. Inclusion criteria included U.S. born Latino, foreign-born Latino, U.S. born non-Latino white (NLW), and European-born NLW women with breast cancer from 1988-2009. The independent variable was defined as patient's nativity status, and the outcomes were defined as stage at diagnosis and receipt of radiation. Logistic regression was performed adjusting for community and patient covariates. Results: A total of 296,055 women were analyzed. Compared to U.S.-born NLW, both U.S.-born Latinas and foreign-born Latinas were more likely to present at a high-stage (OR = 1.18, CI = 1.13 – 1.23; OR: 1.26, CI: 1.22 – 1.31), and were less likely to receive radiation (OR: 0.85, CI: 0.75 – 0.96; OR: 0.80, CI: 0.73 – 0.88). Compared to U.S.-born NLW, foreign-born NLWs were more likely to receive radiation (OR: 1.26, CI: 1.04 – 1.53), yet stage at diagnosis among foreign-born NLWs was not significantly different. Conclusion: Nativity status negatively impacted the quality of breast cancer care for foreign-born Latina patients treated in the U.S., but this negative impact was not observed in foreign-born NLW patients. Lack of cultural competency in health services could explain the disadvantage observed among foreign-born Latinas. Measures should be taken to increase the number of culturally and linguistically concordant physicians to create well-rounded providers that are able to serve diverse populations, as well as to change existing interventions by integrating the positive context of a patient's culture as a means to promote treatment-seeking modification.

P22

Oncofertility Program Implementation Increases Access to Fertility Preservation Options and Assisted Reproductive Procedures in Breast Cancer Patients J. Vu,[1]* N. Llarena,[2] S. Estevez,[2] J.S. Jeruss.[1]
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2. Northwestern University, Chicago, IL.

INTRODUCTION: Young oncology patients incur a risk of temporary or permanent infertility as a result of cancer treatment. Despite guidelines recommending oncologists counsel patients about treatment-related fertility risks, patients are not routinely educated about fertility preservation options before initiating therapy. We hypothesized that a formal oncofertility program would increase provider-driven discussions, fertility specialist referrals, and assisted reproductive procedures in breast cancer patients. METHODS: An oncofertility program was instituted in 2007 that required documentation of fertility preservation discussions for premenopausal breast cancer patients during intake encounters. The program included provider- and patient-centered resources with education regarding available reproductive techniques, a fertility preservation patient navigator, a hotline for referrals, and an online resource tool. We compared the number of discussions, referrals, appointments made, and assisted reproductive procedures performed in pre- (2004-2006, n=277) and post- (2007-2012, n=515) program patient cohorts. Median age was 41 for both cohorts. RESULTS: Discussions about treatment effects on fertility increased after initiation of the oncofertility program, from 9% to 38% ($p < 0.001$). The documented number of patients who expressed an interest in maintaining fertility at the time of diagnosis also increased in the post-program cohort, ($p = 0.0041$), as did referrals to reproductive specialists ($p < 0.0001$), and appointments attended ($p < 0.0001$). Additionally, there was an increase in the number of patients who underwent fertility preservation procedures ($p < 0.0183$) in the post-program cohort. CONCLUSIONS: Institution of an oncofertility program significantly increased the rate of conversations about treatment-related infertility and documented patients expressing fertility concerns. Importantly, establishment of a formal oncofertility program helped to improve patient access to fertility preservation options. Future work will examine the impact of access to fertility preservation on cancer treatment compliance.

P23

Age and Receptor Status Do Not Indicate the Need for Axillary Dissection in Patients Meeting ACOSOG Z0011 Criteria A. Mamtani,* K.J. Van Zee, H.S. Cody III, M. Pilewskie, A. Barrio, A.S. Heerdt, S. Patil, M. Morrow. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: ACOSOG Z0011 provided practice-changing evidence for omission of axillary lymph node dissection (ALND) in women with <3 positive sentinel lymph nodes (SLNs) undergoing breast conservation therapy (BCT). Since most women in ACOSOG Z0011 were postmenopausal with ER-positive cancers, the applicability of these results in younger and ER-negative patients has been questioned. We compared axillary surgery and nodal disease burden in patients with high-risk (HR) disease, defined as triple-negative (TN), HER2-positive (HER2+), or age <50 years, to the remainder of the population, termed average-risk (AR). Methods: From 8/2010 to 7/2015, Z0011-eligible patients (cT1-2N0 having BCT) were prospectively identified and followed. ALND was performed for >2 positive SLNs or extracapsular extension. Clinicopathologic characteristics, axillary surgery, and short-term outcomes in HR and AR patients were compared. Results: Among 646 Z0011-eligible patients,

228 (35%) were HR: 30 (13%) TN, 43 (19%) HER2+, 121 (53%) <50 years old, and 34 (15%) had >1 HR feature; 418 (65%) were AR. Characteristics are summarized in Table 1. HR patients were significantly younger (p<0.0001), with higher-grade tumors (p<0.0001), and more often had abnormal nodes on imaging (p=0.02). SLNB alone was performed in 84% HR vs. 83% AR cases, with a median of 4 vs. 3 SLNs excised (p=0.01), and a median of 1 positive SLN in both groups (p=0.42). 61% HR vs. 68% AR (p=0.51) had additional positive nodes at ALND. Median number of additional positive nodes was 3.5 vs. 3.0 (p=0.38). Adjuvant radiotherapy was completed in 96% HR vs. 92% AR (p=0.05) cases. At a median follow-up of 30 vs. 32 months (range 1-58), there were no isolated axillary recurrences. In the HR vs. AR groups, there were 7 vs. 8 distant, 4 vs. 3 locoregional, and 2 vs. 0 combined locoregional/distant recurrences, respectively. Conclusions: HR patients were no more likely than their AR counterparts to require ALND. In patients requiring ALND, nodal burden did not differ. These findings indicate that ALND is not indicated on the basis of age or receptor status in patients otherwise meeting ACOSOG Z0011 eligibility criteria.

Table 1: Patient and node clinicopathologic characteristics

Patient Clinicopathologic Characteristics					
	High-Risk: n = 228		Average-Risk: n = 418		p-value
	Median	Range	Median	Range	
Patient age (years)	47	28 - 83	62	50 - 92	<0.0001
Clinical tumor size (cm)	2.0	0.5 - 5.0	2.0	0.5 - 8.0	0.14
Pathologic tumor size (cm)	1.8	0.25 - 5.27	1.7	0.1 - 5.2	0.43
	N	%	N	%	
Palpable tumor	113	49.8	144	34.4	0.0002
Abnormal lymph nodes imaged	67	29.4	88	21.0	0.02
Histology: Ductal Lobular/mixed/other	204 24	89.5 10.5	353 65	84.4 15.6	0.08
Lymphovascular invasion	142	62.3	237	56.7	0.17
SLNB: Nodal Results					
	High-Risk: n = 228		Average-Risk: n = 418		p-value
	N	%	N	%	
# of positive sentinel nodes: 1 or 2 ≥ 3	199 29	87.3 12.7	368 50	88.0 12.0	0.78
	Median		Median		
# sentinel nodes excised	4.0		3.0		0.01
cALND: Nodal Results					
	High-Risk: n = 36		Average-Risk: n = 71		p-value
	N	%	N	%	
Additional positive nodes	22	61.1	48	67.6	0.51
	Median	Range	Median	Range	
# additional nodes positive	3.5	1 - 52	3.0	1 - 53	0.38
# additional nodes excised	16.5	6 - 52	14.0	0 - 53	0.07

SLNB: Sentinel lymph node biopsy, cALND: Completion axillary lymph node dissection

P24

Resection of the Primary Tumor Significantly Improves Median Overall Survival in Patients with Stage IV De Novo Inflammatory Breast Cancer R. Menen,* H.Y. Lin, Y. Shen, S.F. Simona, I. Bedrosian, W. Woodward, N. Ueno, V. Valero, G. Babiera. *MD Anderson Cancer Center, Houston, TX.*

Introduction: Inflammatory breast cancer (IBC) is an aggressive, rapidly progressive disease that comprises 2-6% of breast cancers with approximately 25%% of patients presenting with metastatic disease at diagnosis. There remains controversy surrounding the role of locoregional therapy for de novo stage IV non-IBC stage patient and surgical palliation is still the mainstay of therapy for symptomatic patients. Few studies have specifically evaluated the role of primary tumor resection for treatment of de novo stage IV IBC patients. Methods: Using the National Cancer Data Base, female patients diagnosed between 1998 and 2011 with unilateral metastatic T4d adenocarcinoma of the breast as the only cancer were identified. To determine the impact of surgery on overall survival (OS), we conducted propensity score matched analysis to balance confounders of two treatment groups. The propensity to receive surgery was estimated using multivariate logistic model including year of diagnosis, age at diagnosis, race, hormone receptor status, chemotherapy, radiation therapy, facility type, and Charlson-Deyo score. Stratified log-rank test and double robust estimation under the Cox model were used to assess the effect of surgery on OS in the propensity score matched cohort. Results: A total of 1863 patients fulfilled the study criteria. 41% were in the surgery group whereas 59% were in the no-surgery group. In the unmatched cohort (N=1863), median OS of surgery and no-surgery groups were 24 and 13 months, respectively (p<0.001, Log-rank test). In the matched cohort (N=334), the median OS of surgery and no-surgery groups were 25 and 16 months, respectively (p=0.005, Stratified Log-rank test, Figure 1). After adjusting for other risk factors, surgery significantly benefited OS (HR (95% CI) = 0.69 (0.53, 0.88), p= 0.003). Conclusion: This retrospective study demonstrated that resection of the primary tumor significantly improves OS in patients with metastatic IBC. Further prospective studies are needed to change the surgical paradigm in this aggressive disease.

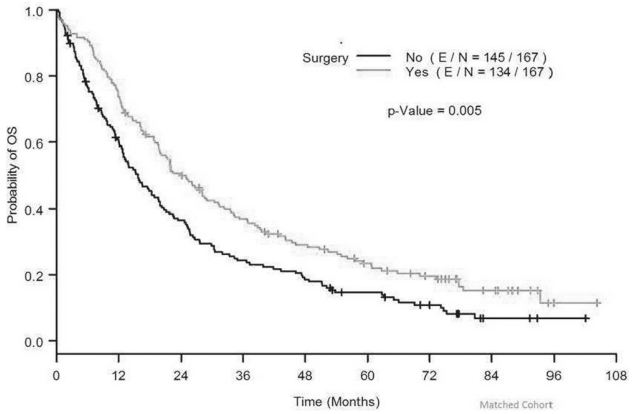


Figure 1: Overall survival in surgery vs no-surgery groups in the Matched Cohort. The green curve represents patients who underwent resection of the primary tumor. The black curve represents patients who did not undergo surgical resection. Median overall survival (OS) in the surgery group was 25 months, compared to 16 months in the no-surgery group (p= 0.005, stratified log-rank test).

P25

Breast Cancer Populations at Risk for Not Receiving Chemotherapy E. Marcinkowski,* L. Goldstein, A. Polverini, J. Yim, C. Vito, L. Taylor, J. Mortimer, L. Kruper. *City of Hope, Duarte, CA.*

Background: The American College of Surgeons Commission on Cancer (CoC) has defined an Accountability Breast Cancer Measure that multi-agent chemotherapy therapy is considered or administered within 120 days of diagnosis for women < age 70 with AJCC T1cN0M0, or Stage IB – III hormone receptor negative breast cancer. The objective of this study is to examine compliance in California. Methods: Using the California Cancer Registry 2004-2011, we evaluated female breast cancer cases meeting the criteria for chemotherapy. We examined rates of compliance and evaluated differences by patient and hospital characteristics using a multiple logistic regression model. Results: Among the 15,187 cases examined, 9,896(65.2%) were compliant. Among these cases, 9,545(96.5%) received chemotherapy, 33(0.3%) were contraindicated, 27(0.3%) were recommended although not given, and 291(2.9%) declined. Predictors of compliance included age at diagnosis, marital status, socioeconomic status (SES), and year of diagnosis (p<.0001), as well as race/ethnicity (p=.0015) and insurance (p=0.0190). Compliance decreased with age and patients age 26-35 (OR=1.74; 95%CI 1.48-2.04), age 36-45 (OR=1.33; 95%CI 1.21-1.47), and age 46-55 (OR=1.19; 95%CI 1.09-1.29) were significantly more compliant than those aged 56-69. Compliance decreased with SES level, lowest SES compared to highest SES (OR=0.69; 95%CI 0.61- 0.78). Compliance rates were significantly lower among minorities when compared to Non-Hispanic Whites: Asian/Pacific Islander (OR= 0.85, 95% CI 0.76 - 0.94), Hispanic (OR=0.86; 95%CI 0.78- 0.94), Black (OR=0.87; 95%CI 0.78- 0.98). Medicaid patients had the lowest rates of compliance when compared to Managed Care/HMO patients (OR=0.69; 95%CI 0.62 - 0.76). Single women had lower rates of compliance compared to married women (OR=0.90; 95%CI 0.82 - 0.99). Conclusion: The study points to disparities in compliance with CoC recommendations for chemotherapy within 120 days of diagnosis of breast cancer. Differences are observed by marital status, age, race/ethnicity, and insurance. These differences highlight the need for improved access to care for at-risk groups: older patients, minorities, those with limited insurance and/or lower SES.

P26

Surgical Treatment of Paget Disease of the Breast: A Report from the National Cancer Data Base A. Hanna,[1]* G. Daisuke,[2] S. Feigenberg,[1] S. Kesmodel,[1] K. Tkaczuk,[1] P. Rosenblatt,[1] E. Nichols,[1] D. Mullins,[2] N. Hanna,[1] E. Bellavance.[1] *1. University of Maryland School of Medicine, Baltimore, MD; 2. University of Maryland School of Pharmacy, Baltimore, MD.*

Introduction: Paget disease (PD) of the breast represents a minority (~2%) of breast malignancies. While the traditional treatment of PD in the setting of an invasive or non-invasive breast cancer is mastectomy (M), recent studies have supported treatment with breast conservation (BC) with adjuvant radiation (R). In this study, we aim to identify the current patterns of surgical management for PD in the setting of breast cancer. Methods: The National Cancer Data Base (NCDB) was used to identify stage I-III unilateral breast carcinoma in female patients 18 – 90 years of age who underwent surgery between 2010 and 2012. Patients with tumors > 4cm or who underwent neoadjuvant chemotherapy were excluded. Data on patient demographics, tumor characteristics, and treatment modalities were collected. Patients with PD were compared to patients without PD. All statistical analyses were two-sided t-tests for continuous variables and chi-squared tests for discrete variables with a p-value cut off of < 0.0001 for significance. Results: Of 502,833 female patients who had surgery between 2010 and 2012 who met our criteria, 1767 patients had PD. Table 1 describes differences in the demographic and tumor presentation of both PD and non-PD patients. The percentage of PD patients receiving BC was significantly lower than non-PD patients (PD = 27% versus non-PD = 65%, P < 0.0001). Of BC patients, 75% received adjuvant R in the PD and 86% non-PD groups. Of the PD patients undergoing M, 18% underwent contralateral prophylactic mastectomy compared to 13% in non-PD patients. Immediate reconstruction rates in PD and non-PD patients were similar (PD = 36% versus non-PD = 38%, P = 0.004). Conclusions: To our knowledge, this is the largest cohort of PD patients that has been reported. Overall, PD patients present with more advanced disease compared with non-PD patients and breast cancers associated with PD are more likely to be hormone receptor negative and Her 2 receptor positive. Despite data supporting BC in PD, the majority of patients reported in the NCDB are treated with mastectomy. Further research is required to determine if more extensive surgery for PD patients affects oncologic outcomes.

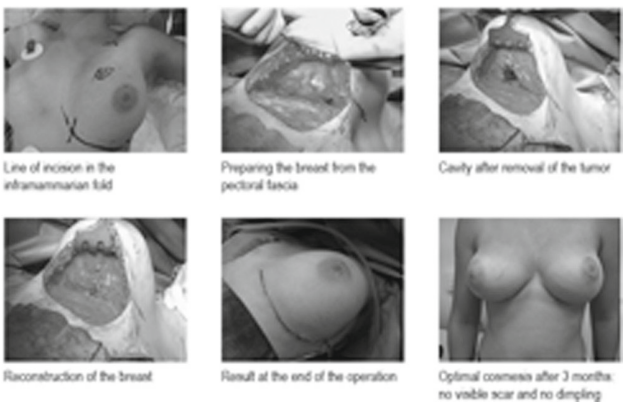
Demographic and Tumor Characteristics

Characteristic		*PD Patients (N=1784)*	*Percent of PD Patients*	*Non-PD Patients*	*Percent of Non-PD Patients*	*p-value*
Median Age (range)		*59 (20 - 90)*		*61 (18 - 90)*		
Race	*White*	*1365*	*77%*	*147354*	*80%*	*0.001*
	Hispanic	*97*	*5%*	*9091*	*5%*	
	Black	*224*	*13%*	*18234*	*10%*	
	Other	*98*	*5%*	*9026*	*5%*	
Pathologic Stage	*I*	*933*	*52%*	*116500*	*63%*	*0.000*
	II	*594*	*33%*	*57494*	*31%*	
	III	*257*	*14%*	*9711*	*5%*	
Histology	*Ductal*	*1158*	*84%*	*151492*	*82%*	*0.177*
	Lobular	*223*	*16%*	*32213*	*18%*	
	Unknown	*403*		*0*		
Tumor Size (mm)	*< 20*	*1132*	*63%*	*127093*	*69%*	*0.000*
	20 - 39	*652*	*37%*	*56612*	*31%*	
Positive Lymph Nodes	*0*	*1026*	*62%*	*132639*	*75%*	*0.000*
	1 - 3	*424*	*26%*	*34431*	*20%*	
	4- 9	*135*	*8%*	*6697*	*4%*	
	10 +	*60*	*4%*	*2486*	*1%*	
	Unknown	*139*		*7452*		
ER Status	*Positive*	*1161*	*67%*	*154851*	*85%*	*0.000*
	Negative	*580*	*33%*	*27381*	*15%*	
	Unknown	*43*		*1473*		
PR Status	*Positive*	*938*	*54%*	*138034*	*76%*	*0.000*
	Negative	*797*	*46%*	*43900*	*24%*	
	Unknown	*49*		*1771*		
Her2 Status	*Positive*	*669*	*42%*	*21415*	*12%*	*0.000*
	Negative	*915*	*58%*	*155332*	*88%*	
	Unknown	*200*		*6958*		

P27

Nearly Invisible Lumpectomy (NIL): Feasible and Safe A. Nijhuis,* J. Bloemen, J. Vogelaar, P. Nijhuis. *Surgery, VieCuri, Utrecht, Netherlands.*

We present the results of the first 50 patients operated upon with this new Nearly Invisible Lumpectomy (NIL) technique. Cosmesis has been fabulous: no dimpling and no visible scar. The technique, its indications and safety are discussed. Methods: The first 50 early-breast cancer patients who were treated with this technique were included between September 2010 and January 2015. Best indications for NIL were tumors located deep in the breast and/or high in the upper quadrants, especially in the medial upper quadrant. Originally, only palpable breast tumors were included. Later on, this technique was also used in patient with non-palpable tumors, even after neoadjuvant chemotherapy. Follow up was according to Dutch national guidelines.Informed consent was obtained in all patients. Technique: 1) inframammarian fold incision, 2) preparing the breast from pectoral fascia, 3) removal of tumor, 4) reconstruction of the breast (see figure). Results: Patients were all female with an average age of 56 years. Median follow up was 26 months. 25 Tumors were palpable, 25 required needle guidance. Average tumor size was 1.6 cm. pT-stage : 2 ypT0, 5pT1b,1 ypT1c, 33pT1c, 9pT2. pN-stage : 1Nx, 36 N0, 3 N1mic, 9 N1, 1 N2. Three woman encountered a bleeding necessitating re-operation. Margins were involved in 3 cases, followed by ablation. In one of the cases, this was already our primary treatment plan but the patient insisted on a conservative treatment. Three patients underwent needle guided lumpectomy after neoadjuvant chemotherapy; all had clear margins. To date, no recurrences have been encountered. Conclusion: NIL is the summum of breast conserving therapy in early-breast cancer: no dimpling or visible scar. The results of the first 50 NIL-procedures demonstrate that this procedure is not only feasible but also safe, even in non-palpable tumors and after neoadjuvant chemotherapy. Special attention has to be paid to hemostasis. To date, no recurrences have been encountered. This new procedure should be offered to early-breast cancer patients, especially in case the tumor is situated deep in the breast or high in the upper quadrants.



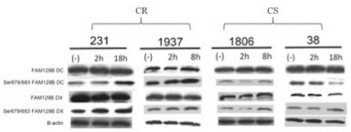
NIL procedure: step-by-step

P28

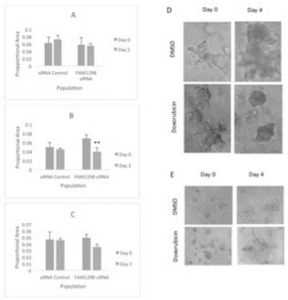
Differential Phosphoproteomics Between Chemosensitive and Resistant Triple Negative Breast Cancer Cells M. Lee,* X. Deng, J. Capri, M. Kohanfars, W.Y. Luo, J. Gornbein, J.P. Whitelegge, H.R. Chang. *UCLA, Los Angeles, CA.*

Introduction: Triple-negative breast cancer (TNBC) has an aggressive clinical behavior for which there is no targeted treatment. We optimized a protocol to analyze the phosphoproteome of chemoresistant (CR) and chemosensitive (CS) TNBC cell lines using mass spectrometry (MS) to discover targeted mechanisms involved in drug resistance. Methods: From prior studies, MDA-MB-231 and HCC1937 were considered CR, and HCC1806 and HCC38 CS. Cells were treated with DMSO, docetaxel (DC), and doxorubicin (DX). Samples were fractionated by hydrophilic interaction liquid chromatography (HILIC), enriched for phosphopeptides with titanium dioxide (TiO2) chromatography, and analyzed with tandem MS. Mean spectral counts were compared with a negative binomial model. Immunoblotting confirmed results. Cells were transfected with FAM129B or control siRNA and treated to assess changes in CR. Results: We found an average of 1063 proteins and 912 phosphorylated proteins for an 86% yield. The average false discovery rate was 4%. We identified 7023 unique phosphosites and 1436 sites in both CR and CS cell lines. With a restrictive p<0.01 and log change>2, 26 phosphosites in the DC group and 37 sites in the DX group were identified. Ser683 and ser696 of FAM129B were significant in both treatment groups. Immunoblotting for FAM129B total protein showed no difference between control and treated groups. Compared to controls, immunoblotting using anti-phospho-ser679/683

FAM129B showed decreased expression in CS cell lines after drug treatment and increased expression in CR lines (Panel 1). After successful knockdown of FAM129B in CR line MDA-MB-231, there was significantly increased susceptibility to DC and DX (Panel 2). Conclusion: We used HILIC and TiO2 enrichment to identify phosphoprotein profiles in complex samples with high yield and low false discovery. FAM129B phosphosites, a protein involved in cell invasion and suppression of apoptosis, had decreased expression after drug treatment in CS cell lines and increased expression in CR lines. Knockdown of FAM129B increased drug susceptibility. Our study suggests that FAM129B phosphorylation is involved in drug resistance of TNBC.



1: Immunoblotting for total protein FAM129Bshows no difference in each cell line between control and after drug treatment. Immunoblotting for ser676/683 of FAM129B shows increased expression after treatment in CR lines and decreased expression in CS lines.

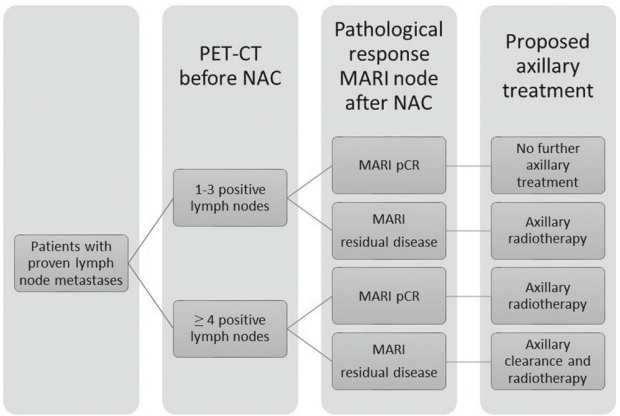


2: siRNA-mediated FAM129B knockdown in doxorubicin-resistant 231 causes significantly increased susceptibility to both doxorubicin and docetaxel in 2D cultures, when compared to a siRNA control (A-C). FAM129B knockdown also reduced doxorubicin resistance in 3D 231 culture (D, E). A) Treatment of transfected 231 with DMSO control. B) Treatment of transfected 231 with 1 μM doxorubicin. C) Treatment of transfected 231 with 5 μM docetaxel. D) Images taken at 100x magnification of siRNA control-transfected 231 treated with DMSO or 1.5μM doxorubicin. E) Images taken at 100x magnification of FAM129B siRNA-transfected 231 treated with DMSO or 1.5μM doxorubicin. (*: P≤0.05; **: P≤0.01; Error bars depict standard error.)

P29

New Strategy to Tailor Axillary Treatment After Neoadjuvant Chemotherapy in Breast Cancer Patients M. Straver,* M. Donker, B.B. Koolen, R.A. Valdes Olmos, E. Rutgers, M.F. Vrancken Peeters. *Surgery, NKI-AvL, Utrecht, Netherlands.*

Background: Tailored treatment of lymph node metastases after neoadjuvant chemotherapy (NAC) remains discussable because of a low accuracy of the sentinel node procedure in patients with proven lymph node metastases. Marking Axillary lymph nodes with Radioactive Iodine seeds (MARI procedure) is proven to be more accurate. We studied the potential of tailored axillary treatment by combining PET-CT to stage the axilla before NAC with the pathological response after NAC measured by the MARI procedure. Patients and methods: Between 2008-2012 patients participated in the MARI trail. Prior to NAC, the number of FDG-avid lymph nodes was assessed and one of the tumour-positive nodes was localized with an I-125 seed. After NAC, the marked node was selectively removed followed by a complementary axillary clearance. The response in the MARI node was indicative for the response in additional lymph nodes with a FNR of 7 % as reported earlier. We now combined PET and MARI data in order to find out the potential reduction in axillary clearances by treating patients according to the attached scheme. Results: Patients were categorised based on PET-CT outcome before NAC. In 65/95 patients, 1-3 PET-positive lymph nodes were observed and in 30 patients, ≥4 PET -positive lymph nodes were observed. Thereafter patients were categorised based on tumour response in the MARI node. When treatment was performed according to the new scheme, we would save 75% axillary clearances. By the results of the axillary clearance, we then calculated potential over and undertreatment. 2/95 patients would potentially be undertreated because residual disease was found in the axillary clearance and based on the MARI outcome no further axillary treatment would be performed. 16/95 patients would potentially be overtreated; the MARI node was the only tumour positive node however these patients were categorised to receive further axillary treatment. Conclusion: In the present study we show that combining PET/CT and the MARI procedure led to a decrease of 75% in the performance of axillary clearances with minimal undertreatment



P30

MRI for Axillary Breast Cancer Metastasis in the Neoadjuvant Setting: A Prospective Study A. Mattingly,* B. Mooney, H. Lin, J. Kiluk, N. Khakpour, S. Hoover, C. Laronga, M.C. Lee. *Breast Surgery, Moffitt Cancer Center, Tampa, FL.*

Background: MRI imaging of the axilla for regional breast cancer metastasis is controversial due to variable specificity. We sought to evaluate breast MRI for nodal metastasis in neoadjuvant patients confirmed by axillary biopsy and surgical pathology. Methods: A single-institution, IRB-approved prospective trial enrolled female breast cancer patients receiving neoadjuvant chemotherapy (NAC) from 2008-2012. Pre- and post-NAC MRI images, pre-NAC axillary US (AUS), axillary biopsy and surgical pathology results were collected. Images were reviewed by radiologist to classify normal vs abnormal axilla, and inadequate images excluded. Kappa coefficient described the strength of agreement between MRI and AUS. Fisher's exact test was used to evaluate MRI for prediction of biopsy results and surgical pathology. Wilcoxon rank-sum test evaluated lymph node results on surgical pathology. Results: 43 Patients enrolled; 33 were N1/N2 pre-NAC and 16% had a pCR in breast and axilla. Pre-NAC MRI was compared to pre-NAC AUS and axillary biopsy; 38 patients had analyzable data. 92% had consistent diagnosis results between MRI and axillary biopsy; strength of agreement was moderate (kappa coefficient = 0.54). Pre-NAC MRI was significantly associated with axillary biopsy results (p=0.014) and had FPR of 60%, FNR 0%, SE 100%, and SP 40%. Pre-NAC MRI was not associated with AUS (p=0.077). Post-NAC MRI was compared to surgical pathology; 38 patients had analyzable data. Only 58% had consistent diagnosis results between MRI and surgical pathology. Strength of agreement was slight (Kappa = 0.16). For post-NAC MRI, FPR was 38%, FNR 46%, SE 55%, and SP 63%. There was no difference in the number of pathologic nodes between the normal and abnormal groups (p=0.102). In post-NAC patients with abnormal MRI, 23.4% had pathologic lymph nodes vs. 2.8% with normal MRI; this did not reach statistical significance (p=0.079). Post-treatment MRI was not associated with lymph node results on surgical pathology (p=0.342). Conclusions: In untreated high risk cases, breast MRI is sensitive for axillary metastasis. Post-treatment breast MRI was not predictive of residual axillary disease.

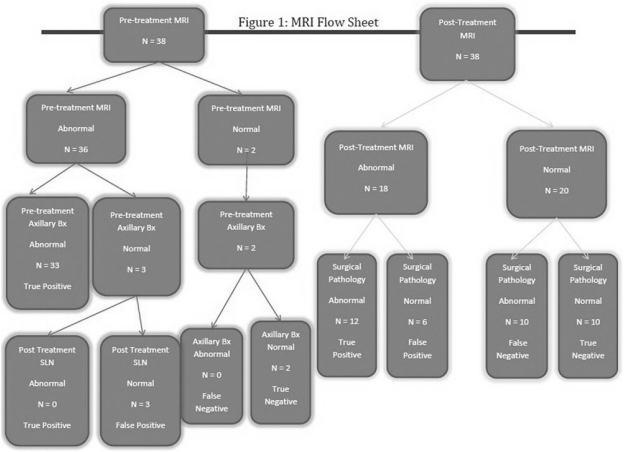


Figure 1:
Left: Pre-treatment MRI flow sheet illustrating true positive, true negative, false positive, and false negative used to calculate SE*, SP*, FPR*, & FNR*.
Right: Post-treatment MRI flow sheet illustrating true positive, true negative, false positive, and false negative use to calculate SE*, SP*, FPR*, & FNR*.
*SE Sensitivity, SP Specificity, FPR False Positive Rate, FNR False Negative rate

P31

Neoadjuvant Chemotherapy Combined with Oncoplastic Reduction for High Stage Breast Cancer Patients J. Broecker,[1]* A. Hart,[2] A. Losken,[2] T.M. Styblo.[3] *1. Emory University School of Medicine, Atlanta, GA; 2. Emory University Department of Plastic and Reconstructive Surgery, Atlanta, GA; 3. Surgical Oncology Winship Cancer Institute of Emory University, Atlanta, GA.*

Objective: Oncoplastic surgery has been shown to be a good alternative to breast conservation surgery alone (BCS) for patients with breast cancer. Its role in patients with advanced disease is unclear. In this study, we evaluate the safety of oncoplastic breast conservation surgery (OBCS) in patients who received neoadjuvant therapy for high stage breast cancer. Methods: The oncologic outcomes of consecutive patients classified as high stage (>T1 or at least N1) that received neoadjuvant therapy followed by BCS at EUH by a single breast surgeon (TMS) from September 2004 until June 2015 were reviewed. Comparisons were made between those who received BCS alone and those who received BCS combined with an oncoplastic reduction. Results: A total of 88 patients were included in this series (48 OBCS and 40 BCS alone). The mean initial tumor size (4.44 cm vs. 2.54 cm, p<0.0001), the weight of the biopsy (150.7 g vs. 70.3 g, p=0.015) and the post-op tumor size (1.39 cm vs. 1.04 cm, p=.308) were all larger in the OBCS group as compared to BCS alone. Nodal metastases following induction therapy were similar in both groups (40 % OBCS vs. 29% BCS alone, p=0.367). The mean follow up was 31.85 months (Range: 1 months – 125 months) and similar in each group. Average percent reduction in tumor size (31.8% vs. 40.9%, p=0.346) and complete pathologic response to induction therapy (44% vs 35%) was higher in the BCT group. Oncologic outcomes were similar for OBCS reduction and BCS groups, respectively: positive margin rate (8.3% vs 7.5% p=1.0), re-excision rate (8.3% vs. 7.5% p=1.0), completion mastectomy rate (6.25% vs. 5% p=1.0), local recurrence rate (1.6% vs. 0%). There have been 2 deaths from breast cancer in each group. Conclusions: The oncoplastic approach in high stage patients treated with neoadjuvant systemic therapy appears to be as safe and effective when compared to BCS alone. The many proven benefits of the oncoplastic approach along with the oncologic safety should make this a reasonable option in high stage patients too.

P32

Impact of Comorbidities on Surgical Outcomes Following Mastectomy in Elderly Breast Cancer Patients: An Analysis of the NSQIP Database T. Moo, S. Mays,* R. Simmons. *Weill Cornell Medical College, New York, NY.*

Background: Approximately 4% of women age 70 will develop breast cancer during the next ten years. There is limited data on surgical outcomes in elderly patients undergoing treatment for breast cancer. This study examines complications following mastectomy in elderly patients and determines how comorbidities impact those outcomes. Methods: The American College of Surgeons National Surgery Quality Improvement Program database was used to examine complications and comorbidities in breast cancer patients 70 or older undergoing mastectomy from 2007-2012. The relationship between complication and comorbidity was characterized using discriptive statistics and Wilcoxon rank-sum test. Variable freqencies were compared using Chi-square or Fisher's exact test with a statistically significant two-sided p-value set at 0.05. Results: We identified 12,026 patients 70 or older who underwent mastectomy. The 30-day overall morbidity rate was 4.22%. Myocardial infarction (MI) was associated with history of bleeding disorder and cerebral vascular accident (CVA) (P<0.05). Prior CVA, transient ischemic attack and MI were associated with post-operative CVA (p<0.05). Chronic obstructive pulmonary disease and steroid use impacted post-operative pneumonia (p<0.05). Bleeding disorder, hypertension, and steroid use impacted urinary tract infection occurrence (p<0.05). Diabetes increased the rate of wound dehiscence (p=0.001). Conclusion: The 30-day morbidity rate of elderly breast cancer patients undergoing mastectomy is low. Although the complication rate is low, certain comorbidities increase the risk of specific complications. Appropriate measures should be taken to optimize comorbidities in elderly patients to further minimize adverse outcomes.

P33

An Evaluation of HER2 Positivity in Invasive Breast Cancers with Associated Ductal Carcinoma In Situ L. Thalheimer,* J. Lloyd, G. Edina, S. Nolano, W.B. Carter, T. Frazier. *The Bryn Mawr Hospital, Bryn Mawr, PA.*

Introduction: Ductal carcinoma in situ (DCIS) accounts for approximately 20-25% of breast malignancies annually. There is limited knowledge about predictors of recurrence and biologic aggressiveness following DCIS. The aim of our study was to evaluate DCIS surrounding invasive ductal carcinomas and compare the HER2 status of these lesions. Methods: All patients diagnosed with invasive ductal carcinoma between January 2012 to December 2013 were included in this retrospective IRB chart review (n=85). Cases with associated or extensive DCIS were then extracted (n=54) and the DCIS was stained for HER-2 and histopathologically evaluated by a single pathologist. Cases without DCIS present on the restained specimens were excluded (n=2). The restained cases were then grouped based on molecular subtypes: Luminal A (n= 12), Luminal B (n=5), triple negative (n=15), $ER^+/PR^-/HER\text{-}2^+$ (n=14), $ER^-/PR^-/HER\text{-}2^+$ (n=6). The HER-2 status of the DCIS was then compared to the HER-2 status of the associated invasive carcinoma. A positive HER2 result was 3+; 2+ DCIS was considered negative for the purpose of this study. Results: Eighty-five patients were diagnosed with invasive ductal carcinoma from January 2012 to December 2013. Of these, 54 had associated or extensive DCIS surrounding their tumors. In the Luminal A group, 4 out of 12 (33.3%) DCIS specimens stained positive for HER-2. In the Luminal B group, 1 out of 5 (20%) stained positive for HER-2. In the triple negative group, 3 out of 15 (20%) stained positive for HER-2. In the $ER^+/PR^-/HER\text{-}2^+$ group, 13 out of 14 (92.9%) stained positive for HER2. In the $ER^-/PR^-/HER\text{-}2^+$ group, 6 out of 6 (100%) stained positive for HER-2. For all HER-2 positive invasive cancers, the surrounding DCIS was positive in 19 of the 20 specimens (95%). For all HER-2 negative invasive cancers, the surrounding DCIS was positive in 8 out of 32 specimens (25%). Conclusions: In our study, 95% of DCIS associated with HER2 positive invasive breast carcinoma was also positive for HER2. This suggests that HER-2 DCIS may undergo a more aggressive transition to invasive cancer and routine staining of DCIS for HER-2 may be of value in determining treatment options.

P34

Outcome Disparities in African American Compared to European American Women with Luminal A Tumors Treated within an Equal Access Health Care System R. Ellsworth,[1]* B. Freeman,[1] N. Costantino,[2] C. Shriver.[1] *1. Clinical Breast Care Project, Murtha Cancer Center, Windber, PA; 2. Windber Research Institute, Windber, PA.*

Background: Breast cancer mortality rates are higher for African American women (AAW) than for any other ethnic group in the US. Recent reports suggest that outcome disparities between AAW and European American women (EAW) is present only in the ER+HER2- subtype and these differences may be attributable to molecular factors. To improve our understanding, pathological characteristics, mortality and molecular profiles from women treated within an equal-access (Department of Defense) health care system were evaluated. Methods: All AAW (n=90) and EAAW (n=308) enrolled in the Clinical Breast Care Project with ER+HER2- tumors who received care at Walter Reed National Military Medical Center were identified. Gene expression profiles were generated from primary breast tumors from 57 AAW and 181 EAW. Pathological characteristics, survival and gene expression analysis were evaluated using chi-square analysis and log-rank tests and ANOVA. Results: Tumors from AAW were significantly more likely to be PR-, Ki67+ and of higher grade. Tumor stage, size and lymph node status did not differ significantly, nor did mortality rates (P=0.932), with 6% of both populations dying of disease. At the molecular level, genes PSPHL and CRYBB2P1 were expressed at significantly higher levels in tumor tissues as well as normal stroma and blood from AAW. Polymorphisms controlling expression of each gene were identified with minor allele frequencies differing significantly between populations but not between cases and controls within each population. Conclusions Survival disparities were not detected in patients with ER+HER2- tumors treated within our equal-access health care system. Molecular differences in tumors from AAW reflect population stratification and are not causal. These data thus suggest that outcome disparities in AAW with ER+HER2- tumors are largely attributable to socioeconomic factors affecting access to screening and treatment, rather than reflecting underlying biological differences. Reduction of disparities in survival may therefore be addressed by improving access to health care in the general population.

P35

Pathologic Concordance of Preoperative Magnetic Resonance Imaging in Breast Cancer Patients Undergoing Contralateral Prophylactic Mastectomy for Symmetry S. Nolano,* L. Thalheimer, E. Yu, W.B. Carter, T. Frazier. *The Bryn Mawr Hospital, Bryn Mawr, PA.*

Introduction: With a large increase in bilateral mastectomies for unilateral breast cancer in the United States, the question of how to best treat the prophylactic side is of concern. The aim of this study was to evaluate whether or not magnetic resonance imaging (MRI) is an accurate predictor of disease in the prophylactic breast tissue. Methods: One hundred five patients diagnosed with unilateral invasive breast cancer choosing to undergo bilateral mastectomies for symmetry who underwent bilateral MRI from January 2009 through December 2014 were included in this retrospective, IRB approved study (n=105). Sixty patients underwent sentinel lymph node biopsy (SL) on the prophylactic side and 45 had no sentinel node mapping. We then reviewed the MRI reports for patients with a finding of lobular carcinoma in situ (LCIS), ductal carcinoma in situ (DCIS), or invasive carcinoma (IC) to assess the concordance. Results: In the sentinel lymph node/MRI group, 4 patients had LCIS on the prophylactic side, 3 patients had DCIS, and 2 had IC. In the MRI only group, 1 patient had LCIS on the prophylactic side and 2 had DCIS. In the SL group, the MRI was concordant with the invasive cancer in both instances. There were 5 cases of DCIS in both groups on prophylactic side and the MRI was concordant in 3 of those cases (60%). Five cases of LCIS were reported on the prophylactic side and the MRI was concordant in 4 of the 5 cases (80%). Of the 60 patients with SL, only 2 had a positive sentinel node which corresponded to the 2 invasive cancers suggested by MRI and confirmed pathologically. Conclusion: While no invasive cancers were missed on MRI, 2 patients with DCIS were not identified. Patients undergoing prophylactic mastectomy for symmetry should have a pre-operative MRI. Suspicious areas noted on pre-operative MRI should be biopsied pre-operatively or undergo sentinel node mapping at the time of surgery.

P36

Tamoxifen Compliance in Duct Carcinoma In Situ (DCIS) L.C. Karavites,[1]* A. Kane,[2] S. Zaveri,[2] Y. Xu,[2] I. Helenowski,[2] S.A. Khan.[2] *1. UIC/Mt. Sinai Hospital, Chicago, IL; 2. Northwestern University, Chicago, IL.*

Tamoxifen reduces the risk of DCIS recurrence and prevents new breast cancer events, but many DCIS patients decline tamoxifen. We aim to identify factors influencing this decision among women with hormone receptor(HR) positive DCIS. Through a retrospective review at Northwestern University, we identified 366 women with HR positive DCIS (1998-2009). Demographics, socio-economic and insurance status, tumor characteristics, use of medical oncology consultation, and tamoxifen use were evaluated. The Wilcoxon rank-sum test was used for continuous and Fisher exact test for categorical variables. The odds of compliance were estimated with the noncompliant and refusal groups combined as the reference category. Multivariate logistic models were developed adjusting for age, size, grade, and radiation therapy (XRT). Of the 366 women offered tamoxifen, 294 accepted and 72 declined. There were no significant differences in mean age, racial distribution or tumor features among the 3 groups. Among those who accepted, 213 were compliant for at least 4 years while 56 were noncompliant and 25 were lost to follow-up. Among noncompliant patients, 68% stopped during the first year of treatment; of these, 86% stopped for a documented adverse effect. Compliant women were more likely to be insured compared to noncompliant and decliner groups; were more likely to have seen a medical oncologist (74%); were followed longer (median 88 vs 79 and 73 months) and were more compliant with XRT than their counterparts. Decliners were more likely to be of average/below average socio-economic status. After adjusting for age, size, and grade, odds ratios revealed that compliant women were more likely to undergo XRT, have insurance and to have seen a medical oncologist. The majority of the women in our study accepted the drug if it was offered to them, and remained adherent. They were also compliant with other aspects of care. The association between insurance status and drug compliance points to a societal need to improve access to care. Further, tamoxifen-compliant women received the recommendation from more than one physician. Having insurance and the counsel of a medical oncologist may increase both acceptance and adherence to tamoxifen.

Table 1. Demographics Among Patients with ER+ DCIS

	Accepted TAM COMPLIANT (n=213)	Accepted TAM NONCOMPLIANT (n=56)	Did Not Accept TAM (n=72)	P-value
Mean Age	60.0±9.5	59.1±10.8	58.2±10.5	0.18
Median Age (range)	60 (34,81)	58 (30,88)	55 (37,81)	
Race				
-NonEuropean	69 (32.6%)	11 (19.6%)	27 (37.5%)	0.08
-European	143 (67.4%)	46 (80.4%)	45 (62.5%)	
DCIS Size (mm)				
-Mean ± standard deviation	23.8±26.9	29.4±43.4	20.9±25.1	0.11
-Median (range)	16 (0, 130)	9 (0, 130)	11 (0, 130)	
Radiation Therapy (BCT only)				
-No	38 (20.8%)	19 (41.3%)	27 (47.4%)	<0.0001
-Yes	144 (78.7%)	25 (54.3%)	30 (53.6%)	
-Unknown	1 (0.5%)	2 (4.3%)	0 (0%)	
New Event				
-Ipsilateral	11 (5.2%)	5 (8.9%)	12 (16.7%)	0.01
-Contralateral	13 (6.1%)	3 (5.4%)	2 (2.8%)	0.61
Length of Follow Up (months)				
- Mean ± standard deviation	88.0±27.6	79.3±36.7	73.0±33.6	0.005
-Median (range)	84 (44,200)	72 (15,187)	74 (2,169)	
Median Income by Zip				
-Below Average	50 (23.6%)	11 (19.6%)	15 (20.8%)	0.02
-Average	19 (9.0%)	6 (10.7%)	18 (25.0%)	
-Above Average	143 (67.4%)	39 (69.6%)	39 (54.2%)	
Medical Oncology Apt				
-No	41 (19.2%)	16 (28.6%)	24 (33.3%)	0.009
-Yes	158 (74.2%)	35 (62.5%)	48 (66.7%)	
-Unknown	14 (6.6%)	5 (8.9%)	0 (0.0%)	
Health Insurance				
-No	12 (5.6%)	15 (25.0%)	13 (18.1%)	<0.0001
-Yes	201 (94.4%)	42 (75.0%)	59 (81.9%)	

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Concomitant Partial Mastectomy and Reduction Mammoplasty is Associated with Increased Postoperative Complications A.U. Friedrich,* A.C. Larkin, B.M. Ward, A. O'Connor, R. Quinlan, J. LaFemina. *Surgery, University of Massachusetts, Southborough, MA.*

INTRODUCTION: Synchronous partial mastectomy and reduction mammoplasty offers the potential for oncologic resection and concomitant improved cosmetic outcomes. It is unclear if women who undergo simultaneous reduction mammoplasty immediately after partial mastectomy are subject

to an increased risk of postoperative complications. We aim to determine if simultaneous partial mastectomy and reduction mammoplasty is associated with a difference in perioperative outcomes. METHODS: The American College of Surgeons (ACS) National Surgical Quality Improvement Project (NSQIP) database was analyzed for all patients undergoing concomitant partial mastectomy and reduction mammoplasty for breast cancer between 2005 and 2012. RESULTS: 33105 patients were identified who underwent partial mastectomy between the years of 2005 and 2012. Of these, 244 patients (0.7%) underwent reduction mammoplasty in the same setting as the oncologic resection. Total operative time was 78 minutes for the lumpectomy-only group and 195 minutes for the simultaneous mammoplasty group (95% CI 77.7–78.7min and 187.0-204.1min, respectively; p<0.001). Overall complications were low in both groups. However concomitant mammoplasty was associated with an increased relative risk of multiple complications, among these superficial surgical site infection (RR 2.3, 95% CI 1.1-4.7, p=0.027), wound infection (RR 5.7, 95% CI 1.8–17.9, p=0.018), wound dehiscence (RR 8.4, 95% CI 2.0–34.9, p=0.018) and postoperative bleed requiring blood transfusions (RR 18.4, 95% CI 5.5–61.0, p<0.001). CONCLUSION: In this analysis of a national cohort of breast cancer patients, partial mastectomy followed by reduction mammoplasty was associated with increased wound complications within 30 days as well as an increased risk of postoperative hemorrhage. Surgeons need to be aware of these risks when planning a combined procedure.

P38

A Contemporary Analysis of Axillary Lymph Node Dissection A. Gomberawalla,[1]* B. Borden,[1] B. Kalesan,[2] M. Chen,[1] B. Taback,[1] P. Ananthakrishnan,[1] S. Feldman.[1] *1. Breast Surgery, Columbia University Medical Center, New York, NY; 2. Boston University School of Medicine, Boston, MA.*

Introduction: The role of axillary lymph node dissection (ALND) has evolved drastically in the last decade. However, despite multiple advances in the treatment of breast cancer, the morbidity of the ALND still bears a large burden on both patient and treating physician. In the setting of an academic contemporary practice, we wanted to evaluate our lymphedema (LE) rate and factors that may be associated with its development. Methods: An IRB approved retrospective chart review was performed. 150 patients underwent ALND (levels 1 and 2) by four surgeons from 2009-2014. LE was defined by the patient's symptoms or by physician assessment. Mean follow up was 32 months (range 6-72 months). Chi square tests and Poisson regression analysis were used to compute statistical significance. Results: The LE rate for our cohort was 31.5%. 47/150 patients underwent neoadjuvant systemic chemotherapy (NAC). The LE rate in this population was significantly lower, 17% compared to 38% in the group who did not receive NAC (p=0.02). Additionally, a higher lymph node (LN) retrieval played a role in increasing one's risk of developing LE, with >20 LN removed having a prevalence ratio of 1.9 (95% CI 1.5-4.1). Both factors remained independent on multivariate analysis. Contrary to previous reports, BMI did not play a significant role in the development of LE. Additionally, post-operative radiation, type of breast surgery or reconstructive option, race/ethnicity, molecular subtype, as well as previous axillary surgery did not influence the rate of LE. Conclusions: In our cohort, the LE rate was on the higher end of what has previously been reported (8-40%); but our patient population now represents those with more advanced disease. Previously thought risk factors did not correlate within our study population. The finding of reduced LE in NAC patients further supports its benefit. Those patients who have more than 20 LN's removed may also represent a focused population for screening and early intervention with decongestive therapy for LE.

P39

Do Nurse-Navigated Treatment Summary-Survivorship Care Plans (TSSCPs) Improve Treatment and Follow-up Compliance in Underserved Populations? C. Manoukian,* K. Ashing, A. Falor, V. Sun, M. Altamirano, L.L. Lai. *Surgery, City of Hope, Duarte, CA.*

Background: Multiple cancer organizations advocate for the use of TSSCPs in cancer patients. To better quantify the benefits of a nurse-navigated, culturally and linguistically responsive TSSCP in underserved breast cancer patients, we compared rates of compliance with treatment and follow up in 26 patients who were treated with TSSCPs to 38 similar controls who were treated without TSSCPs. Methods: We prospectively enrolled 26 consecutive, newly-diagnosed breast cancer patients who were given nurse-navigated TSSCPs under an IRB-approved protocol. At their first clinic visit, a trained nurse educated and assisted the patient in the completion of the TSSCP. The TSSCPs were completed at each visit through 12 months of surveillance. Rates of compliance with treatment and follow up guidelines were compared to 38 similar control patients using a two group Fisher's exact chi-square test. Statistical significance was set at p-value < 0.05. Findings: All patients were treated under Medicaid insurance and 47% were racial and/or ethnic minorities. Time from diagnosis to treatment and time from initial clinic visit to treatment were similar across groups. The rate of compliance with first treatment recommendations was 96% (25/26) in the TSSCP group compared to 79% (30/38) in the non-TSSCP group (p = 0.07). The number of patients compliant with all follow up visits was similar: 22/25 (88%) of TSSCP patients and 22/30 (73%) in non-TSSCP patients (p = 0.31). Of the recommended total follow up appointments, 6/67 in the TSSCP group and 25/120 in the no TSSCP group were "no shows" (p = 0.04). Conclusions: Although the use of nurse-navigated TSSCPs may not improve time to treatment in medically underserved patients, adherence to first treatment recommendations and follow up appointments shows improvement in patients who participate in nurse-navigated TSSCPs. Further study is needed to fully assess the role of nurse-navigated TSSCPs in improving treatment and surveillance compliance rates and how these rates impact clinical outcomes. Acknowledgement: Funded by a Community Grant from the Los Angeles County Affiliate of Susan G. Komen.

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National Trends of the Impact of Rurality on Breast Cancer Surgery E. Canopy,[1]* W. Zahnd,[1] T.M. Breslin,[2] D.J. Rea,[1] J.D. Mellinger,[1] S. Ganai.[1] *1. Surgery, Southern Illinois University School of Medicine, Springfield, IL; 2. Northwestern University Feinberg School of Medicine, Chicago, IL.*

Introduction: Rural disparities in access to breast cancer care may be present with implications for surgical management. This study evaluates contemporary rural-urban differences in surgical therapy for breast cancer. Methods: We conducted a retrospective cohort study of female early-stage breast cancer patients (n=865,238) from the National Cancer Database from 1998-2012. Chi-square trend tests were used to assess rural-urban trends in breast-conserving surgery (BCS), mastectomy with reconstruction (MWR), and contralateral prophylactic mastectomy (CPM). Unadjusted and adjusted logistic regression was used to compare rural-urban differences. Chi-square analysis was performed to assess regional differences in 2012 surgery rates. Results: Rural patients (14%) were more likely to have Medicare insurance, were poorer, less educated, and had more comorbidities than urban patients. They were less likely to be treated at an academic center (9.4% vs. 31.2%) and lived further from their treating facility (50±119 vs. 16±78 miles). Significant trends in breast cancer procedures were noted across the study interval (p<0.05): BCS increased among rural patients while decreased in urban patients; MWR increased in both rural and urban patients; and CPM increased in both rural and urban patients. Even after controlling for demographic, hospital and clinical characteristics, rural patients had lower likelihood of BCS and MWR and higher odds of CPM (Table; p<0.05). By region, CPM rates were higher in rural compared to urban New England, while urban rates were higher in both the Middle and South Atlantic regions (p<0.05). CPM rates were higher in the western US compared to eastern regions regardless of rurality. Significant rural-urban differences in BCS were also seen in several US regions, with most displaying less use of BCS among rural patients compared to urban patients, although this trend was reversed along the Pacific coast. Conclusions: Although many factors influence breast cancer surgical treatment, both rural/urban status and regional geography are significantly associated with BCS, MWR, and CPM. Further analysis of rural disparities and the influence of geography in breast cancer care is warranted.

National Trends of the Impact of Rurality on Breast Cancer Surgery

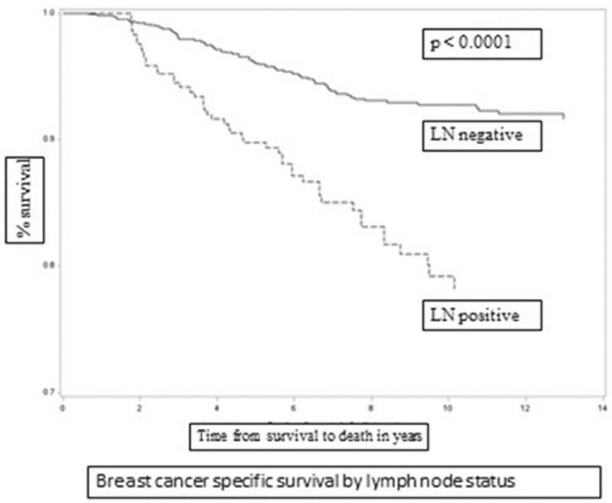
	Rural (%) 1998 and 2012	Urban (%) 1998 and 2012	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)†
Breast Conserving Surgery	53.0% to 54.4%	63.7% to 59.0%	0.78 (0.77 - 0.79)	0.86 (0.85 - 0.88)
Mastectomy with Reconstruction	2.0% to 11.6%	3.0% to 15.4%	0.72 (0.70 - 0.73)	0.94 (0.92 - 0.97)
Contralateral Prophylactic Mastectomy	1.5% to 12.2%	1.4% to 11.8%	1.04 (1.02 - 1.06)	1.08 (1.05 - 1.11)

† Controlled for age, race, location, facility type, insurance status, income, education, tumor size, tumor grade, and Charlson-Deyo score.

P41

Outcomes After Mastectomy and Lumpectomy in Elderly Patients with Early Stage Breast Cancer H. Mogal,* C. Clark, N. Fino, M. Howard-McNatt. *Wake Forest University School of Medicine, Winston-Salem, NC.*

Introduction: Prospective studies have shown equivalent outcomes after mastectomy or breast conservation in patients with invasive breast cancer. However, survival in elderly patients has not been specifically analyzed. Methods: Patients older than 70 years with clinical stage I (pathologic stage I or II) invasive breast cancer, undergoing mastectomy or lumpectomy with or without radiation, who were surveyed within three years of their diagnosis, were identified from the Surveillance Epidemiology and End-Results and Medicare Health Outcomes Survey linked database. Primary end point was breast-cancer specific survival. Results: Of 1784 patients, 596 (33.4%) underwent mastectomy, 918 (51.4 %) underwent lumpectomy with radiation and 270 (15.1%) underwent lumpectomy alone. Significant differences were noted in age, tumor size, AJCC stage, lymph node status (all p<0.0001) and number of positive lymph nodes between the three groups (p=0.003). On univariate analysis, breast cancer-specific survival for patients undergoing lumpectomy with radiation (HR 0.61, CI 0.43-0.85; p=0.004) was superior to mastectomy. Older age (HR 1.3, CI 1.09-1.45, p=0.002), ≥ 2 comorbidities (HR 1.57, CI 1.08-2.26; p=0.02), inability to perform > 2 ADLs (HR 1.61, CI 1.06-2.44; p=0.03), larger tumor size (HR 2.36, CI 1.85-3.02; p<0.0001) and positive lymph nodes (HR 2.83, CI 1.98-4.04; p<0.0001) were associated with increased risk of death from breast cancer. On multivariate analysis, larger tumor size (HR 1.89, CI 1.37-2.57; p<0.0001) and positive lymph node status (HR 1.99, CI 1.36-2.9; p=0.0004) were independent predictors of worse survival. Conclusions: Elderly patients with early stage invasive breast cancer undergoing breast conservation with or without radiation have better cancer-specific survival than those undergoing mastectomy. After adjusting for age, comorbidities, functional impairment and type of surgery, survival is dependent on tumor specific variables. Determination of lymph node status remains important in staging elderly breast cancer patients.

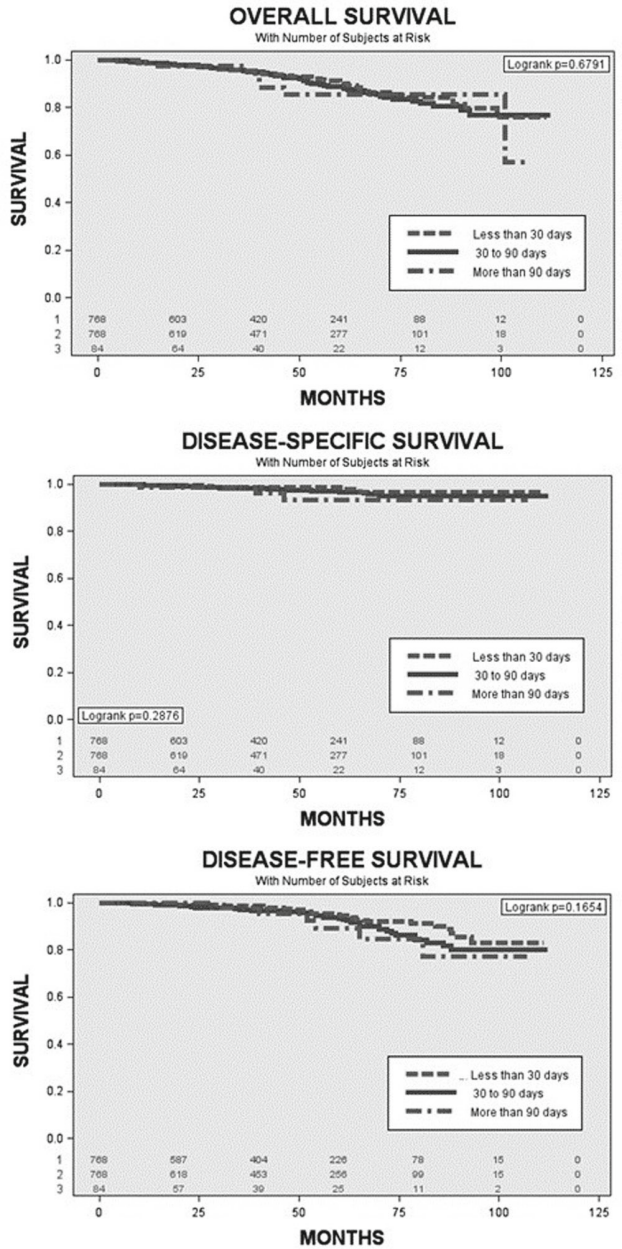


Breast cancer specific survival by lymph node status

P42

Longer Time Intervals from Diagnosis to Surgical Treatment in Breast Cancer: Associated Factors and Survival Impact M. Mariella,* C.W. Kimbrough, K.M. McMasters, N. Ajkay. *Surgery, University of Louisville, Louisville, KY.*

Background Time interval from breast cancer diagnosis to definitive surgery (TI) is increasing, but the impact on outcomes is not well understood. TI longer than 30 days is associated with a greater chance of delay to chemotherapy, which may impact survival. We sought to identify factors associated with longer TI, and the influence on outcome measures. Methods We examined TI for stage 0-III breast cancer patients treated between 2006 and 2015 at a university-based cancer center (excluding neoadjuvant chemotherapy). Univariate (UV) and multivariate (MV) analysis were used to study factors associated with TI <30, 30-90 and >90 days. Kaplan-Meier (KM) plots were used to examine the effect of different TI on overall survival (OS), disease-specific survival (DSS) and disease-free survival (DFS). Results 1620 patients where included with a median follow-up of 47 months. The median TI was 32 days. TI increased in patients from 2011-2015 compared to those from 2006-2010 (35 vs. 30 days, p <0.001). UV analysis comparing TI of <30, 30-90 and >90 days demonstrated significant differences between groups in MRI use, type of surgery, Her2neu status, and insurance coverage. On MV analysis, independent predictors of TI >30 days included patients undergoing mastectomy, both with (OR 3.95, 95% CI 2.88-5.46) and without (OR 1.66, 95% CI 1.31-2.09) reconstruction; MRI use (OR 1.87, 95% CI 1.35-2.60); and age (OR 1.014 per year, 95% CI 1.003-1.026). On KM analysis, no significant differences in terms of OS (p=0.67), DSS (p=0.28) or DFS (p=0.16) were found between the TI groups. When comparing TI <30 vs. >30 days, there was a non-significant trend towards an increased risk of recurrence in patients with TI > 30 days (p=0.07), without significant differences in OS (p=0.42) or DSS (p=0.19). In patients who received adjuvant chemotherapy, there was no association between TI > 30 days and a subsequent delay > 60 days in starting chemotherapy (OR 1.05, 95% CI 0.73-1.53). Conclusions TI has increased in the last 5 years. Type of surgery, MRI use and age are associated with longer TI. Longer TI does not appear to influence outcomes or significantly delay chemotherapy.



Kaplan-Meier curves for overall survival, disease-specific survival and disease-free survival comparing time intervals <30 days, 30-90 days and >90 days.

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Interobserver Agreement for Assessment of Tumor Infiltrating Lymphocytes (TIL) in Breast Cancer S. Swisher,[1] Y. Wu,[1] C. Castaneda,[2] G. Lyons,[1] F. Yang,[1] C. Tapia,[1] X. Wang,[1] R. Bassett,[1] M. Castillo,[2] S. Casavilca,[2] K.K. Hunt,[1] A. Sahin,[1] E. Mittendorf.[1]* *1. Breast Surgical Oncology, MD Anderson Cancer Center, Houston, TX; 2. Instituto Nacional de Enfermedades Neopasicas, Lima, Peru.*

Background: Studies have shown that HER2+ and triple negative breast cancers (TNBC), are immunogenic as evidenced by the presence of TIL. The presence of TIL is prognostic and predictive suggesting TIL may be an important biomarker. Recognizing the need to standardize the approach to quantifying TIL in order for TIL evaluation to be incorporated into clinical care, an International TILs Working Group was convened to formulate consensus recommendations for TIL evaluation. The current study was performed to determine interobserver agreement of TIL assessment using the proposed methodology. Methods: TIL were assessed on a single H&E stained slide obtained from the core biopsy from 75 TNBC patients. Four pathologists independently reviewed each slide and evaluated stromal and intratumoral TIL. Stromal TIL (sTIL) were defined as mononuclear cells within the stroma not in direct contact with tumor cells and were categorized as <10%, 10-50%, or >50%. Intratumoral TIL (iTIL) were defined as mononuclear cells within the tumor nest or in direct contact with tumor cells and were reported as a continuous percentage. The kappa statistic was used to estimate interobserver variability for identification of sTIL; the intraclass correlation coefficient (ICC) was used to estimate the agreement among observers for iTIL. Results: The number of cases in each sTIL category by pathologist are shown in the table. Consistent with published studies, a minority of cases (8%-15%) had a sTIL score of >50%, a previously defined threshold for lymphocyte predominant breast cancer. The kappa statistic for sTIL evaluation was 0.57 (std error=0.04). For iTIL, the ICC calculated to determine internal consistency among raters was 0.65 (95%CI:0.56-0.74; p<0.0001) and to determine agreement among raters was 0.62 (95%CI:0.50-0.72; p<0.0001). Conclusion: Using consensus methodology for TIL evaluation, the interobserver agreement was moderate to substantial for sTIL and the calculated ICC values showed that the pathologists were internally consistent and in agreement with each other when determining iTIL. Use of additional techniques to include special stains are being investigated to improve agreement rates.

Number of cases by category of stromal tumor infiltrating lymphocytes by pathologist

Pathologist	< 10%	10-50%	> 50%
1	43	25	6
2	28	35	11
3	42	24	8
4	37	28	9

P44

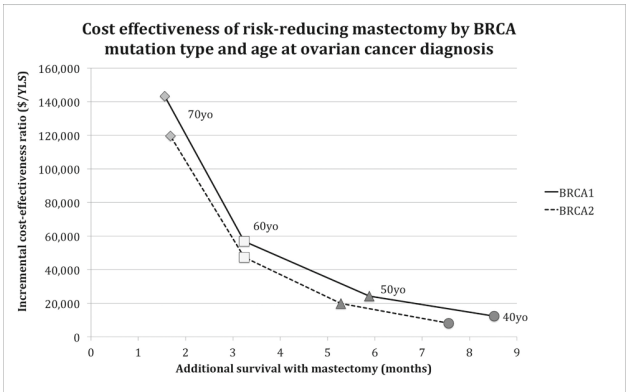
Postoperative Complications in Breast Cancer Patients are Independent of Age B. Ten Wolde,[1]* M. Kuiper,[2] J. Wijgman,[1] M. Keemers,[1] F. van den Wildenberg,[1] J.H. de Wilt,[2] L.J. Strobbe.[1] *1. Surgery, Canisius Wilhelmina Hospital, Nijmegen, Netherlands; 2. Radboud University Medical Center, Nijmegen, Netherlands.*

Introduction: One element regarding treatment choices, is whether fear of age-related increased risk of postoperative complications is valid or whether other variables contribute to the risk of complications. Therefore, the objective of this study is to establish the incidence of postoperative complications in the older breast cancer patients compared to younger patients, to identify risk factors and explore differences between breast-conserving treatment and mastectomy. Methods: 1258 female patients (>18 years) who underwent breast cancer surgery for primary stage I-III breast cancer in 2010-2014 were included in this retrospective cohort study. Incidence of postoperative complications (POC) were compared between the younger (18-70 year, N=1008) and older (≥71 year, N=250) patients. Multivariate logistic regression was performed to identify the correlation between age and developing postoperative complications. Results: 38.3% of the younger and 36.4% of the older patients developed POC (p=0.317). After lumpectomy the incidence of POC was 26.8% vs 18.4% (p=0.024) for respectively the younger and the older patient group. After mastectomy, POC occurred in 35.5% of the younger compared to 50.6% in the older group (p=0.016). Multivariable regression analyses showed increasing age was no predictor for POC (OR 0.592; CI 0.401-0.874, p=0.008), neither was increasing ASA classification. More extensive surgery, increasing BMI and increasing volume of breast tissue removed did increase the odds of developing a POC. Analyses on the ≥71 year group separately revealed only type of surgery to be of influence on developing a POC. 9.6% of patients who had a tumor suitable for breast conserving surgery chose mastectomy instead, with increasing age being a predictor for this decision (OR2.624; CI 1.606-4.288, p=0.000). Conclusion: Fear of increased risk of complications in the older patient is unjustified. Advancing age nor increasing ASA classification are predictors for developing POC. Type of surgery is the most important determinant. Choosing mastectomy while breast conserving surgery is suitable should be discouraged, in particular in the older patient.

P45

Value of Prophylactic Mastectomy in BRCA Mutation Carriers with Ovarian Cancer C.R. Gamble,* L. Havrilesky, S. Hollenbeck, E. Myers, R. Greenup. *Duke University, Durham, NC.*

OBJECTIVE: Women with life-threatening epithelial ovarian cancer (OC) who are at high genetic risk need an informed discussion of options to reduce the additional risk of breast cancer (BC). We wished to determine the survival benefit and costs of risk-reducing mastectomy (RRM) versus breast screening among women with a new diagnosis of OC who are identified as BRCA mutation carriers. METHODS: A decision model was constructed using a modified Markov structure to compare survival and costs associated with two mortality reduction strategies for women with a new diagnosis of stage II-IV OC and a BRCA germline mutation: (1) RRM; and (2) annual MRI and mammography. Outcomes were mean cost, mean overall survival time, and cost-effectiveness of each strategy. We examined four ages at OC diagnosis: 40, 50, 60, and 70. OC and BC disease-specific survival were from SEER data. Published hazard ratios were used to account for the effects of each mutation type on survival. BC incidence in mutation carriers using each strategy was modeled using prospective, published data. Costs were from CMS reimbursements, hospital costs of mastectomy plus reconstruction, and SEER/Medicare. Monte Carlo probabilistic sensitivity analysis was performed. RESULTS: For a BRCA1 carrier diagnosed with OC at age 40, RRM achieves a survival advantage of 8 months compared to annual screening and is highly cost-effective, with an incremental cost effectiveness ratio (ICER) of $12,298/year of life saved (YLS). At ages 50, 60, and 70, RRM provides 6, 3, and 1.5 additional months, with ICERs of $24,255, $56,881, and $143,207 per YLS, respectively. RRM affords a BRCA2 carrier gains of 7, 5, 3, and 2 months, respectively, at ages 40, 50, 60, or 70. It is cost-effective at ages 40, 50, and 60 but is not cost-effective at age 70 (ICER of $119,557/YLS; Figure). CONCLUSIONS: For women with OC diagnosed before age 60 and who are at high genetic risk, RRM achieves modest life expectancy gains, with an acceptable cost increase compared to annual breast screening. Above age 60 at OC diagnosis, RRM is unlikely to be cost-effective, with diminishing gains in life expectancy.



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Utility of 21-Gene Breast Cancer Assay (ODX) Risk Estimate in Invasive Mucinous Breast Cancers A. Gangi,* L. Dossett, M.C. Lee, W. Sun, S. Hoover, C. Laronga. *Surgery, Moffitt Cancer Center, Tampa, FL.*

Introduction: The 21-gene assay (ODX) Recurrence Score (RS) estimates the likelihood of distant recurrence in early-stage, estrogen receptor positive breast cancer patients (pts) and guides adjuvant treatment recommendations. Invasive mucinous breast cancer is presumed to be an indolent subtype. Comparative analyses were performed in pts that had RS-directed adjuvant treatment for invasive mucinous, lobular (ILC), and ductal (IDC) carcinomas. Methods: An IRB-approved, retrospective review of a prospective institutional ODX database was conducted. ODX use was based on NCCN guidelines or physician discretion. Data collected included: demographics, clinical-pathologic features, surgery, margin status, RS, adjuvant treatment and outcomes. RS was categorized as low risk (RS <18), intermediate risk, or high risk (RS>30). Recurrences were classified as locoregional (LRR) and distant (DR). Descriptive statistics were performed; comparisons were made using one-way ANOVA. Results: 616 pts had ODX between 2004-2012: 32 (5.2%) mucinous carcinoma, 73 (11.8%) ILC, and 511 (83.0%) IDC. Women with IDC were younger (57 years versus 61 for both mucinous and ILC, p<0.01). Median tumor size was 1.7cm for mucinous, 1.8cm for ILC and 1.5cm for IDC (p<0.01); mucinous and IDC were more likely to be grade 3 (13% each) than ILC (5%, p<0.01). IDC pts had more node-positive disease (11% IDC, versus 0% mucinous and 4.3% ILC p<0.01). Median RS was lower in pts with mucinous (median 14, range 0-63) versus IDC (median 16, range 2-62) or ILC (median 16, range 0-34, p=0.05). Risk stratification for mucinous carcinoma was low (64%), intermediate (32%) and high (5%). With median follow of 35 months, no mucinous carcinoma pts developed LRR, compared to 2.4% of pts with IDC and 1.4% of pts with ILC (p=0.62). No mucinous carcinoma pts developed DR compared to 2% DR in both IDC and ILC groups (p<0.01). Conclusion: Lower median RS in mucinous histology compared to IDC and ILC supports biologically more indolent disease. However, identification of mucinous carcinomas with more aggressive phenotypes allows for selection of RS-directed adjuvant treatment without compromise of patient outcome.

P47

Investigation of Breast Cancer Cell Dormancy Using a 3-D Cell Culture System E. O'Connell,* J. Wang, O. Grace, H.P. Redmond. *Department of Surgery, Cork University Hospital, Cork, Ireland.*

The persistence of clinically occult cancer cells within the body has been explained by tumour dormancy; the concept that cancer cells may remain in a quiescent non-proliferative state for a prolonged period. We aimed to investigate the role of tumour dormancy in breast cancer cell lines. We aimed to establish a simple reproducible method for three dimensional (3D) culture of MDA MB 231 and MCF7 cells on an extracellular matrix derived gel. The 3D culture model was designed by coating tissue culture plates with growth factor reduced basement membrane extract gel.Growth of cells in 3D culture was monitored by light microscopy with 2x103 cells/well maintained in 2D low glucose culture for control. Cell proliferation was measured by MTT assay and cell counting and cell cycle assessed using flow cytometry. 3D-cultured cells aggregated in clusters from 24hours to 96hours and maintained a static size over following days. 2D-cultured cells formed an adherent monolayer. A significant reduction in cell proliferation was seen between 3D-cultured cells and 2D-cultured cells at 120hours (MDA MB 231(3D) mean optical density (OD)/well=0.97 versus MDA MB 231(2D) mean OD/well=0.13, p<0.05; MCF7(3D) mean OD/well=1.27 versus MCF7(2D) mean OD/well=0.14,p<0.05). 2D cultured cells were distributed through all stages of the cell cycle. 3D wells showed a significant proportion of cells arrested within the G0/G1 phase of the cell cycle. (Mean fraction of cells in G0/G1 stage as proportion of intact positive stained cells in MCF7 cell line in 3D culture versus MCF7 in 2D culture = 0.86 v 0.48, p=0.0004; mean fraction of cells in G0/G1 stage as proportion of intact positive stained cells in MDA MB 231 cell line in 3D culture versus MDA MB 231 in 2D culture = 0.90 v 0.59, p=0.0048.) Conclusion: Our findings suggest that cells in a 3D culture system displayed hallmarks of dormancy. To clarify this hypothesis it will be necessary to stain for the key cellular signalling pathways of dormancy. This will allow us to explore the clinically relevant question of what factors may stimulate stable low burden cancer to develop into active metastatic disease.

P49

Screening Mammography in Women Ages 40-49: More Risks than Benefits? R.Y. Leong,* R. Vaszily, S.P. Cate, A. Paguyo, A. Gillego, T. Fulop, M. Chadha, S.K. Boolbol. *Mount Sinai Beth Israel, New York, NY.*

Background: The National Comprehensive Cancer Network guidelines recommend that average risk women begin mammographic screening at age 40. However, in 2009 the U.S. Preventive Services Task Force (USPSTF) recommended average risk women start biennial screening mammography at 50. For women 40-49, the USPSTF stated that screening mammography before 50 should be individualized. The standard for breast cancer detection rate according to the American College of Radiology (ACR) is at least 2.5 cases per 1000 studies for all ages screened. Aim: In this study, we reviewed our institution's practice for screening mammography, as well as the cancer detection rate in women 40-49. Methods: A retrospective review of all screening mammograms was performed at our institution, in women 40-49, from January 1, 2013 to December 31, 2014. Patients who had BIRADS 0 imaging were reclassified into a final BIRADS category following their diagnostic evaluation. A chart review was performed to obtain pathology information. Results: Over this two

year period, a total of 7,771 screening mammograms were performed. In this age group 7050/7771 (90.7%) mammograms were BIRADS 1 or 2. There were 527/7771 (6.8%) BIRADS 3 studies. The remaining 194/7771 (2.5%) were BIRADS 4 mammograms. Of the 194 biopsies performed, 147(76%) were benign. Pathology revealed 32 atypical biopsies, 7 cases of ductal carcinoma in situ, and 8 cases of invasive ductal carcinoma. One patient with atypia on biopsy had invasive cancer on final surgical pathology. Conclusions: In this group of women 40-49 who had a biopsy based on screening mammography, 15/194 women (7.7%) were diagnosed with breast cancer. Of the 15 patients diagnosed with cancer in this cohort, 8/15 (53.3%) had invasive disease. The breast cancer detection rate in this study was 2 per 1000 mammograms performed. Although this detection rate was lower than the ACR standard, several patients were diagnosed with early stage cancer. There is benefit to screening women in their 40's because our study showed more than half of the patients diagnosed with cancer were found to have invasive disease.

BIRADS Classification

BIRADS	Number of Patients
1	4674 (60.1%)
2	2376 (30.6%)
3	527 (6.8%)
4	194 (2.5%)
5	0

P50

Can Risk Factors be Used to Select Women Aged 40-49 for Breast Cancer Screening? A. Sabbota,* K. Skinner. *Surgery, University of Rochester Medical Center, Rochester, NY.*

Objective: Breast cancer(BC) is the second leading cause of cancer-related death in women, and screening reduces associated mortality. Current USPSTF guidelines recommend routine screening among women 50 to 74 years of age with biennial mammography, leaving women less than 49 years old to be screened on an individual basis. Criteria on which to base these decisions, that successfully identify women with cancer, are needed. We hypothesize that most women aged 40-49 with BC could be identified using known risk factors. Methods: A prospective BC database identified 956 patients treated at our institution between 2009 and 2014. Of these 161 were aged 40-49 with a first diagnosis of BC. Relevant risk factors (age, age of menarche, first live birth, family history of BC, family history of ovarian cancer, previous biopsy, atypia, mammographic density(MD)) were tabulated. 5-year and lifetime risks were calculated using the modified Gail Model. The ratio between the patient's risk and the risk in an average woman was called the 5yr and lifetime relative risks. Results: Table 1 shows the distribution of risk factors in our patients compared to published values for the general population where available. Only 6.2% of these patients would have been identified as high risk using a cutoff of 2 fold increased risk by the Gail model. MD(extremely or heterogeneously dense) was the most prevalent risk factor, but requires a mammogram to define it. Any family history of BC was the next most prevalent risk factor, followed by early menarche, late first birth or nulliparity. Family history of ovarian cancer was uncommon. Only 23% had none of these risk factors, with 31.7%, 34.8%, 10.0%, and 0.6% having 1,2,3, and 4 risk factors, respectively. Adding atypia or prior biopsy would identify an additional 1(0.6%) or 2(1.2%) patients, respectively. Conclusion: The modified Gail model was not an effective tool for determining which 40-49yo women should be screened. Screening based on the presence of any of the common risk factors listed above would identify up to 80% of these younger women with BC. Because MD was the most common risk factor, a baseline mammogram at age 40 to assess density should be considered.

Percent of Breast Cancer Patients, Aged 40-49, with Risk Factors, Compared to the General Population

Risk Factor	General Population Aged 40-49	Breast Cancer patients aged 40-49
Any Family History of Breast Cancer	34.7%	38.5%
Menarche <12yo	12.8%	23.6%
First Birth >34yo OR Nulliparous	26.8%	21.7%
Any Family History of Ovarian Cancer	?	5.2%
Mammographic Density: Extremely dense or Heterogeneously dense	55.6%	77.8%
Prior Biopsy	?	13.0%
History of atypia	?	1.9%
Gail: 5-year relative risk >=2	NA	6.2%
Gail: Lifetime relative risk >=2	NA	3.7%

General population numbers are based on literature review.

P51

Clinical Breast Examination Improves Breast Health Awareness and Stage at Diagnosis Among Peruvian Breast Cancer Patients A. Romanoff,[1]* T. Hayes Constant,[1] M. Cedano Guadiamos,[2] A. Burga Vega,[2] J. Zunt,[1] K. Johnson,[1] B. Anderson.[1] *1. University of Washington, Seattle, WA; 2. Instituto Regional de Enfermedades Neoplasicas del Norte, Trujillo, Peru.*

Background: Worldwide, the majority of breast cancer deaths occur in low and middle income countries (LMICs) due to late presentation and inadequate access to diagnosis and treatment. To better understand the impact of awareness education and clinical breast exam (CBE) in Peru, we studied factors influencing method of detection and stage at diagnosis in breast cancer patients. Methods: A cross-sectional study was carried out at a federally-funded referral cancer center in Trujillo. All breast cancer patients who visited a surgeon from 2/15-5/15 were eligible. Trained personnel conducted individual patient surveys in Spanish, using a validated Breast Cancer Delays Questionnaire. Results: Of 159 eligible women, 113 (71%) participated. 1 cancer (1%) was detected by screening CBE, 7 (6%) by mammography, and 105 (93%) by patient-reported clinical symptoms. A minority of women had previously undergone CBE (52, 46%) or mammogram (23, 20%). Of those diagnosed by symptoms, the mean patient delay interval from symptom discovery until first medical consult was 6.9 months (range 0-129 mo). Income, insurance, previous CBE and previous mammography were significantly associated with screening vs. symptom detected cancer. After controlling for age and socioeconomic variables, women who underwent a previous CBE had 16x greater odds of having screening vs. symptom detected cancer (p=0.01), while previous mammography no longer retained significance. Of 92 women with available stage, those who underwent previous CBE were less likely to be diagnosed with late stage (III or IV) disease compared with those who never had a CBE (15/41, 37% vs. 32/51, 63%, p=0.04). Prior receipt of breast cancer information and self breast exam had no influence on detection method or stage at diagnosis. Conclusion: The vast majority of Peruvian women detected their breast cancer by symptoms. Undergoing a previous CBE is the strongest predictor of detecting a breast cancer by screening, and is associated with earlier stage at cancer diagnosis. Exposure to CBE is more relevant to breast cancer early detection than are more difficult-to-modify socioeconomic variables among women in LMICs.

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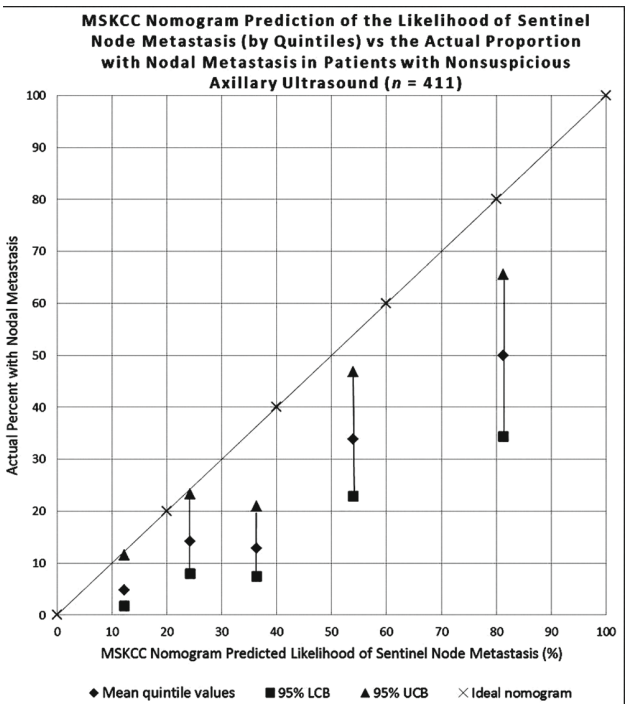
The Impact of Axillary Ultrasound Results on a Sentinel Lymph Node Metastasis Prediction Nomogram T. Chichester,* R. Jackson, C. Mylander, M. Rosman, S. Cologer, R. Andrade, L. Tafra. *Anne Arundel Medical Center, Annapolis, MD.*

Background: Axillary staging for breast cancer is essential for planning treatment and determining prognosis. While surgical staging is the gold standard, improved preoperative staging may be of benefit. The Memorial Sloan Kettering Cancer Center (MSKCC) nomogram calculates the risk of sentinel lymph node metastasis (SLNM) based on clinicopathologic variables, but does not incorporate axillary ultrasound (AXUS) results. Objective: To examine how AXUS findings modify the accuracy of the MSKCC nomogram's prediction of SLNM. Methods: A retrospective analysis of consecutive breast cancers treated at a single institution that received preoperative AXUS, surgical axillary staging, and no neoadjuvant chemotherapy. MSKCC nomogram estimates were calculated for each case, and approximate quintiles were defined by the nomogram's prediction of SLNM. The cohort was dichotomized into

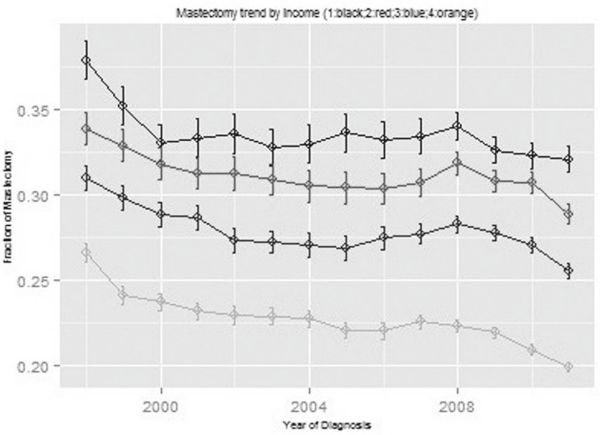
subgroups: those with suspicious versus non-suspicious AXUS. For each subgroup, the proportion of cases with SLNM by surgical pathology was compared to the nomogram estimates. Results: 528 cancers were included; 117 (22%) had suspicious AXUS, and 411 (78%) had non-suspicious AXUS. In the overall cohort, the nomogram prediction of SLNM was higher than the observed proportion with SLNM. However, when AXUS results were considered, the nomogram performance varied based on AXUS results. In the subgroup with non-suspicious AXUS, the nomogram overestimated the likelihood of SLNM, and this was statistically significant in all quintiles (Figure). Conversely, for the subgroup with suspicious AXUS, the nomogram prediction was similar to the observed proportion of patients with SLNM. Conclusions: AXUS stratified patients by likelihood of nodal metastasis and appears to modify the predictive ability of the MSKCC nomogram. A limitation of this study is the purposeful selection for early breast cancers by excluding patients who received neoadjuvant chemotherapy. A revised nomogram incorporating AXUS may improve preoperative prediction of nodal metastasis.



P53

Income and Health Care Utilization May Influence Surgical Choice in Early Stage Breast Cancer R.S. Sweeting,* L. Du, K. Kummerow Broman, Y. Shyr, M.A. Hooks. *Surgical Oncology, Vanderbilt University, Nashville, TN.*

Background: Breast conservation surgery (BCS) among early stage BCS eligible patients is used as a performance marker for accredited breast centers. However, recent studies have revealed a shift towards mastectomy in BCS eligible women. We seek to examine trends stratified by income in order to further define variables that influence surgical choice for mastectomy. Methods: We performed a retrospective cohort analysis of adult women with early stage breast cancer treated from 1/1/1998 to 12/31/2011 using the National Cancer Database. We compared trends by income quartiles for rates of mastectomy, mastectomy with reconstruction and BCS using Pearson chi-squared test. We then assigned a cost to each index procedure using 2012 data from the Healthcare Cost and Utilization Project. We assumed a re-excision rate of 20% with BCS and only one reconstructive procedure in patients undergoing post mastectomy reconstruction. Mean hospital costs were used as a surrogate for patient charges due to extreme heterogeneity of charge calculations in our healthcare system. We then calculated the number of heath care related contacts to assign a burden of utilization to each procedure. A health care contact was defined as required visits associated with the index procedure. Results: The study included 1.2 million women. Rates of mastectomy alone were 0.334, 0.310, 0.227, and 0.223 for the 4 income quartiles in ascending order ($p < 0.0001$). The rates of mastectomy with reconstruction were 0.062, 0.071, 0.081 and 0.113 ($p < 0.0001$). The calculated procedure costs are $10,065 for mastectomy, $22,666 for mastectomy with reconstruction, and $19,006 for BCS. Mastectomy corresponds to 3 health care contacts as opposed to 10 for mastectomy with reconstruction and 34 for BCS. Discussion: Women in lower income categories were more likely to undergo mastectomy, which was associated with the lowest cost and least healthcare utilization. By comparison, mastectomy plus reconstruction was pursued by more women in higher income brackets, and was associated with higher cost. These findings demonstrate that it is important to investigate external socioeconomic barriers which influence surgical choice.



Fractions of patients undergoing mastectomy in order of income category
Category one is the lowest income quartile and category 4 is the highest

P54

TOX3 as an Adjunct Novel Biomarker in Luminal B Breast Cancer J.J. Hong,* A. Seksenyan, B. Knudsen, W. Audeh, J. Kaye. *Surgical Oncology, Cedars-Sinai Medical Center, Los Angeles, CA.*

Background: A breast cancer (BC)-associated SNP is found in an enhancer region of the TOX3 gene, which encodes a nuclear protein expressed in ER^+ mammary epithelial cells but with unknown biological function. We previously reported data implicating TOX3 as a tumor promoter where high expression was associated with poor outcome in patients with luminal B (LumB) breast cancer. The Oncotype DX assay predicts likelihood of distant recurrence in ER^+ early stage BC, improving patient selection for adjuvant chemotherapy. However, LumB subtypes often have an intermediate recurrence score (RS), where the absolute benefit of chemotherapy is unclear. Thus, we investigated whether TOX3 expression might provide additional discriminatory power. Methods: Tumors specimens were retrospectively collected. Tissue microarrays of 177 histologically-defined LumB tumors ($ER^+Her2^{-/+}$ Ki67>14%), 89 of which with associated Oncotype DX data, were stained with an anti-TOX3 monoclonal antibody, to correlate with RS and clinicopathologic outcomes. Results: TOX3 protein was expressed in a significant subset of LumB tumors. Using image analysis to create a histoscore, we found no correlation between TOX3 expression and RS. On multivariable analyses, TOX3 and RS were not significantly associated with RFS after adjusting for stage. In 89 patients with RS, 11% developed recurrence with a 3-year RFS of 91% during the 13 years of follow-up. In 36 patients with intermediate RS, higher T stage, grade III, presence of LVI, and higher Ki-67 were associated with worse RS; 17% developed recurrence with a 3-year RFS rate of 89%. Adding TOX3 to the model including RS and Ki-67 did not improve the predictive accuracy of RFS. Conclusions: Despite overall efficacy of adjuvant chemotherapy in early stage BC, patients are exposed to risks without deriving benefit. The lack of correlation of TOX3 expression and RS may suggest a facet of the biology of ER^+ aggressive cancers that may not be addressed by the Oncotype DX assay. Thus, prospective studies examining recurrence risk and chemotherapy benefit may need to be expanded to further investigate TOX3 expression as an adjunct novel biomarker to guide optimal personalized therapy for BC.

P55

The Role of Social Support in Surgical Decision Making for Black Women with Breast Cancer R.S. Sweeting,* K.B. Wilson. *Vanderbilt University, Nashville, TN.*

Background: Black women with breast cancer have worse survival at every stage as compared with white women. This disparity persists when controlling for standard variables associated with health outcomes. The availability of a social support structure is positively correlated with health outcomes in the literature. This is thought to be due to intangible psychosocial factors and enhanced coping mechanisms. Prior studies demonstrate that black women tend to have fewer networks for social support as compared to white women. We seek to examine the role of social support in the lives of black women with breast cancer, specifically as it relates to surgical decision making and knowledge. Methods: We conducted 20 semi-structured 2 hour interviews in two target cities with black women who have received a diagnosis of breast cancer. We used a snowballing technique to recruit participants beginning with women in the Sisters Network in Nashville TN and Durham NC. After transcription, interviews were analyzed using Atlas-TI software to look for trends in narratives and responses. Results: We found that when asked about surgical choice, the presence or absence of a support person during the time from diagnosis to procedure was viewed by participants to influence surgical choice and the stress of the decision. The identified sources of support included spouses, other family members, close female friends, and experientially similar others. The presence of strong support empowered women to feel as though they were better able to make choices. Women who reported having minimal support or unsupportive individuals had greater difficulty in making empowered and well informed decisions. Conclusion: Many disparities exist for black women in regards to cancer care. Our study demonstrates that the quality and presence of social support plays a role in surgical decision making for black women with breast cancer. It is important that we examine psychosocial morbidity as a contributor to health behaviors and outcomes.

P56

Safety of Immediate Breast Reconstruction Following Neoadjuvant Chemotherapy in Inflammatory Breast Cancer E.M. Aleassa,[2]* S. Niraula,[4] M.W. Pitz,[4] E.L. MacIntosh,[2] T.J. Hayakawa,[3] E.W. Buchel,[3] B. Friesen,[4] O. Bucher,[1] P. Hebbard.[2] *1. Epidemiology and Cancer Registry, Cancer Care Manitoba, Winnipeg, MB, Canada; 2. General Surgery, University of Manitoba, Winnipeg, MB, Canada; 3. Plastic Surgery, University of Manitoba, Winnipeg, MB, Canada; 4. Medical Oncology and Hematology, University of Manitoba, Winnipeg, MB, Canada.*

Introduction: Indications for breast reconstruction surgery after breast cancer surgery are expanding. We hypothesize that immediate breast reconstruction is safe to perform in inflammatory breast cancer (IBC) patients following neoadjuvant chemotherapy. Methods: A retrospective chart review was performed for all locally advanced breast cancer (LABC) and inflammatory breast cancer (IBC) patients receiving neoadjuvant chemotherapy followed by surgery in the province of Manitoba between January 2004 and December 2011. Data gathered included demographics, breast cancer (site and type), surgery (date, type and contralateral procedure), reconstruction (type and timing), recurrence and all-cause mortality. Descriptive data analysis and univariable logistic regression model were used to analyze the date. Results: A total of 286 patients were treated with curative intent during the time period. After excluding patients who had progressive disease on chemotherapy, 199 (69.6%) were included in the study, of which 71 (36%) had IBC. Thirty-two (45%) patients with IBC developed recurrences and 39 (55%) died at last follow-up. Local recurrence occurred in only 1 patient. Fifteen (21%) of the IBC patients had breast reconstruction, including 10 (14%) that were performed at the time of definitive surgery. There was no association between the use of immediate breast reconstruction and the risk of breast cancer recurrence (OR 0.72, 95%CI 0.18-2.8, p =0.63) or death (OR 0.78, 95%CI 0.06-1.1, p= 0.068). Similarly, when looking at the larger group of LABC patients, there was no association between the use of immediate breast reconstruction and the risk of breast cancer recurrence (OR 0.78, 95%CI 0.35-1.8, p=0.56). There was an association between immediate breast reconstruction and the risk of death in all LABC patients (OR 0.37, 95%CI 0.15-0.88), likely reflective of good clinical patient selection for the procedure. Conclusion: Immediate breast reconstruction in IBC patients who have undergone neoadjuvant chemotherapy appears to be safe in appropriately selected patients. This treatment option is routinely offered to appropriate patients in our centre.

P57

Oncoplastic Breast Conserving Surgery is Associated with a Lower Risk of Surgical Site Complications Compared to Standard Breast Conserving Surgery A. Crown,* L. Scovel, E. Scott, D.G. Wechter, J.W. Grumley. *Virginia Mason Medical Center, Seattle, WA.*

Introduction: Oncoplastic breast conserving surgery (BCS) integrates plastic surgery techniques in the excision of breast cancer. Oncoplastic techniques significantly lower rates of re-excision while improving breast cosmesis. Despite these benefits, critics postulate that more extensive surgery may result in higher incidence of surgical site complications. The goal of this study is to compare the surgical site complication rates for oncoplastic BCS with standard BCS. Methods: A single institution retrospective chart review was performed to identify complications following BCS. All patients undergoing BCS for treatment of breast cancer were evaluated. Patients treated from January 2009 to 2010, prior to adoption of oncoplastic techniques, were identified as the standard surgery (SS) group. Patients treated with oncoplastic BCS from January 2013 to 2015 were identified as the oncoplastic surgery (OS) group. All surgical site complications were recorded with the most common being cellulitis, seroma, and superficial wound dehiscence. Demographic and clinical parameters were compared using chi-squared tests. Results: 726 patients were evaluated. 273 patients were treated in the SS group compared with 453 patients in the OS group. 51 patients (18.9%) developed surgical site complications in the SS group compared with 43 patients (9.4%) in the OS group ($p<0.001$). Seroma formation was significantly higher in the SS group (SS 4.4% vs OS 1.8%, p=0.036). Surgical site complication rate was significantly higher when BCS was performed by low volume surgeons (32.6% vs 15.8%, p=0.012). However, when low volume surgeons were excluded from the analysis, the complication rate for SS remained significantly higher than for OS (15.8% vs 9.5%, p=0.017). Despite the differences in surgical site complications, the need for interventions was not statistically different (SS 54.9% vs OS 58.1%, p=0.75). Conclusion: Overall, BCS has a low risk of significant surgical site complications. Despite more extensive surgery associated with oncoplastic BCS, the surgical site complication rate was significantly lower compared to standard BCS technique.

P58

Axillary Surgery in Patients with Ductal Carcinoma In Situ (DCIS): Analysis of the U.S. National Cancer Data Base (NCDB) from 1998-2012 J.L. Bell,* R.E. Heidel, A. Orucevic. *Cancer Institute, University of Tennessee Medical Center, Knoxville, TN.*

Introduction: Lymph node (LN) examination of patients with pure DCIS remains controversial. Recent studies showed a range of 1-22% positivity of sentinel LN in patients with DCIS, but the clinical and biologic significance of these findings is unknown. Methods: We investigated the practice of axillary management in patients with pure DCIS through analysis of the NCDB from 1998-2012. Number of LN examined and positive; facility type; year of diagnosis and clinicopathologic characteristics including overall survival were analyzed (Table 1). Results: 384,420 DCIS cases were analyzed (age range 18-90, mean = 59.7). 32.6% (125,240) had regional LN assessment and 66.4% did not (255,261; missing data in 3919), regardless of type of surgical procedure. 0.1% cases had nodal metastases (261/384,420). LN number harvested ranged widely, mean=4.05. Mean DCIS size was 48 mm. Facility type was not predictive. LN positivity increased from 0.1% in 1998 to 0.3% in 2003; however, fell to 0% in 2004-2012. LN sampling rates increased through the years from 24.4% in 1998 to 37.5% in 2012. 89% of patients were alive and 11% dead at the end of 2012. Positive LN predicted for worse overall survival (OR 3.34, 95% CI 2.52-4.43; p<.001). Younger age and larger tumor size were predictive of positive LN (p=0.01) but grade and race were not (p=0.3). Conclusion: Fifteen-year analysis of NCDB revealed low prevalence of positive LN in patients with DCIS (0.1%), suggesting that the practice of avoiding axillary staging in DCIS patients should be strongly considered. Since positive LN predicted for worse overall survival, the criteria allowing identification of at risk patients warrants further study.

Table 1. NCDB analysis of axillary surgeries in DCIS patients from 1998-2012

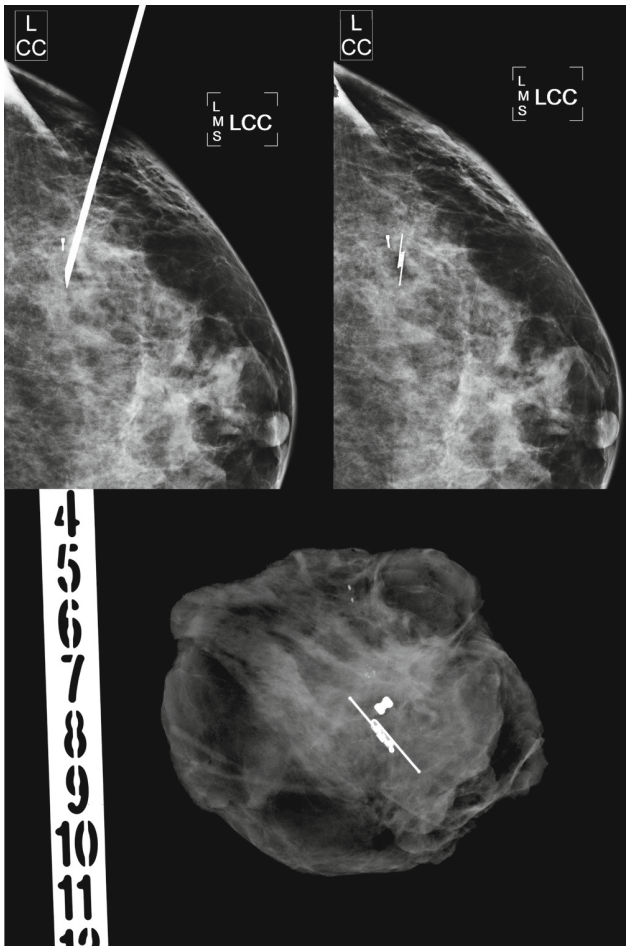
Age (N=384,420)	LN Examined Negative	LN Examined Positive	LN Not Examined	LN Unknown
Age group 18-39	5,864 (1.5%)	31*	6,831 (1.8%)	168*
Age group 40-70	92,996 (24.2%)	177*	182,975 (47.6%)	2,788*
Age group >70	26,119 (6.8%)	53*	65,455 (17%)	963*
Race (N=379,170)	LN Examined Negative	LN Examined Positive	LN Not Examined	LN Unknown
White	104,817 (27.6%)	224*	215,225 (56.8%)	3,334*
Black	14,034 (3.7%)	33*	26,414 (7%)	385*
Other	4682 (1.2%)	3*	9894 (2.6%)	125*
Facility type (N=384,420)	LN Examined Negative	LN Examined Positive	LN Not Examined	LN Unknown
Community Cancer Program	12,903 (3.4%)	23*	28,495 (7.4%)	419*
Comprehensive Community Cancer Program	76,352 (19.9%)	139*	153,693 (40%)	2,255*
Academic/Research Program	35,532 (9.2%)	98*	72,544 (18.9%)	1,216*
Other Cancer Programs	192*	1*	529*	29*
Tumor size (mm) (mean=48mm)(N=384,420)	LN Examined Negative	LN Examined Positive	LN Not Examined	LN Unknown
1-10	286*	5*	940*	11*
11-20	33,925 (8.8%)	37*	92,774 (24.1%)	834*
21-50	34,283 (8.9%)	71*	47,122 (12.3%)	522*
≥51	56,485 (14.7%)	148*	114,425 (29.8%)	2,522*
Number of positive lymph nodes (N=261)	LN Examined Negative	LN Examined Positive	LN Not Examined	LN Unknown
1	N/A	132 (50.6%)	N/A	N/A
2-3	N/A	37 (14.2%)	N/A	N/A
≥4	N/A	92 (35.2%)	N/A	N/A
Histologic grade (N=384,420)	LN Examined Negative	LN Examined Positive	LN Not Examined	LN Unknown
G1	11,217 (2.9%)	24*	38,726 (10.1%)	620*
G2	30,684 (8%)	52*	71,402 (18.6%)	873*
G3 and undifferentiated	49,151 (12.8%)	86*	64,110 (16.7%)	880*
Grade not stated	33,927 (8.8%)	99*	81,023 (21.1%)	1,546*
Vital status (N=358,753)	LN Examined Negative	LN Examined Positive	LN Not Examined	LN Unknown
Dead	10,206 (2.8%)	64*	28,660 (8%)	637*
Alive	105,116 (29.3%)	197*	210,707 (58.7%)	3,166*

Table legend: LN=lymph node; *=<1%

P59

Prospective, Single-Arm, Multi-Site Evaluation of a Non-Radioactive Surgical Guidance Technology for the Location of Non-Palpable Breast Lesions During Excision C.E. Cox,[1]* P. Whitworth,[2] P. Blumencranz,[3] J.M. Cox,[4] R. Prati,[5] S. Russell,[1] E. Carter,[1] J. King,[1] S.C. Shivers.[1] *1. Surgery, University of South Florida, Tampa, FL; 2. Nashville Breast Center, Nashville, TN; 3. Morton Plant Mease Hospital, Clearwater, FL; 4. Tampa Bay Breast Care Specialists, Tampa, FL; 5. Florida Hospital Tampa, Tampa, FL.*

Introduction: This study evaluated a novel FDA-cleared medical device that utilizes non-radioactive electromagnetic wave technology to provide real-time guidance during excisional breast procedures. The technology was developed to address the disadvantages associated with wire localization and advance the progress made with radioactive seed localization. The purpose of this on-going study is to evaluate the performance of the device in guiding the removal of non–palpable breast lesions. Methods: IRB approval was obtained for all institutions. Pts underwent excision with the device, which includes an electromagnetic wave reflective device (reflector), handpiece and console. Using imaging guidance, the reflector was implanted into the target tissue. In the OR, the surgeon used the handpiece to plan the incision and guide the removal of the reflector and surrounding breast tissue. The console provides feedback on handpiece-to-reflector proximity. Primary endpoints include successful reflector placement, localization and retrieval. Results: To date, 114 pts have participated in the study, along with 17 surgeons, 23 radiologists, and 10 institutions. The reflectors were successfully placed in 113/114 (99%) pts with either mammography (52) or ultrasound (62) guidance up to 7 days (avg 1.7 days) before surgery. Thirty-one pts underwent excisional biopsy and 83 pts had a lumpectomy. The intended lesion and reflector were successfully removed in all pts. No adverse events occurred. Pathology is currently available for 113 pts. For 31 pts who had an excisional biopsy, 21 had no invasive or in situ carcinoma identified. For 79 pts with cancer, 67 pts (85%) had clear margins and 9 pts (11%) were recommended for re-excision. Conclusions: The preliminary data show that real–time surgical guidance with the device is an accurate technique for directing the removal of non–palpable breast lesions and reproducible at multiple sites. The study has yielded 100% surgical success with a re–excision rate of 11%. Ongoing accrual to this study will validate these findings with planned enrollment of 150 pts across 10 sites.



Reflector placement (top) and specimen radiograph (bottom).

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Accuracy of Sentinel Lymph Node Dissection (SLND) in Patients with Multicentric Breast Cancer M. Yi,* E. Mittendorf, I. Bedrosian, S. Black, H.M. Kuerer, S.M. DeSnyder, A.S. Caudle, G. Babiera, K.K. Hunt. *University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: National guidelines support use of SLND in the setting of multicentric disease based on the limited data. We evaluated the identification rate, false negative rate (FNR) and recurrence rates in breast cancer patients with multicentric disease who underwent SLND. Methods: Patients with clinical T1-3,N0,M0 breast cancer, who underwent SLND from March 1993 through March 2014 were identified from our institutional database. Patients with recurrent breast cancer, neoadjuvant chemotherapy, previous breast irradiation or axillary surgery were excluded. Patient and tumor characteristics were evaluated and comparisons undertaken between those with multicentric vs unifocal disease. Results: Of 6,720 patients identified; 10% had multicentric disease. A SLN was identified in 99.1% of patients with multicentric and 98.8% with unifocal disease (P=0.5). Of those undergoing SLND with a planned completion axillary dissection (ALND) (N=524), the FNR was 3.8% in the multicentric group (N=52) vs 2.8% in the unifocal group (N=472) (P=0.7).

Patients with multicentric disease were more likely to have isotope injected in the subareolar location (39.9% vs 23.4%, P<0.0001). Incidence of positive SLNs was 30% in multicentric patients vs 18.8% in patients with unifocal disease (P<0.0001). There were no significant differences in SLN identification rates, FNRs or SLN positivity rates in patients with multicentric disease based on injection sites (peritumoral at the site of the largest tumor vs subareolar). A total of 8 (1.2%) patients had regional recurrence in the multicentric group versus 54 (0.9%) in the unifocal group (P =0.5). There were no differences in disease-specific or recurrence-free survival between the multicentric and unifocal groups at a median follow-up of 2.8 years (range: 0.1-14.5 years) and 3.1 years (range: 0-21.7 years), respectively. Conclusions: This large dataset confirms that SLND is appropriate for axillary staging in patients with multicentric disease with local-regional outcomes following SLND equivalent to those in patients with unifocal disease undergoing SLND.

P61

Does a Lower Tumour Stage Give a Higher Pathological Complete Response Rate in Breast Cancer Patients Undergoing Neoadjuvant Chemotherapy? B. Goorts,[2] T. van Nijnatten,[2] L. De Munck,[1] M. Moossdorff,[2] M. Vane,[2]* E. Heuts,[2] M. Lobbes,[2] M. Smidt.[2]
1. Department of Research, Netherlands Comprehensive Cancer Organisation (IKNL), Utrecht, Netherlands; 2. Maastricht University Medical Centre, Maastricht, Netherlands.

Introduction. Pathological complete response of the tumour (pCR) is the best possible response in breast cancer patients treated with neoadjuvant chemotherapy (NCT). It is considered to be a surrogate outcome for (disease free) survival. The aim of this study was to investigate the effect of between clinical tumour stage (cT-stage) on pCR. Furthermore, the effect of pCR per cT-stage on overall survival was analysed. Methods. Using the Netherlands Cancer Registry database, all patients with primary invasive breast cancer treated with NCT between January 2005 and December 2008 were identified. Exclusion criteria were neoadjuvant radio- or endocrine therapy or distant metastases at time of diagnosis. Univariate logistic regression was performed to evaluate the effect of cT-stage on pCR. Subsequently, stepwise logistic regression was used to correct for potential confounders. Kaplan-Meier survival analyses were used to calculate overall survival (OS). Results. A total of 1,930 breast cancer patients treated with NCT were included. The overall pCR rate was 17%. In case of cT1, cT2, cT3 or cT4, pCR rates were 29%, 19%, 13% and 12%, respectively. Lower cT-stage (p<0.001, OR 4.044, 95% CI [2.438;6.706]) was a significant predictor of higher pCR rate (cT1-2 vs cT3-4), independent of and also stronger than positive Her2neu receptor status (p=0.007, OR 1.947, 95% CI [1.201;3.158]), negative oestrogen receptor status (p=0.024, OR 2.046, CI [1.101;3.805]), negative progesterone receptor status (p=0.032, OR 2.108, 95% CI [1.066;4.167]) and high grade (p=0.264, OR 1.348, 95% CI [0.798;2.278]). A significant positive effect of having pCR on 5-year OS was specifically seen in cT3 and cT4 tumours. The OS was 87.9% in cT3 tumours with pCR versus 73.6% without pCR (p=0.007) and 80.7% in cT4 tumours with pCR vs 54.6% without pCR (p<0.001). Conclusion. The most important predictor of pCR is the cT-stage: lower cT-stages have significantly higher pCR rates than higher cT-stages. Patients with cT3 or cT4 tumours who do have pCR, have a significantly higher overall survival compared to patients with cT3 or cT4 tumours without pCR.

Percentage pathological complete response per cT-stage.

cT-stage	% pCR (n)	p-value	OR	95% CI for OR (lower)	95% CI for OR (upper)
1	29 % (49/172)	Ref.	-	-	-
2	19% (152/787)	0.008	0.601	0.413	0.875
3	13% (66/502)	0.000	0.380	0.250	0.578
4	12% (57/469)	0.000	0.347	0.226	0.535

* cT-stage = clinical tumour stage, pCR = patholocial complete response, OR = Odds Ratio.

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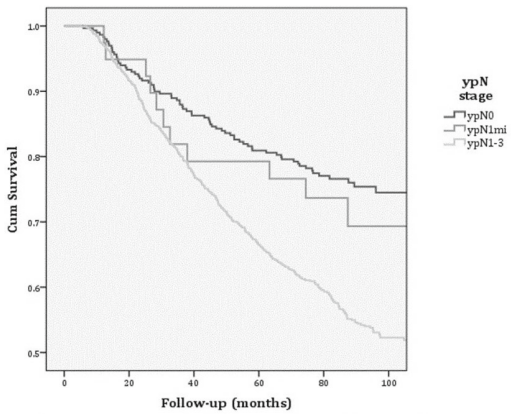
Prognosis of Micrometastases Compared to Complete Nodal Response and Macrometastases in cN+ Breast Cancer Patients After Neoadjuvant Chemotherapy: A Population-Based Study T. van Nijnatten,[1] M. Moossdorff,[1]* L. De Munck,[2] B. Goorts,[1] K. Keymeulen,[1] R. Beets-Tan,[1] M. Lobbes,[1] M. Smidt.[1] *1. Maastricht University Medical Centre, Maastricht, Netherlands; 2. Department of Research, Netherlands Comprehensive Cancer Organisation, Utrecht, Netherlands.*

Purpose The prognosis of residual micrometastases (ypN1mi) after neoadjuvant chemotherapy in clinically node positive (cN+) breast cancer patients is still unclear. The aim of this study was to determine whether the prognosis of ypN1mi in cN+ breast cancer patients, is more similar to prognosis of complete nodal response (ypN0) or residual macrometastases (ypN1-3). Methods Data were obtained from the Netherlands Cancer Registry. All patients were diagnosed between 2005 and 2008 with cN+ primary invasive breast cancer and treated with neoadjuvant chemotherapy, followed by axillary lymph node dissection. Exclusion criteria were ypNx, distant metastases at time of diagnosis, neoadjuvant radio- or endocrine therapy. Disease-free survival (DFS) included any local, regional, or contralateral recurrence or distant metastasis. Kaplan-Meier curves provided information on DFS and overall survival (OS). Uni- and multivariable cox regression analyses were used to determine predictors. Results A total of 1,347 patients were included for analysis. Pathologic nodal stage consisted of 22.2% ypN0, 0.9% ypN0i+, 2.9% ypN1mi and 74.0% ypN1-3.Overall, 39.6% of the patients experienced a recurrence within 5 years. In subgroup analysis, this concerns 25.2% ypN0, 33.3% ypN1mi and 44.5% ypN1-3. In multivariable analyses, no statistical difference for DFS between ypN0 and ypN1mi (p=0.555) or ypN1mi and ypN1-3 (p=0.709) was found. After 8 years, 39.0% of all patients deceased. In subgroup analysis, this concerns 23.7% ypN0, 28.2% ypN1mi and 43.9% ypN1-3. In multivariable analyses, no statistical difference for OS between ypN0 and ypN1mi(p=0.518) or ypN1mi and ypN1-3 (p=0.157) was found. High tumorgrade, absence of pCR in the breast and omission of endocrine therapy in case of hormone positive receptors were identified as independent predictors for worse DFS and OS. Conclusion DSF and OS of residual micrometastases in cN+ breast cancer patients, treated with neoadjuvant chemotherapy and axillary lymph node dissection, seem more similar to patients with a complete nodal response than patients with residual macrometastases.



pN0	296	276	255	239	176	63
pN1(mi)	38	36	30	30	20	8
pN1-3	989	907	762	657	451	171

Figure 1. Kaplan Meier curve of overall survival, subdivided by ypN stage

P63

Long-term Satisfaction and Breast Cancer Outcomes After Bilateral Prophylactic Mastectomy in Women with a Family History of Breast Cancer J.C. Boughey,* T.L. Hoskin, C.N. Heins, L.C. Hartmann, M. Frost. *Surgery, Mayo Clinic, Rochester, MN.*

Background: Awareness and availability of genetic testing is increasing identification of women at high risk of breast cancer. Bilateral prophylactic mastectomy (BPM) significantly decreases breast cancer risk. Herein we present long term follow up data on the efficacy and satisfaction of a large cohort of women who underwent BPM. Methods: Women with a family history of breast cancer who underwent BPM 1960-1993 were mailed questionnaires at two timepoints to assess satisfaction and breast cancer development and medical record review undertaken. Cumulative incidence of breast cancer was calculated from date of BPM to survey follow-up and estimated using the Kaplan-Meier method. Paired comparisons between the two timepoints within patient were performed using the Wilcoxon signed-rank test. Results: Of 639 initial women, 609 patients were alive at time of the first questionnaire and 584 at the second questionnaire and a total of 319 (55%) women completed both. Median length of breast cancer specific follow-up for the cohort overall was 18.4 years with a minimum of 10 years follow-up for >90% of the cohort. Estimated breast cancer incidence was 1.3% (95% CI: 0.3-2.5%) at 20 years. Ten women developed breast cancer after BPM and 4 died of breast cancer at a mean of 3.2 years after breast cancer diagnosis. Among the 319 women with data from both follow-up timepoints, 308 (97%) underwent implant reconstruction. 70 patients (22%) required one reoperation and 130 patients (41%) had ≥2 reoperations. Median patient age was 42 years at BPM and 56 and 64 years at first and second follow-up, respectively. The proportion satisfied with their decision for BPM did not change (p=0.98) with 73% very or somewhat satisfied at both surveys. The proportion saying they would choose BPM again increased significantly between the two timepoints from 71% at the first to 81% at the second survey (p<0.001). Conclusion BPM significantly decreases risk of breast cancer development; this cohort remained at extremely low risk with a 20-year breast cancer incidence estimate of 1.3%. Patient satisfaction remained high with long term follow up.

	N = 639		
Cumulative incidence of breast cancer estimate (95% CI)			
10-year	0.6% (0.01%, 1.3%)		
15-year	0.8% (0.1%, 1.6%)		
20-year	1.3% (0.3%, 2.5%)		
25-year	2.3% (0.6%, 4.2%)		
	N = 319		
	1st follow-up survey	2nd follow-up survey	p-value
Overall How Satisfied with PM			0.98
Missing	12	7	
Very satisfied	108 (35.2%)	108 (34.6%)	
Satisfied	117 (38.1%)	120 (38.5%)	
Neither	36 (11.7%)	33 (10.6%)	
Dissatisfied	27 (8.8%)	33 (10.6%)	
Very dissatisfied	19 (6.2%)	18 (5.8%)	
Choose to have PM again			<0.001
Missing	9	3	
Definitely would	143 (46.1%)	190 (60.1%)	
Probably would	76 (24.5%)	66 (20.9%)	
Unsure	49 (15.8%)	38 (12.0%)	
Probably would not	21 (6.8%)	13 (4.1%)	
Definitely would not	21 (6.8%)	9 (2.8%)	

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Postmastectomy Breast Reconstruction Disparities Across an Academic, Private, and Public Institution in the Same Metropolitan Area L. Perry,[1]* V. Jones,[2] C. Arciero,[1] C. Zhang,[3] Z. Chen,[3] G. Carlson,[1] A. Cheng,[1] A. Losken,[1] M. Rizzo,[1] T.M. Styblo,[1] J. Okoli,[4] S. Gabram.[1] *1. Emory University School of Medicine, Atlanta, GA; 2. City of Hope Cancer Center, Duarte, CA; 3. Rollins School of Public Health, Atlanta, GA; 4. Morehouse School of Medicine, Atlanta, GA.*

BACKGROUND Breast reconstruction is delivered unequally across patient populations. Previous study of a metropolitan hospital system found significantly higher rates of immediate reconstruction at its academic (71%) and private (57%) hospitals as compared to its public hospital (23%)[1]. This disparity was addressed as two plastic surgeons were hired at the public hospital in September 2012. We sought to identify remaining factors influencing rates of breast reconstruction. METHODS We performed an IRB approved, retrospective review of all patients undergoing mastectomy between October 1, 2012 and September 30, 2014 at an academic, private, and public institution in the same metropolitan area. Demographic and clinical data were collected. Univariate and multivariate analyses were utilized to compare factors affecting reconstruction rates across the three sites. RESULTS In all, 456 patients underwent mastectomy (178 academic, 202 private, 76 public), with immediate reconstruction rates of 77%, 61%, and 51%, p<0.001. Of women without reconstruction, 71% were African-American (AA), p<0.001. However, patient populations varied by site, as AA women comprised 26%, 76%, and 84% of academic, private, and public patients, p<0.001. Among academic patients, 97% were referred to plastic surgery, versus 72% of private and 61% of public patients, p<0.001. Referrals may reflect disease severity as clinical stage trended towards significance (p=0.057) and pathologic stage differed across sites, p=0.026. Also, 49% of public patients had a MRM, versus 12% and 23% of academic and private patients, p<0.001. Among patients without reconstruction, 30% of women at the public hospital elected this option, versus 22% and 17% of academic and private patients, p=0.003. CONCLUSIONS Although access to plastic surgery improved rates of breast reconstruction at the public hospital, this rate remains lower than academic and private sites. Underlying differences must be explored and addressed to ensure equal, high quality care for all breast cancer patients, regardless of where they receive treatment. [1] Reconstruction after breast cancer surgery. ASBS poster, 2013.

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Observation Versus Excision of Lobular Neoplasia on Core Needle Biopsy B. Arditi,* M. Wooster, L. Margolies, A. Nayak, C. Weltz, E. Port, I. Bleiweiss, S. Jaffer, H. Schmidt. *Mount Sinai, New York, NY.*

Introduction: Controversy exists surrounding management of lobular neoplasia (LN), either atypical lobular hyperplasia (ALH) or lobular carcinoma in situ (LCIS), diagnosed on core needle biopsy (CNB). Retrospective series of pure ALH and LCIS reported an "upgrade" rate to DCIS or invasive cancer in <10%. Few reports document radiologic/pathologic correlation to exclude cases of discordance that are the likely source of most upgrades, and there is minimal data on outcomes of patients electing interval follow-up imaging and clinical breast exam, in lieu of excision. We reviewed outcome of LN cases undergoing both excision and observation. Methods: Cases of LN alone on CNB between 2001-2014 were reviewed. CNB yielding LN and additional pathologic findings for which surgery was indicated were excluded. Patients must have had either surgical excision or follow-up breast imaging. All cases included were subject to radiologic-pathologic correlation after biopsy. Results: 178 cases were identified. 115 (65%) patients underwent surgery for the LN diagnosis, 54 (30%) patients were followed with imaging for >12 months (mean = 55 months), and 9 (5%) patients were followed for <12 months (mean = 8.2 months). Of the patients who underwent surgical excision, 103/115 (90%) had benign results, and 12/115 (10%) malignant. 7 of these 12 found malignancy at excision when needle biopsy results were considered discordant (5 DCIS, and 2 invasive lobular carcinoma), with the remainder, 5/115 (4%), having a true pathologic upgrade: 3 DCIS, and 2 microinvasive lobular carcinoma. Among 54 patients not having excision, 12/54 (22%) required subsequent CNB with 3 being in the same location as the initial CNB (2 benign, 1 invasive carcinoma 3 yrs later). In the imaging follow up group 1 other patient developed invasive cancer at a different site in the ipsilateral breast. Conclusion: Surgical excision of LN found on breast core biopsy yields a low upgrade rate when careful consideration is given to radiologic/pathologic correlation to exclude cases of discordance. Observation with reliable interval breast imaging is a reasonable alternative for most cases.

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Are Triple Negative Breast Cancer Patients Screened for BRCA Mutations According to NCCN Guidelines? L. Petersen,[1]* S. Aubry,[2] K. Burgess,[2] R. Rao,[2] K. Kopkash,[2] A. Madrigrano.[2] *1. Surgery, University of Michigan, Ann Arbor, MI; 2. Rush University Medical Center, Chicago, IL.*

BACKGROUND: Ten to 25 percent of patients diagnosed with breast cancer have triple negative breast cancer (TNBC), defined as tumors negative for estrogen, progesterone, and Her2-neu receptors. TNBC is more aggressive than receptor positive cancer. The National Comprehensive Cancer Network (NCCN) recommends BRCA genetic testing for women less than age 60 when diagnosed with triple negative breast cancer. METHODS: The Commission on Cancer registry tumor database was queried for triple negative breast can-

cers from 2006 to 2013. Patient demographics were analyzed. Data regarding pathologic details and BRCA testing was collected. Analyses using the Fisher's exact test were conducted (www.graphpad.com). RESULTS: Triple negative breast cancer tumors were identified in the database (n=173). Sixty-one percent (105/173) of patients were less than 60 years of age, and therefore BRCA testing was indicated. Fifteen patients were BRCA positive. Eighty-three percent (87/105) of patients underwent BRCA testing. Seventeen percent (18/105) of patients did not receive BRCA testing that should have under the current guidelines. Patients that did not undergo recommended BRCA testing were more likely to be greater than or equal to 55 years of age (p=0.002), African-American (p=0.001), have Medicaid listed as a primary payer (p=0.021), and have American Joint Commission on Cancer stage 3 disease (p=0.014). CONCLUSIONS: Risk factors for not completing BRCA testing include older age, African-American race, Medicaid insurance status, and stage 3 disease. Health provider awareness of this opportunity for improvement is important to decrease these health disparities.

Comparison of demographics and stage between triple negative patients under the age of 60 that underwent BRCA testing and those that did not

Patient demographics and stage	BRCA testing (n=87)	No BRCA testing (n=18)	p value
Age < 40 years old	20 (23%)	1 (6%)	0.114
Age >/= 55 years old	12 (14%)	9 (50%)	0.002
White	54 (62%)	4 (22%)	0.003
Black	30 (34%)	14 (78%)	0.001
Medicaid	9 (10%)	6 (33%)	0.021
Uninsured	0 (0%)	0 (0%)	1
Grade III	80 (92%)	16 (89%)	0.65
Positive EGFR	28 (32%)	6 (33%)	1
Unfavorable Ki67	60 (69%)	13 (72%)	1
AJCC stage 0	32 (37%)	0 (0%)	1
AJCC stage 1	42 (48%)	5 (28%)	0.592
AJCC stage 2	8 (9%)	7 (39%)	0.605
AJCC stage 3	3 (3%)	6 (33%)	0.014
AJCC stage 4	1 (1%)	0 (0%)	1

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The Impact of Neoadjuvant Chemotherapy on Nodal Disease and Nodal Surgery by Tumor Subtype Z. Al-Hilli,* T.L. Hoskin, C.N. Heins, J.C. Boughey. *Surgery, Mayo Clinic, Rochester, MN.*

Background: Neoadjuvant chemotherapy (NAC) decreases extent of nodal disease and provides the opportunity for conservation of the axilla. The goal of this study was to evaluate the impact of NAC on nodal positivity and nodal surgery using data from the National Cancer Database (NCDB). Methods: NCDB data from 2010-2012 of cT1-4c breast cancers were evaluated. Patients receiving NAC and those undergoing primary surgery (PS) were compared. Patients with neoadjuvant radiation or neoadjuvant hormone therapy were excluded. Axillary surgery was classified according to the number of nodes examined with 1-6 nodes considered sentinel lymph node (SLN) surgery only and >6 nodes examined considered axillary lymph node dissection (ALND). Rates of pathologic node negative status (pN0) and use of SLN surgery were compared between groups using chi-square tests. Results: A total of 267,720 patients were evaluated, of whom 18,775 (7.0%) received NAC and 248,945 (93.0%) had PS. In cN0 patients, rates of pN0 were significantly higher in patients treated with NAC compared to PS in ER+/Her2+ (82.1% vs 78.3%, p=0.002), ER-/Her2+ (90.9% vs 78.4%, p<0.001) and in ER-/Her2- (89.8% vs 85.5%, p<0.001) patients. Stratified by cT stage (see Table), the largest effects were generally seen in cT2-cT4c tumors. Patients with cT2 and T3 tumors had a significantly higher SLN rate for NAC vs PS for each biologic subtype except ER+/Her2- tumors where this was true only for T3 tumors. In cN1-3 patients, rates of pN0 after NAC were 32.4% ER+/Her2+, 14.4% ER+/Her2-, 41.2% ER-/Her2+, 37.0% ER-/Her2- (p<0.01 for all pairwise comparisons). SLN surgery use in the cN1-3 patients was similar across tumor types at 28.3% ER-/Her2+, 26.3% ER-/Her2-, 26.2% ER+/Her2+, and 21.9% ER+/Her2-, with significantly lower rates only for ER+/Her2- compared to every other tumor type (p<0.001). Conclusion: NAC increases rates of pN0 disease among cN0 pts compared to PS. Among cN+ pts, 14-41% undergoing NAC convert to pN0 disease depending on tumor type. Use of less extensive axillary surgery is being adopted after NAC across most tumor types in pts with cN0 and cN+ disease. ER+/Her2- disease has lowest response rates to NAC.

		NAC	PS		NAC	PS	
cN0 patients		% pN0	% pN0	p-value	% SLN	% SLN	p-value
ER+ / HER2+	T1	86.1%	82.8%	0.17	79.2%	81.0%	0.45
	T2	83.4%	68.1%	<0.001	75.9%	67.6%	<0.001
	T3	75.8%	57.9%	<0.001	63.7%	53.5%	0.02
	T4a-c	68.6%	54.6%	0.12	45.1%	40.9%	0.65
ER+ / HER2-	T1	62.8%	85.5%	<0.001	63.1%	85.1%	<0.001
	T2	67.4%	66.8%	0.65	67.6%	68.9%	0.28
	T3	55.0%	50.7%	0.05	56.2%	48.8%	<0.001
	T4a-c	53.0%	50.2%	0.46	47.0%	46.4%	0.88
ER- / HER2+	T1	89.8%	83.3%	0.04	72.7%	79.9%	0.05
	T2	92.7%	70.5%	<0.001	77.5%	66.6%	<0.001
	T3	89.0%	58.7%	<0.001	64.6%	48.3%	0.004
	T4a-c	83.9%	58.8%	0.009	51.8%	50.0%	0.87
ER- / HER2-	T1	88.7%	88.5%	0.86	77.7%	83.9%	<0.001
	T2	91.5%	81.1%	<0.001	80.3%	72.5%	<0.001
	T3	87.0%	78.0%	<0.001	64.2%	57.6%	0.02
	T4a-c	82.0%	69.2%	0.02	52.3%	48.1%	0.52

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Adjuvant Endocrine Therapy Does Not Decrease Breast Cancer Mortality in the Elderly J. Johnson,* J. Bao, F. Amersi, Q. Li, A. Giuliano, A. Chung. *Surgery, Cedars Sinai Medical Center, Los Angeles, CA.*

Introduction: The benefits of adjuvant endocrine therapy (ET) for elderly women with breast cancer are unclear given the diminished life expectancy in this population. The objective of this study was to compare women age ≥ 70 years who received ET after breast conserving surgery (BCS) to those who did not receive ET and to determine the effect of ET on outcomes. Methods: Review of a prospectively maintained database identified 481 women age ≥70 years who underwent BCS for stage I-III estrogen receptor positive breast cancer at a single institution between 2004 and 2013. We compared clinicopathologic and treatment characteristics, overall survival (OS), disease free survival (DFS), breast cancer specific survival (BCSS), and locoregional recurrence (LRR) for those who received ET (n=388) to those who did not receive ET (n=93). Results: Patients who received ET were younger with larger tumors, higher grade, and more frequent lobular histology. They were more likely to undergo sentinel node biopsy (SNB), have positive nodes, and receive radiation (XRT) than those who did not receive ET. No significant differences were observed between the groups in American Society of Anesthesiologist (ASA) scores, use of chemotherapy, progesterone receptor, and Her2 status (Table 1). With median follow-up of 46 months (mean 54 months), multivariable analysis did not find association between use of ET and BCSS (HR 0.68, 95% CI 0.17-2.68), but did associate use of ET with better DFS (HR 0.34, 0.15-0.76), LRR (0.28, 0.10-0.83), and OS (0.44, 0.25-0.77). The risk of dying from a cause other than breast cancer was greater than the risk of breast cancer mortality (risk ratios in no ET and ET, respectively: 8.0, 4.1), any breast cancer recurrence (1.7, 1.7), and LRR (3.4, 4.7). Conclusions: There were significant differences in the clinicopathologic and treatment profiles of elderly women who received or did not receive ET. Although ET was associated with a small absolute improvement in LRR and DFS, patients were more likely to die of causes other than breast cancer than to recur. Use of ET in this age group does not appear to reduce breast cancer mortality.

Table 1. Comparison of Patient and Tumor Characteristics in Patients age ≥ 70 with Breast Cancer treated With and Without Endocrine Therapy

Variable	No ET [1] (n=93) (%)	ET (n=388) (%)	p-value
Mean Age (years)	79	77	<0.01
ASA [2]			0.26
≤2	44 (47)	217 (56)	
≥3	41 (44)	148 (38)	
Mean Tumor Size (mm)	16	19	<0.05
Histology			<0.01
Ductal	73 (78)	285 (73)	
Lobular	3 (3)	49 (13)	
Mixed	13 (14)	51 (13)	
Other	4 (4)	3 (1)	
Grade			<0.05
1	32 (36)	84 (22)	
2	36 (40)	204 (53)	
3	21 (24)	96 (25)	
SNB [3]			<0.01
Yes	64 (69)	326 (84)	
No	29 (31)	62 (16)	
Lymph Nodes			<0.01
Positive	8 (9)	101 (26)	
Negative	56 (60)	225 (58)	
PR [4]	75 (81)	334 (86)	0.19
Her2	7 (8)	31 (8)	1.00
Adjuvant Chemotherapy	10 (11)	43 (10)	0.85
Adjuvant Radiation	42 (45)	299 (77)	<0.01

(1) ET=Endocrine therapy; (2) ASA=American Society of Anesthesiologists score; (3) SNB=Sentinel Node Biopsy; (4) PR=progesterone receptor

P69

DCIS is a Noninvasive Cancer, Not a Risk Factor for Breast Cancer A. Guth,* J. Montes, F. Schnabel, J. Chun, S. Schwartz, E. Kamen, R. Shapiro, D. Axelrod. *Surgery, NYU Langone Medical Center, New York, NY.*

Introduction: Ductal carcinoma in situ (DCIS) and invasive breast cancer have long been viewed as representing two points on the spectrum of one disease. A recent study published by Narod et al. found that women diagnosed with DCIS who developed an invasive recurrence were 18.1 times more likely to die of breast cancer than women who did not. In light of this controversial topic, we investigated DCIS in a contemporary cohort of newly diagnosed women at our institution spanning a five year period. Methods: The institutional Breast Cancer Database was queried for all women with newly diagnosed breast cancer from 2010-2015. Variables included age, race, body mass index (BMI), risk factors, tumor characteristics and outcomes. Statistical analyses included Pearson's Chi Square and Fisher's Exact Tests. Results: Out of a total of 2190 patients, 475 (22%) had pure DCIS while 1715 (78%) had invasive cancer. The median follow up was 3 years. The median age was 59 years (range 22-95). Of the patients with invasive cancer, 36 (2%) had any recurrence. Similarly, of the patients with DCIS, 9 (2%) developed recurrent disease (ipsilateral or contralateral), with 4 patients diagnosed with invasive recurrence (44%). Of the 36 recurrences in patients with invasive cancer, 33% presented with chest wall or distant metastasis. Patients with pure DCIS had a slightly higher proportion of African Americans and Hispanics (11% v. 8%) and higher proportion of women with BMI≥30 who developed an invasive recurrence (78% v. 50%). All recurrences in the pure DCIS cohort were detected by routine screening surveillance, with a majority detected by mammography (89%). Conclusions: Within a relatively short follow up period, we found that the rates of in-breast recurrences were the same in women with pure DCIS compared to women with invasive breast cancer. Also, 44% of women developed invasive breast cancer recurrence after an initial DCIS diagnosis, potentially altering their long term survival. These findings suggest that women with all breast cancers, including DCIS, requires intensive surveillance after initial treatment, as consequences of delayed diagnosis may impact on their long term survival.

P70

A Comparison of the Pathologic Response Rate After Neoadjuvant Chemoradiation in Patients with Locally Advanced Breast Cancer in an Underserved Population A. Keshinro,[1]* N. Huppert,[1] S. Dhage,[1] S. Formenti,[2] K. Joseph.[1] *1. Surgery, Bellevue Medical Center, NYU Langone Medical Center, New York, NY; 2. Cornell Medical Center, New York, NY.*

Introduction: The conventional approach to a locally advanced breast cancer (LABC) consists of neoadjuvant chemotherapy to induce a tumor response, which improves patient outcome, followed by surgery. At our institution, recent advancement using neoadjuvant combined chemotherapy and radiation has been shown to be promising. We report the pathologic response, based on the tumor profiles, in LABC patients after receiving the appropriate neoadjuvant chemoradiation treatment at a NYC public hospital. Methods: Women with stage 2B-3C breast cancer were enrolled into 1 of 2 IRB-approved prospective trials, from 2005 to 2014. The HER2-positive LABC patients were treated with biweekly paclitaxel (30mg/m^2) and weekly trastuzumab (2mg/m^2) for 10weeks. HER2-negative LABC patients were treated with weekly paclitaxel (30mg/m^2) for 12 weeks. Concurrent daily radiation (1.8 Gy per fraction to a total dose of 45 Gy with a tumor boost of 14 Gy at 2 Gy/fraction) was administered to the breast, axillary, and supraclavicular lymph nodes for 6 weeks in both groups. Surgery was performed within 8 weeks of completing chemoradiation and pathological complete response (pCR) was defined as the absence of invasive cancer in breast and lymph nodes and pathological partial response (pPR) as the persistence of <10 microscopic foci of invasive carcinoma in breast or lymph nodes. Results: The mean age of HER2-positive was 48years (range 28-62) and HER2-negative LABC was 47years (range 28-73). Race distribution was as follows: 36% Asian, 30% Black, 20% Hispanic and 14% White. pCR was significantly higher in the HER2-positive patients (47%) compared to the HER2-negative patients (19%). There was no significant difference in the pathological response (pCR and pPR) between the triple negative and hormone receptor positive subsets. Conclusions: The most significant pathological complete response is in the HER2-positive LABC. In the HER2-negative patients, the pathological response is independent of the hormone receptors profile. This is an important treatment option for a population that often presents with advanced and aggressive breast cancer.

Pathologic response rate based on tumor profiles in LABC patients.

	Her2-positive	HR positive	TN	
Pathologic Response	n=17	n=12	n=15	p-value
pCR+pPR	15 (88%)	7 (58%)	13 (87%)	0.257
pCR	8 (47%)	1 (8%)	4 (27%)	0.043
pPR	7 (41%)	6 (50%)	9 (60%)	0.115

HR- Hormone Receptor. TN- Triple Negative. pCR-pathological complete response. pPR- pathological partial response.

P71

Preoperative Axillary Imaging Compared to Sentinel Lymph Node Biopsy Results B.B. Scott,* J.L. Crawford, E.G. McCarthy, C.L. Devin, T. Kaufman, M. Lazar, A. Berger, E. Hsu, T. Tsangaris. *Thomas Jefferson University Hospitals, Philadelphia, PA.*

Introduction: Axillary lymph node status provides critical staging data for breast cancer patients. Axillary ultrasound (AUS) has become a standard pre-operative test to detect malignant nodes and axillary MRI (AMRI) has been shown to have high sensitivity and specificity in studies with limited numbers of patients. The aim of this study was to compare the predictive value of pre-operative AUS and AMRI to sentinel lymph node biopsy (SLNB) results to gauge the possibility of obviating the need for SLNB. Methods: We performed a retrospective review under IRB protocol of all patients who underwent AUS and/or AMRI followed by SLNB of the axilla from Jan. 1, 2013 until July 1, 2015 at a major academic hospital. A total of 626 patients were reviewed. Of these, 276 patients were included in our evaluation. Patients were eliminated based on neoadjuvant chemotherapy, missing data, and previous cancer treated with chemotherapy, radiation, or both. 37 patients received AMRI and 239 received AUS. Pre-operative imaging results were compared to SLNB pathology. Fisher's exact test was used to determine statistical significance. Results: AUS demonstrated less sensitivity (41.5%, p=0002, when compared to SLNB results) at our institution than in previously reported studies, independent of size of tumor. Specificity was 83.4%, consistent with previously reported values. AMRI of tumors smaller than 20 mm was 100% sensitive and 88.2% specific (p=0.0008), however sample size for this group was small (N=22). Positive and negative predictive values for AUS were 42.3% and 83.4% (p=0.0002) while AMRI was 66.7% and 80.0% (p=0.0097) respectively. Conclusions: AUS demonstrated less sensitivity and equivalent specificity at our institution as compared to literature values. While AUS is inexpensive and minimally invasive, these results call into question the efficacy of it prior to SLNB. Although controversial, AMRI showed superior sensitivity and specificity at our institution. In light of these results, we are planning a trial comparing SLNB vs. AMRI alone.

P72

Single Institution Experience of Local Recurrence and Toxicity Following a 2-Day Course of Accelerated Partial Breast Irradiation

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Introduction: Accelerated Partial Breast Irradiation (APBI) has attracted considerable interest due to its shortened course. While intra-operative radiation therapy condenses treatment time to one day, results from the seminal trials have demonstrated inferior outcomes compared to traditional whole breast irradiation. We sought to determine if catheter-based APBI could safely be compressed from ten fractions over five days into a convenient two-day schedule. Methods: We initiated a prospective, multi-institutional phase II trial that sequentially treated three cohorts of women (each n = 30) with three different, progressively hypofractionated radiation schedules, all delivered over two days using a multi-lumen brachytherapy applicator. The first cohort received 7 Gy x 4 fractions and was observed for toxicities for six months. In the absence of predefined toxicities, we progressed to the second cohort, treated with an 8.25 Gy x 3 fractions schedule. The final cohort of patients was to be treated with a two-fraction schedule, but was not enrolled due to sponsor withdrawal and termination of the study. We retrospectively reviewed patient charts to evaluate outcomes after an ultra-short course of APBI. Results: A total of 22/60 women prospectively enrolled to this trial were from our institution. Nine women were treated on the four-fraction schedule and thirteen were treated with three fractions. The median patient age was 64.9 years and median tumor size was 0.8 cm. Median follow up was 31 months. There were no local failures. All cosmetic outcomes were excellent. There were a total of ten grade I toxicities, including seromas, fibrosis and fat necrosis, and three grade II toxicities, a symptomatic seroma, mastitis and wound dehiscence. There was only one reported grade III toxicity, a wound dehiscence requiring operative debridement. Conclusions: In our cohort of 22 women we found that an ultra-short course of image-guided, catheter-based brachytherapy was well tolerated. There was only one grade III toxicity and no local recurrences within our follow up. To our knowledge, this is the first report of a three-fraction schedule of APBI.

Radiation toxicities by grade and by hypofractionation schedule

		Cohort 1 (n=9)	Cohort 2 (n=13)	Totals
Toxicity		7 Gy x 4 fractions	8.25 Gy x 3 fractions	
Grade I	Seroma	2	2	4
	Fibrosis	2	3	5
	Fat Necrosis	1	0	1
Grade II	Seroma	1	0	1
	Mastitis	0	1	1
	Wound Dehiscence	0	1	1
Grade III	Wound Dehiscence	0	1	1
Totals		6	8	14

P73

Relationship Between BMI and Breast Cancer Subtype V. Gershuni,* Y. Li, E. Carrigan, L. Steel, V. Ro, T. Albright, J. Tchou. *Surgery, University of Pennsylvania, Philadelphia, PA.*

Obesity is correlated with insulin resistance and chronic low-grade inflammation that has been linked to various disease states including cancer. We hypothesize that obesity is associated with a carcinogenic metabolic milieu that leads to increased incidence of unfavorable breast cancer (BC) subtypes. Many studies have focused on increased estrogen production from adipocyte aromatase expression and the proliferation of ER+ BC, but few have been able to clearly show a link between obesity and risk of more aggressive BC based on receptor subtype. Deregulated energy balance and insulin resistance associated with obesity negatively impacts growth factor signaling and inflammatory processes. Increased central obesity may promote BC via hyperinsulinemic insulin resistance, secretion of pro-angiogenic adipokines, and chronic low-grade inflammation. Using a single-institution, retrospective chart review of over 1500 women who underwent surgery between 1995 and 2015, we evaluated the association between obesity and BC subtype. Receptor status was used as a surrogate for common BC subtypes: hormone receptor (ER+/PR+), Her 2+, and triple negative. Women were stratified based on BMI at time of diagnosis: healthy (BMI 18-24.9), overweight (BMI 25- 29.9), obese (BMI>30). Potential confounding covariates including age, race and comorbidities such as diabetes were included in multivariate analysis. Our initial analysis of patients (n=343) demonstrated a statistically significant inverse correlation between overweight/obesity and Her2+ (p=0.01). Preliminary survival analysis revealed worse outcomes among overweight patients with Her2+ disease. Women over 50 (p=0.02) and African Americans (p<0.001) were more likely to be overweight or obese. Further analysis is planned to expand our pilot cohort to evaluate the impact of other covariates—which are not commonly available in national databases but are available in our electronic medical record—on the relationship between obesity, metabolic markers, tumor subtype, and clinical outcomes. The ultimate goal is to clarify the relationship between obesity and BC pathogenesis so that prevention strategies can be developed to interrupt the obesity-carcinogenesis link.

P74

Survival Risk in Breast Cancer Related to Delays in Surgical Care

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Introduction: There is no population data evaluating time to therapies and differences in survival. We performed a preliminary analysis using a large national database to evaluate differences in 5-year mortality in groups experiencing different time delays from diagnosis of breast cancer to first surgical intervention. Our hypothesis was that mortality would be significantly affected by delays in surgical therapy. Methods: Using data from the National Cancer Data Base Participant User File, female Breast Cancer cases were identified. 2,782,807 individual cases were divided into groups based on time to surgery: 0-30 days (Group 1), 31-60 days (Group 2), 61-90 days (Group 3), and 91+ days (Group 4). Age, rural living, NCDB analytic stage grouping, and Charleston/Deyo comorbidity scores were examined. The 5-year mortality was determined by group. Separate analyses were also performed excluding stages 3 and 4. Results: The data demonstrates significant differences in baseline characteristics analyzed among the 4 groups and in 5-year mortality (Table 1). When only stages 0, 1, and 2 were considered, 5-year mortality was 9% for Group 1, 7% for Group 2, 8% for Group 3, and 11% for Group 4 (p<0.0001). Conclusion: This is a large data set that demonstrates several differences between groups of women diagnosed with breast cancer with respect to delays to first surgical intervention both in baseline characteristics and 5-year mortality. The 5-year mortality doubles at greater than 90 days, however between 0-90 days there may be no clinical risk to advanced pre-operative imaging studies. We also witnessed a similar trend in mortality when excluding Stages 3 and 4 to limit confounding from patients undergoing neoadjuvant chemotherapy. Further evaluation is being conducted to determine risk factors for delay in surgical treatment in this population and to determine how mortality may be affected. Similar analyses are necessary regarding delays in all treatment modalities include chemotherapy, radiation therapy, and definitive surgical treatment.

Patient Characteristics and 5-year mortality

Variables	Overall Sample n=2782807	Group 1 (0-30 d) n=1632562	Group 2 (31-60 d) n=531736	Group 3 (61-90 d) n=116310	Group 4 (>91 d) n=502199	p-value
Age Median (IQR)	60 (50-71)	61 (50-71)	61 (51-71)	60 (50-70)	58 (49-70)	0.0001
Rural Living	1.72%	1.86%	1.40%	1.21%	1.71%	<0.0001
Charleston/Deyo Mean (SD) Median	.16 (.43) 0	16 (.42) 0	.17 (.44) 0	.19 (.46) 0	.16 (.45) 0	0.0001
Stage 0	19.18%	20.49%	20.51%	24.32%	12.31%	<0.0001
Stage 1	38.84%	41.72%	44.97%	39.05%	23.92%	<0.0001
Stage 2	26.23%	26.77%	25.92%	24.49%	25.18%	<0.0001
Stage 3	8.10%	6.63%	6.32%	8.14%	14.72%	<0.0001
Stage 4	3.57%	1.34%	0.73%	1.15%	14.37%	<0.0001
5 Year Mortality for all stages within each group	12.92	11.11	8.50	10.23	24.13	<0.0001

P75

Local Recurrence After Mastectomy for Breast Cancer in the Current Era: Which Subgroups are Still at Risk?

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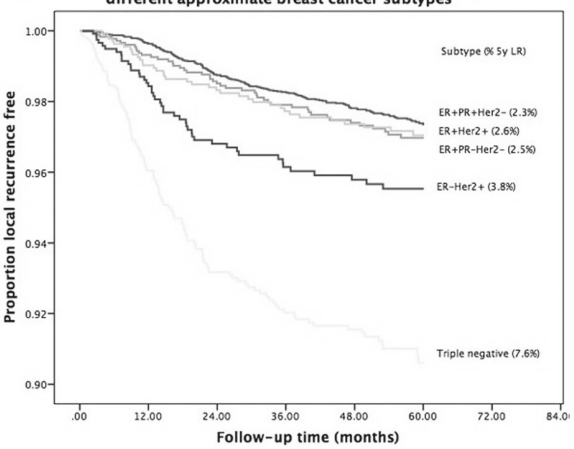
Introduction. Although the incidence of local recurrence (LR) after mastectomy has decreased over the past decade, preventing LR is still a major

goal of locoregional treatment. The indication for post-mastectomy chest wall irradiation is based on presence of certain risk factors. However, emphasis has recently shifted from traditional risk factors to biologic subtypes of breast cancer. This study aims to determine the risk of LR after mastectomy for different approximate subtypes in the current era. Methods. From the National Cancer Registry, all new invasive epithelial breast cancers (M0) diagnosed between 2005-2008 treated with mastectomy were analyzed. Kaplan-Meier analysis was performed to determine risk of LR in different subtypes. Cox regression was used to determine predictors for LR as a first event. Results. From 2005-2008, 22336 breast cancers were treated with mastectomy, of which 5-year follow-up was available for 15382 (69%). Overall, LR was the first event in 477 (3.1%). Risk of LR was significantly different between approximate subtypes (p<0.001): 2.3% in ER+PR+Her2-, 2.5% in ER+PR-Her2-, 2.6% in ER+ Her2+, 3.8% in Er-Her2+ and 7.6% in triple negative tumors (Kaplan-Meier plot in Figure). HER2 positive tumors treated with trastuzumab had fewer LRs (2.6% versus 4.3%, p 0.018) than tumors treated without trastuzumab, as well as ER+ tumors treated with endocrine therapy (1.9% vs 3.4%, p <0.001) compared to no endocrine therapy. Overall, the strongest risk factors on multivariable Cox regression (including radiotherapy as a variable) were T4 tumor (Hazard Ratio 5.342 [95%CI 3.093-9.225], p <0.001), no endocrine therapy (HR 3.224 [2.539-4.094], p<0.001), and >4 positive lymph nodes (HR 2.455 [1.697-3.551], p<0.001). The risk factors varied for the approximate subtypes. Conclusion. In the current era, particularly triple negative tumors are at risk for LR as a first event within 5 years after mastectomy. Trastuzumab and endocrine therapy are associated with a significant reduction of LRs. LR risk assessment, for instance for the indication for radiation therapy, should be based on specific subtype rather than the general breast cancer population.

Figure 1. Kaplan-Meier plot of 5-year local recurrence as a first event in different approximate breast cancer subtypes



No. at risk (months)	0	12	24	36	48
ER+PR+Her2-	7296	6954	6523	6055	5478
ER+PR-Her2-	1822	1669	1537	1399	1252
ER+Her2+	1364	1295	1205	1115	1038
ER-Her2+	1198	1079	936	841	779
Triple negative	1596	1319	1120	997	905

Subtype unknown for 13.7%

P76

Implementation of the Distress Thermometer Among Surgical Breast Cancer Patients at a Comprehensive Breast Center

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Introduction: The Distress Thermometer (DT) is a validated self-assessment tool that enables patients with cancer to convey the source and severity of distress. The objective of this study is to understand the baseline clinical and patient related factors influencing distress scores among newly diagnosed surgical breast cancer patients at a comprehensive breast center. Methods: Patients at Duke University Cancer Center with a new breast cancer diagnosis from July 1, 2013 to March 31, 2015 were included in the study. The cohort was divided into two groups: low distress (DT score ≤ 3) and higher distress (DT ≥ 4). Descriptive statistics were tabulated as frequencies. Univariate analysis was conducted with Chi-Squared, Mann-Whitney, ANOVA, student T-test and Kruskal Wallis. Tests were 2-sided and a p value of <.05 was considered statistically significant. Analyses were conducted in STATA. Results: 466 patients fulfilled inclusion criteria. Average age of the cohort was 60.3 (95% CI 59.0, 61.5). The mean distress score was 4.1 (95% CI 4.3, 4.8). 58% of subjects in the study had a distress score ≥ 4. Low and higher DT groups did not differ by race, marital status, employment, clinical stage or comorbidities. Patients with higher DT were younger (p = 0.0049) and reported a history of a mood disorder (p=0.002). Prevalent sources of distress were emotional problems (worry 56%, sadness 35%, nervousness 54%) and physical complaints (pain 42%, sleep 45%, fatigue 47%). Family (p= 0.001), emotional (p= 0.0001), and physical problems (p=0.001) differed between patients with low DT compared to patients with higher DT. Conclusion: The majority of patients presenting for surgical consultation for breast cancer report elevated levels of distress attributable to both emotional and physical concerns. Younger age and a prior history of a mood disorder increased the likelihood of an elevated distress score. This study underscores the feasibility and potential value of a systematic collection of patient reported outcomes in identifying those patients at greatest need for additional support during their cancer.

P77

The Utility of Screening MRI for Women Diagnosed with Atypical Breast Lesions

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Introduction: The role of screening MRI in women with atypical ductal and lobular hyperplasia (ADH and ALH) and lobular carcinoma in situ (LCIS) is controversial. Our objective was to evaluate the potential utility of this screening modality for these conditions. Methods: A retrospective review of women diagnosed with ADH, ALH, or LCIS who underwent a subsequent breast MRI from 2007-2012 at three institutions within one healthcare system was performed. Exclusion criteria included: prior diagnosis of invasive breast cancer or ductal carcinoma in situ (DCIS), BRCA mutation, or a history of mantle radiation. Patient characteristics, pathology, and follow-up were determined by chart review. Results: Among the atypia cohort of 3090 women, we identified 540 who underwent subsequent MRI. Median age at atypia diagnosis was 49 years (range 26-83). Median follow-up was 3.9 years (range 0-17.9). Diagnoses included: 34% ADH, 22% ALH, 32% LCIS, and 12% severe ADH (or borderline DCIS). There were 1484 MRIs performed, and the median interval between atypia diagnosis and MRI was 3.3 years (range 0-18). 82% (1221 of 1484) were performed for routine screening or short follow-up of prior routine screening, which constituted our main cohort. Of those subsequently diagnosed with breast cancer, 30 patients had had an MRI within the prior 6 months; of the 30 MRIs, 15 were performed for routine screening purposes. Of the routine screening MRIs, the initial atypia included: 1 ADH, 5 ALH, and 9 LCIS (no severe ADH). The final cancer diagnoses included: 8 DCIS, 2 IDC, 3 ILC, and 2 other invasive cancers. Thus, 15 of 540 patients with atypia and MRI screening had an MRI-detected cancer (2.8%), and a total of 15 of 1221 screening MRIs detected cancer (1.2%) Conclusion: Women with atypical breast lesions are at a markedly increased risk for developing breast cancer and should be followed closely. Additional screening with MRI has the potential to detect mammographically occult breast cancer in 2.8% of this high-risk group of patients. Future studies may further delineate additional risk factors that would increase the yield of screening MRIs.

P78

Trends in Sexual Function After Breast Cancer (BrCa) Surgery

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Background: Sexual dysfunction is assumed to be common but understudied in BrCa patients. Existing studies lack data on baseline function, antiestrogen therapy, and surgery making it difficult to quantify the influence of BrCa treatment. Herein, we use the validated Female Sexual Functioning Index (FSFI) to evaluate changes in female sexual function after BrCa surgery. Methods: The FSFI assesses sexual function in 6 domains (desire, arousal, lubrication, orgasm, satisfaction, pain) on a 36-point scale with scores >26.6 indicating better sexual function. We identified 226 women with unilateral BrCa undergoing surgery at our institution from 6/2010-1/2015. All completed

the FSFI preoperatively and at a median of 13mos (range 5-48) postoperatively to assess sexual function. We quantified declines in FSFI scores and considered P values <0.05 as statistically significant. Results: Overall, 119 women had breast conserving surgery (BCS), 40 had unilateral mastectomy (UM), and 67 UM+contralateral prophylactic mastectomy (CPM). Women having BCS and UM were older than UM+CPM (60 vs 48yo, p= <0.001); BCS had lower stage tumors (p=0.014) and lower rates of systemic therapy (p=0.001). No difference existed in percent of married women or rates of any antiestrogen therapy among cohorts but more UM+CPM had reconstruction than UM (88% vs 77%, p=0.038). At baseline, all women had similar FSFI evidence of sexual dysfunction (medians: BCS 26.3, UM 25.2, UM+CPM 23.7; P=0.23). At follow up, sexual function had declined significantly in BCS (23.5, p<0.001) and UM (17.4, p=0.010) but was unchanged in UM+CPM (22.8, p=0.74) women. Interestingly, overall all women maintained their desire for sex (p=0.17). BCS and UM women demonstrated significant declines in all other subscale domains (all p<0.045) while UM+CPM women demonstrated no decline in any subscale domain at follow up but did not exhibit superior sexual function to those having BCS (22.8 vs 23.5, p=0.21). Conclusions: Baseline sexual dysfunction exists in women diagnosed with BrCa . Treatment negatively impacts sexual function. Women having UM have the greatest decline in sexual function. UM+CPM women do not exhibit better sexual function over those having BCS.

P79

Does the Addition of Pertuzumab to Neoadjuvant Treatment for HER2 Positive Patients Result in Increased Nodal Down-staging or Eligibility for Breast Conservation? L. Petersen,[1]* K. Friend,[2] J. Bensenhaver,[1] A. Chang,[1] J.S. Jeruss,[1] L. Newman,[1] M. Sabel.[1] *1. Surgery, University of Michigan, Ann Arbor, MI; 2. Einstein Healthcare Network, Philadelphia, PA.*

BACKGROUND: Dual agent anti-Her-2 neoadjuvant chemotherapy (NAC) has shown improved pathological complete response (pCR) rates. Pertuzamab was approved in September 2013 for use in the neoadjuvant setting. We hypothesized that dual agent NAC for Her-2 positive patients resulted in increased rates of nodal down-staging and increased eligibility for breast conservation. METHODS: Her-2 positive patients that received NAC were identified in an IRB approved database. Patients presenting with abnormal appearing nodes on ultrasound underwent fine needle aspiration (FNA). Patients with a negative axillary ultrasound or FNA underwent sentinel lymph node biopsy (SLNB). Patients with no axillary disease at SLNB had no further axillary surgery after completion of NAC, while those patients with documented axillary disease prior to NAC underwent axillary lymph node dissection (ALND). Statistical analyses of data were performed (www.graphpad.com). RESULTS: 118 Her-2 positive patients received NAC from 2000-2015. The mean patient age was 46 years and mean tumor size was 3.9 cm. 30 of 118 patients (25%) had node-negative disease prior to NAC, while 88/118 (75%) had node-positive disease. 96% (113/118) of patients received anti-Her-2 therapy; 79/113 received trastuzumab without pertuzumab and 34/113 received both trastuzumab and pertuzumab (34/113). Prior to NAC, 27% of the patients in the trastuzumab group were eligible for breast conserving therapy (BCT) vs 50% of the dual-therapy group (p=.02). Compared with trastuzumab alone, following NAC with trastuzumab and pertuzumab, there were increased rates of pCR (68% vs 48%), nodal down-staging (44% vs 39%) and BCT (32% vs 27%), although these failed to reach statistical significance. CONCLUSIONS: Based on the approval of pertuzumab in the neoadjuvant setting, we witnessed an increased use of NAC in patients eligible for BCT at the time of diagnosis. The addition of pertuzumab to NAC for Her-2 positive patients resulted in improved down-staging of both the primary tumor and regional nodes and had an impact on surgical decision making.

Comparison of patients receiving neoadjuvant anti-Her-2 treatment with trastuzumab alone vs trastuzumab and pertuzumab

Patient demographics and outcomes	Trastuzumab (n=79)	Trastuzumab and pertuzumab (n=34)	p value
Age < 40 years old	19/79 (24%)	11/34 (32%)	0.36
White	64/79 (81%)	28/34 (82%)	1
Black	10/79 (13%)	3/34 (9%)	0.75
Tumor < 2 cm	13/77 (17%)	6/34 (18%)	1
Tumor > 2 cm	64/77 (83%)	28/34 (82%)	1
Inflammatory	18/79 (23%)	6/34 (18%)	0.62
Eligible for BCT* prior to NAC**	21/79 (27%)	17/34 (50%)	0.02
New patients eligible for BCT* after NAC**	25/58 (43%)	4/17 (24%)	0.17
Patients that underwent mastectomy	58/79 (73%)	23/34 (68%)	0.65
Underwent bilateral mastectomy	21/79 (27%)	12/34 (35%)	0.37
Patients with pCR***	38/79 (48%)	23/34 (68%)	0.07
Patients with nodal down-staging	31/79 (39%)	15/34 (44%)	0.68

*breast conserving therapy, **neoadjuvant chemotherapy, ***pathologic complete response

P80

Oncoplastic Breast Surgery: Three Years Experience at National Cancer Institute Mexico City R. Vazquez Romo,* J. Bargalló Rocha, S. Villarreal Colín, C. Robles Vidal, J. Corona Rivera, R. Shaw Dulin, A. Herrera Gómez, H. Martínez Said. *Instituto Nacional de Cancerología, Mexico, Distrito Federal, Mexico.*

Background: Oncoplastic breast surgery represent a major advance in breast surgery. It combines the surgical oncological principles with plastic surgery techniques. The goal is the complete excision of the cancer with free margins while maintaining or improving cosmesis. We analyzed the outcomes in oncoplastic breast surgery regarding margin status, immediate complications and easthetics results. Methods: We conducted a retrospective cohort study of 146 patients treated with oncoplastic breast surgery at National Cancer Institute, Mexico, from April 2012 to April 2015. Clinical data of patients, tumor and surgical treatment were included in the analysis. Results: 146 cases were included. Mean patients age was 51.62 years (range 18-78), mean follow up period was 22 months. The mean tumor size was 25.88 mm. Eleven (7.5%) cases were carcionoma In situ, 31(24.7%) were clinical stage (CE) I, 79 (51.4%) and 15(10.3%) were CE II and III respectively and five were benign disease. The oncoplastic techniques used were: lateral mammoplasty 52 (35.6%), peri-areolar mammoplasty 33 (22.6%), Inferior pedicle mammoplasty 23 (15.8%) superior pedicle mammoplasty 14 (9.6%), omegaplasty 18(12.3%) and Grissoti 6 (4.1%). Drainages were no necessary in 105(72%) cases. Of 41 drainages placed 22 (15%) were unilateral and 19 (13%) bilateral. Sixteen (12.3%) patients had an immediate surgical complication. Cosmesis was excellent in 45 (30.8%) good in 50 (34.3%), regular in 18 (12.3%), no specified in 31 (21.2%) and bad in two (1.4%) cases. The rate of positive margins was 22 (15.5%), five of them (3.5%) required a completion mastectomy to achieve free margins. Univariate analysis showed that tumor size; clinical stage, and surgery type were no predictors for positive margin status. Conclusions: Oncoplastic breast surgery results in a low positive margins rate with a low rate of postoperative complications and provides appropriate aesthetic outcomes.

P81

Patient Experience with Breast Reconstruction Following Bilateral Mastectomy in BRCA Mutation Carriers S. Nurudeen,[2]* Y. Chun,[2] H. Guo,[3] W. Barry,[3] S.B. Coopey,[4] J.E. Garber,[3] L.S. Dominici.[1] *1. Surgical Oncology, Dana Farber/Brigham and Women's Cancer Center, Boston, MA; 2. Brigham and Women's Hospital, Boston, MA; 3. Dana Farber Cancer Institute, Boston, MA; 4. Massachusetts General Hospital, Boston, MA.*

Introduction: Increased use of genetic screening has led to growing numbers of patients (pts) identified with BRCA mutations who may consider bilateral mastectomy (BM) for risk-reduction. Reconstruction (recon) choices following BM are often made without complete data informing many aspects of the process. This is likely due to limited data available to inform patient experience. One important issue is the likelihood of further unexpected surgeries following the initial recon. This study seeks to further understand factors associated with unforeseen procedures and prolonged time to completion of recon following BM in BRCA positive pts. Methods: A total of 180 BRCA positive pts who underwent BM with recon from 1997 to 2013 were evaluated retrospectively.

A cox proportional hazard model was used to determine factors associated with time to recon completion. Univariate and multivariate logistic regression was used to assess factors associated with unexpected procedures. Results: Twenty four percent of pts (n=44) underwent a form of autologous recon, while 76% (n=136) underwent implant-based recon. Median time to completion of recon was 0.7 years (95% CI: 0.6-0.9). Pts with non-nipple-sparing mastectomy (HR 0.69, 95% CI 0.37-0.96), tissue expander use (HR 0.63, 95% CI 0.46-0.88), and autologous recon (HR 0.62, 95% CI (0.42-0.92) were less likely to complete recon. Fifty eight percent of pts underwent an unexpected procedure. Unexpected procedures were associated with patient age and type of recon. With an additional 10 years of age, the odds of having an unexpected procedure increased by 77% (OR: 1.77, 95% CI 1.19-2.62, p=0.005) Pts with autologous recon were 2.7 times (95% CI: 1.08-6.74; p=0.03) more likely to have an unexpected procedure. Conclusions: Decisions related to recon following BM in BRCA positive pts are complex and may be made without complete data on surgical issues in favor of anticipated cosmesis. This study demonstrates predictive factors that may prolong time to recon completion and likelihood of unexpected procedures. Patient–centered decision making should be a focus of further studies assessing outcomes following breast recon.

Unexpected Procedures by Reconstruction Type*

	Implant-Based (n=136)	Autologous/Combination (n=44)
	n (%)	n (%)
Unexpected Revisions		
Revision of Nipple-Areolar complex **	36 (26.4%)	27 (61.4%)
Implant Exchange **	59 (43.4%)	8 (18.2%)
Fat grafting/Liposuction	14 (10.3%)	16 (36.4%)
Scar Revision	25 (18.4%)	28 63.6%)
Conversion to Flap	1 (0.7%)	1 (2.3%)
Capsulotomy	3 (2.2%)	0 (0.0%)
Other	1 (0.7%)	1 (2.3%)

*Individual patients were found to have more than one unexpected procedure so total percentage will not equal 100
**Expected initial implant exchange or nipple-areolar complex reconstruction were not included

P82

Body Mass Index, Pathologic Complete Response, and Circulating Tumor Cells After Neoadjuvant Chemotherapy for Breast Cancer O.M. Fayanju,[1]* C. Hall,[2] J. Bauldry,[2] M. Karhade,[2] L. Valad,[2] H.M. Kuerer,[1] S.M. DeSnyder,[1] C.H. Barcenas,[3] A. Lucci.[2] *1. Department of Breast Surgical Oncology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX; 2. Department of Surgical Oncology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX; 3. Department of Breast Medical Oncology, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX.*

INTRODUCTION: Pathologic complete response (pCR) after neoadjuvant chemotherapy (NACT) is an important prognosticator in the management of breast cancer. But as rates of obesity increase in the United States, it is unclear if body mass index (BMI) affects the likelihood of achieving pCR. We describe an analysis of the relationship between BMI at diagnosis and pCR (absence of invasive disease post-NACT) in operable breast cancer patients with known levels of circulating tumor cells (CTCs), another important predictor of breast cancer prognosis. METHODS: Study participants were Stage I-III breast cancer patients diagnosed from 3/2005 to 3/2015 who received NACT as part of a prospective trial on CTCs and whose postoperative pathologic review definitively described pCR. Clinical characteristics potentially associated with pCR including BMI, age, race, tumor size/biomarkers, menopausal status, anthracycline/taxane type, axillary nodal status, and the presence of inflammatory breast cancer or lymphovascular invasion (LVI) were examined with χ^2 tests and logistic regression, as were the relationships between BMI, pCR, and CTCs. We report proportions, adjusted odds ratios (OR), and 95% confidence intervals (CI) significant at 2-tailed $p<0.05$. RESULTS: Of 113 patients, 34 (30%) had pCR; 50 (44%) were obese (BMI≥30), and 91 (81%) had CTC values. There was no difference between obese and non-obese (BMI<30) patients' pCR rates (32% [16/50] vs. 29% [18/63], p=0.69) or CTC levels (39% [11/28] vs. 43% [27/63], p=0.75). There was no association between BMI and pCR (OR 1.21, CI 0.5-2.96, p=0.67) or CTCs and pCR (OR 1.3, CI 0.5-3.33, p=0.59) in bivariate analysis. Higher BMI was not associated with pCR in multivariate analysis (OR 0.82, CI 0.22-3.02, p=0.77) but axillary disease (OR 0.15, CI 0.03-0.72, p=0.02), LVI (OR 0.12, CI 0.02-0.56, p=0.01), and HER2/neu non-amplification (OR 0.33, CI 0.13-0.84, p=0.02) were associated with lower likelihood of pCR. CONCLUSION: BMI does not appear to have a significant impact on pCR attainment or CTC levels after NACT, but the significance of both prognosticators in obese patients warrants further investigation.

P83

National Practice Patterns Among Women with Stage IV Breast Cancer Undergoing Surgery at the Primary Site W.O. Lane,* K. Houck, E.S. Hwang, R. Greenup. *Duke University School of Medicine Department of Surgery, Durham, NC.*

BACKGROUND: Standard of care for primary tumor resection among women with stage IV breast cancer is evolving. Retrospective data suggesting a survival benefit has been criticized due to both selection and observational biases; however, up to 50% of women with stage IV disease undergo surgical resection. In this study, we sought to determine contemporary national practice patterns of surgery among women with stage IV breast cancer in light of pending results from the randomized ECOG 2108 trial. METHODS: Using the ACS NCDB, stage IV breast cancer patients with an intact primary were identified from 2003-2012. Inclusion was limited to those who received systemic therapy prior to surgery to exclude those diagnosed with metastases following resection. Subjects were classified by timing of surgery from diagnosis: < 6months, 6-10months, and >10months. The 6-10month timeframe was chosen to approximate the time interval to surgical resection in the ECOG 2108 trial. Baseline clinicopathologic variables were compared between groups. RESULTS: In total, 8,242 subjects were identified. The majority were white (78%), had private insurance (57%), low comorbidity index (87%), and received care at an academic or comprehensive care center (88%). The majority underwent modified radical mastectomy (52.1%). The clinicopathologic features were similar between timing groups. The majority underwent surgery >6 (46%) or 6-10 months (43%) from time of diagnosis. During the study period, the number of stage IV patients undergoing surgery doubled; however, those undergoing surgery <6 months dropped from 55% to 43% of resections per year while the proportion undergoing surgery 6-10 months from diagnosis increased from 35% to 48% ($p<0.0001$). CONCLUSIONS: The number of women with stage IV cancer undergoing primary site resection increased from 2003-2013, with the greatest increase among women undergoing surgery 6-10 months from diagnosis. This likely corresponds to patients who are resected following a full course of chemotherapy and therefore parallels the ECOG 2108 inclusion criteria. Further analysis will determine whether the timing of surgery impacts breast cancer outcomes.

P84

Clinical, Radiologic and Pathologic Findings After Use of Spiral 3-Dimensional Bioabsorbable Lumpectomy Marker C.S. Kaufman,[1]* W.H. Hall,[2] V.S. Behrndt,[3] G.M. Wolgamot,[4] L.M. Hill,[5] R. Caro,[6] S. Nix,[6] E. Evans,[6] K. Zacharias,[6] N. Schnell.[6] *1. Surgery, University of Washington, Bellingham, WA; 2. Northwest Radiation Oncology Associates, Bellingham, WA; 3. Northwest Radiologists, Bellingham, WA; 4. Northwest Pathologists, Bellingham, WA; 5. Bellingham Regional Breast Center, Bellingham, WA; 6. Bellingham Ambulatory Surgery Center, Bellingham, WA.*

Introduction: A novel bioabsorbable three-dimensional tissue marker has been utilized to aid in targeting radiation therapy to the breast cancer lumpectomy site. Over 1,000 patients across the country have had markers placed and a national registry trial is underway. The goals are: 1) to aid radiation treatment by marking the margins closest to the excised tumor site; 2) to avoid radiation targeting of inadvertent seroma from oncoplastic surgery; 3) to orient for re-excision; and 4) to provide a 3-D structure that allows fibrosis to add volume that may contribute to cosmesis. With widespread use of this new device and its gradual absorption, it is pertinent to document the long term clinical, imaging and pathologic findings so clinicians with varied experience may know what to expect. Methods: Consecutive lumpectomy patients who were candidates for targeted radiation therapy were implanted with the 3-D bioabsorbable marker from May 2014 to September 2015. After informed consent, each of 38 patient's charts were reviewed to gather clinical, imaging and pathologic findings. Routine imaging with mammography and ultrasound were obtained at 6 and 12 months post lumpectomy. Patients requiring re-excision were examined for pathologic findings related to the device. Results: Clinically the lumpectomy site was firm/dense in 94% of patients at 3 months

(n = 34), but in only 57% at one year (n = 14). Two patients had removal at one month and at 12 months for reasons unrelated to the tissue marker. Histologic examination demonstrated typical foreign body reaction and organization without remarkable changes due to tissue marker. Six month images show maintenance of the unique array of clips of the device while at one year, mammograms demonstrate that half the patients had clips coalescing as the tissue marker dissolves while maintaining the volume of the cavity. Cosmetic outcome has been good to excellent measured at 6 and 12 months. Conclusion: The natural history of the clinical, imaging and pathologic aspects of a novel radiation therapy tissue marker is described. This is valuable new information for surgeons to properly inform and follow these patients over time.

P85

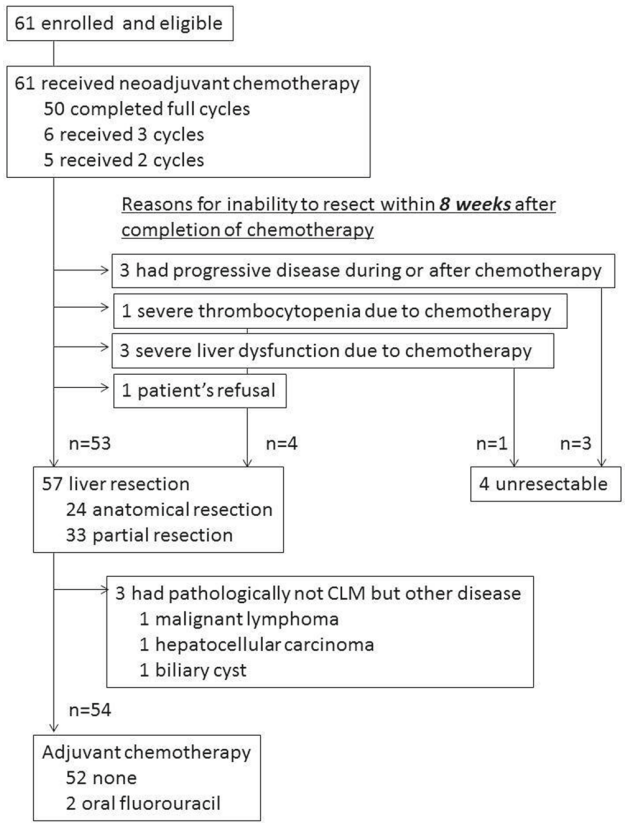
How Fast Can the Immune Response Eliminate Murine Cancer Cells from a Different Background? E. Katsuta, S. DeMasi, K.P. Terracina, H. Aoki, M. Aoki, P. Mukhopadhyay, S. Spiegel, K. Takabe.* *Surgical Oncology, Virginia Commonwealth University, Richmond, VA.*

INTRODUCTION: This study aimed to establish an improved breast cancer orthotopic model. Utilizing this new model, we investigated the growth of tumor after implantation of murine cancer cell derived from different strain mice. METHODS: Different amount of matrigel were injected into mice mammary glands. Three weeks after inoculation, tumorigenesis were compared between various number of murine breast cancer E0771 cells in Matrigel. $1x10^4$ of 4T1-luc2 cells, derived from Balb/C mice, were orthotopically implanted into mammary fat bad of Balb/C or C57BL6 mice. Tumor growth was monitored by bioluminescence imaging. RESULTS: We found that implantation of the cells will be more efficient with less variability when the cells are suspended in Matrigel compared with PBS. Maximum volume of Matrigel inoculated without spillage was 20 μl and 30 μl in #2 and #4 gland, respectively. Therefore, we implanted these amount of Matrigel in the subsequent experiments. To determine the difference of tumor development, 5×10^4, 10^5, 5×10^5, 10^6 E0771 cells suspended in Matrigel were inoculated. Three weeks after inoculation, tumorigenesis occurred in 0%, 13%, 75%, 75%, 100%, respectively. Utilizing 4T1-luc2 cells in Matrigel suspended cell implantation method, we investigated how long the mouse-derived cancer cells survive in mice from a different background. The fold increase in tumor growth in both backgrounds were nearly identical 24 h after inoculation at 5-fold increase measured by bioluminescence imaging. By 7 days after inoculation, 4T1-luc2 cells in C57BL6 reached a maximum increase of approximately 720-fold their Day 0 size, whereas the tumor in Balb/C had almost a 2000-fold increase in tumor size. The Balb/C tumor continued to increase rapidly to reach an almost 3000-fold increase in size, while the C57BL6 mice tumors swiftly decreased from Day 7 and was eliminated by Day 14. CONCLUSIONS: In this study, we established improved breast cancer orthotopic model with Matrigel. Utilizing this new model, we found that cancer cells will continue to grow until one week, then it will eliminated by 2 weeks when implanted into different background strain mice.

P86

Early Results of Phase II Trial of Neoadjuvant Chemotherapy with S-1 and Oxaliplatin Plus Bevacizumab for Colorectal Liver Metastasis K. Uehara,[1]* H. Goto,[2] K. Hiramatsu,[3] S. Kobayashi,[4] E. Sakamoto,[5] A. Maeda,[6] E. Takeuchi,[7] Y. Okada,[8] Y. Tojima,[9] R. Yamamoto,[10] Y. Okamoto,[11] M. Nagino.[1] *1. Nagoya University Hospital, Nagoya, Aichi, Japan; 2. Anjo Kosei Hospital, Anjo, Aichi, Japan; 3. Toyohashi Municipal Hospital, Toyohashi, Aichi, Japan; 4. Toyota Kosei Hospital, Toyota, Aichi, Japan; 5. Nagoya Daini Red Cross Hospital, Nagoya, Nagoya, Japan; 6. Ogaki Municipal Hospital, Ogaki, Gifu, Japan; 7. Japanese Red Cross Nagoya Daiichi Hospital, Nagoya, Aichi, Japan; 8. Handa City Hospital, Handa, Aichi, Japan; 9. Chukyo Hospital, Nagoya, Aichi, Japan; 10. Kasugai Municipal Hospital, Kasugai, Aichi, Japan; 11. Shizuoka Saiseikai General Hospital, Shizuoka, Shizuoka, Japan.*

Background. This phase II trial was designed to evaluate the safety and efficacy of neoadjuvant chemotherapy (NAC) with S-1 and oxaliplatin (SOX) plus bevacizumab (Bev) in patients with colorectal liver metastasis (CRLM). Methods. Patients who had initially resectable CRLM received SOX plus Bev as NAC. Treatment was administered for 4 cycles, but the 4th cycle did not include Bev. Results. Between December 2010 and August 2014, 61 patients were enrolled in this study and all patients started NAC. The most frequent grade >3 hematologic toxicity involved neutropenia in 5 patients (8.2%). Non-hematologic toxicities of grade >3 were diarrhea in 3.3% of patients. The completion rate of the scheduled 4 cycles of NAC was 82.0%. The reasons for discontinuation of chemotherapy were adverse events in 6 patients (9.8%), misgivings about disappearance of the tumor in 3 patients (4.9%), and progressive disease on the interim assessment in 2 patients (3.3%). Three patients (4.9%) developed severe liver dysfunction due to NAC and could not receive liver resection within 8 weeks after completion of chemotherapy. Although 2 of the 3 patients underwent liver resection after recovery of the liver function, 1 patient finally abandoned resection. Three patients (4.9%) judged as having progressive disease during or after NAC and did not receive liver resection. As a consequence, 57 patients underwent liver resection after NAC. Pathological findings showed that, among the 57 resected patients, 3 patients did not have CRLM but had other disease. Finally, 47 patients achieved R0 resection for CRLM and the rate in the entire cohort was 77.0%. A pathological complete response was observed in 13% and good tumor regression was exhibited in 21.5%. Conclusions. NAC with SOX plus Bev has an acceptable toxicity profile. However, accuracy of preoperative diagnosis and liver dysfunction due to NAC were serious problems. This trial suggested that we could not ignore the disadvantage of NAC. Oncologists should keep these facts in their mind and indication to NAC should be strictly selected. (UMIN number, 000004706.)



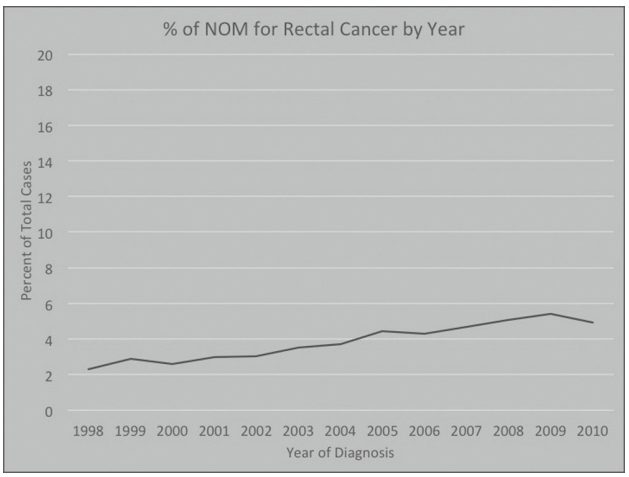
Trial profile

P87

Innovation or Disparity? National Trends in Non-operative Management of Rectal Adenocarcinoma C.T. Ellis,* C. Samuel, K. Stitzenberg. *Surgery, University of North Carolina, Chapel Hill, NC.*

BACKGROUND: While surgical resection has always been the cornerstone of curative treatment for rectal cancer, preoperative chemoradiation for stage II/III rectal cancer results in up to 49% of patients with a clinical complete response. As a result, many have questioned whether surgery can be omitted for this group of patients. Currently, there is insufficient evidence on the safety and efficacy of chemoradiation-only, or non-operative management (NOM), to support the wholesale adoption of this treatment paradigm.

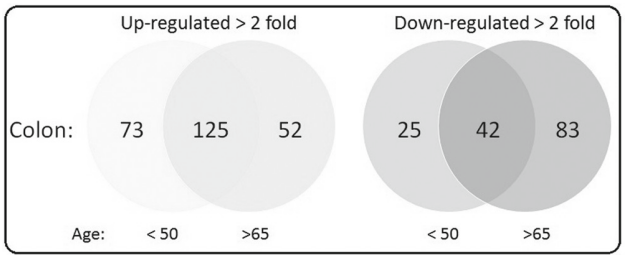
Despite this, anecdotal evidence suggests there is a trend for increased use of NOM. Our objective was to examine trends in the use of NOM for rectal cancer over time as well as patient- and facility-level factors associated with its use. METHODS: We included all incident cases of invasive, non-metastatic, rectal adenocarcinoma reported to the National Cancer Data Base (NCDB) from 1998–2010. We performed univariate and multivariate analyses to assess NOM use over time as well as patient- and facility-level predictors of NOM. RESULTS: 146,135 patients met inclusion criteria: 5,741 had NOM and 140,394 had surgery +/- additional therapy. From 1998-2010, the use of NOM doubled from 2.4% to 5% of all cases annually. Patients who were Black (AOR=1.71, 95%CI=1.57-1.86), uninsured (AOR=2.35, 95%CI=2.08-2.65), Medicaid-enrolled (AOR=2.10, 95%CI=1.90-2.33), and those treated at low-volume facilities (AOR=1.53, 95%CI=1.42-1.64) were more likely to receive NOM than White, privately insured, and high-volume facility patients, respectively. Additionally, NOM was more common in the South (AOR=1.53, 95%CI=1.32-1.76) and Pacific (AOR=1.82, 95%CI=1.57-2.12) as compared with the Northeast. CONCLUSIONS: NOM is an innovative approach that demonstrate promise in the treatment of rectal cancer. Pursing this approach in the context of a clinical trial and with well-informed patients would be appropriate. We observed evidence of increasing NOM utilization; however, this increase is occurring more frequently in Black and uninsured/Medicaid patients, raising concern that increased NOM use may actually represent increasing disparities in rectal cancer care rather than innovation.



P88

Comprehensive Genomic Analysis of Colon Tumors Reveals Differences in Molecular Patterns Between Early- and Late-onset Tumors J. Jandova,* V. Nfonsam. *Surgery/Pathology, University of Arizona, Tucson, AZ.*

Introduction: Although the overall incidence of colon cancer (CC) in the US has decreased over the past three decades, recent literature indicates an alarming increase of CC in individuals under the age of 50. More importantly, younger patients often present with more advanced and aggressive disease. Despite alarming increase in incidence of early-onset (EO) CC, the etiology is not quite understood. Increased frequency of EOCC, poorer prognosis and lack of molecular data emphasizes a need for improved and novel molecular markers for use in the treatment and prognosis of this disease. Methods: Two cohorts of patients with sporadic EO and late-onset (LO) CC were identified. Six tumors and six matching non-involved tissues from patients under 50 and over 65 were obtained. Patients with Lynch syndrome, familial adenomatous polyposis and inflammatory bowel disease were excluded from study. De-paraffinized tissues were macro-dissected from FFPE sections, RNA isolated and used for NanoString nCounter mRNA gene expression analysis to assess expression levels of up to 800 cancer genes. Statistical analysis was performed using the Gene Expression R-script module within the nCounter software v2.5. Results: We analyzed and compared expression profiles of EO and LO CC tumors to their matched non-involved tissues in order to identify genes that are unique to colon neoplasm. Out of 770 cancer pathway genes assayed, 265 genes were differentially expressed between EOCC and LOCC. From all differentially expressed genes found in CC tumors, changes in expression were statistically significant in 147 genes ($p<0.05$). Ninety eight genes were uniquely expressed in EOCC with 73 genes being up- and 25 genes down-regulated with a fold change higher than two. Conclusions: Results of this study suggest that EOCC is characterized by distinct molecular events compared to LO disease. Studies of larger patient cohorts might validate these findings and offer the possibilities of finding novel molecular markers for treatment of young patients with CC and help to enhance the search for newer, faster and noninvasive detection modalities.



P89

The Incidence of Secondary Pelvic Tumors After Previous (Chemo) Radiation for Rectal Cancer A. Rombouts,[1]* N. Hugen,[1] M. Elferink,[2] T. Feuth,[1] P. Poortmans,[1] I.D. Nagtegaal,[1] J.H. de Wilt.[1] *1. Surgery, RadboudUMC, Nijmegen, Netherlands; 2. Dutch Cancer Registration IKNL, Utrecht, Utrecht, Netherlands.*

Introduction: The aim of this study was to analyze the association between radiotherapy(RT) for rectal cancer and the development of second primary tumors. Methods: Data on all surgically treated primary rectal cancer patients diagnosed between 1989 and 2007 were retrieved from a population-based cancer registry and retrospectively reviewed. Patients with metastatic disease were excluded. To estimate the cumulative incidence of a second tumor, Fine and Gray's competing risk model was used with death as a competing event. Standardized incidence ratios (SIR's) were calculated for comparison with the incidence of primary tumors in the general population, taking in account sex, age and calendar year. Results: The cohort consisted of 29,214 patients of which 15,454 patients had undergone (chemo)RT. Median follow-up was 6.2 years (range 0-24). 3655 patients were diagnosed with at least one second primary tumor of which 808 patients had pelvic tumors. The SIR for any second tumor in rectal cancer patients was 1.14 (95% confidence interval [CI] 1.10-1.17), resulting in 23.3/10,0000 excess cases per year. Compared with patients who received preoperative RT, the cumulative incidence risk of second tumors in the pelvis was higher in patients without RT (subhazard ratio [SHR] 1.59, 95%CI 1.35-1.86) and in patients who received post-operative RT (SHR 1.41, 95%CI 1.13-1.75; Figure 1). Organ-specific analyses showed that patients without RT more often developed second prostate tumors than patients who received pre-operative RT (SHR 2.06, 95%CI 1.67-2.54). Patients who did not receive RT or received post-operative RT also had an increased risk of a second primary tumor in the rectum(sigmoid) (SHR 2.23, 95% CI 1.26-3.95 and SHR 2.22, 95%CI 1.05-4.69). Patients without RT had worse overall survival then patients who received RT (hazard ratio 1.22, 95%CI 1.19-1.26). Conclusion: In this nationwide study, patients with previous rectal cancer had a slightly increased probability of developing another primary tumor compared with the general population. We found a protective effect of pre-operative RT on the development of secondary pelvic tumors, predominantly for prostate cancer in men.

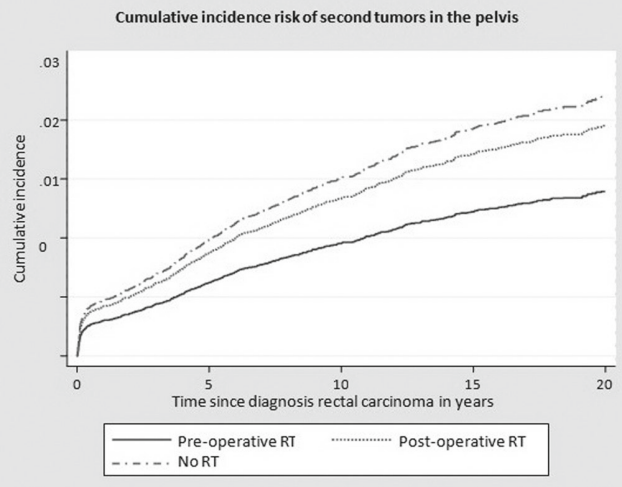


Figure 1

P90

Oncologic Outcomes Following Laparoscopic Versus Open Resection of pT4 Colon Cancer: A Systematic Review and Meta-analysis A. Feinberg,[1]* T. Chesney,[1] S.A. Acuna,[1] T. Sammour,[2] F.A. Qureshy.[1] *1. University of Toronto, Toronto, ON, Canada; 2. The Royal Melbourne Hospital, Melbourne, VIC, Australia.*

Purpose: Locally advanced colon cancer is considered a relative contraindication for laparoscopic resection and clinical trials addressing the oncologic safety are lacking. The aim of this study was to compare the oncologic outcomes associated with laparoscopic versus conventional open surgery for locally advanced colon cancers. Methods: We systematically searched the literature using MEDLINE, EMBASE, CENTRAL, and ClinicalTrials.gov (inception to August 6, 2015) for studies comparing curative intent laparoscopic and open surgery for colon cancer. Two independent reviewers selected studies, extracted data, and assessed the risk of bias. Eligible studies included any controlled trials or observational studies that reported disease free survival, overall survival, resection margins and lymph node harvest. Studies were included if it was possible to determine outcomes for the T4 colon cancers separately, either reported in the manuscript or calculated with individual patient data (IPD). Meta-analyses were done using random-effects models. Results: Of 2878 identified studies; 5 observational studies met eligibility criteria with a total of 1268 patients (675 laparoscopic, 593 open). There was no significant difference in overall survival (HR 1.28, 95%CI 0.94-1.72), disease free survival (HR 1.20, 95%CI 0.90-1.61) or positive surgical margins (OR 0.89, 95%CI 0.17-4.77) between the groups. The open group had a larger lymph node retrieval (pooled mean difference 2.26 nodes, 95%CI 0.58-3.93). The pooled rate of conversion to from laparoscopy to an open procedure was 18.6% (95%CI 9.3%-27.9%). Conclusion: Based on the available literature, minimally invasive resection of selected locally advanced colon cancer is oncologically safe. There is a small increase in lymph node harvest with open resections but it is unclear whether this is clinically significant. Surgeons should be prepared for a significant rate of conversion to laparotomy as required to perform en bloc resection.

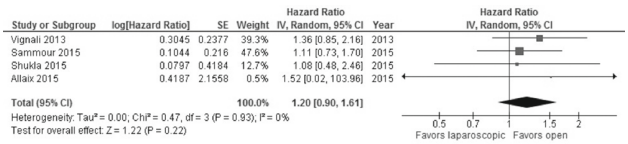


Figure 1: Forest Plot for Disease Free Survival

P91

Mesorectal Pathologic Assessment in Two Grades Predicts Accurately Recurrence, Positive Circumferential Margin and Correlates with Survival R.A. Salcedo Hernandez,* L.S. Lino-Silva, A. Herrera-Gomez, M.A. García-Gómez, R. Loaeza-Belmont. *Instituto Nacional de Cancerologia, Mexico City, Mexico.*

Background. Total Mesorectal Excision is the standard surgical treatment of colorectal cancer (CRC) proved to reduce overall recurrence and their pathological quality grading may influence survival and recurrences. We aimed to determine the prognostic value of the mesorectal quality gradified in a 2-grade system compared with the classic 3-grade system. Methods. Consecutive patients in a 5yr. period with rectal resection for CRC were prospectively included (n=103). Mesorectum was assessed in 3- grades (complete/nearly complete/incomplete) and compared with a 2-grade classification (Adequate/inadequate), data were compared and correlated with outcomes. Results. The 73% of patients received preoperative chemoradiotherapy, 59(57.2%) received a Low Anterior Resection, 35(34%) Abdomino-perineal resection and 9(8.2%) an excenteration. Laparoscopic resection was performed in 31 cases (30%). Major complications occurred in 18 patients (17.4%). Mesorectum was reported as complete in 62(60.25%), nearly complete in 22(21.35 %) and incomplete in 19 (18.4%). Quality reassessment was reported as Adequate in 84 patients (81.5%) and inadequate in 19. The data analyzed in the 2-grade classification showed a R0 resection in 91.7% of patients with adequate mesorectum vs 68.4% with inadequate (p=.008); inadequate mesorectum recurred in 47.4% vs 22.6% (p=.029) in adequate. The 71.4% of the patients with adequate mesorectum are alive free of disease vs 36.8% of patients with inadequate mesorectum (p=.030). The 3-grade system failed to predict accurately survival, with the 5-year-OS of 78.9% for complete, 80.4% for nearly complete and 42% for incomplete mesorectum (p=0.235). The 2-grade system showed a 5-year-OS of 79.3% for Adequate vs. 42% for patients with inadequate mesorectum (p=0.048). In the multivariate analysis, only recurrence was an independent adverse prognostic factor. Conclusion. Worse recurrence rates occurred after an incomplete mesorectum, it correlated with more incomplete (R1/R2) resections and positive CRM. The differences in outcome between a 3-grade classification were minimal into categories “complete and nearly complete”.

Evaluation of the TME quality in two categories

Mesorectum	
Adequate	• Intact mesorectum with only minor irregularities or one or more defects greater than 5 mm deep within the mesorectum but no visible muscular propia. • No visible muscular propia. • No coning • Smooth CRM on transverse sections or only light irregularities in the contour.
Inadequate	• Non bulky mesorectum with evident defects. • Irregular CRM on transverse sections. • Exposed muscularis propia. • Coning in the distal end of the specimen.
Sphincteric complex	
Adequate	• Cylindrical specimen with no or lightly waist effect. • Levators removed en bloc. • No significant defects or perforations
Inadequate	• Significant waist effect. • Perforation or missing areas of muscularis propria.

P92

Factors Affecting Quality of Life Post-Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in Patients with Peritoneal Carcinomatosis from Colorectal Cancer: A Prospective Study C. Chia,[1]* C. Lim,[2] G. Tan,[1] K. Soo,[1] M. Teo.[1] *1. National Cancer Centre Singapore, Department of Surgical Oncology, Singapore, Singapore; 2. Division of Clinical Trials and Epidemiological Sciences, National Cancer Centre Singapore, Singapore, Singapore.*

Background: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for peritoneal carcinomatosis from colorectal cancer have been accepted as standard of care in many institutions worldwide. While many studies have shown a good quality of life post surgery, few have been performed prospectively and even fewer have focused on colorectal cancer patients. We conducted a prospective quality of life (QOL) study on patients undergoing CRS and HIPEC for peritoneal carcinomatosis from colorectal cancer. Methods: All patients who had undergone CRS and HIPEC for peritoneal carcinomatosis from colorectal cancer at our institution from March 2012 to January 2015 were included. A total of 23 patients who underwent 25

procedures were included. The European Organization for the Research and Treatment of Cancer Core Quality of Life Questionnaire (EORTC QLQ-C30) and the colorectal module (EORTC QLQ-CR29) were administered to the patients. The questionnaire was administered at baseline prior to surgery and thereafter at 3, 6 and 12 months. Results: There were 9 males and 16 females. The median age was 52 years old (range 25-71). The median follow up was 18.5 months (range 3.2 – 36.9). Median disease- free survival was 12.9months (95% CI, 2.5-19.3). Amongst functional scales, the largest decreases from baseline were observed in physical and role functioning scores at 3 months. These scores returned to baseline levels at 6 months. There were significant increases in emotional and social functioning scores at 6 and/or 12 months. Amongst symptom scales, there were improvements in almost all symptoms at 6 and 12 months, especially the fatigue and appetite scores. A higher PCI score, longer duration of peritonectomy, the presence of a stoma and a recurrence within 3 months were associated with a poorer quality of life. Conclusions: Quality of life post CRS and HIPEC generally improved or returned to baseline in all categories by 6 to 12 months after the surgery. Patients can achieve a good quality of life similar to their baseline after CRS and HIPEC.

P93

Is Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy Cost-effective for Metastatic Colorectal Cancer?
Z. Lee,[1]* C. Chia,[2] M. Teo.[2] *1. Singhealth, Singapore, Singapore; 2. National Cancer Centre Singapore, Singapore, Singapore.*

Background Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) have improved survival outcomes with acceptable morbidity for colorectal peritoneal carcinomatosis. However, the cost effectiveness has not been extensively evaluated. This study examines the cost effectiveness of CRS and HIPEC in comparison to palliative chemotherapy. Methodology We performed a retrospective review of a prospectively maintained database of 52 patients with colorectal peritoneal carcinomatosis who underwent CRS and HIPEC procedures from April 1999 to September 2013 at the National Cancer Centre Singapore. The reference group was 21 colorectal cancer patients with only peritoneal metastasis who underwent palliative chemotherapy from January 2008 to March 2014. All costs incurred for both treatment arms, including any subsequent admissions, were included. Overall survival was defined as the duration from the initiation of treatment to the last follow-up or death. Results The average cost of CRS and HIPEC per patient was $83,720.33 while the average cost of palliative chemotherapy per patient was $44,479.01. The median overall survival of patients on CRS and HIPEC was 47.0 months (range 6- 135) and the cost per life year attained was $21,365.19. The median overall survival for patients on palliative chemotherapy was 9 months (range 2 - 34) and the cost per life year was $59.305.35. A lower proportion of patients with CRS and HIPEC required readmissions after initial therapy as compared to those on palliative chemotherapy (65% vs 86%). More patients on palliative chemo required 2 or more readmissions than patients who underwent CRS and HIPEC (58% vs 50%) Conclusion The cost per life of year attained for CRS and HIPEC was lower than that for palliative chemotherapy with significantly prolonged survival and lower readmission rates. It is less than Singapore's GDP per capital of S$71,318, making it extremely cost effective by WHO Criteria. With previously published data from NCCS that showed CRS and HIPEC resulted in improved survival as well as quality of life, it is a good management option for selected patients with colorectal peritoneal metastasis.

P94

C6-Ceramide Restores Cetuximab Chemo-Enhancement in KRAS Mutant Colorectal Cancer Cells
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Background: Cetuximab is beneficial for patients with metastatic KRAS Wild type colorectal cancer only. C6-Ceramide can act synergistically with chemotherapy to induce cancer cell death. The aim of this study was to compare growth inhibition percentage of cytostatics 5-fluoruracil, oxaliplatin, and Cet with or without C6-Cer in KRAS WT and KRAS mutant CRC cell lines (SW48 and SW480). Material and Methods: Both cell lines were incubated with IC50 concentrations of test drugs. Drug concentrations included 0.8μM for 5-FU, 0.04μM for Ox, 25 μg/mL for Cet, and C6-Cer concentrations ranged from 5 to 10 μM. Cell survival was assessed 72h after using 0.4% Trypan Blue. Results: With above mentioned concentrations, C6-Cer's GIP was 78.3% for SW-480 (vs. 33.33% for SW-48). It was also noted that the addition of C6-Cer to a combination of steady concentrations of Ox, Cet and 5-FU increased GIP with an especially significant effect on SW-480. Addition of 5 and 7.5μM resulted in doubling of GIP (75% and 86.25%, respectively, vs 32.5% of 5-FU + Ox + Cet). The greatest effect was seen when 10μM of C6-Cer was added to the IC50 concentrations of chemotherapeutic agents (using the 25μg/mL concentration of Cet), where GIP increased from 32.5% to 92.5% in SW-480. Same concentration of drugs increased GIP for SW-48 to a similar 93.5%. Conclusion: C6-Cer appears to have direct inhibitory properties, especially on KRAS Mut cells. Additionally when added to Ox, 5-FU and Cet, C6-Cer reversed the apparent insensitivity of KRAS Mut to Cet. Also, the study showed C6-Cer can provide additional synergism to their cytostatic properties in KRAS WT CRC cell lines. The true mechanism of these observations is still undergoing analysis, however the effect of isolated C6-Cer on KRAS Mut raises possibility of a different pathway that could bypass EFGR pathway. We believe the results of this study provide a starting point for clinical studies with C6-Ceramide in patients with relapsing or metastatic KRAS Mut CRC in combination with standard chemotherapy plus molecular target agents hoping they will translate into clinical benefit for this difficult to treat patient population.

P95

Outcomes of Primary Colorectal Sarcomas: A National Cancer Data Base (NCDB) Review
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Introduction: Primary Colorectal Sarcomas (PCRS) are a rare entity with anecdotally poor outcomes. Given the lack of available literature, we sought to conduct a retrospective review using a national database to inform surgeons and oncologists of the characteristics and outcomes for these rare and difficult to manage tumors. Methods: The National Cancer Data Base (NCDB) was queried for patients who underwent a colon or rectal resection and had a pathologically confirmed primary sarcoma of the colon or rectum between 1998 and 2012. Patients with adenocarcinoma (AC) of the colon or rectum were used as a comparison cohort. Overall survival was the primary outcome. Unadjusted survival analysis was performed using the Kaplan-Meier method. Cox proportional hazards model was used to control for age, sex, Charlson-Deyo comorbidity, grade, tumor size, margins status, radiation, and chemotherapy. Results: 451 patients with PCRS and 746,272 patients with AC were identified. PCRS patients tended to be younger (23.7% age 18-50 vs 13.1%, $p<0.001$), have large tumors (62.2% size >50mm vs 32.0%, $p<0.001$), less node positive disease (8.9% vs 36.3%, $p<0.001$), and high grade tumors (41.0% vs 17.5%, $p<0.001$). Sex, race, comorbidity, and 90-day mortality were similar between groups ($p>0.05$). Of the 451 patients with PCRS, 70 (15.5%) received chemotherapy and 56 (12.4%) received radiation. Overall, PCRS patients had significantly worse 60 month survival than patients with AC (44.2% vs. 52.3%, $p<0.01$). Within PCRS, upon multivariable Cox Proportional Hazard regression, high grade tumor, age 50-80 years, positive or unknown margins, and large tumor size were predictive of decreased overall survival while female sex predicted decreased mortality hazard. Neither chemotherapy nor radiation resulted in a survival benefit compared to no chemotherapy or radiation (all $p>0.05$, Table 1). Conclusion: PCRS are rare, and present at a younger age and higher grade than AC of the colon and rectum. In addition, PCRS have significantly worse long term survival compared to AC. Chemotherapy and radiation may not improve survival in patients with PCRS.

Table 1. Multivariable Cox Proportional Hazards Model of overall survival within Primary Colorectal Sarcomas (PCRS).

	HR	95% CI	p value
Tumor Grade, low (reference)			
High	2.24	1.20, 4.18	**0.01**
Unknown	1.72	0.87, 3.39	0.12
Age, 18-50 years (reference)			
50-80 years	1.88	1.02, 3.47	**0.04**
80-90 years	1.39	0.57, 3.40	0.47
Sex, Male (reference)			
Female	0.49	0.31, 0.78	**0.01**
CDCC, Score 0 (reference)			
1	1.28	0.70, 2.33	0.43
2+	1.38	0.66, 2.88	0.39
Tumors Size, <50 mm (reference)			
>50 mm	2.63	1.57, 4.39	**<0.01**
Margins, Negative (reference)			
Positive	2.27	1.14, 4.52	**0.02**
Unknown	2.29	1.21, 4.37	**0.01**
Chemotherapy, Given (reference)			
No Chemotherapy	0.70	0.36, 1.35	0.28
Unknown	0.95	0.28, 3.25	0.94
Radiation, None (reference)			
Radiation	0.55	0.25, 1.21	0.14

P96

Endoscopic Resection and Laparoscopic Surgery for Early Colorectal Cancer: A Case-Matched Study J. Baek,* S. Park, W. Lee. *Dept. of Surgery, Gachon University Gil Medical Center, Incheon, Korea (the Republic of).*

Background: Recently, endoscopic resection (ER) such as colonoscopic polypectomy, endoscopic mucosal resection, and endoscopic submucosal dissection is increasingly being used to eliminate early colorectal cancer, despite the technical difficulties associated with the procedure. Laparoscopic surgery (LS) for colorectal cancer is an alternative to conventional open surgery, and ER was lately introduced as another alternative. In present study, we compared ER with LS for oncologic outcomes, effectiveness as minimally invasive treatments for early colorectal cancer. Methods: The study included 154 patients (77 patients undergoing ER, LS, respectively) who were diagnosed with early rectal cancer and treated at a tertiary single institution between April 2008 and September 2014. The patients were matched for T stage of colorectal cancer. The clinical outcomes of ER and LS were retrospectively evaluated. Data were analyzed according to the intention-to-treatment principle. Results: The mean hospital stay for all admissions was 3.4 days in the ER group and 11.5 days in the LS group ($p<0.001$). The median follow up was 36.5 months for all of patients. The survival rate, such as overall survival, and disease-free survival were not significant between two groups, respectively. The complication rate was also not significant. But, ER group showed high transition rate (33.8%, ER followed by LS) due to resection margin involvement. And longer hospital stay and high complication were shown in transition cases ($p<0.05$) Conclusion: For early colorectal cancer, ER was comparable with LS in terms of safety and oncologic outcomes. But, ER group was shown high transition rate and longer hospital stay, high complication rate in transition cases. The choice of treatment should be individualized and discussed with a multidisciplinary teram.

P97

Derivation of Stringent Transcriptomic Signatures from Multi-sampling of Colorectal Tumours K. Koh,[2]* N. Shannon,[1] Q. Tan,[1] W. Wang,[2] K. Li,[2] S. Lek,[2] T. Skanthakumar,[2] K. Soo,[2] B. Teh,[2] C. Ong,[1] M. Teo.[2] *1. Singapore General Hospital, Singapore, Singapore; 2. National Cancer Centre Singapore, Singapore, Singapore.*

Introduction Currently, most genomic research on cancer examines only one sample each of tumor vs normal. Since tumors exist as a heterogeneous entity, such research generate large lists of putative targets. This study aimed to examine the impact of sampling multiple tumor or normal from the same patient on identification of a tumor vs normal signature in colorectal cancer. Method RNA sequencing was performed on four samples representing two normal mucosa (M1/2) and two tumor samples (T1/2). Data was analysed using DNANexus to align reads using TopHat and pairwise comparisons made between each sample using cuffdiff. A FDR p-value <0.01 was used to identify differentially expressed genes. For assessment of putative targets using multiple samples, venn diagrams were used to count the number of dysregulated genes present in multiple pairwise comparisons. Results As expected, the largest signature was seen comparing a single tumor and normal sample (65 for T2 vs M1, 438 for T1 vs M2). If using single tumor sample, then two normal samples are able to reduce the number of genes by 34-59% (180/273 for T1 vs M1±M2 to 180/438 for T1 vs M2±M1). If using a single normal sample, then two tumor samples are able to reduce the number of genes by 35-87% (55/84 for M2 vs T2±T1 to 55/438 for M2 vs T1±T2). When using two tumor samples, addition of a second normal sample further reduced the number of genes by a further 44-60% (22/39 for T1/T2 vs M1±M2, 22/55 for T1/T2 vs M2±M1). Conclusion Surgeons have exclusive access to allow multi-sampling of tumors which permits profiling for more stringent molecular signature of tumor vs normal. This provides a benefit of 34-87% reduction in a putative signature by the addition of a second sample, or up to 66-95% reduction using two of each samples.

P98

Inhibition of Colon Cancer Growth and Migration by Polyamine Synthesis Inhibition and AMP Kinase Activation Y. Zhang,[1] L. Rodriguez,[2] G. Peng,[1] E. Hsueh.[1]* *1. Surgery, Saint Louis University, St. Louis, MO; 2. National Cancer Institute, Bethesda, MD.*

Metformin (Met) can inhibit cancer cell growth via activation of AMP kinase. Colon cancer over-expresses ODC, a key enzyme in polyamine biosynthesis. We hypothesized that combination of Met and DMFO (ODC inhibitor) can inhibit tumor cell proliferation and migration of colon cancer cells. HCT-116 and HT-29 colon cancer cells were treated with Met, DFMO, or combination (M+D). Colon cancer cell proliferation and migration were assessed. Western blot was performed for AMP kinase, mTOR, p70S6K, 4E-BP, 1LC3A/B, and Beclin-1 expression. Annexin V assay and fluorescence microscopy of LC3A/B were performed. For in vivo evaluation, HT-29 cells were injected SQ into BALB/c nu mice in 4 groups: group 1 - vehicle and drinking water (W), group 2 - 2% (w/v) DFMO in W; group 3 - IP Met (250 mg/kg/day), group 4 - M+D. Tumor volume and weight were measured. Data were presented as means ± SD. Student's t test was used for comparison between groups. Dose- and time-dependent inhibition of cell proliferation and migration was observed with either Met or DFMO in both HCT-116 and HT-29 cells. Enhanced inhibition was observed with M+D (5 mM DFMO and 5 mM Met) on both cell migration and proliferation at 24 hours compared with either drug alone and significantly greater in mismatch-repair defective HCT-116 cells. There was synergistic inhibition of ODC expression with M+D versus DFMO alone ($p<0.01$) and significant enhancement of AMPK activation versus Met alone ($p<0.01$). The combination resulted in significant inhibition of mTOR signaling with decreased phosphorylation p70S6K and 4E-BP1. Autophagy and apoptosis were both enhanced in M+D group versus either drug alone. In vivo experiment confirmed synergistic anti-proliferative effect of M+D with average HT-29 tumor weight of 1471 mg for control group compared with 923 mg for group 2 ($p<0.05$), 1095 mg for group 3 ($p< 0.05$), and 503 mg for M+D group ($p< 0.001$). Met and DFMO have synergistic effect in inhibition of colon cancer proliferation and migration. The combination of Met and DFMO induced colon cancer cell death via apoptosis and autophagy through activation of AMPK pathway and suppression of the Akt/mTOR signaling pathway.

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Full Length LGR5-Positive Cells have Chemoresistant Characteristics in Colorectal Cancer H. Takahashi,* H. Osawa, J. Nishimura, N. Haraguchi, T. Hata, H. Yamamoto, I. Takemasa, T. Mizushima, Y. Doki, M. Mori. *Gastrointestinal Surgery, Osaka University Faculty of Medicine, Suita, Osaka, Japan.*

LGR5 is a target of Wnt signaling and considered both a cancer stem cell marker and intestinal stem cell marker. Transcript variants of LGR5 have been reported in soft tissue sarcoma, but whether LGR5 isoforms exist in colorectal cancer is unknown. Here, we report firstly two splice variants of LGR5 were expressed in the human intestine crypt columnar based cells. One lacked exon 5 and the other lacked exons 5-8. Only full length LGR5 (LGR5FL) appeared during cell cycle arrest, whereas the transcript variants appeared when the cell cycle was proceeding. Considering both splice variants of LGR5 lacked exon5, we made anti-LGR5 exon 5 antibody which can recognize LGR5FL specifically. Immunohistochemistry and in situ hybridization showed that LGR5FL-positive cells were negative for Ki-67. Moreover, comparing pre-chemotherapy and post-chemotherapy specimens, the population of LGR5FL-positive cells significantly increased with therapy ($P<0.01$). These findings suggested LGR5FL-positive cells did not have cell proliferative

character and have the feature of resistant to anti-tumor drugs. Designing therapeutic strategies that target LGR5FL-positive cells seems to be important in colorectal cancer.

P100

Epigenetic Alterations by MicroRNAs in Carcinogenesis of Colorectal Cancer T. Hata,* H. Yamamoto, D. Okuzaki, H. Ogawa, M. Konno, H. Takahashi, N. Haraguchi, J. Nishimura, T. Hata, I. Takemasa, T. Sato, T. Mizushima, H. Ishii, Y. Doki, M. Mori. *Osaka University, Suita, Japan.*

Introduction; MicroRNAs (miRs) are essential factors for epigenetic modulations, and, in many types of cancer, epigenetic disorders get accumulated in the course of carcinogenesis, including aberrant expression of miRs. Our group previously reported the function of miRs (miR-200c, 302, 369) which had an ability to change epigenetic profiles to pluripotent state, and inhibited malignant potential for cancer cells. The aim of this study is to investigate the effect of these miRs on tumorigenesis in a mouse model of adenoma-carcinoma progression using CPC/Apc mouse, and analyze gene expression and epigenetic profiles. Materials and Methods; MiRs (miR-200c, 302, 369) were injected from a tail vein of CPC/Apc mice, using super carbonate apatite system for the nucleic acid delivery. Colonoscopy was performed every four weeks, and the number of tumors was counted. The RNA and miR expression were analyzed with Agilent Technologies. Gene expression of interest was also quantified by qRT-PCR in clinical samples from colorectal cancer. In vitro experiments, the functional role of candidate genes was assessed based on a colony formation assay using rat IEC18 cells. Results; Incidence of tumors was suppressed in mice treated with miRs (MIR group), compared with non-treated mice (NC group) (p=0.026). In microarray analysis, the expression of pluripotent markers such as OCT3/4 and SOX2 increased in normal mucosa of MIR group. We focused on MAF gene, which encodes a transcription factor Maf, displaying an inverse correlation of increase in normal mucosa of MIR group and decrease in tumor of NC group, compared to normal mucosa of NC group. MAF expression decreased in clinical tumor tissues compared to corresponding normal mucosa (p=0.045). In vitro, knockdown of MAF expression led to an increase of colony-forming ability of IEC18 cells. The effect of forced expression of MAF and methylation of MAF are under investigation. Conclusions; Our findings indicate that these miRs have potential to suppress the incidence of tumors in vivo, and regulate MAF expression. Further analyses for the function and regulation mechanism are required.

P101

Predictors of Severe Morbidity After Cytoreductive Surgery and HIPEC in Patients with Colorectal Peritoneal Carcinomatosis G. Simkens,* T. van Oudheusden, M. Luyer, S. Nienhuijs, G. Nieuwenhuijzen, H. Rutten, I. de Hingh. *Surgical Oncology, Catharina Hospital Eindhoven, Eindhoven, Noord-Brabant, Netherlands.*

Introduction: Severe morbidity after cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is, besides the obvious short-term consequences, associated with impaired long-term outcomes. Risk factors for severe morbidity in patients with peritoneal carcinomatosis (PC) of colorectal origin are poorly defined. This study aims to identify risk factors for severe morbidity after CRS + HIPEC in patients with colorectal PC. Methods: Patients with colorectal PC who underwent CRS + HIPEC between 2007 and 2015 in a tertiary referral center were categorized and compared between those with and without severe morbidity. Risk factors were identified using logistic regression analysis. Morbidity was graded according to the Clavien-Dindo Classification for Surgical complications, with grade ≥3 indicating severe morbidity. Results: A total of 211 patients were included. In these patients, the median PCI score was 8 [0 - 25] and complete macroscopic (R1) cytoreduction was achieved in 93.8%. In total, 53 patients (25.1%) developed severe morbidity with grade ≥3. Identified independant risk factors for severe morbidity were extensive prior surgery (odds ratio (OR) 4.3), a positive recent smoking history (OR 4.0), a poor physical performance status (OR 2.9) and extensive cytoreduction (OR 1.2 per additional resection). Patients with an increased number of risk factors more often had severe morbidity and higher reoperation, readmission and mortality rates. Furthermore, an internally validated preoperative prediction model for severe morbidity with an area under the ROC curve of 70% was constructed. This model was able to adequately distinguish high risk patients from low risk patients prior to CRS + HIPEC. Conclusion: The current study identified risk factors for severe morbidity after CRS + HIPEC in colorectal PC patients. Patients with a combination of risk factors have a substantial risk of severe morbidity and therefore should be carefully selected for CRS + HIPEC. The preoperative decision model can be a valuable additional tool in this process of patient selection.

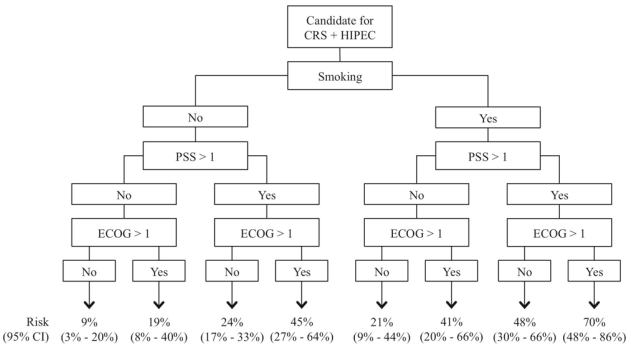


Figure 2. Risk of severe morbidity after CRS + HIPEC according to major preoperative risk factors

P102

Molecular Targeting B-RAF Mutant Colorectal Cancer: Novel AMPK-induced Autophagy Mechanism T. Sueda,* D. Sakai, K. Kawamoto, M. Konno, N. Nishida, J. Koseki, H. Takahashi, N. Haraguchi, J. Nishimura, T. Hata, I. Takemasa, T. Mizushima, H. Yamamoto, T. Sato, H. Ishii, Y. Doki, M. Mori. *Osaka University, Suita, Japan.*

Although $BRAF^{V600E}$ mutation is associated with adverse clinical outcomes in patients with colorectal cancer (CRC), the mechanism how they responded to therapeutic $BRAF^{V600E}$ inhibitors remains understood imperfectly. In this issue, autophagy has been emerged recently as a mechanism of chemo-resistance in cancer cells, but its biological effects remain inconsistent, which may underscore the significance of uncharacterized roles of autophagy. To examine the detailed mechanism, we investigated the role of autophagy by immunoblots, MTT, and apoptosis assay in $BRAF^{V600E}$ CRC cell lines including HT29 and RKO. Here we showed that selective BRAF inhibitors elicited the induction of autophagy as well as therapeutic resistance in $BRAF^{V600E}$, but not $BRAF^{wild\text{-}type}$, CRC cells. Furthermore, we demonstrated that pharmacological or siRNA inhibition of autophagy resulted in the restoration of sensitivity to the exposure to selective BRAF inhibitors in the BRAF mutant CRC cells. Moreover, to clarify the underlined mechanisms for selective BRAF inhibitors-induced autophagy, we performed the expensive analysis of the protein expression levels, which may link the BRAF genotypes with the autophagy phenotypes. We found finally that the phosphorylation of AMPK is involved in the selective BRAF inhibitor-induced autophagy. Indeed, we were able to show that the genetic knockdown of oncogenic BRAF signaling led to the stimulation of AMPK activity in an association with the downstream signaling, Mek-Erk-p90Rsk phosphorylation cascades. The present data demonstrated that AMPK played a critical role in the autophagy-dependent cytoprotections in BRAF mutant CRC cells, and that AMPK was negatively correlated with $BRAF^{V600E}$-dependent activation of Mek-Erk-Rsk signaling in one hand, while it positively correlated with Unc-51-like kinase 1 (ULK1), an initiator of autophagy, in another hand. As sum, the present study demonstrated clearly that the single inhibition of $BRAF^{V600E}$ was supposed to elicit the activation of AMPK, which further induced autophagy, suggesting the further rationale that the simultaneous targeting for autophagy could be beneficial to overcome the chemo-resistance of $BRAF^{V600E}$ CRC cells.

P103

Histopathological Features of Patients with Synchronous Colorectal Peritoneal Metastases Strongly Influence Treatment and Survival G. Simkens,[1]* L. Razenberg,[1] V. Lemmens,[2] G. Nieuwenhuijzen,[1] G. Creemers,[1] I. de Hingh.[1] *1. Surgical Oncology, Catharina Hospital Eindhoven, Eindhoven, Noord-Brabant, Netherlands; 2. Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, Netherlands.*

Introduction: Approximately 5% of the patients with colorectal cancer present with synchronous peritoneal metastases (PM). Currently, it is unclear

how both treatment choice and outcome are influenced by histological subtype and the presence of concomitant systemic/locoregional lymph node metastases. Therefore, this study assessed the impact of these histopathological features on treatment choice and outcome in patients with synchronous colorectal PM. Methods: This population-based study included all patients diagnosed with synchronous PM in the Netherlands between 2005 and 2014. Data was extracted from the National Cancer Registry (IKNL). Patients were compared based on histological subtype; adenocarcinoma (AC), mucinous adenocarcinoma (MC), or signet ring cell carcinoma (SRCC). Results: In total, 5516 patients were included, of which 71.8% had an AC, 21.2% an MC, and 7.0% had an SRCC. After multivariate cox regression analysis, the hazard ratio (HR) for treatment with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) compared to best supportive care was 0.16 in AC patients, 0.20 in MC patients, and 0.13 in SRCC patients. This implies the survival benefit of CRS + HIPEC was comparable in all histological subtypes. Patients without locoregional lymph node metastases benefitted the most of CRS + HIPEC (median survival: 56.8 months). Patients with AC histological subtype were treated with CRS + HIPEC less often compared to MS and SRCC patients (6.2% vs. 13.3% and 11.2%, respectively). Patients with concomitant systemic metastases were treated with curative intent occasionally. Furthermore, the use of CRS + HIPEC increased over time, especially in AC and MC patients. Conclusions: Histological subtype and the presence of systemic metastases influenced treatment choice in patients with synchronous colorectal PM. The relative survival benefit of CRS + HIPEC was comparable in all histological subgroups. These results can be used to optimize the treatment strategy for patients with synchronous colorectal PM.

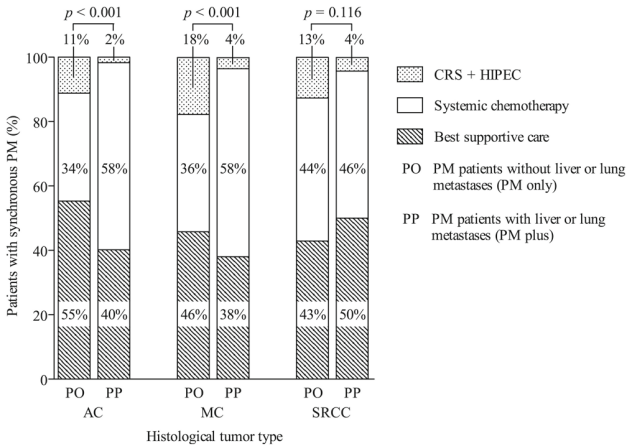
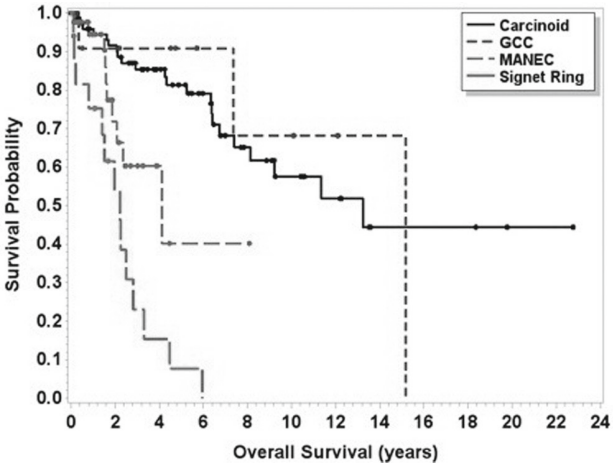


Figure 1. Treatment type in patients with synchronous colorectal peritoneal metastases (PM) according to histological subtype and stratified for the presence of other systemic metastases; AC adenocarcinoma, MC mucinous adenocarcinoma, SRCC signet ring cell carcinoma, CRS cytoreductive surgery, HIPEC hyperthermic intraperitoneal chemotherapy

P104

Mixed Adeno-Neuroendocrine Carcinoma: An Aggressive Clinical Entity S.A. Brathwaite,* J. Rock, M.M. Yearsley, T. Bekaii-Saab, L. Wei, W.L. Frankel, J. Hays, C. Wu, S. Abdel-Misih. *General Surgery, The Ohio State University Wexner Medical Center, Columbus, OH.*

Background Mixed adeno-neuroendocrine carcinoma (MANEC) is a rare pathologic diagnosis recently defined by the World Health Organization in 2010. Due to poor understanding of MANEC as a clinical entity there is significant variation in the management of these patients. The aim of our study is to characterize MANEC to develop evidence-based treatment strategies. Methods The patient database at our institution was queried for the diagnosis of MANEC and 46 patients were identified. For comparison, the database was also queried for goblet cell carcinoid (GCC) of the appendix, signet ring cell carcinoma and carcinoid/neuroendocrine tumor of the appendix. Charts were then retrospectively reviewed for clinicopathologic characteristics, patient treatment and survival data. Results The median age of diagnosis of MANEC was 55 years. Eighty-seven percent of MANEC arose from the appendix, with 28% of patients undergoing appendectomy and 35% undergoing right hemicolectomy (RHC) as their index operation. Immunohistochemical staining was positive for Chromogranin (82%), Synaptophysin (97%) and CD56 (67%). Sixty-seven percent of patients presented with Stage IV disease and 41% had positive lymph nodes. Median overall survival was 4.1 years, which was statistically significant (p=<0.0001) in comparison to carcinoid tumors (13.2 years, p=0.0025), GCC (15.2 years, p=0.37) and signet ring carcinoma (2.2 years, p=0.056) (Figure 1). Conclusions MANEC is a more aggressive clinical entity than both GCC of the appendix and carcinoid/neuroendocrine tumors of the appendix. Based on these findings we recommend patients with MANEC tumors undergo aggressive multidisciplinary management.



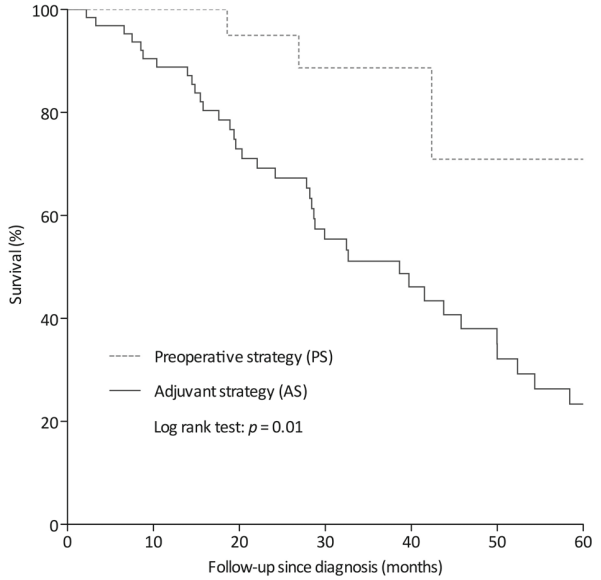
Kaplan Meier survival curve for patients with carcinoid tumors, GCC, MANEC and signet ring cell carcinoma.

P105

Timing of Systemic Treatment in Patients Undergoing Cytoreductive Surgery and HIPEC for Peritoneal Metastases of Colorectal Origin R. Devilee,[1] G. Simkens,[1]* T. van Oudheusden,[1] H. Rutten,[1] G. Creemers,[1] B. ten Tije,[2] G. Nieuwenhuijzen,[1] I. de Hingh.[1] *1. Surgical Oncology, Catharina Hospital Eindhoven, Eindhoven, Noord-Brabant, Netherlands; 2. Amphia Hospital, Eindhoven, Noord-Brabant, Netherlands.*

Introduction: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) can result in long-term survival in selected patients with colorectal peritoneal metastases (PM). Most patients are additionally treated with systemic chemotherapy but timing (adjuvant versus preoperative) varies between treatment centers. The aim of this study was to compare short and long-term outcomes in patients with synchronous colorectal PM treated with CRS + HIPEC who received adjuvant or preoperative chemotherapy. Methods: Patients with synchronous colorectal PM who underwent macroscopically complete CRS + HIPEC were included in this study. Data were collected from a prospective database containing all patients between 2007 and 2014. Perioperative outcome and survival were compared between patients planned for adjuvant chemotherapy (adjuvant strategy [AS]) or preoperative chemotherapy, followed by adjuvant systemic chemotherapy if possible (preoperative strategy [PS]). Results: A total of 88 patients with synchronous colorectal PM were included of whom 24 patients (27%) were treated with preoperative chemotherapy. The peritoneal cancer index (PCI) score was lower (8.4 ± 4.6 vs. 6.3 ± 3.7, p=0.04) in patients receiving preoperative chemotherapy. The severe complication rate was 17% in the AS-group versus 21% in the PS-group (p=0.76). In the AS-group, 11% did not receive adjuvant chemotherapy, mainly due to postoperative complications. In the PS-group, 88% of the patients were treated with adjuvant chemotherapy in addition to the preoperative treatment. Median survival since diagnosis was 38.6 months in the AS-group, whereas median survival was not reached in the PS-group (p=0.01). Three-year overall survival rates were 51% and 89%, respectively. Conclusion: Treatment with preoperative chemotherapy was associated with improved long-term survival after CRS + HIPEC compared to adjuvant chemotherapy. Ideally, a randomized controlled trial should be

performed to investigate the optimal timing of systemic chemotherapy in PM patients. By doing so, the survival of these patients may be further improved.



No. at risk

NS	24	23	18	13	5	3	1
AS	64	55	39	28	18	12	6

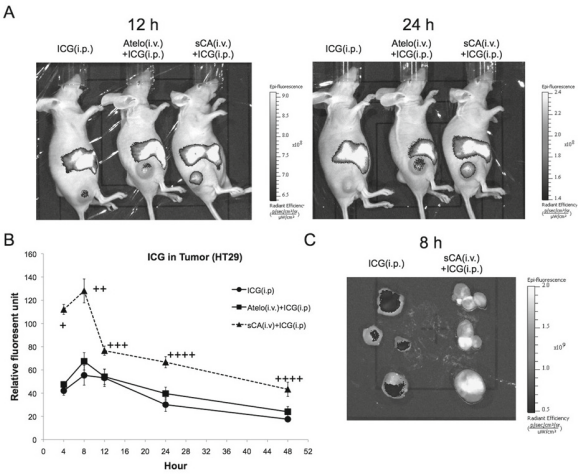
Figure 1. Log-rank survival analysis comparing survival of patients in the AS- and PS-group calculated from date of diagnosis of the primary tumor

P106

Super Carbonate Apatite Nanoparticles Can Adjunctively Reduce Tumor Interstitial Fluid Pressure and Enhance the Uptake of Chemicals into Tumor X. Wu,[1]* H. Yamamoto,[2] H. Hirose,[1] Y. Yamamoto,[1] H. Ueno,[3] M. Mori.[4] *1. CancerStem Tech Inc., Ibaraki, Osaka, Japan; 2. Department of Molecular Pathology, Division of Health Sciences, Graduate School of Medicine and Health Science, Osaka University, Suita, Osaka, Japan; 3. Department of Stem Cell Pathology, Kansai Medical University, Hirakata, Osaka, Japan; 4. Department of Surgery, Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan.*

Background Nanoparticles have been developed to delivery therapeutic agents to tumors for decades. However, penetrating into tumor against the increased interstitial fluid pressure (IFP) remains a major challenge in cancer treatment, so that it results in inefficient uptake of nanoparticles or therapeutic agents. So far we have introduced an in vivo pH-sensitive delivery system for doxorubicin or siRNA using super carbonate apatite (sCA) nanoparticles, which consisted of inorganic ions. In this study, we report a unique characteristic of sCA itself, not as a delivery system, that the empty sCA alone markedly reduces the solid tumor IFP and enhances the uptake of agents into solid tumors. Methods and Results Tumor IFP of colon cancer HT29 xenografts in mice was measured under anesthesia using pressure measurement systems with 1.6 Fr fluied-filled catheter. We found that the tumor IFP at 2.5 h - 4 h after the intravenous injection of sCA markedly decreased to 13.4 ± 1.8 mmHg, which was significantly lower than that of control group (30.9 ± 2.9 mmHg, $P < 0.0001$). To further investigate whether the decreased IFP in tumor would lead to enhanced uptake of agents supplied from the tumor vessels, sCA and indocyanine green (ICG) were simultaneously administered via the separate routes to the mice bearing HT29 tumor; sCA was administered i.v. (intravenously) and ICG was administered i.p. (intraperitoneally). We found by IVIS imaging system that sCA enhanced intratumoral uptake of ICG, whereas atelocollagen (Atelo) did not have such effects (Figure 1A). Time course studies showed that ICG levels in tumors with treatment of sCA (i.v.) + ICG (i.p.) were significantly higher throughout the examined time points than those treated with ICG alone ($P = 0.0142$ for 4 h, $P = 0.0139$ for 8 h; Figure 1B). Ex vivo imaging of the tumors treated with sCA (i.v.) + ICG (i.p.) at 8 h post administration confirmed higher fluorescence intensity than the tumors treated with ICG (i.p.) alone (Figure 1C). Conclusion Our data suggest that sCA itself can reduce tumor interstitial fluid pressure and enhance the uptake of agents into tumors.

Figure 1



In vivo and ex vivo IVIS imaging of ICG. sCA and ICG were simultaneously administered to mice through the separate routes; sCA was administered i.v. (intravenously) and ICG was administered through the i.p. (intraperitoneal) route. (A) ICG levels in HT29 tumors with treatment of sCA plus ICG were significantly higher at 12 h and 24 h. (B) Time course studies of ICG intensity in HT29 tumor. Data represent mean ± SEM. ICG (i.p.) group vs sCA (i.v.) + ICG (i.p.) group. $^{+}P=0.0142$, $^{++}P=0.0139$, $^{+++}P=0.0433$, $^{++++}P=0.0304$ (n=4, Wilcoxon rank test) (C) The uptake of ICG in tumor between the two groups at 8 h.

P107

Exploring the Clinical Utility of MULE as a Biomarker in Colorectal Cancer W. Wang,[1]* P. Reilly,[1] N. Shannon,[1] Q. Tan,[2] K. Koh,[1] K. Li,[1] S. Lek,[1] T. Skanthakumar,[1] K. Soo,[1] C. Ong,[2] M. Teo.[1] *1. National Cancer Centre Singapore, Singapore, Singapore; 2. Singapore General Hospital, Singapore, Singapore.*

Aim MULE is a member of the E3 ubiquitin ligase family which has both tumour suppressor and oncogenic effects. It has also been shown to promote metastasis via the TIAM1 pathway and is consistently demonstrated to be overexpressed in colorectal cancer (CRC). We hypothesized that MULE overexpression can lead to aggressive tumour biology and consequently poor prognosis. In this study, we look at the clinical relevance of MULE overexpression in CRC, specifically with regards to patient outcomes. Methods We interrogated molecular profiles of colorectal cancers using publicly available datasets and identified treatment-naïve CRC patients who had available tissue samples from an existing institutional database. Tissue microarrays (TMAs) constructed from these samples (n=238) were stained, scored for MULE expression and then correlated with retrospectively collected clinic-pathological data. We also collected samples of primary and metastatic tissue from patients with advanced CRC (n=17). Results From our in-silico analysis, we found that MULE expression increased from normal mucosa to primary colorectal tumour samples to metastatic tissue. Expression was also highest in malignant epithelial component as compared to the leukocyte and stromal components. This was validated on immunohistochemistry of colorectal tumour samples. From a prognostic perspective, although not statistically significant, samples with low MULE staining displayed a trend towards poorer overall and recurrence-free survival as compared to samples with high MULE staining($p=0.385$ and 0.173 respectively). Conclusion Although our study has not demonstrated a prognostic effect of MULE, the differential expressions of stromal and inflammatory components as compared to tumour cells suggest that MULE might exert different effects on each component. A stepwise increase in MULE expression from normal mucosa to tumour cells and metastatic tissues suggests that MULE might still have a clinical role as a diagnostic biomarker.

P108

Patients with Squamous Cell Cancers of the Anal Canal are at Risk for Second Cancers R. Nelson, L.L. Lai.* *Surgery, City of Hope, Duarte, CA.*

Introduction: Over the last decade, squamous cell carcinoma of the anal canal (SCCA) has emerged as a human papilloma virus (HPV)-related cancer. Chemoradiation for SCCA has resulted in favorable survival. Although the risk of HPV-related second cancers in patients with SCCA has been shown to be very high, the risk of other second cancers remains unknown. We sought to determine the risk and type of second cancers to better inform on survivorship issues. Methods: We conducted a cohort analysis of secondary primary cancer standardized incidence ratios (SIRs) following the diagnosis of SCCA using the SEER dataset. Our index case cohort includes patients from 1992-2012 with at least 6 months of event-free follow-up. A comprehensive study of sites and incidence of second cancers was conducted. HPV-related second cancers were excluded. Data was analyzed using SIRs adjusted by person years at risk. Significance was determined if the exact method 99% confidence intervals (CIs) did not include 1.0. Calculated excess risk statistics are expressed as per 10,000 person years. Findings: Of 10,483 SCCA patients identified, 346 developed 367 second cancers resulting in an SIR (observed/expected ratio) of 2.5 (CI 2.2–2.9). SIRs were elevated for cancer sites related to tobacco use such as larynx (3.02, CI 1.4–5.7) and lung (2.3, CI 1.9–2.8); to co-infection with other viruses such as liver (2.4, CI 1.3 – 4.1), leukemia (1.6, CI 0.9-2.6), lymphoma (2.7, CI 2.0–3.6) and Kaposi Sarcoma (28.7, CI 16.5-46.2). Excess risk analysis demonstrated marked increased risk at these disease sites. The highest risk of second cancers was in the first 5 years after the index SCCA but remained elevated even after 15 years. Conclusions: Patients with SCCA have significantly increased risk of developing second cancers related to tobacco use or to co-infection with other viruses such as HCV and HIV. Given the excess risk for second cancers, screening for second cancers in SCCA survivors may improve overall survival in this population.

Second cancers in patients with SCCA

Second cancer site	Observed	Expected	Observed/Expected (SIR) 99% CI
All	367	146	2.51 (2.19 - 2.87)*
Liver	22	9	2.44 (1.31 - 4.13)*
Larynx	15	5	3.02 (1.39 - 5.68)*
Lung	195	85	2.30 (1.90 - 2.76)*
Lymphoma	81	30	2.71 (2.00 - 3.59)*
Leukemia	27	16	1.64 (0.94 - 2.64)
Kaposi Sarcoma	27	1	28.69 (16.46 - 46.22)*

SEER13 1992-2012.
Latency period set at minimum of 6 months from index primary diagnosis.
*Incidence rate significantly higher than expected (using exact method and 99% CIs).

P109

Pelvic Exenterations Can be Performed Safely: A Morbidity and Mortality Analysis of the First 90 Days After Surgery N.A. Borja,* A. El Mokdad, I. Nassour, H. Hirsch, H. Zhu, S. Kehoe, V. Margulis, T. Chong, C. Balch, M.A. Choti, P. Polanco, G. Balch. *Surgery, UT Southwestern, Dallas, TX.*

INTRODUCTION: Pelvic exenteration can achieve cure for patients with locally advanced pelvic malignancies, and palliate symptoms when cure is unattainable. However, concern over high patient 30-day major morbidity and mortality, which has been reported to exceed 50% and 10% respectively, has limited its use. Here we provide the first large patient series with 90 day perioperative outcomes. METHODS: Patients with locally advanced pelvic malignancies treated at a single institution from 2008-2015 were studied through a prospectively maintained database. Statistical analysis of patient factors and postoperative complications was analyzed using the chi-square and Fisher's exact test. RESULTS: Seventy-eight patients underwent total (47%) or partial exenteration (53%), for either primary (71%) or recurrent (29%) disease. Most patients had colorectal adenocarcinomas (80%). The majority of patients received preoperative chemotherapy (77%) and preoperative radiation (58%). R0 resection was achieved in 70% of cases. The median hospital LOS was 10 days (IQR 7-15). The 90-day readmission rate was 33.3%. The overall 90-day complication rate was 66.6%, with 19.2% as major (Clavien III-IV), and 47.4% as minor (Clavien I-II). The most common major complication was intra-abdominal abscess (5 patients), which was managed in all cases with percutaneous drainage. The 30-day mortality was 1.3%, and at 90 days was 2.6%, with both deaths related to pulmonary complications. Interestingly, the type of exenteration performed was not associated with increased risk for complications, nor was patient age, ASA class, operative time, blood loss, flap reconstruction, or pathologic margins. Only preoperative radiation (p=0.009) was associated with a higher rate of complications. CONCLUSIONS: Our 90-day major morbidity rate of 19% and mortality rate of 2.6% in this large series demonstrates that pelvic exenteration can be performed with acceptable outcomes in patients with locally advanced pelvic malignancies, and should be more readily considered, even in the palliative setting.

Associations between Patient Factors and 90-day Morbidity

Patient Characteristics (n=78)	No Complication (n=24)	Minor Complication (n=37)	Major Complication (n=15)	P-value
Patient Age	-	-	-	
<55 years (n=38)	31.6% (12)	42.1% (16)	26.3% (10)	p = 0.561
≥55 years (n=40)	30.0% (12)	52.5% (21)	17.5% (7)	
Patient Comorbidities	-	-	-	
ASA 1, 2 (n=30)	40.0% (12)	40.0% (12)	20.0% (6)	p = 0.370
ASA 3, 4, 5 (n=43)	25.0%(12)	52.1% (25)	22.9% (11)	
Disease Presentation	-	-	-	
Primary Malignancy (n=52)	32.7% (17)	48.1% (25)	19.2% (10)	p = 0.728
Recurrent Malignancy (n=21)	23.8% (5)	57.2% (12)	19.0% (4)	
Preoperative Chemotherapy	-	-	-	
Yes (n=59)	27.1% (16)	50.8% (30)	22.1% (13)	p = 0.499
No (n=18)	44.4% (8)	33.3% (6)	22.3% (4)	
Preoperative Radiation	-	-	-	
Yes (n=44)	18.2% (8)	50.0% (22)	31.8% (14)	p = 0.009 **
No (n=33)	48.5% (16)	42.4% (14)	9.1% (3)	
Type of Exenteration	-	-	-	
Total (n=37)	21.6% (8)	51.4% (19)	27.0% (10)	p = 0.220
Partial (n=41)	39.0% (16)	43.9% (18)	17.1% (7)	
Reconstruction	-	-	-	
Muscle Flap (n=44)	34.1% (15)	50.0% (22)	15.9% (7)	p = 0.348
No muscle flap (n=34)	26.5% (9)	44.1% (15)	29.4% (10)	
Operative Time	-	-	-	
<460 minutes (n=38)	39.4% (15)	44.7% (17)	15.8% (6)	p = 0.205
≥460 minutes (n=40)	22.5% (9)	50.0% (20)	27.5% (11)	
Estimated Blood Loss	-	-	-	
<600 mL (n=38)	31.6% (12)	42.1% (16))	26.3% (10)	p = 0.618
≥600 mL (n=39)	30.8% (12)	51.3% (20)	17.9% (7)	
Intraoperative pRBC Transfusion	-	-	-	
Yes (n=29)	24.1% (7)	51. 7% (15)	24.1% (7)	p = 0.573
No (n=45)	35.6% (16)	42.2% (19)	22.2% (10)	
Margin Status	-	-	-	
R0 resection (n=54)	37.0% (20)	44.5% (24)	18.5% (10)	p = 0.173
R1/R2 resection (n=24)	16.7% (4)	54.2% (13)	29.1% (7)	

P110

First In-Human Intraoperative Optical Imaging of Peritoneal Carcinomatosis of Colorectal Origin Using a VEGF Targeted Near-Infrared Fluorescent Tracer: A Feasibility Study S.J. de Jongh,[1]* N.J. Harlaar,[1] M. Koller,[1] B.L. van Leeuwen,[1] P.H. Hemmer,[1] R.J. van Ginkel,[1] L.B. Been,[1] J.S. de Jong,[2] G. Kats,[1] M.D. Linssen,[1] A. Jorritsma-Smit,[1] W.B. Nagengast,[1] V. Ntziachristos,[3] G.M. van Dam.[1]
1. University Medical Centre Groningen, Groningen, Netherlands; 2. University Medical Centre Utrecht, Utrecht, Netherlands; 3. Technical University of Munich, Munich, Netherlands.

Introduction Optimal cytoreduction (CRS) in addition to Hyperthermic IntraPEritoneal Chemotherapy (HIPEC) is essential for the curative treatment of peritoneal carcinomatosis (PC). Currently, peritoneal lesions with a size of several millimeters can easily be missed with visual and tactile inspection. Better tumor detection could lead to improved radical cytoreduction. In this study we used near-infrared fluorescence (NIRF) imaging to enhance detectability of peritoneal metastases. Methods Patients scheduled for CRS and HIPEC were included in this feasibility study (n=7). The NIRF tracer bevacizumab-800CW targeting VEGF-A was administered intravenously 2 days prior to surgery. The peritoneal cancer index (PCI) was estimated by two surgeons independently, first by inspection and palpation, subsequently using the NIR intraoperative camera system. Biopsies were taken from fluorescent and non-fluorescent areas for ex-vivo validation and correlation of fluorescence. Results No (serious) adverse events related to tracer administration occurred in any of the patients. In total 87 peritoneal lesions were imaged and histologically analyzed. Thirty-one out of 58 fluorescent lesions were confirmed peritoneal metastases. All 23 non-fluorescent lesions were

cancer negative, indicating a sensitivity of 100%. Additionally, this method detected a positive resection margin and para-aortal lymph node metastasis that would not have been identified otherwise (Figure). Despite the relatively high false positive rate (47%), the PCI decreased 2.9 points on average per patient. Fluorescence was strongly correlated with vital tumor tissue ex-vivo at a microscopic level, with a tumor-to-normal ratio of 6,92 ± 2,47 (mean ± sd). Conclusion Intraoperative NIRF-imaging of PC during CRS is technically feasible and safe. This sensitive technique can lead to an optimal cytoreduction and stage migration, due to better patient selection, thus potentially preventing over and under treatment. We state that these results are promising for a subsequent phase II study.

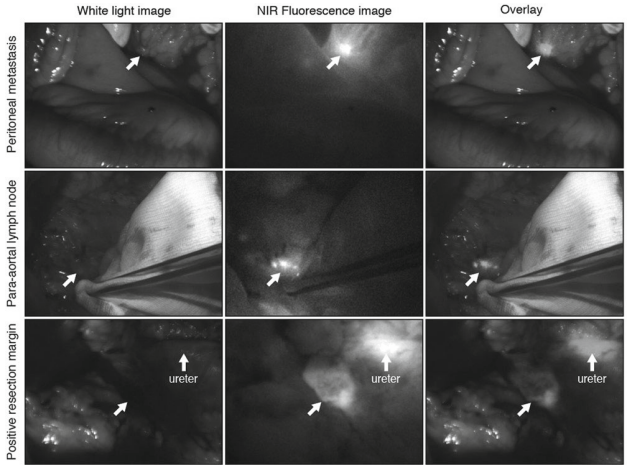


Figure: Intraoperative images captured by the NIRF camera system from a peritoneal metastasis (panel A to C), para-aortal lymph node metastasis (panel D to F) and positive resection margin (G to I), all confirmed by histopathology (indicated with a white arrow). Both the para-aortal lymph node and the positive resection margin were initially missed by visual and tactile inspection, however detected using the camera system. Physiological excretion of bevacizumab-IRDye-800CW was seen via the ureter (panel G to I).

P111

Validation of Verwaal's Prognostic Score in an Asian population D. Ng,* G. Tan, C. Chia, M. Kumar, K. Soo, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction Cytoreductive Surgery(CRS)and hyperthermic intraperitoneal chemotherapy(HIPEC)have afforded prolonged survival in selected cases of colorectal cancer with peritoneal metastases. Established prognostic factors include Peritoneal Carcinomatosis Index and Completeness of Cytoreductive Score. A Prognostic Score for prediction of survival outcome after CRS+HIPEC was developed by Verwaal et al. based on patients with colorectal cancer with peritoneal metastases treated at the Netherlands Cancer Institute. Verwaal's Prognostic Score(VPS)has not been validated in any external cohort and thus its universal applicability remains unproven. We aim to evaluate the predictive accuracy of the Prognostic Score in a cohort of patients treated at an Asian institution. Materials and Methods: Between 2000 and 2015, 50 adult patients underwent CRS+HIPEC for colorectal cancer with peritoneal metastases. The variables included in VPS are location of the primary tumour(colon or rectum), grade of malignancy, histological appearance (signet cell or non-signet cell) and number of affected regions(1-7)in the abdomen. The Prognostic Score was validated by assessing its extent of discrimination. This was quantified using Harrell's concordance index(c-index). The variables included in VPS were also evaluated in our population to assess if they were statistically significant. Survival-related univariate comparisons were performed using the log rank test. Results The concordance index associated with VPS was 0.59. On univariate analysis, grade of malignancy(p-value:0.01), histological appearance(p-value:0.01)and number of affected regions(p-value: 0.05)were significant for overall survival while location of primary tumour (p-value: 0.448) was not. No factor was significant on multivariate analysis. Conclusion The observed concordance index demonstrates a moderate level of predictive accuracy. All variables included in VPS are closely aligned with that of our population except location of primary tumour. This could be due to our preferential selection of colonic primaries for CRS+HIPEC. Hence, to increase the accuracy of the Prognostic Score, modification is required for a predominantly Asian population.

P112

Robotic Versus Laparoscopic Surgery for Rectal Cancer: An Analysis of the Nationwide Inpatient Sample (NIS) Database M. Julien,* M. Shabahang, J. Blansfield, K. Halm, K. Long. *Geisinger Medical Center, Danville, PA.*

Introduction: Robotic surgery has gained popularity in surgical oncology. The objective of this study was to compare robotic to laparoscopic surgery in patients who have rectal cancer surgery with regard to clinicopathologic and economic parameters. Methods: A retrospective analysis of all elective rectal cancer surgeries performed laparoscopically or robotically between January 1st 2009 and December 31st 2012 was conducted using the Healthcare Cost and Utilization Project's Nationwide Inpatient Sample (NIS) database. Results: Robotic procedures accounted for 158(17%) of the 913 of rectal cancer procedures included in the study. Overall, urban teaching hospitals performed the highest portion (65%) of robotic rectal cancer procedures and more often in males overall (62%). Univariate analysis between robotic and laparoscopic cohorts showed broad similarity in patient sociodemographic as the groups were not statistically different with respect to age (62.4yo v 62.4yo, p=0.90), gender (61.3% male v 66.5% male, p=0.22), race (72.9% white v 67.7% white, p=0.41), risk of mortality (p=0.75), severity of illness (p=0.81), income quartile (p=0.80) or primary payer (p=0.32). Length of stay was decreased in the robotic group; 6 days vs 5 (p=0.001). On multivariate analysis, robotic surgery was associated with significantly higher hospital charges ($12,512; 95% CL $7027-$17504) and a significantly lower conversion to an open procedure rate1% compared to 12% in the laparoscopic group. Inpatient outcomes with robotic procedures were also comparable to laparoscopic procedures; specifically the infection rate (4.4% v 3.7%, p=0.67), pulmonary (2.5% v 1.3%), gastrointestinal (2.53% v 3.44% p=0.56), cardiovascular (1.3% vs 1.3% p=0.95), and operative complications (1.3% vs 2.1% p=0.48), as well as inpatient mortality(0.6% vs 0.8% p=0.83). Conclusions: Overall the patient selection and perioperative outcomes are similar between patients undergoing laparoscopic and robotic rectal surgery. Most importantly, it appears that despite higher costs of robotic rectal resection, the rate of conversion to open procedures is significantly lower than similar laparoscopic procedures.

P113

The Relationship of Socioeconomic Disparities with Age-Related Rates of Colorectal Cancer in the United States E. Gabriel,* E. Al-Sukhni, K. Attwood, P. Boland, S. Nurkin. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction Although the overall incidence of colorectal adenocarcinoma (CRC) in the US is decreasing, the incidence for patients under age 50 is increasing. The aim of this study was to identify socioeconomic disparities associated with the age-related, increasing rate of CRC. Methods The National Cancer Data Base (NCDB) was used to identify patients with CRC from 1998-2011. Patients were stratified by age (< 50 vs > 60); ages 50-60 were omitted from the analysis to minimize overlapping trends between the two age groups. Relative frequencies (RF) of CRC by year were plotted against common socioeconomic variables (gender, race, education, income). Changes in RF over time were calculated using linear regression. Times from diagnosis to treatment (surgery, neoadjuvant/adjuvant therapy, or systemic therapy) were also compared. Results A total of 516,185 patients were studied; 395,710 with colon and 120,475 with rectal cancer. Patients < 50 had higher RF for stage III/IV CRC per year compared to > 60 (Figure 1 A/C), with the highest rates of increase in stage III colon cancer. Conversely, patients had lower RF for stage I/II CRC per year with a similar rate of decrease in both stage II colon and rectal cancer (each 0.18% per year). Patients < 50 had higher RF for CRC if they were male, black or Hispanic, and less educated. For males, RF of colon and rectal cancer increased yearly by 0.02% and 0.04%, respectively. RF of rectal cancer for black patients < 50 increased 0.06% per year, but decreased by 0.05% per year for colon cancer. Hispanic patients had the highest rates of increase for both colon (RF = 0.30% per year, Fig 1B) and rectal cancer (RF = 0.25% per year, Fig 1D). No clinically significant differences were observed for time to any treatment. Conclusions The rate of CRC among younger patients (< 50) in the US has been increasing, but this study shows that higher RFs are dispropor-

tionately comprised of more advanced (stage III/IV) cancer. These findings warrant further investigation to develop improved strategies for the earlier detection of CRC in patients < 50, with particular emphasis on the identified populations that have disparate trends in CRC.

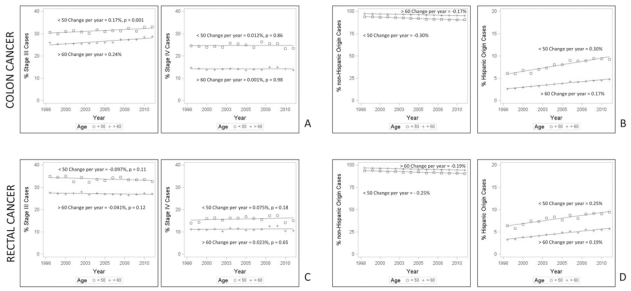


Figure 1. Top panel shows relative frequencies (RF) of stage III (left) and IV (right) colon cancer from 1998-2011, whereas bottom panel shows RF of rectal cancer. Patients aged < 50 years have higher RF of both colon (A) and rectal (C) cancer compared to age > 60. The largest socioeconomic disparity was identified among Hispanic patients. Younger, Hispanic patients have higher RF for colon (A) and rectal (B) cancer with the steepest change per year in colon (B, right). All differences between < 50 and > 60 are significant to p < 0.001. Percent change per year of each curve is significant to p < 0.001, unless otherwise stated.

P114

Can Mapping Procedures Prior to Definitive Wide Local Excision for Perianal Paget's Disease Decrease Local Recurrence Rates?
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Introduction: The microscopic extent of perianal Paget's disease is difficult to determine due to its infiltrative and discontinuous nature. Wide local excision with generous margins is standard therapy but positive margins are common and local recurrence rates are reported between 40 and 60%. Methods: We perform serial mapping procedures to identify the microscopic extent of disease prior to definitive resection. Each mapping procedure involves drawing gridlines at one centimeter intervals around the area of macroscopic disease. Representative punch biopsies are taken and their locations according to the grid are documented. Photos are taken to reproduce the grid for future procedures. Repeat mapping procedures are performed based on the location of positive biopsies until circumferential negative biopsies have been obtained. Definitive resection is planned based on the final negative biopsy locations. Results: Over the past 10 years, 19 patients were treated for perianal Paget's disease. The mean number of biopsies taken during the first mapping procedure was 36 which yielded an average of 10 positive biopsies. Second and third mapping procedures were required in 9 and 1 patient respectively. The median size of final resection defect was 105 cm2 (range 50 – 625cm2). Complex reconstruction was required in all but two patients. Five patients (26%) had invasive disease. Over the study period, only two patients developed local recurrences (11%), each with a disease-free interval of approximately 16 months. One of these patients suffered from anal sphincter dysfunction and elected to have recurrence treated with abdominoperineal resection. She remains without evidence of disease nine years later. The second patient with recurrence has refused treatment. Median follow-up in the remaining disease-free patients with >6 month of follow up (n=13) is 32 months (range 6 to 74 months). Conclusions: Serial mapping procedures prior to definitive resection for perianal Paget's disease appears to provide better long-term local control but longer follow up is necessary.

P115

To Screen or Not to Screen: Colonoscopy, a Story of Successful Population-Based Screening
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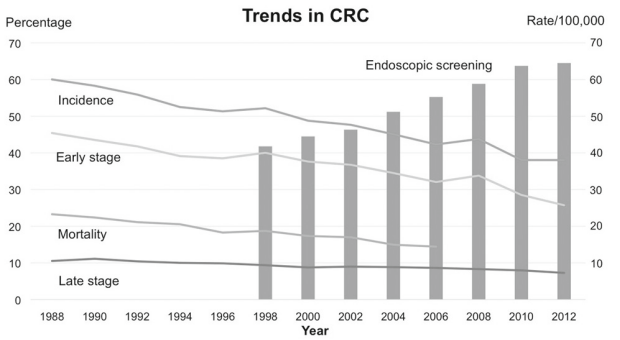
Screening for neoplasia of the breast and prostate has come under increasing scrutiny. However, little is understood regarding the temporal impact of screening on incidence and mortality for colorectal cancer (CRC). Methods: We selected states that had both CRC screening prevalence estimates from The Behavioral Risk Factor Surveillance System (BRFSS) and cancer registry data from The Surveillance, Epidemiology, and End Results (SEER) data from 1988-2012. We used SEER*Stat to compute age-adjusted incidence and mortality rates by state. Correlation coefficients were computed for change in screening. Results: The states California, Connecticut, Georgia, Hawaii, Iowa, New Mexico, and Utah were included. Each state had unique population and tumor characteristics for age, gender, race, socioeconomic status, stage of presentation, and location of the primary, $p < 0.0001$. Over the study period for ages 50 +, there was an increase in screening endoscopy (41 to 64%, R^2 =0.77, p<0.0001) and a slight decrease in fecal occult blood testing (25 to 23%, R^2 =0.28, p<0.0001). Similar trends were noted by state. There was an inverse relationship between increased screening endoscopy and incidence of CRC over time (60.03 to 34.68/100.000, R^2 =0.95 and p=<0.0001); this was pronounced for early disease (45.4 to 25.7/100,000, p=< 0.0001) and minimal for late stage disease (10.5 to 7.2/100,000, p=0.014). There was a comparable trend in mortality (23.27 to 13.47 per 100.000) (Figure 1). When evaluating states individually, the association between increasing endoscopic screening and the trends in incidence and mortality were robust (R^2 0.75 – 0.92 and R^2 0.65-0.95, respectively, p<0.0001). However, when states were analyzed collectively the association of screening with decreases in incidence and mortality was weaker (R^2 =0.27, p=0.005 and R^2 = 0.65, respectively, p=0.06). Conclusions: Increased screening for CRC coincides with a decrease in incidence and mortality, disproportionality decreasing early stage cancer. This correlation is very strong within states but diminished between states, suggesting factors in addition to screening are influencing the epidemiology of CRC.



Trend in colorectal cancer: Endoscopic screening, incidence, stage of presentation and mortality.

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The Role of Glutaminase C and Glutamine Metabolism in Epithelial-Mesenchymal Transition in Colorectal Cancer
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Introduction Glutamine is a crucial source of nutrition for cancer, in which enhanced catabolism of glutamine allows for a greater rate of proliferation and propensity to metastasize. The mitochondrial enzyme glutaminase C metabolizes glutamine and is the initial enzyme of the glutamine-catabolizing chain, its expression being up-regulated in malignancies, including in colorectal cancer. Glutaminase C is already a target for cancer treatment, but its association with metastasis in colorectal cancer is unknown. The link between the two cardinal features of cancer, glutamine metabolism and epithelial-mesenchymal transition, a cellular phenotype associated with metastasis, will be explored in colorectal cancer. Methods Following lysis, whole cell extracts of colorectal cancer cell lines were immunoblotted for gluaminase C and E-cadherin, an important marker of the epithelial phenotype. Glutaminase C knockdown in colorectal cancer cell lines was conducted by small interfering RNA or short hairpin RNA, following which the whole cell extracts were immunoblotted for epithelial (E-cadherin) and mesenchymal (vimentin) markers. Cell migration of colorectal cancer cells were analysed using the wound-healing assay. Results There was an inverse relationship between glutaminase C and E-cadherin expression in colorectal cancer cell lines of differing genetic background. Furthermore, knockdown of glutaminase C demonstrated an increase in expression of E-cadherin and decrease in expression of vimentin. Knockdown of glutaminase C also resulted in decreased cell migration of colorectal cancer cells. Conclusion In colorectal cancer cells, glutaminase C expression plays an important role in epithelial-mesenchymal transition, a phenotype that is associated with metastasis. The downstream mechanisms of glutaminase C-induced epithelial-mesenchymal transition will be investigated further.

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Liposomal Indocyanine Green for Intraoperative Imaging of the Ureters and Prevention of Iatrogenic Damage E. Nizri,[1]* Y. Friedman-Levy,[2] G. Lahat,[1] S. Eyal,[2] S. Magdassi.[2] *1. General Surgery, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; 2. Hebrew University, Jerusalem, Israel.*

Introduction: The identification of the ureters is a critical step during colorectal resection procedures, commonly complicated by increased intra abdominal fat and the use of laparoscopic techniques which limit tactile perception. Indocyanine green (ICG) is a near infra-red dye approved for human use but it is metabolized by the liver, and appears in the urine only in negligible amount. Our aim was to test whether liposomal formulation of ICG could drive its excretion through the urinary pathways. Methods: Liposomal ICG was prepared by sonication. Characterization of the liposomes in vitro was done by fluorometry, diffuse light scattering (DLS) and electron microscopy. After in vitro characterization, the liposomes were i.v. injected to FVB mice and ureteral identification was tested after colonic mobilization. The mean intensity of ureters fluorescence was calculated as ureters/retroperitoneal ratio (URR), Results: We produced liposomes at 30nm, 60nm and 100nm. In all liposomes, ICG was located inside the membrane, with no dye outside the liposomes. The sizes of the liposomes were concordant when measured by DLS and microscopy. The latter also revealed a lipid bilayer and round particles. In vivo, at 8mg/kg ICG, all the liposomal formulations were superior to free ICG, with URR of 4.86±0.45, 5.5±0.85, 4.23±1.11 for the 30nm, 60nm and 100nm liposomes, respectively vs. 1.64±0.16 for free ICG ($p<0.001$). Urine samples taken from mice showed increased fluorescence from animals treated with the liposomal formulation, indicating indeed that ICG was secreted to the urine. For signal optimization, we further used the 60nm formulation. We next tried different ICG doses, namely, 4mg/kg and 16mg/kg. As expected, decrease of ICG dose led to decrease in the URR. However, the 16mg/kg dose did not increase URR due to increased retroperitnoneal (background) fluorescence. The URR was correlated to the blood fluorescent intensity, raising the possibility that the liposome main mechanism of action is the prevention of ICG liver uptake. Conclusions: Liposomal ICG is secreted to the urinary pathways and enables ureter identification without dissection.

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The Role of Positron-Emission Tomography/Computed Tomography in Patients with Colorectal Liver Metastases Who are Candidates for Liver Resection: Is It Useful? T. Hiraide,[1]* T. Sakaguchi,[1] H. Kikuchi,[1] S. Furuhashi,[1] R. Kiuchi,[1] M. Takeda,[1] Y. Shibasaki,[1] Y. Morita,[1] K. Fukumoto,[2] K. Hiroyuki.[1] *1. Second Department of Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan; 2. Iwata City Hospital, Iwata, Japan.*

Background: This study aimed to analyze the role of F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) as a preoperative diagnostic modality in patients with colorectal cancer liver metastasis (CRLM) who were candidates for liver resection. Methods: In the first term (2002 - 2008), we intended to identify the criteria under which PET was recommended in a retrospective analysis of 50 patients with CRLM. In the second term (2008 - 2013), 30 of 45 patients with CRLM underwent PET/CT by these criteria. The ability of PET/CT to detect extrahepatic lesions was compared with conventional radiologic modalities, such as enhanced CT and magnetic resonance imaging (MRI). Results: In the first term, all 25 non-PET patients underwent hepatectomy, while hepatectomy was canceled in six of 25 PET patients due to extrahepatic lesions. The prognosis after hepatectomy was similar between the PET and non-PET patients. Since each hepatectomy-canceled patient showed Fong's clinical risk scores (CRS) of three or higher, we determined that the preoperative PET/CT should be performed when the CRS was greater than or equal to three. In the second term, extrahepatic lesions were identified in four of the 30 PET patients. These lesions were detectable under enhanced multi-detector row CT (MDCT). The lesion detection rate for PET/CT was similar to that of MDCT. Disease quickly recurred after hepatectomy in the PET group (median disease-free duration 11.5 months versus 40.5 months), suggesting that preoperative PET/CT did not benefit hepatectomy-candidates with CRLM. Conclusions: In the hepatectomy-candidates with CRLM, PET/CT is not always a necessary diagnostic modality.

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Evolution of Lymph Nodes Detected by Pathologist in Colorectal Cancer: A Comparison of National Cancer Data Base and Surveillance, Epidemiology and End Results Program (SEER) Between 1998-2010 S. Saha,* M. Hicks, V. Onkoba, J. Gernand, M. Arora, H. Gayar, A. Ahsan, W. Liu, P. Ng, D. Wiese. *McLaren Flint, Flint, MI.*

Introduction The most important prognostic factor for colorectal cancer (CRCa) is the status of the lymph nodes (LNs). LN status directly correlates with the number (No) of LNs detected by the pathologist. Since 2012, emphasis has been made to identify at least 12 patients (Pt.) for adequate staging. Hence, a comparative analysis between National Cancer Data Base (NCBD) and Surveillance, Epidemiology and End Results Program (SEER) to determine the trend in average (Avg.) no. of LNs detected as well as no. of positive LNs for CRCa pts between 1998-2010. Methods Between 1998-2010, there were 295,554 patients (Pts) for colon (C) and 56,913 Pts for rectal (R) cancer (Ca) in NCBD and 141,943 Pts for C and 32,837 for R Ca in SEER, after excluding for incomplete data regarding age, sex, grade, no. of nodes, no. of positive LNs, and TNM stage. Statistical dependence was evaluated using Spearman's rank correlation coefficient. Results Between 1998-2010 among NCBD and SEER CCa Pts, avg. no. of LNs detected increased gradually from 12.6 to 18.5 in NCBD and from 12.5 to 19.06 in SEER. For R Ca Pts, LN yield also increased from 11.02 to 14.98 in NCBD and 9.53 to 13.07 in SEER respectively. No. of the LNs in CCa also increased from 3.87 to 5.81 in NCBD vs 3.81 to 4.49 in SEER. Conclusions Between 1998-2010, among NCDB and SEER Pts, there has been a gradual increase in the LN yield, avg. of positive LNs for CRCa Pts. across the nation. Whether the increase in survival during this period is due to LN yield or other biological factors needs to be determined by a mutli-institutional study.

Table I. Lymph node yield (LNY) and average number of positive (+ve) LNs detected for rectal and colon cancer patients of the NCDB and SEER.

	NCDB	NCDB	NCDB	NCDB	SEER	SEER	SEER	SEER
Year of Diagnosis	LNY Rectal	Avg # +ve LNs Rectal	LNY Colon	Avg # +ve LNs Colon	LNY Rectal	Avg # +ve LNs Rectal	LNY Colon	Avg # +ve LNs Colon
1998	11.02	4.13	12.57	3.87	9.53	4.26	12.46	3.81
1999	11.01	4.06	12.68	3.93	9.03	4.08	12.56	3.92
2000	11.09	4.20	12.95	3.85	9.04	4.16	12.37	3.85
2001	11.34	4.24	13.29	3.89	9.24	4.02	12.80	3.96
2002	11.45	3.93	13.76	3.97	9.72	3.95	13.25	3.98
2003	11.20	4.01	13.17	5.37	9.58	4.20	13.79	4.10
2004	11.90	4.02	13.54	5.88	10.74	4.12	14.27	4.12
2005	12.09	4.16	14.30	5.85	10.62	4.12	15.06	4.30
2006	13.45	4.20	15.39	6.24	11.79	4.03	15.97	4.48
2007	14.32	4.22	17.21	6.44	12.42	4.21	17.56	4.57
2008	14.80	4.28	17.84	6.60	12.87	4.41	18.10	4.70
2009	14.79	4.32	18.36	6.57	12.89	4.28	18.79	4.64
2010	14.98	4.02	18.54	5.81	13.07	3.97	19.06	4.49

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Emergency Room Utilization by Patients with Colorectal Cancer: Predictors of Use and Subsequent Admission N. Wasif,[1]* L.R. Sangaralingham,[2] D. Etzioni,[1] H. Van Houten,[2] D. Asante,[2] N. Shah.[2] *1. Surgery, Mayo Clinic in Arizona, Phoenix, AZ; 2. Mayo Clinic in Minnesota, Rochester, MN.*

Introduction Utilization of emergency room (ER) services by cancer patients has not been well studied. Our primary objective is to assess the utilization of ER services by patients diagnosed with colorectal cancer and to identify predictors of use and admission from the ER. Methods We utilized administrative claims data from a commercial insurer (Optum Labs Data Warehouse) to retrospectively identify privately insured and Medicare Advantage patients who were diagnosed with colorectal cancer between 2008 and 2013. The primary outcomes were ER utilization or admission from the ER within six months of diagnosis. Logistic regression analysis was used to identify predictors of ER utilization and subsequent hospitalization. Results Of 23138 patients with colorectal cancer, 7085 (30.6%) had at least one ER visit within six months of the index diagnosis. ER utilization increased from 26.4% in 2008 to 35.8% in 2013 ($p<0.001$). Compared to patients with no ER visit, those who visited the ER tended to be older (mean age 66 vs. 60, $p<0.001$), White (62% vs. 57%, $p<0.001$), and have more co-morbidities (Charlson score 3+ 68% vs. 52%, $p<0.001$). The most common reasons for

ER utilization were abdominal pain (16.4%), chest pain (11.3%), and other acute lower respiratory infections (7.8%). Of the 10,959 ER visits recorded, 1509 (13.8%) resulted in a hospital admission. In these patients, the most common diagnoses were abdominal pain (36%), GI hemorrhage (33%) and intestinal obstruction (27%). Predictors of ER visits included advancing age, more recent diagnosis, co-morbidity, and receipt of chemotherapy or radiation. Advancing age and co-morbidity, in addition to having had a prior surgical resection, were also predictors of admission following an ER visit (Table 1). Conclusions A third of patients recently diagnosed with colorectal cancer visit the ER, and 14% are subsequently admitted for inpatient care. We identify a high risk subset of patients that could be targeted with strategies designed to address problems in the outpatient setting and hence decrease ER utilization and subsequent admissions.

	Predictors of ER Visits (n= 23,128)			Predictors of Admission (n = 7085)		
Covariates	Odds Ratio	95% CI	p value	Odds Ratio	95% CI	p value
Gender						
Male	Ref					
Female	1.03	0.97-1.09	0.41	1.04	0.89-1.20	0.63
Race						
White	Ref					
Other	0.99	0.93-1.05	0.70	0.97	1.83-1.14	0.73
Age						
18-44	Ref					
45-54	**0.81**	0.71-0.92	***0.001***	1.20	0.50-2.86	0.68
55-64	**0.73**	0.65-0.83	***<.0001***	1.86	0.83-4.17	0.13
65-74	**1.45**	1.28-1.65	***<.0001***	**11.22**	5.24-24.04	***<.0001***
75+	**2.37**	2.09-2.68	***<.0001***	**17.45**	8.18-37.21	***<.0001***
Year of Diagnosis						
2008	Ref					
2009	0.99	0.88-1.10	0.79	0.94	0.70-1.26	0.66
2010	1.05	0.95-1.17	0.35	0.88	0.66-1.17	0.37
2011	**1.12**	1.01-1.24	***0.03***	**0.72**	0.54-0.95	***0.02***
2012	**1.23**	1.11-1.36	***<.0001***	0.90	0.70-1.19	0.48
2013	**1.35**	1.22-1.49	***<.0001***	0.90	0.69-1.17	0.43
Charlson Score						
0-2	Ref					
3+	**1.58**	1.49-1.68	***<.0001***	**1.27**	1.06-1.52	***0.01***
Chemotherapy						
No	Ref					
Yes	**1.38**	1.23-1.55	***<.0001***	0.48	0.32-0.72	***<.0001***
Surgery						
No						
Yes	1.08	0.99-1.18	0.09	**1.72**	1.35-2.18	***<.0001***
Radiation						
No	Ref					
Yes	**1.43**	1.21-1.67	***<.0001***	0.68	0.42-1.07	0.10

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Extended Pelvic and Sacral Resection in the Surgical Management of Recurrent Low Rectal Cancer W.S. Gawad,* M.M. Khafagy, M.A. Gameil, N.M. Mokhtar, O.M. Mansour, M.M. Lotayeif, M.M. Negm. *National Cancer Institute - NCI, Cairo, Egypt.*

Background: The incidence of rectal cancer recurrence after surgery is 5-45%. Extended pelvic resection which entails En-bloc resection of the tumor and adjacent involved organs provides the only true possible curative option for patients with locally recurrent rectal cancer. Aim: To evaluate the surgical and oncological outcome of such treatment. Patients & Methods: Between 2008 and 2013 a consecutive series of 50 patients with locally recurrent rectal cancer underwent abdominosacral resection (ASR) in 24 patients, total pelvic exentration with sacral resection in 12 patients and extended pelvic exentration in 14 patients. Patients with sacral resection were 35, with the level of sacral division at S 2-3 interface in 13 patients, at S 3-4 in 18 patients and S 4-5 in 4patients. Results: Fivty patients, male to female ratio 1.7:1, mean age 45 years (range 25-65Y) underwent extended pelvic resection in the form of pelvic exentration and abdominosacral resection. The morbidity, re-admission and mortality rates were 55%, 37.5%, and 5% respectively. Mortality occurred in 3 patients due to enteric fistula and abdominal sepsis. A R0 and R1 sacral resection were achieved in 63% and 37% respectively. Forty-five patients underwent curative resection and showed significantly improved survival with 5-year survival rate of 26.3% compared to 5 patients with palliative resection in a survival rate of 0%. Conclusion: Extended pelvic resection as pelvic exentration and sacral resection for locally recurrent rectal cancer are effective procedures with tolerable mortality rate and acceptable outcome. The associated morbidity remains high and deserves vigilant follow up.

P122

Extent of Adjuvant Chemotherapy Use in Stage II and Stage III Colon Cancer through Examination of a National Cancer Data Base (NCDB) K. Nagatomo,* A. Lefkowitz, N. Carp, V. Siripurapu. *Main Line Health, Philadelphia, PA.*

Introduction: The aim is to investigate stage II and stage III colon cancer (CC) treatment nationwide. Chemotherapy (AC) use in stage II CC is accepted treatment in those with poor prognostic features. Standard of care for stage III CC is AC and shows 30-40% decrease in relapse and disease specific mortality. Methods: A total of 1,063,631 colon cancer cases in NCDB between the years of 1998 to 2012 were evaluated. This was sub-analyzed for stage II and III CC and AC treatment. Comparison of pathologic stage II and III colon cancer for AC use by age group and years of diagnosis (1998-2005 vs 2006-2012) was performed. All data was imported into SPSS and labeled using PUF SPSS import. All variables were analyzed in SPSS using one- and two-way frequency tables and crosstabs. Raw counts and percentages were calculated in the resulting tables. Results: Age analysis of colon cancer reports their mean, median and mode of age as 71, 69.1 and 77 respectively. Gender breakdown is 52% male and 48% female. Ethnicity breakdown is 81% Caucasian, 12% African American, 4% Hispanic, 2% Asian. Of stage II CC 20% are treated by AC with only 65% of stage 3 treated by AC. Extent of Stage II diseases treated by AC was 36.4% for ages 18-58y, compared to 63.7% for ages 59-90y. In addition, extent of stage III disease treated by AC was 32.5% for ages 18-58y and 67.5% for ages 59-90 y. Interestingly, 18% of stage II and 65% of stage III colon cancer were treated with AC in 1998-2005 whereas 22% of stage II and 60% of stage III colon cancer were treated with AC in 2006-2012. Conclusions: The database notes a significant difference in ethnic groups being captured by the NCDB. Stage II colon cancer seems to be vastly over-treated based on analysis of this database. Stage 3 CC treatment by AC is surprisingly low even taking into account age stratification. Our study shows a 4% increase in AC use in stage II colon cancer from 1998-2005 to 2006-2012 compared to a 5% reduction of extent of AC use in 2006-2012 from 1998-2005 for stage III colon cancer. AC use is possibly overused for stage II diseases and more conservatively for stage III diseases.

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The Interaction of Primary Histology and Extent of Surgery on Overall Survival in Appendiceal Cancer K. Peng,* R.J. Gray, B.A. Pockaj, C. Stucky, N. Wasif. *Mayo Clinic, Phoenix, AZ.*

Introduction Cancer of the appendix is an 'orphan' cancer that is often found incidentally following a routine appendectomy. Although subsequent colectomy is often recommended, an improvement in long-term survival has not been clearly demonstrated. We postulate that the underlying histology predicts the utility of a colectomy. Methods The National Cancer Database was used as the data source for this study. Patients diagnosed with appendix cancer from 1998-2006 were identified and divided into mucinous adenocarcinoma (MA), non-mucinous adenocarcinoma (NMA), goblet cell carcinoid (GCC), carcinoid and signet cell histology. Patients were re-staged using AJCC 7th edition criteria and all patients with Stage IV tumors were excluded from subsequent analyses. The association between colectomy and overall survival was studied using Cox regression analyses after controlling for age, sex, race, co-morbidity, grade, T stage and N stage. Results Our study population consisted of 12,160 patients, with breakdown by histology as follows: 4.9% signet cell, 12.8% GCC, 22.4% carcinoid, 27.7% MA, and 32.3% NMA. Sex distribution was almost equal (50.5% men) and the median age was 58. Stage distribution was 29.3% Stage I, 49.2% Stage II, and 21.5% Stage III. Overall, 25.6% patients underwent appendectomy, 55.9% colectomy, 11.1% had no surgery and 7.5% were unknown. On adjusted analyses, an association between colectomy and improved long-term survival compared to appendectomy alone was seen only for signet cell (HR 0.64, 95%CI 0.43-0.95) and NMA (HR 0.66, 95%CI 0.57-0.77). Compared to appendectomy alone, colectomy was not associated with improved long-term survival for carcinoids >2cm in size (HR 0.79, 95%CI 0.56-1.2) or MA (HR 0.93, 95%CI 0.78-1.12), and was associated with worse survival for GCC (HR 1.76, 95% CI 1.02-3.05). Conclusions An association between colectomy and improved long-term survival for appendix

cancer is seen only for signet cell and NMA and not for MA or carcinoid tumors >2cm in size. The decision to perform a colectomy for Stage I-III appendix cancer should take into consideration primary histology.

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Inhibition of the AIM (Adhesion, Invasion, Migration) Pathway Limits Tumor Cell Metastatic Properties M.E. Stack,* A. Uppal, S. Wightman, G. Oshima, S.P. Pitroda, M. Beckett, N.N. Khodarev, R.S. Rock, R.R. Weichselbaum, M.C. Posner. *Surgery, University of Chicago, Chicago, IL.*

Introduction: Oligometastasis represents a distinct state of limited metastasis between local and widely metastatic cancer. We previously identified the 14q32 micro-RNA cluster as a mediator of an oligmetastatic phenotype by targeting the AIM pathway, a functional motif of genes that enhances the ability of cancer cells that have escaped the primary tumor to undergo metastatic growth by regulating cell adhesion, ECM interactions and cell motility. Here we demonstrate the effectiveness of four different migration inhibitors on the AIM pathway. Methods: MDA-MB-231, human breast cancer cells, and HCT116, human colon cancer cells, were treated in vitro with four migration inhibitors targeting different proteins involved in migration, invasion and adhesion, including Y-27632 (ROCK2 inhibitor), SMIFH2 (formin inhibitor), CK-666 (Arp2/3 inhibitor), and 4-HAP (myosin II activator). Proliferation assays were done to screen for doses without significant effect on tumor cell growth. In vitro adhesion, migration and invasion assays were then performed in order to generate dose-response curves. Results: Proliferation assays revealed doses below 50uM for Y-27632, 10uM for SMIFH2, 50uM for CK-666 and 4uM for 4-HAP had no significant effect on growth for both MB231 and HCT116 cells. In both cell lines, we found a significant decrease in cell adhesion following treatment with each inhibitor in a dose-dependent manner ranging from a 36-78% reduction (p-values <0.05). Similarly, we found a significant decrease in cell migration and invasion for both cell lines, ranging from a 56% to 89% reduction and a 50% to 97% reduction respectively (p-values <0.05). MB231 demonstrated a more sensitive response profile. The compound 4-HAP was the most potent inhibitor, requiring doses ranging from 1-4uM to exhibit significant inhibition on adhesion, migration and invasion. Conclusions: The AIM pathway has been implicated as a key factor in differentiating oligometastatic and polymetastatic phenotypes. Selective inhibition of the AIM pathway with migration inhibitors may promote an oligometastatic phenotype by limiting circulating tumor cells' ability to adhere, migrate and invade

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Predictors of Tumor Response and Survival After Preoperative Chemoradiotherapy for Locally Advanced Rectal Adenocarcinoma R. Silva-Martínez,* M. Ramirez-Ramirez, M. Gutierrez de la Barrera, P. Luna-Perez. *Hospital de Oncología IMSS CMN SXXI, México, Distrito Federal, Mexico.*

Background. Pathologic response after preoperative chemoradiotherapy (PCRT) is associated as prognostic indicator for local control and survival in patients with locally advanced rectal adenocarcinoma. However, is hard to predict who will be responders. Many parameters for predicting tumor response and survival have been identified; they are based in tumor characteristics. Little information about the immune/inflammatory relation has been reported. Objective. Identify single, practical and reproducible parameters to predict tumor response and survival to PCRT for locally advanced rectal cancer. Material and methods. Retrospective analysis was performed. Inclusion criteria were: tumor location between 0-10 cm of the anal verge, pre-treatment tumor stage II-III determined by CT and/or endorectal US. Pretreatment CEA level of 5 and neutrophil/lymphocyte ratio (NLR) of 4 was established mean ROC curve. Pathologic response was determined by Mandard classification. Patients received 45-50.4 Gy + 5-FU (450 mg/m^2 days 1–5 and 28–32 of RT or capecitabine. 4-8 weeks after PCRT surgery was performed. Results. From 2005 to 2011, 121 males and 101 females were treated. Median age was 57 years. 39 and 183 patients had pretreatment: stage II and III, respectively. 145 patients had NLR <4 and 77 >4. 107 had CEA <5ng and 115 >5 ng. Univariate and multivariate analysis of pathologic response according studied covariates is depicted on Table 1. After follow-up of 56 months, 5-year survival in those patients with PCR, near PCR, and no response was: 73%, 64% and 48%, respectively (p=0.001). 5-year survival in those with NLR <4 was 77%, conversely 45% in those with >4 (p=0.019). 5-year survival in patients with CEA<5ng was76%, conversely 58% of those with >5ng. Conclusion. Practical parameters as primary tumor stage, pretreatment CEA levels and NLR are predictors of response and survival for rectal cancer patients treated with PCRT and surgery.

Pathological Response

Covariate	No Response (%)	Near Complete Response (%)	Complete Response (%)	p	OR (CI)
CEA <5	33 (37.5)	32 (47.1)	42 (63.6)	0.006	2.8 (1.4-5.6)
CEA >5	55 (62.5)	36 (52.9)	24 (36.4)		
Stage II	13 (14.7)	6 (8.8)	20 (30.3)	0.003	4.9 (2.0-12.2)
Stage III	75 (85.2)	62 (91.2)	46 (69.7)		
NLR<4	41 (46.6)	42 (61.8)	62 (93.9)	<0.001	18 (5.7-56)
NLR>4	47 (53.4)	26 (38.2)	4 (6.1)		

p value = chi square.
OR = Odds Ratio by Logistic Regression

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ACA Solutions for Colorectal Cancer Workup: Affordable Care? J. Perone,* K. Olino, J.R. Zatarain, A. Gajjar, D. Tyler, K. Brown. *UTMB- Galveston, Galveston, TX.*

INTRODUCTION: Appropriate workup and staging for colorectal cancer (CRC) may be done as an outpatient (OP) or inpatient (IP) depending on clinical and socio-economic factors. Uninsured patients or patients with high-deductible plans face barriers to OP services, resulting in potentially unnecessary admissions. We hypothesize that uninsured patients are more often worked up as an IP, at greater expense than insured patients. METHODS: We performed a retrospective review of patients with a confirmed diagnosis of colorectal adenocarcinoma over an 18-month period at our institution. We included patients for whom we could identify encounters related to staging workup: colonoscopy, pathology review, CT chest/abdomen/pelvis and CEA. We recorded whether each encounter was OP or IP, and the associated charges. We compared the rates of IP workup and total charges based on insurance status. RESULTS: Of 81 patients, 32 had commercial insurance, 35 had Medicare, 7 had Medicaid, and 7 were uninsured. The average age was 64 ± 14 years, and 34 patients (42%) were women. 16% presented with stage I disease, 33% with stage II, 20% with stage III, and 28% with stage IV. Uninsured and Medicaid patients were twice as likely to have IP workup compared to commercially insured patients. Average IP stay for workup was 13 days for uninsured, 22 for Medicaid and 6 for commercially insured patients. The total average charges were higher for uninsured ($64,518) and Medicaid ($78,707) patients vs Medicare ($49,943) and commercially insured ($29,207, p= 0.018, ANOVA). Uninsured and Medicaid patients had 87% and 93% of workup charges from IP care, vs 62% for commercially insured. CONCLUSION: This exploratory analysis suggests uninsured patients generate higher charges for standard workup for CRC. This may be a result of a higher proportion of the workup being done as an inpatient. Medicaid patients, considered under-insured, have a similar practice and charge pattern to uninsured patients. These data suggest that expanding Medicaid and offering high-deductible health plans may not be a cost-effective solution to caring for uninsured patients. Strategies aimed at making out-patient services more available may be more cost-effective.

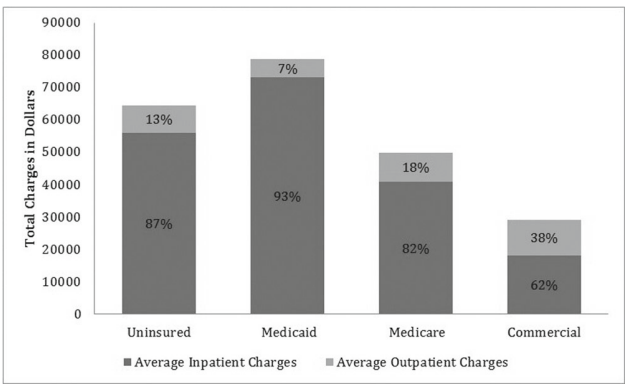


Figure 1. Total charges and inpatient/outpatient distribution by insurance status

P127

Detecting Peritoneal Surface Malignancies with Cathepsin-Based Fluorescent Imaging System C.H. Chan,* L. Liesenfeld, I. Ferreiro-Neira, J.C. Cusack. *Massachusetts General Hospital, Boston, MA.*

Background: Peritoneal surface malignancies, including peritoneal metastasis of appendiceal and colorectal cancers, are often considered incurable. The ability to detect microscopic peritoneal metastasis intraoperatively may guide surgical therapy. In this study, we aim to evaluate the suitability of a hand-held cathepsin-based fluorescent imaging system for intraoperative detection of appendiceal and colorectal peritoneal metastasis. Methods: Peritoneal tumors and normal peritoneal tissues were collected from patients with appendiceal and colorectal peritoneal metastasis. Expression of different cathepsins (CTS-B, -D, -F, -G, -K, -L, -O, and -S) was determined by quantitative RT-PCR and immunohistochemistry. The hand-held cathepsin-based fluorescent imaging system was used to detect peritoneal xenografts derived from human colon cancer cells (HT29, LoVo and HCT116) in nu/nu mice. Results: While the expression levels of CTS-B, -D, -L and -S could be higher in peritoneal tumors than normal peritoneum with a median (range) of 6.1 (2.9 – 25.8), 2.0 (1.0 – 15.8), 1.4 (0.8 – 7.0) and 2.1 (1.6 – 13.9) folds by quantitative RT-PCR, respectively, CTS-B was consistently the major contributor of the overall cathepsin expression in appendiceal and colonic peritoneal tumors, including adenocarcinomas and low-grade appendiceal mucinous neoplasms. Using peritoneal xenograft mouse models, small barely visible colonic peritoneal tumors (< 2.5 mm in maximum diameter) could be detected by the hand-held cathepsin-based fluorescent imaging system. Conclusions: Since cathepsin expression is higher in peritoneal tumors than underlying peritoneum, the hand-held cathepsin-based fluorescent imaging system could be useful for intraoperative detection of microscopic peritoneal metastasis. It may guide future surgical therapy and clinical trial is warranted.

P128

Perioperative Outcomes for Robotic Total Mesorectal Excision After Preoperative Chemoradiation for Rectal Cancer I. Nassour,* N.A. Borja, A. El Mokdad, H. Hirsch, M.A. Choti, J. Meyer, P. Polanco, G. Balch. *University of Texas Southwestern, Dallas, TX.*

Background: Laparoscopic total mesorectal excision (TME) after preoperative chemoradiation therapy (P-CRT) for mid to low rectal cancer was shown to be safe and feasible by a recent randomized trial (COREAN trial). However, the safety and short-term efficacy for robotic assisted laparoscopic TME has not been demonstrated. This study is a review of the perioperative outcomes of robotic TME after P-CRT for mid to low rectal cancer at our institution. Methods: All patients that underwent robotic TME after P-CRT for rectal cancer were retrospectively reviewed in our prospectively maintained, IRB-approved surgical oncology database. All relevant demographic, clinical, operative, pathology and perioperative data were analyzed. These were compared to the COREAN trial results. Results: From 2010 to 2014, 42 patients underwent robotic TME for rectal cancer after P-CRT. Mean patient age was 60+/-13. Robotic low anterior resections (R-LAR) were performed in 69% and 31% had a robotic abdominoperineal resection (R-APR). A majority were obese patients as 74% had a BMI≥25, and 50% had an ASA≥3. Conversion to open rate was 9.5% (n=4) but 3 of these were within the first 8 cases. Median estimated blood loss was 105 ml (50-400 ml). The 30-day major complication rate (Clavien III-IV) was 11.9% (n=5) and 90-day rate was 14.2% (n=6). One patient (2.4%) had an anastomotic leak. There were no mortalities within 90-days from operation. Median length of stay was 7 days (6-12 days). Pathological complete response was 19% while 24% had no response. The average number of lymph nodes harvested was 14.2+/-9.5. The circumferential resection margin was negative in 95.2% (n=40) of patients. Conclusion: As compared to laparoscopic TME patients in the COREAN trial, the robotic patients in our series were more obese and had a higher ASA classification. Our conversion rate was slightly higher, but this was related to the learning curve. All other short-term outcomes were similar. It appears that robotic TME is safe and feasible after P-CRT even among a more obese and higher risk population than previously reported in large series.

Characteristics and perioperative outcomes among patients undergoing total mesorectal excision: COREAN trial laparoscopic surgery cohort vs. UTSW robotic surgery cohort

Characteristics and Perioperative Outcomes	Laparoscopic (n=170)	Robotic (n=42)	p value
BMI > 25	63 (37.0%)	31 (74%)	<0.0001*
ASA 3 or 4	5 (2.9%)	21 (50.0%)	<0.0001*
Conversion to open procedure	2 (1.2%)	4 (9.5%)	0.0035*
Complication rate	36 (21.2%)	6 (14.2%)	0.3157*
Mortality	0 (0.0%)	0 (0.0%)	1.0000
Anastomotic Leak	2 (1.2%)	1 (2.4%)	0.4862‡
Positive Resection Margin	5 (2.9%)	2 (4.8%)	0.6273‡
EBL (mL)	200 (100-300)	105 (50-400)	N/A
Postoperative hospital stay (days)	8 (7-12)	7 (6-12)	N/A
Average LN harvest	17 (12-22)	14 (8-16)	N/A

Data are reported as n(%) or median (IQR)
*Chi square test
‡ Fisher's exact test

P129

Utility of Positron Emission Tomography (PET) Scans in the Management of Patients with Peritoneal Disease W. Wang,[1] G. Tan,[1] J. Wong,[2]* T. Skanthakumar,[1] M. Teo.[1] *1. National Cancer Centre Singapore, Singapore, Singapore; 2. Singapore General Hospital, Singapore, Singapore.*

Introduction Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) confer survival benefit to selected patients with peritoneal carcinomatosis but may be associated with significant morbidity. Accurate preoperative assessment of disease burden and the exclusion of distant metastases are crucial in selecting the appropriate patient. This study looks at the utility of PET scans in preoperative evaluation as compared to other imaging studies such as computed tomographic (CT) and magnetic resonance imaging (MRI) scans. Methods Data was retrospectively collected from patients considered for CRS and HIPEC and who had a PET scan performed. Results of the PET scans were then compared against previous CT and/or MRI scans. Patient and tumor factors were subsequently analyzed to identify the group of patients who were most likely to benefit from PET imaging. Results A total of 324 patients were considered for CRS and HIPEC from January 2011 to November 2014. PET imaging was performed for 100 (30.9%) patients. PET scan was of limited use in 52 patients as it either provided no additional information when compared with conventional CT/MRI imaging (n=30) or showed lesions of minimal FDG uptake (n=22). Of the latter, mucinous adenocarcinoma (72.7%, n=16) was the most common histological subtype. In the 48 patients where PET was useful, it was diagnostic for 22 patients who had it as their only imaging modality and provided definitive answers for 26 patients who had indeterminate lesions on CT and MRI scans. Amongst the latter, PET scan confirmed the diagnosis of peritoneal disease in 10 patients, identified extra-peritoneal disease and/or nodal metastases in 12 and excluded peritoneal disease in 4 patients. Adenocarcinoma (38.4%, n=10) was the most common histologic subtype in patients with originally indeterminate imaging findings. Conclusion In the evaluation of patients with peritoneal disease, PET scans may provide additional diagnostic information when compared with conventional imaging technologies. However, their utility may be limited to patients with indeterminate lesions, suspected extra-peritoneal disease and non-mucinous tumours.

P130

Exploring the Trend in Referrals for Consideration of CRS and HIPEC to Understand the Attitudes of Clinicians in the Development of a National Cancer Centre Program in Peritoneal Disease Z. Yong,[1]* W. Wang,[2] G. Tan,[2] T. Skanthakumar,[2] M. Teo.[2] *1. Department of General Surgery, Singapore General Hospital, Singapore, Singapore; 2. National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) improve survival in selected patients with peritoneal carcinomatosis. However, only a small proportion of patients who are potentially eligible for the procedure are referred for consideration. By studying the trends of patients considered for CRS and HIPEC in our center, we hope to better understand the demographics of our patient cohort and the attitudes of physicians involved towards CRS and HIPEC. Methods: Patients who were considered for CRS and HIPEC between 5 January 2011 and 15

December 2014 were identified from the institutional database and included in the study. Patient demographics and clinicopathological data were retrospectively collected from electronic records and clinical charts. Results: 324 patients were considered for CRS and HIPEC during the duration of the study. Referrals were most commonly from oncology-related departments (54.6%, n=177). This was followed by referrals from other hospitals (17.6%, n=57), overseas self-referrals (16.0%, n=52) and other non-oncologic departments (11.7%, n=38). Referrals made by the surgical oncologists, medical oncologists and overseas self-referrals showed an increasing trend over the years. Of patients considered for the procedure, 45.4% (n=147) were recommended at the tumor board to proceed. 16 (4.9%) patients defaulted or opted for another treatment and 6 (1.9%) were medically unfit, leaving 125 who underwent a laparotomy with the plan for CRS and HIPEC. Conclusions: There is growing acceptance of CRS and HIPEC in patients and oncologic-related departments. However, adoption remains low in non-oncologic departments. Dissemination of information and well-defined clinical recommendations can help the physicians identify and select potentially eligible patients for consideration of CRS and HIPEC.

P131

Prognostic Significance of Nodal Count and Lymph Node Ratio in Irradiated Rectal Cancer W.P. Ceelen,* W. Willaert, M. Varewyck, E. Goetghebeur, P. Pattyn. *Surgery, Ghent University, Ghent, Belgium.*

Purpose To examine how lymph node count (LNC) and lymph node ratio (LNR) correlate with overall survival (OS) in rectal cancer after surgery alone, neoadjuvant short term radiotherapy with immediate surgery (SRT), or chemoradiation with deferred surgery (CRT). Methods Data were used from the Belgian PROCARE rectal cancer registry. The effect of neoadjuvant therapy type on LNC was examined using Poisson loglinear analysis. The association of LNC and LNR with overall survival (OS) was studied using Cox proportional hazards models. Results Data from 4037 patients were available. A significant effect of neoadjuvant therapy on LNC was found (P<0.001): compared to surgery alone, LNC was reduced by 12.3% after SRT and by 31.3% after CRT. In patients with surgery alone, the probability of finding node positive disease increased with LNC while after SRT and CRT, no increase was noted for more than 12 and 18 examined nodes, respectively. The correlation of LNC with OS was significantly affected by neoadjuvant treatment type: per node examined, we found a decrease in hazard of death of 2.7% after surgery alone and 1.5% after SRT, but no effect after CRT. In a model including only stage III patients, the LNR (P=0.02) but not (y)pN stage was significantly correlated with OS regardless of neoadjuvant therapy. Specifically, a LNR >0.4 was associated with a significantly worse outcome. Conclusions Nodal counts are reduced in a dose dependent manner by neoadjuvant treatment in rectal cancer. After chemoradiation, the LNC does not confer any prognostic information. A LNR of >0.4 is associated with a significantly worse outcome in stage III disease, regardless of neoadjuvant therapy type.

P132

Platinum Distribution of Platinum After Clinical (H)IPEC Using Laser Ablation Inductively Coupled Plasma Mass Spectrometry C. Carlier,* S. van Malderen, F. Vanhaecke, W.P. Ceelen. *Surgery, Ghent University, Ghent, Belgium.*

Background: Cytoreductive surgery (CRS) followed by intraperitoneal chemoperfusion (IPEC) with platinum (Pt) – based drugs benefits selected patients with peritoneal carcinomatosis. However, little is known about the tumor tissue penetration of these drugs after IPEC, and on the effect of combined hyperthermia on Pt distribution. Highly sensitive bioimaging with laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) may allow detailed insight in the tissue distribution of Pt. Methods: Tumor tissue samples were obtained from two patients with PC from gastric and ovarian cancer, who underwent CRS followed by 90min. of IPEC (38°C) or HIPEC (40°C) with cisplatin (120mg/m^2), respectively. A single tumor nodule from each patient was removed after (H)IPEC and freeze-dried in liquid nitrogen. To analyze penetration depth, distribution and concentrations of Pt within these tumors, LA-ICP-MS was used. Ablation was performed with an Analyte G2 193nm ArF* excimer laser, coupled to an XSeries 2 ICP-quadrupole-MS. Calibration of the system was achieved using four gelatin standards, spiked gravimetrically by 1001 ± 5μg/ml Pt and 1000 ± 5μg/ml Indium standards. Micro droplets (200-300μg) of gelatin were placed onto a microscope slide and ablated quantitatively. Results: Figure 1 depict LA-ICP-MS images showed that the distribution of Pt can be observed with high sensitivity (5.1x10^3 c.p.s/μg g^{-1}). In general, distribution, penetration and concentrations of Pt are limited to the outer layer of the tumor and influenced by tumor type, temperature and tissue density. While the dense tumor derived from ovarian cancer treated with HIPEC demonstrate a Pt-gradient, a more uniformly Pt-distribution can be observed in the less dense tumor derived from gastric cancer treated with IPEC. Conclusion: LA-ICP-MS is a highly sensitive technique for the analysis of Pt distribution in human tumor sections. Additionally, these data can be correlated to histological images and wil be of particular interest to investigate the influence of tumor microenvironment on IP drug delivery.

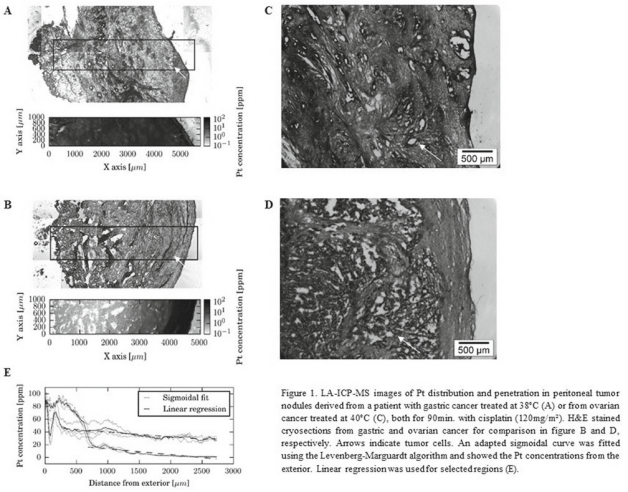


Figure 1. LA-ICP-MS images of Pt distribution and penetration in peritoneal tumor nodules derived from a patient with gastric cancer treated at 38°C (A) or from ovarian cancer treated at 40°C (C), both for 90min. with cisplatin (120mg/m²). H&E stained cryosections from gastric and ovarian cancer for comparison in figure B and D, respectively. Arrows indicate tumor cells. An adapted sigmoidal curve was fitted using the Levenberg-Marguardt algorithm and showed the Pt concentrations from the exterior. Linear regression was used for selected regions (E).

P133

The VEGFR Inhibitor Cediranib Improves the Efficacy of Fractionated Radiotherapy in a Colorectal Xenograft Model E. Melsens,* B. Verberckmoes, B. Descamps, C. Vanhove, P. Pattyn, W.P. Ceelen. *Surgery, Ghent University, Ghent, Belgium.*

Background The efficacy of radiotherapy (RT) depends on the presence of molecular oxygen. Several lines of evidence suggest that anti-angiogenic therapy 'normalizes' tumor microvascular structure and function, leading to improved blood supply, oxygenation, and RT efficacy. Here, we examined whether Cediranib, a pan–VEGF receptor tyrosine kinase inhibitor, improves microvascular function and tumor control in a mouse colorectal cancer model. Methods CRC xenografts (HT29) were grown for 14 days in athymic nude mice. Animals were treated for 5 consecutive days with vehicle, RT (1.8Gy daily), Cediranib (6mg/kg PO), or combined therapy. Tumor volume was measured with calipers. Functional vascular changes were analyzed by dynamic contrast enhanced-MRI (DCE-MRI), oxygenation and interstitial fluid pressure (IFP) probes and histology (Hoechst 33342, pimonidazole). To investigate structural vascular changes, a second set of mice were fitted with titanium dorsal skinfold window chambers (DSWC), wherein a HT29 tumor cell suspension was injected. In vivo fluorescence microscopy (IVM) was performed before and after treatment. Results Tumor growth in the combination group was significantly delayed (P < 0.0001) compared to controls or monotherapy (Fig1), with a tumor doubling time of 13.16 days with RT versus 27.13 days with combination treatment. Perfused and hypoxic areas on histology were not significantly different between groups. Further results of the in vivo fluorescence microscopy, probe measurements and DCE-MRI will be presented. Conclusion The combination of external RT with the VEGFR-inhibitor Cediranib enhances tumor control in a colorectal xenograft mouse model. The imaged structural and functional vascular changes elucidate the concept of vascular normalization and its potential therapeutic window.

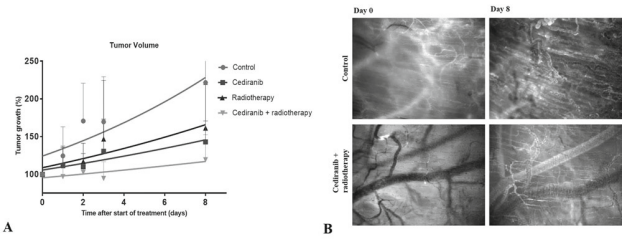


Figure 1. (A) Exponential growth curve of subcutaneous tumors showing a progressive growth delay with Cediranib, radiotherapy and combination therapy (P<0.0001). Values are presented as a mean with standard error bar. (B) Screenshots of in vivo fluorescence videos (100x magnification) of dorsal skinfold window chambers after IV injection of FITC-dextran. Day 0 shows images after implantation of the chamber with a normal microvasculature. Day 8 shows images after tumor inoculation and 5 days of treatment. The control group shows visibly more dilated and tortuous tumoral vessels than the combination group.

P134

Genipin-Crosslinked Gelatin Microspheres as a Strategy to Prevent Postsurgical Peritoneal Adhesions K. De Clercq,* W.P. Ceelen, C. Vervaet, J. Remon. *Surgery, Ghent University, Ghent, Belgium.*

Background Postoperative adhesions remain a major problem in abdominal surgery. Complications associated with adhesions include small bowel obstruction, female infertility and chronic abdominal pain. Severe adhesions commonly occuring after cytoreductive surgery compromise the effect of postsurgical intraperitoneal (IP) chemotherapy. The aim of this work was to develop biocompatible microspheres that can simultaneously prevent peritoneal adhesion formation and improve IP chemotherapy by providing local drug release over a prolonged period. Methods Genipin-crosslinked gelatin microspheres (GP-MS) were prepared by emulsification and characterized in vitro and in vivo (particle size, morphology, degree of crosslinking, cytotoxicity, biocompatibility and -degradation). Peritoneal adhesions were induced in Balb/c mice (n=24) using abraded peritoneal wall-cecum model. Mice received an IP injection of either 50 mg GP-MS in 2 ml physiological saline (n=12) or 2 ml physiological saline (n=12). Adhesions were scored on day 2, 7 and 14. Results GP-MS are non-toxic and biodegradable. A bluish colour was observed due to crosslinking reaction. A more intense dark blue coloration was noticed at higher genipin concentration and higher degree of crosslinking. This allows visual observation of the distribution pattern of GP-MS. GP-MS distribute similar to the flow of peritoneal fluid. None of the mice who received GP-MS developed adhesions (n=12, score 0) whereas peritoneal adhesions were seen in all control mice (n=12, score 3). Conclusion GP-MS are able to prevent peritoneal adhesions. IP drug release experiments using paclitaxel as drug will be performed to evaluate the potential dual effect of GP-MS as peritoneal adhesions prevention strategy and drug delivery system.

P135

Propensity Score Matched Analysis of Postoperative Outcome After Hyperthermic or Normothermic Intraperitoneal Chemoperfusion F. Gremonprez,* P. Pattyn, W. Willaert, W.P. Ceelen. *Surgery, Ghent University, Ghent, Belgium.*

Background: Cytoreductive surgery with intraperitoneal chemotherapy (IPC) is a cornerstone in the treatment of peritoneal carcinomatosis (PC). Remarkably, there is no consensus on IPC perfusion duration, drugs or temperature. Experimental and clinical studies have been equivocal on the necessity of hyperthermia. We aimed to assess outcome after hyperthermic (39° - 42 °C) or normothermic intraperitoneal chemoperfusion (37°C - 38°C) after debulking surgery for colorectal cancer (CRC). Methods: A comprehensive prospective database is kept of all IPC patients. From 1999 to 2014, 480 patients underwent IPC with oxaliplatin (200-460 mg/m^2) for PC of CRC origin. Due to the non-random allocation of IPC temperature, patients were propensity score matched according to possible confounders (nearest neighbor; SPSS 21, R 2.14.2). Results: 99 patients were eligible for analysis. Baseline characteristics did not differ significantly between the hyperthermia (H) and normothermia (N) groups. 62 patients were matched according to propensity score. There was no significant difference in the primary endpoint of severe morbidity (≥III Dindo-Clavien; H 32.3% and N 25.8%, p = 0.780). Secondary endpoints sowed a difference in infectious and wound complications; i.e. H 45.2% and N 12.9% (p = 0.011). Hospital stay was longer in the hyperthermia group before matching (p = 0.031), but significance was not reached in the matched groups (p = 0.081). Local recurrence and survival analyses are ongoing and will be presented. Conclusion: Severe morbidity is comparable to reports in the literature (30.3%). While the frequency of severe complications does not differ between groups, there is an increased number of infectious and wound problems after hyperthermic IPC. The efficacy of hyperthermia needs to be evaluated in a randomized controlled trial.

P136

Changes in Apparent Diffusion Coefficient Evaluated with Diffusion Weighted MRI May Predict Complete Pathologic Response After Neoadjuvant Therapy for Rectal Cancer: A Meta-analysis V. Desiato,[1]* A. Rosman,[2] E. Newman,[1] R. Berman,[1] H. Pachter,[1] M. Melis.[1] *1. Surgery, NYU School of Medicine, New York, NY; 2. Mount Sinai School of Medicine, New York, NY.*

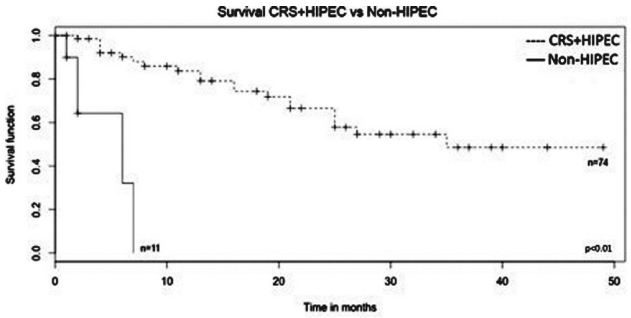
Background: A complete pathological response (pCR) is observed in 9-38% of all patients undergoing neo-adjuvant chemo-radiation therapy (CRT) for locally advanced rectal cancer (ARC). Imaging techniques that can reliably assess CRT results may enhance identification of those pCR patients for which surgery may potentially be avoided. Recently, several studies have suggested that diffusion-weighted magnetic resonance imaging (DW-MRI) may predict pathologic response by measuring tumor apparent diffusion coefficient (ADC). ADC can be measured before (pre-ADC) and/or after CRT (post-ADC). Both pre- and post-ADC, as well as the variation between pre- and post-ADC (Δ-ADC) can be used to assess pCR. We aimed to assess the reliability of ADC at predicting pCR in ARC patients treated with CRT. To determine the most effective ADC timing to evaluate pCR. Methods: A systematic review of available literature was conducted to compare all the studies of DW-MRI for identification of pCR after CRT for ARC. For each parameter (pre-ADC, post-ADC and Δ-ADC) we pooled sensitivity and specificity and calculated the area (AUC) under the summary receiver operating characteristics (sROC) curve. Results: We found 10 prospective and 8 retrospective studies examining correlation of ADC and CRT results. Overall, pCR rate was 25%. Pooled sensitivity, specificity, and AUC were: 0.743, 0.755, and 0.841 for pre-ADC; 0.745, 0.706, and 0.782 for post-ADC; and 0.832, 0.806, and 0.895 for Δ-ADC. Conclusions: Our meta-analysis confirms that at least 25% of patients with ARC experiences pCR after CRT. DW-MRI is a promising technique for assessment of CRT results and Δ-ADC appears to be the most effective parameter for prediction of pCR.

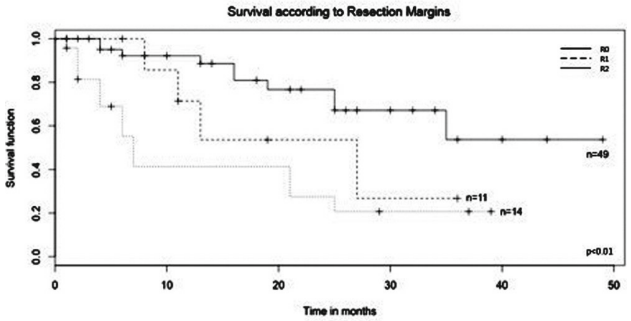
P137

Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC): Can We Improve Survival with Less Postoperative Complications? O. Picado Roque, C. Ripat, R. Vega, G. Tiesi, E. Paulus, L. Sánchez, H. Bahna, F. Marchetti, E. Avisar, D. Franceschi, A. Livingstone, D. Yakoub, M. Möller.* *Surgical Oncology, University of Miami Miller School of Medicine, Miami, FL.*

BACKGROUND: CRS+HIPEC to treat peritoneal surface malignancies (PSM) is commonly associated with significant post-operative complications. The aim of this study was to determine predictors of survival and factors associated with post-operative complications in these patients. METHODS: Records of all patients with PSM were retrospectively reviewed (Jan 2011-Aug 2015). Comorbidities, chemotherapy, peritoneal cancer index (PCI), extent and margins of resections, OR time, EBL, ICU and hospital length of stay (LOS) were analyzed in uni- and multivariate models using Cox proportional hazards regression. Log-rank testing was used to calculate overall survival (OS). RESULTS: 85 out of 142 patients with PSM were eligible for CRS+HIPEC, 11 of those were unresectable. Median age 54 yrs (23–74). Primary tumor sites were mostly in the appendix and colon (68%). Median operative time: 8.5 hrs(4–13), median EBL: 500cc(150–2500). Median pre-operative PCI score was 14(2–37). R0, R1 and R2 was achieved in 65%, 15%, and 20%, respectively. Number of organs resected was 1, 1-2 and ≥3 in 15%, 23% and 62%, respectively. Median ICU and LOS were 4 d(0–52) and 8 d(1-88), respectively. 30 day mortality was 0%. Post-op complications included chemotherapy induced neutropenia (22%), surgical complications: fistula (7%), ileus and leak (5% each), intra-abdominal abscess and wound infection (4% each). R0 patients had the least morbidity (p<0.02) and wound infection rate (p<0.03) while R2 patients had the most pleural effusion (p<0.003). OS for CRS+HIPEC patients was 31 vs. 4 months in non CRS+HIPEC patients (p<0.01). Median OS was 35, 13 and 6 mo for R0, R1 and R2 (p<0.01). Predictors of OS were pre and post-operative PCI (HR:1.05, p=0.01 and HR:1.07, p<0.01, respectively) on univariate analysis and LOS (HR:1.05, p<0.01) and abdominal wall implants resection (HR:3.98, p<0.01) on multivariate analysis. CONCLUSION: Extensive CRS+HIPEC is achievable with low surgical complications. Patients with

longer LOS and/or abdominal wall implants resection are more prone to early death. Resection margin is the most significant predictor of survival.

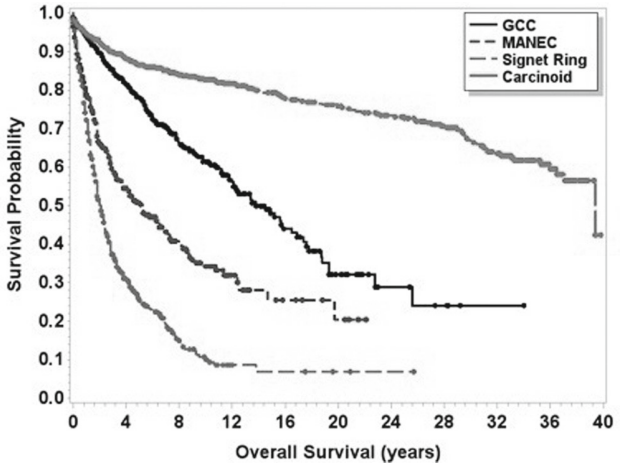




P138

Mixed Adeno-Neuroendocrine Carcinoma (MANEC): A Population-Based Study of the Surveillance, Epidemiology and End Results (SEER) Registry S.A. Brathwaite,* M.M. Yearsley, T. Bekaii-Saab, L. Wei, W.L. Frankel, J. Hays, C. Wu, S. Abdel-Misih. *General Surgery, The Ohio State University Wexner Medical Center, Columbus, OH.*

Background Mixed adeno-neuroendocrine carcinoma (MANEC) is a rare pathologic diagnosis recently defined by the World Health Organization (WHO) in 2010. Prior to definition by the WHO, tumors with both adenocarcinoma and neuroendocrine components were given multiple pathologic designations making it difficult to characterize the disease. The aim of our study is to better characterize MANEC to understand the natural history and prognosis. Methods The Surveillance, Epidemiology and End Results (SEER) program database was queried for all patients age 18 years of age or older between 1973-2012 who had the diagnosis composite carcinoid (n=431) of the colon and rectum. Composite carcinoid tumors refer to tumors that have both adenocarcinoma and carcinoid tumor components present, consistent with the pathologic diagnosis MANEC. For comparison the database was also queried for carcinoid tumor of the appendix (n=951), signet ring cell carcinoma of the appendix (n=579) and goblet cell carcinoid (GCC) tumors of the appendix (n=944). The data was retrospectively reviewed and clinicopathologic characteristics, treatment regimens and survival data were obtained. Results The median age of diagnosis of MANEC tumors was 62 years of age. Seventy-four percent of patients were white and 49% were female. Fifty-eight percent and 15% of MANEC tumors arose in the appendix and cecum, respectively. Forty-two percent of patients underwent hemicolectomy and 31% had partial/subtotal colectomy as their surgical management. Median overall survival for MANEC was 5.2 years (95% CI 3.8-6.8), which was statistically significant (p<0.0001) in comparison to 13.8 years (95% CI 12.1-16.5) for GCC, 2 years (95% CI 1.8-2.3) for signet ring cell carcinoma and 39.4 years (95% CI 37.1 – NA) for carcinoid tumors (Figure 1). Conclusions MANEC is a more aggressive clinical entity than both GCC of the appendix and carcinoid tumors of the appendix. Based on these findings patients with MANEC tumors should undergo aggressive multidisciplinary management.



Kaplan Meier survival curve for patients with carcinoid tumors, GCC, MANEC and signet ring cell carcinoma.

P142

Readmission Rates of Patients Undergoing Resection of a Colorectal Primary: An Analysis of SEER-Medicare A. Gustin, P.D. Lorimer,* K.K. Walsh, R.C. Kirks, Y. Han, S.L. White, J.C. Salo, J.S. Hill. *Levine Cancer Institute, Charlotte, NC.*

Background Hospital readmission rates are increasingly reported in this era of value-based care. Predictive models are utilized to risk-adjust patient populations; however there are few studies investigating this topic after surgery for colorectal cancer. The present study utilizes a large national dataset to further understand readmissions in this population. Methods SEER-Medicare was queried for patients with primary colorectal cancer (1998-2009). Patients ages 66+ who underwent colorectal resection were identified with ICD9 procedure/CPT codes. Patients discharged to home, a skilled nursing facility (SNF) or acute inpatient rehabilitation (AR) were included. Demographics, socioeconomic factors, length of stay (LOS), day of admission and discharge, and discharge destination were analyzed for effect on readmissions. Readmission rates at 14 and 30 days were analyzed using multivariate logistic regression models. Cochran-Armitage time trends were performed to examine the relationship of discharge day of the week and discharge location over the course of the week. Results 93,047 patients met inclusion criteria. The median age was 77; 56% male. The overall readmission rate at 14 days was 9.1% (30 day=13.4%). Readmissions were higher in males (OR1.14 [1.10,1.20]), blacks (OR1.22 [1.13,1.32]), those with the least education (OR1.23 [1.15,1.31]), a LOS>6 days (OR1.21 [1.12,1.30]), and Charlson >0 (OR1.31 [1.23,1.38]). Patients discharged home were less likely to be readmitted than those discharged to non-home destinations (OR0.58 [0.55,0.61]). On subgroup analysis, patients discharged home were increasingly likely to be readmitted as the week progressed (p<0.01). No significant difference with regard to day of discharge was seen in patients readmitted from SNF or AR. Subset readmission rates based on discharge destination are seen in table 1. Conclusions Readmissions were more likely in males, blacks, patients with LOS >6 days, Charlson score >0, and patients discharged to a non-home location. Patients who were discharged home later in the week were more likely to be readmitted. This would suggest that improvements in preparing patients for discharge to home are needed.

Table 1: Readmission Rates by Weekday and Discharge Destination

Destination	Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Total
Home, n (%)	7450 (10.3%)	12312 (17.0%)	12536 (17.3%)	11841 (16.3%)	9907 (13.7%)	10296 (14.2%)	8172 (11.2%)	72514
Skilled Nursing Facility	565 (3.0%)	3180 (16.7%)	3591 (18.8%)	3535 (18.5%)	3055 (16.0%)	3776 (19.8%)	1360 (7.2%)	19062
Inpatient Rehabilitation Facility	21 (1.4%)	243 (16.5%)	291 (19.8%)	291 (19.8%)	248 (16.9%)	304 (20.6%)	73 (5.0%)	1471
Total	8036	15735	16418	15667	13210	14376	9605	93047

P143

Degree of Intraperitoneal Hyperthermia During HIPEC Predicts Overall Survival V. Phuoc,* D. Dean, R.E. Royal, G.N. Mann, B. Badgwell, P. Mansfield, K. Fournier. *Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Trimodality therapy including systemic chemotherapy, cytoreductive surgery (CRS), and hyperthermic intraperitoneal chemotherapy (HIPEC) has become a standard treatment option for patients with a variety of peritoneal surface malignancies. The impact of the hyperthermia component of this regimen on overall survival and disease recurrence is poorly understood, despite being common practice. Methods: An IRB-approved, single-institution, retrospective review of 101 patients who underwent CRS and HIPEC from 2007 to 2012 was conducted. Continuous multi-site intraperitoneal regional temperature probe measurements were collected during HIPEC. Parameters evaluated included mean and median temperature for all anatomic regions monitored, overall survival, time to recurrence, completeness of cytoreduction score (CCR), peritoneal carcinomatosis index (PCI), and perfusate volume returned. Results: 32 patients (31.7%) developed a recurrence, at a mean time of 18.8 months after CRS and HIPEC. Degree of hyperthermia was assigned to three groups based on mean temperature of measured regions during perfusion. Multivariate logistic regression was used to analyze overall survival as a function of hyperthermia for each region perfused, PCI, CCR, and volume of perfusate returned. Degree of hyperthermia in the right upper quadrant (but not other regions monitored) and CCR were both found to be independent predictors of overall survival ($p = 0.024$ and 0.010 respectively). Simple linear regression modeling showed a relationship (adjusted R-squared 0.465) between degree of RUQ hyperthermia and time to recurrence. Conclusions: Although it has been long assumed that hyperthermia is an important component of peritoneal chemotherapeutic perfusion after CRS, this is the first study to demonstrate an overall survival and time-to-recurrence benefit for increasing intraperitoneal hyperthermia during HIPEC. Regional right upper quadrant temperature monitoring during HIPEC may be warranted, as inflow and outflow temperatures may not be sufficiently accurate.

P144

Molecular Profiling: Prognostic Biomarkers in Patients Presenting with Peritoneal Carcinomatosis of the Appendix and Colon Treated with Cytoreductive Surgery and Perioperative Intraperitoneal Chemotherapy C. Ihemelandu.* *Surgery, Washington Hospital Center, Washington, DC.*

Introduction: Prognostic biomarkers are helpful in matching patients to molecularly targeted therapies. Our aim was to analyze and compare the molecular profile and prognostic biomarkers in patients presenting with peritoneal carcinomatosis (PC) of the appendix or colon. Methods: A retrospective analysis of a prospectively maintained database of patients treated with CRS and POIC for PC of appendix and colon from 2013-2015, and who had molecular profiling for biomarkers of drug sensitivity with a CLIA-certified laboratory. IHC and FISH assays were performed with up to 30 biomarkers. Gene sequencing for KRAS, EGFR, PIK3CA, BRAF and other biomarkers were done. Results: Thirty-nine patients were included, of which 18(46.2%) had appendiceal vs. 21(53.8%) colonic PC cases. There were 20(51.3%) males vs. 19(48.7%) females. Mean age at presentation was 53.8 vs. 51.1years respectively for appendix and colon cancer. No significant difference was noted between the two tumor types in over 50 biomarkers analyzed, including BRAF mutations 1(5.6%) vs. 2(9.5%) p=. 643, KRAS mutation 7(38.9%) vs. 9(42.9%) p=. 802, EGFR 10(55.6%) vs. 8(38.1%) p=. 276, TS 4(22.2%) vs. 6(28.6%) p=. 651, and TOPO1 15(83.3%) vs. 12(57.1%) p=. 077. The colonic tumors however showed a higher expression of PIK3CA 5(25.0%) vs. 0(0.0%) for the appendiceal tumors. Conclusion: - The Appendiceal tumor biomarker profile showed considerable homogeneity to that of the colonic tumors. Therapeutic options possible based upon the targets noted include TOPO1 inhibitors, EGFR inhibitors, and BRAF inhibitors.

P145

Mutant-Allele Tumor Heterogeneity (MATH) Scores Correlate with Stage of Colon Cancer A. Rajput.* *Surgery, University of New Mexico Comprehensive Cancer Center, Albuquerque, NM.*

Background: Colorectal cancer remains a leading cause of cancer related mortality worldwide. The vast majority of these deaths are from metastatic disease. An important clinical question that remains unanswered is which patients with stage II (lymph node negative) and stage III (lymph node positive) disease are at risk for developing metastasis. The purpose of this study was to determine if a bioinformatics approach to measure intra-tumoral heterogeneity could be used to classify patients with colon cancer by stage of disease. Methods: Eleven patients with either AJCC stage II, III or IV colon cancers were identified. Normal and tumor DNA were extracted from formalin fixed, paraffin embedded tissues. Samples were analyzed using the Ion Ampliseq comprehensive Cancer panel assay and sequencing was performed on the Ion Proton next-generation sequencing instrument. Mutant allele frequencies were determined and a calculated MATH score was used to quantify tumor heterogeneity. The MATH score is calculated as 100 x median absolute deviation (MAD)/median, and describes the ratio of the width of the data to the center of the distribution of mutant-allele fractions among tumor-specific mutated loci. Results: For tumors with a lack of heterogeneity, there is a distinct cluster of variants at approximately 50% variant allele frequency and smaller clusters at 0% and 100% (Figure 1A). A number of samples demonstrated a more complex composition reflective of increased tumor heterogeneity as shown in Figure 1B. The calculated MATH scores showed that there is a strong association between the MATH score and the stage of disease (Figure 1C). Conclusions: The bioinformatics approach using the MATH score allows the classification of colon cancer patients by stage of disease. The degree of heterogeneity is thought to lead to the outgrowth of therapy-resistant clones and thus to metastatic disease. This novel approach of analyzing tumor heterogeneity as a reflection of the "shape" of the bioinformatics data may provide a useful biomarker for staging patients with colon cancer and importantly, may allow a means of identifying patients who are likely to develop metastatic disease

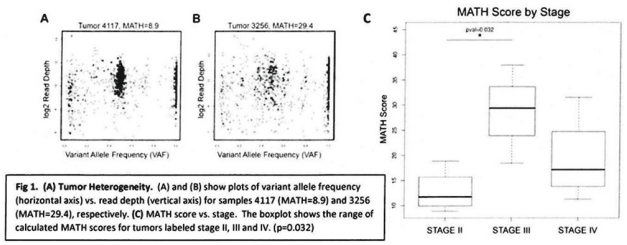


Fig 1. (A) Tumor Heterogeneity. (A) and (B) show plots of variant allele frequency (horizontal axis) vs. read depth (vertical axis) for samples 4117 (MATH=8.9) and 3256 (MATH=29.4), respectively. (C) MATH score vs. stage. The boxplot shows the range of calculated MATH scores for tumors labeled stage II, III and IV. (p=0.032)

P146

Frequent BRAF Mutations in Colonic High-Grade Neuroendocrine Carcinoma C. Padmanabhan,[1]* E. Liu,[3] K. Dahlman,[1] J. Berlin,[1] R. Gonzalez,[2] Y. Guo,[1] C. Shi,[1] K. Idrees.[1] *1. General Surgery, Vanderbilt University, Nashville, TN; 2. University of Rochester, Rochester, NY; 3. Rocky Mountain Cancer Centers, Denver, CO.*

Introduction The WHO 2010 has classified GI neuroendocrine neoplasms into well-differentiated neuroendocrine tumor (NET) and high-grade neuroendocrine carcinoma (NEC) based on mitosis and proliferative rate. NEC is more aggressive than NET and most patients die within several months of diagnosis. Whole genome sequencing has provided insight into the genetic underpinnings of NET but much less is known about NEC. The aim of the study is to perform genomic profiling of NEC to better characterize the underlying mutations in this aggressive disease. Methods We identified 9 patients who underwent biopsy or resection for NEC between 1/1/05 - 6/30/13 with histological blocks available. Whole genomic sequencing (WGS) was performed on DNA extracted from tissue from 2 patients with ≥80% tumor cellularity using the Illumina HiSeq 2500 platform. Validation and mutational analysis of the BRAF gene was performed on 2 WGS patients and on additional 7 patients via Sanger sequencing of exon 11 and 15 to identify BRAF mutations. Results 7 of 9 patients (78%) presented with liver metastasis at the initial diagnosis (Table). 8 of the patients died of disease within 25 months (ranging from 3 to 25 months) post-operatively. In the 2 NECs on which we performed WGS, we identified BRAF mutations on exon 15. The first patient (case S1) presented with a cecal high-grade NEC and had an A1781G:p.D594G mutation in exon 15 of BRAF. The second patient (case S2) presented with high-grade NEC in the descending colon and had a c.1799T>A: p.V600E mutation in exon 15 of BRAF. An additional 7 colonic NECs were analyzed using Sanger Sequencing of exons 11 and 15 for BRAF mutations. 2 of 7 had BRAF V600E mutations. Overall, BRAF mutations were present in 4 of 9 (44%) colonic NECs. Interestingly, all 3 cases with BRAF V600E mutation were large cell NECs, whereas the case with a BRAF D594G mutation was a small cell carcinoma. Conclusion High

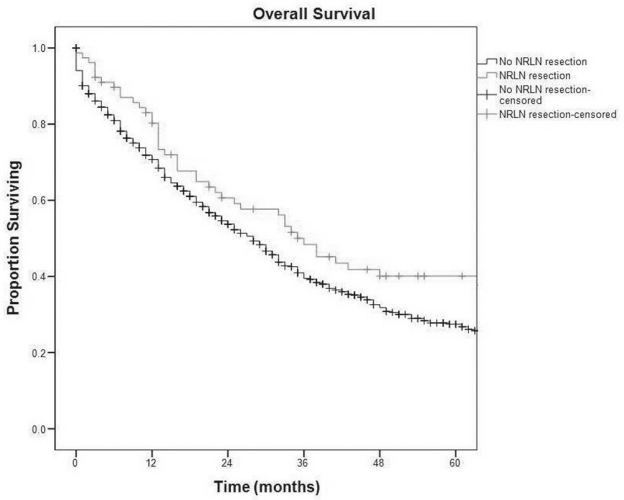
grade colonic NEC is a rare but aggressive tumor with high frequency (44%) of activating BRAF mutations. Further investigation is warranted to ascertain the incidence of BRAF mutations in a larger population as BRAF inhibition may be a potential avenue of targeted treatment for these patients.

Case#	Gender	Age (yrs)	Location	Stage	Histological Subtype	BRAF exon 11	BRAF exon 15	Status	Survival (months)
S1	F	69	Cecum	TxNxM1	Small cell	WT	A1781G; p.D594G	DOD	12
S2	F	65	Descending colon	T3N1M0	Large cell	WT	c.1799T>A; p.V600E	DOD	20
S4	M	59	Sigmoid	T2N1M1	Small cell	WT	WT	DOD	21
S5	F	52	Rectum	TxNxM1	Large cell	WT	WT	DOD	25
S6	F	63	Cecum	TxNxM1	Small cell	WT	WT	DOD	14
S8	F	62	Sigmoid	T3N2M0	Large cell	WT	c.1799T>A; p.V600E	DOD	16
S10	F	60	Transverse colon	T4N1M1	Small cell	WT	WT	DOD	3
S12	M	30	Sigmoid	TxNxM1	Small cell	WT	WT	AWD	38
S13	F	66	Cecum	T3N1M1	Large cell	WT	c.1799T>A; p.V600E	DOD	21

P147

Resection of Non-regional Lymph Node Metastasis in Patients with Colorectal Cancer C. Bailey,* K. Idrees, A. Parikh. *Vanderbilt University Medical Center, Nashville, TN.*

Background: Approximately 20% of patients with colorectal cancer (CRC) present with metastatic disease-most commonly to the liver or lungs. Successful resection of these metastatic foci leads to significant long-term survival. Less commonly, patients present with isolated metastasis to non-regional lymph nodes (NRLN) and little is known regarding the role of resection in these patients. The primary aim of this study is to evaluate the outcomes of patients with CRC who undergo resection of NRLN metastasis. Methods: A retrospective cohort study of patients diagnosed with CRC and NRLN metastasis was performed using the Surveillance, Epidemiology, and End Results database (2004-2012). Demographic and clinical factors were compared for patients who underwent resection of NRLN metastasis and those who had not. Kaplan-Meier and log-rank analysis was used for survival analysis. Logistic regression analysis was used to assess factors associated with resection of NRLN metastasis. Results: A total of 22,848 patients presented with metastatic CRC and underwent primary tumor resection. Of these, 786 (3.4%) presented with isolated NRLN metastasis and 78 (9.9%) underwent NRLN resection. Patients who underwent resection were more likely to be male, have rectal cancer, and poorly or undifferentiated grade tumors. Median overall survival (OS) was significantly improved for patients who underwent resection compared to those who did not (36 vs. 28 months, p=0.036)[Figure]. In patients with colon cancer (N=602), median OS was 33 vs. 21 months (p=0.042) for those who underwent resection compared to those who did not, whereas in patients with rectal cancer (N=184), the median OS was 45 vs. 38 months (p=0.977), respectively. In multivariate analysis, rectal cancer (OR 1.84, 95% CI 1.08 to 3.13) and poorly or undifferentiated grade tumors (OR 1.64, 95% CI 1.01 to 2.66) were associated with increased NRLN resection. Conclusion: Resection of NRLN metastasis in patients with CRC is associated with an overall survival benefit, particularly among patients with colon cancer. Further studies are needed to identify which specific patient subgroups would best benefit from this resection strategy.



P148

Impact of KRAS/BRAF Mutations in Patients with Colorectal Peritoneal Metastases G. Wright,* A. Zureikat, J.F. Pingpank, M. Holtzman, S. Ahrendt, L. Ramalingam, H. Zeh III, D. Bartlett, M.A. Choudry. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

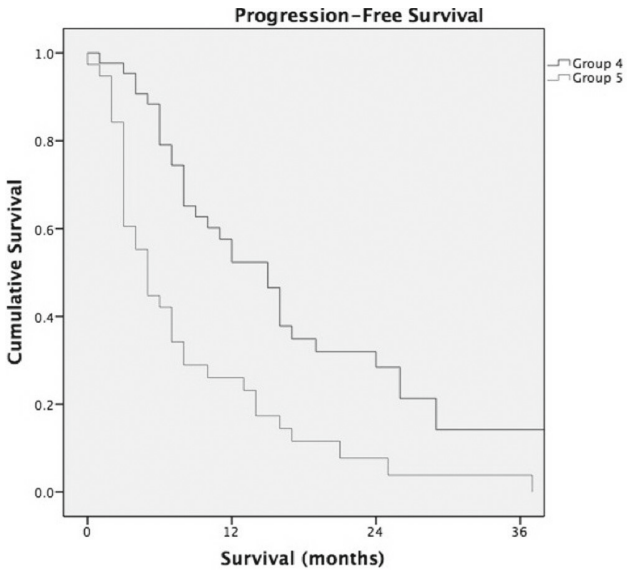
Introduction: KRAS/BRAF mutations have been identified as negative prognostic factors in colorectal cancer. The impact of KRAS/BRAF mutational status on oncologic outcomes in patients with colorectal peritoneal metastases is unclear. Methods: From a prospective database of patients undergoing multimodality therapy, including cytoreductive surgery with hyperthermic intraperitoneal chemoperfusion (CRS-HIPEC) and systemic chemotherapy for colorectal peritoneal metastases, we analyzed perioperative, clinicopathologic and oncologic outcome data for 111 patients with KRAS, BRAF and MSI testing. Kaplan-Meier survival curves and multivariate Cox-regression models identified prognostic factors effecting survival. Results: Mutational analysis revealed 52 KRAS/BRAF wild-type (wtKRAS/BRAF) patients (47%), while KRAS (mutKRAS) and BRAF (mutBRAF) mutations were identified in 44 patients (40%) and 15 patients (14%), respectively. The MSI status was similar among the three mutational groups. There was no difference in administration of preoperative systemic chemotherapy based on mutational status. KRAS/BRAF wild-type patients were more likely to have poorly differentiated tumors (wtKRAS/BRAF 53%; mutKRAS= 23%, mutBRAF= 33%; p=0.06) and signet-ring cells (wtKRAS/BRAF= 28%, mutKRAS= 5%, mutBRAF= 0%; p=0.002). There was no difference in the peritoneal cancer index or ability to achieve complete cytoreduction (residual tumor nodules < 2.5mm) among the three mutational groups. After a median follow-up time from surgery of 14 months, there was a trend towards worse overall survival in the BRAF mutated group (wtKRAS/BRAF= 22 months, mutKRAS= 29 months, mutBRAF= 14 months; p=0.39). In a multivariate Cox-regression model of patients with wtKRAS/BRAF, lack of administration of EGFR inhibitor was an independent predictor of poor survival (HR 3.96; p=0.04). Conclusion: The frequency of KRAS/BRAF mutations in colorectal peritoneal metastases is similar to primary colorectal cancer and other sites of metastases. Similarly, BRAF mutation has prognostic significance while KRAS mutation is predictive of response to EGFR therapy, as reported in primary colorectal cancer and other sites of metastases.

P149

CEA Level Predicts Oncologic Outcomes Following Surgical Resection of Colorectal Peritoneal Metastases G. Wright,* A. Zureikat, J.F. Pingpank, M. Holtzman, S. Ahrendt, L. Ramalingam, H. Zeh III, D. Bartlett, M.A. Choudry. *University of Pittsburgh Medical Center, Department of Surgical Oncology, Pittsburgh, PA.*

Introduction: Post-operative normalization of CEA level predicts long-term survival following resection of colorectal liver metastases. We hypothesized

that changes in CEA levels would be predictive of oncologic outcomes in patients undergoing multimodality therapy for colorectal peritoneal metastases. Methods: From a prospective database of patients undergoing multimodality therapy, including cytoreductive surgery with hyperthermic intraperitoneal chemoperfusion (CRS-HIPEC) and systemic chemotherapy for colorectal peritoneal metastases, we analyzed CEA levels at various time-points of therapy; Group 1 (n=140): normal preoperative CEA; Group 2 (n=42): elevated preoperative CEA that normalized or decreased ≥50% with preoperative systemic chemotherapy; Group 3 (n=112): persistently elevated preoperative CEA level; Group 4 (n=44): elevated preoperative CEA that normalized or decreased ≥50% postoperatively following CRS-HIPEC; and Group 5 (n=38): persistently elevated postoperative CEA level. Kaplan-Meier survival curves were analyzed. Results: In patients with elevated preoperative CEA level (Groups 2/3), CEA returned to normal or decreased by ≥50% in 28% following administration of systemic chemotherapy. Patients with non-mucinous histology were more likely to demonstrate CEA response to preoperative chemotherapy (42% vs. 11%, p<0.001). For patients in Group 3, CEA returned to normal or decreased by ≥50% in 54% of patients following CRS-HIPEC (Group 4). Patients with persistently elevated postoperative CEA (Group 5) had a higher incidence of perineural/perivascular invasion and were less likely to undergo complete macroscopic resection (CC-0) than patients in Group 4. Moreover, patients in Group 4 demonstrated significantly improved PFS (15 vs. 5 months, p<0.001) (Fig. 1) and a trend towards improved overall survival (29 vs. 15 months, p=0.18) than Group 5. Conclusion: Systemic chemotherapy may have limited effect on colorectal peritoneal metastases as suggested by poor CEA response to therapy, particularly in mucinous tumor histology. CEA response to CRS-HIPEC is predictive of disease control and perhaps long-term survival.



Progression-Free Survival of Patients with Elevated Preoperative CEA Based on Postoperative CEA Response

P150

Establishing the Proper Timing of Surgical Decision-making in Rectal Cancer: Before or After Neoadjuvant Therapy? A Prospective Study for T3 Cancers of the Distal 1/3 of the Rectum

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INTRODUCTION: Some within the surgical community still adhere to the thought that surgical decisions regarding timing and sphincter preservation in rectal cancer management should be based upon the original presentation despite neoadjuvant downstaging. We examine the oncologic outcomes of T3 cancers arising in the distal 1/3 of the rectum, where APR would be uniformly advised upon original presentation. We hypothesize that using neoadjuvant therapy and sphincter preserving surgery (SPS) in which surgical decision-making relies exclusively upon a post-neoadjuvant downstaged cancer allows expanded sphincter preservation for patients without sacrificing oncologic outcomes. METHODS: From a prospectively maintained rectal cancer database we identified 192 consecutive T3 cancers of the distal 1/3 of the rectum treated with neoadjuvant therapy (mean 5374 cGy, range 3000-7295 cGy) and underwent either APR (n=41), radical SPS (n=109) [transanal abdominal transanal proctosigmoidectomy (TATA; n=107) or low anterior resection (LAR; n=2)], or local excision (n=42) [transanal excision (TAE; n=15) or transanal endoscopic microsurgery (TEM; n=27)]. Oncologic outcomes including local recurrence (LR), distant metastasis (DM), and survival were analyzed. Sphincter preservation was offered to all patients except those whose cancer remained fixed after completion of neoadjuvant therapy. RESULTS: Average time from completion of neoadjuvant treatment to surgery was SPS (10.9 weeks) and APR (15.2 weeks). Mean follow up was 48.6 months (range 0-240 months). LR and KM5YAS for SPS vs. APR were 6.6%, 95% and 7.3%, 72%, respectively (p=0.87, p<0.0001). Distant metastasis developed in 22.5% SPS and 24.4% APR (p=0.80). CONCLUSIONS: This study demonstrates that by holding the decision regarding sphincter preservation until after completion of neoadjuvant therapy allows for avoidance of a colostomy in 79% with no adverse oncologic effects. In our opinion, the data offers convincing evidence that the appropriate timing of surgical decision-making rests upon the status of the rectal cancer post-neoadjuvant treatment.

Tumor Characteristics and Oncological Outcomes

	TEM (n=27)	TAE (n=15)	Radical SPS (n=109)	All SPS (n=151)	APR (n=41)
Tumor Fixity Mobile Tethered Early Fixed Fixed	 12 (44.4%) 14 (51.9%) 1 (3.7%) 0 (0%)	 9 (60%) 6 (40%) 0 (0%) 0 (0%)	 43 (3.9%) 46 (42.2%) 14 (12.8%) 0 (0%)	 64 (42.2%) 66 (43.7%) 15 (9.9%) 0 (0%)	 6 (14.6%) 20 (48.8%) 12 (29.3%) 1 (2.4%)
Mean tumor distance from anorectal ring cm (range)	1.1 (-1 to 3)	0.8 (-0.5 to 3)	1.2 (-1.5 to 3)	1.2 (-1.5 to 3)	-0.3 (-4 to 3)
Distance from anorectal ring < -1 cm -1-0 cm 0.1-1.5 cm 1.6-3.0 cm	 1 (3.7%) 5 (18.5%) 13 (48.1%) 8 (29.6%)	 0 (0%) 5 (33.3%) 7 (46.7%) 3 (20%)	 1 (0.9%) 14 (12.8%) 58 (53.2%) 36 (33%)	 2 (1.3%) 24 (15.9%) 78 (51.6%) 47 (31.1%)	 8 (19.5%) 21 (51.2%) 7 (17.1%) 5 (12.2%)
Distal margins Average cm (range)	0.43 (0.3-0.7)	Not available	1.8 (0.1-8)	1.9 (0.1-8)	3.2 (1-7.5)
Proximal margins Average cm (range)	0.3 (0.015-0.3)	Not available	25.9 (13-64)	26 (1.5-64)	21.2 (2.4-42)
CRM positivity (≤1mm)	0 (0%)	0 (0%)	5 (4.6%)	5 (3.3%)	7 (17.1%)
ypT Stage ypT0 (complete response) ypT1 ypT2 ypT3 ypT4	 6 (22.2%) 6 (22.2%) 9 (33.3%) 5 (18.5%) 1 (3.7%)	 5 (33.3%) 1 (6.7%) 5 (33.3%) 4 (26.6%) 0 (0%)	 22 (20.2%) 4 (3.7%) 41 (37.6%) 41 (37.6%) 1 (0.92%)	 37 (24.5%) 11 (7.3%) 67 (44.4%) 70 (46.4%) 6 (4%)	 4 (9.8%) 0 (0%) 12 (29.3%) 20 (48.8%) 4 (9.8%)
Local Recurrence (LR)	1 (3.7%)	4 (26.7%)	5 (4.6%)	10 (6.6%)	3 (7.3%)
Distant Metastasis (DM)	4 (14.8%)	4 (26.7%)	26 (24.3%)	34 (22.5%)	10 (24.4%)
KM5YAS	100%	82%	98%	95%	72%

P151

Hospital Treatment Intensity and Guideline-Concordant Care for Resected Stage II/III Colorectal Cancer

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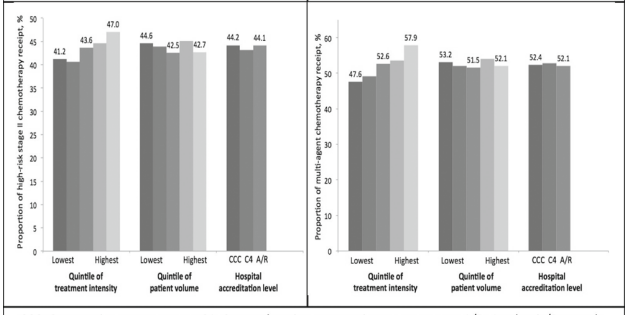
BACKGROUND: Variation in guideline-concordant colorectal cancer (CRC) care is poorly understood. Many have attributed better care to treatment at high volume hospitals or hospitals with cancer center accreditation. We previously demonstrated wide variation in hospital treatment intensity for metastatic CRC. The extent to which these hospital treatment patterns are associated with guideline concordant care for high-risk stage II and stage III CRC is unknown. METHODS: We used data from the National Cancer Data Base Colorectal PUF from 2006-12 (N=488,317 patients in 1,045 hospitals). We first quantified hospitals' overall treatment intensity by their relative treatment utilization for patients with metastatic CRC. We then assessed the receipt of postoperative chemotherapy in high-risk stage II and stage III disease. To assess the relative influence of hospital treatment intensity on other care patterns, we compared adjusted adjuvant chemotherapy rates across levels of treatment intensity and other hospital attributes such as patient volume and accreditation levels. RESULTS: Treatment intensity for metastatic CRC varied widely across hospitals as expected. Compared to other hospital attributes, treatment intensity was the best predictor of receiving postoperative adjuvant care across disease stages. For example, patients with high-risk stage II disease were more likely to receive postop chemotherapy in high-intensity hospitals (47.0%) than high-volume hospitals (42.7%). Similarly, patients with stage III

disease were more likely to receive multi-agent chemotherapy in high-intensity hospitals (57.9%) than high-volume hospitals (52.1%). For both stage II and III disease, adjuvant chemotherapy increased in a stepwise fashion according to hospital treatment intensity, but not patient volume or accreditation levels (Figure 1) CONCLUSIONS: Hospital care intensity for metastatic CRC predicts treatment intensity for other disease stages, and is a stronger predictor of guideline-concordant care than other structural hospital attributes. Investigating hospital treatment intensity patterns may help identify barriers and facilitators to receiving high-quality cancer care.

Figure: adjusted receipt of multi-agent chemotherapy in high-risk stage II and stage III colorectal cancer, NCDB 2006-2012



CCC: Community cancer center; C4: Comprehensive community cancer center; A/R: Academic/Research

P153

Care Coordination in Elderly Colon Cancer Patients R. Hoffman,* K.D. Simmons, C.B. Aarons, R.R. Kelz. *Surgery, University of Pennsylvania, Philadelphia, PA.*

Background: Navigating the healthcare system is suggested as a reason for breaches in evidence based treatment in elderly patients yet there is little supporting data. We aimed to describe the colon cancer patient experience using administrative claims data. Methods: Patients 66-84yrs who underwent resection for stage II/III colon cancer were identified within the 2005-2009 SEER-Medicare database. The patient experience was defined by the occurrence and timing of physician encounters. Six specialists were targeted: surgeon, medical oncologist (MO), radiation oncologist (RO), emergency medicine (EM), gastroenterologist (GI) and primary care (PCP). Stage-specific adherence to NCCN guideline-based therapy (GBT) was determined. Multivariate logistic regression was used to determine the association between receipt of GBT with multiple specialist visits. Results: A total of 12,911 patients were identified; 6816(52.8%) stage II and 6095(47.2%) stage III. Patients were aged 80-84yrs (28.6%); 75-79yrs (28.3%); 70-74yrs (25.0%); 66-69yrs (17.9%). Within a median of 15 days (IQR 5,36) from the cancer operation,12726 (98.6%) patients had 4 distinct visits. The first occurred within a median of 1 day (IQR 1,5); the second within 4d (IQR 2,16); the third within 8d (IQR 4,27), and the fourth within 15d (IQR 5,36). 19%(2479) saw 0 specialists and 36.6%(4726) saw 2-4 specialists. Multiple specialist types were seen on the same date 901 times (7.0%). The number of patients who saw their surgeon or oncologist decreased with increasing age (24.2% to 15.3% and 46.1% to 31.5%, respectively, $p<0.001$) and the median times to see these specialists also decreased with increasing age (24 to 15 days, $p<0.001$ and 23 to 10 days, $p<0.001$). On multivariate analysis, seeing 2 (OR2.19, 95%CI 1.56-3.07) or 3 (OR2.24, 95%CI 1.45-4.07) specialists was associated with an increased odds of receiving GBT for stage III patients. Conclusions: A minority of elderly cancer patients receive same day multidisciplinary care or see a surgeon or oncologist early in their post-operative course. The coordination of complex cancer care may be improved by further examining processes related to the provision of same-day multidisciplinary visits.

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Radical Surgery for Advanced Right Colic Cancer: Lymph Node Dissection in the Era of Complete Mesocolic Excision S. Tsukamoto,* H. Ochiai, D. Shida, G. Morizono, M. Tanaka, Y. Kanemitsu. *National Cancer Center Hospital, Tokyo, Japan.*

Aims: D3 lymph node dissection, in which the draining lymphatics and lymph nodes along the feeding vessels to the surroundings of the root are removed with bowel resection, is a standard surgery for advanced colon cancer in Japan. Recently, it is reported that the improvement of prognosis by performing complete mesocolic excision similar to Japanese D3 lymph node dissection from western country. However, the range of lymph node dissection is controversial whether the dissection should be performed along with superior mesenteric artery (SMA) or vein (SMV) for right colon cancer. We examined the appropriate range of D3 lymph node dissection for advanced right colic cancer in this study. We show a procedure of laparoscopic right hemicolectomy with D3 lymph node dissection along with SMA. Methods: Between 1980 and 2012, 791 patients who underwent radical surgery with D3 lymph node dissection for right-sided colon cancer were eligible for this retrospective study. We performed lymph node dissection along with SMV in the early period, and SMA in the latter period. The ratio of lymph node metastases along with SMA and SMV was investigated. Procedure; we expose the ileocolic artery, and cut the root of the artery. By incising along the SMA, the lymph nodes of the mesocolon are completely removed. The cutting point for the middle colic artery is at the bifurcation of the left and right branches. Results: The lymph node metastasis along with SMA and SMV were 28 cases (4.1%) in all cases. The number of retrieved lymph node was 30 in the early period, and 49 in the latter period. The rate of lymph node metastases along with SMA and SMV was increased 4.0% in the early period to 5.6% in the latter period. Conclusion: To dissect along with SMA leads to secure the wide margin for lymph node metastases. Further assessment for improving patient outcomes of the range of lymph node dissection is awaited.

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Benefit of Surgical Resection of the Primary Tumor in Stage IV Colorectal Cancer with Unresectable Metastasis S. Maroney,* C. Chavez de Paz, R.E. Mark, C. Garberoglio, E. Raskin, S. Maheswari, N. Solomon. *General Surgery, Loma Linda University Hospital, Loma Linda, CA.*

INTRODUCTION: Resection of the primary tumor in patients with unresectable metastatic colorectal cancer is often performed for palliation. Our goal was to determine if resection of the primary tumor in patients with unresectable metastatic colorectal cancer is associated with improved survival. METHODS: This is a Retrospective Cohort Study of the National Cancer Data Base from 2004-2012. The study population included all patients with synchronous metastatic colorectal adenocarcinoma undergoing definitive surgery of the primary tumor. Patients were excluded from the study if they had surgical intervention on the sites of metastasis. Primary outcome was overall survival of patients undergoing definitive surgical resection for the primary colorectal cancer versus no surgery. RESULTS: Of the 118,828 patients with unresectable Stage IV colorectal adenocarcinoma, 52% underwent surgical resection of the primary site. In the subset of patients undergoing chemotherapy, actuarial survival curves for surgical resection were associated with improved median survival when compared to patients treated with multi-agent or single-agent chemotherapy alone (23 vs 14 months, $p<0.001$; 19 vs 9 months, $p<0.001$). Using multivariate analysis with propensity score matching in patients undergoing multi-agent or single-agent chemotherapy, surgery demonstrated a protective effect on survival (HR=0.499; 95% CI [0.49-0.51]; HR=0.579; 95% CI [0.54-0.63]) CONCLUSIONS: Our results show that in patients with synchronous unresectable Stage IV colorectal adenocarcinoma undergoing multi-agent chemotherapy, after adjusting for confounding variables, definitive surgery of the primary site was associated with improved overall survival. Large randomized controlled trials are needed to determine if there is a causal relationship between surgery and increased overall survival in this patient population.

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Racial Disparities in Thyroid Cancer Surgery H.B. Castillo Valladares,* J. Malinowski, G.G. Callender. *Surgery, Yale School of Medicine, New Haven, CT.*

BACKGROUND Although thyroid cancer surgery (TCS) is associated with excellent outcomes, studies have established survival rate differences based on race. We sought to determine the impact of race on the surgical management of thyroid cancer, evaluating differences in recommendation for surgery and refusal of surgery. METHODS The Surveillance, Epidemiology, and End Results registry identified 137,483 patients with thyroid cancer from 1988-2012. Associations between race, surgery recommendation, and surgery refusal were evaluated using logistic regression. Survival analysis was performed using the Cox model. Analyses were stratified by cancer type: papillary (PTC), medullary (MTC), follicular (FTC), and anaplastic (ATC). RESULTS The majority of the sample was white (82%), female (75%), had PTC (87%), and underwent TCS (95%). TCS was less often recommended to blacks (Odds ratio (OR) 1.3, 95% confidence interval (CI) 1.2-1.5), and patients of unknown race (OR 3.1, CI 2.4-3.9) compared to whites. American Indian/Alaska Natives (AI) and Asian/Pacific Islanders (API) refused surgery more often compared to whites (OR 4.5, CI 1.9-10.4; OR 2.96, CI 2.2-3.9). Blacks had poorer 5-year survival compared to whites (Hazard ratio (HR) 1.14, CI 1.02-1.3). Race did not predict surgery recommendation or refusal for MTC or ATC patients. Among PTC patients, blacks, API, and patients of unknown race were recommended surgery less often compared to whites (OR 1.2, CI 1.01-1.5; OR 1.3, CI 1.1-1.5; OR 3.1 CI 2.4-4.1). Among FTC patients, patients of unknown race were recommended surgery less often compared to whites (OR 2.7, CI 1.02-7). AI and API PTC patients and API FTC patients refused surgery more often compared to whites (OR 4.3, CI 1.5-12.1; OR 2.6 CI 1.9-3.8; OR 3.1 CI 1.3-7.8). AI PTC patients had poorer 5-year survival compared to whites (HR 1.6, CI 1.05-2.6); we found no survival differences based on race for MTC, FTC, and ATC. CONCLUSION Racial disparities in recommendation and acceptance of TCS exist, affecting black, API, AI, and patients of unknown race. Future studies should evaluate system- and patient-level factors perpetuating the disparities observed.

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Resection of Primary Gastrointestinal Neuroendocrine Tumor Improves Overall Survival with or without Treatment of Liver Metastases A. Lewis,* M.A. White, M. Raoof, P. Ituarte, R. Kauffman, S. Warner, L. Melstrom, Y. Fong, G. Singh. *Surgery, City of Hope, Duarte, CA.*

Introduction: There is mounting evidence that resection of the primary tumor offers a survival benefit in metastatic gastrointestinal neuroendocrine tumors (GI-NET); however, few studies have examined the effect of primary site and grade on resection and survival. This study seeks to determine outcomes of primary tumor resection in metastatic neuroendocrine tumors across all primary tumor sites. Methods: This is a retrospective study of patients with metastatic GI-NET at the time of presentation between 2005-2011 using the California Cancer Registry (CCR) dataset merged with the California Office of Statewide Health Planning and Development (OSHPD) inpatient longitudinal database. Primary outcome was Overall Survival (OS). Univariate and multivariate (MV) analyses were performed using the chi-squared test and cox proportional hazard, respectively. OS was estimated using the Kaplan-Meier method and log-rank test. Results: A total of 854 patients with GI-NET metastases on presentation underwent 392 primary resections. Liver metastases were found in 467 patients and 161 received liver treatment(s). Resection of the primary tumor improved OS in patients with untreated metastases (median survival 8 vs 34 months, $p < 0.001$). On MV analysis adjusted for demographics, tumor stage, grade, chemotherapy use, Charlson comorbidity index, primary tumor location, or treatment of liver metastases, resection of the primary tumor with or without liver treatment improved OS in comparison to no treatment at all as shown in Table 1 (HR 0.5, $p < 0.001$ and 0.39, $p < 0.001$, respectively). Low-grade tumors were more likely to undergo primary resection than high-grade (73.8% vs 51.5%, respectively. $p < 0.0001$); however, primary resection offered a survival benefit across all grades (low-grade, HR 0.38, $p = 0.002$ and high-grade, HR 0.62, $p = 0.025$). Conclusions: Resection of the primary tumor in GI-NET is associated with a better survival, with or without liver treatment, irrespective of grade.

Resection of Primary Tumor in Stage IV GI-NET

Site	No Liver Treatment				Liver Treatment			
	N	Median (months)	5-yr OS (%) (1)	p-value	N	Median (months)	5-yr OS (%) (1)	p-value
Overall								
No 1° Rx	203	7	17.7	<0.001	75	18	30.7	<0.001
1° Rx	103	26	44.7		86	45	55.8	
Stomach								
No 1° Rx	23	3	8.7	0.8	5	8	20	0.52
1° Rx	3	12	0		3	20	0	
Pancreas								
No 1° Rx	138	11	21.7	0.011	54	18	31.5	0.007
1° Rx	9	Not Reached	66.9		35	Not Reached	60	
Small Bowel								
No 1° Rx	11	7	18.2	<0.001	7	45	42.8	0.35
1° Rx	48	Not Reached	68.8		31	Not Reached	74.2	
Large Bowel								
No 1° Rx	31	2	6.5	0.026	9	8	22.2	0.33
1° Rx	43	5	16.3		17	15	23.5	

Table 1. (1) 5-year absolute OS reported.

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Prognostic Significance of Diagnosed Hereditary Syndrome in Patients with Malignant Pheochromocytoma and Paraganglioma W. Li,* M.T. Stang, K.L. McCoy, S.M. Challinor, M. Hogg, S.E. Carty, L. Yip. *University of Pittsburgh, Pittsburgh, PA.*

Introduction: Pheochromocytoma (PHEO) and extra-adrenal paragangliomas (PG) are components of a number of hereditary syndromes. Both can be malignant and prognosis is variable. The study aim was to determine if outcomes for malignant PHEO/PG differ in patients with hereditary compared to nonhereditary disease. Methods: Retrospective single institution review of all patients with histologic PHEO and/or PG from 2000-2015. Malignant disease was diagnosed if lymphatic or distant metastasis was documented. Hereditary disease was determined by genetic testing when available and/or detailed pedigree analysis. Demographic, clinical, pathologic, and survival comparisons were calculated using student t-test, chi-square and Kaplan-Meier analysis. Results: Forty-six patients with malignant PHEO/PG included 19 (41%) hereditary and 27 presumed nonhereditary patients. Patients with hereditary disease were younger both at initial PHEO/PG diagnosis (mean age 35 v. 49 y, p=.008) and at time of malignant diagnosis (mean age, 40 v. 53 y, p=.017). Patient characteristics were not otherwise different in those with hereditary or nonhereditary malignant PHEO/PG including gender (p=.8), tumor site (p=.4), surgical resection (p=1), use of XRT (p=1) or use of chemotherapy (p=.3). Overall mean survival was 12.8 years with 5-year survival of 71%. By Kaplan- Meier analysis, survival was not affected by PHEO vs. PG (p=.4), presence of synchronous vs. metachronous metastasis (p=.4), or use of treatment modalities including surgery (p=.8), chemotherapy (p=1), or XRT (p=.7). However, poorer prognosis was observed in men (mean survival 6.6 vs. 16.3 years, HR 3.4, p=.01,) and in those with nonhereditary disease (mean survival 10.3 vs. 12.8 years, HR 2.6, p=.05). Overall, men with nonhereditary malignant PHEO/PG had the shortest mean survival (4.8 years, p=.004). Conclusions: In malignant PHEO/PG, patients with hereditary disease are younger at diagnosis, but have similar disease characteristics and received equivalent treatment as patients with malignant nonhereditary disease. Malignant PHEO/PG in men with presumed nonhereditary disease is associated with the worst prognosis.

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Outcomes of Cytoreductive Surgery for Well-Differentiated Metastatic Neuroendocrine Tumors in the Setting of Extrahepatic Metastases J. Hallet,[1]* S. Koudjanian,[2] K. Beyfuss,[2] N. Coburn,[1] P. Karanicolas,[1] S. Singh,[1] C. Law.[1] *1. Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada; 2. Sunnybrook Research Institute, Toronto, ON, Canada.*

Background: Neuroendocrine tumors (NETs) have a unique indolent biology. Management focuses on tumor and hormonal burden reduction. Data on cytoreduction with extra-hepatic disease remain limited. We sought to define the outcomes of cytoreduction for metastatic NETs in the setting of extra-hepatic metastatic disease. Methods: Patients undergoing cytoreductive surgery for G1 or G2 (WHO 2010 classification) NETs in the setting of extra-hepatic metastases (with or without intra-hepatic disease) were identified from an institutional database (2003-2014). Primary outcomes included post-operative hormonal response (>10% urinary 5HIAA drop), progression-free and overall survival (PFS, OS). Secondary outcomes were 30-day post-operative major

morbidity (Clavien grade III-V), mortality, and length of stay. Results: 55 patients were identified, with median age of 59.3 years old. Most had small bowel primaries (80%), and 49.1% were G1. Few patients (13%) had exclusively extra-hepatic metastases, with the remainder presenting combined intra and extra-hepatic metastases. Resection most commonly included liver (87%), small bowel (22%), mesenteric (25%) and retroperitoneal (11%) nodes, and peritoneum (7%). 30-day major morbidity (Clavien III-V) was 18%, with 3.6% mortality. Median length of stay was 7 days (inter-quartile range: 5-9). Liver embolization was performed in 31% after surgery, at a median of 15 months following surgery. Overall, post-operative hormonal response occurred in 70%. Median drop in 5HIAA was 60%. 41 (75%) patients received LASA, more commonly so with small bowel primaries, but without difference in grade, carcinoid syndrome presentation or 5HIAA response to surgery. At median follow-up of 37 months (range 22-93), 45 (82%) patients were alive and 23 (41.8%) had progressed. 5-year OS was 77% and 5-year PFS was 51%. Conclusion: Cytoreduction of metastatic well-differentiated NET in the setting of extra-hepatic metastatic disease provides significant tumoral and hormonal control, with favourable PFS and OS. Aggressive surgical management of metastatic NET appears indicated even with extra-hepatic disease.

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Functional Polymorphisms in Antioxidant Genes and Occurrence of Recurrent Disease in Patients with Hurthle Cell Carcinoma

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Background: Common functional polymorphisms in antioxidant genes can decrease antioxidant defense. The resulting higher level of oxidative stress has been associated with increased risk for cancers. There are no data on polymorphisms in antioxidant genes in Hurthle cell adenoma (HCA) and Hurthle cell carcinoma (HCC). We investigated if they are associated with development or clinical course of HCC. Material and methods: We analyzed 139 patients with Hurthle cell neoplasm. HCC, HCA and benign multinodular goiter (MNG) were diagnosed by pathomorphology. Two to three cores of normal tissue were obtained from formalin fixed paraffin embedded specimens for DNA extraction using QiaAmp Mini kit (Qiagene, Hilden, Germany). Genotyping of GSTP1 rs1695, GSTP1 rs1138272, GPX1 rs1050450, CAT rs1001179, SOD2 rs4880 was carried out using fluorescence-based competitive allele-specific KASPar assay (Kbiosciences, Herts, UK). Amplifications were performed in PCR system 9700 AB. Fluorescence was measured on 7500 Real Time PCR System AB and allele discrimination data analyzed with 7500 System SDS Software. Logistic regression was used to compare genotype distributions between patient groups. All statistical analyses were carried out using IBM SPPS Statistics version 19.0. Results: HCC, HCA and MNG were diagnosed in 53, 47 and 39 patients, respectively. Metastatic disease and recurrence of HCC were diagnosed in 20 and 16 out of 53 HCC patients, respectively. Genotypes and allele frequencies of investigated polymorphisms did not deviate from Hardy-Weinberg equilibrium in patients with HCC, HCA and MNG. Under the dominant genetic model we observed no differences in the genotype frequency distribution of the investigated polymorphisms when HCA and MNG group was compared to HCC group for diagnosis of HCC or for presence of metastatic disease. However, GPX rs1050450 polymorphism was associated with recurrent disease (p=0.040). No associations were observed between GSTP1 haplotypes and diagnosis of HCA/MNG versus HCC, presence of metastatic disease or recurrent disease. Conclusion: GPX polymorphism may influence the risk for recurrent disease in HCC.

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Small Bowel Neuroendocrine Tumors:

A Critical Analysis of Diagnostic Work-up and Operative Approach

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Background: Small bowel neuroendocrine tumors (SB-NET) are rare, and often small and multifocal. They are difficult to localize preoperatively and can be overlooked during operative exploration. The optimal work-up and operative approach is not known. Methods: Patients who underwent resection of SB-NET at a single institution from 2000-2014 were included. Primary aim was to describe the diagnostic work-up, pathologic characteristics, and compare minimally-invasive (MIS) to open resection. Results: 93pts underwent resection for SB-NET. Median age was 61yrs; 52% were male. On presentation, 71% of pts were symptomatic and underwent an average of 3 diagnostic tests prior to resection: 45% had octreoscans, which identified the region of primary disease in 85%; 11% had small bowel enteroscopy, with a 10% diagnostic yield; 19% had capsule endoscopy, which saw a lesion in 83%, but in only 21% was the correct number of tumors seen. The diagnostic yield of capsule was 28% overall, but 82% in pts presenting with GI bleeding. 79pts (85%) underwent curative-intent resections. Median tumor size was 1.8cm and multiple primary tumors were seen in 34pts(42%), of whom 50% had >3 tumors. 37% had metastatic and 70% had LN positive disease. 27pts underwent MIS resections vs 66 open. MIS pts were younger (56vs61yrs;p0.035) and less likely to have obstructive symptoms (4vs24%;p=0.19) and metastatic disease at resection (19vs44%;p=0.038). Compared to open, the MIS group had smaller (1.7vs2.4cm;p=0.03) and fewer tumors resected (2vs5;p=0.049), but similar LN yield (13vs12;p=0.7). In pts without metastases undergoing curative-intent resection, MIS approach was still associated with fewer tumors removed compared to open (1.5vs4;p=0.034). Conclusion: Capsule endoscopy appears to be better than small bowel enteroscopy at identifying occult small bowel neuroendocrine tumors, particularly when pts present with bleeding, but still may underestimate tumor burden. While MIS may be appropriate in select patients, recognizing the limitations of preoperative evaluation is critical when selecting the operative approach for these tumors, as heightened operative vigilance is often required.

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Demographic and Economic Disparities in the Presentation and Management of Carcinoid Tumor: A National Perspective

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Background: Demographic and economic factors have been frequently identified in the healthcare system as determinant factors in certain diseases. In this study, we aim to examine the association of selected demographic and economic factors with carcinoid tumor. Methods: A cross-sectional study utilizing the Nationwide Inpatient Sample (NIS) database for 2003-2010. The study population included adult patients (≥18 years) with carcinoid tumor who were admitted for treatment. Results: A total of 3,422 discharge records were included. Gastrointestinal, metastatic and/or undifferentiated tumors were more common in males (p<0.05 each). Younger patients (≤65 years), and Blacks were more likely to present with gastrointestinal carcinoid tumor than elsewhere in the body (p<0.05 each). Alternatively, patients within the age group (45 – 65 years) or on Medicaid were more likely to have malignant carcinoid tumor regardless of the site (p<0.05 each). Women were more likely to undergo major operative procedure [OR: 1.33, 95%CI: (1.06, 1.68), p=0.014]. While patients with Medicaid coverage were at higher risk of postoperative complications [OR: 1.93, 95%CI: (1.26, 2.96), p=0.003]. Patients managed in low volume hospitals (1 case/year) were more likely to have a longer hospital stay (> 8 days) (p<0.05). Conclusion: The presentation and outcomes of carcinoid tumor appear to be associated with the patient's demographic and economic background, underlying the disparity in carcinoid tumor management.

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Access to Care and Outcomes for Neuroendocrine Tumors: Does Socioeconomic Status Matter? A Population-Based Analysis

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Introduction: Despite rising incidence, Neuroendocrine Tumors (NET) are a poorly understood malignancy lacking standardized care. Differences in socioeconomic status (SES) may further worsen the impact of non-standardized care. Variations in care in this setting may provide insight into improving healthcare delivery. We examined the impact of SES on NET peri-diagnostic care patterns and outcomes. Methods: We conducted a population-based cohort study, within a universal heatlthcare system, of adults with NET. NET cases identified from a provincial cancer registry (1994-2009) were divided into low (1st and 2nd income quintiles) and high SES (3rd, 4th, 5th quintiles). Utilization Band (RUB) captured expected healthcare need based on baseline

comorbidities. We compared peri-diagnostic healthcare utilization (-60 days to +6 months), metastatic recurrence, and overall survival (OS) between groups. Results: Of 4966 NET patients, 38.3% had low SES. Age, gender, and RUB did not differ among groups (p=0.13). Neither primary NET sites (p=0.15) nor metastatic presentation differed (p=0.31). Patients with low SES had higher mean number of physician visits (20.1±19.9 vs 18.1±16.5; p=) and imaging studies (56±50 vs 52±44; p=0.009) leading to NET diagnosis. Primary tumor resection (p=0.14), hepatectomy (p=0.45), systemic therapy (p=0.38), and liver embolization (p=0.13) rates did not differ with SES. Metastatic recurrence was more likely with low SES (41.1% vs 37.6%; p=0.01) over a 61.7 months median follow-up. 10-year OS was inferior with low SES (47.1% vs 52.2%; p<0.01). Low SES was associated with worse OS (HR 1.16; 95%CI: 1.06-1.26) after adjustment for age, gender, comorbidity burden, primary NET site, and rural living. Conclusion: Low SES was associated with need for more physician visits and imaging to reach NET diagnosis, but not with more common advanced stage presentation or impact on patterns of therapy. Long-term outcomes were inferior for low SES patients, with more frequent metastatic recurrence and worse 10-year OS. This data provides further insight for future directives in enhancing healthcare delivery particularly in NET patients with low SES.

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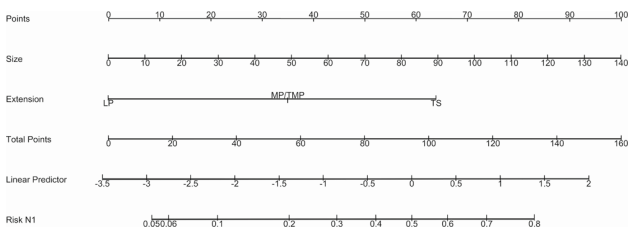
Novel Nomogram Combining Depth of Invasion and Size Can Accurately Predict the Benefit of Regional Lymphadenectomy for Appendiceal Neuroendocrine Tumors (A-NET) C. Mosquera,* H. Vora, T. Fitzgerald. *Brody School of Medicine, Division of Surgical Oncology, Greenville, NC.*

The need for regional lymphadenectomy for A-NET is predicated on the risk of nodal metastasis. Although depth of invasion is predictive of nodal metastases in other gastrointestinal NET, current guideline recommendations for A-NET are based solely upon size. Methods: Patients with A-NET from 1988-2012 were identified within the SEER registry. Depth of invasion was defined as limited to lamina propria (LP), invading or through muscularis propria (MP), and through serosa (TS). Results: A total of 1,024 patients met inclusion criteria, with majority being female (55.7%), white (86.8%), and node-negative (81.1%). On univariate analysis, risk of nodal metastases was associated with size (<1 cm 1.9%, 1-2 cm 19.7%, 2-4 cm 32.5%, and > 4 cm 37.2%), depth of invasion (LP 4.1%, MP 17.4% and TS 44.3%) and extent of surgery (appendectomy 8.7% vs colectomy 31.9%), p<0.0001. On multivariate analysis, size (<1 cm vs 1-2 cm HR 8.80, vs 2-4 cm HR 15.68, and vs >4 cm HR 15.16), depth of invasion (LP vs TS HR 6.67) and extent of surgery (appendectomy vs colectomy HR 2.98), continued to be associated with nodal involvement, p<0.0001. When only patients with colectomy were considered results were similar on both univariate and multivariate analyses. On univariate survival analysis, size [<1cm 95.6%, 1-2cm 94.9%, 2-4cm 88.4%, and > 4cm 73.7% 5-year disease-specific survival (5-y DSS)], depth of invasion (LP 96.9%, MP 93.2%, and TS 77.1% 5-y DSS), extent of surgery (appendectomy 94.4% and colectomy 87.1%), and N stage (N0 94.7% and N1 77.7%) predicted survival, p<0.002. In a Cox regression model, extent of surgery and N stage continued to predict survival. A nomogram (Figure 1) was created to predict the risk of nodal metastases, AUC=0.83. Conclusion: This simple nomogram, which incorporates size and tumor extension, accurately predicts the risk for regional nodal metastases in appendiceal NET. In addition to providing valuable information on risk for regional nodal metastases, depth of invasion independently predicts survival.



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Focused Parathyroidectomy without Intraoperative Parathormone Testing is Safe After Preoperative Localization with ^{18}F-Fluorocholine PET/CT M. Hocevar,[1]* S. Rep,[2] L. Lezaic,[2] T. Kocjan,[3] B. Peric,[1] J. Zgajnar.[1] *1. Surgical Oncology, Institute of Oncology, Ljubljana, Slovenia; 2. University Clinic Center, Department of Nuclear Medicine, Ljubljana, Slovenia; 3. University Clinic Center, Department of Endocrinology, Ljubljana, Slovenia.*

A focused surgical approach based on pre-operative localization replaced the classical four-gland exploration in patients with primary hyperparathyroidism (PHP). Sestamibi scanning and ultrasound are most often used localization modalities with reported sensitivity of 54–100% for identification of single gland disease. The aim of this study was to analyze the results of pre-operative localization with ^{18}F-Fluorocholine PET/CT (FCh-PET) in patients with PHP. A retrospective review of 151 patients with PHP who underwent surgery after pre-operative localization with FCh-PET was performed. Only a focused parathyroidectomy without ioPTH testing had been done in patients with single adenoma on FCh-PET. Primary outcome was operative failure, defined as persistent PHP. According to pre-operative FCh-PET 126 (83,4%) patients had single adenoma, 22 (14,5%) multiglandular disease and the test was negative in only two patients. Intraoperative failure experienced 4/126 patients (3,3%) with single adenoma. Removed parathyroid glands were normal in three and hyperplastic in one patient with intraoperative failure. A limited bilateral neck exploration with ioPTH testing was used in 14/22 patients with double adenoma according to pre-operative FCh-PET. In 6/14 patients surgery confirmed double adenoma while 8 patients had only a single adenoma and all 14 patients were cured. A classical four-gland exploration without ioPTH testing was used in 8/22 patients with more than two pathological glands according to pre-operative FCh-PET. All 8 patients had hyperplasia and two experienced intraoperative failure. In two patients with negative FCh-PET a classical four-gland exploration without ioPTH testing was used. One patient had a single adenoma and was cured and only normal parathyroid glands were found in the other patient with intraoperative failure. A preoperative localization with FCh-PET is a reliable test in patients with PHP. Patients with a single adenoma on FCh-PET can safely undergo a focused parathyroidectomy without ioPTH testing.

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Reevaluating the Significance of Multifocality in Sporadic Medullary Thyroid Carcinoma (MTC) E. Grubbs,* F. Nieves-Munoz, M. Hu, L. Feng, N.D. Perrier, J.E. Lee, G. Cote, M.D. Williams, R. Gagel. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Tumor multifocality (MF) is common in hereditary MTC and has been superseded by RET gene sequencing in identifying the disease's germline origin. The existence of MF in sporadic MTC (sMTC) is less certain, and may represent widespread lymphovascular invasion (LVI) versus a true polyclonal event. Its incidence and significance in sMTC varies in the literature. Therefore, we evaluated our single institutional experience to further define incidence and clinicopathologic associations of MF in sMTC. Methods: Thyroidectomy specimens of patients (pts) undergoing primary surgery for MTC at a single institution were evaluated for pathologic features including extrathyroidal extension (ETE), LVI, MF, C-cell hyperplasia (CCH) and laterality. MF was noted when tumor nodules appear distinct, separated by normal thyroid parenchyma. Results: 76 pts underwent primary surgery for confirmed sMTC at our institution from 2006-2015 at a median age of 56.4 years (range 23.2-84.9). 44 (58%) of pts were female and the T stage was 30%, 29%, 25% and 16% for T1,T2,T3,T4; N stage was 38%,7%, and 53% for N0, N1a, N1b, and M stage was 62%,16%, 22% for M0,M1,MX. 11 (14%) sMTC were MF (9 unilateral and 2 bilateral). MF was associated with LVI (p=.02), nodal metastasis (p=.005) and macroscopic nodal involvement (p=.0005); 10 of 11 MF had documented LVI with all 11 having nodal metastasis. MF was also associated with ETE (p=.0001) (present in all 11 MF). Only 2 pts with MF also had CCH which was not significantly associated (p=.61). Median follow up of the sMTC cohort was 30.7 months (range 1.0-97.0); 9 (12%) died of MTC during this time period. Disease specific survival (DSS) for sMTC was associated with M stage but not T or N stage, ETE, MF, CCH, or LVI (Table). Conclusion: Multifocality in sMTC is rarer in this series than in the literature, especially if defined by bilaterality; MF fails to add significance to clinical management/outcomes. The association of MF with only unilateral involvement, LVI, and nodal disease favors an etiology of a multinodular process via lymphovascular

spread; rare MF bilaterality may represent a true polyclonal process requiring molecular validation.

Disease specific survival (DSS) in sporadic medullary thyroid cancer by staging and pathology characteristics

Variable	DSS rate at 3 years (95%CI)	DSS rate at 5 years (95%CI)	p-value
Age	-	-	
<50 years	0.91 (0.79,1.00)	0.91 (0.79,1.00)	0.44
>50 years	0.84 (0.73,0.97)	0.79 (0.66,0.95)	
T stage	-	-	
T1/T2	0.92 (0.83,1.00)	0.92(0.83,1.00)	0.09
T3/T4	0.78 (0.63,0.97)	0.70(0.52,0.95	
N stage	-	-	
N0	0.96 (0.88,1.00)	0.96(0.88,1.00)	0.09
N1	0.80 (0.68,0.95)	0.75(0.61,0.93)	
M stage	-	-	
M0	0.94 (0.87,1.00)	0.94 (0.87,1.00)	0.0001
M1	0.58 (0.36,0.94)	0.39 (0.15,0.99)	
Multifocality	-	-	
No	0.87 (0.78,0.97)	0.87 (0.78,0.97)	0.29
Yes	0.82 (0.62,1.00)	0.65(0.39,1.00)	
Extrathyroidal extension	-	-	
No	0.93(0.84,1.00)	0.93(0.84,1.00)	0.06
Yes	0.79(0.65,0.96)	0.72(0.55,0.94)	
Lymphovascular invasion	-	-	
No	0.96(0.88,1.00)	0.96 (0.88,1.00)	0.06
Yes	0.78(0.65,0.94)	0.71(0.55,0.92)	
C-cell hyperplasia	-	-	
No	0.86(0.76,0.97)	0.80(0.66,0.97)	0.26
Yes	1.00 (1.00,1.00)	1.00(1.00,1.00)	

P169

Thyroglobulin Measurement in Fine-Needle Aspiration Improves the Diagnosis of Cervical Lymph Node Metastases in Papillary Thyroid Carcinoma Z. Al-Hilli,* V. Strajina, T. McKenzie, G.B. Thompson, D.R. Farley, M.L. Richards. *Mayo Clinic, Rochester, MN.*

Introduction: Papillary thyroid carcinoma (PTC) is frequently associated with cervical lymph node metastases. Current guidelines recommend performing ultrasound (US) guided fine-needle aspiration cytology (FNAC) for suspicious nodes to guide further management. There are no specific recommendations for the use of FNA thyroglobulin assay (FNA-Tg). We investigated the diagnostic value of performing FNAC and FNA-Tg alone and in combination. Methods: Patient demographics, pre-operative investigations, type of surgery and final lymph node pathology were collected in patients with PTC who underwent lateral neck lymphadenectomy and central compartment re-exploration from Jan 2000-July 2015. Sensitivities and specificities were obtained for FNAC and FNA-Tg. Patients with both diagnostic studies performed were compared using McNemar's test of paired proportion. Patient, imaging and lymph node characteristics were correlated with test accuracy. Results: 480 patients underwent 706 lateral neck dissections or central compartment re-exploration for PTC. The mean age was 44 years, with a male to female ratio of 1:1.6. All patients underwent US. FNAC alone was performed prior to 425(60%) operations, FNAC with FNA-Tg in 106(15%) and 175(25%) proceeded directly to surgery without biopsy. The sensitivity, specificity, positive predictive value, negative predictive value and accuracy of each test are shown in Table 1. Performing FNA-Tg alone was superior to FNAC alone (sensitivity 94% vs 92%, p=0.017). The addition of FNA-Tg to the FNAC increased the detection of metastatic PTC by 16.7%. Inversely, the addition of FNAC to FNA-Tg increased the detection of metastatic PTC by 4.9%. Increasing lymph node size (>2cm) and extent of surgery correlated with test accuracy (p=0.02 and 0.01). There was no relation to test accuracy for patient age >45, gender, lymph node level and US interpretation. Conclusion: FNA-Tg is more accurate than FNAC at diagnosing cervical lymph node metastases in PTC. It should be considered an important adjunct to FNAC to avoid missing metastatic disease in patients who may benefit from lymphadenectomy.

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	Accuracy
FNAC	480/520 (92.3%)	8/11 (72.7%)	480/483 (99.4%)	8/48 (16.7%)	488/531 (91.9%)
FNA-Tg	96/102 (94.1%)	1/4 (25%)	96/99 (97%)	1/7 (14.3%)	97/106 (91.5%)
FNAC and FNA-Tg	101/102 (99%)	1/4 (25%)	101/104 (97.1%)	1/2 (50%)	102/106 (96.2%)

P170

Adjuvant Radiation Therapy in Patients Undergoing Curative Intent Resection for Adrenocortical Carcinoma: A Multi-Institutional Experience I. Hatzaras,[1]* R. Rao,[1] T.B. Tran,[2] L.M. Postlewait,[3] S.K. Maithel,[3] J. Prescott,[7] T.M. Pawlik,[7] T. Wang,[10] J. Phay,[5] R.C. Fields,[6] L. Jin,[6] S. Weber,[4] A.I. Salem,[4] J. Sicklick,[12] S. Gad,[12] A. Yopp,[8] J. Mansour,[8] Q. Duh,[13] N. Seiser,[13] C.C. Solorzano,[9] C.M. Kiernan,[9] K. Votanopoulos,[11] E.A. Levine,[11] E. Newman,[1] G. Poultsides,[2] H. Pachter.[1] *1. Department of Surgery, NYU Langone Medical Center, New York, NY; 2. Department of Surgery, Stanford University, Palo Alto, CA; 3. Department of Surgery, Emory University, Atlanta, GA; 4. Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 5. Department of Surgery, Ohio State University, Columbus, OH; 6. Department of Surgery, Washington University, St. Louis, MO; 7. Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD; 8. Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX; 9. Department of Surgery, Vanderbilt University Medical Center, Nashville, TN; 10. Department of Surgery, Medical College of Wisconsin, Milwaukee, WI; 11. Department of Surgery, Wake Forest University School of Medicine, Winston-Salem, NC; 12. Department of Surgery, University of California, San Diego, San Diego, CA; 13. Department of Surgery, University of California, San Francisco, San Francisco, CA.*

Background: The role of adjuvant radiation (RT) for adrenocortical carcinoma (ACC) is uncertain. We combined the experience of thirteen centers in the U.S. to explore the impact of adjuvant RT in ACC. Methods: Patients were identified from a retrospective database of 234 patients who underwent surgery for ACC between 1993 to 2014. Descriptive statistics were used to characterize demographics, comorbidities, surgical approach, margin status, pathologic characteristics, and high-risk features (tumor rupture, large tumor size, and positive resection margin). We also reviewed the potential synergistic effect of receiving RT with adjuvant Mitotane. Cox proportional hazards regression was used to identify predictors of local / regional recurrence and overall survival. Propensity score matching was used to eliminate selection bias and evaluate the potential prognostic benefit of RT. Results: Adjuvant RT data was available in 208 (89%%) patients, of which 20 (9.6%) received RT with a median dose of 50Gy. Twelve patients received RT plus Mitotane. The median follow up of the entire cohort was 17.8 months. T and N stage was proportionally distributed between the RT and no RT groups. The RT group had a higher rate of margins positive resection (57.9% vs. 30.6%, p=0.017). Median survival was comparable between the two cohorts (38.2 vs. 47.3 months, p = 0.74) as was recurrence-free survival (RFS) (6.7 vs. 9.8 months, p = 0.54). RT had no benefit in the subgroup with high-risk features. Lastly, there was no benefit in the RT plus Mitotane regimen compared to surgery only (median survival: 38.2 vs. 41.3 months, p = 0.9, RFS: 4.1 vs. 9.8 months, p = 0.016). Upon propensity score matching, with a surgery only control group, RT was found to improve RFS [HR= 0.128, 95% CI (0.027, 0.603), p=0.009] but not overall survival [p=0.9]. Conclusions: After curative intent resection for ACC, adjuvant RT may offer improved local control, but not overall survival, compared with observation. The potential synergistic effect of Mitotane in addition to RT did not yield improved prognosis. Further studies are needed to explore the potential benefit of RT.

P171

Number of Lymph Nodes Examined Predicts Survival in Node Negative Appendiceal Carcinoids M. Raoof,* S. Dumitra, G. Singh, Y. Fong, B. Lee. *City of Hope Medical Center, Duarte, CA.*

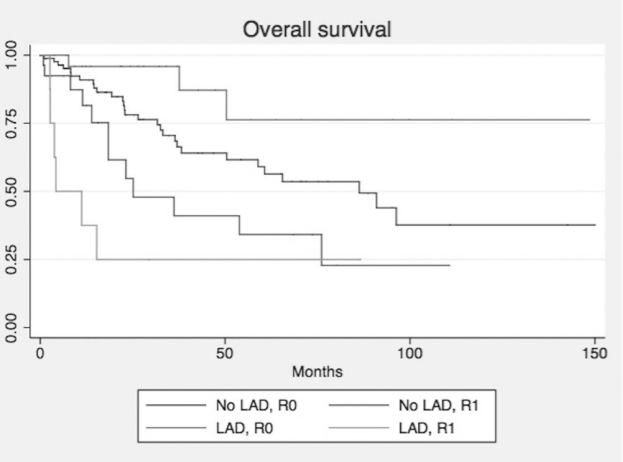
Background: Surgical resection is the primary therapy for local and locally advanced carcinoid tumors of the appendix. The extent of surgery is largely dictated by the size of the tumor. Tumors >2 cm require a right hemicolectomy with associated mesenteric lymphadenectomy. What constitutes an adequate mesenteric lymphadenectomy is not known. Methods: This is a study of a contemporary cohort from NCI's SEER database (Jan, 2004- Nov, 2012). Patients with non-metastatic appendiceal carcinoid tumors were included. Surgical extent was defined as limited (appendectomy or illeocecectomy) or extended (hemicolectomy). Primary outcome was overall survival (OS). Survival analysis was performed using the Kaplan-Meier and Cox-proportional hazards model. Results: Of the total 1104 patients that met the inclusion criteria, 52% were female, 88% were white and majority were middle aged (40-

60y) 45%. Majority of the tumors were <2 cm (49.3%) and lymph node(LN) negative 85%. Median LN retrieved were 10 (IQR 0-17). Median follow-up was 32 months (IQR 10-61). A multivariate Cox-proportional hazard model demonstrated that increasing age, tumor size > 3cm, tumor spread to contiguous organs, LN positivity and LN count <11 (HR 1.78: 95%CI 1.17-2.69; p=0.006) are associated with worse OS. Five-year overall survival increased with the number of LN retrieved (LN 1-10, 81.4%; LN >10, 85.9%, p=0.035). Stratified analysis by LN status demonstrated that LN count <11 was an independent predictor of worse OS in node negative patients (HR 2.10: 95%CI 1.25-3.53; p=0.005) but not node positive patients (p=0.65). Subset analysis by tumors size demonstrated that prognostic value of LN count <11 was only significant for tumors greater than 3 cm (HR 2.32: 95%CI 1.15-2.03; p=0.018). Conclusion: This is the largest study to date that looks at prognostic significance of LN count for appendiceal carcinoids. The number of LNs evaluated is an independent prognostic factor in pathologic node-negative, appendiceal carcinoid tumors measuring greater than 3 cm. This data supports performing a formal lymphadenectomy (>10 LN) even if no mesenteric disease is visible for adequate staging.

P172

Lymphadenectomy for Adrenocortical Carcinoma: Is there a Therapeutic Benefit? J. Gerry,[1]* L.M. Postlewait,[2] S. Maithel,[2] J. Prescott,[3] T. Wang,[4] J.A. Glenn,[4] J. Phay,[5] K. Keplinger,[5] R.C. Fields,[6] L. Jin,[6] S. Weber,[7] A.I. Salem,[7] J. Sicklick,[8] S. Gad,[8] A. Yopp,[9] J. Mansour,[9] Q. Duh,[10] N. Seiser,[10] C.C. Solorzano,[11] C.M. Kiernan,[11] K. Votanopoulos,[12] E.A. Levine,[12] I. Hatzaras,[13] R. Shenoy,[13] T.M. Pawlik,[3] G. Poultsides.[1] *1. Stanford University School of Medicine, Stanford, CA; 2. Emory University, Atlanta, GA; 3. The Johns Hopkins University School of Medicine, Baltimore, MD; 4. Medical College of Wisconsin, Milwaukee, WI; 5. The Ohio State University, Columbus, OH; 6. Washington University School of Medicine, St. Louis, MO; 7. University of Wisconsin School of Medicine and Public Health, Madison, WI; 8. University of California San Diego, San Diego, CA; 9. University of Texas Southwestern Medical Center, Dallas, TX; 10. University of California San Francisco, San Francisco, CA; 11. Vanderbilt University, Nashville, TN; 12. Wake Forest Baptist Medical Center, Winston-Salem, NC; 13. New York University School of Medicine, New York, NY.*

Introduction: Lymph node metastasis is an established predictor of poor outcome for adrenocortical carcinoma (ACC), however routine lymphadenectomy during surgical resection of ACC is not widely performed and it is therapeutic role remains unclear. Methods: Patients who underwent curative-intent resection for localized ACC from 1993 to 2014 were identified from a multi-institutional database. Patients were stratified into two groups based on the surgeon's effort or not to perform lymphadenectomy. Clinical, pathologic, and outcomes data were compared between the two groups. Results: Of 188 patients identified, an effort to perform lymphadenectomy was documented in 49 (26%). Factors associated with lymphadenectomy were tumor size (median, 11.0 vs. 9.2 cm, p<0.001), preoperative imaging showing irregular tumor edge (88% vs. 71%, p=0.021) or suspicious lymph nodes (43% vs. 13%, p<0.001). Lymphadenectomy more commonly involved removal of adjacent organs (80% vs. 40%, p<0.001), but was not associated with significantly higher blood loss (650 vs. 525 ml, p=0.31). Median number of lymph nodes harvested was higher in the lymphadenectomy group (5 vs. 0, p<0.001), but the frequency of T3/4 tumors (63% vs. 50%, P=0.11) and R1 resection (27% vs. 26%, p=0.54) were similar. Rates of metastatic disease were also similar (18% vs. 16%, p=0.68). In-hospital mortality (2% vs. 0.7%, p=0.47) and morbidity rates (49% vs. 43%, p=0.52), as well as use of post-operative chemotherapy (18% vs. 12%, p=0.29) or radiation (11% vs. 11%, p=1.00) were similar. Metastatic disease excluded, overall survival after resection was not different between the two groups. However, on subset analysis incorporating margin status, it was noted that in the setting of an R0 resection the attempt to perform a lymphadenectomy was associated with significantly improved overall survival (Figure, p<0.001). Conclusions: When an R0 resection can be achieved for ACC, the effort to perform a lymphadenectomy is associated with significantly improved survival. Achieving negative margins and dissecting regional lymph nodes are two modifiable factors in the hands of the surgeon, which can affect long-term outcome after ACC resection.



LAD, effort to perform lymphadenectomy

P173

Double Balloon Enteroscopy in the Diagnosis of Multifocal Small Bowel Neuroendocrine Tumors: Clinical Utility or Over Utilization? J. Johnson,[1]* A. Harit,[1] N. Manguso,[1] A. Gangi,[2] N. Nissen,[1] J. Mirocha,[1] A. Hendifar,[1] F. Amersi.[1] *1. Surgery, Cedars Sinai Medical Center, Los Angeles, CA; 2. Moffitt Cancer Center, Tampa, FL.*

Background: Small bowel (SB) neuroendocrine tumors (NET) are multifocal in up to 35% of patients (pts). It is unclear whether double balloon enteroscopy (DBE) is a useful adjunct in the identification of multifocal disease. The aim of this study is to compare the accuracy of DBE to intra-operative surgical evaluation of the SB, and to compare the extent of surgical resection between pts who underwent DBE prior to surgery, pts who underwent surgical resection without prior DBE, and patients who had NET found incidentally at the time of surgery. Methods: Retrospective analysis of our database identified 178 pts with SB NET between 2006-2013. Final analysis included only patients with jejunal or ileal NETs who underwent pre-operative evaluation and surgical resection at our institution. Results: 83 pts met study criteria, of whom 44 (53%) underwent DBE. Sixteen (36%) pts had complete DBE, 14 (32%) had either an upper/ lower DBE, 14 (32%) pts had intraluminal or mesenteric disease precluding DBE. When compared to final pathology after surgical resection, DBE predicted the number of lesions in 19 (43%) pts and underestimated number of lesions in 18 (41%) pts. Surgeon palpation was accurate in 28 (64%) pts. and underestimated disease in 9 (20%) pts. For pts with multifocal NET on pathology, DBE was accurate in predicting distance between lesions (clustered vs. distant) in 14 (61%) of 23 pts. When comparing extent of surgical resection performed after DBE to resection without prior DBE, or resection for an incidentally found NET, there were no significant differences in the number of bowel segments resected (p=0.79) or the length of bowel resected (p=0.62). A significant difference in the final number of lesions identified by pathology between these groups was due to more lesions resected following DBE than in patients who had incidental NET found at surgery (p<0.01). Conclusions: DBE was less accurate than intra-operative surgical palpation in identifying SB NET. DBE did not significantly affect the extent of SB resection and may have limited utility in the routine preoperative evaluation of patients with SB NET.

P174

Significance of Intravenous Thrombus in the Management of Adrenocortical Carcinoma: Prognosis and Surgical Implications S. Ahmed,[1]* T. Tran,[2] E.A. Levine,[1] S. Weber,[3] A.I. Salem,[3] L.M. Postlewait,[4] S.K. Maithel,[4] T. Wang,[5] I. Hatzaras,[6] R. Shenoy,[6] J. Phay,[7] L. Shirley,[7] R.C. Fields,[8] L. Jin,[8] T.M. Pawlik,[9] J. Prescott,[9] J. Sicklick,[10] S. Gad,[10] A. Yopp,[11] J. Mansour,[11] Q. Duh,[12] N. Seiser,[12] C.C. Solorzano,[13] C.M. Kiernan,[13] G.A. Poultsides,[2] K. Votanopoulos.[1] *1. Department of Surgery, Wake Forest Baptist Medical Center, Winston-Salem, NC; 2. Department of Surgery, Stanford University School of Medicine, Stanford, CA; 3. Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 4. Department of Surgery, Emory University, Atlanta, GA; 5. Department of Surgery, Medical College of Wisconsin, Milwaukee, WI; 6. Department of Surgery, New York University School of Medicine, New York, NY; 7. Department of Surgery, The Ohio State University, Columbus, OH; 8. Department of Surgery, Washington University School of Medicine, St. Louis, MO; 9. Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD; 10. Department of Surgery, University of California San Diego, San Diego, CA; 11. Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX; 12. Department of Surgery, University of California San Francisco, San Francisco, CA; 13. Department of Surgery, Vanderbilt University, Nashville, TN.*

Background: Adrenocortical carcinoma (ACC) is a rare malignancy associated with poor outcomes. The prognostic significance of intravenous thrombus (IT) remains poorly defined. Method: Patients who underwent surgery for ACC between 1993 and 2014 were identified from 13 academic institutions participating in the U.S. ACC group study. Patient demographics, tumor characteristics, operative approach, perioperative morbidity and mortality as well as long-term survival were compared between ACC patients with and without IT. Results: 29 (10.9%) out of total 264 ACC patients had IT. IT was noted to be more common in women (69 vs 31%; p<0001) but not associated with laterality (left adrenal tumor 50 vs 57.39%; p=0.8) or tumor size (mean size 12.12 vs 12.75cm; p=0.6). Patients with IT had higher rates of thoraco-abdominal surgical approach (42.86 vs 12.5%; p=0.005), higher intraoperative blood loss (mean 2958 vs 1165ml; p=0.0006) and higher in-hospital mortality (8 vs 1.43%; p=0.03) while Clavien-Dindo Grade III/IV morbidity (17.24% vs 8.5%; p=0.26), length of hospital stay (7.51 vs 10.08 days; p=0.08), and readmission rates (4 vs 18.68%; p=0.07) were not statistically different between the two groups. Overall survival in patients with R0 resection was worse for those with IT compared to those without IT (median survival 2.71 vs 8.02 yrs; p=0.03), despite observing no differences in R0 resection rates between groups (62.1 vs 70.2% p=0.58). On multivariate analysis, improved survival was associated with decreased length of stay (p=0.02) and ASA class II status (p=0.02). Open abdominal (n=16) versus thoraco-abdominal (n=12) approaches for patients with IT did not impact survival (p=0.57). Conclusion: Intravenous thrombus of ACC is associated with decreased overall survival even after an R0 resection. Decreased survival and higher in-hospital mortality merit judicious patient selection.

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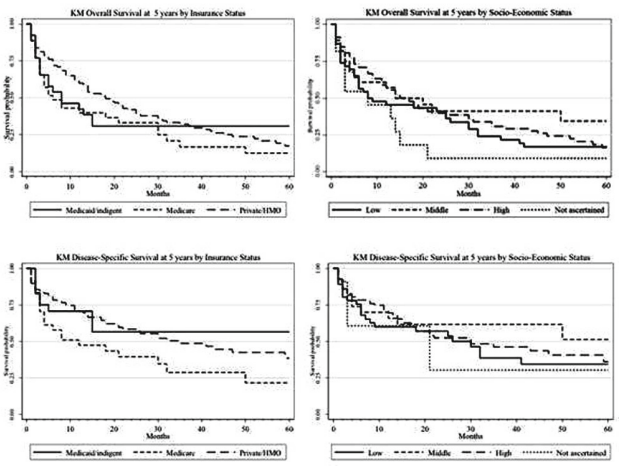
External Radiotherapy in Patients with Iodine Refractory Differentiated Thyroid Cancer A.H. Groen,[1]* D. van Dijk,[1] T.P. Links,[2] H.P. Bijl,[3] J. Plukker.[1] *1. University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands; 2. University of Groningen, University Medical Center Groningen, Department of Endocrinology, Groningen, Netherlands; 3. University of Groningen, University Medical Center Groningen, Department of Radiation Oncology, Groningen, Netherlands.*

Introduction: The role of external beam radiotherapy (EBRT) remains controversial in the treatment of patients with iodine refractory differentiated thyroid cancer (DTC). The primary aim of this study is to evaluate the locoregional (LR) control and overall survival (OS) of EBRT for microscopic (R1) or macroscopic (R2) residual disease in iodine refractory DTC after initial thyroidectomy. Methods: Between January 1990 and November 2011, 41 patients with iodine refractory DTC were treated with EBRT for locoregional residual (i.e. R1, n=24 or R2, n=17) disease in our tertiary referral center. Patients who received radiotherapy for distant metastases were excluded. Locoregional recurrent disease was identified by either clinical or radiographic progression. The median dose of EBRT was 66 (range 45-72) Gy, the median follow-up after EBRT was 40 (range 4-194) months. Kaplan Meier estimates were performed for LR control and OS. Results: The 2 and 4 year LR control rates after EBRT were respectively 90.9% and 85.5% for R1 residual disease and 79.0% and 53.3% for R2 residual disease. The 2 and 4 year overall survival rates after EBRT were respectively 87.3% and 73.5% for R1 residual disease and 63.0% and 43.2% for R2 residual disease. A significant difference was found between the groups with R1 and R2 residual disease, regarding LR control (p=0.011) and OS (p=0.004). Conclusion: This retrospective study shows that postoperative EBRT provides durable LR control and OS in patients with iodine refractory DTC. Patients with macroscopic residual disease have a significantly worse outcome.

P176

Socioeconomic and Insurance Status are Not Associated with Liver Directed Therapy Utilization or Survival in Neuroendocrine Tumors Metastatic to the Liver M.A. White,* A. Lewis, A. Falor, P. Ituarte, S. Warner, Y. Fong, G. Singh, L. Melstrom. *Surgical Oncology, City of Hope, Arcadia, CA.*

Introduction: Neuroendocrine tumors (NET) are often indolent and recurrent, requiring multiple treatments and significant resources. Liver directed therapy (LDT) has been associated with improved survival in this population. The aim of this study is to determine if lower socioeconomic status (SES) and those without private insurance are less likely to receive LDT and thus have a worse survival. Methods: The California Cancer Registry linked with patient hospital records was used to identify patients from 2005-11 with gastrointestinal NET with liver-only metastases. We evaluated basic demographics, SES and insurance payer type as variables associated with overall and disease specific survival. Multivariable survival analysis was used to identify factors associated with differences in outcome. Results: A total of 178 patients were identified with NETs metastatic to the liver only. Pancreas was the most common site of origin at 53% (96), followed by colon/rectum/appendix (45), small bowel (26) and stomach (11). Private insurance accounted for 66% (117) of patients and the remaining had Medicare (20%, 35) or Medicaid/no insurance (15%, 26). Just over 52% (93) of patients were considered to be high SES, 16% middle (28) and 26% low (46). Only 67 patients (38%) received any LDT. There was no significant association between receipt of LDT and either SES or type of insurance. There were no significant differences in 5-year overall and disease specific survival based on SES or type of insurance (Figure 1). Multivariable analysis identified only younger age (HR 1.02, p = 0.004), receipt of LDTs (HR 0.36, p <0.001), and small bowel primary (HR 0.23, p = 0.003) as factors associated with improved survival. Conclusion: While disparities are notable for many cancer populations, our results do not show an inferior outcome with metastatic neuroendocrine tumors in patients that have low SES or federal health insurance. It is possible that patients with low socioeconomic status or lack of private insurance are more often treated in tertiary care centers that may have greater expertise in caring for these complex patients.



P177

Small Change for Big Gains: Process Optimization for Sample Processing Provides Substantial Savings K.A. Caddell,[1]* C. Travis,[2] L. Kim,[1] J. Yeh.[1] *1. UNC, Department of Surgery, Chapel Hill, NC; 2. Brown University, Department of Surgery, Providence, RI.*

BACKGROUND Over 100,000 patients undergo parathyroidectomy per year. Intraoperative parathyroid hormone (IOPTH) monitoring is used to verify removal of offending glands, with a decrease of more than 50% associated with adequate resection. This requires multiple samples to be processed per case. Longer operating times are associated with increased cost and risk to the patient, and the trend toward bundled payments for procedures highlights the role of process optimization to reduce cost and improve patient care. METHODS We performed a prospective study of IOPTH turnaround times at our institution. Time from specimen collection to result was collected for 1 year in; 1) main hospital operating room (OR) with samples processed in the core lab (MC), 2) ambulatory surgery center (ASC) with processing in adjacent satellite lab, 3) the main OR with processing in adjacent anteroom (MA). Comparisons were made between groups using t-tests, coefficient of variation, and f-tests. RESULTS 304 samples were collected and analyzed from 64 cases (avg 4.78/case). Average "time to result" was 29 (range (23-50), coefficient of variation (CV) 20.2%) minutes for MA samples, 32 ((21-98), CV 19.8%) for ASC, and 36 ((22-71), CV 25.6%) for MC. Sample processing closer to the OR (ASC and MA) showed a significant reduction in turnaround time compared to MC samples (p=0.002 and 0.001 for ASC vs MC, MA vs MC). Variance between groups also favored MA samples compared to MC or ASC samples (F=.001 and .002). Based on average $/minute OR utilization at our institution, this is a potential savings of $365/case. CONCLUSIONS Prospective review of IOPTH processing at our institution strongly supports the concept that relocation of necessary equipment and staff for IOPTH measurement closer to the OR is cost effective and cost saving. While variation existed in each setting based on personnel experience and transport time, the data show a statistically significant increase in efficiency with proximity of sample processing and reporting. As bundled payments gain traction, cost minimizing strategies such as this will be key to maintaining efficiency, profitability and patient care.

P178

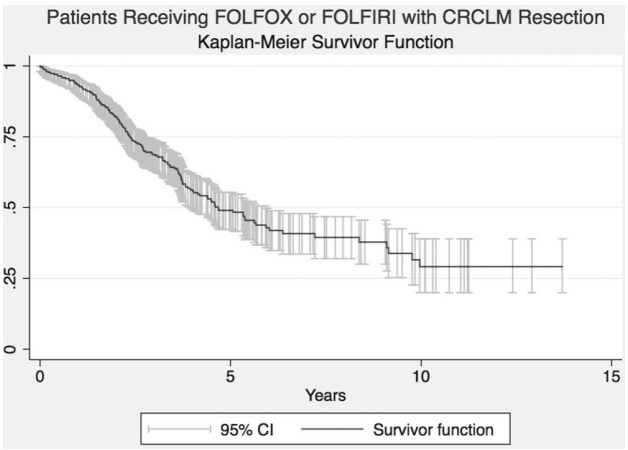
Relative Recurrence of Differentiated Thyroid Cancer Following Radioactive Iodine Ablation After Lobectomy Versus Total Thyroidectomy: A Systematic Analysis E. Dawson,* F. Murad, E. Kandil. *Surgery, Tulane University School of Medicine, New Orleans, LA.*

Background: Total thyroidectomy is the treatment of choice for differentiated thyroid cancer; however, recent studies have shown that radioactive iodine (RAI) can ablate the remaining thyroid lobe using lower doses than previously believed. RAI after lobectomy is an attractive alternative compared to completion thyroidectomy due to the risks associated with redo surgery, especially in patients who had recurrent laryngeal nerve injury or oncological resection at initial operation. Objective and Methods: To assess differences in recurrence of differentiated thyroid carcinoma after initial treatment with lobectomy followed by RAI ablation versus total thyroidectomy. We performed a meta-analysis of studies comparing outcomes in these two groups. PubMed, Web of Science, and Embase were searched for English language studies comparing recurrence in these two groups. Pooled estimates of hazard ratio, mean radiation dose for ablation, and their 95% confidence intervals were calculated using a fixed effects model. Heterogeneity was assessed using the Q and I^2 statistics. Results: Initial literature search resulted in 223 studies. After review of the manuscripts, three studies were found to meet inclusion criteria by two independent reviewers and were included in the qualitative analysis. The pooled hazard ratio was 1.512 (0.864-2.160). Moderate heterogeneity was observed, Q value of 4.53 (p=0.103) and I^2 of 55%. Mean radiation required for ablation of remaining lobe was 89.784 mCi (60.10-119.48) compared to 80.235 mCi (56.08-104.39) for ablation of thyroid remnant after total thyroidectomy. Two sample t-test showed no significant difference in the cumulative radiation dose between groups (p<.05). Conclusion: We found no significant difference in recurrence rate between RAI following lobectomy versus total thyroidectomy. Additionally, there was no significant difference between radiation doses for ablation after lobectomy versus total thyroidectomy. Based on our analysis, RAI after lobectomy represents a valid alternative to total thyroidectomy in patients with well-differentiated thyroid cancer.

P180

With Modern Chemotherapy Prognostic Models Underestimate Which Patients May Benefit from Hepatic Resection for Colorectal Liver Metastases R. Smalley,[1]* C. Collura,[2] C. Miller,[1] D. Berger,[2] K. Tanabe,[2] C.R. Ferrone.[2] *1. Harvard Medical School, Boston, MA; 2. Massachusetts General Hospital, Boston, MA.*

Introduction: With modern chemotherapy, FOLFOX and FOLFIRI, and safer hepatic resections historic prognostic models may not optimally identify patients who will benefit from resection of their colorectal cancer liver metastases (CRCLM). Our aim was to evaluate the performance of models developed by Fong, Nordlinger, Jaeck, and Iwatsaki in this modern patient population. Methods: Retrospective review of the clinicopathologic data of patients receiving FOLFOX or FOLFIRI and undergoing resection of their CRCLM between 2000-2014 was performed. Actual patient outcomes were compared to those predicted by four commonly used prognostic scores. Results: Of the 357 patients identified, the median age was 60 years and 47% were female. Synchronous disease, defined as liver metastases within 6 months, was identified in 67%. Actuarial 5yr survival was 49%. In this modern patient population, none of the 4 models divided the patients into groups with survival differences poor enough to recommend against resection. The Nordlinger model's highest risk group had a 2yr survival of 43% in the original study, vs. 80% in our population. Similarly, the Fong model showed a 5yr survival of 20% and 25% in their patients with scores of 3 and 4, respectively, vs. 5yr survival of 51% and 38% in our population. Of 19 independent predictive variables examined between the 4 models, only the number of tumors and age greater than 60 showed statistical significance in our patient population. None of the 4 models had pseudo R^2 values greater than 0.08. Conclusion: The 4 models all showed significant limitations in predictive ability. Patients receiving modern chemotherapy and with a poor prognosis predicted by the Nordlinger and Fong models, may still demonstrate good overall survival and should be considered for metastasectomy.



P181

Liver Resection Following Selective Internal Radiation Treatment with Yttrium-90: A Bi-Institutional Analysis G. Wright,[1]* J. Marsh,[4] M. Varma,[2] M. Doherty,[2] D. Bartlett,[1] M. Chung.[3] *1. University of Pittsburgh, Department of Surgical Oncology, Pittsburgh, PA; 2. Advanced Radiology Services, Grand Rapids, MI; 3. Spectrum Health Medical Group, Division of Surgical Oncology, Grand Rapids, MI; 4. University of Pittsburgh, Division of Hepatobiliary and Pancreatic Surgery, Pittsburgh, PA.*

Introduction: Treatment with yttrium-90 (Y90) is typically reserved for patients with unresectable tumors, though select patients demonstrate a favorable response and become candidates for surgical resection. Methods: Patients who underwent selective internal radiation treatment with Y90 microspheres followed by liver resection at two institutions were included. Data gathered included demographics, tumor characteristics, response to Y90, surgical details, perioperative outcomes, and survival. Results: There were 12 patients who met the inclusion criteria. Patients had few co-morbidities (median CCI = 0 (0-6)) and mild liver disease (median MELD = 6 (6-11)). Diagnoses included

metastatic colorectal adenocarcinoma (n=6), neuroendocrine tumor (n=1), and ocular melanoma (n=1) in addition to hepatocellular carcinoma (n=4). The majority had multifocal disease (n=8). Median time from liver disease diagnosis to Y90 treatment was 5.5 (2–92) months. RECIST criteria following Y90 were:complete response (n=2), partial response (n=7), stable disease (n=2), progressive disease (n=1). Median time from Y90 treatment to surgery was 9.5 (3–20) months. Surgical approach included right hepatectomy (n=3), extended right hepatectomy (n=5), extended left hepatectomy (n=1), segmentectomy with ablation (n=2), segmentectomy with isolated liver perfusion (n=1). Mean OR time was 244±69 minutes and median EBL was 700 (400–1500) mL. Length of stay was 7 (4–31) days, with a 42% readmission rate. The 90-day morbidity and mortality rates were 42% and 8%, respectively. One mortality occurred on POD #77 following sequelae from ARDS and post-hepatectomy liver failure in a patient who underwent right hepatectomy with caudate lobectomy. Recurrence and survival data are listed in Table 1 with median follow-up of 12 months. True medians have yet to be reached. Conclusion: Liver resection following Y90 embolization is a challenging surgical procedure, though appears to be safe and feasible at high volume centers. There is potential for extending disease-free and overall survival in properly selected patients in the current era of multimodal therapy utilization for malignant liver disease.

Table 1. Oncologic Outcomes for Liver Resection Following Y90 Treatment

Variables	N (median:range)
Disease recurrence	4/11 (36.4%)
Postoperative disease-free interval	12 (3-43) months
Alive at follow-up	8 (66.7%)
Alive without disease	7 (58.3%)
Overall post-operative survival	14 (3-43) months
Overall survival from liver disease diagnosis	39 (16-122) months

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Racial Disparity or Different Biology? Variations in the Outcomes and Survival in Hepatocellular Carcinoma E. Alkhalili,* A. Greenbaum, R. Rodriguez, K. Caldwell, O. Estrada Munoz, J. O'Neill, I. Nir, K. Morris. *Surgery, University of New Mexico, Albuquerque, NM.*

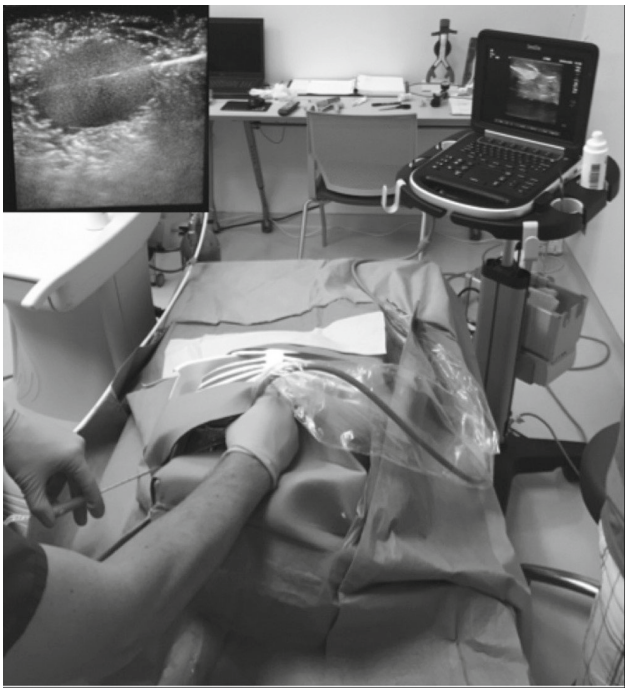
Introduction Prior studies have shown that the incidence and treatment outcomes of hepatocellular carcinoma (HCC) differ between racial groups. We investigated if there were differences in disease presentation, treatments offered and survival between the three major ethnicities in our state; Non-Hispanic Whites (NHW), Native Americans (NA) and Hispanics (H). Methods A retrospective chart review of patients with HCC treated at our cancer center between 2000 and 2014 was performed. Patients' demographics, etiology of cirrhosis, Child-Pugh classification, disease stage and treatments offered were analyzed using ANOVA and Chi square test. Overall (OS) and disease-free (DFS) survivals were compared using Kaplan-Meier and Cox regression models. Results 326 patients were identified; 106 (32.5%) NHW, 183 (56.1%) H, and 37 (11.4%) NA. There was no difference in age, disease stage, resectability, and rate of offering surgery or chemotherapy. Advanced cirrhosis (Child-Pugh B/C) was more common in H 58.4% and NA 59.4% than NHW 46.6% (p=0.01). NA had a higher incidence of non-Hep B non-Hep C HCC (NBNC-HCC) when compared to NHW and H (62.2% vs 30.2% vs 31.7%, p<0.001). NA had a higher prevalence of NASH cirrhosis when compared to NHW and H (16.2% vs 2.8% vs 6.5%, p=0.01). Among patients who met criteria for transarterial chemoembolization (TACE) and/or radiofrequency ablation (RFA) therapy, NHW were more likely to receive it than NA or H (57.5% vs 41.7% vs 38.4%, p=0.04). H had worse OS (HR 1.37,CI 1.04-1.80,p=0.02) and DFS (HR 1.80,CI 1.16-2.81,p<0.01) when compared to NHW. Median survivals for NA, NHW, H were 24, 14, and 11 months, respectively (p=0.01). Conclusions While there was no difference in disease stage or resectability, NA and H were more likely to have advanced cirrhosis. Furthermore, NA and H were less likely to undergo TACE/RFA therapy than NHW. NA had the best survival which may be attributed to higher incidence of NBNC-HCC, whereas H had the worst survival. Further studies are needed to evaluate more aggressive screening in Hispanics given their prognosis and interventions to eliminate disparities in receiving TACE/RFA therapy.

Variable	Non-Hispanic White (N=106)	Hispanic (N=183)	Native American (N=37)	p-value
Age: Mean (SD)	59 (9.9)	58.7 (10)	61.6 (9.8)	0.28
Sex				0.02
Male	89 (83.9%)	150 (81.9%)	21 (56.7%)	
Female	17 (16.1%)	33 (18.1%)	16 (43.3%)	
Stage				0.44
I	30 (28.3%)	51 (27.9%)	8 (21.6%)	
II	32 (30.2%)	43 (23.5%)	9 (24.3%)	
III	21 (19.8%)	48 (26.2%)	14 (37.8%)	
IV	23 (21.7%)	41 (22.4%)	6 (16.3%)	
Resectability				0.61
Yes	59 (55.7%)	104 (56.8%)	24 (64.9%)	
No	47 (44.3%)	79 (43.2%)	13 (35.1%)	
TACE/RFA received	38/66 (57.5%)	43/112 (38.4%)	10/24 (41.7%)	0.04
Chemotherapy received	25 (23.6%)	36 (19.7%)	9 (24.3%)	0.67

P183

Development of Laparoscopic and Open Models for Training and Assessing Image-guided Liver Tumor Ablation K. Diab,[1]* K. Olino,[2] S. Agle,[2] S. Kochat,[1] K. Kahrig,[2] S. Delao,[2] D. Tyler,[2] K. Brown.[2] *1. University of Texas Medical Branch, Galveston, TX; 2. University of Texas Medical Branch, Department of Surgery, Galveston, TX.*

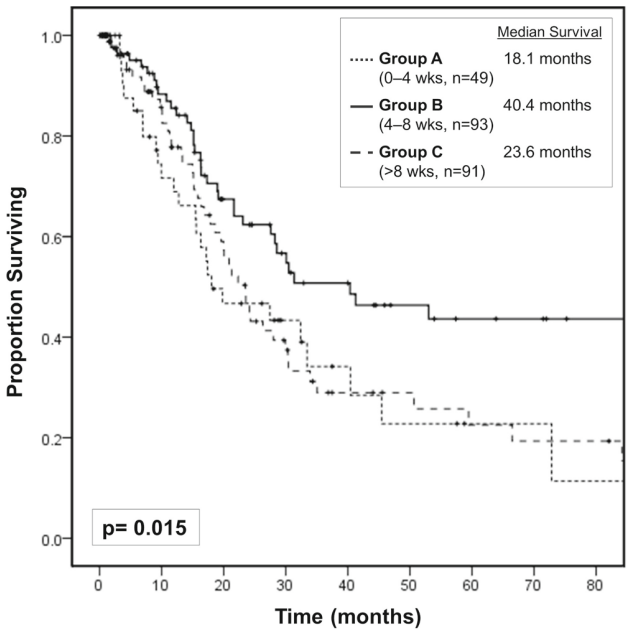
Introduction: Image-guided laparoscopic or open microwave ablation (MWA) is a technically demanding procedure, involving advanced visual-spatial perception skills for accurate tumor targeting. It is currently taught in one-time courses or during clinical cases, which does not allow the learner to engage in deliberate practice to achieve proficiency. This study describes a high fidelity simulation-based training model to teach MWA, and assesses participant feedback on the model's performance. Methods: We created simulated tumors using a mixture of 3% agarose, 3% cellulose, 7% glycerol, and 0.05% methylene blue. Tumors were injected into porcine livers or created ex vivo and implanted into bovine livers. We assessed tumor visibility with ultrasound. We constructed a simulated abdomen to create a high-fidelity context with physical constraints for open or laparoscopic surgery. Total cost of the model including liver and tumors was $30. We recruited physicians with experience in ultrasound and tumor ablation to perform simulated ablations using our model, and collected feedback on the model's realism and utility for training using a 10-point Likert-type scale. Results: The thicker bovine liver allowed more challenging tumor depths, but required tumor to be created externally then implanted. Tumors appeared hyperechoic and were clearly visualized on ultrasound. One interventional radiology fellow, 3 surgical oncologists and 1 vascular surgeon performed a total of 7 ablations. Time from needle insertion to ablation was 4-12 minutes, with 2-4 needle passes and 5-13 repositionings. Examination of ablation zone revealed 40-80% of the tumor volumes were ablated. Participants rated the model's realism at 4/5 and utility for training at 5/5 . Conclusions: We have created a cost-effective, high-fidelity model of MWA, which can facilitate a deliberate practice curriculum. Trainees can practice to proficiency with clear target metrics prior to participating in clinical cases. Participants felt the technical and decision-making challenges in model accurately reflected clinical cases.



P184

The Optimal Time-Interval to Re-resection for Incidentally Discovered Gallbladder Cancer: A Multi-Institution Analysis from the U.S. Extrahepatic Biliary Malignancy Consortium C.G. Ethun,[1]* L.M. Postlewait,[1] N. Le,[1] T.M. Pawlik,[2] S. Buettner,[2] G.A. Poultsides,[8] T. Tran,[8] K. Idrees,[3] C.A. Isom,[3] R.C. Fields,[4] L. Jin,[4] S. Weber,[5] A.I. Salem,[5] R.C. Martin,[6] C. Scoggins,[6] P. Shen,[7] H. Mogal,[7] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] G. Vitiello,[10] D.A. Kooby,[1] S.K. Maithel.[1] *1. Emory University, Atlanta, GA; 2. The Johns Hopkins Hospital, Baltimore, MD; 3. Vanderbilt University Medical Center, Nashville, TN; 4. Washington University School of Medicine, St. Louis, MO; 5. University of Wisconsin School of Medicine and Public Health, Madison, WI; 6. University of Louisville, Louisville, KY; 7. Wake Forest University, Winston-Salem, NC; 8. Stanford University Medical Center, Stanford, CA; 9. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 10. New York University, New York, NY.*

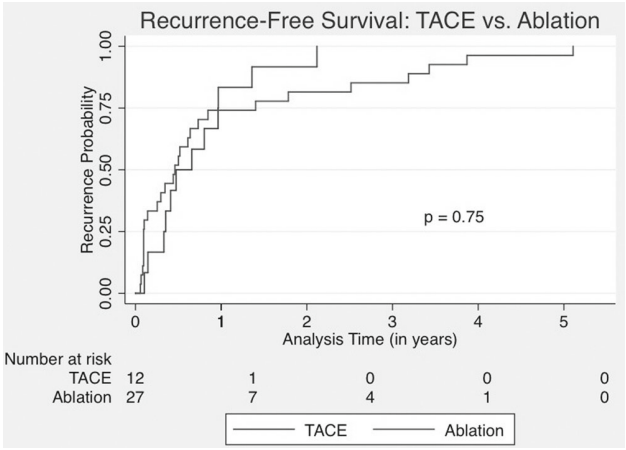
Background: Current recommendation is to perform re-resection for select patients with incidentally discovered gallbladder cancer. The interval time to re-resection that optimizes both patient selection and long-term survival is not known. Methods: All patients with incidentally discovered gallbladder cancer who underwent re-resection at 10 institutions from 01/2000-05/2015 were included. The interval time to re-resection was analyzed. Primary outcome was overall survival (OS). Results: Of 449pts with gallbladder cancer, 233 (52%) were discovered incidentally and underwent attempted re-resection at 3 different time-intervals from the date of original cholecystectomy: Group A: 0-4wks (49pts, 21%); B: 4-8wks (91pts, 39%); C: >8wks (93pts, 40%). All 3 groups were similar with regards to T-stage, LN involvement, grade, and post-operative complications. Group A tended to have distant disease found less frequently at the time of re-resection (11%vs20%vs19%; p=0.38) and was least likely to have residual disease on pathologic analysis (29%vs47%vs49%; p=0.048). Despite these findings, patients who underwent attempted re-resection between 4-8 weeks had the longest median OS (Group B: 40.4mo) compared to those who underwent early (Group A: 18.1mo) or late (Group C: 23.6mo) re-exploration (Figure; p=0.015). A 4-8 week time interval to re-resection, presence of residual disease, advanced T-stage, LN involvement, high grade, and positive margin were associated with decreased OS on UV Cox regression (all p<0.05). Only 4-8 week time interval (HR 0.43, 95%CI 0.21-0.90; p=0.02), advanced T-stage (HR 2.65, 95%CI 1.16-6.09; p=0.02), and margin positivity (HR 2.46, 95%CI 1.16-5.22; p=0.02) persisted on MV analysis. Conclusion: The optimal time-interval for attempted re-resection for incidentally discovered gallbladder cancer appears to be between 4-8 weeks after the date of the original cholecystectomy.



P185

Management Strategies for Patients with Solitary Hepatocellular Carcinoma ≤3 cm A.N. Martin,* D. Das, L.E. Johnston, T.W. Bauer, R.B. Adams, V.M. Zaydfudim. *University of Virginia, Charlottesville, VA.*

Introduction: Optimal treatment for small hepatocellular carcinoma (HCC) ≤3 cm remains controversial. Although liver transplantation is considered the standard of care, a paucity of donor organs has led to persistent use of resection and non-operative treatment modalities, including ablation and transcatheter arterial chemoembolization (TACE). We sought to compare survival among patients managed with resection and bridge to transplantation as well as ablation and chemoembolization. Methods: Patients diagnosed with solitary HCC ≤3 cm between 2005 and 2014 were included in the study. The primary outcome, recurrence-free survival (RFS), was defined from the date of surgery, ablation or TACE until evidence of radiographic recurrence. Overall survival (OS) was measured from date of treatment until date of last follow-up or death. Kaplan-Meier survival functions with log-rank tests were used to estimate recurrence-free survival (RFS) and overall survival (OS). Results: Among 161 patients with solitary HCC ≤3 cm, 11 (6.9%) did not receive treatment and 5 (3.1%) underwent external beam radiation; these 16 patients were excluded. The remaining 145 patients had a median age of 63 years (±9.2), median follow-up time of 2.5 years (±2.6), and were predominantly male (68%) and cirrhotic (95%). Twenty-six patients underwent liver transplantation as primary treatment with 5-year OS of 75% (median survival not reached). There were 35 patients bridged to transplantation with TACE, ablation, or resection; these patients had equivalent OS and RFS compared to 41 patients managed with resection as their definitive treatment (both p≥0.30). Among patients not treated with resection or bridged to transplant, definitive treatment with TACE or ablation led to 5-year OS of 23% and 35%, respectively (p=0.26). 1-year recurrence-free survival for patients treated with TACE or RFA also did not differ and was 17% and 26%, respectively (p=0.75, figure). Conclusions: Among patients with HCC ≤3 cm, those who are bridged to transplant with liver-directed therapy have similar survival to patients treated with primary resection. Management with TACE or ablation without transplantation results in similar RFS and OS.



P186

The Treatment Outcomes After Hepatectomy for Advanced Hepatocellular Carcinoma Y. Okamura,* T. Sugiura, T. Ito, Y. Yamamoto, R. Ashida, K. Uesaka. *Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center Hospital, Sunto-Nagaizumi, Japan.*

Background and objectives: Most Japanese institutions perform surgical resection for advanced hepatocellular carcinoma (HCC). To identify the prognostic factors and the treatment outcomes of patients with advanced HCC after hepatectomy, we performed the following analyses. Methods: A total of 559 patients were included in the present study. At our institution, surgical resection is the first choice of treatment for advanced HCC if the tumor conditions and liver function allow hepatectomy.We analyzed the surgical outcomes for HCC with portal vein invasion (vp) and/or the presence of a bilobular tumor. Results: One hundred and one patients with vp were identified. There comprised 69, 14, 13 and 5 patients with vp1, vp2, vp3 and vp4, respectively. The median survival time (MST) of the patients with vp was significantly poorer than that of the patients without vp (65.8 vs. 100.1 months, P<0.001). The MST of the patients with vp1, vp2, vp3 and vp4 was 81.9, 34.7, 70.7 and 88.8 months, respectively. No significant differences were observed among the four groups (P = 0.378). A multivariate analysis revealed hepatic vein invasion (hazard ratio [HR] 2.46, 95% confidence interval [CI] 1.34-4.52, P=0.004) and preoperative AST>40 U/L (HR 2.16, 95% CI 1.20-3.88, P=0.010) to be significant independent predictors in HCC with vp. One hundred and forty-four patients with multiple HCC were identified. Of these, there were 51 patients with bilobular HCC. The MST of the patients with multiple HCC was significantly poorer than that of the patients with solitary HCC (75.3 vs. 100.1 months, P=0.026). The MST of the patients with bilobular HCC was significantly poorer than that of the patients with unilobular multiple HCC (69.6 vs. 87.4 months, P=0.026). A multivariate analysis identified patients > 75 years of age (HR 2.46, 95% CI 1.44-9.83, P = 0.007) and those with portal vein invasion (HR 2.87, 95% CI 1.09-7.67, P = 0.034) to be significant independent predictors in bilobular HCC. Conclusions: The present study revealed that a favorable prognosis could therefore be expected when the indications for surgery are appropriately determined, even for patients with advanced HCC.

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Use of Loco-regional Treatment for HCC: Trans-arterial Chemoembolization and Ablation Work Better Together A. Winer,[1]* Y. Rosen,[2] F. Lu,[2] R. Berman,[1] E. Newman,[1] M. Melis,[1] G. Miller,[1] H. Pachter,[1] I. Hatzaras.[1] *1. Department of Surgery, NYU Langone Medical Center, New York, NY; 2. NYU Langone Medical Center, New York, NY.*

Introduction: Hepatocellular Carcinoma (HCC) is the second leading cause of cancer-related death worldwide. Loco-regional treatment modalities for HCC include Trans-Arterial Chemoembolization (TACE) and Radiofrequency/Microwave Ablation (RFA/MWA). Several studies have shown that dual therapy with both TACE and ablation is beneficial, though data is limited. We retrospectively studied all HCC patients treated with either TACE, ablation, or dual therapy at a tertiary referral public hospital to determine differences in survival. Methods: Following IRB approval, all patients diagnosed with HCC and treated with TACE and/or ablation (1998-2013) at our institution were retrospectively analyzed for date of diagnosis, treatment-type, length of follow-up, and survival. Patients were excluded if they did not undergo TACE or RFA/MWA, or underwent other additional treatment, such as surgery. Primary outcomes were overall survival at 2 and 5 years after diagnosis. Kaplan Meier curves were generated and statistics with Log-rank testing and hazard ratios (HR) were performed. Results: Of 509 patients diagnosed with HCC, 109 (21.4%) met inclusion criteria. 60 were treated with TACE alone, 30 with ablation alone, and 19 were treated with both, either concomitantly or in sequence. Median follow-up and overall median survival was 15.5, 19, and 52 months for TACE, ablation, and dual therapy, respectively. Survival at 2 years was 35.6%, 40.0% and 84.2%, and at 5 years was 11.9%, 13.3% and 42.1% for TACE, ablation, and combination groups respectively. Kaplan Meier analysis (fig. 1) revealed that survival was significantly increased in the combination therapy group vs. RFA or TACE alone at both 2 (p=0.0009) and 5 years (p=0.0006). However, there was no significant difference in survival when comparing TACE vs. RFA/MWA at either 2 (HR= 1.22, p=0.49) or 5 years (HR=1.18, p=0.48). Conclusion: Our study suggests a greater survival benefit for patients treated with TACE and RFA/MWA versus either modality alone. Further studies are needed to clarify which patients may benefit the most from the combined approach, particularly in light of the limited resources of a public hospital.

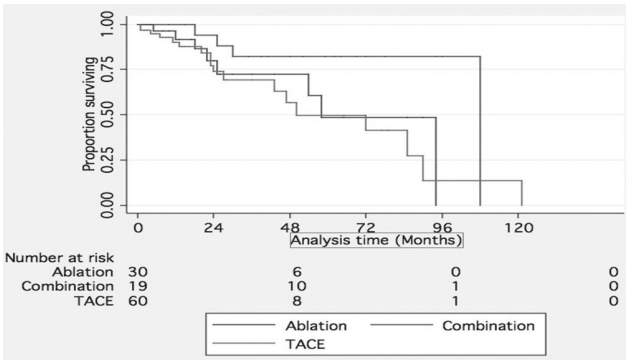

Figure 1: Overall Survival Analysis, Per Modality of Treatment.

P188

The Mechanism of Upregulating c-Met Expression During Preoperative Chemo-radiation Therapy in Pancreatic Ductal Adenocarcinoma H. Tomihara,* D. Yamada, H. Eguchi, H. Ogawa, T. Asaoka, T. Noda, H. Wada, K. Kawamoto, K. Gotoh, M. Mori, Y. Doki. *Osaka University, Osaka, Japan.*

Introduction: The preoperative therapy for pancreatic ductal adenocarcinoma, PDAC, has emerged as a reasonable strategy and expanded the indication of surgery. However, even after the preoperative therapy, viable cancer cells still remain in PDAC tissues, indicating some of these cells have the resistance to preoperative therapies. In the present study, c-Met expression, known as a HGF receptor and a pancreatic cancer stem cell marker, was investigated using surgically resected specimens after chemo-radiation therapy (CRT), and the mechanisms of c-Met alteration in cancer cells during CRT were investigated. Methods: We employed consecutive 92 patients who underwent R0 resection with or without preoperative CRT in 2007 to 2012. Immunohistochemistry (IHC) for c-Met was performed, and the relations between c-Met expression and clinicopathological features were examined. The change of c-Met expression under radiation in PDAC cells were investigated in vitro by qRT-PCR, Western blotting, flow cytometry, and IHC. Results: By IHC, every PDAC tissue showed different c-Met expression. When PDAC patients were divided to c-Met high or low group according to c-Met protein level, c-Met high group showed significantly shorter overall survival than that of low group (median survival time; 46.8 vs 23.7 months, P=0.0004). The multivariate analysis of clinicopathological features revealed preoperative CRT was an independent increasing factor. When radiation was exposed to cancer cells, mRNA expression and protein level of c-Met were increased. By a microarray analysis of cancer cells with or without radiation exposure, miR-181b was selected as a candidate gene upregulating c-Met expression. MiR-181b is known as an inhibitor of ETS-1, which has shown to play a dominant role

in c-Met transcription. While radiation exposure suppressed the expression of miR-181b in PDAC cells, c-Met expression was upregulated via ETS-1 increase. Conclusions: C-Met upregulation through the suppression of miR-181b and the elevation of ETS-1 can be a novel target in overcoming the resistance to preoperative therapies.

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Hepatic Microenvironment: What Tips the Balance Towards Metastasis? F. Hand,[1]* C. Harmon,[1] L. Elliott,[2] F. Caiazza,[2] J. Geoghegan,[3] E. Ryan,[2] C. O'Farrelly.[1] *1. Trinity Biomedical Sciences Institute, Dublin, Ireland; 2. Centre for Colorectal Disease, School of Medicine and Medical Science, University College Dublin, Dublin, Ireland; 3. Department of Hepatobiliary and Liver Transplant Surgery, St. Vincent's University Hospital, Elm Park, Dublin, Ireland.*

Introduction The liver is ideally placed as an immune surveillance organ owing to its unique blood supply. It maintains a tolerogenic environment in response to gut antigens and commensal pathogens presented to it via the portal vein. The healthy hepatic microenvironment is rich in Natural Killer (NK) cells which play a key role in the livers powerful anti-tumour repertoire. They are important effector targets for immune strategies in the treatment of malignancy, yet despite this, the liver is the most common solid organ to form metastases. Patients and Methods Twenty-five patients with colorectal liver metastases (CRLM) undergoing liver resection were prospectively recruited to this study. Biopsies of freshly resected tumour, tumour adjacent liver and liver at the distal resection margin were cultured in vitro to obtain metastatic conditioned media (CM). Using an antibody array metastatic CM was screened for 102 cytokines and proinflammatory mediators and compared to CM obtained from healthy control liver. Differentially expressed cytokines (n=12) were quantified using luminex-based multiplex analysis. Furthermore, healthy NK cells were treated with metastatic CM and their function assessed by flow cytometry. Results Several cytokines demonstrated altered expression in the metastatic microenvironment when compared to healthy control liver. Metastatic liver was characterised by increased expression of several proinflammatory mediators including IL6 (p=0.03), VEGF (p=0.006) and RANTES (p=0.006). Furthermore, increased expression of LIF (p=0.0008) GMCSF (p=0.04) and IP10 (0.01) were noted at the distal resection margin when compared to control. When treated with metastatic CM from tumour, tumour adjacent and distal biopsy sites, NK cells demonstrated reduced IFNg production. Conclusion Healthy human liver has an evolved anti-tumour immune repertoire. The rich cytokine profile of the metastatic microenvironment is both pro-inflammatory and immunosuppressive with direct effects on NK cell function. These proinflammatory mediators may provide a mechanism for potentiating tumour growth and metastatic recurrence.

P190

Morphomic Analysis and Frailty Assessment Improves Prediction of NSQIP Serious Complications Following Pancreaticoduodenectomy in Older Adults A.J. Benjamin,[1]* A. Schneider,[1] M. Buschmann,[1] B. Derstine,[2] J.F. Friedman,[2] S. Wang,[2] W. Dale,[1] K. Roggin.[1] *1. Surgery, University of Chicago, Chicago, IL; 2. University of Michigan, Ann Arbor, MI.*

Introduction: Radiographic sarcopenia, measured by psoas muscle area and density in Hounsfeld units (HU) at L3 /L4, combined with clinical and frailty assessments, predicts clinically important pancreaticoduodenectomy (PD) outcomes, including serious complications defined by NSQIP. Previous reports suggest morphomic analysis provides a more comprehensive analysis of body composition compared to psoas muscle evaluation alone. We hypothesized that morphomic analysis would both reproduce our previous post-PD outcome prediction models and improve predictive accuracy over geriatric assessments (GA) of frailty. Methods: Prior to PD, enrolled patients (n=59) underwent comprehensive GAs. Non-contrast CT scans were processed to measure morphomic variables including: psoas area and density, dorsal muscle group area and density, subcutaneous fat, visceral fat, and total body area. Associations with NSQIP serious complications (Grade III+) were tested using univariate Wilcox Rank Sum and multivariate elastic net regression models. Elastic net models were constructed by randomly selecting 60% of the cases and cross-validating on the remaining 40%. Results: On univariate analysis NSQIP serious complications were associated with decreased psoas density (average HU at L3, p=0.006), Fried's frailty exhaustion (p=0.037), estimated blood loss (p=0.022), and morphomic measures including: dorsal muscle group low density muscle area (p=0.011), visceral fat area (p=0.009), and visceral fat average HU (p=0.006). A predictive model based on demographics, GA, and morphomics improved prediction of NSQIP serious complications (AUC=0.853). When compared to a clinical "base model" of age, BMI, ASA score, and Charlson comorbidity score (AUC=0.685) or the "base model" + Fried's exhaustion + average psoas HU (AUC=0.800). Fried's exhaustion and psoas average HU remained statistically significant in the final model. Conclusion: Morphomic analysis of CT scans provides information that improves prediction of post-PD outcomes compared to models utilizing measurement of psoas L3/L4 area and density alone. The best model includes both morphomic analysis and GA.

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Gemcitabine/Capecitabine for Advanced Biliary Cancer: Less Toxicity with Favorable Outcomes E. Gabriel,* K. Attwood, S. Hochwald, B. Kuvshinoff, W. Ma, R. Iyer. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction The results of the ABC-2 trial established gemcitabine plus cisplatin (gem-cis) as a standard regimen for advanced biliary cancer. Although no randomized trial has been done with gemcitabine plus capecitabine (gem-cap), this regimen has established benefits. We report our experience with outcomes and toxicity. Methods This is a single institution, retrospective study from 2005 to 2015 of patients with advanced biliary cancer, including intrahepatic and extrahepatic cholangiocarcinoma (IHCC/EHCC) and gallbladder carcinoma (GBC). Overall survival (OS) and progression-free survival (PFS) were reported using Kaplan-Meier methods. Results A total of 372 patients were identified. Of these, 227 (61.0%) had chemotherapy data at our institution. A total of 153 patients (41.1%) received gem-cap, of which 133 (86.9%) received it in the first line. The majority of patients (67.4%) had metastatic disease; 32.6% were locally advanced. Twenty-seven patients (17.6%) received it as adjuvant therapy, of which 16 (10.5%) also received adjuvant radiation. Forty-four patients (33.1%) received a second line of chemotherapy and 12 (9.0%) received a third line. Disease sites included: 48.9% IHCC, 24.0% EHCC and 27.1% GBC. Median follow-up was 45.1 months (mo). The median OS and PFS were 13.0 mo (95% CI 10.7-17.4) and 8.0 mo (6.0-9.3), respectively. Patients with metastatic disease had poorer OS and PFS compared to locally advanced disease: median OS – 11.4 vs 16.3 mo (p=0.01); median PFS – 6.9 vs 10.4 mo (p<0.001). There was no statistically significant differences in OS/PFS by disease site. Overall, 69 patients (55.6%) experienced a grade 3/4 toxicity. The most common (35.7%) was a hematologic toxicity (neutropenia or thrombocytopenia) followed by infection (27.5%). Other adverse events included elevated LFT's (9.3%) and non-hematologic events (22.5%), including fatigue (6.8%) and hand-foot syndrome (6.0%). Conclusions Gem-cap provides a similar PFS to gem-cis based on historical comparison with the ABC-2 trial. Gem-cap may offer the advantage of fewer adverse events (55.6%) as compared to the 70.7% reported in ABC-2. Prospective comparison of these two regimens is therefore warranted.

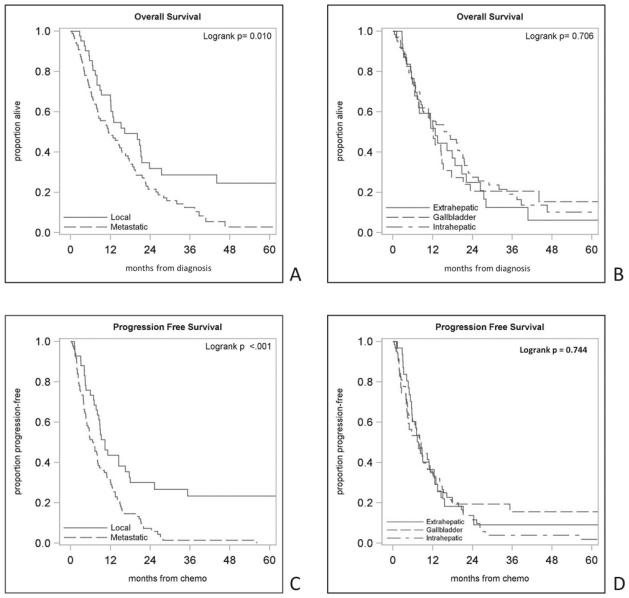

Figure 1. Overall survival (OS) and progression free survival (PFS) for patients with biliary cancer who received first-line gemcitabine plus capecitabine.
Top panel shows OS by extent of disease (A, locally advanced vs metastatic) and by disease site (B, extrahepatic cholangiocarcinoma, gallbladder carcinoma, intrahepatic cholangiocarcinoma. Bottom panel shows PFS by extent (C) and disease site (D).

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Conditional Survival Probability of Long-term Survival After Resection of Hilar Cholangiocarcinoma S. Buettner,[1]* G. Margonis,[1] Y. Kim,[1] C.G. Ethun,[2] S.K. Maithel,[2] G.A. Poultsides,[3] T. Tran,[3] K. Idrees,[4] C.A. Isom,[4] R.C. Fields,[5] B.A. Krasnick,[5] S. Weber,[6] A.I. Salem,[6] R.C. Martin,[7] C. Scoggins,[7] P. Shen,[8] H. Mogal,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] T.M. Pawlik.[1]
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Introduction: Traditional survival analyses focus on factors determined at the time of surgery and therefore may not be accurate over time. Conditional survival(CS) estimates future prognosis based on survival time accrued following treatment. We sought to define differences between actuarial and CS among patients after resection of peri-hilar cholangiocarcinoma(PHCC). Methods: 242 patients who underwent resection for PHCC between 2000-2014 were identified from 10 major HPB centers. Cox proportional hazard models were used to evaluate factors associated with overall survival. CS estimates were calculated as the probability of surviving an additional 3 years at "x" years after surgery using the formula $CS_3=S_{(x+3)}/S_x$. Results: Median patient age was 67 yrs(IQR:57-73) and the majority (73.6%) of patients had a major hepatic resection. Surgical margin status was R0 (n=160;66.1%) or R1 (n=82;33.9%). Tumor grade was well-(n=43;17.8%), moderate-(n=131;58.2%) or poorly-(n=51;22.2%) differentiated. Most patients had T1(13.8%) or T2(66.4%) disease, while a smaller subset had T3(17.3%) or T4(2.6%) disease. Lymph node metastasis were present in 79 (37.1%) patients. While actuarial survival decreased over time from 46.3% at 2 years to 18.2% at 5 years following surgery, 3-year CS increased over time among those patients who survived. The CS_3 at 2 years (i.e. the probability of surviving to postoperative year 5 after having already survived to postoperative year 2) was 39.3% and increased to 54.4% at postoperative year 5(Table). Factors associated with worse OS included lymph node metastasis(HR:1.72; 95%CI,1.23-2.40) and perineural invasion(HR:1.54;95%CI,1.02-2.33)(both P<0.05). Calculated CS_3 for high-risk patients exceeded the actuarial survival. For example, patients with peri-neural invasion had an actuarial survival of 15.4% at 5 years versus a CS_3 at 2 years of 37.6% (Δ=22.2%). Conclusions: CS provides a more dynamic means to estimate future survival among patients who have accrued survival time. CS can be particularly helpful in estimating future survival of high-risk patients who were predicted to have short survival times based on traditional prognostic models.

Patients Who Reach a Certain Survival Point After Resection of Hilar Cholangiocarcinoma Given That They Have Already Survived a Certain Amount of Time

Total Survival Time, (year)	If the Patient Has Survived to Time "X", the chance of future survival (%)						
	1 y	2 y	3 y	4 y	5 y	6 y	7 y
1							
2	60.8						
3	44.9	73.9					
4	35.0	57.5	77.8				
5	23.9	39.3	53.2	68.4			
6	17.6	28.9	39.2	50.4	73.6		
7	14.7	24.2	32.7	42.1	61.5	83.6	
8	13.0	21.4	28.9	37.2	54.4	73.9	88.4

P193

Assessing Tools for the Management of Non-Colorectal Non-Neuroendocrine Liver Metastases: External Validation of a Prognostic Model M.E. Tsang,[1]* A.L. Mahar,[2] G. Martel,[3] J. Hawel,[4] J. Rekman,[3] C. Boulanger-Gobeil,[5] D. Hurlbut,[2] M. Meschino,[4] C. Morin,[5] S.P. Cleary,[6] S. Gallinger,[6] S. Nanji,[2] F.K. Balaa,[3] P. Karanicolas,[1] D. Jalink,[2] J. Ouellet,[5] R. Hernandez-Alejandro,[4] A.C. Wei,[6] J. Hallet.[1]
1. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 2. Queen's University, Kingston, ON, Canada; 3. The Ottawa Hospital, Ottawa, ON, Canada; 4. London Health Sciences Centre, London, ON, Canada; 5. Centre Hospitalier Universitaire de Québec, Québec City, QC, Canada; 6. University Health Network, Toronto, ON, Canada.

Introduction: Selection criteria and benefits for resection of non-colorectal non-neuroendocrine liver metastases (NCNNELM) remain debated. The Adam prognostic score was developed for patient selection, but not validated. We performed an external validation of the Adam score in an independent contemporary North American cohort. Methods: Patients with resected NCNNELM were identified from multiple institutions (2000-2014). Risk groups were based on Adam score (primary tumour characteristics, disease-free interval, extra-hepatic metastases, major hepatectomy, R2 resection). TRIPOD guidelines for prediction tool development and validation were followed. Necessary data on score development were not available for a formal external validation. Discrimination was thus qualitatively evaluated by visually inspecting overall survival (OS) curves' separation between risk groups, calculating the slope of the continuous score on OS (Cox regression), and comparison of OS hazards between risk groups. Results: 165 patients were included (84 deaths, median follow-up in survivors 68 months): 53 (32.1%) low-risk, 85 (51.5%) intermediate-risk, and 27 (16.4%) high-risk. Breast primary was less frequent (12%) and mean disease free interval longer (48 months), than in the Adam cohort. There was no separation of OS curves among risk groups, with 5-year OS of 60.1% (low), 57.1% (intermediate), and 55.6% (high). OS was superior to the Adam cohort (low 46%, intermediate 33%, high 0%). The slope of the score (parameter estimate) below 1 (0.02) indicated lower discrimination than in the Adam cohort. Hazard ratios of 1.05 (0.63-1.70) for low vs. intermediate, 0.87 (0.46-1.64) for low vs. high, and 0.83 (0.46-1.49) for intermediate vs. high, demonstrated lack of discrimination in OS among risk groups. Conclusion: While long-term survival is achievable, these results suggest that discrimination of the Adam score is not maintained in a North American cohort of resected NCNNELM. It is not generalizable to this population, likely due to different case-mix and initial patient selection for resection. Score recalibration is required for use in specific practice settings.

			Adam Cohort* (n=1452)	Validation Cohort (n=165)
Prognostic score variables	**Extrahepatic metastases** – n (%)	Absent	1133 (78)	115 (70)
		Present	319 (22)	50 (30)
	Major hepatectomy (>3 segments) – n (%)	No	799 (45)	66 (40)
		Yes	654 (55)	99 (60)
	R2 resection – n (%)	No	1321 (91)	157 (95)
		Yes	131 (9)	8 (5)
	Age (years old) – median (range)		53 (10-87)	56 (20-83)
	Disease-free interval (months) – mean (range)		38 (0-448)	48 (0-485)
	Primary tumour characteristics – n (%)	Breast primary	454 (31)	20 (12)
		Squamous histology	71 (5)	4 (2)
		Melanoma	148 (10)	26 (16)
		Other	779 (54)	115 (70)
Survival analysis	**Follow-up for all patients** (months) – median (range)		31 (0–258)	42 (0-180)
	5-year overall survival – % (95% confidence interval)	Overall	36 (NR)	58.1 (49.8-65.5)
		Low-risk	46 (NR)	60.8 (45.6-73.0)
		Intermediate-risk	33 (NR)	57.1 (45.2-67.3)
		High-risk	2 (NR)	55.6 (35.2-71.8)

NR Not Reported
*Based on prognostic score development publication: Adam R et al, Ann Surg. 2006;244(4):524-535.

Qualitative comparison of characteristics and outcomes of the derivation and validation cohorts.

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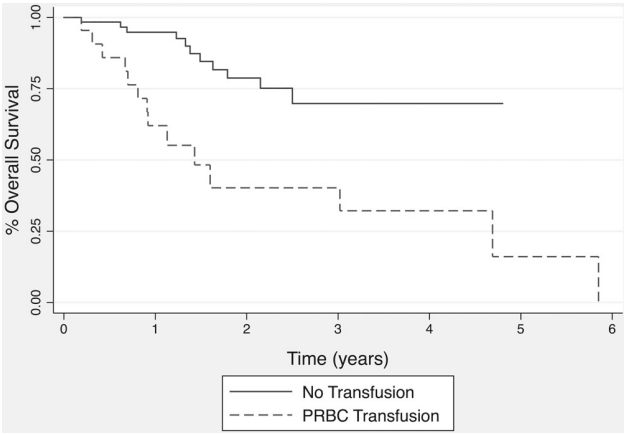
Rates and Patterns of Recurrence Following Complete Resection of Hilar Cholangiocarcinoma: Results from the U.S. Extrahepatic Biliary Consortium H. Mogal,[1]* S. O'Connor,[1] N. Fino,[1] C.G. Ethun,[2] T.M. Pawlik,[3] G.A. Poultsides,[4] T.B. Tran,[4] K. Idrees,[5] C.A. Isom,[5] R.C. Fields,[6] L. Jin,[6] S. Weber,[7] A.I. Salem,[7] R.C. Martin,[8] C. Scoggins,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] S.K. Maithel,[2] P. Shen.[1] *1. Wake Forest University School of Medicine, Winston-Salem, NC; 2. Winship Cancer Institute, Emory University, Atlanta, GA; 3. Johns Hopkins School of Medicine, Baltimore, MD; 4. Stanford University Medical Center, Stanford, CA; 5. Vanderbilt University Medical Center, Nashville, TN; 6. Washington University School of Medicine, Saint Louis, MO; 7. University of Wisconsin School of Medicine and Public Health, Madison, WI; 8. University of Louisville, Louisville, KY; 9. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 10. New York University, New York, NY.*

Background: Data for incidence and patterns of recurrence after surgical resection of Hilar cholangiocarcinoma have been derived largely from single institution series. We sought to assess factors associated with recurrence, recurrence patterns and their impact on outcomes. Methods: Patients with Hilar cholangiocarcinoma that underwent R0/R1 resection without 30-day mortality from surgery were analyzed from a 10-institution database. Results: 193 patients with recurrence data available were identified. Of these 95 (49%) recurred with median time to recurrence of 15.2 months and overall survival (OS) of 24.3 months. Univariate analysis identified age (HR 1.02, CI 1.004-1.036; p=0.01), pre-op CA 19-9 (HR 1.02, CI 1.004-1.035; p=0.02), positive lymph nodes (HR 1.72, CI 1.187-2.478; p=0.004) and perineural invasion (HR 1.78, CI 1.125-2.802, p=0.01) as factors predicting worse disease free survival. On multivariate analysis, only age (HR 1.032, CI 1.01-1.06, p=0.007) and pre-op CA 19-9 (HR 1.02, CI 1.01-1.04, p=0.013) remained significant. 67 patients (70.5%) had distant recurrence (DR) with or without locoregional recurrence (LR) while 28 patients (29.5%) had LR only. Of patients that had DR, 42 (63.6%) had liver, 23 (34.9%) had peritoneal, 8 (12.1%) had lung and 5 (7.6%) had other sites including distant nodal metastases. Median time to recurrence (13.6 vs 17.7 months, p=0.07), time from recurrence to death (5.9 vs 4.5 months, p=0.72) and OS (24.4 vs 25.3 months, p=0.3), was not significantly different between patients who had LR or DR with or without LR. Among patients that recurred, tumor size, lymph node status, resection status (R0/R1), extent of resection and adjuvant therapy were not significantly associated with the type of recurrence. Conclusion: Hilar cholangiocarcinoma is an aggressive cancer with high rates of predominantly distant recurrence associated with poor survival. Further investigation is warranted to determine the role and potential type of adjuvant therapy in order to improve outcomes after surgical resection.

P195

Transfused Blood from Older Donors is Associated with Improved Survival in Patients Undergoing Hepatic Surgery for Non-Hepatocellular Malignancies A.N. Lopez,[1] T.K. Jenkins,[1] S.L. Thompson,[2] E.M. Downey,[2] J. Sikora,[3] J.R. Pelletier,[3] I. Zendejas,[4] R.M. Thomas.[4]* *1. University of Florida, College of Medicine, Gainesville, FL; 2. Life-South Community Blood Centers, Gainesville, FL; 3. University of Florida, Department of Pathology, Immunology, and Laboratory Medicine, Gainesville, FL; 4. University of Florida, Department of Surgery, Gainesville, FL.*

Intro: The negative role of packed red blood cells (PRBC) on cancer outcomes is actively debated but little research has focused on factors of the donated blood. We sought to investigate PRBC factors that affect survival in patients undergoing hepatic surgery for cancer and hypothesized that leukocyte reduced (LR) blood or PRBC from older donors would portend improved outcomes. Methods: An IRB approved retrospective database of patients undergoing potentially curative hepatectomy or operative ablation of cancers of non-hepatocellular origin from 2005-2014 was used. Clinicopathologic data were recorded including PRBC transfusion ±72hr of surgery, storage age and donor age of PRBC, and LR status. Kaplan-Meier and Cox regression were used to determine predictors of recurrence free survival (RFS) and overall survival (OS). Results: A total of 172 patients were identified, 94 non-transfused (NTx) and 78 transfused (Tx). Cases included 59% major resections (≥4 segments), 30% minor, and 11% ablation only. Metastatic colorectal cancer was the indication in 73% of cases. Mean PRBC transfused was 3.9 units (range 1-53). No differences existed between NTx and Tx cohorts except operative blood loss (OBL) [mean 430ml vs 940ml, respectively;p<0.01]. Multivariate factors for reduced RFS and OS in the Tx cohort were OBL >700ml [HR 2.8, CI 1.3-6.4;p=0.01) and patient age >59yr [HR 1.6, CI 0.8-3.2;p=0.03], respectively, but PRBC donor age >50yr was a positive predictor of OS [HR 0.4, CI 0.1-1.3;p=0.03]. As OBL may be a confounder, cohort analysis of patients with OBL <700ml still demonstrated worse OS after PRBC transfusion [HR 4.1, CI 1.8-9.3;p<0.01]. Use of LR PRBC and age of stored PRBC had no effect on RFS or OS. Conclusion: In patients undergoing operative intervention for hepatic malignancy, perioperative use of PRBC may worsen OS even after controlling for OBL. PRBC from donors >50yr may have a protective effect but LR PRBC does not appear to have any effect. Greater cohort numbers may help strengthen these associations and cytokine analysis of those receiving PRBC may provide insight into an immunologic role of blood donor age.



Kaplan-Meier OS analysis of patients who underwent potentially curative operative intervention for malignancies of non-hepatocellular origin stratified to patients with operative blood loss ⟨700ml.

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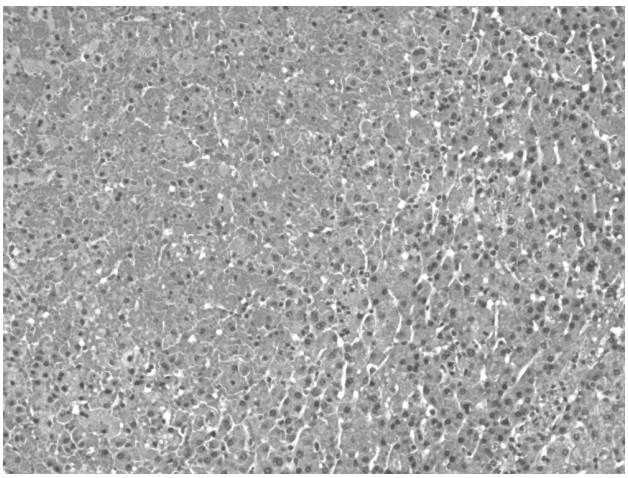
High Frequency Irreversible Electroporation (HFIRE): A Novel Method of Targeted Cell Death I. Siddiqui,[1]* E. Baker,[1] E. Latouche,[2] M. Dewitt,[2] J. Swet,[1] D. Vrochides,[1] D. Iannitti,[1] R. Davalos,[2] I. Mckillop.[1] *1. Carolinas Medical Center, Charlotte, NC; 2. Virginia Tech, Wake Forest University, Blacksburg, VA.*

Introduction –Electroporation unlike ablation is excellent in inducing cell death via apoptosis but has disadvantages of electrical conduction via cardiac

and nervous tissue. We hypothesized a novel high-frequency IRE (H-FIRE) system employing ultra-short bipolar pulses would obviate the need for cardiac synchronization and paralytics while maintaining measurable effect on cell death Methods - . Female swine (55-65Kg) were used. Two H-FIRE electrodes were inserted into the liver (1.5cm spacing). In the absence of paralytics H-FIRE pulses were delivered (2250V, 2-5-2 pulse configuration) at different on times (100 vs 200μs) or number of pulses (100 vs 300). Next electrodes were placed across major hepatic vascular structures and H-FIRE performed. At conclusion tissue was resected and analyzed histologically. Results - . 24 H-FIREs were performed (mean ablation time 275secs). No EKG abnormalities or changes in vital signs were measured during H-FIRE procedures. In 1/24 H-FIREs minor twitching of the rectus abdominis was recorded coinciding with pulse delivery. Histologically, tissues had effective electroporation as evidenced by cell death and caspase activity. Blinded scoring was performed for necrosis and apoptosis. Areas of cell death were predictable. No significant vascular damage or coagulated/thermally-desiccated blood was detected within major vessels following H-FIRE. Conclusion – H-FIRE is a novel way of liver electroporation. It produces predictable cell apoptosis without the requirement of paralytics and alteration of electrocardiographic signals, while preserving underlying vascular integrity. It's application in cancer cell death needs to be studied, but it has a potential for clinical use in targeting tumors with minimal morbidity.



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Management of Massive (>10cm) Hepatocellular Carcinoma at a Tertiary Referral Public Hospital Y. Rosen,[2]* A. Winer,[1] F. Lu,[2] R. Berman,[3] M. Melis,[3] G. Miller,[3] H. Pachter,[3] E. Newman,[3] I. Hatzaras.[3] *1. Department of Internal Medicine, NYU Langone Medical Center, New York, NY; 2. NYU Langone Medical Center, New York, NY; 3. Department of Surgery, NYU Langone Medical Center, New York, NY.*

Background: There is relative paucity of data regarding patients who present to North American centers with massive (>10 cm) hepatocellular carcinoma (HCC). We sought to assess the prognosis of patients with massive HCC who presented at a tertiary referral public hospital. Methods: We identified all patients with a diagnosis of HCC who were evaluated at Bellevue Hospital Center, New York from 1998 to 2013 and collected relevant demographic and clinical information. We categorized patients according to the treatment modality they received (resection, TACE, sorafenib, or best supportive care). Survival analysis was performed among the subgroups using Cox proportional hazards regression. Results: There were 509 patients with HCC identified, of which 122 (24%) had a massive HCC. Median tumor size was 14 cm (IQR = 12 - 17.6cm). Other demographics are summarized in table 1. 11 patients received TACE, 14 received resection and 87 received best supportive care and/or Sorafanib; 10 received combination treatment and were excluded from the analysis. With best supportive care, patients had a median survival of 3.0 months. Resection had median survival 16.8 months and showed significant survival benefit over best supportive care ($p < 0.001$) with hazard ratio 0.19 (95% CI 0.08-0.46). TACE had median survival 13.4 months and showed a significant survival benefit over best supportive care ($p < 0.001$) with hazard ratio 0.30 (95% CI 0.13-0.72). We lacked the statistical power to detect a difference comparing resection and TACE. Sorafenib treatment showed no statistically significant benefit (median survival 1.43 months vs. best supportive care 3.43 months, $p = 0.53$). In multivariate analysis, patients of Asian race had worse prognosis (HR = 2.13); tumor size, metastasis, vascular invasion on imaging, AFP levels, and unadjusted MELD score all failed to predict survival. Discussion: Patients with massive HCC benefited from resection or TACE, independent of standard markers of disease severity. Clinically this implies that the presence of large, advanced HCC does not preclude performing life-extending procedures. Resection or TACE should not be withheld for patients with massive HCC.

Covariate	Supportive care *(n = 86)*		TACE *(n = 11)*			Resection *(n = 14)*		
	Median	IQR	Median	IQR		Median	IQR	
Tumor Size	14.5 cm	12-18 cm	17 cm	14-17 cm	p = 0.23	12 cm	11-14 cm	p = 0.04
AFP level at diagnosis	1511.1	29-19116	9261.5	3060-94553	p = 0.1	25621	1123-117218	p = 0.09
Unadjusted MELD score	10	8-14	9	8-10	p = 0.12	9	7-10	p = 0.04
Age	50	42-61	38	36-51	p = 0.1	49	36-58	p = 0.31
	Patients	% of patients	Patients	% of patients		Patients	% of patients	
Portal vein invasion on imaging	49	57%	6	55%	p = 1	2	14%	p = <0.01
Hepatic vein invasion on imaging	22	25%	1	9%	p = 0.29	1	7%	p = 0.18
Metastases on imaging	34	40%	7	64%	p = 0.19	7	50%	p = 0.56
Female sex	10	12%	1	9%	p = 1	2	14%	p = 1
Asian race	45	52%	7	64%	p = 0.53	10	71%	p = 0.25
Sorafenib treatment	17	20%	2	18%	p = 0.05	1	7%	p = 0.24
History of hepatitis B infection	51	60%	10	91%	p = 1	11	79%	p = 0.31

Table 1: Patient Group Characteristics.

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National Treatment Patterns of Hepatocellular Carcinoma Among Patients with Hepatitis B and C Infection: A Surveillance, Epidemiology, and End Results-Medicare Analysis C. Scally,* H. Yin, H. Nathan, S.L. Wong. *Department of Surgery, University of Michigan, Ann Arbor, MI.*

INTRODUCTION: The incidence of hepatocellular carcinoma (HCC) is increasing; mortality can only be improved with earlier detection to allow effective therapeutic intervention. The majority of HCC cases are related to chronic Hepatitis B and C infection (HBV/HCV). Given the increasing prevalence of HBV/HCV, a better understanding of HCC in this population is needed. METHODS: Patients diagnosed with both HBV/HCV and HCC were identified from SEER-Medicare linked data (2005-09, with follow-up to 2011). Patient and tumor factors were analyzed, along with the initial mode of treatment. We then compared these pts to those without accompanying diagnoses of HBV/HCV. RESULTS: 1723 HCC pts with HBV/HCV and 2360 HCC pts without HBV/HCV were identified. Among those with HBV/HCV, median age at diagnosis was 73 yrs. 63% of pts were male; 50% were white, 26% Asian, 11% African-American. The majority of pts presented with locoregional (81%) disease. However, only a small number underwent cancer directed therapy: surgical resection (n= 116, 6.7%), liver transplant (n=59, 3.4%), or liver directed therapy (chemoembolization, radiofrequency ablation) (n=358, 20.8%). The majority of pts received no therapy. Compared to white and Asian pts, African Americans were less likely to receive surgical resection or liver-directed therapy (25.0% v 18.4 %, p = .006). Among pt with HBV/HCV, mortality was higher (89%) than those without HBV/HCV (85%, p <.001). This higher rate of mortality occurred despite HBV/HCV pts having similar rates of surgical resection (6.7% vs 5.5%, p = .09) and higher rates of liver directed therapy (20% vs 8.6%, p < .001). Pts with HBV/HCV presented with similar tumor staging as those without HBV/HCV. CONCLUSION: Although many HCC patients present with localized disease, only a small proportion undergo potentially curative therapy. Pts with HBV/HCV have worse outcomes than pts without HBV/HCV despite similar treatment patterns. Timely diagnosis and access to screening in at-risk HBV/HCV pts may allow for earlier detection of HCC and identify pts amenable to surgical intervention.

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Adjuvant Chemotherapy for Intrahepatic Cholangiocarcinoma Does Not Improve Survival: National Cancer Data Base Analysis J.A. Santamaria-Barria,* D. Roife, L.S. Kao, C.J. Wray. *Department of Surgery, University of Texas Health Science Center at Houston, Houston, TX.*

Introduction: To date no convincing evidence suggests a benefit of adjuvant chemotherapy following resection or ablation for the treatment of intrahepatic

cholangiocarcinoma (ICC). Our hypothesis is adjuvant chemotherapy improves survival following surgical or ablative treatment of ICC. Methods: The national cancer database was queried for all ICC cases from 1998-2012. We included patients who received adjuvant chemotherapy within 120 days after resection or ablation. Exclusion criteria were unknown stage, surgical treatment, or vital status. The effect of adjuvant chemotherapy was estimated using a standard Cox proportional hazards model stratified by stage. To account for nonrandomized treatment assignment, the average treatment effect of chemotherapy was calculated using inverse probability of treatment weighting with propensity scores. Results: 2,798 patients (n=1470 female) met inclusion criteria. 16,654 patients had no surgical or ablative treatment. Treatment included n=2537 resections and n=261 ablations. The median survival for patients undergoing resection was 30.3 months, and for patients that were ablated was 16.9 months. In the multivariate Cox regression (adjusted by adjuvant chemotherapy, age, sex, and hospital type), resection was associated with improved survival (HR 0.59, 95% CI: 0.38 to 0.90) when compared to ablation; however, adjuvant chemotherapy was not associated with improved survival. Using propensity scores and inverse probability of treatment weighting, the average treatment effect of adjuvant chemotherapy following resection did not increase survival (+1.32 months, 95% CI:-8.7 to +11.4). However, adjuvant chemotherapy following ablation significantly reduced survival (-8.6 months, 95% CI: -15.2 to -1.96). Conclusion: Amongst patients undergoing hepatic resection for ICC, the effects of adjuvant chemotherapy remain uncertain. For those patients undergoing ablation, there is a clinically significant reduction in survival. Future randomized trials should focus on evaluating adjuvant chemotherapy in patients undergoing resection and on alternative strategies for improving survival in patients undergoing ablation.

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Coordinated Minimally Invasive Multi-Stage Surgery for Stage IV Colorectal Cancer C. Conrad,* D. Weissinger, H. Shiozaki, T.A. Aloia, B. Bednarski, C.A. Messick, Y. Chun, J. Vauthey, G. Chang, Y. You. *Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction Minimally-invasive surgery (MIS) is increasingly performed for colorectal cancer (CRC) and liver metastases (LM). Perioperative benefits and oncologic adequacy have been separately demonstrated for each. However, coordinated minimally-invasive multi-stage surgery for CRC with resectable LM has not been investigated. We evaluated the perioperative and oncologic safety of this novel approach. Methods Thirty-one consecutive patients who underwent MIS resections for both CRC and for synchronous(n=23) or metachronous(n=8) LM between 2011-2015 were retrospectively reviewed for clinicopathologic characteristics and multimodality treatments. Outcome measures included perioperative morbidity, pathologic assessment, and return to intended oncologic therapy (RIOT). Results The median age at CRC diagnosis was 55 years and 16 (52%) were female. Most (80%) primary tumors arose from the sigmoid (n=14) and rectum (n=11, median 8cm from the anal verge). For patients with synchronous LM, 17(74%) received preoperative chemotherapy and 4(17%), pelvic radiation. Resection sequence was reverse (liver-first, n=5, 22%; 0 conversion during CRC resection), combined (n=9, 39%), or classic (CRC-first, n=9, 39%; 1 conversion during LM resection). Overall, CRCs required 2-stage resection with temporary diversion in 8 (26%) patients, while hepatectomy was 2-stage with portal vein embolization (PVE) in 5 (22%) patients (with post-PVE procedure performed open). Perioperative outcomes highlighted low morbidity and short hospital stay (Table). All were rendered disease-free, with R0 resection in 94% for CRC (2 with 1mm radial margin) and 94% for LM (2 with R1 resection; median free margin: 4mm). A median of 24 nodes [interquartile range, IQR: 17, 34] nwere resected with CRCs. All patients returned to their intended oncological therapy at a median of 6.5 [IQR: 5.1, 7.6] weeks post-resection. Conclusion Coordinated curative-intent MIS for CRC with resectable LM affords favorable peri-operative morbidity rates, excellent pathologic outcomes, and timely RIOT. Advanced planning of multi-stage resections, including port and ostomy site placements, is required. Long-term oncologic results will await future studies.

Summary of peri-operative outcomes of coordinated minimally-invasive surgery for CRC with resectable liver metastases

	Primary CRC (No., %)	Liver Metastases (No., %)
Total patients	N=31	N=31
Surgical Approach	Laparoscopic (14, 45%) Robotic (12, 39%) Lap-hand assisted (5, 16%)	Laparoscopic (25, 81%) Lap hand-assisted (5, 16%) Robotic (1, 3%)
Surgical Procedure *	LAR (18, 58%) Segmental colectomy (10, 32%) APR (2, 7%) TPC (1, 3%)	Major hepatectomy (8, 26%) Minor hepatectomy (23, 74%)
Estimated blood loss, cc Median [IQR]	100 [50,200]	100 [50, 100]
Intra-operative/In-hospital Transfusion	1 (3%)	0
Length of hospital stay, days Median [IQR]	4.5 [3, 5.3]	3.3 [4, 5.8]
30-day/In-hospital morbidity, Any	4 (12.9%)	6 (19%)
30-day/In-hospital morbidity, Grade 3 or higher **	1 (3%)	3 (9.7%)

IQR=interquartile range.
*** Surgical Procedures:** LAR=low anterior resection; APR=abdominal perineal resection; TPC=total proctocolectomy. Major hepatectomy = wedge resection of 3 or more segments, anatomic resection of 2 or more segments, left/right hepatectomy, extended left/right hepatectomy. Minor hepatectomy = wedge resection of fewer than 3 segments; anatomic resection of 1 segment.
**** Grade 3 morbidity** was defined as a complication requiring surgical, endoscopic, or interventional radiology intervention. No Grade 4 or 5 complication occurred.

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Patient Ratings of Hospital Care Using the HCAHPS Survey Following Pancreatic Surgery are Influenced by Pain Management and Not Postoperative Complications T. Nguyen,* J. Peng, C. O'Rourke, N. Anzlovar, D. Bokar, R. Walsh, G. Morris-Stiff. *Cleveland Clinic, Cleveland, OH.*

Introduction: Patient perception is an important quality metric of hospital care and is linked to Medicare reimbursement. The aim of this study is to determine whether there is an association between Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey results and surgical complications in patients who underwent pancreatic surgery. Methods: Patients who underwent pancreatic surgery between 2009 and 2013 at a single institution and returned an HCAHPS survey were included. Patient complications were obtained from the American College of Surgeons National Surgical Quality Improvement Project database. Results: Seventy-nine patients who underwent pancreatic surgery completed HCAHPS surveys. The majority of patients underwent surgery for malignant (n=51, 65%) or benign (n=21, 27%) neoplasms. Forty-five (57%) patients had no post-operative complications, 19 (24%) had minor complications and 15 (19%) had major complications within 30 days. There was no significant difference on HCAHPS survey results in patients with and without complications in regards to ratings of the hospital, physician staff communication, or pain control. Higher ratings on pain control and whether pain was addressed were significantly associated with higher hospital ratings ($p< 0.001$ and $p=0.003$) and how strongly the patient would recommend the hospital ($p=0.037$ and $p=0.038$). Conclusion: In pancreatic surgery patients, pain management was a significant influence on patient satisfaction. Favorable surgical outcomes based on post-operative complications were not associated with higher HCAHPS ratings. This warrants further study in a larger, multi-institutional study to evaluate the use the HCAHPS scores as a quality metric for pancreatic resections.

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Intrahepatic Cholangiocarcinoma: Ambitious Operations and Outcomes M. Raoof,* S. Dumitra, P. Ituarte, L. Melstrom, S. Warner, Y. Fong, G. Singh. *City of Hope Medical Center, Duarte, CA.*

Background: Data from specialized institutions suggests that resection for large (>7cm) and mutifocal intrahepatic cholangiocarcinoma (ICC) is safe and feasible. We aim to study this hypothesis using a population-based dataset. Methods: This is a study of a contemporary cohort from California Cancer Registry database (2004-2011) that was merged with Office of Statewide Health Planning and Development inpatient database. All patients with ICC

that underwent resection or ablation were included. Tumors were classified into two groups; intrahepatic, small (<7cm) & solitary (ISS) vs. extraheapatic extension, large or multifocal (ELM). Mortality was recorded at 90 days. Overall survival (OS) analysis was performed using the Kaplan-Meier and Cox-proportional hazard model. Results: Of the total 275 patients that met the inclusion criteria, 55% were female, 52% were white and median age was 65 years (IQR 55-72). Majority of patients had >3 segment resection 59% (Ablation 10%, 1-3 segments 30%). Portal lymphadenectomy was performed in 45% of patients. Vascular Invasion was found in 22% of patients, 14% were bilobar and 20% were node positive. Median follow up was 23 months (IQR 13-40). Number of ISS tumors (139, 50.5%) and ELM tumors (136, 49.5%) was similar. The two groups were comparable in regards to age, sex, race, comorbidities, extent of surgery, portal lymphadenectomy, node positivity. ELM tumors were more likely to have vessel invasion (27% vs. 17%, p=0.048) and be bilobar (26% vs. 2%, p<0.001). There was no significant difference in overall complication rate (ISS 34%, ELM 27%, p=0.19) and mortality rate (both groups <1%, p=0.32). A multivariate Cox-proportional hazard model demonstrated that age >60 years, >1 comorbidity, high grade tumors, ELM tumors (HR 1.63: 95%CI 1.11-2.40; p=0.013) and LN positivity (HR 2.30: 95%CI 1.49-3.54; p<0.001) are independently associated with worse OS. (Figure 1) Conclusion: Surgical resection of tumors > 7cm, multifocal lesions involving contiguous extrahepatic organs is safe with acceptable morbidity and mortality. Age > 60 years, grade, comorbidity, ELM tumors and LN positivity are independent predictors of worse OS.

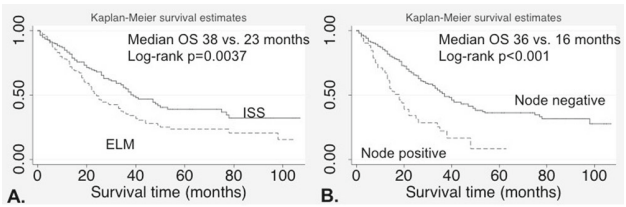

Figure 1. Kaplan-Meier survival estimates of Overall Survival. A. Intrahepatic, small and solitary (ISS) vs. Extrahepatic extension, large and multifocal (ELM). B. Lymph Node positive vs. negative.

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PD-L1 Expression is an Unfavorable Prognostic Factor in Hepatocellular Carcinoma M. Baek,[1]* H. Jung,[1] T. Ahn,[1] S. Park,[1] S. Bae,[1] D. Jung.[2] *1. Surgery, Soonchunhyang University Hospital, Cheonan, Korea (the Republic of); 2. Soonchunhyang University, Cheonan, Korea (the Republic of).*

Background: The programmed death-1 (PD-1) and programmed death ligand-1 (PD-L1) pathway have been shown to be involved in tumor-induced immunosuppression. Immunotherapy has become a key strategy for cancer treatment and programmed cell death 1 (PD-1) and its ligand (PD-L1) have recently emerged as important targets. Hepatocellular carcinoma (HCC) is a highly aggressive and rapidly growing tumor. Effective methods of early diagnosis, monitoring metastasis and recurrence are not available. Recently, overexpression of programmed cell death-1 (PD-1) and its` ligand (PD-L1) correlate with poor outcome in some cancers. However, expressions of PD-L1 and clinical outcomes in hepatocellular carcinoma have not been known. We analyzed the expression of PD-L1 in hepatocellular carcinoma to evaluate its potential as biomarker and target for immunotherapeutic strategies. Methods: Formalin-fixed paraffin-embedded samples were obtained from 85 patients with HCC who underwent surgery. The expression of PD-L1 was evaluated by immunohistochemical stains. Two independent pathologists determined semiquantitatively by assessing the percentage of positively stained cells and intensity of staining. Results: Multivariate analysis revealed the PD-L1 [hazard ratio (HR), 6.765; 95% confidence interval (CI), 2.899-15.789; p=0.001], tumor size [HR, 2.499; 95% CI, 1.325-4.713; p=0.005] were independent prognostic value for overall and disease free survival in hepatocellular carcinoma patients. Patients with high expression of PD-L1 had a significantly poorer survival and recurrence than patients with low expression (p<0.001). Conclusion: PD-L1 overexpression in HCC patients is related on survival and recurrence. Patients with high expression of PD-L1 had a worse outcome than patients with low expression. Further evaluation of the PD-1 and PDLs as a predictive biomarker in HCC is warranted.

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Extent of Lymph Node Burden Provides Enhanced Prognostic Value for Pancreatic Adenocarcinoma C. Yabar,* J. Metkus, J. Epstein, G. Kozak, H. Lavu, C. Yeo, J. Winter. *Department of Surgery, Jefferson Pancreas, Biliary and Related Cancer Center, Thomas Jefferson University, Philadelphia, PA.*

Background: While numerous studies have examined the impact of metastatic lymph node burden on survival, the full prognostic potential of this information remains unfulfilled. Methods: 637 patients underwent resection for pancreatic ductal adenocarcinoma (PDA) between 2002 and 2014 at Thomas Jefferson University. Positive lymph node count (LNC) and positive lymph node ratio (LNR) were analyzed as predictors of cancer-specific outcomes. Results: Overall median survival in the cohort was 18.7. Excluding those who were lost to follow-up or expired in the first 90 postoperative days, patients with node-positive disease (N1) had a median survival of 16.9 months (n=496, 70%) compared to 27.5 months (n=191, 30%) for patients with node-negative (N0) disease (HR= 1.9, p<0.001). Overall survival decremented with increased nodal disease, but plateaued at LNC above 4 (HR 2.5 vs. N0, p<0.001) and LNR above 0.4 (HR 2.4, p<0.001). In contrast to historical cohorts with metastatic disease, long-term survival was relatively common with extensive nodal disease (LNC≥4); 18, 24, and 36-month survivals were 37%, 24%, and 14%, respectively. Increased lymph node disease burden (both LNC and LNR) were also predictive of a systemic recurrence pattern (p<0.001) and an increased postoperative CA 19-9 level (linear regression, slope 970, p=0.044). Conclusion: Lymph node burden portends a worse prognosis, but levels off at a certain point (LNC>4 or LNR>0.4). Microscopic regional spread beyond these thresholds does not negatively influence longevity, and long-term survival is relatively common compared to patients with metastatic disease. A high lymph node disease burden is a surrogate marker for occult systemic disease, as evidenced by high postoperative CA 19-9 and a distant recurrence pattern.

Table 1: Predictors of Total Survival Time

Covariate	Median (mo.)	Univariate Hazard Ratio	95% CI	*P* value
Total pts (n=606)	18.7	-	-	-
Positive lymph node no.				
0	27.5	1.00	-	-
1	19.7	1.58	1.07-1.85	0.014
2	17.6	1.68	1.20-2.19	0.002
3	18.7	1.83	1.58-2.97	<0.001
4+	14.6	2.46	1.80-3.14	<0.001
Lymph node ratio*				
0	24.1	1.00	-	-
.1	19.9	1.41	1.17-2.13	0.003
.2	17.3	1.62	1.20-2.35	0.003
.3	15.4	2.16	1.30-2.57	0.001
.4+	13.2	2.38	1.90-3.19	<0.001

*rounded to the nearest tenth

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Towards an Absolute Bilirubin Threshold for Preoperative Biliary Decompression in Patients Undergoing Whipple C. Mosquera,[2]* V.G. Dorismond,[1] E.E. Zervos.[2] *1. Brody School of Medicine, Greenville, NC; 2. Brody School of Medicine, Division of Surgical Oncology, Greenville, NC.*

There is no consensus as to when preoperative biliary decompression is indicated in patients with obstructive jaundice prior to pancreatoduodenectomy. The purpose of this study is to identify a bilirubin level whereby biliary decompression provides clear benefit despite potential drawbacks. Methods: Serial logistic regression analyses were undertaken to identify the bilirubin threshold upon which biliary decompression was associated with significant improvement in overall complications, mayor complications (Clavien-Dindo ≥3), length of stay, readmission rates and mortality. Results: Biliary decompression independently predicted a higher incidence of overall complications in patients presenting with bilirubin ≤10mg/dl, (p=0.02). For patients with bilirubin >10mg/dl - <15mg/dl, there were no differences in complications, mortality, length of stay or readmissions. Biliary decompression in patients with bilirubin ≥15mg/dl independently predicted fewer overall (72% vs 100%), and mayor complications (11 % vs 50%), p<0.05, and lower readmission rates (27.7% vs 62.5%), p=0.02. Patients not undergoing biliary decompression underwent resection on average two weeks sooner than those having decompression (4.7 days vs 17.2 days), p=0.01, with no significant change in bilirubin levels between presentation and surgery. Patients with bilirubin < 15mg/dl at

presentation, who underwent biliary decompression, had a bilirubin decrease of more than 50% (6.3mg/dl to 2.5mg/dl), and the time to resection increased by more than one week (28 days vs 20.4 days), p<0.001. Conclusion: All patients presenting with bilirubin ≥15mg/dl should undergo preoperative biliary decompression to minimize the risk of complications and readmissions. Patients presenting with bilirubin ≤10 mg/dl should forego stent placement to avoid stent related complications without clear benefit. The decision to stent between >10mg/dl to <15 mg/dl should be made on a case by case basis, taking into account anticipated bilirubin level at the time of surgery.

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Primary Malignancy is an Independent Determinant of Morbidity and Mortality Following Liver Resection M.W. Fromer,* J.P. Gaughan, U.M. Atabek, F.R. Spitz. *Cooper University Hospital, Camden, NJ.*

BACKGROUND: Although outcomes following liver resection have improved due to recent advances, there remains considerable perioperative morbidity and mortality with these procedures. Previous studies suggest a primary liver cancer diagnosis is associated with poorer outcomes, but the extent to which this is attributable to a higher degree of hepatic dysfunction is unclear. To better delineate how a primary cancer diagnosis contributes to the morbidity and mortality of hepatectomy, we performed a matched pair analysis of primary vs. secondary malignancies with a national database. METHODS: The ACS-NSQIP database (2005-2013) was analyzed to select cases of elective liver resection. The associated diagnoses were sorted as follows: 1) primary cancers of the liver parenchyma or intrahepatic bile ducts and 2) secondary metastatic neoplasms. A literature review identified factors found to impact hepatectomy outcomes; these variables were evaluated by a univariate analysis. The most predictive factors were used to create similar groups from each diagnosis category via propensity score matching. Multivariate regression was used to validate results in the wider study population. Outcomes data were compared using $\chi 2$ and Fisher exact tests with odds ratios and 95% confidence intervals. RESULTS: Matched groups of 4,838 patients were similar with regard to all variables, including indicators of liver function and extent of resection. Primary malignancies were associated with a significantly increased incidence of sepsis, organ space surgical site infection, deep vein thrombosis, renal failure, return to the operating room, pneumonia, reintubation, failure to wean from the ventilator, and cardiac arrest. The mortality rate for primary neoplasms was 4.6% at 30 days (versus 1.6%); this represents a risk of death three times (95%CI 2.20-3.81, p<0.0001) higher in cancers of hepatic origin. CONCLUSIONS: Hepatectomy carries substantially higher perioperative risk when performed for primary liver cancers, independent of hepatic function and resection extent. This knowledge will help to improve treatment planning, patient education, and resource allocation in oncologic liver resection.

Outcomes of Propensity Score Matched Groups (Metastatic versus Primary Hepatic Malignancies)

Outcome at 30 days	Metastatic	Primary		
	N= 4838 (%)	N= 4838 (%)	p-value	Odds Ratio (95% CI)
Operative time	247m (SD 116)	251m (SD 136)	0.133	
Length of Hospital Stay	7.46d (SD 6.8)	8.33d (SD 7.9)	<0.0001	
Patients with Transfusions	631 (13.0)	759 (15.7)	0.0002	1.24 (1.11-1.39)
Urinary Tract Infection	116 (2.4)	175 (3.6)	0.0005	1.53 (1.20-1.94)
Superficial SSI	183 (3.8)	223 (4.6)	0.048	1.22 (1.01-1.50)
Deep SSI	56 (1.2)	27 (0.56)	0.002	0.48 (0.30-0.76)
Organ Space SSI	236 (4.9)	338 (7.0)	<0.0001	1.46 (1.23-1.74)
Sepsis	235 (4.9)	336 (7.0)	<0.0001	1.46 (1.23-1.74)
Pulmonary Embolism	64 (1.3)	72 (1.5)	0.546	1.13 (0.80-1.58)
Deep Vein Thrombosis	88 (1.8)	140 (2.9)	0.0006	1.61 (1.23-2.11)
Stroke	22 (0.5)	13 (0.3)	0.175	0.59 (0.30-1.17)
Myocardial Infarction	33 (0.7)	25 (0.5)	0.357	0.76 (0.45-1.27)
Wound Dehiscence	33 (0.7)	27 (0.6)	0.518	0.82 (0.49-1.36)
Renal Failure	47 (1.0)	97 (2.0)	<0.0001	2.09 (1.47-2.96)
Return to Operating Room	150 (3.1)	215 (4.4)	0.0006	1.45 (1.18-1.80)
Pneumonia	139 (2.9)	186 (3.8)	0.009	1.35 (1.08-1.69)
Reintubation	144 (3.0)	248 (5.1)	<0.0001	1.76 (1.43-2.17)
Failure to Wean at 48hrs.	142 (2.9)	228 (4.7)	<0.0001	1.64 (1.32-2.02)
Cardiac Arrest	30 (0.6)	63 (1.3)	0.0008	2.11 (1.37-3.27)
Major Morbidity	1419 (29.3)	2015 (41.6)	<0.0001	1.72 (1.58-1.87)
Mortality	71 (1.6)	203 (4.6)	<0.0001	2.90 (2.20-3.81)

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The Utility of MELD Score in Predicting Mortality Following Liver Resection for Metastasis M.W. Fromer,* J.P. Gaughan, U.M. Atabek, F.R. Spitz. *Cooper University Hospital, Camden, NJ.*

BACKGROUND: The MELD score has been demonstrated previously to be predictive of hepatectomy outcomes in mixed patient samples of primary and secondary liver cancers. Because MELD score is a measure of hepatic dysfunction, prior conclusions may rely on the high prevalence of cirrhosis seen with primary lesions. The utility of the score has not been clearly verified in purely metastatic populations, where cirrhosis is less common. We hypothesized that MELD score would prove to be an independent determinant of perioperative mortality in patients undergoing hepatic metastasectomy. METHODS: The ACS-NSQIP database 2005-13 was analyzed to select liver resections performed for metastases. The data were randomly sorted into a training set (80%) and a validation set (20%). A receiver operating characteristic (ROC) analysis determined the MELD score with the best sensitivity and specificity for 30-day mortality. A literature review identified variables found to impact hepatectomy outcomes. Significant factors were included in a multivariable analysis with backward selection. A risk calculator was generated from a final multivariable model using MELD as a continuous variable. RESULTS: A preoperative MELD score of 7.5 was identified by ROC (sensitivity 72%, specificity 73%, c-statistic 0.77). Of all patients above this threshold, 4.9% died at 30 days, vs. 0.7% below. This group represented 28.2% of the total population but accounted for 72.4% of all deaths (p<0.001). The multivariable analysis revealed the risk of death with MELD >7.5 to be increased by 69% (OR=1.69, 95%CI 1.26-2.28, p<0.001). In all, 12 significant perioperative predictors were identified. A risk calculator was successfully developed with 81% correct classification and similar event rates; parameter estimates, c-statistics, and event rates were comparable when applied to the validation set. CONCLUSIONS: A MELD score over 7 is an important predictor of death following hepatectomy for metastasis and may prompt a more detailed surgical assessment with the provided risk calculator. Attention to MELD score in the preoperative setting will improve treatment planning and patient education prior to oncologic liver resection.

MELD Score >7.5 in Multivariable Analysis with Backward Selection

Perioperative Characteristic	p-value	Odds Ratio (95% CI)
Age	<0.0001	1.03 (1.02-1.04)
ASA Classification (3/4)	<0.0001	2.38 (1.80-3.14)
Metabolic Syndrome	0.0017	1.79 (1.25-2.57)
Preop Albumin	<0.0001	0.43 (0.34-0.54)
Preop Hematocrit <39	0.0017	1.95 (1.28-2.95)
Preop AST >30	0.0007	1.63 (1.23-2.17)
Preop Alkaline Phosphatase >93	0.0388	1.36 (1.02-1.81)
Preop Platelet Count <100	0.0007	2.16 (1.39-3.36)
Preop Weight Loss >10%	0.0157	1.62 (1.10-2.40)
Major Hepatic Resection	<0.0001	1.40 (1.25-1.56)
Cardiovascular Comorbidity	0.0092	1.52 (1.11-2.08)
MELD Score >7.5	0.0005	1.69 (1.26-2.28)

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Lymph Node Yield Between Open and Laparoscopic Portal Lymphadenectomy C.T. Ong,* D.P. Nussbaum, Z. Sun, D. Blazer, M. Worni. *Duke University Medical Center, Durham, NC.*

Background: Gallbladder cancer (GBC), intrahepatic cholangiocarcinoma (IHC), and fibrolamellar hepatocellular carcinoma (FL-HCC) are rare hepatobiliary malignancies with poor prognoses. For these cancers, portal lymphadenectomy is recommended for prognostic and possibly therapeutic value. Though minimally invasive approaches to resection of hepatobiliary malignancies are increasing in utilization, the impact of these techniques on lymph node (LN) retrieval is unknown. Methods: Patients 18 years or older were selected from the 2010-2012 National Cancer Database with surgically resected non-metastatic GBC, IHC, and FL-HCC. Predictors of laparoscopic over open surgery were identified by univariate and multivariate logistic regression. The number of harvested LNs was analyzed with negative binomial/Poisson regression while multivariable-adjusted predicted LN yields were calculated for comparison. Subgroup analyses were performed for patients undergoing dedicated regional lymph node surgery and by facility type. Results: 4173 patients were identified (GBC: n=3045, 73%, IHC: n=1069, 26%, and FL-HCC: n=59, 1.4%). Resections were open in 2174 (52%) and laparoscopic in 1999 (48%) patients. 416 (10%) patients were converted from laparoscopic to open surgery. After multivariable adjustment, intention to treat

by laparoscopic approach was more likely if patients were female, older, operated on at academic centers, or had more comorbidities, GBC, T1/2 disease, or smaller tumors compared to their counterparts. The LN yield was greater overall in patients undergoing open procedures (p<0.001) and among patients undergoing dedicated regional lymphadenectomy (p<0.001) [Table]. In a subgroup analysis of academic centers, there was no difference in LN harvest between laparoscopic and open resection. Conclusions: Study of this large national database demonstrates LN retrieval after portal lymphadenectomy appears to be inferior in laparoscopic compared to open surgical resections. However, restricting our analysis to academic centers shows similar retrieval rates. These results underscore the importance of maintaining sound oncologic principles as minimally invasive techniques for hepatobiliary surgery emerge.

Measured and predicted lymph node yield between open and laparoscopic resection

	Overall: intention to treat				
	Measured (n, %)		Multivariable adjusted predicted values (negative binomial regression, %)		
Number of lymph nodes	Open	Laparoscopic	Open	Laparoscopic	p-value
0	882 (40.6)	1125 (56.3)	44.0	55.2	<0.001
1	457 (21.0)	437 (21.9)	16.6	18.0	
2	190 (8.7)	110 (5.5)	9.9	9.4	
3	158 (7.3)	87 (4.4)	6.6	5.5	
4	94 (4.3)	48 (2.4)	4.7	3.5	
5	78 (3.6)	42 (2.1)	3.5	2.3	
6	48 (2.2)	24 (1.2)	2.7	1.6	
7	47 (2.2)	25 (1.3)	2.1	1.1	
8	32 (1.5)	18 (0.9)	1.6	0.8	
9	35 (1.6)	15 (0.8)	1.3	0.6	
≥10	148 (6.8)	58 (2.9)	7.0	2.0	
Unknown	5 (0.2)	10 (0.5)			
	Among patients with dedicated LN surgery: intention to treat				
	Measured (n, %)		Multivariable adjusted predicted values (Poisson regression, %)		
Number of lymph nodes	Open	Laparoscopic	Open	Laparoscopic	p-value
0	16 (1.3)	18 (2.1)	2.1	5.0	<0.001
1	435 (34.0)	416 (48.2)	7.4	14.0	
2	190 (14.8)	109 (12.6)	13.7	20.5	
3	158 (12.3)	87 (10.1)	17.8	20.8	
4	93 (7.3)	48 (5.6)	17.9	16.5	
5	78 (6.1)	42 (4.9)	15.0	10.9	
6	48 (3.8)	24 (2.8)	10.9	6.3	
7	47 (3.7)	25 (2.9)	7.0	3.3	
8	32 (2.5)	18 (2.1)	4.1	1.5	
9	35 (2.7)	15 (1.7)	2.2	0.7	
≥10	148 (11.6)	58 (6.7)	1.1	0.3	
Unknown	1 (0.1)	3 (0.4)			

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Effect of Preoperative Bilirubin on Outcomes of Completely Resected Hilar Cholangiocarcinoma: A Multi-Institutional Analysis H. Mogal,[1]* R. Dodson,[1] N. Fino,[1] C.G. Ethun,[2] T.M. Pawlik,[3] G. Poultsides,[4] T. Tran,[4] K. Idrees,[5] C.A. Isom,[5] R.C. Fields,[6] L. Jin,[6] S. Weber,[7] A.I. Salem,[7] R.C. Martin,[8] C. Scoggins,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] S.K. Maithel,[2] P. Shen.[1] *1. Wake Forest University School of Medicine, Winston-Salem, NC; 2. Winship Cancer Institute, Emory University, Atlanta, GA; 3. Johns Hopkins School of Medicine, Baltimore, MD; 4. Stanford University Medical Center, Stanford, CA; 5. Vanderbilt University Medical Center, Nashville, TN; 6. Washington University School of Medicine, Saint Louis, MO; 7. University of Wisconsin School of Medicine and Public Health, Madison, WI; 8. University of Louisville, Louisville, KY; 9. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 10. New York University, New York, NY.*

Background: Perioperative and long-term outcomes of patients with Hilar cholangiocarcinoma (HC) and preoperative hyperbilirubinemia have not been clearly defined. Methods: Patients with HC undergoing hepatectomy with a complete (R0/R1) resection between 2000 and 2014 were identified within a 10-institution prospectively maintained database. Using receiver operating characteristic curves from logistic regression models, a peak bilirubin cutoff point that minimized the difference between the sensitivity and specificity, was determined. Factors affecting perioperative complications were estimated using logistic regression. Results: 191 of 328 (58.2%) patients who underwent complete resection with a hepatectomy, with available preoperative bilirubin data were analyzed. 37.2% (n=71) had bilirubin > 7.9. Patients with higher preoperative bilirubin were more likely to have a higher CA 19-9 (1776±3721.5 vs 302.1±518.6, p=0.0006), more comorbidities (1.6±0.8 vs 1.4±0.9), preoperative biliary drainage (PBD) (91.4% vs 75.6%, p=0.007), positive lymph nodes (48.5% vs 31.5%, p=0.025) and perioperative death (14.5% vs 5.2%, p=0.2092). Multivariate analysis identified PBD (OR 3.2, CI 1.4-7.5; p=0.008) and smoking (OR 2.3, CI 1.2-4.4; p=0.016) to be independent predictors of any and major complications. Peak bilirubin > 7.9 (OR 3.1, CI 1.1-8.9; p=0.04) and preoperative systemic sepsis (PSS) (OR 5.0, CI 1.2-21.5; p=0.03) were associated with increased risk of postoperative mortality. However, on multivariate analysis only PSS was significant (OR 14.4, CI 2.2-93.9; p=0.005); 5/13 (23.1%) of patients with PSS died within 30 days after surgery. Conclusions: PSS portends increased operative mortality in HC patients undergoing hepatectomy, independent of preoperative peak bilirubin levels. Prevention and aggressive treatment of PSS should be the priority in the preoperative optimization of these patients.

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Curative Resection for Hilar Cholangiocarcinoma: Does Adjuvant Therapy Impact Overall Survival? A Multi-Institution Analysis from the U.S. Extrahepatic Biliary Malignancy Consortium B.A. Krasnick,[1]* L. Jin,[1] J.T. Davidson,[1] C.G. Ethun,[2] T.M. Pawlik,[3] G.A. Poultsides,[4] T. Tran,[4] K. Idrees,[5] C.A. Isom,[5] S. Weber,[6] A.I. Salem,[6] W. Hawkins,[1] S. Strasberg,[1] R.C. Martin,[7] C. Scoggins,[7] P. Shen,[8] H. Mogal,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] S.K. Maithel,[2] R.C. Fields.[1] *1. Washington University School of Medicine, St. Louis, MO; 2. Emory University, Atlanta, GA; 3. The Johns Hopkins Hospital, Baltimore, MD; 4. Stanford University Medical Center, Stanford, CA; 5. Vanderbilt University Medical Center, Nashville, TN; 6. University of Wisconsin School of Medicine and Public Health, Madison, WI; 7. University of Louisville, Louisville, KY; 8. Wake Forest University, Winston-Salem, NC; 9. The Ohio State University School of Medicine, Columbus, OH; 10. New York University, New York, NY.*

Introduction: Surgical resection is the cornerstone of curative therapy for localized hilar cholangiocarcinoma. However, the effect of adjuvant therapy on survival is unclear. We analyzed the impact of adjuvant therapy on overall survival (OS) in those patients undergoing curative resection for hilar cholangiocarcinoma. Methods: We reviewed 294 patients who underwent curative resections for hilar cholangiocarcinoma between 1998 and 2015 from ten institutions participating in the U.S Extrahepatic Biliary Malignancy consortium. We analyzed the impact of adjuvant therapy on the primary outcome of OS. Probability of OS was calculated in the method of Kaplan and Meier and analyzed using multivariate Cox regression analysis. Statistical significance was set at p≤0.05. Results: Median follow up was 20 months. Mean age was 65 years. OS at 5 years was 16%. A total of 146 patients (50%) received adjuvant therapy. Of these 146 patients, 44 patients underwent solely chemotherapy, 5 underwent only radiation therapy, and 97 underwent combined chemotherapy and radiation therapy. On univariate analysis, patients who received adjuvant therapy and those who did not had similar demographic and preoperative features, with the major difference being in the rate of lymph node (LN) positive disease (50% in the adjuvant group vs. 19% in the no adjuvant therapy group, p<0.001). In a multivariate Cox regression analysis, adjuvant therapy conferred a significant protective effect on OS (HR 0.57, p=0.008, 95% CI 0.38-0.86), even when adjusting for age, tumor size, R0 resection status, ASA classification, and LN positivity. Increasing age (HR 1.026, p=0.004, 95% CI 1.01-1.04) and LN positivity (HR 1.95, p=0.002, 95% CI 1.28-2.98) both significantly predicted decreased survival. Conclusion: Adjuvant therapy is associated with improved OS in resected hilar cholangiocarcinoma. This association remains even after adjusting for poor prognostic features. We acknowledge that there is an inherent selection bias when looking at those who underwent adjuvant therapy, and thus future prospective randomized trials are needed.

Multivariate Cox Regression Model Looking at Overall Survival in Hilar Cholangiocarcinoma

Variable	HR	95% CI	p-Value
Adjuvant Therapy	0.575	0.383-0.864	0.008
Size >20mm	1.144	0.761-1.720	0.518
LN Positive	1.954	1.280-2.984	0.002
R0 Resection	1.141	0.800-1.627	0.466
Age	1.026	1.008-1.044	0.004
ASA Classification	0.872	0.634-1.199	0.399

Abbreviations: HR, Hazard Ratio; CI, Confidence Interval.

P212

Tumor-Associated Macrophage Infiltration in Colorectal Cancer Liver Metastases is Associated with Better Outcome M.J. Cavnar,[1]* S. Turcotte,[2] S.C. Katz,[3] M. D'Angelica,[1] P.T. Kingham,[1] P. Allen,[1] W.R. Jarnagin,[1] R.P. DeMatteo.[1] *1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Centre Hospitalier de l'Universite de Montreal, Montreal, QC, Canada; 3. Roger Williams Medical Center, Providence, RI.*

INTRODUCTION: Tumor-associated macrophages (TAMs) are believed to support tumor growth in most human cancers. However, there are several exceptions, notably primary colorectal adenocarcinoma, where higher TAM infiltration has been correlated with better outcome. Little is known about the importance of TAMs in colorectal cancer liver metastases (CLMs). We postulated that TAMs would similarly have a favorable association with outcome in CLMs. METHODS: A tissue microarray was previously constructed using three 0.6mm cores per patient from CLMs resected with curative intent at our institution from 1998 to 2000 (n=158). We performed immunohistochemistry for the macrophage marker CD68 and quantified expression using MIRAX SCAN and Metamorph Image Analysis software. CD68 density was correlated to overall survival (OS), time-to-recurrence (TTR), and expression of CD3, CD4, CD8, FoxP3, and MHC-I. The median value was used to stratify CD68 expression for survival analysis with the Kaplan-Meier method and log-rank test. RESULTS: Median follow-up for all patients was 42 mo (n=158), and 115 mo (n=44) for survivors. Median OS and TTR were 46 and 20 mo. TTR was higher in patients with $CD68^{hi}$ tumors compared to $CD68^{low}$ (Figure; 21 vs. 16 mo, p=0.021). OS was not different (42 vs 45 mo, p=0.30). CD68 density correlated with parameters previously associated with improved outcome using 2-tailed Spearman correlation (CD3 R=0.18, p=0.023; CD8 R=0.27, p=0.001; CD4 R=0.27, p=0.001; MHC-I R=0.30, p<0.001). Consistently, CD68 correlated with a low ratio of FoxP3/CD8 (R=-0.023, p=0.005), but not with FoxP3 alone, which was not associated with outcome alone. CONCLUSIONS: High TAM infiltration in CLMs is associated with longer TTR and more often observed in metastases rich in T cells and expressing high levels of MHC-I, parameters that are strongly associated with better outcomes.

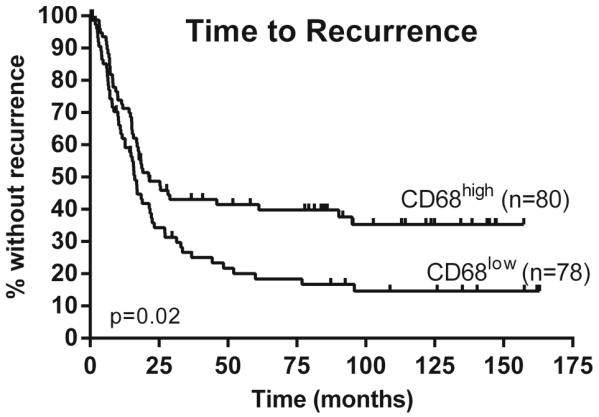


Figure. Kaplan-Meier curves of patients with CLM stratified by CD68 expression, compared by log-rank test.

P213

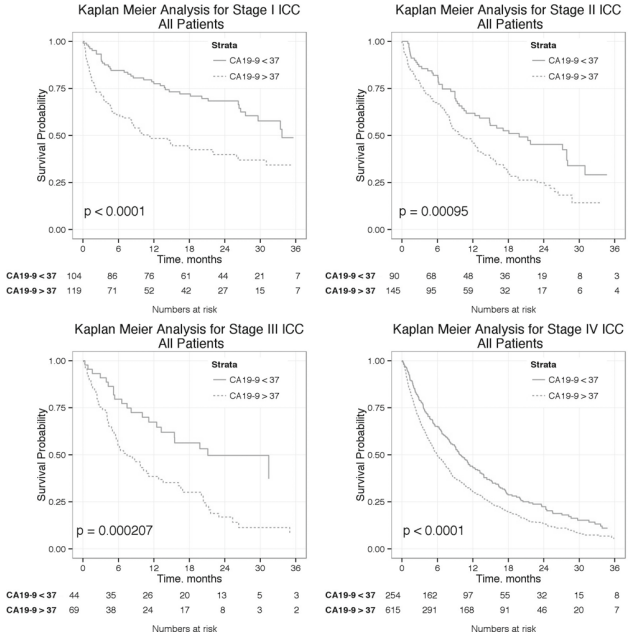
Initial Treatment of Unresectable Neuroendocrine Tumor Liver Metastases with Trans-Arterial Chemoembolization Using Streptozotocin: A 10-Year Experience M. Dhir,* J. Marsh, A. Tsung, N.B. Amesur, P. Orons, E. Santos, D.A. Geller. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: The majority of patients with neuroendocrine tumor liver metastases (NELM) present with multi-focal disease and are not surgical candidates. We present our 10 year experience with intrahepatic transarterial chemoembolization (TACE) with streptozotocin in patients with initially unresectable NELM. Methodology: Patients with unresectable neuroendocrine tumor liver metastasis treated with TACE at a single institution from 2005 to 2015 were identified from a hospital registry. All patients had a pathologic diagnosis of neuroendocrine tumor. Our initial approach was to use single agent streptozotocin TACE treating only one hepatic lobe at a time. If patients did not respond or progressed on streptozotocin, then doxorubicin or cisplatin was utilized depending on the cardiac and renal function. Results: 76 patients with NELM were treated with 360 TACE treatments over the last 10 years were identified from an institutional registry after IRB approval. Median age was 61 years and 46% of the patients were males. Sites of origin include small intestine 36%, pancreas 21%, large intestine 13%, lung 12%, and unknown in 17%. Median number of TACE treatments per patient was 4 (range 1-16). 76% had bilobar disease, 30% had extrahepatic disease, 59% had carcinoid symptoms, 68% presented with synchronous disease, and 62% had prior resection of primary tumor. TACE treatment with streptozotocin was very well tolerated with 6.1% of treatments being associated with transient side effects including hyper/hypotension, bradycardia, or post-embolization syndrome. There were no 30 day mortalities. 83% of patients also received monthly depot octreotide injections. Median overall survival from the time of diagnosis of NELM was 77 months. 55% of the patients who had carcinoid syndrome reported improved symptoms after TACE treatments. Conclusions: In patients with unresectable NELM, TACE treatment with streptozotocin is very well tolerated with minimal toxicity, and can lead to diminished carcinoid syndrome and excellent long term survival. This is a novel, conservative approach for the initial treatment of unresectable NELM.

P214

CA19-9 Level in Intrahepatic Cholangiocarcinoma is Independently Associated with Increased Mortality Hazard and Aggressive Tumor Biology: A NCDB Study J.R. Bergquist,* R.T. Groeschl, M.C. Tee, R.L. Smoot, D.M. Nagorney, E.B. Habermann, M.J. Truty. *Surgery, Mayo Clinic, Rochester, MN.*

Introduction: Triage of patients with elevated CA19-9 in intrahepatic cholangiocarcinoma (ICC) remains undefined. We hypothesized that any elevation of CA 19-9 above normal should be considered biologically borderline and prompt a multidisciplinary therapy approach. Methods: The National Cancer Data Base (2008-2011) was reviewed for patients with ICC and measured CA 19-9. Non-secretors were analyzed separately. Patients were stratified by CA 19-9 above and below normal reference range (37 U/mL). Unadjusted Kaplan-Meier analysis and adjusted Cox proportional hazards modeling of overall survival (OS) were performed. Results: 1734 patients with measured CA 19-9 were identified. Of these, 148 (8.5%) were non-secretors, 435 (25.1%) had normal CA 19-9 levels, and 1151 (66.4%) had elevated levels. 294 patients (16.9%) did not have sufficient information for staging. Among Stage I patients (N=223), 26 (11.6%) were non-secretors, 78 (34.9%) had normal levels, and 119 (53.5%) had elevated levels. Demographics and peri-operative outcomes were similar between CA 19-9 groups in all stages. Stage-specific survival was decreased in all stages for patients with elevated CA 19-9, and the difference in survival was greatest in Stage I (see figure). Cox modeling adjusting for patient comorbidity, pathologic, and adjuvant treatment variables revealed elevated CA 19-9 independently confers increased mortality hazard overall (HR 1.43, p<0.01) and in all stages (HR's 1.85, 1.48, 2.10, and 1.24, all p<0.03 in Stage 1-4 respectively). For comparison, nodal status and margin positivity conferred increased mortality hazards of 1.38 (p=0.06) and 1.87 (p<0.01) respectively. Conclusions: Elevated CA 19-9 is an independent risk factor for mortality similar in magnitude to nodal and margin status and this may merit its consideration for inclusion as a new staging variable. A multi-disciplinary therapeutic approach should be considered in patients with ICC and any CA 19-9 elevation above normal.



Unadjusted stage specific survival in Intrahepatic Cholangiocarcinoma stratified by CA 19-9 level above and below normal

P215

A Risk Calculator for Oncological Outcomes in Patients Considering Hepatic Resection for Hepatocellular Carcinoma K.T. Ostapoff,* K. Attwood, S. Kurenov, B. Kuvshinoff, M. Kukar, S. Hochwald, S. Nurkin. *Roswell Park Cancer Institute, Buffalo, NY.*

Background: Although hepatocellular carcinoma (HCC) patients are common worldwide, few undergo surgical resection. No available program exists to predict survival following HCC resection to assist with the decision to proceed with surgery or other treatment modalities. Methods: Oncologic outcomes were analyzed using the National Cancer Database (NCDB) from 1998-2006. Patients with HCC selected underwent wedge resection, partial hepatectomy or formal hepatectomy. Patients were excluded with metastatic disease or neoadjuvant treatment. Outcomes included 1, 3 and 5 year overall survival (OS). Data was randomly divided into testing (n=4364) and validation cohorts (n=1091). Regression analyses of the testing cohort were used to construct prediction models, then optimized using the validation cohort. These models were incorporated into a web-based portable application for predicting survival after curative resection. Results: HCC patients (n =5455) demonstrated a median survival of 36 months (95% CI 34.0-38.0) months with 1, 3, 5 year OS of 73% (95% CI 72– 74%), 50% (95% CI 49 – 51%) and 36% (95% CI 35-38%) respectively. Patient demographics include median age 65, male 66%, histology code HCC not otherwise specified 93.7% and median tumor size was 60 mm. Patients had analytic stage 1 (25%), stage 2 (29%) and stage 3 (45%). AFP was elevated in 63% of patients. In the patients in which cirrhosis was documented (n=452) 38.3% had biopsy proven cirrhosis. Factors assessed for significance in survival calculator included age, sex, Charleson-Deyo score, histology, grade, tumor size, node status, clinical stage, AFP level, presence of cirrhosis, surgery, margin type, and adjuvant therapy. The OS prediction model included age, sex, race, tumor size, grade, histology and analytic stage (Figure 1). Conclusion: Our model was able to predict overall 1, 3 and 5 year survival based on clinical factors. By using national database a user-friendly, point of care web-based mobile application was developed to assist in decision making for resection for HCC patients. Further work is ongoing to include perioperative outcomes with this calculator.

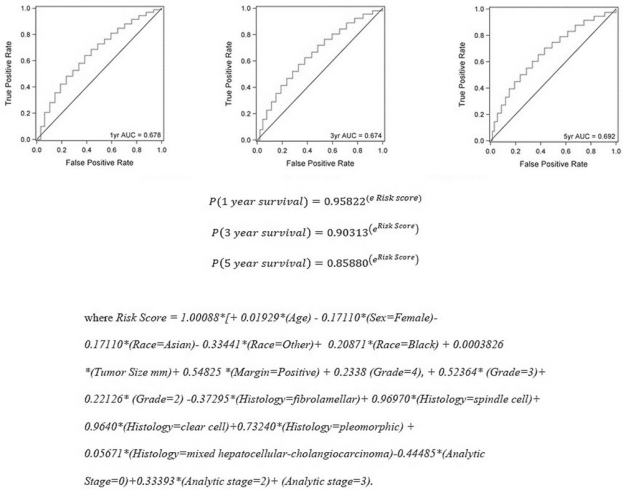
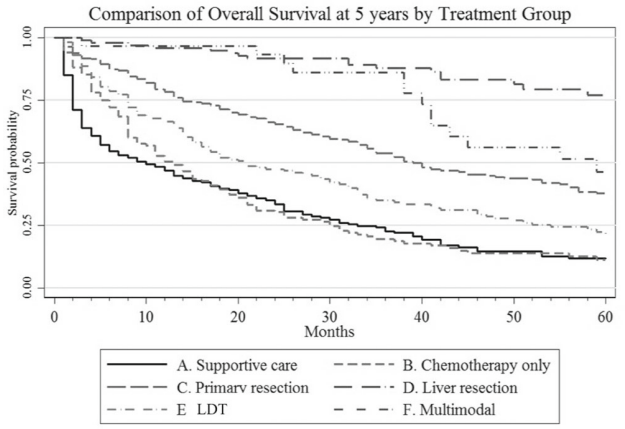


Figure 1. Model Predicting 1, 3 and 5 Overall Survival for HCC resection patients

P216

Are We Maximizing Liver Treatment for Metastases in Neuroendocrine Tumors? A. Lewis,* M.A. White, P. Ituarte, G. Singh, J. Kessler. *Surgery, City of Hope, Duarte, CA.*

Objectives: Neuroendocrine tumors (NET) commonly present at a late stage. The liver is the most common site of metastatic disease and the most likely site to result in patient mortality. Currently, no consensus exists for how to treat patients with hepatic metastases. The aim of our study was to evaluate the current standard treatments and assess their effect on patient survival. Methods: This is a retrospective study of patients with metastatic NET between 2005-2011 using the California Cancer Registry (CCR) dataset. Patients were evaluated based upon demographics, primary site, and presence of extrahepatic. Five-year overall survival (OS) was estimated by the Kaplan-Meier method and log-rank test. Multivariate analysis was performed using Cox proportional hazard. Results: A total of 1029 patients with liver metastases (22.1% of all NETs) were identified and presented with primary NETs of the pancreas (n=387, 37.6%), small bowel (n=289, 28.1%), colon/rectum (n=277, 26.9%), and stomach (n=76, 7.4%). Hepatic metastases were documented at presentation in 86.1% of these patients. Only 12.3% underwent liver resection, 14.5% chemoembolization, 4.9% radioembolization, and 3.9% multiple liver directed modalities for their hepatic metastases. A significant improvement in OS measured from the time of liver treatment was found in patients treated with surgery or liver targeted treatments ($p<0.001$; see figure). Multivariate analysis found older age (HR 0.97, CI 0.96-0.98, $p<0.001$), male sex (HR 0.64, CI 0.48-0.86, $p=0.003$), higher grade (HR 0.6, CI 0.38-0.96, $p=0.033$) or unknown grade (HR 0.59, CI 0.41-0.84, $p=0.004$), positive lymph nodes (HR 0.42, CI 0.18-0.97, $p=0.042$), and colon primary (HR 0.51, CI 0.32-0.8, $p=0.003$) were associated with a lower liver treatment rate. Conclusion: Liver resection and liver targeted therapies are associated with significantly improved survival in patients with hepatic metastases from NET compared to supportive care or systemic chemotherapy. The low rate of liver treatment suggests an underutilization of multimodal modal treatment options for liver metastases.



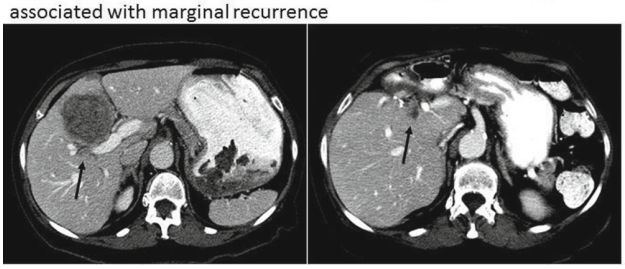
LDT = Liver-directed therapies

P217

Radiographic Predictors of Intrahepatic Recurrence After Resection of Colorectal Liver Metastases V. Phuoc,* Y. Chun, J. Vauthey, T. Newhook, C. Conrad, T.A. Aloia, H. Kang, S. Yedururi, E.M. Loyer. *Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: After resection of colorectal liver metastases (CLM), over 60% of patients will develop intrahepatic recurrence. Perioperative chemotherapy has been shown in randomized fashion to improve progression-free survival. The objective of this study was to identify radiographic predictors of intrahepatic recurrence after resection of CLM in patients treated with preoperative chemotherapy. Methods: A retrospective review was performed of patients who developed intrahepatic recurrence after resection of CLM following chemotherapy. Pre-chemotherapy and postoperative computed tomography (CT) scans were compared to identify radiographic correlates of recurrence. Median follow-up was 41 months (range, 8-132 months). Results: Among 88 patients who met study criteria, intrahepatic recurrence was identified at a median of 9 months after hepatic resection (range, 1-66 months). Fifty-five patients (63%) underwent anatomic major hepatectomy (resection of ≥ 3 segments), and 25 patients (28%) underwent R1 resection (tumor cells < 1 mm from transection line). The most frequent radiographic finding associated with intrahepatic recurrence was disappearing liver metastases (DLM) after chemotherapy in 20 patients (23%). Seventeen patients (19%) had a close radiographic margin associated with marginal recurrence, despite a negative pathologic margin in 6 of the 17 patients. Four patients had both DLM and close radiographic margin. The remaining 47 patients developed de novo metastases unexplained by preoperative CT. Seven patients had tumor infiltration of the interlobular fissures (figure), which was significantly associated with marginal recurrence (n=5, marginal recurrence vs. n=2, DLM or unexplained, $p < 0.001$). Conclusion: In this study, 47% of patients who developed intrahepatic recurrence after resection of CLM following preoperative chemotherapy demonstrated CT findings predictive of recurrence. DLM represent a significant cause of intrahepatic recurrence. Tumor infiltration of interlobular fissures may require anatomic hepatectomy or wider resection margins to avoid marginal recurrence.

Figure. Tumor infiltration of interlobular fissure (black arrow) is associated with marginal recurrence



P218

Interim Results of a Screening Protocol for Early Detection of Pancreatic Cancer in Asymptomatic High-risk Patients A. Gangi,* M.P. Malafa, J.B. Klapman. *Surgery, Moffitt Cancer Center, Tampa, FL.*

Background: Pancreatic cancer (PC) is the 4th leading cause of cancer deaths in the US but is rarely diagnosed at an early curable stage. Early detection of PC will have measurable improved outcomes in affected patients. This study sets out to evaluate if EUS can detect early stage pre-cancerous or cancerous changes in the pancreas of high risk (HR) patients. Methods: After IRB review, a clinical trial (NCT01662609) to evaluate HR patients was opened to accrual. Study subjects met specified inclusion and exclusion criteria as described in Table 1. Enrolled subjects underwent EUS followed by screening as defined by study protocol: subjects with normal EUS underwent repeat EUS at 1 year; subjects with abnormal EUS underwent fine needle aspiration (FNA) if a mass or cyst was found and measured ≥ 5mm and did not undergo FNA if the lesion measured < 5mm. Those with indeterminate or benign FNA underwent pancreatic CT scan with repeat EUS/FNA at 3 or 6 months respectively. Those with positive FNA were treated appropriately based on findings. Patients with mass/cyst < 5mm underwent repeat EUS/FNA at 3 months. Targeted follow-up is 5 years. Results: Of the 52 subjects accrued thus far, 41 were available for interim analysis. Twenty-seven (67%) subjects had a normal EUS while 14 (34%) subjects had abnormal findings. Two patients had large cysts with FNA consistent with an intraductal papillary mucinous neoplasms (IPMN). These 2 subjects ultimately underwent surgical resection. The 12 remaining subjects had at least 1 subcentimeter lesion and are being routinely screened per the outlined protocol. Conclusion: EUS screening of asymptomatic individuals who are at high risk for pancreatic cancer as defined by our inclusion criteria frequently detects abnormal lesions in the pancreas. These lesions include high risk IPMNs that warrant surgical resection. Our results validate the results of other high risk screening protocols and support the screening of individuals who are at high risk for development of pancreatic cancer.

Table 1. Eligibility Criteria

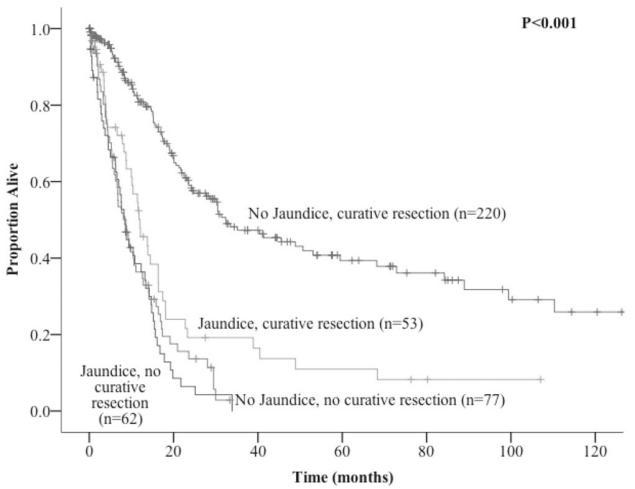
Inclusion Criteria:
2 or more relatives with pancreatic cancer (PC), one of whom is a 1st degree relative
If only 2 family members are affected, then both must have had PC and one must be a 1st degree relative
If >2 family members on the same side of the family are affected, at least 1 must be a 1st degree relative
Patients must be 40 years of age or older or 10 years younger than the youngest affected individual
All patients with Hereditary Pancreatitis
Patients with Peutz-Jeughers Syndrome (PJS) who are age 30 or greater
Patients with Familial Atypical Multiple Mole Melanoma Syndrome (FAMMM)
Patients with BRCA2 mutation and at least one 1st or 2nd degree relative with documented PC
Patients must be willing to undergo:
EUS with possible FNA
Surgical evaluation for abnormal EUS/FNA findings
Radiographic evaluation if screening findings are abnormal
Exclusion Criteria:
Medical contraindications to undergoing endoscopy or obstruction of the GI tract that precludes passage of the endoscope
Personal history of pancreatic adenocarcinoma
Previous partial or complete resection of the pancreas for PC
Prior partial or total gastrectomy with Billroth II or Roux-en-Y anastomosis
Previous CT, MRI/MRCP, or EUS of the abdomen in the past 3 years
Coexisting cancer in other organs or acquired immunodeficiency syndrome/human immunodeficiency virus (AIDS/HIV)
Life expectancy < 5 years
Pregnancy

P219

Gallbladder Cancer Presenting with Jaundice: Uniformly Fatal or Still Potentially Curable? T.B. Tran,[1]* J.A. Norton,[1] C.G. Ethun,[2] T.M. Pawlik,[3] S. Buettner,[3] K. Idrees,[4] C.A. Isom,[4] R.C. Fields,[5] B.A. Krasnick,[5] S. Weber,[6] A.I. Salem,[6] R.C. Martin,[7] C. Scoggins,[7] P. Shen,[8] H. Mogal,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] S.K. Maithel,[2] G.A. Poultsides.[1] *1. Surgery, Stanford University, Stanford, CA; 2. Emory University, Atlanta, GA; 3. John Hopkins Hospital, Baltimore, MD; 4. Vanderbilt University, Nashville, TN; 5. Washington University, St. Louis, MO; 6. University of Wisconsin, Madison, WI; 7. University of Louisville, Louisville, KY; 8. Wake Forest University, Winston-Salem, NC; 9. The Ohio State University, Columbus, OH; 10. New York University, New York, NY.*

INTRODUCTION: The prognosis of patients with gallbladder cancer (GBC) who present with jaundice has historically been considered dismal, however recent Eastern literature has demonstrated that surgical resection can be associated with long-term survival. The objective of this study was to utilize a contemporary, Western, multi-institutional dataset to examine the prognostic significance of preoperative jaundice on short- and long-term outcomes after GBC resection. METHODS: Patients with GBC managed surgically from

2000 to 2015 in 10 academic institutions participating in the U.S. Extrahepatic Biliary Malignancy Consortium were stratified based on the presence of preoperative jaundice (bilirubin > 3 mg/ml or requiring preoperative biliary drainage). Postoperative morbidity, mortality, and overall survival were compared. RESULTS: Of 449 patients with GBC evaluated for resection, 301 (67%) eventually underwent curative-intent resection. Resectability for cure was much lower in patients with preoperative jaundice (48% vs. 79%, p<0.001). Of 273 patients who underwent curative-intent resection and had available preoperative bilirubin levels, 53 (19%) had preoperative jaundice and were noted to have tumors of T3/4 stage (63% vs 42%, P=0.008), with lymph node metastasis (63% vs. 41%; p=0.014), lymphovascular invasion (68% vs 39%; p=0.003), and R1 margins (37 vs. 9%; p<0.001). Patients with jaundice more commonly required CBD (55% vs 32%, P=0.004), major liver (25% vs. 7%; p<0.001) and portal vein resection (8% vs. 0.5%; p=0.006), as well as intraoperative blood transfusion (29 % vs. 11%; p=0.002). Overall morbidity (57% vs. 38%; p=0.031) and in-hospital mortality (7.5% vs. 1.4%; p=0.029) rates were higher in patients with jaundice. Overall survival after curative-intent resection was worse in patients with jaundice (median 12 vs 33 months; Figure, p<0.001). CONCLUSIONS: Half of GBC patients presenting with jaundice are not resectable for cure and when they are, their 5-year survival is 12%. These patients should not be excluded from multidisciplinary treatment strategies that include surgery, however expectations should be clearly set and selection should be cautious.



P220

30-Day Readmission After Liver Resection for Hepatocellular Carcinoma S. Tohme,* A. Chidi, P. Varley, A. Tsung. *General Surgery, University of Pittsburgh, Pittsburgh, PA.*

Introduction: Liver resection can confer long-term benefits for patients with hepatocellular carcinoma, however this complex procedure can be associated with high postoperative morbidity and subsequent hospital readmission. Although 30-day readmission rates are increasingly used to determine hospital reimbursement, the impact of readmission on perioperative outcomes remains unclear. Methods: We conducted a retrospective cohort study using records from the National Cancer Database. We included all adult patients diagnosed with HCC between 2003 and 2011 who underwent liver resection. We performed Wilcoxon rank sum and Chi-square tests and included variables reaching p<0.20 in univariable logistic regression in a multivariable model. We also aggregated patient data at the hospital level and used Kruskal-Wallis tests to determine whether hospitals with higher readmission rates had higher 30- and 90-day mortality rates. Results: Of the 8,635 patients who underwent liver resection for HCC, 503 (5.8%) were readmitted within 30 days of discharge. Patients who were readmitted were younger, diagnosed at later stages, had higher Charlson-Deyo scores. There were also regional differences in readmisison. 535 (6.2%) of all patients died within 30 days of surgery. At the patient level, readmission was associated with a significantly lower risk of 30-day mortality (adjusted OR: 0.44, 95%CI:0.15 – 0.79). Of the 8,100 patients who were alive at 30 days, 404 (5.0%) died within 90 days of discharge. Readmission was significantly associated with increased 90-day mortality (adjusted OR: 2.19, 95%CI:1.58-3.03). Hospital-level readmission rates were not significantly associated with 30-day or 90-day mortality. Conclusion: For patients with hepatocellular carcinoma, hospital readmission after liver resection is associated with a lower risk of 30 day mortality but increased risk of 90 day mortality. These results suggest that readmission may be beneficial in the short term in managing potentially life-threatening postoperative complications; however, this advantage is reversed at 90 days. However, on the hospital level, rate of readmission is not associated with overall hospital outcomes after liver reseciton.

P221

The Effect of Postoperative Morbidity on Long-term Survival After Curative Resection for Extrahepatic Biliary Tumors: A Multi-Institution Analysis from the U.S. Extrahepatic Biliary Malignancy Consortium L. Jin,[1]* B.A. Krasnick,[1] J.T. Davidson,[1] C.G. Ethun,[2] T.M. Pawlik,[3] G.A. Poultsides,[4] T.B. Tran,[4] K. Idrees,[5] C.A. Isom,[5] S. Weber,[6] A.I. Salem,[6] W. Hawkins,[1] S. Strasberg,[1] R.C. Martin,[7] C. Scoggins,[7] P. Shen,[8] H. Mogal,[8] C.R. Schmidt,[9] E.W. Beal,[9] I. Hatzaras,[10] R. Shenoy,[10] S.K. Maithel,[2] R.C. Fields.[1] *1. Washington University in St. Louis School of Medicine, St. Louis, MO; 2. Emory University, Atlanta, GA; 3. The Johns Hopkins Hospital, Baltimore, MD; 4. Stanford University Medical Center, Stanford, CA; 5. Vanderbilt University Medical Center, Nashville, TN; 6. University of Wisconsin School of Medicine and Public Health, Madison, WI; 7. University of Louisville, Louisville, KY; 8. Wake Forest University, Winston-Salem, NC; 9. Ohio State University Comprehensive Cancer Center, Columbus, OH; 10. New York University, New York, NY.*

Introduction: Surgical resection is the cornerstone of curative therapy for extrahepatic biliary tumors (EHBTs) Postoperative complications (POCs) can negatively impact survival after oncologic resection. We evaluated the impact of POCs on survival after resection of EHBTs. Methods: We analyzed 914 patients from ten institutions of the U.S. Extrahepatic Biliary Malignancy Consortium who underwent curative resection for EHBT, including gallbladder adenocarcinoma (n=389), and hilar (n=295) and distal (n=294) cholangiocarcinoma between 1998 and 2015. POCs were graded using the modified Clavien-Dindo system. Overall survival (OS) probabilities were estimated using the method of Kaplan and Meier and analyzed using multivariate Cox regression. Results: Median follow-up was 20 months. The median age was 66 years, and the overall complication rate was 54%. Complication rates were significantly higher in patients with distal or hilar cholangiocarcinoma (62%) when compared with gallbladder cancer (41%, p<0.001). For all cancer types, patients who experienced POCs had lower five year OS when compared with those who did not (18% vs 28%, p<0.001). On multivariate Cox regression, POC remained an independent predictor for decreased OS (HR 1.5, 95% CI 1.3-1.9, p<0.001), even when controlling for age, ASA, tumor size and lymph node status (Table). Amongst patients who experienced POCs, survival did not differ by greatest Clavien grade of complication experienced (p=0.89), however patients who had 2 or more POCs did have decreased long term survival when compared with patients with only a single POC (HR 1.5, 95% CI 1.2-1.8, p=0.001). Conclusions: Postoperative complications adversely affect long-term outcomes after curative resection for extra-hepatic biliary tumors. While any complication grade did not have a significant impact on long-term survival, increasing number of POCs did significantly worsen the prognosis for OS.

Table. Multivariate Cox Regression of Factors Associated with Overall Survival

Variable	*HR*	*95% CI*	*p value*
Complication	1.5	1.3-1.9	<0.001
Age (continuous)	1.01	1.01-1.02	0.02
ASA class ≥3	1.1	0.9-1.3	0.41
R0 resection	1.5	1.2-1.8	<0.001
Tumor size ≥2 cm	1.3	0.9-1.7	0.05
Lymph node positive disease	1.7	1.4-2.2	<0.001

Abbreviations: HR, hazard ratio; CI, confidence interval.

P222

Morbidity and Mortality of Surgical Palliation in Stage IV Pancreatic Cancer B.N. Reames,* S.P. Shubeck, S.L. Wong, H. Nathan. *Department of Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: Surgical vs. endoscopic palliation of patients with metastatic pancreatic cancer (MPanCa) is controversial. In this study, we sought to examine the utilization and outcomes of palliative procedures in MPanCa patients. Methods: This retrospective cohort study used SEER-Medicare data to identify patients ≥65 years diagnosed with MPanCa during 2005-2009 who underwent a non-therapeutic or palliative procedure. Procedure type [non-therapeutic exploration (ExLap) vs. palliative (PAL)] and indications for operation were identified using ICD-9 codes. Serious complications were defined as complications associated with prolonged length of stay (LOS >75th percentile). Multivariable logistic and linear regressions were used to adjust for patient characteristics, comorbidities, and procedure year, in order to analyze outcomes (adjusted odds ratios, AOR) and costs, respectively. Results: Of 6,266 MPanCa patients who underwent surgery, 866 (14%) underwent PAL. Gastrojejunostomy was the most common PAL (510, 59%), followed by double bypass (217, 25%), feeding enterostomy (74, 9%) and biliary bypass (65, 8%). Almost half (385, 45%) of PAL patients did not have a diagnosis of intestinal or biliary obstruction. Mortality within 30 days of discharge among PAL patients was 20%, and only 81 patients (9%) survived 1 year. Compared to patients undergoing ExLap, PAL patients were much more likely to experience a serious complication (19% vs. 8%, AOR 2.9), had longer lengths of stay (median LOS 14 days vs. 7 days), and were less likely to receive chemotherapy within 30 days of surgery (14% vs. 33%, AOR 0.32) (all p<0.001). Adjusted 30-day episode payments were $15861 higher for patients undergoing PAL compared to ExLap (p<0.001). Conclusions: Patients with MPanCa who undergo PAL surgery experience significant morbidity, and nearly 20% die within 30 days of discharge. Non-surgical palliation should be considered for MPanCa in order to expedite receipt of chemotherapy, minimize hospital LOS, and reduce resource utilization.

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Conditional Probability of Survival in Gallbladder Carcinoma: An Apt Prognostic Tool for Long-term Survivors R. Rajeev,* N.G. Berger, A. Hammad, J. Miura, F. Johnston, T. Gamblin, K. Turaga. *Surgical Oncology, Medical College of Wisconsin, Milwaukee, WI.*

Background: Gallbladder carcinoma (GBC) often presents in an advanced stage and despite radical resection and nodal harvest, prognosis remains poor. Conventional survival statistics do not account for time elapsed from diagnosis and may not carry relevant prognostic information for long term survivors. This study sought to estimate the conditional probability of survival (CS) in patients of GBC. Methods: Patients with GBC were identified from the Surveillance, Epidemiology and End Results (SEER) database (1988-2012). Overall probability of survival (OS) was estimated using Kaplan-Meier method. Cumulative incidence method was employed to calculate CS. Results: Of 15,046 GBC patients identified, Stage IV disease was the most common presentation (n=5625). Surgical intervention was reported in 9,720(65%) patients with cholecystectomies (n=8254) outnumbering radical resections (n=1116). 3-year OS for all stages was 18% and conditional probability of surviving additional 3 years (CS_3) at 1, 2 and 3 years from diagnosis was 42%, 57% and 66% respectively. Stage III and IV disease had 3-year OS rates of 19% and 3% respectively while CS_3 increased progressively with each year survived(33% and 17% at 1 year, 51% and 34% at 2 years, 60% and 56% at 3 years). Discussion: Conditional probability of survival is favorable in patients surviving one year from diagnosis and shows an increasing trend with time. Improvements in survival are more substantial in patients with adverse initial prognosis. Conditional survival provides valuable information on prognosis to patients after curative surgery and can be the basis of follow-up guidelines.

3-year overall survival and conditional survival rates of gallbladder cancer, stratified by patient, tumor and therapy characteristics

	3-year OS (%)	3-year CS at 1 year (%)	3-year CS at 2 years (%)	3-year CS at 3 years (%)
Total population	18	42	57	66
Prognostic groups				
Stage I	52	63	71	71
Stage II	45	55	61	69
Stage III	19	33	51	60
Stage IV	3	17	34	56
Surgery receipt				
No surgery	3	25	48	59
Cholecystectomy	26	45	58	67
Radical surgery	22	40	60	68

CS - conditional survival. OS - overall survival

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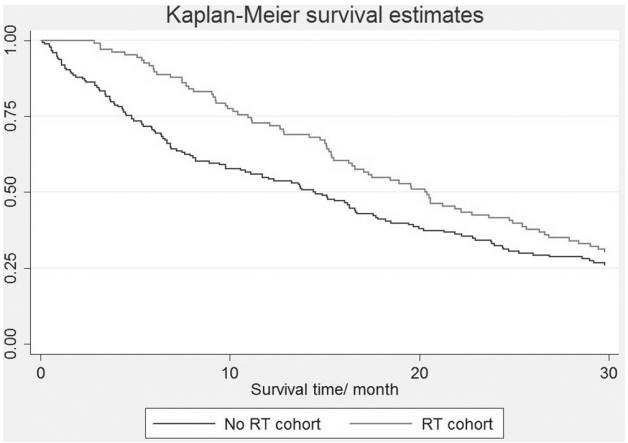
Radiotherapy for Intrahepatic Cholangiocarcinoma: An Analysis of the National Cancer Data Base A.Y. Hammad, J. Miura, N.G. Berger,* F. Johnston, K. Christians, S. Tsai, K. Turaga, T. Gamblin. *Surgery, Medical College of Wisconsin, Milwaukee, WI.*

Background: The role of radiotherapy (RT) for surgically resected intrahepatic cholangiocarcinoma (ICC) remains poorly defined. Radiotherapy is often considered when a positive resection margin exists. The present study sought to examine the impact of radiotherapy following liver resection. Methods: Patients with early stage ICC, who underwent surgical resection, were identified from the National Cancer Database (1998-2011). Patients were stratified by resection margin status and receipt of RT. Survival was analyzed by Kaplan-Meier method and a multivariate regression model was used to identify predictors of survival. Results: A total of 2,182 patients were identified. R0 status was obtained in 1,624 patients (74.4%), while RT was delivered to 405 patients (R0=209, R1/R2=196). In the R1/R2 group, 196 patients received RT vs. 362 R1/R2 patients that did not receive RT. The median overall survival for R0 patients was 32m compared to 16.5m in patients with R1/R2 margins (p<0.001). RT appeared to trend toward improving survival for R1/R2 patients, though this was not significant (20.4m vs. 14.5m, p=0.191). In a multivariate model accounting for age, sex, comorbidities, disease stage and resection margins, RT was not a predictor of survival. Negative predictors of survival included age>65years (Hazards Ratio [HR]: 1.20 (95%CI: 1.04-1.39), p=0.013), and positive resection margins (HR: 1.95 (95%CI: 1.65-2.30), p<0.001). Female sex was the only positive predictor of survival identified (HR: 0.76 (95%CI: 0.65 -0.88), p<0.001). Conclusion: Surgical resection with negative margins provides the best outcome for patients with ICC. Radiotherapy does not appear to significantly impact survival in patients with positive resection margins.



Kaplan Meier curve examining radiotherapy in patients with positive resection margins

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Regression in Thin Melanoma is Associated with Nodal Recurrence After a Negative Sentinel Node Biopsy J.C. Rubinstein,* G. Han, L. Jackson, K. Bulloch, S. Ariyan, D. Narayan, B. Gould Rothberg, D. Han. *General Surgery, Yale University, Guilford, CT.*

Introduction Prognostic markers for nodal metastasis in patients with thin melanoma are debated. We present a single institution study looking at factors predictive of nodal disease in thin melanoma patients. Methods Retrospective review of a single institution database from 1997 to 2012 identified 252 patients with thin melanoma (≤1 mm) who underwent a sentinel node biopsy (SNB). Node-positive patients included both positive SNB patients and negative SNB patients who developed a nodal recurrence in the dissected nodal basin (false-negative SNB). Clinicopathologic characteristics were correlated with nodal status and outcome based on Fisher's exact test and Cox's proportional hazard regression, respectively. Results Median age was 55.5 years and 52% of patients were female. Median follow-up time was 45.5 months. A total of 12/252 patients (4.8%) were node-positive including 6 positive SNB (2.4%) and 6 false-negative SNB (2.4%) patients. No clinicopathologic factors were significantly correlated with nodal disease, but male gender (p=0.06) and head/neck location (p=0.07) trended toward significance. For the 6 false-negative SNB patients, median time to nodal recurrence was 37.5 months. Overall, regression was seen in 16% of cases. None of the 6 positive SNB cases had regression, but regression was seen in 60% of false-negative SNB cases. Both age (OR: 1.09, 95% CI: 1.01– 1.17; p=0.02) and regression (OR: 8.33, 95% CI: 1.34–52.63; p=0.02) were significantly associated with nodal recurrence after a negative SNB on univariable analysis. Conclusion Nodal disease in thin melanoma patients was seen in 4.8% of cases with half detected by SNB. Although regression was not correlated with nodal metastasis, it did predict for a false-negative SNB. Patients with thin melanoma and regression may need more intensive surveillance after a negative SNB. Further study is needed to determine if the same immune mechanisms that result in regression in the primary tumor also lead to regression in lymph nodes, which may decrease detection of melanoma metastases during SNB.

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Breslow Thickness Measurements of Melanomas Around AJCC Staging Cut-off Points: Imprecision and Terminal Digit Bias have Implications for Staging and Patient Management L. Ge,[1]* R. Vilain,[1] S. Lo,[1] K. Aivazian,[2] R. Scolyer,[1] J. Thompson.[1] *1. Melanoma Institute Australia, Sydney, NSW, Australia; 2. Royal Prince Alfred Hospital, Sydney, NSW, Australia.*

Introduction: Breslow thickness is the most important prognostic factor in clinically localized primary cutaneous melanomas and its accuracy has important implications for staging and management. A review of our institution's database and a statewide melanoma database found an unexpectedly large number of melanomas reported as exactly 1.00mm thick. Our study sought to determine the possible causes for this biologically implausible finding. Methods: Using our institution's database, 200 cases of invasive cutaneous melanoma with a recorded Breslow thickness measurement between 0.9 and 1.1mm were selected. 125 of these were suitable for review. Their thickness was re-measured and recorded to 2 decimal places by two independent pathologists. Results: Concordance of measurements between the two pathologists was high (intraclass correlation coefficient 0.816, 95%CI 0.733-0.873. The original measurements showed clustering at 0.9mm, 1.0mm and 1.1mm, whereas the review measurements did not. The original measurements staged 84 cases (72%) as T1 and 33 cases (28%) as T2. The reviewed measurements staged 58 cases (50%) as T1 and 59 cases (50%) as T2. This staging difference was statistically significant (p<0.001). Conclusions: Our study demonstrated imprecision in Breslow thickness measurements and its significant impact on staging. Two potential sources of error are the lack of standardized measurement guidelines and the phenomenon of terminal digit bias, which has not previously been identified in this field. Educating pathologists about this phenomenon and standardizing guidelines may improve the precision and accuracy around critical staging cut-off points.

Original and Reviewed Staging

		Review staging (Number of cases)		
		T1	T2	Total
Original staging (Number of cases)	T1 (% withing original staging)	53 (63%)	31 (37%)	84 (100%)
	T2 (% within original staging)	5 (15%)	28 (85%)	33 (100%)
	Total (% within original staging)	58 (50%)	59 (50%)	117 (100%)

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Molecular Profiling and Clinical Outcomes in Malignant Melanoma: Experience at a NCI-Designated Cancer Center F.S. Zih,[1]* N. Kulkarni,[1] D.A. Escalante,[2] C. Meade,[2] N. Osevala,[2] M. Zibelman,[1] S. Movva,[1] K.S. Gustafson,[1] H. Wu,[1] S. Reddy,[1] M. Lango,[1] A.J. Olszanski,[1] J. Farma.[1] *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Temple University Hospital, Philadelphia, PA.*

INTRODUCTION: The use of molecular profiling has become increasingly important in providing valuable prognostic information on primary cancers beyond conventional staging modalities. Our institution has been using next generation sequencing (NGS) to examine mutations in 50 cancer-related genes in various tumors. Here we examine the use of molecular profiling of malignant melanoma (MM) in predicting clinical outcomes. METHODS: Patients with primary or recurrent MM of all stages were included in the study. Using NGS, we analyzed tissue samples for mutations in targeted regions of 50 cancer-related genes. Clinical and pathologic data, overall (OS) and disease-free (DFS) survival were collected. RESULTS: We collected specimens from 93 patients with MM. Median age at diagnosis was 67 (range 24-90) and 66% were male (n=61). Median follow-up was 12.4 months. 44 patients had recurrent melanoma, 22 (24%) had distant metastases and 13 (14%) had in-transit disease. At last follow-up, 43 patients had no evidence of disease, 29 were alive with disease, 16 died of disease and 2 died of other causes. In total 157 mutations were identified, affecting 34 unique genes. No mutations were found in 12.9% of patients (n=12), 44% of patients (n=41) had only one mutation and 43% (n=40) had 2 or more mutations. 32 (34%) patients had mutations in the RAS family; 27 (29%) had BRAF mutations. The most frequently identified mutations included NRAS (n=28), TP53 (n=23), BRAF V600 (n=22), and CDKN2A (n=14). Fifty-one patients had specimens from their primary tumor available for analysis. Of the 51 patients, 41 had adequate follow-up data and the median DFS was 18 months. In this subgroup 12 patients (29%) had disease recurrence. Patients with 2 or more mutations had a significantly worse DFS (p=0.026). (Figure 1) CONCLUSIONS: Using our NGS platform, patients with primary MM who have 2 or more mutations may have a higher risk of tumor recurrence. We will further examine this subgroup to correlate molecular pathways with patterns of recurrence.

Figure 1. Disease-free Survival in patients with primary malignant melanoma analyzed by next generation sequencing (n=41)

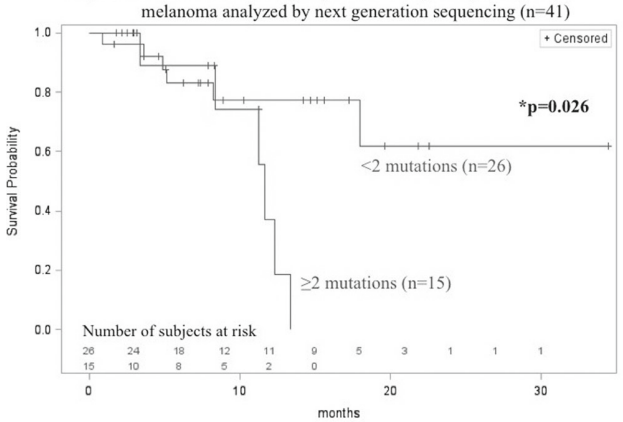

Figure 1. Disease-free Survival in patients with primary malignant melanoma analyzed by next generation sequencing

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Prognostic Significance of Sentinel Node Status in Patients with Thick Melanoma D. Bello,* G. Han, L. Jackson, K. Bulloch, S. Ariyan, D. Narayan, B. Gould Rothberg, D. Han. *Surgery, Yale-New Haven Hospital, New Haven, CT.*

Introduction: Sentinel lymph node biopsy (SLNB) is recommended for patients with intermediate thickness melanoma, but use of SLNB in patients with thick melanoma is debated. We present a single institution study looking at factors predictive of SLN metastasis and outcome in thick melanoma patients. Methods: Retrospective review of a single institution database from 1997 to 2012 identified 147 patients with thick primary cutaneous melanoma (≥4mm) who had a SLNB. Clinicopathologic characteristics were correlated with nodal status and outcome. Results: Median age was 67 years and 61.9% of patients were male. Median tumor thickness was 5.5 mm and a positive SLN was seen in 54/147 (36.7%) cases. Univariable analysis showed that tumor thickness, mitotic rate and tumor location were significantly correlated with SLN metastasis ($p<0.05$). On multivariable analysis, only tumor thickness significantly predicted a positive SLN (OR: 1.14, 95% CI: 1.02-1.28; $p=0.02$). Completion nodal dissection (CND) was performed in 48/54 (88.9%) positive SLN patients with additional nodal disease found in 13/48 (27.1%) CND cases. Median follow-up was 34.6 months. Overall survival (OS) and melanoma-specific survival (MSS) were significantly worse for positive versus negative SLN patients; 5-year OS was 34.3% and 56.9% for positive and negative SLN patients ($p<0.01$), respectively, while 5-year MSS was 36.3% and 73.4% for positive and negative SLN patients ($p<0.01$), respectively. Multivariable analysis showed that age (HR: 1.04, 95% CI: 1.01-1.07; $p=0.02$) and SLN status (HR: 2.24, 95% CI: 1.03-4.88; $p=0.04$) significantly predicted OS while only SLN status (HR: 3.85, 95% CI: 2.13-6.97; $p<0.01$) significantly predicted MSS. Conclusions: Tumor thickness predicts SLN status in thick melanomas. Furthermore, SLN status is prognostic for OS and MSS in thick melanoma patients with positive SLN patients having significantly worse OS and MSS compared with negative SLN patients. These findings show that SLNB should be recommended for thick melanoma patients, particularly since detection of SLN metastasis can identify patients for potential systemic therapy and treatment of nodal disease at a microscopic stage.

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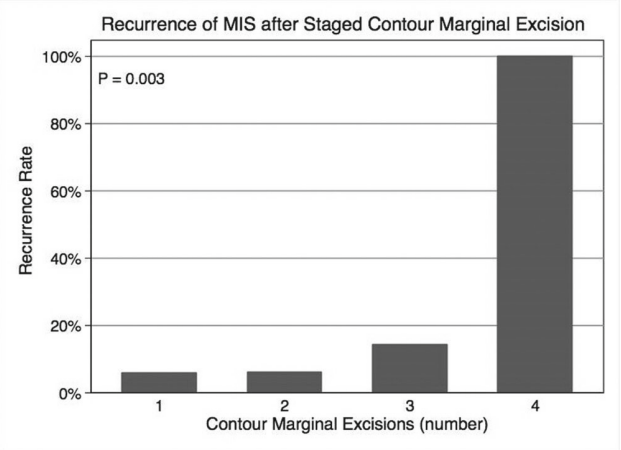
Treatment of Melanoma In Situ with Staged Contoured Marginal Excisions E.S. Glazer,* C.F. Porubsky, J.D. Francis, J. Ibanez, N. Castner, A.A. Sarnaik, V.K. Sondak, J.S. Zager, W. Cruse. *Surgical Oncology, Moffitt Cancer Center, Tampa, FL.*

Introduction: Melanoma-in-situ (MIS) on the head & neck can pose a treatment dilemma due to microscopically positive margins after excision. Initial contoured excisions of the margin around the tumor can provide negative margins prior to the central tumor excision & reconstruction. The excised margins consist of 2 mm strips of normal appearing skin around the tumor. We hypothesized that contoured marginal excision (CME) followed by central tumor resection is an effective method to treat MIS. Methods: Clinicopathological, surgical, & recurrence data were abstracted for all patients who underwent staged CME followed by central tumor resection for MIS on the head or neck from 2006-15. Patients with an invasive melanoma component ≥ 0.75 mm at initial biopsy were excluded. Statistical analyses included χ^2 and regression. Results: 166 patients were identified. 55% were male; the average age was 69 years (range 30 to 92 years). 17% of patients had an invasive melanoma component at initial biopsy (< 0.75 mm depth). 3% of patients without an invasive component on the initial biopsy had invasive melanoma in the central tumor resection specimen. The median number of CMEs was 1 (range 1 to 4). The median clinical margin was 5 mm (range 1 to 20 mm). Final margins were negative in 95% of patients; 20% of patients required ≥ 2 CMEs to achieve negative margins. 9 patients with only MIS & negative margins had a recurrence at a median follow up of 26 months (range 3 to 31 months). For these patients, the recurrence rate was associated with the number of CMEs ($P = 0.003$, figure). On multivariate logistic regression analysis, recurrence was associated with the number of CMEs ($P = 0.03$) and tumor diameter ($P = 0.03$). Reconstruction was completed with flaps (36%), skin grafts (59%), wound matrix (2%), & primary closure (3%). Conclusions: Staged CME followed by central tumor resection is an effective method to treat MIS. Without it, 20% of patients would have had reconstruction on a positive margin. Even with careful preoperative sampling, some patients felt to have MIS will be found to have invasive melanoma on final excision. Requiring ≥ 2 CMEs and large tumor diameter are markers for aggressive tumor biology.



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Videoscopic Ilioinguinal Lymphadenectomy for Lymph Node Metastases from Melanoma A. Sommariva,* S. Pasquali, C. Cona, L. Saadeh, L.G. Campana, M. Meroni, C.R. Rossi. *Surgical Oncology, Veneto Institute of Oncology, IOV-IRCCS, Padova, Italy.*

Background: Ilioinguinal lymph node (LN) dissection for melanoma patients is associated with a high rate of wound related morbidity, including infection, dehiscence/necrosis and seroma/lymphocele. Videoscopic groin lymphadenectomy has recently been proposed for treating LN metastases from melanoma with the main goal of reducing post-operative wound-related morbidity through the virtual elimination of surgical incision. This was a prospective single centre trial aimed at investigating feasibility, safety and postoperative outomes of videoscopic ilioinguinal lymphadenectomy (VIIL) in patients with inguinal melanoma LN metastases. Methods: The trial was conducted under an approved protocol reviewed by the local Ethics Committee. Patients without distant metastasis and either positive SLNB or clinically positive inguinal LNs were prospectively enrolled. The inguinal step was performed via three trocars positioned at the apex of the femoral triangle. After subcutaneous inflation, a formal inguinal LN dissection was performed. For the iliac step, after insertion of three trocars in the pro-peritoneal space along the midline and creation of pneumo-pelvis, the external iliac and obturator LNs were excised. Clinicopathologic and postoperative outcome data were recorded. Results: Between September 2011 and June 2014, 24 videoscopic ilioinguinal lymphadenectomies were performed. Median duration of surgery was 270 minutes (IQR 245-300). Conversion to open dissection occurred in 4 patients (16.6%). Conversion did not occurr during the final 10 procedures. Blood loss was minimal and blood transfusions were never required. The median number of excised LNs was 21 (IQR, 15-25). After a median follow-up of 18 months, regional LN recurrence was observed in two patients (8.3%). No significant impairment in global QoL was observed. Conclusions: This prospective trial demonstrated the technical feasibility, safety profile and favourable post-operative outcomes of VIIL for melanoma patients with groin LN metastases. Before considering VIIL in clinical practice, this technique should be compared with open surgery within prospective randomized trials.

Post-operative complications (Clavien Dindo Classification)	Grade I N (%)	Grade II N (%)	Grade III A-B N (%)	Total N (%)
Infection	3 (12)	0	1 (4)	4 (17)
Seroma	2 (8)	5 (21)	0	7 (29)
Wound dehiscence	0	0	0	0
Post-operative bleeding	2 (8)	0	0	2 (8)

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Lymph Node Ratio is Less Prognostic in Melanoma When Minimum Node Retrieval Thresholds are Not Met M.A. Healy,* E.L. Reynolds, M. Banerjee, S.L. Wong. *Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: Lymph node ratio (LNR) has been proposed as a prognostic indicator in melanoma, to take number of nodes examined into account and to mitigate the effect of low lymph node yields. However, it is unclear if

LNR offers superior prognostication over consideration of number of positive nodes and number of nodes examined. Moreover, it is unclear if the prognostic value of LNR changes if a certain threshold number of nodes are examined. We sought to evaluate whether the prognostic value of LNR exceeds that of positive nodes and nodes examined, and whether the prognostic value of LNR changes if thresholds of nodes examined are met for axillary lymph node dissection (ALND) and inguinal lymph node dissection (ILND). Methods: Using the National Cancer Data Base Participant User File, we identified 74,692 incident cases of melanoma with lymph node dissection from 2000 to 2012 at 1,372 hospitals. Using Cox proportional hazards regression analysis, we compared prognostic models using LNR vs. total positive nodes and total nodes examined. Our main outcome measures were hazard ratios (HR) of mortality and Harrell's C (C), which indicates predictive ability. We then repeated this analysis, stratifying by total nodes examined: greater than vs. less than 10 nodes for ALND and greater than vs. less than 5 nodes for ILND. Results: LNR was associated with a HR of 1.33 (95% CI 1.32 – 1.34), with C 0.628 (95% CI 0.625 – 0.631). A multivariate model using total positive nodes and total nodes examined was not significantly different, with C 0.625 (95% CI 0.621 – 0.630). In ALND, LNR was associated with C 0.626 (95% CI 0.610 – 0.643) in cases when a 10 node threshold was met vs. 0.554 (95% CI 0.551 – 0.558) when less than 10 nodes were examined. Likewise in ILND, LNR was associated with C 0.679 (95% CI 0.664 – 0.694) when 5 or more lymph nodes were examined vs. C 0.601 (95% CI 0.595 – 0.606) when less than 5 nodes were examined. Conclusion: In melanoma, LNR provides no prognostic superiority versus using measures of total positive nodes and total nodes examined. Moreover, the prognostic value of LNR diminishes when minimum node retrieval thresholds are not met in ALND and ILND.

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Tissue Harvesting for Adoptive T-Cell Therapy with "Young" Tumor Infiltrating Lymphocytes for the Treatment of Metastatic Melanoma D. Zippel,* M. Besser, G. Markel, R. Ben-Avi, R. Shapira-Frommer, J. Schachter. *Chaim Sheba Medical Center, Ramat Gan, Israel.*

Adoptive cell transfer (ACT) using autologous tumor-infiltrating lymphocytes (TIL) has been shown to yield objective responses in 30% of metastatic melanoma patients. To date, 155 patients have been enrolled in the ACT "young" TIL program at the Ella Lemelbaum Institute for melanoma, in the Chaim Sheba Medical Center. This study analyzes the tissue harvesting data and surgical aspects of ACT. Methods:The data of 155 patients who underwent tissue harvesting, for the purpose of undergoing adoptive cell therapy with IL-2 for metastatic melanoma was analyzed. Results:155 patients had 200 tumor specimens surgically harvested to procure TIL for ACT. OF these, 89 patients were able to undergo the treatment protocol with infusion of TIL with IL-2 after lymph-depleting chemotherapy. 16 patients are still ongoing, with their TIL cultures frozen for future use. 50 patients who underwent surgery did not complete the treatment plan. Of these, 35 patients withdrew because of clinical deterioration, including two deaths from chemotherapy related toxicity, while in 15 patients, TIL cultures could not be generated. The most common source of tumor tissue harvested were subcutaneous nodules, accounting for 40% of tissue excisions. 23% were lymph node excisions and 20% were lung nodule excisions. The remaining tissue harvests were from visceral or CNS metastases. Serious surgical adverse events included abdominal dehiscence requiring relaparotomy, pancreatic leak requiring drainage, and a pleural effusion requiring drainage. There was no surgery related mortality. Objective clinical responses were recorded in 33% of treated patients. Discussion:Tissue harvesting for ACT can be safely and successfully accomplished from a variety of tissue sources, encompassing a wide range of surgical procedures. It is critically important to minimize surgical morbidity to facilitate treatment with adoptive cell therapy, which necessitates adequate performance status, in order to undergo chemotherapy and TIL/IL2 infusion. TIL cultures were not generated in 10% of patients accrued. ACT remains an important vehicle for immunotherapy to metastatic melanoma patients.

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Identifying the Low-risk Subgroups Among Intermediate Thickness Melanoma Patients J.M. Chang,[1]* H.E. Kosiorek,[1] A.C. Dueck,[1] S.P. Leong,[2] J.T. Vetto,[3] R.L. White,[4] E. Avisar,[7] J.S. Zager,[5] C. Garberoglio,[6] B.A. Pockaj.[1] *1. Mayo Clinic, Phoenix, AZ; 2. Center for Melanoma Research and Treatment, California Pacific Medical Center, San Francisco, CA; 3. Oregon Health & Science University, Portland, OR; 4. Levine Cancer Institute, Carolinas Medical Center, Charlotte, NC; 5. Moffitt Cancer Center, Tampa, FL; 6. Loma Linda University School of Medicine, Loma Linda, CA; 7. University of Miami Miller School of Medicine, Miami, FL.*

Introduction: Guidelines for melanoma recommend sentinel lymph node biopsy (SLNB) in all patients with melanomas ≧1mm thickness. Recent single institution studies have found tumors <1.5mm to be a low risk group for positive SLNB. We tested that finding using a multicenter database. Methods: We performed a retrospective review of the Sentinel Lymph Node Working Group multicenter database. Patients with intermediate thickness melanoma (1.01–4mm) who underwent SLNB were identified. Predictors were compared between patients with positive vs. negative SLNB. Multivariate analysis included forward logistic regression to determine potential predictors of SLNB positivity. Results: 3460 patients were analyzed, 584 (17%) had a positive SLNB. Median age was 57.8 years and 59% of patients were men. Univariate factors associated with a positive SLNB included age <60 ($p<0.001$), tumor on the trunk/lower extremity ($p<0.001$), Breslow depth ≥2mm ($p<0.001$), Clark level IV/V ($p=0.003$), ulceration ($p<0.001$), lymphovascular invasion ($p<0.001$), mitotic rate ≥1/mm^2 ($p=0.01$), and microsatellitosis ($p<0.001$). Multivariate analysis revealed age, location, and Breslow depth as significant predictors of positive SLNB. Rate of SLNB positivity decreased with age ≥60, but did not reach significance when comparing age groups 60-69 vs 70-79 vs 80+ years old (13.9% vs 13.9% vs 11.5%, $p=0.60$). Head/neck/upper extremity melanoma had a similar risk. The cutoff for identifying a lower risk group by Breslow thickness varied from 1.5-2 mm by age and location (Table); patients with head/neck/upper extremity melanoma with a thickness <2mm melanoma had <10% of SLN positivity regardless of age. Patients ≥60 with lower extremity or trunk melanoma and <2 mm melanoma had ~10% risk of SLN positivity. All other subgroups had SLNB positivity rates >10%. Conclusions: Significant heterogeneity of risk of SLNB positivity exists among patients with intermediate thickness melanoma. Low risk subgroups can be found among patients ≥60 years of age with a Breslow thickness of 1.01-1.99mm if located on the head/neck/upper extremity. This data can be used to help guide studies and clinical trials regarding high and low risk melanoma subgroups.

Table. Rates of positive sentinel lymph node biopsies based on age, Breslow thickness, and tumor location.

Breslow Thickness (mm)	Head/Neck or Upper Extremity (%positive SLNB*)		Lower Extremity or Trunk (%positive SLNB*)		Total
	Age <60	Age ≥60	Age <60	Age ≥60	
1.01-1.49	22/241 (9%)	17/232 (7%)	60/465 (13%)	26/234 (11%)	125/1172 (11%)
1.50-1.99	9/126 (7%)	14/155 (9%)	73/301 (24%)	18/174 (10%)	114/756 (15%)
2.0-2.99	28/160 (18%)	31/223 (14%)	91/313 (29%)	55/252 (22%)	205/948 (22%)
3.0-4.0	21/89 (24%)	22/130 (17%)	59/153 (39%)	30/139 (22%)	132/511 (26%)
Total	80/616 (13%)	84/740 (11%)	283/1232 (23%)	129/799 (16%)	576/3387 (17%)

*SLNB - Sentinel Lymph Node Biopsy. Rates of positive sentinel lymph node biopsies based on age, Breslow thickness, and tumor location (N=3,387 with known age, Breslow thickness, and tumor location).

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Preliminary Feasibility Data from the Melanoma Margins Trial (MelMarT) Pilot Study: Australian and New Zealand Melanoma Trials Group (ANZMTG) Study 03.12 M. Moncrieff,[1]* R. Saw,[2] A. Spillane,[2] J. Thompson,[2] E. Paton,[3] D. Gyorki,[4] R. Pritchard-Jones,[5] E. Wilson,[6] P. Matteucci,[7] N. Crampton,[8] D. Oudit,[9] M. Henderson.[4] *1. Plastic & Reconstructive Surgery, Norfolk & Norwich University Hospital, Norwich, Norfolk, United Kingdom; 2. Melanoma Institute of Australia, Sydney, NSW, Australia; 3. Australia & New Zealand Melanoma Trials Group (ANZMTG), Sydney, NSW, Australia; 4. Peter MacCallum Cancer Centre, Melbourne, VIC, Australia; 5. Mersey Centre for Plastic Surgery & Burns, Liverpool, United Kingdom; 6. North Bristol NHS Trust, Bristol, United Kingdom; 7. Hull & East Yorkshire NHS Trust, Hull, East Yorkshire, United Kingdom; 8. Gold Coast Melanoma Clinic, Coolangatta, QLD, Australia; 9. Christie Hospital NHS Trust, Manchester, United Kingdom.*

Introduction: In primary cutaneous melanoma, a secondary wider excision around the original biopsy scar is recommended to reduce the risk of local recurrence and improve patient outcome. Currently, there is no uniform guidance on wide excision margins for tumours >1mm Breslow thickness (AJCC stage pT2-4). MelMarT is a phase III, non-inferiority, randomised control trial, investigating the safety and effectiveness of 1cm versus 2cm wider excision margins for pT2a-4b in patients undergoing staging with sentinel lymph node biopsy. The pilot phase, investigating the feasibility of the full trial, includes 11 sites in the UK (8) and Australia (3). Methods: Data was extracted from the centrally-administered ANZMTG database based in Sydney, Australia from January to August 2015. Results: 75 patients were recruited to the study in the preliminary period from a screened population of 322 (23.3%) and an eligible cohort of 157 patients (47.8%). In the UK, 143 patients were screened of whom 72 (50%) were eligible: 26 (18%) declined enrolment and 46 (32%) were recruited (64% of all eligible patients). In Australia, 179 patients were screened of whom 85 (47%) were eligible: 27 (15%) declined enrolment, 29 (16%) were unable to be recruited for (now-resolved) technical reasons and 29 (16%) were recruited (34% of all eligible patients). Overall, 165 (52.2%) patients were ineligible to participate and the reasons are outlined in Table 1. The joint-highest reason for ineligibility was incomplete excision of the primary melanoma at diagnostic biopsy, of which the overwhelming majority were Australian cases. Conclusion: The preliminary feasibility data from MelMarT are very encouraging. Almost 2 in 3 eligible UK subjects and almost 1 in 2 subjects overall have been recruited indicating a ready willingness of patients to participate. The proportions of exclusion criteria reflect variations in practice; however the data indicate that the protocol is broadly applicable across international healthcare services. Future data, including those from additional sites in Europe & North America, will provide further feasibility information.

Table 1

Exclusion Criterion	N	%
Incomplete Excision	34	20.7
Life Expectancy <10 yrs	34	20.7
Microsatellites	21	12.7
Desmoplastic/Neurotropic Melanoma	18	11.0
2cm margin not possible	14	8.5
Previously Diagnosed Melanoma	10	6.1
Immunocompromised	8	4.9
Previous Cancer	6	3.7
Melanocytic Lesion of Uncertain Malignant Potential	5	3.0
Subungual Melanoma	4	2.4
[Other]	11	6.7
Total	165	100

P236

BRAF Inhibitors for Neoadjuvant Treatment in Irresectable or Marginally Resectable Stage III Melanoma D. Zippel,[1]* E. Ben-Ami,[1] R. Shapira-Frommer,[1] G. Markel,[1] A. Nissan,[1] H. Gutman,[2] J. Schachter,[1] S. Schneebaum.[3] *1. Chaim Sheba Medical Center, Ramat Gan, Israel; 2. Rabin Medical Center, Beilinson Campus, Petach Tikva, Israel; 3. Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.*

Stage III melanoma is potentially curable by surgery alone. Some patients present with bulky nodal masses, making surgery difficult and morbid. 50% of melanoma patients harbor a V600E mutation in the BRAF protooncogene, allowing possible treatment with a BRAF inhibitor. BRAF inhibitors are capable of achieving a rapid and considerable response in bulky tumors, and thus facilitate complete and safe resection in patients otherwise marginally resectable or irresectable. Based on this, we preoperatively treated patients with BRAF inhibitors with the goal of achieving successful resection in this clinical setting. V600E+ patients with stage III melanoma who were deemed marginally resectable or irresectable by surgeons specialized in melanoma surgery, were treated with either Vemurafenib or Dabrafanib, for a period of 6-8 weeks prior to planned surgery. The main outcome was successfully achieving complete resection of all bulky nodal tissue with minimum morbidity. Secondary outcome was pathological response. 11 patients fitting the criteria were treated preoperatively. 7 patients received Vemurafenib . 4 patients received Dabrafanib and 2 patients received concurrent. All patients were reassessed for surgery after 6 weeks. 10/11 patients exhibited a marked clinical response prior to surgery. Successful resection was accomplished in all patients. 4 patients had a complete pathological response. The remaining 7 patients, had residual tumor,albeit in conjunction with extensive necrosis and fibrosis. Of these, 2 had only micrometastasis in their nodes. Although common practice in locally advanced breast and rectal cancer, using neoadjuvant treatment with the aim of facilitating surgery is not well defined in melanoma. A main goal of neoadjuvant treatment is to allow surgical resection in situations where surgery would otherwise be unsafe or unduly morbid. As BRAF inhibition often results in a rapid and considerable shrinkage of tumor mass, targeted therapy in BRAF mutated patients may serve as the ideal neoadjuvant agent to permit safe and complete surgical resection. This data may offer promise of a new potential concept in surgical therapy of locally advanced melanoma.

P237

Isolated Limb Perfusion in Merkel Cell Carcinoma Offers High Complete Response and Durable Local-Regional Control: Systematic Review and Institutional Experience C.A. Thiels,[1]* A.B. Gonzalez Juarrero,[1] R.J. Gray,[2] J.W. Jakub.[1] *1. Surgery, Mayo Clinic, Rochester, MN; 2. Mayo Clinic, Phoenix, AZ.*

Introduction: Merkel cell carcinoma (MCC) has a propensity for local recurrence and regional lymph node metastases. Hyperthermic isolated limb perfusion (HILP) has an established role in the management of melanoma with recurrent intralymphatic contamination, but the role for MCC is less well defined. Our aim was to review our experience with HILP for MCC in the context of a systematic review of the literature. Methods: Retrospective review of our intuitional experience with HILP for MCC was conducted (2009-2015). Literature search was performed by an expert librarian on MEDLINE, EMBASE, Cochrane Database of Systematic Reviews, Web of Science and Scopus through April 2015 and 10 studies met inclusion criteria. Isolated limb infusion cases were excluded. Results: 4 patients (pts) underwent HILP for MCC over the study period. There were no major complications and all were discharged on POD #2. Complete response was achieved in all 4 pts. Unfortunately, early metastatic recurrence developed in 2 pts, 1 of whom died at 8 months (complicated by leukemia) with the other 1 is alive at 7 months post-op. The remaining 2 pts were NED at death (36 months) or last follow up (36 months). On systematic review we identified 12 pts that underwent HILP for MCC for a total of 16 cases. 13 pts had a complete response while 1 pt had no response and in 2 pts response rate was not reported. 3 pts developed local-regional recurrence and 6 distant metastases following regional perfusion, all within 6 months. Overall median follow-up was 14.5 months and was 27 months in the 8 pts without recurrence (Table). Conclusion: Our institutional experience and systemic review suggest HILP for MCC is safe and has a high complete response rate. HILP is an acceptable therapeutic modality for obtaining durable loco-regional control in this population. Unfortunately, early distant metastatic disease remains a significant cause of mortality. Patients with in-transit disease from MCC and no evidence of distant disease should be discussed in a multidisciplinary fashion in an environment where regional perfusion can be strongly considered.

Outcome of patients who underwent Hyperthermic isolated limb perfusion (HILP) for Merkel Cell Carcinoma.

Study	Limb (Vessel Cannulated)	Complications	Response	Loco-regional Recurrence (months)	Distant Metastatic Disease (months)	Status at Last Follow-up (months)
Mayo AZ/A	Upper (Axillary)	Urinary Retention	CR	No	No	DWD (36)
Mayo MN/A	Lower (Femoral)	Wound Infection	CR	No	No	NED (36)
Mayo MN/B	Lower (Iliac)	Cellulitis	CR	No	Yes (3.6)	DOD (8)
Mayo MN/C	Lower (Femoral)	Heat Lamp Burn	CR	No	Yes (2.5)	AWD (7)
Bassi et al .	Lower (NR)	NR	NR	Yes	Yes (5)	DOD (13)
Dawson et al.	Lower (NR)	Transient neutropenia	CR	No	No	NED (<1)
Duprat et al.	Lower (Iliac)	CPK Elevation	CR	Yes (24)	No	DOD (31)
Feun et al.	Lower (NR)	NR	CR	No	No	NED (>120)
Grandpeix et al.	Lower (NR)	Local skin changes	CR	No	No	NED (60)
Gupta et al.	Lower (Iliac)	None	CR	No	No	NED (18)
Lampreave et al.	Lower (Popliteal)	Severe swelling & painful skin lesions	CR	No	No	NED (6)
Olieman et al. A	Lower (Femoral)	None	CR	Yes (12)	No	NED (37)
Olieman et al. B	Upper (Axillary)	None	NR	Yes (8)	Yes (1)	DOD (16)
Olieman et al. C	Upper (Axillary)	None	PR	No	Yes (3)	DOD (7)
Ponte et al.	Lower (Iliac)	None	CR	No	Yes (2)	DOD (4)
Wood et al.	Lower (Femoral)	NR	CR	No	No	NED (12)

Legend: NR (not recorded), CR (Complete response), PR (partial response), NED (no evidence of disease), DOD (died of disease), DWD (died without disease), AWD (alive with disease), and CPK (Creatinine Phosphokinase).

P238

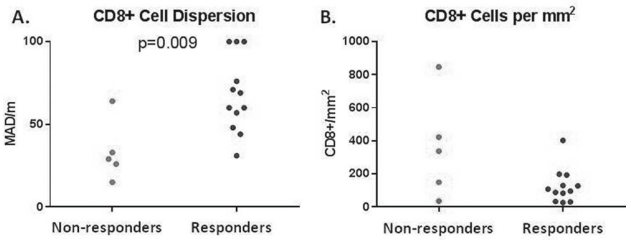
Sentinel Node Biopsy for T1 Melanoma in Patients 75 Years of Age or Older Does Not Change Clinical Outcomes D. Schuitevoerder,[1]* J. Fortino,[2] J.T. Vetto.[2] *1. Oregon Health & Science University, Department of Surgery, Portland, OR; 2. Oregon Health & Science University, Department of Surgery, Division of Surgical Oncology, Portland, OR.*

Introduction: NCCN guidelines recommend consideration of sentinel node biopsy (SNB) for T1 melanomas with high-risk features (mitoses, ulceration, or thickness >0.75mm). Recent studies suggest a decreased rate of SNB positivity and increased disease related mortality with increasing age for melanomas >1mm thick. The objective of this study was to determine the incidence of positive SNB, overall and disease free survival in patients ≥75 years old with T1 melanoma. Methods: A retrospective review of prospectively gathered data correlated from a university-based tumor registry and an IRB approved, melanoma SNB database. Results: A total of 190 clinically node negative patients, ≥75 years old, with T1 melanoma were reviewed. Twenty-four had SNB; the remaining one hundred sixty-six did not. As expected, tumor thickness (0.46 vs 0.83mm, p<0.001) and the proportion of lesions with mitoses (8 vs 33%) or ulceration (0.6 vs 8%) were all higher in the SNB group. Despite this, there was no difference in overall or disease free survival (p = 0.6 and 0.9 respectively) between the two groups. Twenty-two of the twenty-four patients with SNB and thirty-five of the one hundred sixty-six patients without had lesions with high-risk features. When these high-risk patients were compared the group without SNB was on average older (83 vs 80, p = 0.02), however there was no significant difference in average melanoma thickness (0.78 vs 0.85mm, p = 0.14), presence of ulceration (p = 0.31) or mitoses (p = 0.79), or overall or disease free survival (p = 0.21 and 0.14 respectively). Of the patients who underwent SNB, none had nodal metastasis. Four patients in the entire data set had recurrence, one in the SNB group at 3 years. Conclusion: Patients ≥75 years of age have low rates of SNB positivity and similar recurrence rates compared to those without SNB in this age group, even in the presence of high risk features. These findings suggest that patients with T1 melanomas who are 75 years of age or older can be safely managed without SNB.

P239

Predicting Response to BRAF-Targeted Therapy Using an Immune Signature J.A. Cintolo-Gonzalez,[1]* M. Hammond,[1] D. Frederick,[1] N. Lawrence,[1] A. Piris,[2] K. Flaherty,[1] J. Wargo,[3] Z. Cooper,[3] M. Hoang,[1] L. Kwong,[3] G. Boland.[1] *1. Surgery, Massachusetts General Hospital, Boston, MA; 2. Brigham and Women's Hospital, Boston, MA; 3. University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Our group has previously shown correlation between immune activation signatures and resistance patterns to BRAF-inhibitor (BRAFi) therapy using RNA-seq and Reverse Phase Protein Array (RPPA). We now expand on this work by using immunohistochemistry (IHC) to assess immune infiltrates within tumor samples of patients both pre- and on-treatment with BRAF-inhibitor (BRAF-i) or combination BRAF-i/MEK-inhibitor (MEK-i) therapy to validate the correlation of an immune signature with clinical outcomes using a technically-feasible approach. Methods: Serial tumor and blood samples were collected from patients with metastatic melanoma enrolled in clinical trials with targeted therapies according to institutional review board (IRB) protocols. Patient samples were securely linked to relevant clinical information including response as measured by Response Evaluation Criteria in Solid Tumors (RECIST) criteria. Formalin-fixed, paraffin-embedded tumors were stained by IHC for CD4/8 using CD4 (M)+ CD8 (RM) Prediluted Multiplex Cocktail (Biocare Medical). Slides were scored by clinical dermatopathologists. Median absolute deviation divided by the median (MAD/m score) is a normalized, non-parametric measurement of dispersion and was used for analysis to allow inter-tumor comparisons. Results: Response to anti-BRAF therapy (RECIST) correlated with dispersion of $CD8^+$ T cells as represented by MAD/m rather than with the total number of $CD8^+$ cells per area. In other words, tumors with more spatially dispersed tumor infiltrating $CD8^+$ cells had a less robust response, while those with higher levels of focally concentrated $CD8^+$ cells demonstrated a more significant RECIST response, particularly at tumor-stromal interfaces (Figure 1). Through this work, we uncovered a nuanced association between the immune signature identified through RNA-seq/RPPA and the spatial CD8+ cell dispersion by IHC in patients previously analyzed via RNA-seq/RPPA and validated the findings in a larger cohort of patients (n=25 patients). Conclusion: We propose the scoring of $CD8^+$ T cell presence/location may be an effective and feasible approach to predicting patient response to BRAFi therapy.



Pretreatment tumors demonstrating differences in CD8 dispersion (A) and density (B) in responders versus non-responders to BRAF-targeted therapy.

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Predictors of Early Recurrence in Patients with Melanoma Nodal Micrometastases M. Peters,* E.K. Bartlett, R. Roses, B.J. Czerniecki, D.L. Fraker, R.R. Kelz, G. Karakousis. *Hospital of the University of Pennsylvania, Philadelphia, PA.*

Introduction: Stage III malignant melanoma with nodal micrometastases represents a group with heterogeneous prognosis. Prior studies demonstrating the significance of various patient and tumor characteristics associated with survival are limited in terms of data on predictors of early recurrence and patterns of recurrence. We sought to identify factors associated with early recurrence as this subgroup may be particularly considered for adjuvant therapy trials. Methods: Patients with nodal micrometastases were identified from a database of consecutive patients with melanoma who underwent sentinel lymph node (SLN) biopsy at our institution between 1996-2011. Patient and tumor factors were recorded. Patients routinely underwent completion lymph node dissection (88%). Univariate analysis and multivariate logistic regression were applied to identify factors significantly associated with melanoma recurrence within one year of SLN biopsy. Results: Among 2013 patients who underwent SLN biopsy, 263 had positive sentinel nodes. The overall recurrence rate was 45% (n=118) with median time to recurrence of 1.2 years (IQR 0.63, 2.2). Median follow-up was 3.5 years for the overall group and 8.6 years for never recurring patients. In patients with recurrence, 43% (n=51) had recurrence within 1 year of SLN biopsy (early recurrence). Sites of first recurrence in patients with early recurrence were 14% (n=7) loco-regional, 33% (n=17) distant and 41% (n=21) both locoregional and distant recurrent disease. Median survival time among early recurrence patients was 1.5 years. Multiple patient and tumor factors were significantly associated with early recurrence by univariate analysis (see Table 1). In reduced multivariate analysis, significant factors associated with early recurrence were age >70, male gender and N2/N3 nodal status. Among males over 70, early recurrence was observed in 40% (n=14). Conclusion: Age over 70, male gender, and nodal burden are significantly associated with early recurrence in patients with nodal micrometastases. These factors could aid in counseling, surveillance, and consideration of patients for adjuvant therapies.

Prognostic Factors Associated with Early Recurrence								
Factors	Number (%)		Univariate Analysis		Multivariate Analysis		Reduced Model	
	Recurrence ≤1 year	No Recurrence < 1 year	OR	p-value	OR	p-value	OR	p-value
Age >70	17 (33)	33 (16)	2.71	.005	2.23	.082	2.68	.008
Male Sex	41 (80)	120 (57)	3.14	.003	2.52	.034	2.85	.007
Primary Site								
Extremity	21 (41)	19 (9)	Ref	Ref	Ref	Ref	Ref	Ref
Trunk	22 (43)	104 (49)	0.90	.746	.97	.937	--	--
Head & Neck	8 (16)	89 (42)	1.78	.243	2.40	.156	--	--
T3/T4	41 (80)	122 (58)	3.02	.004	2.26	.128	--	--
Mitoses ≥1	46 (90)	159 (75)	3.91	.070	3.80	.215	--	--
Ulceration	26 (51)	59 (28)	2.78	.002	1.63	.250	--	--
Vertical Growth	34 (67)	111 (52)	1.84	.089	1.03	.953	--	--
Lymphovascular Invasion	15 (29)	27 (13)	2.89	.005	1.24	.474	--	--
Absence of Tumor-Infiltrating Lymphocytes	26 (51)	138 (65)	2.03	.034	1.64	.722	--	--
Satellites	20 (39)	26 (12)	4.15	<.001	2.08	.858	--	--
N2/N3	27 (53)	65 (31)	2.54	.003	2.07	.070	2.56	.005
Adjuvant Therapy	18 (35)	63 (30)	1.31	.422	1.24	.603	--	--

Table 1. Reduced multivariate analysis model determining significant factors associated with recurrence of melanoma within one year of diagnosis

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MITF in Primary Melanoma Increases the Accuracy of Melanoma Nomogram in Predicting the Lymph Node Status S. Naffouje,[1]* R. Naffouje,[2] J. Chen,[1] G.I. Salti.[1] *1. University of Illinois at Chicago Medical Center, Chicago, IL; 2. Weiss Memorial Hospital, Chicago, IL.*

Introduction: Microphthalmia Transcription Factor (Mitf) is an important regulator of melanocytes homeostasis and differentiation. We proved that the grade of Mitf staining in primary melanoma cells can be a prognostic marker of the nodal status. Recently, there has been an industrious effort to identify the lymph node status in cutaneous melanoma using noninvasive tools such as serum markers or characteristics of the primary tumor. A nomogram has been established by Memorial Sloan Kettering Cancer Center (MSKCC) based on features of the primary melanoma to predict the status of the Sentinel Lymph Node (SLN). Herein, we apply the same statistical method to our patients to validate the nomogram. In addition, we add Mitf as an independent predictive factor, and assess its effect on the nomogram in predicting the SLN involvement. Methods: A total of 171 patients diagnosed with cutaneous melanoma were included. All patients underwent tumor resection with node biopsy or dissection. Demographic and histopathological data was collected according to MSKCC nomogram. We used Mitf staining grade of ≥50% (Mitf≥50) as an additional characteristic of the primary tumor. At first, logistic regression was used to fit the data without considering Mitf to validate the MSKCC's nomogram. We then proceed to reapply the analysis with Mitf as an independent predictor. Likelihood ratio test was conducted to test the effect of the addition of Mitf≥50 into the model. Results: In comparison of receiver operating curves from our logistic regression to those of MSKCC's nomogram, our logistic regression generated an Area Under the Curve (AUC) of 0.714 for prediction of positive nodes, compared to MSKCC's AUC of 0.591. However, none of the coefficients' differences was statistically significant. Inclusion of Mitf≥50 as an additional independent factor in the analysis improved the model fit significantly with a new AUC of 0.878 (vs. 0.714; $p<0.001$, likelihood ratio test). Conclusion: The nomogram described by MSKCC is a valuable tool in predicting SLN involvement in primary melanoma. Moreover, addition of 'Mitf≥50' significantly improves the accuracy of the nomogram in predicting the SLN status.

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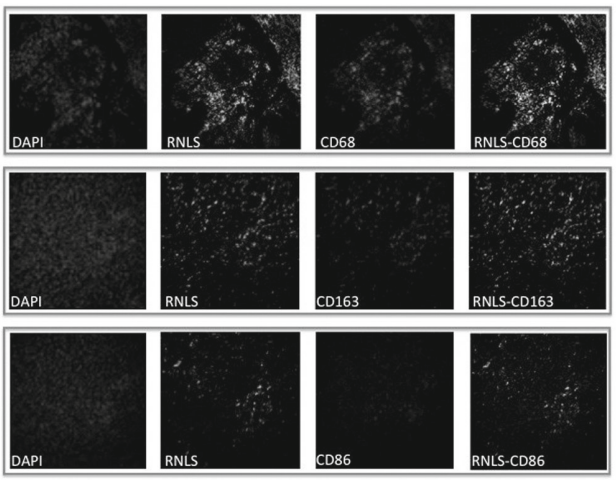
Suppression of Renalase in TAMs Enhances Melanoma Invasion and Metastasis L. Hollander,* X. Guo, G.V. Desir, C.H. Cha. *Yale University, West Hartford, CT.*

Background: Renalase (RNLS) is a secreted flavoprotein that functions as a survival factor for cells and organs exposed to ischemic and toxic injury. We recently found it has a significant impact on the progression of melanoma and is secreted by both tumor and stromal cells, specifically tumor-associated macrophages (TAMs). We chose to study the impact of TAM-secreted RNLS on the invasive and metastatic capabilities of melanoma. Methods: A nude xenograft mouse model utilizing non-RNLS-producing human melanoma cells A375.S2 was initially evaluated to determine the source of RNLS. Macrophages were collected from both wild type (WT) and RNLS knockout (RNLS KO) C57Bl6 mice for direct comparison. A syngeneic metastatic model was then investigated in these two groups with the B16-F10 melanoma cell line. After a two-week incubation period, the mice were sacrificed, the gross metastatic disease burden was carefully calculated, and the lung tissue was collected for further mRNA and protein study, including that from control WT and RNLS KO mice. Results: Review of the IF images demonstrated the majority of peri- and intra-tumoral RNLS originates from the TAMs. Macrophages collected from either the WT or RNLS KO mice were found to have vastly different morphologies and general function. Gross study of the metastatic mice revealed significantly increased invasion and metastasis in the RNLS KO group. The KO mice demonstrated near complete parenchymal replacement with metastatic disease (94.8% ± 1.0% vs. 42.9% ± 5.8% pulmonary mets, $p<0.001$) as well as an increased number of additional organs involved (3.2 ± 0.2 vs. 1.2 ± 0.2 organs with mets, $p<0.001$). Protein analysis revealed an increased expression of monocyte chemoattractant protein-1 (MCP-1) associated with RNLS silencing. MCP-1 is primarily secreted by macrophages and is known to regulate the migration and infiltration of certain immune cells, modify the tumor immune response, and mediate angiogenesis in melanoma. Conclusion: These data suggest silencing RNLS in TAMs enhances the invasion and metastatic progression of melanoma via the upregulation of MCP-1 and present a possible therapeutic pathway for the treatment of metastatic melanoma.



Immunofluorescence of RNLS and macrophage overlap in melanoma. Blue color is nuclei, green is RNLS, and red is for macrophages (CD68 pan-macrophage marker, CD163 M2/TAM macrophage marker, CD86 M1 macrophage marker). There is a high degree of overlap between RNLS and macrophages, more specifically, the M2/TAM subtype.

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Fluorescent Nanodiamonds Engage Innate Immune Effector Cells: Potential Anti-Tumor Efficacy L.P. Suarez-Kelly,[3]* A.R. Campbell,[3] A.A. Rampersaud,[1] I.V. Rampersaud,[1] A. Bumb,[2] M. Wang,[2] W.E. Carson III.[3] *1. Columbus NanoWorks, Inc., Columbus, OH; 2. Bikanta Corp., Columbus, OH; 3. The Arthur G. James Comprehensive Cancer Center and Richard J. Solove Research Institute, Columbus, OH.*

Background: Fluorescent nanodiamonds (FND) are nontoxic, infinitely photostable, and contain nitrogen-vacancy centers that emit fluorescence in the near infrared region, all of which support the potential for FND in an array of biomedical applications. Natural killer (NK) cells and phagocytic cells such as monocytes/macrophages (M/M) are part of the innate immune system (IIS) and are crucial to the control of carcinogenesis. FND-mediated stimulation of the IIS may serve as a powerful strategy to promote anti-tumor activity against

cancer cells. Methods: Uncoated FND containing NV centers were fabricated with a mean size between 20-50 nm. FND uptake and intracellular localization was evaluated via confocal microscopy in the murine macrophage cell line RAW264.7. FND uptake, cell viability, and cell surface marker expression in freshly harvested NK cells and M/M from healthy human donors were evaluated by flow cytometry and trypan blue staining. Results: Following 24h treatment, FND were detected in the cytoplasm of RAW 264.7 murine macrophage cells. Incubation of NK cells and M/M with uncoated FND (6.25-200 mcg/mL) resulted in a dose-dependent increase in FND uptake, with M/M displaying substantially greater uptake compared to NK cells. Importantly, FND treatment did not affect cell viability. Immune cell activation by FND was examined by flow cytometry: NK cells demonstrated increased expression of CD69 and NKG2D (30% and 14% increase, respectively), while M/M demonstrated only a slight increase in the expression of activation markers CD86 and HLA-DR. Conclusion: Treatment of innate immune cells with FND resulted in dose-dependent FND uptake with positive effects on immune cell activation and no adverse effects on cell viability. Given that the surface of FND may be modified to express immunomodulatory agents (e.g., TLR agonists), this may provide a tool for promoting innate immune cell activation and anti-tumor activity through application of FND in the perioperative setting. Future studies will harness the infinite fluorescence of FND to facilitate labeling and in vivo tracking of innate immune cells within the tumor microenvironment using standard imaging techniques.

P244

Characteristics, Treatment and Outcomes of Invasive Malignant Melanoma in Giant Pigmented Nevi in Adults: 976 Cases from the National Cancer Data Base A. Turkeltaub,[1]* T. Pezzi,[1] C. Pezzi,[2] H. Dao, Jr..[3] *1. Baylor College of Medicine, Houston, TX; 2. Abington Memorial Jefferson Health, Abington, PA; 3. Baylor College of Medicine, Department of Dermatology, Houston, TX.*

Introduction: Invasive malignant melanoma (MM) arising in a giant pigmented nevus (GPN) in adults is rare. This study describes the presentation, patterns of treatment, and survival of MM in a GPN. **Methods:** Adult patients with invasive MM in a GPN reported to the National Cancer Data Base (NCDB) from 1998-2012 were evaluated for patient and tumor characteristics at initial presentation, first course of treatment, and overall survival. For comparison, data from adult patients presenting with invasive nodular melanoma (NM) and superficial spreading melanoma (SSM) was used. **Results:** Of 541,250 patients with MM in the NCDB during the study period, 976 (0.2%) adult patients with invasive MM in a GPN were identified. For comparison, 111,870 patients with invasive SSM, and 35,962 patients with NM were analyzed. The mean age of patients with MM in a GPN was 52.4 years. Compared to patients with SSM, those with MM in a GPN were younger, had a thicker Breslow depth (1.40 mm vs. 0.98 mm, p<0.0005), more positive lymph nodes (10.9% vs. 7.6%, p=0.002), and more distant metastasis (2.5% vs. 0.5%, p<0.0005). Compared to patients with NM, those with MM in a GPN had a thinner Breslow depth (1.4 mm vs. 3.4 mm, p<0.0005), less positive lymph nodes (10.9% vs. 27.5%, p<0.0005), less distant metastasis (2.5% vs 4.4%, p<0.0005), ulceration (9.5% vs. 49.9%, p<0.0005), or presence of one or more mitosis (46.6% vs. 91.1%, p<0.0005). Multivariate cox regression revealed age > 65 years (HR: 2.9), Breslow thickness > 2 mm (HR: 2.9), ulceration (HR: 2.4), distant metastasis (HR: 6.9), and positive margins (HR: 2.9) as independent predictors of survival in patients with MM in a GPN. Having MM in a GPN was not in itself a significant predictor of overall survival, (HR: 0.97) when compared to SSM. **Conclusion:** Melanoma in a GPN occurs rarely in adults, with a mean age of diagnosis of 52.4 years. These rare tumors are treated primarily with surgery. The overall survival of patients with MM in a GPN is similar to SSM. Clinicians should be aware of the risk of MM in GPN in adults.

Patient, tumor and treatment characteristics for malignant melanoma by histologic type, National Cancer Data Base, 1998-2012*

	Malignant melanoma in giant pigment nevus	Nodular melanoma*	Superficial spreading melanoma*
Sample size (n)	976	35,962	111,870
Mean age (yrs)	52.4	62.5 (p < 0.0005)	56.1 (p < 0.0005)
Female gender (%)	46.0	37.9 (p < 0.0005)	46.4 (p = 0.452)
Caucasian (%)	96.9	97.5 (p = 0.200)	97.6 (p = 0.157)
Mean Breslow depth (mm)	1.4	3.4 (p < 0.0005)	1.0 (p < 0.0005)
# of mitosis/mm2	1.9	5.3 (p < 0.0005)	1.7 (p =0.637)
One or more mitosis present (%)	46.6	91.1 (p < 0.0005)	48.7 (p = 0.648)
Ulceration present (%)	9.5	49.9 (p < 0.0005)	10.7 (p=0.343)
Positive lymph nodes (%)	10.9	27.5 (p < 0.0005)	7.6 (p = 0.002)
Evidence of distant metastasis on presentation (%)	2.5	4.4 (p < 0.0005)	0.5 (p < 0.0005)
AJCC Stage 0 (%)	0.8	0.2	0.7
Stage I	68.6	19.0	77.8
Stage II	16.9	46.10	12.9
Stage III	11.6	30.0	8.0
Stage IV	2.1	4.8	0.5
Received primary site surgery (%)	98.1	98.9 (p = 0.085)	99.5 (p = 0.002)
Received lymph node surgery (%)	59.7	76.6 (p < 0.0005)	50.8 (p < 0.0005)
Margins Positive (%)	4.2	5.4 (p = 0.068)	2.8 (p = 0.038)
Received radiation (%)	1.2	4.2	0.6
Received chemotherapy (%)	2.3	4.6	0.8
Received Immunotherapy (%)	4.4	12.1	3.1
1 year survival	97.0	90.0	98.0
5 year survival	85.0	57.0	86.0
10 year survival	74.0	42.0	73.0

*p value as compared with MM in a GPN
*Survival data excludes cases diagnosed in 2012

P245

Completion Lymphadenectomy Does Not Confer a Survival Advantage in Intermediate Thickness Melanoma C. Mosquera,* H. Vora, T. Fitzgerald. *Brody School of Medicine, Division of Surgical Oncology, Greenville, NC.*

MSLTI and other data have clearly defined the prognostic and potential therapeutic value of SLN biopsy for intermediate thickness melanoma. The role for completion lymphadenectomy is, however, unclear and the subject of the ongoing MSLT-II trial. Methods: From 2003-2012, patients with tumors 1-4 mm in thickness with positive sentinel nodes were identified within the SEER registry. Patients were divided into two groups: 1) completion lymphadenectomy (CL) and 2) observation (O). Results: A total of 2,993 patients met inclusion criteria, with a majority being male (61.9%), white (97.9%), with extremity primaries (48.6%), no ulceration (61.2%), Clark level IV (70.7%), and Breslow thickness of 2.01-4.0 (52.7%). On univariate analysis, CL was associated with younger mean age (55.7 vs. 59.2, p<0.0001), male gender (68.8% vs. 62.7%, p=0.0006), and primary site (head and neck 65.9%, trunk 70.7%, vs. extremity 69.3%, p=0.0003), but not ulceration (65.9% vs. 67.3%; p=0.4403), Clark level (II 61.4%, III 67.5%, IV 67.1%, vs. V 64.4%, p=0.7682), or Breslow thickness (1.01-2.0mm 65.6% vs. 2.01-4.0mm 67.3%; p=0.3082). On multivariate analysis only male gender was associated with CL (OR 0.70, p=0.0001). On univariate survival analysis ulceration [59.2% vs. 78.2%, disease-specific 5-year (5-y DSS), (p<0.0001)], Clark level (II 91.2%, III 77.8%, IV 71.5%, vs. V 53.9% 5-y DSS, p<0.0001), and Breslow thickness (1.01-2.0mm 77.9% vs. 2.01-4.0mm 65.4% 5-y DSS, p<0.0001) were associated with survival. However, CL was not (p=0.2974). On cox regression analysis relationships between male gender (HR 1.21), ulceration (HR 1.72), Clark level (II vs. IV, HR 0.26; II vs. V, HR 0.16), and Breslow thickness (HR 0.72) persisted. However, CLwhen included in this model, was not associated with improved survival. Conclusions: SLN biopsy has both prognostic and potential therapeutic value in intermediate thickness melanoma, however, these data suggest that completion lymphadenectomy adds no therapeutic value.

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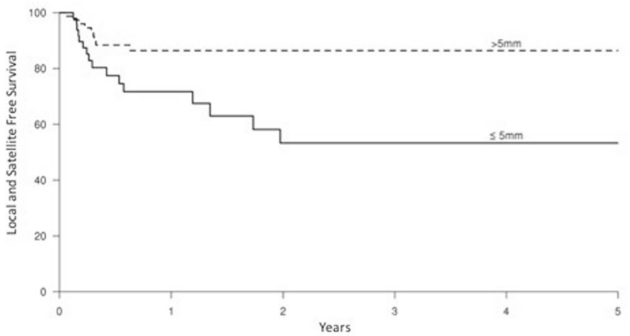
Patterns of Failure Following Excision of In-Transit Lesions in Melanoma and Influence of Excision Margins A.B. Gonzalez,* C.L. Baum, J.D. Brewer, S.J. Vera, J.W. Jakub. *Mayo Clinic, Guaynabo, PR.*

Introduction: Most local, satellite and in-transit (IT) events are the result of intralymphatic contamination and have a similarly poor prognosis. There are no guidelines for excision margins of IT lesions. Wider margins may impact future events within 2cm of the lesion, but are unlikely to otherwise influence the natural history of the disease. We sought to determine if margin width influenced the risk of recurrences within 2cm of the IT lesion and describe the patterns of failure. Methods: Patients undergoing margin negative excision for their first in-transit melanoma, without evidence of distant metastatic disease over a 10-year period (5/05-9/14) were included. Gross margins are those clinically measured by the surgeon. Factors associated with local and satellite recurrence (within 2cm of the excision scar) were analyzed with Cox proportional hazard analysis. Results: 261 patients presented with in-transit disease over the study period and 150 patients met the strict inclusion criteria. 112(75%) patients presented with a single IT lesion and 38(25%) with multiple lesions. 26(17%) patients experienced a local/satellite recurrence, 29(19%) an IT recurrence, 6(4%) a regional nodal recurrence and 37(25%) distant failure as their first event, 46(31%) remain free of disease and 6(4%) have died from other causes. Median time to next local or satellite recurrence was 7 months and 20.4 months for the 46 patients who remain alive without recurrence or death. The overall survival free of local or satellite recurrence at 2 years was 73%. A gross margin ≤5mm compared with >5mm was associated with an increased risk of local or satellite recurrence [p=0.009, OR 2.97(1.31-6.72)]. (Figure 1) Microscopic margins ≤2mm were not associated with an increased risk of local or satellite recurrence compared with microscopic margins >2mm [p= 0.78, OR 1.15(0.44-2.99)]. Conclusions: Approximately 2/3 of patients with an IT event experience future melanoma recurrences. A clinical margin of >5mm is associated with a lower risk of recurrence within 2cm, regardless of the distance of a negative microscopic margin; however, the majority of patients fail beyond this site.



P247

microRNA Profiling of Distant Metastatic Melanoma N. Latchana,[1]* J.H. Howard,[1] A.A. Gru,[2] X. Zhang,[1] P. Fadda,[1] W.E. Carson III.[1] *1. The Ohio State University, Columbus, OH; 2. University of Virginia, Charlottesville, VA.*

Introduction: Metastatic malignant melanoma has a propensity for hepatic and pulmonary involvement which portends a poor prognosis with a 1 year survival rate of 33-53%. Efficacious targeted therapeutic approaches are needed. MicroRNAs (miR) are small nucleotide inhibitors of protein translation. The miR profiles of melanoma metastases involving different organs is unknown. We hypothesize that differences exist in the patterns of microRNA expression in melanoma metastatic to liver and lung. Methods: RNA was extracted from formalin fixed, paraffin embedded human tissue samples of metastatic melanoma involving liver and lung as well as benign nevi and primary cutaneous non-metastatic melanoma as controls (n=6 each). Purified RNA was hybridized with a panel of nCounter capture and reporter probes and immobilized on a NanoString cartridge. Florescence intensity of each sample was measured by an nCounter Digital analyzer and included 5 negative and 5 positive controls as well as 5 housekeeping genes. Linear regression was performed using ANOVA. Results: Primary cutaneous non-metastatic melanoma had greater than 2.5 fold down-regulation of miR-493, miR-551a, and miR-4454 relative to benign nevi (P<0.0007). Metastatic melanoma to liver had differential expression of 14 miRs compared to benign nevi and 20 different miRs compared to primary cutaneous non-metastatic melanoma controls (P<0.0008). Metastatic melanoma to lung had had differential expression of 15 miRs compared to benign nevi and 12 different miRs compared to primary cutaneous non-metastatic melanoma controls (P<0.0008). Compared to metastatic melanoma to the lung, metastatic melanoma to liver was associated with greater than 2 fold up-regulation of miR-122, miR194, miR-885, miR-455 and greater than 1.3 fold down-regulation of miR-199, miR-200c, and miR221 (P<0.006). Conclusions: Metastatic melanoma to lung and liver may have different microRNA profiles suggesting potential insights for future therapeutic approaches.

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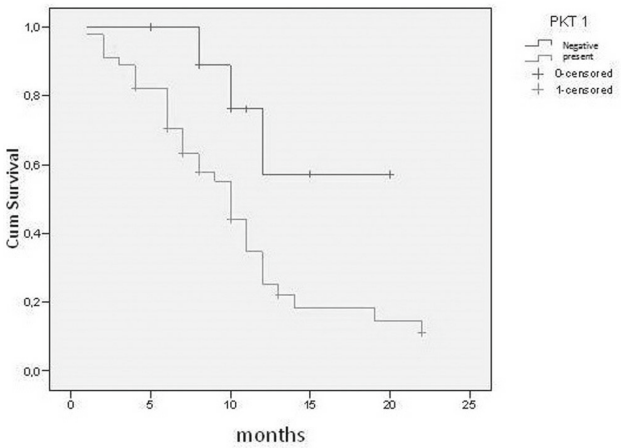
Cell-Free DNA V600E Measurements During Therapy with Vemurafenib in Metastatic Melanoma Patients P. Rutkowski,[1]* K. Kozak,[1] A. Kowalik,[2] A. Gos,[1] M. Jurkowska,[3] B. Wasag,[4] N. Krawczynska,[4] J. Stepniak,[1] T. Switaj,[1] H. Kosela-Paterczyk,[1] B. Jagielska,[1] J.A. Siedlecki,[1] J. Limon,[4] I. Lugowska.[1] *1. Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; 2. Holycross Cancer Center, Kielce, Poland; 3. Genomed, Warsaw, Poland; 4. Medical University of Gdansk, Gdansk, Poland.*

Background: Cell-free DNA (cfDNA) in peripheral blood represents a promising non-invasive diagnostic and prognostic biomarker. We assessed the status of BRAF V600E mutation in cfDNA isolated from plasma to estimate the sensitivity and specificity of two molecular methods and correlation between concentration of plasma cfDNA V600E and clinical outcomes of metastatic melanoma (MM) BRAF(+) patients (pts) treated with vemurafenib. Material and methods: Plasma samples of 64 pts with BRAF-mutated MM treated with vemurafenib in 2013-2014 were collected at 2 different time points: 1) prior to 1st dose of vemurafenib and 2) after 4-8 weeks of treatment. BRAF mutations were assessed using tumor tissue-derived DNA and cfDNA from plasma samples. Mutational analysis of cfDNA for BRAF V600E was performed using droplet digital PCR (ddPCR) and cobas® 4800 BRAF V600 test. We analyzed the association between cfDNA mutation status and progression-free and overall survival (PFS,OS). Results: At 1st time point cfDNA V600E was detected by ddPCR in 80% of pts, and only in 42% of pts using Cobas test. Patients in whom the V600E mutation was detected in cfDNA at baseline (ddPCR) had significantly shorter median PFS and OS than those without detected mutation (ND) in cfDNA (6.6 vs 12.5 months, p=0.035 and 10 months vs not reached, p=0.025, respectively). Conversely, ND cfDNA V600E (in patients with initially positive ddPCR) after 4-8 weeks of treatment with vemurafenib was associated with poorer prognosis (p=0.05). Conclusions: Monitoring plasma cfDNA levels of BRAF V600E mutations may have prognostic value for advanced BRAF-mutated melanoma pts treated with vemurafenib. Undetectable cfDNA V600E before initiation of therapy may be a predictive marker associated with better outcomes. Our results indicate that ddPCR is highly sensitive and probably cost-effective method for plasma BRAF mutation testing.



Overall survival according to presence of V600E mutation in cfDNA at baseline (ddPCR)

P249

Intraoperative Frozen Section (FS) Analysis of Sentinel Lymph Nodes (SLNs) in Melanoma has a High False Negative Rate but Allows Patients with Larger Volume Disease to be Spared a Second Operation A. Fahy,[1]* T.E. Grotz,[1] A. Glasgow,[2] E.B. Haberman,[2] L.A. Erickson,[3] T.J. Hieken,[2] G.L. Keeney,[3] J.W. Jakub.[2] *1. Department of Surgery, Mayo Clinic, Rochester, MN; 2. Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Mayo Clinic, Rochester, MN; 3. Department of Pathology, Mayo Clinic, Rochester, MN.*

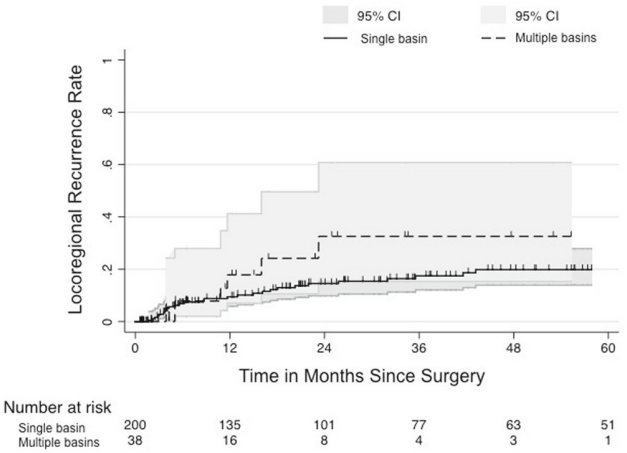
Background: Intraoperative FS analysis of the SLN may allow for definitive lymph node dissection at one operation, sparing patients a second procedure. We aimed to evaluate the accuracy and merit of FS analysis of SLNs in melanoma. Methods: Patients with trunk/extremity melanoma who underwent FS analysis of the SLN between 1/2000 and 12/2010 at our institution were included. Surgical and pathological characteristics, recurrence and survival were analyzed. Comparisons were made using chi squares and Fisher's exact t-test when applicable. Results: 568 patients were identified with a T stage distribution was 145 T1, 235 T2, 123 T3, 54 T4, 11Tx. Median followup was 4.4 years. 133 patients (23%) were SLN positive by permanent section evaluation with H&E and IHC. Of the 133 SLN positive patients, 63 (47.4%) were identified on FS. Of the 70 (52.6%) SLN metastases not identified on FS, 16 (23%) were seen only on IHC. There were no intraoperative FS false positives corresponding to a FS PPV of 100%. The false negative rate was 53%, the negative predictive value was 88% and the overall accuracy of FS was 89%. For patients who had a positive node on FS, 17/63 (27%) had additional positive nodes on lymph node dissection, versus only 1 of the 70 (1.4%) patients whose positive nodes were not detected on FS ($p<0.001$). Of the 26 patients who's SLN metastasis was >2mm, 22 were detected on FS (84%), and SLN metastasis >2mm led to a greater likelihood of further positive nodes on lymph node dissection (45.8% for SLN metastasis >2mm versus 5.5% for SLN metastasis <2mm, $p<0.0001$). Our node positive and regional recurrence rates based on T stage are comparable with the literature for non-FS institutions (Table 1) Conclusions: FS analysis of SLNs in melanoma has a 100% PPV although a high false negative rate. Patients with positive SLNs on FS had a larger volume of disease and were more likely to have further positive nodes and may benefit more from a LND than those with FS negative SLN. FS did not result in understaging and spared approximately half of the patients a second operation.

T stage	Permanent section SLN + (% of T stage)	Frozen section+ SLN (% of permanent section)	LN Recurrence (% of overall group)	LN recurrence in SLN positive patients	LN recurrence in SLN negative patients	Disease Free Survival at 5 years
T1a (n=98)	7 (7%)	2 (29%)	4 (4%)	0/7 (0%)	4/91 (4%)	93.1%
T1b (n= 47)	6 (13%)	2 (33%)	1 (2%)	1/6 (17%)	0/41 (0%)	97.3%
T2a (n = 208)	28 (13%)	9 (32%)	7 (3%)	4/28 (14%)	3/180 (2%)	93.8%
T2b (n= 27)	8 (30%)	5 (63%)	5 (19%)	2/8 (25%)	3/19 (17%)	78%
T3a (n = 84)	24 (29%)	7 (30%)	13 (15%)	4/24 (16%)	9/60 (15%)	87%
T3b (n= 39)	20 (51%)	10 (50%)	5 (13%)	4/20 (20%)	1/19 (5%)	83%
T4a (n= 29)	14 (48%)	8 (57%)	7 (24%)	7/14 (50%)	0/15 (0%)	73%
T4b (n = 25)	19 (76%)	16 (84%)	8 (32%)	6/19 (32%)	2/6 (33%)	54%
Tx (n =11)	6 (55%)	4 (67%)	2 (18%)	1/6 (17%)	1/5 (20%)	75%
Overall (n=571)	**132 (23%)**	**63 (47%)**	**52 (9%)**	**29 (22%)**	**23 (5%)**	**88%**

P250

Sentinel Lymph Node Drainage to Multiple Basins in Head and Neck Melanoma C.L. Stewart,* B.C. Chapman, A.L. Gleisner, J. Merkow, N. Pearlman, C. Gajdos, M.D. McCarter, N. Kounalakis. *Surgery, University of Colorado School of Medicine, Aurora, CO.*

Introduction: Sentinel lymph nodes (SLN) from head and neck melanomas are challenging to localize and can drain to multiple lymph node basins. In this study we determined the frequency of head and neck SLN drainage to multiple lymphatic basins and asked if this was associated with nodal positivity, recurrence of disease, or survival in a large single center cohort. Methods: We queried patients diagnosed with a head and neck melanoma who had a SLN biopsy performed from 1/1998-6/2015. Demographic and clinical characteristics were compared using Student's t-test, chi-square analysis, log-rank test, and Kaplan-Meier curves where appropriate. Results: We identified 250 patients with head and neck melanomas who had a SLN biopsy performed. SLN were biopsied from the following locations: 204 neck, 61 parotid, 24 periauricular, 3 occipital, 1 axillary. There were 39 (15.6%) patients with SLN identified in two basins (most commonly neck and parotid, 24 patients), and two patients (0.8%) with SLN in three basins. These patients were similar to those with SLN drainage to a single basin in age (54.4 vs 54.0 years), gender distribution (70.7% vs 75.6% male), and Breslow depth (2.18 vs 2.13 mm) (all $p>0.05$). Patients with SLN found in multiple basins had higher numbers of SLN recovered (2 vs 3 nodes, $p=0.003$). The percentage of patients whose melanoma drained to multiple basins with a positive SLN (9/38, 23.7%) was similar to patients with a negative SLN (32/212, 15.0%, $x^2=1.73$, $p=0.19$). Outcomes were also similar between patients draining to multiple basins versus a single basin for 3-year locoregional recurrence rates (32.6 vs. 17.5), distant recurrence rates (21.3 vs 16.6), and overall survival (90.0% vs 82.6%) (all $p>0.05$). There was a trend on the Kaplan-Meier curve, however, towards more locoregional recurrence in the multiple basin group (figure). Conclusions: Most head and neck melanomas have sentinel lymph nodes that drain to the neck, and drainage to multiple basins is common. Drainage to multiple basins does not seem to be associated with increased lymph node positivity, recurrence, or survival, but a potential trend in locoregional recurrence warrants further investigation to confirm.

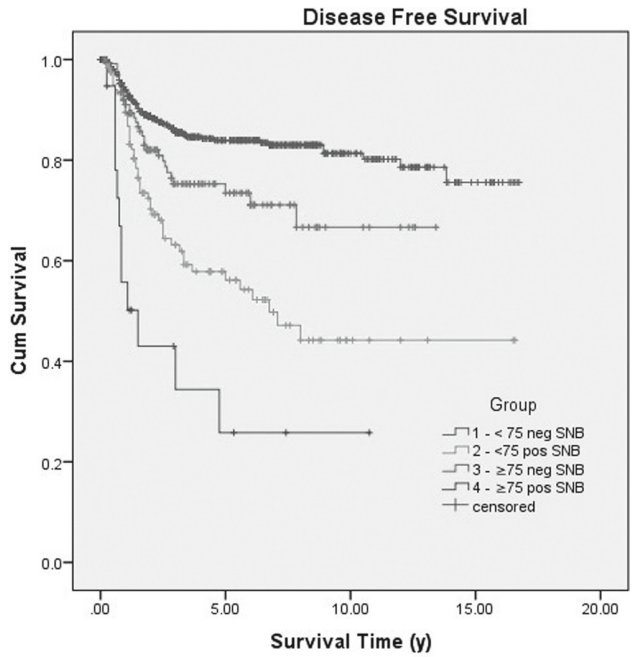


P251

Sentinel Node Status in Patients 75 Years of Age or Older with Melanoma >1mm Thick is an Important Predictor of Disease Recurrence D. Schuitevoerder,[1]* J. Fortino,[2] J.T. Vetto.[2] *1. Oregon Health & Science University, Department of Surgery, Portland, OR; 2. Oregon Health & Science University, Department of Surgery, Division of Surgical Oncology, Portland, OR.*

Introduction: Current NCCN guidelines recommend sentinel node biopsy (SNB) for all melanomas >1mm thick. Recent studies are conflicting regarding the utility of SNB in patients ≥75 years of age with T2-T4 melanoma. The objectives of this study were to determine the incidence of SNB positivity, predictors of disease recurrence, overall and disease free survival among such patients. Methods: Retrospective review of prospectively gathered data correlated from a university-based tumor registry and an IRB approved, melanoma SNB database. Results: A total of 868 clinically node negative patients with melanoma >1mm thick were reviewed. Of these, 712 were <75 years old and the remaining 156 patients were ≥75. There was a trend toward a decreased rate of node positivity in the group ≥75 years of age (13 vs 18%), however this did not reach statistical significance ($p = 0.1$). As expected patients ≥75 years of age had a significantly lower overall survival ($p < 0.001$) independent of nodal status. Disease free survival was significantly lower in patients with positive SNB regardless of age ($p <0.001$). However, among patients with positive SNB, those ≥75 years of age had significantly lower median disease free survival (1.5 vs 6.75 years, $p = 0.005$). Disease free survival was negatively associated with age ≥75 years old [hazard ratio (HR) 1.56, 95%

confidence interval (CI) 1.08-2.27], positive nodal status (HR 3.32, 95% CI 2.36-4.66), head and neck location (HR 2.03, 95% CI 1.36-3.02), as well as ulceration (HR 2.18, 95% CI 1.53-3.1), and tumor thickness (HR 1.09, 95% CI 1.04-1.14). Conclusion: Although patients aged 75 or older showed a trend toward decreased sentinel node positivity, a diagnosis of nodal metastasis was associated with a significant decrease in median disease free survival compared to younger patients. Given this important prognostic information, SNB should continue to be offered to patients 75 years of age or older, if deemed suitable surgical candidates.



P252

Withanolides Inhibit Glycolysis, Growth, Migration, and Invasion in Melanomas through Induction of Reactive Oxygen Species

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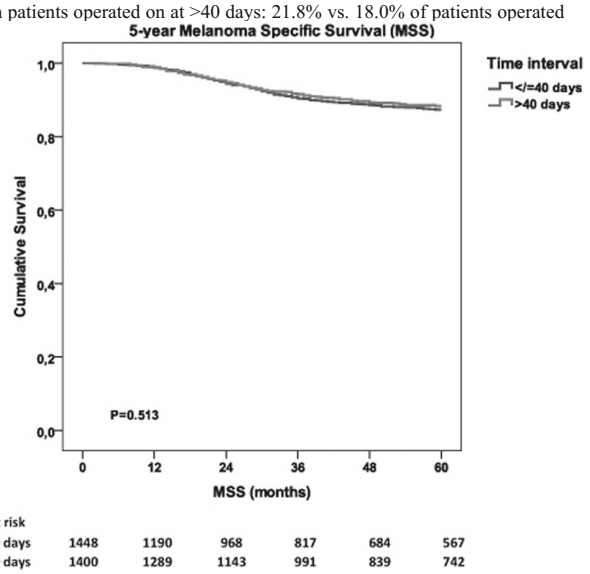
Introduction: Formation of reactive oxygen species (ROS) in melanoma has been shown to play a critical role in both pathogenesis and treatment effects. Our previous studies have shown that 4,19,27-triacetyl withalongolide A (WGA-TA) inhibits heat shock protein (HSP) 90 chaperone function, creates ROS, and leads to apoptotic cellular death. We hypothesized that the ROS induced by WGA-TA in melanoma cells inhibits pro-survival and glycolytic pathways, and decreases invasion and migration. Methods: Using genetically validated human melanoma cell lines (SKMEL28, UACC257) CellTiter-Glo (CTG) assays identified 72 h IC_{50} concentrations for WGA-TA, +/- N-acetylcysteine (NAC) and 2-deoxyglucose (2DG). H_2DCFDA assay quantified ROS formation. Following 24 h treatment with varying concentrations of WGA-TA (+/-NAC, 2-DG), Western blot (WB) was used to evaluate PI3K/mTOR, MAPK, HSPs, apoptotic and glycolytic proteins. Migration/invasion were assessed by scratch/Boyden chamber assays. Results: WGA-TA IC_{50}=202 and 28 nM (SKMEL28, UACC257, respectively) by CTG. IC_{50} increased to >20 μM with NAC treatment, and improved to 113 and 20 nM with 2DG treatment. After 6h of 5 μM WGA-TA treatment, ROS production increased 2-fold vs control ($p<0.05$), which was abrogated by NAC treatment ($p<0.005$). After 24hrs of WGA-TA treatment, WB showed >95% reductions in HSF1, Akt, P-Akt, mTOR, P-mTOR, 70% reductions in BRAF, unchanged HSP90 levels and a 5-fold increase in HSP32. Glycolysis was inhibited with reductions in phosphofructokinase (>80%) and pyruvate kinase 1/2 (>90%) vs. controls. This lead to apoptotic death via PARP and caspase 3 cleavage, again abrogated with NAC treatment. On functional evaluation, WGA-TA inhibited migration >70% ($p<0.05$) and invasion >90% ($p<0.01$) vs. controls, again NAC treatment returned this effect to that of controls. Conclusion: WGA-TA is a novel small molecule therapeutic for melanoma that inhibits HSP90 chaperone function and induces ROS leading to inhibition of the PI3K, MAPK and glycolytic pathways, with functional inhibition of tumor cell migration and invasion. These promising in vitro results warrant additional translational validation.

P253

Effects of Time Interval Between Primary Melanoma Excision and Sentinel Node Biopsy on Positivity Rate and Survival

C.M. Oude Ophuis,[1]* A. van Akkooi,[2] P. Rutkowski,[3] C.A. Voit,[4] J. Stepniak,[3] M. Wouters,[2] D.J. Grunhagen,[1] C. Verhoef.[1] *1. Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; 2. Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, Netherlands; 3. Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; 4. Charité – University Medicine Berlin, Berlin, Germany.*

INTRODUCTION Worldwide, sentinel node biopsy (SNB) has become essential for adequate staging of melanoma patients. Most (inter)national guidelines advocate to perform wide local excision and SNB as soon as possible. Aim: to assess the role of time interval between primary melanoma excision and SNB on melanoma specific survival (MSS). METHODS A retrospective cohort study was performed concerning melanoma patients from 4 EORTC Melanoma Group tertiary referral centers undergoing SNB between 1997-2013. A total of 2,848 patients were included. Differences in baseline characteristics, sentinel node (SN) positivity, MSS, and disease free survival (DFS) were investigated for time interval until SNB. RESULTS Median time interval until SNB was 40 days (interquartile range(IQR) 26–55 days), median follow-up was 52 months (IQR 23–94 months). Median Breslow thickness was 2.00mm (IQR 1.15–3.50mm), 799 patients (28.1%) had ulcerated tumors. Of all patients, 565 (19.8%) had a positive SN. SN positivity was higher in patients operated on at >40 days: 21.8% vs. 18.0% of patients operated



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The Additional Value of S-100B in a Risk Stratifying Model for the Prediction of Non-Sentinel Node Positivity in Melanoma Patients

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Introduction. Completion lymph node dissection (CLND) in sentinel node (SN) positive melanoma patients is accompanied with significant morbidity, while metastases in non-sentinel nodes (NSNs) are only found in approximately 20%. Previously, models have been developed to predict NSN positivity. The aim of this study was to test whether incorporation of S-100B into a prediction model would increase its accuracy, to enable patient selection in

whom CLND could safely be omitted. Methods. All registered clinicopathologic factors were tested for their association with NSN positivity in SN-positive patients who underwent CLND. A prediction model was developed with backwards selection in a multivariable logistic regression model, incorporating all predictive factors. The Area Under the Curve (AUC) was calculated in a model with and without S-100B. A weighted risk score, 'S-100B Non-Sentinel Node Risk Score' (SN-SNORS), was derived. Results. NSN positivity was present in 24 patients (21.8%). The following factors were independently associated with NSN positivity on a 10% significance level: sex, histology, number of harvested SNs, number of positive SNs, extra-nodal growth and S-100B value. The AUC for this model was good: 0.84 (95%CI 0.76-0.92). In a model without S-100B the AUC was 0.79 (95%CI 0.69-0.89), the difference was not significant (p=0.32). SN-SNORS was the sum of scores for six parameters: sex (female=1, male=5), histology (superficial spreading=1, nodular=4, other=3), number of SNs (0.5 per SN), number of positive SNs (3 per SN), extra-nodal growth (no=1, yes=10) and S-100B in µg/l (0-0.05 =0, 0.06-0.10=3, 0.11-0.15=6, 0.16-0.20=9, >0.20=12). SN-SNORS of 0-10, 11-20 and 21-30 were associated with low (4.7%), intermediate (22.5%) and high (55.6%) risk of NSN involvement. (Table 1) Conclusions. Incorporating S-100B into a prediction model shows a trend towards strengthening its predictive value. A weighted score (SN-SNORS) accurately stratifies the risk of NSN involvement in melanoma patients. If validated in future studies, prediction of prognosis and patient selection for CLND will be more accurate using this decision model.

Table 1. Final SN-SNORS System for Stratification of Risk of NSN positivity.

Predictive parameter	OR (95%CI)	SN-SNORS (points)
Sex	-	-
Female	1.0	1
Male	5.05 (1.38-18.37)	5
Histology	-	-
Superficial	1.0	1
Nodular	3.93 (1.24-12.48)	4
Other	3.35 (0.38-29.48)	3
Number of SNs harvested	0.43 (0.19-0.95)	0.5 per SN
Number of SNs positive	2.75 (0.96-7.90)	3 per SN
Extra-nodal growth SN	-	-
No	1.0	1
Yes	67.5 (3.3-1389)	10
S-100B (µg/l)		-
0.0-0.05		0
0.06-0.10	2.88 (1.07-7.71)	3
0.11-0.15		6
0.16-0.20		9
> 0.20		12
Total SN-SNORS	Risk of NSN involvement	
0-10	Low (4.7%)	
11-20	Intermediate (22.5%)	
21-30	High (55.6%)	

Abbreviations: SN-SNORS; S-100B Non-Sentinel Node Risk Score, SN; Sentinel Node, NSN; Non-Sentinel Node.

P255

Factors Associated with Non-Performance of Sentinel Node Biopsy for Intermediate Thickness Melanoma: A National Study of 5,133 Patients L. Youngwirth,* M. Adam, P. Mosca, S. Roman, J.A. Sosa, R. Scheri. *Duke University Medical Center, Durham, NC.*

Introduction: Despite the demonstrated importance of sentinel node biopsy (SNB) for clinically localized intermediate thickness melanoma, it is suspected that many patients still do not undergo this procedure. This study sought to determine factors associated with non-performance of SNB. Methods: The National Cancer Data Base (2000-2012) was queried for patients with a diagnosis of melanoma. Inclusion was limited to patients with intermediate thickness melanoma (1–4mm) without clinically positive lymph nodes or distant metastases. Patients were divided into two groups: patients with/out regional lymph node surgery (RLNS). RLNS is defined as removal of regional lymph nodes, including SNB. Patient demographic, clinical, and pathologic characteristics at diagnosis were determined. Multivariable analyses were performed to identify factors associated with RLNS and survival. Results: 5,133 patients met inclusion criteria; 31.4% did not undergo RLNS. Compared to patients who underwent RLNS, these patients were older (69 years vs 59 years respectively, p<0.01) and more likely to have a higher comorbidity score (14% vs 11%, p<0.01), be treated at a non-academic facility (60% vs 51%, p<0.01), and have tumors located on the head and neck (37% vs 19%, p<0.01). After adjustment, increasing patient age (OR=0.97, p<0.01), non-white race (OR=0.43, p=0.01), higher comorbidity score (OR=0.40, p=0.01), treatment at a non-academic facility (OR=0.62, p<0.01), and tumors located on the head and neck (OR=0.51, p<0.01) were associated with non-performance of RLNS. After adjustment, positive lymph nodes identified during RLNS (HR=2.16, p<0.01) and non-performance of RLNS (HR=1.74, p<0.01) were associated with compromised survival. Conclusion: Nearly one third of patients with intermediate thickness melanoma do not undergo RLNS. Older, more medically complex patients and those with tumors located on the head and neck or treated at non-academic medical centers are at increased risk for non-performance of RLNS. These at-risk patients should be offered SNB to provide better risk stratification for survival and appropriate referral for adjuvant therapy.

P256

A Novel, Endovascular Approach to Hyperthermic Isolated Limb Infusion (HILI) for Advanced Locoregional Melanoma of the Lower Extremity A.C. Kim,* A.E. Boniakowski, N.H. Osborne, J.E. Rectenwald, M. Cohen. *Surgery, University of Michigan Health Systems, Ann Arbor, MI.*

BACKGROUND For patients with locally advanced melanoma confined to an extremity, hyperthermic isolated limb infusion (HILI) with regional heated chemotherapy (i.e. melphalan) can be an effective treatment option. Contemporary HILI protocols utilize endovascular access followed by regional limb occlusion by tourniquet isolation. This traditional approach is limited by its inability to treat high inguinal disease, proximal to an upper thigh tourniquet. We have developed an endovascular HILI technique using two percutaneous catheters and a high flow pump without a formal tourniquet. We hypothesize that this minimally invasive technique will provide excellent comprehensive regional chemotherapy compared to traditional HILI methods. METHODS We examined the outcomes of three patients, who underwent HILI via an exclusive 2-catheter percutaneous approach to the lower extremity, including intraoperative/post-operative complication and 6-months response rates. An ultrasound-guided access of the contralateral common femoral artery and vein were performed to establish an "up and over" access to the affected limb. Specialized occlusion catheters (Stryker 9Fr Merci or 8Fr Flowgate) were then positioned above the level of the inguinal ligament in the external iliac vessels. Following systemic heparinization, catheter balloon occlusion achieved complete limb isolation and the infusion circuit was established through connection of the catheters to the Belmont® Rapid Infuser with a weight-based Melphalan dose delivered over 30 min. RESULTS All patients successfully underwent HILI with this new technique. There were no observed intraoperative or post-operative complications. Total blood loss ranged from 20 to 250 mL. Infusion flow rates averaged 350 ml/min for 30 minutes with 50-80 milligrams of Melphalan in the circuit. All patients ambulated on POD #1 with an avg. length of stay of 2±0.5 days, and are alive with complete tumor responses at 6 month follow-up. CONCLUSION This novel percutaneous non-tourniquet HILI technique provides excellent regional oncologic control with lower morbidity and should be considered for appropriate patients.

P257

Copy Number Alterations Determined by Array CGH Influence Prognosis in Stage III Metastatic Melanomas M. Jurkowska,[1] E. Mierzejewska,[2] K. Sobecka,[2] A. Gos,[1] H. Kosela-Paterczyk,[1] A. Kowalik,[3] I. Lugowska,[1] B. Nowakowska,[2] J.A. Siedlecki,[1] P. Rutkowski.[1]* *1. Department of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland; 2. Institute of Mother and Child, Warsaw, Poland; 3. Holycross Cancer Center, Kielce, Poland.*

The presence of multiple chromosomal aberrations is a hallmark of malignant melanoma. Array comparative genomic hybridization (aCGH) was used here to determine genetic changes in cutaneous melanoma metastases to the regional lymph nodes. Methods: Clinical and genetic data of 56 cutaneous melanoma patients (targeted-therapy naïve) in stage III after therapeutic lymph node dissection due to palpable nodal metastases were analyzed. All tests were performed on DNA derived from FFPE metastatic lymph node samples. aCGH was performed using 60K microarrays from Oxford Gene Technology. NGS Ion AmpliSeq™ Cancer Hotspot Panel v2 was used to analyze 50 most often mutated oncogenes and tumor suppressors, including MAPK pathway members (BRAF and NRAS). In statistical analysis Chi2 or Fisher's exact tests, uni- and multivariate Cox proportional hazards models were used. Results: All samples had aCGH-detectable imbalances. Median 22 (1-56) imbalances

(gains and losses) per sample were identified. The 41 recurrent (affecting ≥6 samples) imbalances were defined. Both total number and chromosomal location of imbalances influenced overall survival (OS). Presence of >20 gains/losses per sample (p=0.047) as well as recurrent changes affecting 1p36.33, 3p25.3, 11p15.5, 16p13.3, 16q24, 17p11.2, whole chromosomes 9 and 10 were significantly associated with better OS while 3q22.3, p15.33, 6p25.3, 16q13, 17q21.33 and 22q11 imbalances indicated poor prognosis (all p≤0.005). Number of gains/losses correlated neither with MAPK activation nor with total mutated genes in AmpliSeq™ panel. Gains at 3p25.3, 22q11.21 were present predominantly in MAPK(-) samples while other like gain of 1p36.33, loss 3q22.3 correlated with MAPK(+) status (p<0.05). In particular the gain at 6p25.3-p12 positively correlated with NRAS activating mutation (p=0.032). Conclusion: The detected quantitative changes may play a role in the progression of metastatic melanoma and may be used as markers in evaluating good/poor prognosis. The study was supported by the Polish National Science Centre (grant no.2011/03/B/NZ5/04513)

P258

Disease Recurrence Patterns of Head and Neck Melanoma

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Brown University/Rhode Island Hospital, Providence, RI.

Introduction The surgical management of head and neck melanoma (HNM) presents unique challenges associated with local anatomy affecting optimal excision margins, emphasis on cosmesis, and potentially increased difficulty and morbidity of sentinel lymph node biopsy (SLNB). We examined the influence of such factors on local, regional, and distant recurrence of HNM. Methods Retrospective analysis of a prospective database of all melanoma patients who underwent operation for HNM from Jan 2005 to Jan 2015. Patient demographics, tumor characteristics, operations, and recurrence were recorded. Results 231 patients underwent HNM operations; 63 (27.3%) had melanoma in situ, 78 thin (≤1 mm; 46.4%), 67 intermediate-thickness (1.01-4.0 mm; 40.0%), and 23 thick (>4 mm; 13.7%). Median patient age was 69 years (range 6-94) and median tumor thickness was 1.1 mm (range 0.17-20.0). SLNB was performed on 76 patients (32.9%), of which 9 (11.8%) were positive. Therapeutic lymph node dissection was performed on 12 patients (5.2%); parotidectomy was done on 9 patients (3.9%) as part of SLNB (n=4) or node dissection (n=5). 20 patients (8.7%) did not meet National Comprehensive Cancer Network (NCCN) guidelines for excision margins, while 33 patients (14.3%) did not undergo SLNB as recommended. Recurrence developed in 26 patients (11.3%), comprised of 9 local (3.9%), 4 regional (1.7%), and 13 distant (5.6%). Local recurrence was associated with greater tumor thickness (p=0.0030) and need for complex wound coverage (p=0.0030) but not older age (p=0.55) or excision margins (p=0.79). Distant recurrence was associated with greater tumor thickness (p=0.0043) and positive SLNB (p=0.0002) but not older age (p=0.63) or nonperformance of recommended SLNB (p=0.08). Conclusions Although previous studies have suggested that HNM is associated with a higher probability of local and distant recurrence, these data suggest that HNM lesions have recurrence rates with extremity and trunk sites. Smaller excision margins and nonperformance of SLNB as indicated by NCCN guidelines did not influence local or distant recurrence, respectively. Outcomes following HNM treatment should be expected to be similar to that of truncal and extremity melanoma.

P259

Sentinel Lymph Node Biopsy in Octogenarians with Very Thick Melanomas Does Not Impact Survival

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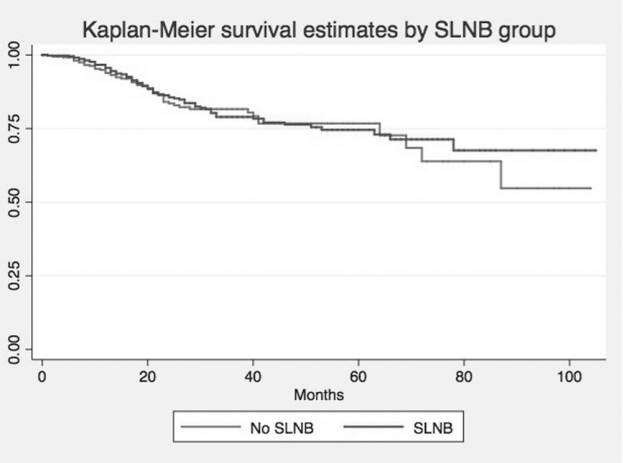
INTRODUCTION: Up to 25% of all melanoma is diagnosed in patients older than 75. Approximately 40% of melanoma deaths occur in this population, yet the impact of sentinel lymph node biopsy (SLNB) in octogenarians with thick melanomas (>4mm) remains unknown. The aim of this study is to conduct a contemporary propensity score analysis of a large database to guide surgical decision-making in this population. METHODS: We conducted an adequately powered propensity-matched analysis of the prospectively collected SEER database (2004-2012). Patients >80 with nonmetastatic, clinically negative LN and thick melanomas (>4 mm) that underwent surgical resection were divided into SLNB and no SLNB groups. Primary outcome was disease-specific survival (DSS). Predictors of SLNB were identified using logistic regression and predictors of survival were identified using Cox proportional hazards model. RESULTS: Of the 883 patients who met the inclusion criteria, 480 (54.4%) underwent SLNB while 403 (45.6%) did not. Patients in the SLNB group tended to be younger, have less thick melanomas (4-8mm), no ulceration, and were diagnosed from 2010 to 2012. In the univariate and multivariate analysis, SLNB had no impact on survival (HR 0.77 (0.51-1.16), p=0.21). Ulceration was associated with decreased survival (HR 1.91 (1.26-2.90), p=0.002) while females lived longer without disease(HR 0.65 (0.45-0.94), p=0.021). After propensity matching for all known variables, SLNB persistently had no impact on DS survival (HR 0.89 (0.56-1.41), p=0.619), and neither did thick melanomas or ulceration in this population. CONCLUSION: SLNB in very thick melanomas in octogenarians had no impact on disease specific survival or overall survival. Further clinical studies need to address this question in this rapidly growing patient population who might be exposed to potentially unnecessary surgical risk.



No DS survival advantage in the SLNB group when compared to the group who did not udergo SLNB(p=0.706) in octagenerians with very thick melanomas

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Treatment with Neoadjuvant Targeted Therapy Yields High Response Rates and Pathologic Complete Responses in Patients with Resectable Metastatic Melanoma

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Introduction: The current standard-of-care (SOC) in resectable metastatic melanoma (stages IIIB/IIIC) is upfront surgery, however up to 70% of patients (pts) treated in this way will relapse and die of disease. The treatment of unresectable metastatic melanoma has been revolutionized through the use of BRAF-targeted therapy and immune checkpoint blockade. We hypothesized that treatment with neoadjuvant targeted therapy would result in a high response rate in this pt population, which may be associated with improved clinical outcomes. Methods: To establish proof-of-concept we treated 9 pts with resectable BRAF-mutant metastatic melanoma with targeted therapy (dabrafenib + trametinib) in the neoadjuvant setting. Tumor measurements were performed pre-treatment and just prior to surgical resection (at week 8-12), and longitudinal blood and tumor biopsies were also acquired. Immune analysis (via 12-marker IHC panel) was performed on pre-treatment, on-treatment and surgical samples when feasible. RECIST responses were determined prior to surgery and pathologic responses assessed on surgical specimens. Results: Eighty-nine % of pts responded (2 CR, 6 PR). Surgical specimen evaluation demonstrated a pathologic CR (pCR) in 4 pts (with no viable tumor cells), and PR in 2 pts (< 50% viable tumor cells). Immune marker analysis (PD-L1, PD-1, CD4, CD8, & FoxP3) demonstrated up-regulation in surgical

specimens compared to pre-treatment tumor biopsies, with the highest immune infiltrate seen in tumors that demonstrated pCRs. Conclusion: This regimen is highly active in this pt population, the high RECIST response rate appears to be associated with an even higher pCR rate, and responses, at least in part, are immune mediated. These data prompted a phase 2 randomized controlled trial investigating this neoadjuvant treatment compared to SOC upfront surgery, with longitudinal tissue and blood sampling to assess for molecular and immune determinants of response, as well as actionable strategies to overcome therapeutic resistance. Results from this and related trials may ultimately help change the SOC.

P261

Head and Neck Melanoma: Differences at Presentation and Treatment Obstacles W.P. Hewgley,* X. Huang, N.M. Hinkle, M.D. Fleming. *College of Medicine, University of Tennessee Health Science Center, Memphis, TN.*

Introduction: Head and neck melanoma (HNM) characteristics differ from other cutaneous melanomas (CM) despite having the same surgical treatment protocol. Also, HNMs present greater surgical complexity due to varied lymphatic drainage patterns, difficulty in excising adequate margins, and cosmetic coverage issues following resection. Methods: This is a retrospective review of 181 HNM cases from a single academic tertiary-care center between June 2003 and January 2014. Pathological data, oncologic outcomes, and surgical treatment were analyzed and compared to published data for CM not arising from the head and neck. Results: A significantly higher percentage of HNM patients presented with melanoma in-situ compared to all other CM (36.4% V 15.7%, $P < 0.0001$). In patients with indications for sentinel lymph node biopsy (SLNB) (99 patients, 54.7%), sentinel lymph node (SLN) positivity (11 out of 86 successful SLNBs, 12.8%) was not significantly different between HNM and published data for non-head and neck CM ($P = 0.74$). This finding contrasts recent reports that HNM may exhibit a lower SLN-positive rate. However, the success rate of SLNB was significantly lower for HNM compared to other CM (88.7% V 94.8%, $P < 0.01$). Out of 11 patients with unsuccessful SLNB, five failed to map on lymphoscintigraphy, and in six patients the sentinel node was unable to be found intra-operatively. Additionally, treatment discrepancies were found in surgical margins of HNM compared to other CM. In wide local excision procedures, 7.1% of excision margins were smaller than NCCN guideline recommends based on Breslow thickness (10 of 141 patients with recorded margins and thickness). Conclusion: Head and neck melanomas present more often as melanoma in-situ than other CM. HNMs presenting at later stages carry similar risk of initial regional node metastasis as other non-head and neck CM. Despite this similar risk, surgical treatment for HNM patients may be complicated by higher failure rates in SLNB and a greater frequency in not obtaining recommended excisional margins due to concerns of cosmesis or function.

P262

Ipilimumab Treatment is Effective for Patients with Melanoma, Whether at Initial Diagnosis or at the Time of Recurrent Disease J.T. Au,* D. Nguyen, J. Farma, A.J. Olszanski, S. Reddy. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

BACKGROUND Ipilimumab, an anti-CTLA4 antibody, is a proven effective treatment for patients with metastatic melanoma (MM), but it is not clear if response is dependent on when ipilimumab is administered. We hypothesized that ipilimumab treatment is equally effective regardless of whether it is administered at initial diagnosis or upon recurrence of melanoma. METHOD A retrospective review of patients with MM started on ipilimumab from 2011-2014 was conducted at a tertiary cancer center. The primary outcomes studied were overall response (defined by complete and partial response), and mortality. RESULTS Of 59 melanoma patients started on ipilimumab for MM, 16 patients (27.1%) were treated at initial diagnosis and 43 patients (72.9%) upon recurrence. Thirty-five patients (30.5%) had prior other treatment besides surgery, such as radiation, immunotherapy, and BRAF inhibitors. After treatment with ipilimumab, 1 patient was lost to follow-up, 4 were not assessable due to lack of measurable disease, and 5 had a mixed response. Of the remaining 49 patients evaluated by RECIST criteria, there were 4 with a complete response (8.16%), 4 with a partial response (8.16%), 4 with stable disease (8.16%), and 37 with progressive disease (75.5%), leading to an overall response rate of 16.3%. There was no significant difference in overall response rate whether ipilimumab was introduced on initial diagnosis or upon recurrence. At a mean time to follow up of 12.0 months, mortality was reduced from 73.2% in patients with no apparent response, to 12.5% in those with a response to ipilimumab ($p=0.001$). CONCLUSION Our findings suggest that a response to ipilimumab is not dependent on the timing of therapy initiation, whether at initial diagnosis or at the time of recurrent disease. Those who respond to ipilimumab have an improvement in overall survival.

P263

Plasma microRNA Dynamics Following Surgical Resection of Metastatic Melanoma N. Latchana,[1]* J.H. Howard,[1] A.A. Gru,[2] X. Zhang,[1] P. Fadda,[1] W.E. Carson III.[1] *1. General Surgery, The Ohio State University, Columbus, OH; 2. University of Virginia, Charlottesville, VA.*

Introduction: MicroRNAs (miR) are noncoding RNAs that inhibit protein translation and regulate melanoma progression however, changes in plasma miR expression patterns following surgical resection of metastatic melanoma are unknown. We hypothesize differences in miR expression profiles exist in patients following complete surgical resection of solitary metastatic melanoma. Methods: Blood collection before and after complete (R-0) surgical resection was performed in 6 individuals with solitary melanoma metastases. RNA extraction was performed and miRs were hybridized with unique fluorescent reporter probes. miR complexes were immobilized on a Nanostring cartridge and florescence was quantified by an nCounter Digital analyzer. The analysis included 5 negative and 5 positive controls as well as 5 housekeeping genes. Statistical analysis was applied using linear mixed effect model. Results: Pre-surgical and post-surgical metastatic melanoma plasma samples contained 216 miRs with expression above baseline. Comparison of plasma following surgical resection to pre-resection samples revealed differential expression of 25 miRs including: miR-let-7a, miR-let7g, miR-15a, miR-16, miR-22, miR-30b, miR-126, miR-140, miR-145, miR-148a, miR-150, miR-191, miR-378i, miR-449c, miR-494, miR-513b, miR-548aa, miR-571, miR-587, miR-891b, miR-1260a, miR1268a, miR-1976, miR-4268, miR-4454 ($P<0.05$). Utilizing $P<0.0046$ as a stringent cutoff to control for 1 false positive among the 216 miRs revealed post-surgical melanoma plasma samples had up-regulation of miR-1260a ($P=0.0007$) and 3.1 fold downregulation of miR-150-5p ($P=0.0026$) relative to pre-surgical samples. Conclusion: Differential expression of miR 150-5p and miR-1260a is present in plasma following surgical resection of metastatic melanoma. Further investigation into plasma miRs is warranted for its utility as a non-invasive marker of melanoma recurrence or persistence post-surgery.

P264

Molecular Profiling and Clinical Outcomes in Patients with In-Transit Recurrence of Melanoma J. Farma,[1] N. Kulkarni,[1] D.A. Escalante,[2] C. Meade,[2] N. Osevala,[2] M. Zibelman,[1] K.S. Gustafson,[1] H. Wu,[1] M. Lango,[1] S. Reddy,[1] S. Movva,[1] A.J. Olszanski,[1] F.S. Zih.[1]* *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Temple University Hospital, Philadelphia, PA.*

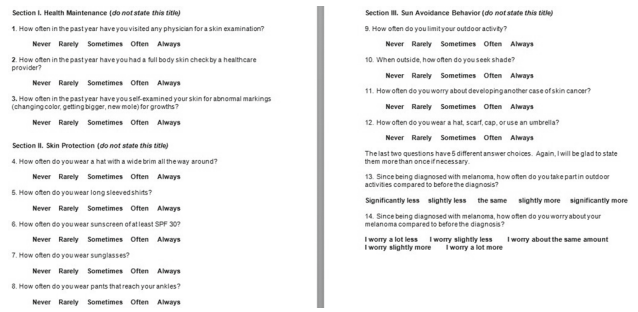
INTRODUCTION: The use of molecular profiling has become increasingly important in providing valuable information on primary cancers with the potential to uncover actionable mutations and provide prognostic information. Our institution has been using next generation sequencing (NGS) to examine mutations in 50 cancer-related genes. Here we examine the use of molecular profiling of patients who presented with in-transit recurrence of their melanoma METHODS: Patients with in-transit recurrence of malignant melanoma (MM) were included in the study. Using NGS, we analyzed tissue samples for mutations in targeted regions of 50 cancer-related genes. Clinical and pathologic data were collected. RESULTS: We performed NGS on 93 patients with MM, of these 13 patients presented with in-transit recurrence. Median age at diagnosis was 67 years (range 37-90) and 54% were male (n=7). Location of the primary included head and neck (n=1), lower extremity (n=5) and upper extremity (n=7). At presentation, three were stage I, two were stage II and nine were stage III. Of the tissue tested nine were from in-transit nodules and four were from the primary tumor. In total 30 mutations were identified, affecting 16 unique genes. No mutations were found in 15% of patients (n=2), while 38% of patients (n=5) had only one mutation, 8% (n=1) had 2 mutations, 15% (n=2) had 3 mutations, 15% (n=2) had 4 mutations. One patient (8%) had 9 mutations. The most frequently identified mutations included NRAS (n=6), TP53 (n=4), BRAF V600 (n=2), ATM (n=2), FLT3 (n=2), KRAS (n=2) and PDGFRA (n=2). CONCLUSIONS: Using our NGS platform in patients with in-transit melanoma we identified the most common mutations are NRAS in

46% and TP53 in 31% of patients. Further studies will identify and correlate specific patterns of mutation with treatment response and survival outcomes.

P265

Are there Gender-Based Differences in Skin Protection Behaviors Post Cutaneous Melanoma Treatment? J. Shih, J. Chen, A. Mullane, A.D. Tran, C. Thomas, N. Aydin, S. Misra.* *TTUHSC, Amarillo, TX.*

Introduction: Skin protection behaviors and environmental exposures play a crucial role in the development and subsequent management of melanoma. Patients with previous melanoma also have increased risk of developing subsequent melanoma. However, not much is studied on skin protection behaviors practiced by patients post melanoma treatment, especially in high risk patients. Methods: Patients diagnosed and surgically treated for cutaneous melanomas over the last six years in a geographical high risk area for melanoma were surveyed. Telephone surveys with a standardized script using categorical answers for how often each patient engaged in skin protective behaviors were used (Survey Sample Chart 1). Patient demographics, tumor characteristics, treatment modalities including extent of surgery were analyzed. Descriptive statistics were used to quantify the extent of behavioral modifications. Results: 117 surveys were obtained, 59 males and 58 females with ages ranging from 14 - 88 years. Males (62%) more often used a wide brim hat than females (38%), $p<0.05$. Females (61%) more often seek shade when outside than males (39%), $p<0.05$. 86% of patients reported skin self-examination for abnormal markings more often. 94% reported wearing skin protective clothing more often. 76% females and 56% males reported limiting their outdoor activity more often. 81% of patients worry more about their melanoma compared to before their diagnosis; females greater than males. 57% of patients reported wearing sunscreen greater than SPF 30 less often. Conclusion: Larger percentage of females than males adopted behavioral changes to prevent future cutaneous melanoma. However, male study participants were more likely to protect the face than females through use of a wide brim hat or cap. This could possibly be due to behavioral change, but we hypothesize it is more likely that males have careers involving agriculture or livestock in this area of the country. In addition, it is essential to educate patients to increase sunscreen application. There was a trend towards younger patients adapting more skin protection behaviors than patients older than 65 years of age.



Section I. Health Maintenance (*do not state this title*)

1. How often in the past year have you visited any physician for a skin examination?
Never Rarely Sometimes Often Always

2. How often in the past year have you had a full body skin check by a healthcare provider?
Never Rarely Sometimes Often Always

3. How often in the past year have you self-examined your skin for abnormal markings (changing color, getting bigger, new mole) for growths?
Never Rarely Sometimes Often Always

Section II. Skin Protection (*do not state this title*)

4. How often do you wear a hat with a wide brim all the way around?
Never Rarely Sometimes Often Always

5. How often do you wear long sleeved shirts?
Never Rarely Sometimes Often Always

6. How often do you wear sunscreen of at least SPF 30?
Never Rarely Sometimes Often Always

7. How often do you wear sunglasses?
Never Rarely Sometimes Often Always

8. How often do you wear pants that reach your ankles?
Never Rarely Sometimes Often Always

Section III. Sun Avoidance Behavior (*do not state this title*)

9. How often do you limit your outdoor activity?
Never Rarely Sometimes Often Always

10. When outside, how often do you seek shade?
Never Rarely Sometimes Often Always

11. How often do you worry about developing another case of skin cancer?
Never Rarely Sometimes Often Always

12. How often do you wear a hat, scarf, cap, or use an umbrella?
Never Rarely Sometimes Often Always

The last two questions have 5 different answer choices. Again, I will be glad to state them more than once if necessary.

13. Since being diagnosed with melanoma, how often do you take part in outdoor activities compared to before the diagnosis?
Significantly less slightly less the same slightly more significantly more

14. Since being diagnosed with melanoma, how often do you worry about your melanoma compared to before the diagnosis?
I worry a lot less I worry slightly less I worry about the same amount
I worry slightly more I worry a lot more

P266

The Incidence and Prognostic Significance of Acquired Genetic Mutations Among High-risk Primary Melanoma Patients Undergoing Surgery C. Del Guzzo,* A. Levin, K. Collins, P. De La Cruz, B. Taback. *Columbia University Medical Center, New York, NY.*

Introduction: Acquired mutations in BRAF, NRAS and c-KIT provide useful therapeutic targets for patients with metastatic melanoma. However, their prognostic utility in patients with earlier stage disease has not been clearly assessed. In this study, we evaluated the incidence and prognostic utility of genetic mutations in patients with high-risk cutaneous melanomas presenting for surgery to our melanoma center. Methods: A single institution prospective study of patients diagnosed with cutaneous melanoma presenting with AJCC stage IIB or greater who were deemed surgical candidates for complete disease resection. Tumors were evaluated for BRAF (exons 11 and 15), NRAS (exons 1, 2, and 3) and c-KIT (exons 2, 9, 10, 11, 13, 14, 15, 17, 18) mutations. Tumor tissue was collected from 53 patients of whom we excluded 5 patients with mucosal melanoma, 4 patients with unknown primary tumors, 4 patients with tissue insufficient for analysis, and 3 patients with a lower AJCC stage. Results: Among the 37 patient tumors tested: 14 (38%) had BRAF mutation, 16 (43%) had NRAS mutation and none had c-KIT mutation. Seven (19%) patients were wild-type. There was no significant difference between mean patient age in years (69, 63 and 71), Breslow thickness in millimeters (2.5, 2.5, 3.0) and percent lymph node positivity (43%, 19%, 43%) and the presence of mutated BRAF, NRAS or wild-type status. Mean time from initial diagnosis to first recurrence was 19.5 months for BRAF mutants, 22.5 months for NRAS mutants and 30 months for wild-type patients. Conclusions: In this study of high-risk melanoma patients, referred for surgery, with similar clinical-pathologic prognostic features, a greater proportion harbored NRAS mutations. Furthermore, there was a trend towards earlier recurrence among patients with a BRAF or NRAS mutation. Mutational analysis may not only have predictive utility for guiding therapy in patients with metastatic disease but may be of prognostic importance for earlier stage high-risk patients. Larger studies in similar cohorts of patients are ongoing.

P267

Non Surgical Management and Interval Cholecystectomy is Preferred for Acute Cholecystitis in Cancer Patients D. Santos,* B. Badgwell. *Surgical Oncology, MD Anderson, Houston, TX.*

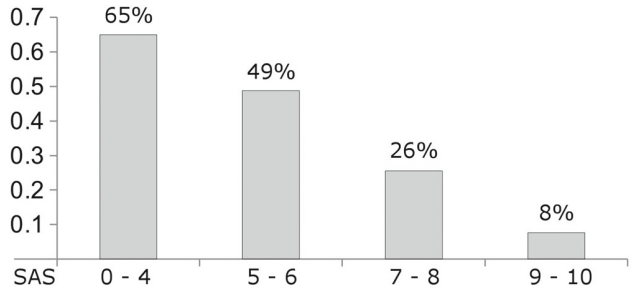
Background: Early cholecystectomy (EC) for acute cholecystitis (AC) is standard of care, however, cancer patients on chemotherapy with immunosuppression or poor prognosis may not be optimal candidates for this approach. Hypothesis: Observation (OBS) and percutaneous cholecystostomy tube (PCT) placement are effective for initial management, but interval cholecystectomy is necessary to prevent recurrent symptoms and delays in chemotherapy. Design: Retrospective cohort study of patients presenting to the surgical oncology service from January 2001 to December 2014 for acute cholecystitis. Setting: Academic tertiary referral center Methods: Adult patients presenting with clinical symptoms of AC and at least one positive imaging study were included. Patients were divided into three groups based on clinician decision to treat with OBS, PCT, or EC. The primary endpoint of successful treatment was resolution of abdominal pain and discharge. If initial management failed to resolve AC, rates of change to different treatment strategies were calculated. The interval cholecystectomy rate was calculated for patients managed nonsurgically. Patient characteristics were compared using Kruskal Wallis and Chi-square tests. Results: 259 patients underwent consultation, and 126 patients met study criteria. 81 patients were selected for OBS, 33 for PCT, and 12 for EC. Patients with abdominal tenderness were more likely to undergo PCT placement ($p = 0.05$) and patients with the highest platelet counts were more likely to have surgery ($p = 0.04$). 97/126 (77%) patients had advanced malignancy, and 37/126 (29%) were not surgical candidates. 65/81 (80%) were successfully observed and 31/33 (94%) were successfully managed with PCT. Interval cholecystectomy was required for 34/126 (27%) of patients managed non-operatively. The median time to interval cholecystectomy after PCT placement was 70 days, and OBS patients was 33 days. Conclusion: The majority of cancer patients with acute cholecystitis will not be managed with early cholecystectomy. PCT has a higher success rate than observation. Interval cholecystectomy is frequently required and can delay chemotherapy by several weeks.

P268

Surgical APGAR Score Predicts Major Complications of the Patients After Hepatectomy I. Mitsiev,[1]* D. Yu,[2] D. Taber,[2] J. McGillicuddy,[2] C. Bratton,[2] P. Baliga,[2] K. Chavin.[2] *1. General Surgery, Greenville Health System, Greenville, SC; 2. Medical University of South Carolina, Charleston, SC.*

Introduction Hepatectomy is a complex procedure with high morbidity and mortality. Early prediction and prevention of major complications is of great value for optimization of patient care. Surgical APGAR score (SAS) during the operation has been validated to predict complications after general, gynecological, and urological procedures. Identifying SAS as a predictor for major complications after hepatectomy might help improving the overall outcome. Methods 119 patients undergoing liver resection between Jan 2002 and Jan 2012 were included in this study. 132 variables were collected and analyzed, including demographics, preoperative, perioperative, and postoperative indices. Major complications were categorized based on established definitions, including Clavien-Dindo's classification for Surgical Complications. Pearson's chi-square test was used for nominal variables and Wilcoxon singed rank test was used for continuous variables; discrimination was computed with the c-statistic from a univariable logistic regression. Results A total of 119 patients (41 men, 78 women; mean age 50.33 years) undergoing liver resection

during the study period were identified. Major complications were associated with gender, age, comorbidity index, and hepatitis. Surgical APGAR score ($p = 0.001$), together with estimated amount of blood loss ($p = 0.0003$), and lowest heart rate ($p = 0.0183$), was significantly associated with major complications. Comparing to the patients with scores of 9 or 10, the relative risk of the patients with scores from 0 to 4, 5 to 6, and 7 to 8, was 22.285, 11.40, and 4.114, ($p = 0.0065$, 0.0254, or 0.1957) respectively. Conclusion Surgical APGAR score provides accurate risk stratification for major postoperative complications after hepatectomy.



Complication rate related to Surgical APGAR Score

P269

Biphasic Learning Curve of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion: Technical Competence and Refinement of Patient Selection N. Shannon,* C. Ong, G. Tan, C. Chia, K. Soo, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemoperfusion (HIPEC) is routinely used to treat selected patients with peritoneal carcinomatoses, but can be associated with relatively high complication rates, prolonged hospital stay, and potential mortality. Our objective was to determine the learning curve of CRS/HIPEC in our institution, representing the largest Asian cohort to date. Methods: 150 consecutive patients with peritoneal carcinomatosis treated with CRS/HIPEC between 2001-2014 were grouped into three cohorts of 50 patients and studied. Primary outcomes included severe morbidity (Clavien-Dindo grade III-V), duration of ICU and hospital stay. Secondary outcomes were duration of peritonectomy and rate of incomplete cytoreduction (CC score 2-3). P-values indicate trend across all cohorts. Results: Overall median age was 52 years. There was no significant difference in age, sex, or histological type across cohorts. Duration required to accumulate each cohort decreased over the study period (8.9, 2.3, 1.4 years). Overall rates of incomplete cytoreduction (2%), severe morbidity (22%), and 60-day mortality (2.7%) were comparable to previously reported data. Decreases in rate of serious morbidity, (38%, 30%, 10%, $p<0.01$), duration of ICU stay (2.9, 2.2, 2.4 days, $p=0.029$) and total hospital stay (23, 23, 17 days, $p=0.053$) were seen across consecutive cohorts. A significant decrease in duration of peritonectomy occured after the first cohort (10.4, 7.9, 8.1 hours, $p<0.01$). Rate of incomplete cytoreduction also decreased (4.6%, 2.1%, 0%, $p=0.29$) despite an increase in average PCI score (10.2, 14.4, 12.3, $p<0.01$). Conclusions: Whilst 50 cases were adequate for familiarity with the procedure and decreased average operation time, significant improvement in the rate of serious morbidity was only observed after 100 operations. This may reflect an initial period of training in which technical competence is achieved, followed by a subsequent period characterised by increasingly complex cases (higher PCI score) and refinement of patient selection.

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Development of a Simulated Interprofessional Geriatric Surgery Curriculum: Challenges and Opportunities T. Nguyen,* M. Tan, R. Bharadwaj, A. Mishra, L. Covington, D. Cassida, J. Smoot, G. Gilbert, N. Aydin, R. Jordan, S. Misra. *Texas Tech University Health Sciences Center, Grand Prairie, TX.*

Background: Majority of oncology patients are elderly with unique needs that require significant Interprofessional teamwork. The benefits of using simulation to deal with delicate clinical issues are well documented. Given the limited teaching exposure for this patient population, we implemented a simulation based, Interprofessional (IPE) Geriatric Surgery education curriculum. Method: Faculty from the School of Medicine, Pharmacy, Nursing and Simulation lab collaborated on developing educational scenarios focusing on common perioperative surgical issues faced by the elderly including post-operative dementia, delirium, polypharmacy, malnutrition and frailty. A standardized patient was trained to simulate these real-life issues. Students from all three disciplines collaborated during a two hour simulated, IPE session to learn these topics. A pre and post learning exam was administered to assess change in knowledge. Students' assessment of the IPE and simulated group exercise was analyzed on a 5 point Likert scale. Results: Organizing multiple faculty schedules was an organizational challenge but was doable given the shared interest and with help from senior educational leadership. Sixteen students participated from the three schools. 93% of students felt the session improved their knowledge of the geriatric field while 81% reported improved knowledge about team structure, communication and felt an improved sense of their roles in a healthcare setting. 100% of students' stated that they would like more IPE training as it leads to improved patient safety and outcomes. Conclusion: As students graduate from book-based learning to clinical training, it is necessary to provide them with the confidence and knowledge to approach patients in various clinical settings. By performing in a controlled, low risk environment, students are awarded the opportunity to learn about vulnerable populations. Students express a positive experience overall with this learning approach and reported a better understanding of the importance of IPE training. Senior education leadership support is crucial in establishing an IPE based simulation curriculum.

Student Feedback of Stimulated Training Session

Responses	Improvement in knowledge of the geriatrics field	Improvement in knowledge of team structure	Improvement in knowledge of leadership roles	Improvement in knowledge of mutual support	Improvement in knowledge of situational monitoring	Improvement in knowledge of communication
Made it much better	50%	25%	0%	18.75%	6.25%	25%
Made it better	43.75%	56.25%	43.75%	50%	68.75%	56.25%
No change	6.25%	18.75%	56.25%	31.25%	25%	18.75%
Made it worse	0%	0%	0%	0%	0%	0%
Made it much worse	0%	0%	0%	0%	0%	0%
Total %	100%	100%	100%	100%	100%	100%

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Isolated Chemotherapeutic Perfusion as Neoadjuvant Therapy for Advanced/Unresectable Pelvic Malignancy H. Wanebo,[3]* G. Begossi,[2] J. Belliveau,[1] E. Gustafson.[1] *1. Surgical Oncology, Roger Williams Medical Center, Providence, RI; 2. Alta Bates Summit Medical Center, Oakland, CA; 3. Roger Williams Medcenter; Brown University, Providence, RI.*

Introduction: Previous chemo radiation usually precludes neoadjuvant therapy for advanced pelvic malignancy. Neoadjuvant isolated pelvic perfusion (IPP) provides higher tissue drug levels with less toxicity than systemic therapy and may enhance resectability . We have performed 113 IPP in 75 such patients (59 for pre-op therapy and 16 palliative). Methods: There were 50 pts with advanced, irradiated, recurrent rectal cancer (34 pre-op and 16 palliative), 8 pts had advanced anal SCC, 6 pts with pelvic sarcoma, 4 pts with pelvic melanoma, and 7 other advanced cancers (endometrial (2), ovarian (3), and bladder (2 pts). Hyperthermic IPP for 60 mins utilized regimens targeted to malignancy type. High dose IPP with stem cell support was utilized in 3 advanced chemo resistant pts. Results: Neoadjuvant IPP in 26 recurrent rectal cancer pts rendered 15 potentially resectable, achieving a complete path CR in 2 patients and facilitating curative pelvic resection in 7 pts. The remaining 8 pts were non-resected because of medical status (5) or pt refusal (3). Median survival post IPP was 24 mos in 15 resectable pts, 30 mos in the 7 resected pts (2 survived > 5 yrs) and 8 mos in 11 non-resectable pts. It was 23 and 8 (resected vs non resected) months in 8 advanced SCC anal pts and 28 and 24mo in advanced gyn cancer pts (endometrial/ovarian),13 mos in 4 advanced melanoma pts, and only 5 mos in 6 sarcoma pts (1 resectable). High dose IPP with stem cell support induced significant regression (with resection) in 2 of 3 pts with advanced chemo resistant (Endometrial/Melanoma) malignancy. Overall, of 59 neoadjuvant pts, 34 (58%) responded to IPP, 21 (36%) were resected, and the remaining 25 pts (42%) were considered reasonably palliated. Conclusion:

IPP has promise in augmenting resectability (or palliating) selected patients with advanced pelvic malignancy not amenable to primary resection or previously treated with conventional chemo RT+/- surgery. . IPP responsive tumors included recurrent rectal and anorectal cancers, and localized gyn cancers and melanoma. Sarcomas were quite resistant. Biologic therapy or stem cell support are viable future options to enhance outcome of IPP.

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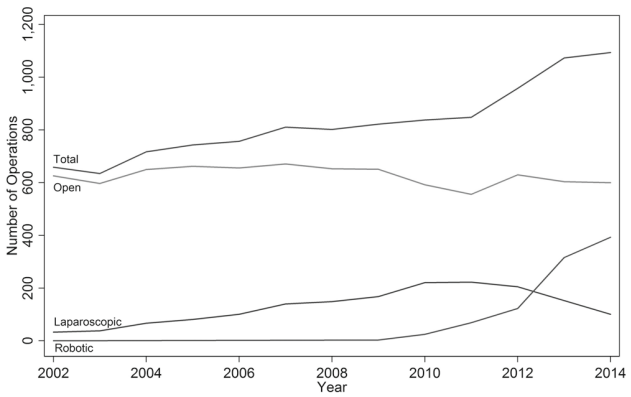
Evolution of Minimally Invasive Surgery at a Tertiary Cancer Center: Analysis of 10,000 Intraabdominal Cases L.V. Selby,* R.P. DeMatteo, W.R. Jarnagin, J. Garcia-Aguilar, P. Allen, P.T. Kingham, M. Weiser, M.F. Brennan, V.E. Strong. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Patients and providers are increasingly interested in the safety and efficacy of minimally invasive surgery (MIS) for the treatment of solid tumors. We reviewed thirteen years of institutional experience with the use of MIS techniques (both laparoscopic and robotic) for the resection of intra-abdominal malignancy. Methods: Following IRB approval, we queried operating room records since 2002 to identify patients undergoing distal pancreatectomy, gastrectomy, colectomy, and proctectomy. Operative Current Procedural Terminology (CPT) codes were used to classify all relevant operations as open or MIS. Results: In total we identified 10,757 relevant operations, 24% (2,609 / 10,757) of which were MIS. In 2002 only 5% (33 / 656) of all relevant resections were MIS, increasing to 21% (171 / 821) by 2009 and 45% (494 / 1,094) in 2014 (Figure 1). This increase reflects two distinct periods of adoption of MIS techniques: pre-2009 and post-2009. Prior to 2009, all MIS procedures were laparoscopic, accounting for 19% (149 / 802) of all resections in 2008. Since its introduction in 2009, robotic surgery has rapidly become the predominant MIS modality; increasing from 0.4% (3 / 822) of all resections when first introduced, to 36% (393 / 1,094) of all resections in 2014. Robotic approaches currently represent 80% (393 / 494) of all MIS resections. MIS volume has come in addition to, not instead of, resections performed open; we consistently perform approximately 600 open resections yearly (623 in 2002, 600 in 2014). Post-operative mortality has remained less than 1% for both open and MIS resections and the perioperative complication rate for MIS resections has remained equivalent to, or better than, open resections. Conclusion: Utilization of MIS techniques has increased substantially since 2002, and since 2009 robotic surgery is the predominant approach. We have demonstrated the safe adoption of MIS for the resection of intra-abdominal malignancies at a large volume specialty cancer center.



P273

Prognostic Significance of Neutrophil/Lymphocyte Ratio (NLR) and Platelet/Lymphocyte ratio (PLR) in Predicting Outcomes for Peritoneal Carcinomatosis Patients Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy W. Loh,[2]* S. Tan,[1] G. Tan,[2] C. Chia,[2] M. Teo.[2] *1. General Surgery, Ministry of Health Holdings, Singapore, Singapore; 2. Singhealth, Singapore, Singapore.*

Background: Laboratory markers of systemic inflammation have demonstrated utility and cost-effectiveness in the prediction of clinical outcome in various cancer subtypes. However, its significance in Peritoneal Carinomatosis (PC) patients is hitherto undetermined. The aim of the present study is to evaluate the prognostic value of the neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) in PC patients who have undergone cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in a single institution. Method: Data was prospectively collected from 168 consecutive patients who underwent CRS and HIPEC between 2001 and 2014, where pre-operative NLR and PLR were obtained. The primary endpoints in our study were overall survival (OS) and disease-free survival (DFS). Preliminary Results: 97 patients of which 126 women (75.0%) and 42 males (25.0%) with a mean age of 50.3 ± 12.9 years were included. Primary tumors were ovarian cancer (n = 58), colorectal cancer (n = 56), appendiceal cancer (n = 37), primary peritoneal carcinoma/mesothelioma (n = 17). The median DFS for NLR>2.5 was significantly poorer at 11.67 months (95% CI 8.24 – 13.85) compared to NLR<2.5 at 17.87 months (95% CI 15.25 – 19.42) (p = 0.006). Kaplan-Meier survival analysis demonstrated that a higher NLR resulted in poorer DFS compared to lower NLR (Log-Rank Test p = 0.012). Multivariate Cox-regression model established a significant relationship between NLR and DFS (HR = 1.78 95% CI 1.55 – 1.89 p = 0.032). A higher PLR ratio significantly yielded in a poorer DFS on the Kaplan-Meier survival curve (Log-Rank test p = 0.025). Correlation of both NLR and PLR with OS did not yield any statistical significance. Conclusion: Our study shows that inflammatory scores, in particular NLR, can prognosticate the recurrence risk and survival of PC patients post CRS and HIPEC.

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Rethinking Priorities: Incremental Cost of Complications for Elective Resection C.K. Zogg,[1]* S. Murphy,[1] N.R. Changoor,[1] P. Najjar,[1] T.C. Tsai,[1] J.W. Scott,[1] J.A. Rose Jr.,[1] E.J. Lilley,[1] D.L. Zogg,[2] T.M. Pawlik,[3] A.H. Haider.[1] *1. Surgery, Center for Surgery and Public Health, Harvard Medical School and Harvard T.H. Chan School of Public Health, Department of Surgery, Brigham and Women's Hospital, Boston, MA; 2. Minnesota Gastroenterology, PA, Saint Paul, MN; 3. Division of Surgical Oncology, Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD.*

Introduction: Rising healthcare costs ($207 billion/year among cancer patients by 2020) have led to increasing focus on the need to achieve a better understanding of the association between costs and quality. Evidence from elective colectomies suggests a mismatch between management strategies (e.g. pay-for-performance) and complications influencing hospital costs. The objective of this study was to compare incremental costs associated with complications of major gastrointestinal (GI) elective resections using national data. Methods: Data from the 2003-2011 National Inpatient Sample were queried for adult (≥18y) patients undergoing elective resections with primary admitting diagnoses of malignant neoplasm: esophagus, stomach, colon, liver, pancreas, rectum. Based on system-based complications considered relevant to long-term treatment of elective operations for GI conditions, stratified differences in risk-adjusted incremental hospital costs and complication probabilities were compared [GLM (family gamma, link log), post-estimation marginal effects]. Secondary clinical outcomes included: in-hospital mortality, non-routine discharge, LOS. Changes in complication probabilities over time (9y of data) were also assayed. Results: A total of 137,854 patients were included, weighted to represent 677,498 patients nationwide. 23.6% experienced complications: 45.8% esophageal, 31.9% gastric, 21.1% colonic, 22.9% hepatic, 32.2% pancreatic, 23.5% rectal. Annual risk-adjusted incremental costs for each amounted to >$302 million overall. Magnitudes of complication prevalences/costs varied by complication group. Infectious complications contributed the most ($72.8 million/year), followed by pulmonary ($60.7 million), GI ($55.5 million). Total annual index hospital costs for elective GI resections amounted to >$1.6 billion: 17.8% due to complications (7.5% CMS complications; 7.1% SSI). Conclusion: The results highlight a need to consider the varied/broad impact of complications, offering a stratified paradigm for surgical priority setting. As we move forward in the development of novel/adaptation of existing interventions, it will be essential to weigh the cost of complications in evidence-based ways.

Table. Risk-adjusted predicted mean incremental costs (95%CI) in 2015 USD, stratified by complication type, among a nationally representative population-weighted sample (select complications shown)

	No Comp.	Any Comp.	Infection	Pulmonary	Gastrointestinal
	(base cost)	(incremental cost)	(incremental cost)	(incremental cost)	(incremental cost)
Esophageal	$40,963.70 ($37,969-43,958)	$37,732.94 ($33,248-42,216) p<0.001	$38,011.56 ($32,358-43,664) p<0.001	$24,716.54 ($20,460-28,972) p<0.001	$20,795.35 ($13,749-27,841) p<0.001
Gastric	$26,760.56 ($25,516-28,005)	$30,662.69 ($27,656-33,668) p<0.001	$29,604.46 ($26,517-32,691) p<0.001	$20,323.15 ($17,912-22,734) p<0.001	$14,669.54 ($12,105-17,233) p<0.001
Colonic	$15,139.05 ($14,858-15,419)	$11,838.10 ($11,295-12,380) p<0.001	$14,355.76 ($13,605-15,105) p<0.001	$9,697.77 ($9,105-10,290) p<0.001	$5,117.26 ($4,741-5,492) p<0.001
Hepatic	$21,175.49 ($20,281-23,223)	$29,762.09 ($25,469-34,054) p<0.001	$28,434.47 ($24,649-32,219) p<0.001	$18,494.37 ($14,529-22,459) p<0.001	$12,149.71 ($9,207-15,092) p<0.001
Pancreatic	$32,467.53 ($30,669-34,265)	$25,613.46 $23,056-28,170) p<0.001	$27,237.60 ($24,225-30,249) p<0.001	$16,333.73 ($13,715-18,951) p<0.001	$9,016.57 ($6,729-11,303) p<0.001
Rectal	$17,605.09 ($17,103-18,106)	$13,514.39 ($12,646-14,382) p<0.001	$14,911.60 ($13,853-15,969) p<0.001	$10,601.72 ($9,640-11,562) p<0.001	$6,110.83 ($5,493-6,728) p<0.001

Physiologic system-based complication groups included: mechanical wounds, infections, urinary complications, pulmonary complications, gastrointestinal complications, cardiovascular complications, systemic complications, and complications during surgery (Zogg et al. Ann Surg 2015). Models accounted for potential confounding due to patient characteristics (age, sex, race/ethnicity, insurance type, median income quartile, CCI, and year) and hospital-level factors (hospital volume, teaching-location, and geographical region). Calculation of incremental additions also accounted for the potential influence of multiple complications by adjusting for the occurrence of all other complications to yield isolated, complication-specific effects.
Modeling used NIS-provided population weights generalized with STATA's "svy" command to account for patient clustering within hospital-level variables and to extrapolate the sample to a nationally representative version of the US population. Predicted mean differences were calculated using post-estimation marginal effects following GLM with link log, family gamma, to account for the highly skewed nature of the data.

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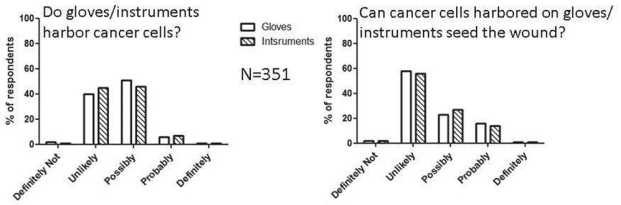
Glove and Instrument Handling in Cancer Cases: A Survey of Surgeons' Beliefs and Practices D. Berger-Richardson,* A. Govindarajan, R. Gladdy, A. McCart, C.J. Swallow. *Surgery, University of Toronto, Toronto, ON, Canada.*

Introduction: Based on empirical observation, the changing of gloves and instruments following the extirpative phase of cancer surgery is variably practiced amongst surgeons. Standardizing such a practice has potential to reduce locoregional and wound recurrences. However, the evidence that gloves/instruments act as vectors of cancer cell seeding is weak. Purpose: To explore surgeons' beliefs and practices regarding glove/instrument handling during cancer surgery, and identify triggers to change. Methods: A survey consisting of multiple choice and free response questions was mailed to all 945 general surgeons listed in the public registry kept by the College of Physicians and Surgeons of Ontario (Canada). Inclusion criteria were: 1) staff surgeon; 2) perform cancer resections; 3) in active practice in Ontario. Results: 438 surveys were returned (46%). 87 not meeting inclusion criteria were excluded from analysis. Respondent characteristics confirmed that the survey reached the target demographic, with variation in years in practice, type of practice (academic, community), and fellowship training that reflects the population of general surgeons in Ontario. 52% of respondents reported that they change gloves during cancer resections with the intent of decreasing the risk of tumor seeding. 41% of respondents change instruments for this purpose (p<0.01 vs. gloves). The most common rationale cited for changing gloves/instruments was "gut feeling" (42%), followed by "clinical training" (40%); "clinical evidence" was cited by only 3%. 73% of respondents take measures to protect the wound during laparoscopic cancer resection (wound protector, specimen retrieval bag) vs. 45% during open resection (wound barriers, irrigation) (p<0.01). Respondents believe that gloves and instruments are equally likely to harbor malignant cells, but the majority do not believe that these retained cells contribute to tumor seeding (Figure). Conclusion: Amongst surgeons who perform cancer resections, there is no consensus as to how gloves and instruments should be handled. Future studies should determine whether surgical gloves and instruments harbor malignant cells that are capable of seeding wounds.



P276

Rural Residence Correlates with Low Volume Surgical Centers and Poorer Survival for Pancreatic Adenocarcinoma B.J. Flink,[1]* Y. Liu,[2] R. Rochat,[2] D.A. Kooby,[2] J. Lipscomb,[2] T.W. Gillespie.[2] *1. Atlanta VA Medical Center, Decatur, GA; 2. Emory University, Atlanta, GA.*

Introduction: Pancreatic adenocarcinoma (PA) is a lethal cancer with over 41,000 new cases diagnosed annually in the United States. Previous studies demonstrate improved PA patient outcomes when surgery occurs in high volume (HV) centers. We examined pancreatic resection at HV centers and its relationship to rurality (rural, urban, metro) and overall survival (OS). Methods: Using the National Cancer Data Base from 2003 to 2011, we identified PA patients who underwent resection with curative intent. HV resection was defined according to the American Cancer Society and National Comprehensive Care Network volume standards, recommending resection at a center performing ≥ 15 per year. Rurality was categorized using Rural Urban Continuum Codes with "rural" the least populated and "metro" the most populated. Univariate and multivariate logistic regression models were used to examine receipt of HV resection, while univariate, multivariate and stratified Cox regression models were used to analyze OS. Results: Of 14,824 patients, 8,275 (55.8%) were resected at HV centers. The majority (80.8%) of patients resided in metro areas, 17.1% in urban areas and only 2.1% in rural areas. Both rural and urban patients had reduced odds of HV resection as compared with metro patients and this disparity was more pronounced on multivariate analysis (OR 0.31-0.4; Table 1). In the full model, HV resection was associated with improved OS (HR 0.88 [95% CI 0.79-0.99]) while rurality was not (Table 1). However, stratification by volume revealed that rural patients had poorer OS amongst patients at low volume centers (HR 1.65 [95% CI 1.06-2.56]; Table 1). Conclusions: Patients in rural and urban areas receive less benefit from HV resection compared to those in metro areas. Furthermore, rural patients have poorer OS amongst patients who do not receive HV resection. To our knowledge, this is the first study to examine rurality and HV resection for PA and thus, the reasons for these findings should be pursued. Given our findings and the improved outcomes associated with HV resection for PA, efforts to improve access to HV centers for patients living outside metro areas are warranted.

Table 1: Multivariate Regression for HV Resection and Overall Survival by Rurality

Logistic Regression Models for HV Resection			
Rurality	n (%)	OR (95% CI)	
		Univariate	Multivariate
Metro	11116 (80.8)	Ref	Ref
Urban	2360 (17.2)	0.9 (0.83-0.99)*	0.4 (0.35-0.47)*
Rural	284 (2.1)	0.69 (0.55-0.88)*	0.31 (0.22-0.42)*
Cox Regression Models for Overall Survival			
Rurality	HR (95% CI)		
	Full Model	Stratified by Center Volume	
		Low Volume (<15 cases/year)	High Volume (≥15 cases/year)
Metro	Ref	Ref	Ref
Urban	1.04 (0.92-1.18)	1.12 (0.93-1.35)	1.04 (0.92-1.18)
Rural	1.15 (0.84-1.58)	1.65 (1.06-2.56)*	1.13 (0.83-1.55)

*=p<0.05; Multivariate models were adjusted for demographic factors, comorbidities, tumor, and treatment factors

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Disseminated Cancer Further Increases the Risk of Venous Thromboembolism in Patients Undergoing Major Abdominal Surgery for Malignancy A. Teng,* G. Bellini, C. Yang, K. Rose. *Mt Sinai St.Luke's Roosevelt, New York, NY.*

Introduction-Pulmonary embolism (PE) and deep venous thrombosis (DVT) are major complications of abdominal operations. We aimed to study the absolute incidence of venous thromboembolism (VTE), factors associated with VTE, and outcomes for patients undergoing major abdominal surgery for malignancy. Methods-The NSQIP database from 2005-12 was utilized to study major abdominal operations (esophagectomy, gastrectomy, pancreatectomy, enterectomy, hepatectomy, colectomy and proctectomy) in patients with an ICD-9 cancer diagnosis. Predictors of VTE and their relation to survival were identified. Results-In a cohort of 17,201 patients, the absolute incidence of DVT was 2.5% (n=424), and PE was 1.3%(n=222) during the 30-day period. The highest rate of VTE occurred after esophagectomy (5.8%) followed by hepatectomy (3.9%), colectomy and proctectomy (3.7%), pancreatectomy (3.2%), gastrectomy (2.5%) and enterectomy (1.4%). Patients who developed VTE had longer operative times (356 vs 319 min, p<0.001), more transfusions (17.5% vs 12.1%, p<0.001), and experienced a higher rate of return to the operating room (17.8% vs 7.2%, p<0.001) compared to those who did not. Furthermore, patients who experienced VTE events also experienced a higher rate of infectious complications (organ space 18.8 vs 7.3%, p<0.001;sepsis 20.8 vs 8.2%, p<0.001; wound disruption 2.7 vs 1.6%, p=0.03). On multivariate analysis, age between 61-79, BMI >20, dependent functional status, disseminated cancer, radiation therapy, history of dyspnea with exertion, and operative time >248 min were all associated with occurrence of VTE (Table 1). Occurrence of VTE was associated with mortality on multivariate analysis (OR 2.7 CI 1.9-3.8, p<0.001). Conclusion-Malignancy is a well-known risk factor for VTE. However, this study demonstrates that disseminated cancer further increased this risk almost 2 fold after a major abdominal operation. Furthermore, bleeding complications, long operations, increased BMI, and poor functional status all increased risks of VTE. Surveillance strategies need to be implemented for those cancer patients who have multiple risk factors for VTE.

Multivariate Analysis of Factors Significantly Associated with VTE Requiring Therapy

Prognostic Factors	VTE Requiring Therapy	
	Adjusted OR (95% CI)	p value
Age		
≤60	Referent	
61-79	1.6 (1.3- 2.0)	<.0001
>=80	1.3 (0.9- 1.9)	0.1246
BMI, kg/m2		
0-20	Referent	
21-35	1.5 (1.1- 2.1)	0.0216
>35	2.1 (1.4- 3.3)	0.0007
Functional status before surgery		
Independent	Referent	
Partially dependent	2.1 (1.4- 3.1)	0.0002
Totally dependent	2.4 (0.8- 6.9)	0.1127
Disseminated cancer	1.9 (1.3- 2.7)	0.0006
Radiotherapy	1.9 (1.5- 2.5)	<.0001
Pulmonary history		
No dyspnea	Referent	
Dyspnea at rest	1.0 (0.3- 3.1)	0.9677
Dyspnea with exertion	1.5 (1.2- 2.0)	0.0015
Systemic Sepsis	2.0 (1.3- 3.1)	0.0016
Operation Time (min)		
<=168	Referent	
169-248	1.5 (1.0- 2.2)	0.0377
>248	2.0 (1.4- 2.8)	<.0001

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The Ergonomic Hazards of Operating: Symptoms and Injuries in Oncologic Surgeons R.K. Voss,* J. Cormier, K.D. Cromwell, Y. Chiang, J.E. Lee, D.L. Urbauer, C. Stucky. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Background: Occupational symptoms and injuries incurred over a surgical career are underreported. We sought to determine the frequency, risk factors, and consequences of occupational injuries in a group of oncologic surgeons in a tertiary care center. Methods: A systematic review of the surgical ergonomics literature was conducted and individual survey items compiled. Domains and items/questions were vetted using an iterative process by a panel of experts. A 31-item questionnaire was piloted by distribution to oncologic surgeons, recording demographics, symptoms, and occupational injury. Univariate and multivariate logistic regression were performed to identify factors associated with occupational injury. Results: 127 surveys were completed for an overall response rate of 58%. 39.4% of respondents were female, and 42.5% of surgeons had practiced 10 or more years. The most commonly reported symptoms were fatigue (78.0%), discomfort (75.6%), stiffness (72.2%), back pain (66.9%), neck pain (65.4%), and shoulder pain (54.2%). Table 1 shows selected injury and treatment results. Primary sources of discomfort were sustained awkward posture and environmental factors. Over 40% of surgeons modified their practice because of symptoms. 27.6% of oncologic surgeons sustained an injury or developed a chronic ailment they attributed to operating. Of those injured, 71.9% received treatment, with 17.4% of those treated requiring surgery for their injury. Age and years in practice were included in univariate logistic regression models but were not significantly associated with injury. In multivariate analysis, factors significantly associated with occupational injury were: male gender (OR 3.00 [95%CI 1.08-8.38]), average case length of 4 hours or longer (OR 2.72 [1.08-6.87]), always or often using a step to operate (OR 3.06 [1.02-9.15]), and neck pain (OR 4.81 [1.64-14.12]). Conclusion: The majority of oncologic surgeons experience musculoskeletal symptoms from operating. Of the 28% of surgeons with an injury or condition attributed to operating, the majority will require some form of treatment. Additional research into specific risk factors for occupational injury in oncologic surgeons is needed.

Table 1: Selected results from the occupational symptom and injury survey of oncologic surgeons, describing the perceived sources of discomfort, injuries, and treatments utilized by surgeons for injuries.

Sources of Discomfort in the Operating Room*	**%**
Sustained awkward posture	87.4
Environmental factors	37.0
Excessive exertion	26.0
Other	12.6
Do not have discomfort	3.2
Most Commonly Reported Occupational Injuries or Conditions*	**%**
Cervical spine pain/discomfort	37.9
Musculoskeletal fatigue	36.2
Vertebral disc injury/herniation	22.4
Generalized pain	17.2
Peripheral neuropathy or numbness	12.1
Carpal tunnel syndrome	10.3
Tendonitis	8.6
Most Utilized Treatments Among Surgeons for Occupational Injury*	**%**
Therapy (physical or occupational)	56.5
Medication	56.5
Complementary medicine	39.1
Surgery	17.4
Other (rest, compression, immobilization)	17.4
Trigger point injections	13.0

*Respondents allowed to select multiple choices so totals may not equal 100%

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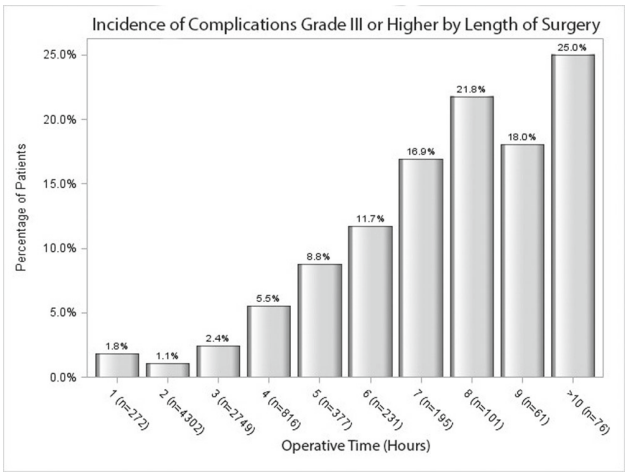
Readmissions and Complications After Robotic Surgery: Experience of 9,234 Operations at a Comprehensive Cancer Center
B. Yuh,* C. Lau, E. Han, J. Kim, E. Maghami, E. Yu, A. Pigazzi, P. Lin, D. Raz, G. Singh, M. Wakabayashi, Y. Fong. *City of Hope, Duarte, CA.*

Introduction The adoption of robotic surgery has progressed without significant study to its safety in various surgical disciplines. Standardized assessment of adverse events after oncologic surgery is necessary for quality improvement, particularly with novel technology. Methods Between 2003 and 2015, 9234 unique robotic operations were performed at a single cancer institute. A review of a prospectively collected database was performed. Readmissions to the hospital were summarized along with complications of grade II or higher within 30 days according to the modified Clavien-Dindo classification. Multivariable logistic regression was used to identify predictors of complications and readmission. Results Prostatectomy (n=6782), hysterectomy (n=589), nephrectomy (n=470), radical cystectomy (n=390), lung resection (n=261), colectomy (n=230), and esophageal-gastric (n=130) were the most common operations. Intraoperative complications occurred in 36 surgeries (0.4%) while 31 (0.3%) required conversion to an open procedure. Overall, 810 patients experienced complications (9%, highest grade II (n=498), III (n=234), IV (n=69)). Five patients died from cardiopulmonary complications. The most frequent complications were ileus (17%,), anemia (10%), cardiac arrhythmia (6%), anastomotic leak (5%), deep vein thrombosis/pulmonary embolus (5%), and wound infection (4%). 355 patients required readmission (4%) with the most common reasons being ileus (13%), pelvic abscess (7%), dehydration (6%), and anastomotic leak (6%). With a multivariable analysis, longer operative time (Figure 1), longer hospital stay, and age > 70 were significantly associated with the incidence of overall complications and complications of grade III or higher (p<.01). Longer operative time, cystectomy, transoral surgery, and lobectomy were risk factors for readmission (p<.02) while hysterectomy and prostatectomy were associated with lower risk (p<.002). Conclusions Robotic surgery appears safe for oncologic surgery with acceptable readmission and major complication rates. Patients with longer surgeries or of older age were more likely to experience complications or readmission.



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Melanoma Quality Assessment Program in a Community Hospital Setting
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Introduction: There have been numerous calls for quality assessment of melanoma care in the United States, including a 2009 Consensus Panels, with endorsement of 26 quality measures. [(1)] To date, there have been no reports of hospital compliance with these measures. Methods: High validity quality indicators were adopted, with the addition of 3 contemporary measures, for a total of 29 quality measures. A data abstraction tool, a 26 page abstraction manual and electronic database were developed. Data was abstracted by medically trained abstractors. Results: A total of 117 cases of malignant melanoma were treated from January 1, 2011 to August 31, 2015. Male to female ratio was 59:58 with median age of 54 (range 18 to 91). Primary tumor location was identified as head & neck (18.8%), trunk (48.7%), extremity (30.7%), and metastatic lesion (1.7%). Primary tumor excision was performed in 71 patients, and 70 (98.6%) had surgical margins documented in operative report; appropriate margin distance was selected for 69 (97.2%), and a final clear histological margin in 73 of 76 (96.1%). Among patients with clinical Stage IB and II disease (n=36), 100% underwent sentinel lymph node (SLN) biopsy. SLN was identified in 47/48 (97.9%). Among patients undergoing regional lymphadenectomy (n=6) an adequate node count was achieved in 5 (83.3%). No radiology imaging was performed in any of 61 patients with clinical Stage 0, I, or IIA (100%). 12 patients identified to have Stage III/IV disease were all referred to medical oncology. Pathology reports were standardized and reporting included Breslow thickness (98.4%), Clark level (91.9%), ulceration (91.9%), margin status (96.8%), satellitosis (85.5%), anatomic location (100%), regression (85.5%), and mitotic rate (93.2%). Histological serial sectioning was performed for 44 (93.6%) of 47 patients with SLN biopsy. Conclusions: Development of a robust melanoma quality program in a community hospital setting is feasible. High quality surgical and comprehensive care for malignant melanoma can be established in the community hospital setting and is verifiable through quality asessment.

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Key Gaps in Pathologic Reporting for Appendiceal Mucinous Neoplasms: Time for Universal Synoptic Reporting?
E. Al-Sukhni,* C. LeVea, J. Kane, J. Skitzki, V. Francescutti. *Roswell Park Cancer Institute, Buffalo, NY.*

INTRODUCTION: The prognosis of appendiceal mucinous neoplasms (AMN) is directly related to their histopathology. Existing classification schemes encompass tumors with widely divergent clinical behaviors within a single diagnosis, making it difficult for clinicians to interpret pathology reports to counsel patients on optimal management. We sought to examine pathology reports generated for AMN for inclusion of essential histologic features determined by expert pathologists and surgeons. METHODS: Pathology reports of appendectomy specimens with a diagnosis of AMN (2002-2015) at our center ("internal") and from referring institutions ("external") were retrospectively reviewed for inclusion of five essential items: layer of invasion, mucin dissection (low grade neoplasms only), perforation, margins, and serosal implants. RESULTS: Sixty-nine patients were included, 54 with external reports available. Benign/low grade tumors comprised 29.0% and 27.8% of internal and external reports, respectively. Thirty-seven internal reports (53.6%) were signed out by specialist GI pathologists. External reports were 66.7% complete for layer of invasion, 26.7% for mucin dissection, 64.8% for perforation, 68.5% for margins, 53.7% for serosal implants, and 18.5% for all items (Table). Internal reports were 75.4% complete for layer of invasion, 40.0% for mucin dissection, 40.6% for perforation, 82.6% for margins, 69.6% for serosal implants, and 17.4% for all items. Reports were more often complete for invasive tumors. Rates of complete internal reports were similar between specialist and non-specialist GI pathologists (16.2% and 18.8%, respectively). Eight external (14.8%) and 24 internal reports (34.8%) were synoptic. Synoptic reports were more likely to be complete for all key items both external (29.2% vs 11.1% in non-synoptic) and internal (50% vs 13% in non-synoptic). Use of synoptic reports increased completeness rates among both specialist and non-specialist GI pathologists. CONCLUSIONS: Most pathology reports are incomplete for essential features needed for management and discussion of AMN with patients. Synoptic reports improve completeness of reporting for these tumors.

Completeness of pathologic reports for essential histopathologic items in appendiceal mucinous neoplasms

	Internal reports			External reports		
	Benign/low grade (n=20)	Invasive (n=49)	All patients (n=69)	Benign/low grade (n=15)	Invasive (n=39)	All patients (n=54)
Item	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Layer of invasion	9 (45.0)	43 (87.8)	52 (75.4)	2 (13.3)	34 (87.2)	36 (66.7)
Mucin dissection	8 (40.0)	n/a	8 (40.0)	4 (26.7)	n/a	4 (26.7)
Perforation	9 (45.0)	19 (38.8)	28 (40.6)	8 (53.3)	27 (69.2)	35 (64.8)
Margins	13 (65.0)	44 (89.8)	57 (82.6)	6 (40.0)	31 (79.5)	37 (68.5)
Serosal implants	14 (70.0)	34 (69.4)	48 (69.6)	9 (60.0)	20 (51.3)	29 (53.7)
All items	1 (5.0)	11 (22.5)	12 (17.4)	1 (6.7)	9 (23.1)	10 (18.5)

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Differences in Psychosocial Distress Screening Scores Between Black and White Cancer Patients T. Schwartz,[1] J. Keller,[1]* J. Dunn,[2] J. Veerapong,[1] L. Hinyard.[3] *1. Saint Louis University School of Medicine, Saint Louis, MO; 2. Saint Louis University Cancer Center, Saint Louis, MO; 3. Saint Louis University Center for Outcomes Research, Saint Louis, MO.*

Introduction: Acknowledgment of distress is critically important when developing and implementing a treatment plan for cancer patients. The NCCN psychosocial distress screening tool has been accepted as an effective method of identifying and characterizing distress. Racial differences in distress scores have not been previously described. The purpose of the study was to compare the distress screening scores of black and white cancer patients. Methods: We reviewed the distress screening scores for all black and white cancer patients at St Louis University Cancer Center between January-July 2015. Only black and white patients were included, as there were too few patients of other races to be used in a statistical analysis. Patients without a total distress score were excluded. Only the first completed form was used in the analysis. Chi-square was used for comparisons between race for individual stressors and Mann-Whitney U was used to compare total score between black and white patients. Results: We analyzed distress screening tools completed by 1332 cancer patients. There was nearly equal male (51.73%) and female (48.27%) representation. The majority of patients were white (77.25%), and there was no statistically significant difference between black and white patients on the total distress score. There were differences in individual stressors according to race (Table 1). Black patients had a greater proportion of distress in the housing, insurance/financial, transportation, dealing with children, ability to have children, spiritual/religious and depression categories when compared to white patients. White patients had a greater proportion of distress in the nervousness category. No racial differences were detected in the child care, work/school, treatment decisions, dealing with partner, family health issues, fears, sadness, worry or loss of interest categories. Conclusion: We identified differences in individual stressors between black and white cancer patients. Attention to these differences is paramount to ensure comprehensive care is appropriately provided to all cancer patients and their individual needs are met and addressed.

Chi-square analysis comparing scores for individual stressor categories between black and white cancer patients

Individual Stressor Category	White (N=1029)	Black (N=303)	Chi-square	p-value
Child Care	12 (1.17)	5 (1.65)	0.435	0.51
Housing	33 (3.21)	19 (6.27)	5.856	0.016
Insurance/Financial	98 (9.52)	46 (15.18)	7.771	0.005
Transportation	43 (4.18)	34 (11.22)	21.31	<0.0001
Work/School	69 (6.71)	21 (6.93)	0.019	0.891
Treatment Decisions	154 (14.97)	41 (13.53)	0.386	0.535
Dealing with children	31 (3.01)	18 (5.94)	5.66	0.017
Dealing with partner	36 (3.50)	14 (4.62)	0.816	0.366
Ability to have children	7 (0.68)	9 (2.97)	10.344	0.001
Family health issues	116 (11.27)	31 (10.23)	0.259	0.611
Depression	160 (15.55)	64 (21.12)	5.197	0.023
Fears	196 (19.05)	61 (20.13)	0.177	0.674
Nervousness	281 (27.31)	63 (20.79)	5.188	0.023
Sadness	138 (13.41)	54 (17.82)	3.691	0.055
Worry	307 (29.83)	87 (28.71)	0.1414	0.707
Loss of interest	93 (9.04)	38 (12.54)	3.24	0.072
Spiritual/religious concerns	11 (1.07)	9 (2.97)	5.721	0.017

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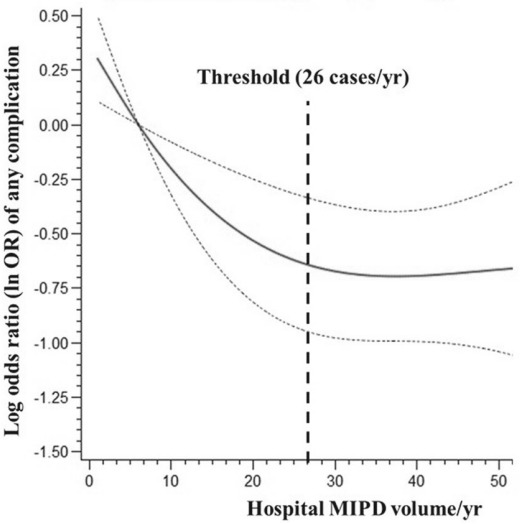
Defining a Hospital Volume Threshold for Minimally Invasive Pancreaticoduodenectomy in the U.S. M. Abdelgadir Adam,[1]* S. Thomas,[2] T. Pappas,[1] S. Roman,[1] J.A. Sosa.[1] *1. Department of Surgery, Duke University Medical Center, Durham, NC; 2. Department of Biostatistics, Duke University, Durham, NC.*

Background: There is increasing interest in expanding utilization of minimally invasive pancreaticoduodenectomy (MIPD). This procedure is complex, with some data suggesting a significant association between hospital volume and outcomes. Our aim was to determine if there is a MIPD hospital volume threshold for which patient outcomes could be optimized. Methods: Adult patients undergoing MIPD were identified from the Healthcare Cost and Utilization Project National Inpatient Sample, 2000-2012. Multivariable models with restrictive cubic splines were employed to identify a hospital volume threshold by plotting annual hospital volume against the adjusted likelihood of postoperative complications. Results: 940 patients underwent MIPD; 86% had cancer, 12% benign conditions/pancreatitis. Overall, 6% of patients had an intraoperative complication, 49% had postoperative complications, and 4% died in-hospital. After adjustment for demographic and clinical characteristics, increasing hospital volume was associated with reduced complications (p=0.001); the likelihood of experiencing a complication declined as hospital volume increased up to 26 cases/yr (p<0.01), with no further reduction thereafter (Figure 1). Median hospital volume was 6 cases/yr (range 1-60 cases/yr). The overwhelming majority of patients (89%) underwent the procedure at a low-volume (<26 cases/yr) hospital. While clinical and pathologic characteristics were similar among low- and high-volume (≥26 cases/yr) hospitals, patients undergoing MIPD at low-volume hospitals were more likely to experience postoperative complications (50% vs 33% high-volume, p=0.0001) and longer hospitalizations (median 10 vs 9 days high-volume, p=0.0004). Patients treated at low- vs. high-volume centers also were more likely to experience multiple complications (24% vs 16%, respectively, p=0.001). Conclusions: Hospital volume is significantly associated with improved outcomes from MIPD, with a threshold of 26 cases/yr. However, the majority of patients undergo MIPD at low-volume hospitals. Protocols outlining minimum procedural volume thresholds should be considered to facilitate safer dissemination of this complex, novel procedure.

Figure 1. Threshold for institutional annual volume of minimally invasive pancreaticoduodenectomy (MIPD) optimizing patient outcomes



P284

Outcomes After Pelvic Exenteration: Do Positive Margins Matter? A Multidisciplinary Cohort of Patients at Two Institutions M. Kitano,[1]* E.L. Jones,[2] B. Smith,[1] N.J. Lyell,[3] A.L. Gleisner,[2] G. Cheng,[2] M.D. McCarter,[2] F.J. Backes,[1] S. Abdel-Misih.[1] *1. Division of Surgical Oncology, The Ohio State University Wexner Medical Center, Columbus, OH; 2. University of Colorado, Denver, CO; 3. The Ohio State University, Columbus, OH.*

Introduction: Pelvic exenteration is a major surgical procedure often associated with high morbidity and mortality, however, it may be the only treatment option in some patients with locally advanced or recurrent pelvic malignancies. Although R0 resection is a major predictor of long-term survival in majority of solid tumors, it is often a challenge to attain negative margins in patients undergoing pelvic exenteration. Our study's aim was to determine the effect of margin status on overall survival and to analyze clinicopathologic features associated with survival in patients undergoing pelvic exenteration. Methods: A retrospective chart review was performed in patients who underwent pelvic exenteration at two institutions: from January 2000 to January 2014 and from January 2002 to January 2015. Patient demographics, operative complications, and overall outcomes were recorded. Overall survival was calculated using the Kaplan-Meir method. Chi-square test was used on clinicopathologic characteristics and multivariate analysis was performed with Cox proportional hazards. Results: A total of 211 patients underwent pelvic exenteration with 67, 79, and 65 patients having colorectal, gynecologic, and urologic histology, respec-

tively. Sixty patients (28%) were male with a median age of 56 years. The median length of follow-up was 19 months (range 1-151; IQR 7-55). A margin negative resection was significantly associated with improved survival for all malignancies (p=0.001) (Table 1). The presence of positive lymph nodes, type of exenteration, pre-operative nutritional status did not impact overall survival. Patients undergoing pelvic exenteration for gynecologic and urologic malignancies had better overall survival as compared to patients undergoing exenteration for colorectal cancer (p=0.0147). Conclusion: Patients undergoing pelvic exenteration with positive margins have decreased survival regardless of their type of malignancy associated. Patients requiring pelvic exenteration for colorectal cancer have worse overall survival compared to patients undergoing pelvic exenteration for gynecological and urological malignancies.

Result

		Hazard Ratio (95% CI)	p=value
Diagnosis	Colorectal	1.00	
	GYN	0.57 (0.32-1.02)	0.057
	GU	0.94 (0.49-1.80)	0.855
	Positive lymph nodes	1.07 (0.61-1.87)	0.822
	Positive margins	2.36 (1.44-3.84)	0.001
Surgery	Total exenteration	1.00	
	Anterior exenteration	0.72 (0.36-1.42)	0.339
	Posterior exenteration	0.55 (0.19-1.59)	0.270
	Albumin	0.82 (0.63-1.07)	0.139

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Current Trends in Diagnosis and Treatment of Merkel Cell Carcinoma Based on T Stage J. Li,* V. Siripurapu, A. Lefkowitz, N. Carp. *Main Line Health, Philadelphia, PA.*

Introduction: Merkel Cell Carcinoma (MCC) is a neuroendocrine skin malignancy, with increasing incidence in the past 20 years. Prone to loco-regional recurrence, it is treated with wide excision, possible nodal excision and radiation therapy based on stage. The aim of this study is to observe practice trends based on primary tumor T stages in a large population identified by a national database. Methods: All data was obtained from the National Cancer Data Base. Patients diagnosed with MCC between 1998 and 2012 were analyzed. Data files were imported into SPSS and labeled using the PUF SPSS import program. All variables were analyzed in SPSS using one- and two-way frequency tables and crosstabs. Raw counts and percentages were calculated. Results: 36,794 subjects were identified. The majority of subjects are found to be elderly (mean= 65.31 years, mode= 90) and male (57%). Primary lesions were equally found in either laterality (35.4% vs. 37.6%, right vs. left). No pathological T status is recorded in 65.3% with the majority of staged lesions being T1 (59.7%). Negative margins were achieved in 68.5% of in situ, 92.2% of T1, 82.8% of T2, 77.5% of T3, 66.2% of T4, with 87% of staged lesions with known margins. Node status was not noted in 69.9% with the majority of staged lesions found to be node negative (21.7%). For lesions with both T and N staging, node positivity increased with advanced T stages (1.2% of in situ, 19.0% of T1, 41.9% of T2, 38.1% of T3, 39.1% of T4 lesions). In regards to radiation, 8.0% of in situ, 36.2% of T1, 41.5% of T2, 37.3% of T3, 47.8% of T4, and 29.7% of overall lesions received therapy. Conclusions: MCC is predisposed to unilateral diagnosis in older males. The majority of lesions are poorly staged with most staged lesions being T1. Negative margins are poorly obtained with in-situ lesions and T4 lesions. Use of radiation is not widespread and least likely in in situ lesions and most common in T4 lesions, likely correlated to increased nodal involvement at higher T stages. As a tumor that is unusually sensitive to radiation, the data suggests a significant portion of higher staged tumors are undertreated

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Has Regionalization of Cancer Surgery in the United States Influenced Access to Care? N. Wasif,* Y.H. Chang, A. Mathur, R.J. Gray, B.A. Pockaj, D. Etzioni. *Surgery, Mayo Clinic in Arizona, Phoenix, AZ.*

Introduction Demonstration of the volume-outcome relationship has driven regionalization of complex cancer surgery in the United States. Our goal was to characterize hospital and patient level changes secondary to centralization of complex cancer surgery and study how these influence access to care. Methods The National Cancer Database (NCDB) was used to identify patients undergoing surgery for colon, esophageal, liver and pancreatic cancer from 1998-2009. Annual hospital volume for each cancer was categorized using quartiles (low <25th, medium 25-75th, high >75th). Predictors of treatment at a high volume (HV) center were analyzed using logistic regression analyses (controlling for age, race, education, income, insurance, and facility type) for likelihood of surgery at a HV hospital. Results The mean number of curative intent surgeries per hospital from 1998-2009 increased for all primary cancer types from except colon (liver +140%, pancreas +71%, esophagus +28%, colon -4.0%), as did the proportion of patients undergoing surgery at a HV hospital (pancreas +17.4%, esophagus +15.2%, liver +12.4%, colon +1.3%). The percentage of hospitals categorized as HV increased from baseline for all cancers except colon: esophagus +6.3%, liver +1.5%, pancreas +4.5%, and colon +0.6%. For all cancer types an increase in the median distance traveled for surgery was seen for patients undergoing surgery at HV hospitals (p <0.001 for trend for all); Figure 1. The likelihood of undergoing surgery at a HV hospital increased by 4% per year (adjusted OR 1.04, 95% CI 1.03-1.05) for pancreatic, liver and esophageal cancer. However, patients who were Black, uninsured, or had a median household income of <30k dollars were less likely to undergo surgery at a HV hospital. Conclusions Regionalization of cancer surgery is evident by an increase in the mean number of procedures per hospital either with (pancreas and esophagus) or without (liver) an increase in the proportion of HV hospitals. Patients are 44% more likely to undergo surgery at a HV institution in 2009 compared to 1998. They are traveling further for surgery at a HV hospital, but are less likely to do so if they are Black, uninsured, or poor.

Figure 1

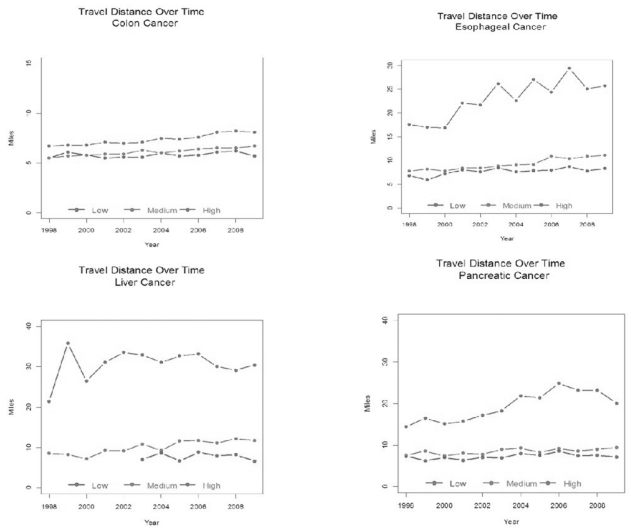

Figure 1

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Surgery for Gastric Cancer is Poorly Centralized M. McCall,[1]* P. Graham,[1] A. Bouchard-Fortier,[1] H. Stuart,[2] D.E. Schiller,[3] O.F. Bathe,[1] L.A. Mack.[1] *1. Surgery, University of Calgary, Calgary, AB, Canada; 2. University of Miami, Miami, FL; 3. University of Alberta, Edmonton, AB, Canada.*

Surgery represents the main curative modality for gastric cancer, with stage-specific survival rates varying across institutions. Variations are not only related to tumor biology, but also to disparities in the delivery of surgical therapy. A recent appropriateness study, employing expert opinion, set guidelines for the delivery of care. These included tenets related to surgeon volume and surgical technique. We sought to review the delivery of gastric cancer surgical care in the Canadian province of Alberta, an area with over 4 million people, focusing on surgeon volume and outcomes. With the end-goal of making positive changes to the way in which care is delivered, we planned this as a population-based assessment of our current baseline. Using the Alberta Cancer Registry we reviewed 320 patients diagnosed with gastric cancer in the province of Alberta between 2008 and 2012. Curative-intent surgery was performed on 274 patients in twelve hospitals by 61 individual surgeons performing on average 4.4 resections over the study period (range 1 – 37, median 2). Comparing the four surgeons with the highest volume (range 18-37 procedures, 37.2% of total operative volume) to the remainder, they performed proportionately more diagnostic laparoscopies prior to resection (53.3% vs

22.8% of cases, p<0.05), fewer subtotal gastrectomies (55.9% vs 72% of total cases, p<0.05) collected significanty more lymph nodes (19.0 vs 15.5, p<0.05) and achieved a lower positive margin rate (3.9% vs 8.9%, p=ns). There was no overall or disease-specific survival difference between these two groups after an average follow-up of 30.3 months, although the high-volume surgeons treated a significantly higher percentage of stage 3 patients (45% vs 32.1% of total cases, p<0.05). Despite centralization of other malignancies, there has not been centralization of gastric cancer surgery in our province. Referral of more cases to designated surgeons could lead to improved surgical quality metrics and outcomes and avoid potential bias such as stage migration. While overall survival was not necessarily improved in the hands of high volume surgeons, a more centralized delivery of care would result in the emergence of a more uniform care pathway.

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A New Application of Irreversible Electroporation Ablation as Adjunctive Treatment for Margin Enhancement to Improve Local Control During Close R0 and R1 Resections E.L. Simmerman,* E.J. Kruse. *Surgical Oncology, Georgia Regents University Medical Center, Augusta, GA.*

Introduction: Irreversible electroporation (IRE) is a relatively new ablation technique utilized as a focal therapy to target areas of significant tumor burden. As loco-regional therapy is becoming more common to improve survival and downstage disease, IRE is being utilized more frequently. We have utilized IRE intra-operatively at our institution for adjunctive treatment of primary and metastatic tumors at the time of surgical resection to achieve local control where an R1 resection is likely. Methods: This was a retrospective chart review at a single tertiary institution. The study included patients receiving IRE from November 2013 through September 2015. Patients received IRE treatment at the time of resection of primary and/or metastatic tumors for margin enhancement. Primary tumors included liver, pancreatic, retroperitoneal, extremity, pelvic, and breast cancers. Excluded from the study were patients undergoing treatment for palliation only or for pure ablation. Results: Of the 46 patients who received IRE ablation treatment, 27 patients (58.7%) received treatment for margin enhancement. 3 patients (11.1%) had negative margins, 15 patients (55.6%) had positive margins, 5 patients (18.5%) had 1mm margins, 3 patients (11.1%) had 2mm margins, and 1 patient (3.7%) had 9mm margins. Median follow-up was 11 months. 24 patients (88.9%) had no local recurrence, 3 patients (11.1%) had a local recurrence, and 8 patients (29.6%) had a distant recurrence. Of the 3 patients found to have a local recurrence one patient failed to complete her second staged operation and another patient underwent incomplete treatment due to intra-operative machine failure. Conclusions: Our institution demonstrated a low local recurrence rate of only 11.1% in patients treated with intra-operative IRE for margin enhancement. This may be a useful adjunct at the time of surgical resection to help achieve local control in difficult areas where an R1 resection is likely. This topic will require further investigation with prospective trials and more extensive follow-up.

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Extent and Impact of Colorectal Cancer Surgery Regionalization in Canada R.Y. Liu,* G. Kephart, G. Porter. *Dalhousie University, Halifax, NS, Canada.*

Introduction: Many studies have demonstrated an association between hospital volume of cancer surgery and outcomes. However, the quantification of regionalization, and its impact, remains unclear in colorectal cancer. The objective of this study was to describe the extent of regionalization of colorectal cancer surgery to high volume centers in Canada, and to examine the association of regionalization with perioperative outcomes. Methods: Discharge abstract data was used to identify a population based cohort of all patients from 9 of 10 Canadian provinces undergoing resection for colon or rectal cancer from 1999-2010. Hospitals were divided into groups based on quartile volume cut points in the first year, and regionalization was quantified as proportion of cases performed at high volume centers. Multiple regression models were used to examine the relationship between regionalization and the short-term outcomes of perioperative mortality and hospital length of stay (LOS). Results: Over the 11 years of the study, there were 100797 colon cancer and 60326 rectal cancer resections. Statistically significant regionalization was identified; in rectal cancer there was an average 5.5% relative increase in proportion of cases done at high volume centers (p=0.016) whereas in colon cancer the average yearly relative increase was 2.9% (p<0.001). Perioperative mortality decreased over time for both colon (4.1% to 2.7%) and rectal (2.3% to 2.02%) cancer resections over the study period. Regionalization was associated with lower odds of mortality for colon resections (OR 0.988, 95%CI 0.976-0.999) but not for rectal resections. Regionalization was associated with shorter LOS for both colon (-0.14 days/%), and rectal: (-0.13 days/%) resections. Conclusions: A modest degree of regionalization has occurred for colon and rectal cancer surgery in Canada. Regionalization was associated with shorter LOS for both colon and rectal cancer resections and decreased mortality for colon resections. This study suggest that regionalization of colorectal cancer surgery may result in modest short term outcome benefits; further research is required to evaluate the impact on oncologic outcomes.

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Improved Survival in Patients with Hepatocellular Carcinoma at Higher Volume Hospitals A. Mokdad,* A. Singal, J. Mansour, H. Zhu, H. Zhu, A. Yopp. *Surgery, University of Texas Southwestern, Dallas, TX.*

Introduction Improved survival at higher hospital volume is seen in high-risk surgical procedures. It is unknown if this relationship exists, within a cancer type, across all forms of treatment. We hypothesize hospital volume is correlated with survival in hepatocellular carcinoma (HCC) for both surgical and non-surgical treatments. Methods Using Texas Cancer Registry from 2001 through 2011, we examined survival among 17,231 HCC patients diagnosed at 322 hospitals. Hospitals were stratified into low and high volume by mean annual number of HCC patients using Contal's outcome-based method. Cox regression with shared frailty was used to account for hierarchal data structure and evaluate the association between facility volume and survival. We evaluated the relation between treatment use and volume using mixed effects logistic regression. Results Annual hospital volume was significantly associated with improved survival after adjusting for patient variables and tumor stage (HR 0.95; 95% CI 0.94,0.98) (Figure 1). An annual volume cutpoint of 24 patients demonstrated maximum mortality difference between low- and high-volume hospitals. A majority (61%) of patients were seen in the 21 high-volume hospitals. Median survival was 9.2 and 4.7 months at low- and high-volume hospitals, respectively (p< 0.01). A survival difference was observed between low- and high-volume hospitals at all tumor stages: localized (8.6 vs. 16.2 months, p<0.01), regional (4.5 vs. 6.4, p<0.01), and distant tumors (2.6 vs. 3, p<0.01). Patients at high-volume hospitals presented more commonly with localized disease (56% vs. 50%; p<0.01) and were more likely to receive curative treatment (22% vs. 12%, p<0.01). On multivariable analysis, hospital volume was significantly associated with increased overall treatment utilization (OR 1.3; 95% CI 1.2,1.4), and curative treatment use (OR 1.3; 95% CI 1.1,1.4). Conclusion Hospital volume is significantly associated with improved survival for both surgical and non-surgical therapies among patients with HCC. Improved survival may be mediated by increased use of curative treatments, and referral of HCC patients to high-volume hospitals should be considered if/when possible.

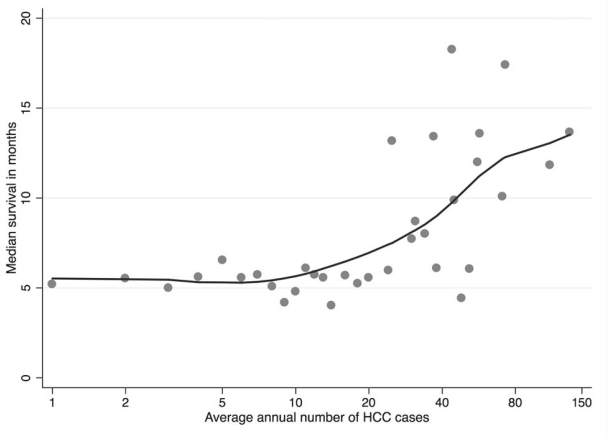

Figure 1: Overall median survival by facility volume in patients with HCC

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Infectious Complications Following Colorectal Cancer Surgery are Associated with Worse Long-term Survival A. Mokdad,* G. Balch, H. Hirsch, M.A. Choti, I. Nassour, N.A. Borja, C. Balch, P. Polanco.
Surgery, University of Texas Southwestern, Dallas, TX.

Introduction Colorectal cancer surgery is associated with significant postoperative morbidity, which may have long-term implications on patient outcomes. We hypothesize that operative complications following surgery for colorectal cancer are associated with increased recurrence and worse survival. Methods Using a prospectively maintained database, we reviewed patients with colorectal cancer that underwent a curative resection from 2008 to 2015. Patients were categorized by presence of any complication within 90 days from surgery and by type of complication, infectious and non-infectious. We compared clinical, pathological, and perioperative data using t-test, chi-squared test, and ANOVA. We compared overall (OS) and recurrence free survival (RFS) using Kaplan Meier and log-rank test. Multivariable Cox regression was used to compare mortality and recurrence. Results Two hundred and twenty-nine patients underwent 104 colon and 125 rectal cancer resections (20 pelvic exenterations, 83 low anterior and 17 abdominoperineal resections) were followed for a median of 23 months. Fifty percent were completed minimally invasively. Postoperative complications occurred in 52%; 19% had a major complication (Clavien-Dindo 3-4). Postoperative complications were more likely to occur in open (61% vs. 38%, p<0.01) and rectal operations (63% vs. 42%, p=0.02). On multivariable analysis, OS and RFS were not statistically different in patients with complications. Patients with infectious complications had worse 3-year survival when compared to patients with non-infectious complications and without complications (58%,69%,76%, p=0.04). Recurrence at 3 years was also significantly different among the three groups (p=0.03) (Figure 1). Infectious complications remained associated with worse overall survival (HR 1.8; 95% CI 1.02,3.26) and recurrence free survival (HR 1.9; 95% CI 1.06,3.39) after adjusting for patient, tumor, and perioperative data. Conclusion Infectious complications following colorectal cancer surgery are associated with worse OS and RFS independent of tumor stage, type of surgery, and technique. Current research is ongoing to explore possible etiologies of this association.

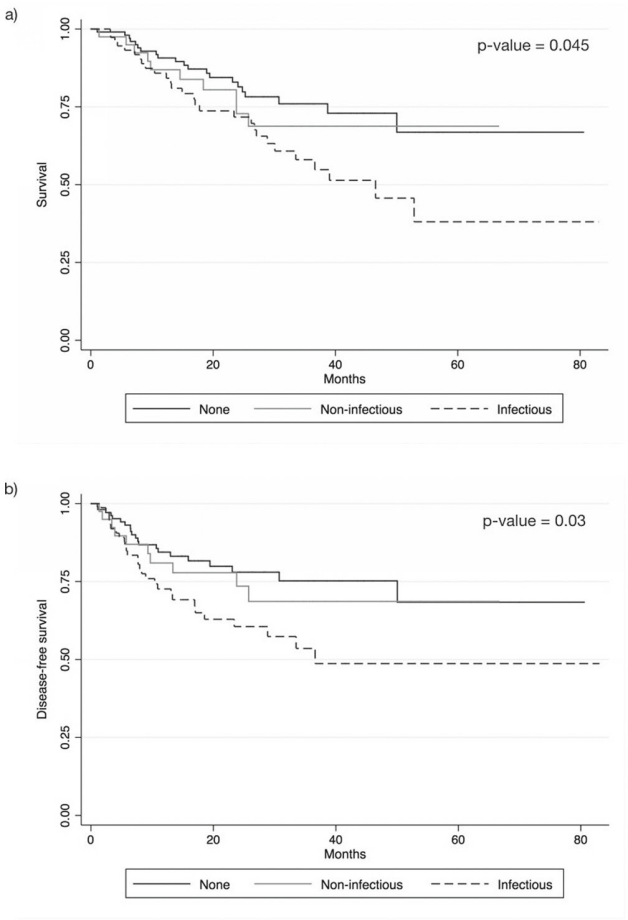

Figure 1. Comparison of overall survival (a) and recurrence free survival (b) by complication type, infectious and non-infectious.

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Increases in the Global Incidence of Young Adult Colorectal Cancer (YA CRC) Pose Critical Challenges for the International Surgical Oncology Community J. Singh,[1]* R. Mendelsohn,[2] S. Winawer,[2] A. Zauber,[2] E. Kantor,[2] D. Ahnen,[3] J. Lowery,[3] D. Bal,[1] C. Sardo Molmenti,[4] T. Weber.[1] *1. State University of New York Health Sciences Center, Brooklyn, NY; 2. Memorial Sloan Kettering Cancer Center, New York, NY; 3. University of Denver, Denver, CO; 4. Columbia University College of Physicians and Surgeons, New York, NY.*

INTRODUCTION: Expanding on our recent presentations, the objectives in this study were to: 1. Investigate YA CRC incidence trends from a global perspective and 2. Identify emerging YA CRC clinical management and translational research priorities for the international Surgical Oncology community. METHODS: We reviewed current WHO GLOBCAN data (http://globocan.iarc.fr) on 1.3 million CRC cases worldwide in 2012 and, under expert guidance, searched PubMed for current literature using multiple terms including "Population Based", "Young Adult" and "Early Age Onset" Colorectal Cancer. RESULTS: WHO data show YA CRC incidence rates steadily increasing over the past 2 decades among multiple developed countries including Australia where an 85-100% increase among 20-29 year age group was observed between 1990 and 2010. Similar trends are observed in "resource constrained" countries including India, Egypt, Saudi Arabia and Nigeria. For all affected countries these trends are largely driven by an increasing incidence of rectal cancer. Currently in the U.S. approximately 1 in 5 rectal cancers occurs in individuals under 50 years of age. Symptomatic late stage diagnosis is a consistent finding as are adverse pathologies including high grade, poor differentiation, mucinous and signet ring features. The definitive cause(s) for the vast majority of these cases remain unknown. Importantly, the known hereditary CRC

syndromes account for 22% or less of reported cases. CONCLUSIONS: These global, population based, expertly curated data confirm a dramatic international increase in YA CRC incidence over several decades. Our results highlight significant opportunities for the Surgical Oncology community to lead international efforts to: 1. Define risk factors and risk stratification strategies for YA CRC 2. Promote prevention and detection at the earliest possible stage 3. Develop treatment strategies designed to preserve fertility and maximize quality of life for the steadily increasing numbers of young adults in the U.S. and around the world diagnosed with CRC.

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Missed Opportunity: Atypical Hyperplasia and Low Rates of Chemoprevention in the Community Cancer Center Experience

A. Tameron,* K. Raque, P. Heath, E. Dunki-Jacobs, C. Ho, M.P. Bramlage, L.R. Hussain, B.A. Wexelman. *General Surgery, TriHealth-Good Samaritan Hospital, Cincinnati, OH.*

Introduction: Four percent of benign breast biopsies are atypical ductal (ADH) or atypical lobular hyperplasia (ALH). Atypical hyperplasia (AH) confers 4X increased risk for future breast cancer. Current NCCN guidelines advise anti-estrogen chemoprevention such as tamoxifen for risk reduction. We seek to understand patterns of risk reduction for this high risk population in routine clinical practice. Methods: Retrospective chart review was performed of all AH diagnoses in our health system from 2012- 2014. Cases were excluded if AH diagnosis was made after a breast cancer diagnosis, or no documentation existed in the EMR post biopsy. Patient demographics, surgical and high risk management were reviewed. Referral to medical oncology for pharmacologic risk reduction, anti-estrogen initiation, and screening breast MRI were analyzed using Fisher's exact and Mann-Whitney U test, $p<0.05$. Results: Review identified 126 patients with AH during the 3 year period. Limitations included some surgeons not using the central EMR, or performing surgery/MRIs at outside facilities. Surgical excisional biopsy was performed in 108 (90.8%) of patients (5.6% unknown). Pathology was upgraded in 18 (15.1%) patients: 4 (22.2%) combined ADH/ALH, 6 (33.3%) DCIS, 5 (27.7%) LCIS, 3 (16.8%) invasive cancer. Medical oncology referral was documented in 15.8%. Hormone therapy was recommended/started in 10 (9.4%), most commonly Tamoxifen. MRIs were performed in 12.5% of patients. Referral to medical oncology was observed in older women (63 vs 56 yrs; $p < .05$). Medicare beneficiaries were less likely to be prescribed hormone therapy than other insurance groups (15% vs 3%; $p<.05$). No other factors were statistically significant for incidence of referral, anti-estrogen therapy or MRI screening. Conclusion: The majority of AH patients do not receive comprehensive risk reduction for the prevention of subsequent breast cancer despite documented high risk. While most undergo surgical excision, anti-estrogen therapy and Breast MRI are utilized at very low rates. The management of AH provides an opportunity for improvement in the quality of care of breast patients in the community setting.

	N	%
Age (average, years)	57.6	
Race		
Asian	1	0.8%
Black	12	9.5%%
White	110	87.3%
Other	3	2.4%
Insurance		
COMMERCIAL	89	70.6%
MANAGED MEDICAID	5	4.0%
MANAGED MEDICARE	9	7.1%
MEDICAID	1	0.8%
MEDICARE	21	16.7%
SELF PAY	1	0.8%
Surgical Excision Performed	108	90.8%
Pathology Upgraded at surgery	18	15.1%
ADH & ALH	4	22.2%
DCIS	6	33.3%
LCIS	5	27.7%
IDC	1	5.6%
ILC	1	5.6%
Invasive Papillary Carcinoma	1	5.6%
Medical Oncology Referral	18	15.8%
Anti-Estrogen Therapy Recommended/ initiated	11	9.4%
Tamoxifen	6	60.0%
Anastrazole	3	30.0%
Raloxifene	1	10.0%
Subsequent Breast MRI	15	12.5%

Table 1: Demographics and management of atypical hyperplasia, N=126

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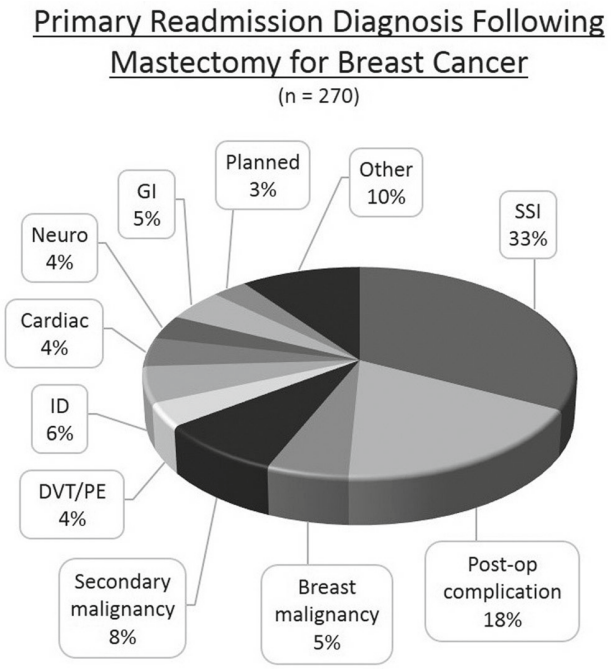
Indications for Readmission Following Mastectomy for Breast Cancer: An Assessment of Patient and Operative Factors

J. Yu,* M. Olsen, J. Margenthaler. *Washington University School of Medicine, Saint Louis, MO.*

Background More than one-third of all women diagnosed with breast cancer each year in the US will undergo mastectomy, and readmissions in these patients remain a costly problem with major potential for intervention. In this study, we investigate the impact of patient demographics and operative factors on hospital readmission within 30 days following mastectomy for breast cancer. Methods Using the Healthcare Cost and Utilization Project State Inpatient Database for California in 2011, we examined indications for readmission in women over age 18 undergoing mastectomy for invasive breast cancer, breast cancer in situ, or history of breast cancer. Clinical data assessment was performed using ICD-9 codes and the Elixhauser comorbidity index. Chi-square tests and logistic regression were used to analyze patient and operative factors and associations with 30-day hospital readmission. Results Of 5,284 women who underwent unilateral or bilateral mastectomy, 270 (5.1%) were readmitted within 30 days after surgery. The most frequent primary readmission diagnoses were surgical site infection (87, 32.2%) and hematoma (18, 6.7%). On univariate analysis, increasing length of stay (LOS) during the index admission for mastectomy was significantly associated with 30-day readmission (mean 1.9 vs. 3.3 days, $p<0.0001$), and readmitted patients were significantly more likely to have comorbidities, including diabetes and obesity, and less likely to have private insurance as a primary payer ($p<0.05$). Using all variables reaching a significance level of $p=0.2$, multivariable logistic regression showed continued significance of increasing index LOS; for example, women admitted for 3-4 days vs. 1 day had more than twice the odds of being readmitted within 30 days (OR 2.38, 95% CI 1.69-3.35, $p<0.0001$). Also, women with private insurance had a 30% decrease in odds of readmission (OR 0.70, 95%CI 0.51-0.96, $p=0.027$). Conclusions Increasing LOS during the index admission after

mastectomy for breast cancer and primary payer are significant predictors of 30-day readmission. Further investigation is needed to analyze epidemiologic influences on LOS and on specific causes for readmission.



P295

Accuracy of Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio in Predicting Node Positivity and Metastatic Disease in Patients with Gastrointestinal Malignancies K. Baughen,[4] I. Nora,[5] S. Kucera,[2] A. Patel,[3] R. Brown,[3] J. Lee,[7] R. Shridhar,[6] K. Meredith.[1]* *1. Florida State University, SMH Campus, Sarasota, FL; 2. Florida Digestive Health System, Sarasota, FL; 3. Florida Cancer Specialists, Sarasota, FL; 4. Brown University, Providence, RI; 5. Sarasota Memorial Healthcare System, Sarasota, FL; 6. University of Central Florida, Florida Hospital Orlando, Orlando, FL; 7. Florida Interventional Specialists, Sarasota, FL.*

Background: Accurate predictors of node positivity and metastatic disease for patients with gastrointestinal (GI) malignancies are currently lacking. Neutrophil-lymphocyte ratio (NLR), and platelet lymphocyte ratio (PLR) have been introduced as a possible prognostic scoring system. We sought to evaluate the accuracy of NLR and PLR in predicting advanced disease in patients with GI malignancies. Methods: We queried a prospective GI oncology database to identify 116 patients. NLR and PLR were calculated from complete blood counts before and after neoadjuvant therapy (NT) and pre-operatively in patients not treated with NT. The associations between NLR and PLR and the clinicopathologic parameters were assessed via χ^2 or Fisher's exact tests where appropriate. All the tests were two-sided, and $p < 0.05$ was considered statistically significant. Results: We identified 49(42.2%) esophageal, 34(29.3%) pancreatic, 14(12.1%) colorectal, 13(11.2%) gastric, and 6(5.2%) biliary cancers. There were 36(31%) LN-, 52(44.8%) LN+ and 28(24.2%) patients with metastatic disease. The median NLR for LN – patients was 1.78 (0.2-4.5) and for LN + and metastatic patients was 4.48 (2.38-24.1) $p<0.00001$. The median PLR for LN– patients was 123 (66-207) and for LN+ and metastatic patients was 212 (112-2185) $p<0.00001$. The sensitivity (SENS), specificity (SPEC), positive predictive value (PPV) and negative predictive value (NPV) for a NLR >2.25 was 98.8%, 72.2%, 89%, and 96% respectively with an overall accuracy of 91%. The SENS, SPEC, PPV, and NPV for PLR>140 was 95%, 78%, 90%, and 88% respectively with an overall accuracy of 90%. Utilizing both NLR >2.25 and PLR >140 the SENS, SPEC, PPV and NPV was 95%, 89%, 95%, and 89% respectively and the overall accuracy was 93%. Conclusions: NLR and PLR can be used to identify patients with node positivity and metastatic disease. Individually, NLR has a higher sensitivity and NPV while PLR has a higher specificity and PPV. However, the combination of NLR and PLR has the highest accuracy of predicting advanced disease among all gastrointestinal malignancies.

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Fall Risk as a Predictor of Failure to Rescue After Palliative Surgery for Advanced Cancer A. Blakely,[1]* D. Kim,[1] D.S. Heffernan,[1] J. McPhillips,[2] K.P. Charpentier,[1] T.J. Miner.[1] *1. Brown University/ Rhode Island Hospital, Providence, RI; 2. Rhode Island Hospital, Providence, RI.*

Introduction Evaluation of failure to rescue has become a major focus of interventions to improve surgical outcomes. Early recognition of advanced cancer patients at risk of not overcoming complications is especially challenging when discriminating perioperative morbidity from disease progression. We evaluated fall risk score (FRS) as a measure of frailty and recovery following palliative operations. Methods Retrospective review of a prospectively-maintained palliative surgery database was performed, Nov 2003 to Mar 2015. FRS, composed of physical and mental functional status (0-5=normal, 6-34=at-risk), was measured pre- and post-op. Results 160 patients had palliative-intent operations to deliberately treat cancer-related symptoms or improve quality of life. Primary tumors were pancreas (n=58, 36.3%), colorectal (n=19, 11.9%), stomach (n=13, 6.3%), melanoma (n=12, 7.5%), and other (n=58, 36.3%). 137 patients (85.6%) had a pre-op FRS (median 3, interquartile range [IQR] 0-8), of whom 97 (70.8%) had an FRS at 1 week post-op (median 4, IQR 2-8). Median max FRS was 8 (IQR 3-13). Median length of stay (LOS) was 7 days (IQR 4-9.5). 44 patients (27.5%) had complications by 30 days; 14 (31.8%) were grade 3-4. Mortality at 30 days was 5.0% and at 90 days was 15.8%. Max FRS≥6 was associated with longer LOS (p=0.0022). High-grade complications were associated with 1-week (p=0.043) but not pre-op (p=0.88) or max (p=0.93) FRS≥6. Pre-op FRS≥6 was associated with increased mortality at 30 (p=0.0002) and 90 days (p=0.026) as was 1-week FRS≥6 (p=0.043, p=0.0068, respectively), whereas max FRS≥6 was not (p=0.087, p=0.72, respectively). Conclusions FRS assessment may provide an objective assessment of recovery and better identify patients at risk of failure to rescue after palliative operations. Pre-op and 1-week post-op FRS≥6 were associated with increased 30- and 90-day mortality. Max FRS≥6 was not associated with complications or mortality, suggesting that transiently elevated FRS was not predictive of outcomes in patients with good pre-op functional status. Patients failing to regain their pre-op functional status at 1 week post-op were at increased risk of mortality well beyond operation.

Fall Risk Score

Safety Risk Factor Assessment	Points
Confusion / disorientation / agitation	6
Depression	1
Prescribed benzodiazepine or antiepileptic	3
Potential drug / EtOH withdrawal	1
Unable to rise from chair independently	6
History of fall within last 6 months	4
Altered elimination of bowels / bladder	5
Generalized weakness	2
Dizziness or lightheadedness	2
Sensory loss: hearing	2
Sensory loss: visual acuity	2
FINAL RISK SCORE =	

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Surrogate Indicators of Surgical Quality are Associated with Survival Following Treatment for Hepatocellular Carcinoma D. Roife,* J.A. Santamaria, L.S. Kao, C. Wray. *UTHealth, Houston, TX.*

Introduction: Quality and core measures have been publicly reported for over 10 years. However, these data have not included disease-specific survival for cancer patients. We hypothesize that hospital level measures of surgical quality are associated with long-term survival following treatment for hepatocellular carcinoma (HCC). Methods: The national cancer data base (NCDB) was queried for all cases of HCC from 1998—2012. Inclusion criteria were known vital status and type of surgical resection (ablation or transplantation not included). Individual hospitals were de-identified. Quality markers for

individual hospitals were defined as mean length of stay (LOS), 30- and 90day death rate and 30day readmit rate. Other variables included: age, gender, race, Charlson Comorbidity score, median income and time period. A Cox proportional hazards model stratified by stage was used to estimate the treatment effect of adjuvant therapy. To minimize confounding, survival was estimated for patients that survived greater than 30 days. Results: A total of 16,202 patients underwent surgical resection for HCC at 1,051 hospitals. Calculated by unique hospital, median 30day death rate was 4.6% (IQR 6.4)), 90day death rate was 9.6% (IQR 9.0), 30day readmit rate was 2.6% (IQR 5.5) and mean LOS was 8.0 days (IQR 2.7). In the multivariate Cox regression (see table), 30day death rate was significantly associated with worse survival (HR 1.90, 95%CI:1.23-2.94). Longer LOS was also associated with worse survival (HR 1.03, 95% CI:1.02-1.04). Interestingly, higher hospital readmit rates were associated with improved survival (HR 0.47, 95%CI:0.27-0.80). Conclusions: Patients surviving more than 30 days following surgery, yet treated in higher 30 day mortality hospitals, experienced worse survival outcomes. These results suggest hospital level markers of surgical quality for hepatocellular carcinoma are associated with long-term survival. Individual hospitals should critically review disease specific outcomes following surgical resection in order to identify and target areas for quality improvement.

	HR	p-value	95% CI
30 day death rate	1.90	<0.05	1.23-2.94
30 day readmit rate	0.47	<0.05	0.27-0.80
LOS	1.03	<0.05	1.02-1.04
Age	1.01	<0.05	1.00-1.02
Female Gender	0.82	<0.05	0.77-0.87
Median Income *			
$38-47.9k	0.91	<0.05	0.84-0.99
$48-62.9k	0.90	<0.05	0.82-0.97
>$63k	0.81	<0.05	0.75-0.88

*=<$38k referent value

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Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Ratio Can be Used to Predict Recurrences for All Gastrointestinal Malignancies M.P. Doepker,[3] K. Baughen,[4] I. Nora,[6] R. Shridhar,[2] R. Brown,[5] A. Patel,[5] A.I. Salem,[7] K. Meredith.[1]* *1. Florida State University, SMH Campus, Sarasota, FL; 2. University of Central Florida, Florida Hospital Orlando, Orlando, FL; 3. Moffitt Cancer Center, Tampa, FL; 4. Brown University, Providence, RI; 5. Florida Cancer Specialists, Sarasota, FL; 6. University of Dublin, Dublin, Ireland; 7. University of Wisconsin, Madison, WI.*

Background: Accurate predictors of recurrence for patients with gastrointestinal (GI) malignancies are currently lacking. Neutrophil-lymphocyte ratio (NLR), and platelet-lymphocyte ratio (PLR) have been introduced as possible predictors of advanced disease. We sought to evaluate the utility of NLR and PLR in predicting systemic recurrence in patients with GI malignancies. Methods: We queried a prospective GI oncology database to identify patients who had undergone surgery for GI malignancies. Patients were excluded if metastatic disease was identified at surgery. NLR and PLR were calculated from complete blood counts. The associations between NLR and PLR and the clinicopathologic parameters were assessed via χ^2 or Fisher's exact tests where appropriate. All the tests were two-sided, and $p < 0.05$ was considered statistically significant. Results: We identified 93 patients diagnosed with: 41(44.1%) esophageal, 25(26.9%) pancreatic, 12(12.9%) colorectal, 11(11.8%) gastric, and 4(4.3%) biliary cancers. The mean age and follow-up was 70.2±10.9 years and 16±16.6 months, respectively. There were 40(43%) LN-, and 53(57%) LN+ patients. Systemic recurrences were identified in 27(27.6%) patients: 9(9.7%) in LN- and 18(19.4%) LN+ patients, p=0.04. Recurrences were identified in 4(16%) pancreatic, 14(34%) esophageal, 4(33%) colorectal, 3(37.5%) gastric, and 2(50%) biliary cancer patients. The median time to recurrence was 6 (3-26) months. Sites of recurrences included: liver 12(44.4%), lung 5(18.5%), peritoneal 5(18.5%), nodal 4(14.8%), and bone 1(3.8%). The median NLR for recurrent v/s non-recurrent patients was 6.8(3.4-17) and 3.8(0.28-14.4) respectively, p<0.0001. The median PLR for recurrent and non-recurrent patients was 281(122-657) and 199(14-452) respectively, p=0.02. Conclusions: Elevation of NLR and PLR can be used to identify patients with recurrence after surgery for GI malignancies. NLR and PLR may be more accurate then disease specific tumor markers in predicting recurrence. Additionally, failure of normalization of NLR and PLR 3 months post-surgical resection may indicate early recurrence.

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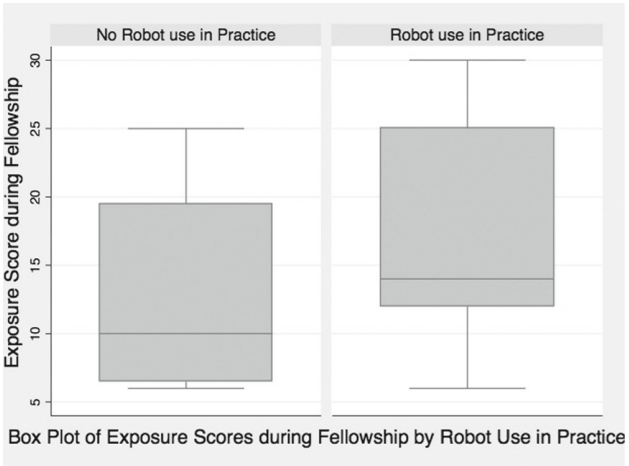
Shaping Future Surgical Oncologists: Robotic Exposure During Surgical Oncology Fellowship is the Most Significant Predictor of Robot Use in Practice F. Tozzi,* S. Dumitra, A. Lewis, B. Lee, L.L. Lai, L. Goldstein, G. Singh, Y. Fong, Y. Woo. *City of Hope, Duarte, CA.*

Introduction: More than 10,000 robot-assisted cases have been completed since the inception of the first surgical robotic system at City of Hope National Medical Center. The adoption of this technology has consequently exposed our surgical oncology trainees to this technology during their fellowship. The goal of this project is to understand the impact of robotic surgery exposure during training on the current practice of past-fellows. Methods: A Web-based questionnaire with volunteer participation was distributed electronically to the surgical oncologists who trained at City of Hope from 2005 to 2014. Categorical, ordinal and continuous questions were created to obtain the current practice, level of exposure to robotic training and the integration of this technology once in practice. Robotic exposure score was calculated for each participant. We used descriptive and inferential statistics to analyze the responses. Results: 62% (13/21) of participants adopted robotic technology in their current practice. The primary application was in colorectal (36%), pancreas (20%), foregut (15%), and liver (8%) surgeries. Exposure scores were significantly higher among robotic adopters vs non-adopters. (mean 17.6 vs 12.9, p=0.005) . 46% of robotic surgeons sought additional training after completing their fellowship. There was no difference in the type (p=0.49) and scope (p=0.35) of practice between surgeons adopting robot technology vs not. Surgeons adopting the robot tended to perceive their fellowship robotic training as adequate (38% vs 25%). Conclusions: Exposure to robotic surgery during fellowship training has a significant positive impact on the adoption of robotic technology once in practice. However, the majority of robot adopters completed further robotic training post fellowship. This study confirms the need to develop and validate a standardized curriculum in robotic surgery training during fellowship tailored to the trainees' interests and needs.



P300

Underutilization of Palliative Care Consultations in Patients with Hepatobiliary Malignancies B. Fahy,* K. Morris, I. Nir, A. Rajput. *Surgery, University of New Mexico, Albuquerque, NM.*

INTRODUCTION: The National Comprehensive Cancer Network (NCCN) has developed criteria to identify patients who should be considered for palliative care consultation (PCC). Current utilization of these guidelines among surgical oncology patients is unknown. Patients treated for hepatobiliary (HPB) malignancies frequently experience high symptom burden and thus may benefit from PCC. METHODS: A retrospective review of 107 patients who underwent surgical treatment of HPB malignancies from 1/2012 to 2/2014 was performed to determine the number of patients who would meet NCCN guidelines for PCC and the indication for PCC. The number of PCC performed among this cohort was recorded. RESULTS: Fifty patients (47%) met NCCN guidelines for PCC. Indications for PCC included severe comorbid conditions (N=20), palliative procedure performed (N=12), history of drug or alcohol abuse (N=8), complex intensive care unit course (N=7), and high risk for

poor pain management (N=3). Primary liver tumors were associated with the highest rate of indication for PCC (19/34, 56%) while bile duct tumors were associated with the lowest rate (12/34, 35%). Patients for whom PCC was likely to be indicated tended to be older than patients in whom PCC was not indicated (65 years vs. 59 years, respectively). The actual number of PCC performed was one (0.9%): a patient with a liver tumor who had both a complex intensive care unit course and severe comorbid conditions. CONCLUSIONS: PCC is rarely performed in patients undergoing surgical treatment for HPB malignancies. Utilization of NCCN guidelines to identify patients who may benefit from PCC would result in a significant increase in PCC for patients with HPB malignancies.

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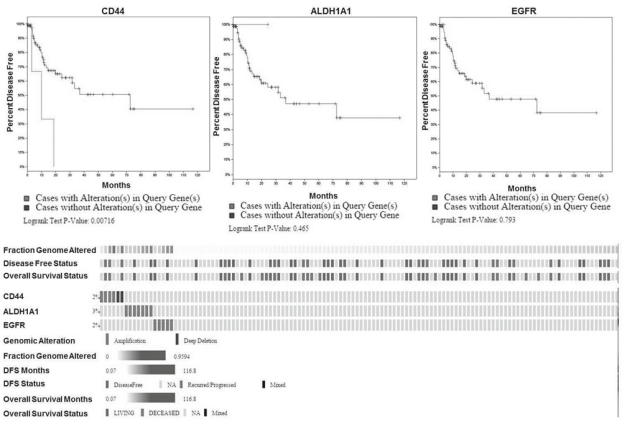
Genomic Alterations in Cancer Stem Cell Marker CD44 Predict Oncologic Outcome in Soft Tissue Sarcoma T. Henderson,[1]* M. Chen,[2] S. Grossenbacher,[2] S. Park,[2] C. Li,[3] C. Chiu,[3] A. Monjazeb,[2] R. Bold,[2] W. Murphy,[2] R. Canter.[2] *1. University of Vermont College of Medicine, Burlington, VT; 2. University of California Davis Medical Center, Sacramento, CA; 3. University of California, Davis, Sacramento, CA.*

Background: Cancer stem cells (CSCs) have been shown to resist chemotherapy and promote metastasis after cytotoxic treatment. The objective of our study was to determine if CSC markers (ALDH, CD44, and EGFR) predicted worse outcomes in soft tissue sarcoma (STS). Methods: We queried an institutional database of 23 STS patients from 2003 to 2015 to create a tissue microarray (TMA) for immunohistochemical (IHC) staining. Specimens were evaluated for IHC expression of CSC markers ALDH, CD44, and EGFR by a blinded pathologist. The Sarcoma Cancer Genome Atlas (https://tcga-data.nci.nih.gov) was queried for clinical and genomic data. Disease-specific (DSS) and overall survival (OS) were assessed by univariate and Kaplan-Meier analysis. Results: Of the 23 patients, 16 (70%) were female, 18 (78%) were high grade, 12 (52%) were extremity, and 7 (30%) were retroperitoneal. With a median follow up of 27 months, 9 (39%) experienced distant recurrence, and 4 (17%) died of disease. At time of diagnosis, mean H-score (±SEM) for CD44, ALDH1A1, and EGFR were 169±27, 77±15, and 144±23, respectively. On univariate analysis, there was a trend for increased CD44 score to predict both worse DSS and OS (HR = 1.01, 95% CI 1-1.02, p=.056), while ALDH and EGFR scores did not. Finally, we analyzed 74 TCGA STS cases with complete clinical and genomic data, observing that CD44 copy number alterations (CNA) predicted worse DSS (9.89 months vs. 72.5 months, P=0.007) and a trend for worse OS (14.03 months vs. 38.6 months, P=0.12), while ALDH1A1 and EGFR CNA did not (Figure 1). Conclusion: Analysis of both institutional IHC and national TCGA data shows a significant effect of elevated baseline CD44 expression, but not ALDH or EGFR, on worse oncologic outcomes in STS. CD44 may therefore be a novel prognostic and/or predictive biomarker in STS, and further study of CD44 targeting appears indicated.



P302

Radiation Independently Improves Survival for Patients with Early Stage Adult-type Soft Tissue Sarcoma and Positive Margins B. Lau,* D. Lee, K.T. Huynh, J. Lee, M. Goldfarb. *Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA.*

INTRODUCTION: There are no definitive guidelines for use of adjuvant radiation (RT) in patients with early stage adult-type soft tissue sarcomas (STS) with positive margins. Current guidelines encourage consideration for local control, but no studies have shown a survival benefit and lower tumor stages have not been studied. METHODS: 3239 patients with clinical stage I-II adult-type STS (lipomatous, clear cell/hemangiosarcoma, fibromatous, synovial, and myosarcomas excluding rhabdomyosarcoma) with positive margins and no preoperative radiation were identified in the National Cancer Database. Factors associated with receiving adjuvant RT and impact on overall survival (OS) were explored with multivariate analyses. RESULTS: Less than half the cohort received RT (42.5%). Patients that were uninsured (HR:1.56, CI 1.03-2.37), with myosarcoma (HR:1.32, CI 1.21-2.17), lower grade, and larger >20cm (HR:1.62, CI 1.21-2.18) all had a greater likelihood of receiving RT. Conversely, STS located outside the trunk and synovial sarcoma less commonly received RT. Age, race/ethnicity, comorbidities, socioeconomic status or the extent of margin positivity did not impact receipt of RT. Controlling for all other factors, receipt of radiation was independently associated with improved OS (HR 0.73, CI 0.64-0.84). In the entire cohort, Black race (HR:0.70, CI 0.53-0.93), Hispanic ethnicity (HR:0.64, CI 0.43-0.95), lower extremity location (HR.0.64, CI 0.54-0.76) had better OS, while government insurance (HR:2.45, CI 2.08-2.87) and macroscopically positive margins (HR:2.11, CI 1.66-2.69), increasing age, non-lipomatous tumors, increasing comorbidities, larger tumor size and higher grade all increased mortality. The influence of RT on OS was not different when stratified by histology, age, insurance, tumor size, stage or grade. CONCLUSIONS: RT use for early stage STS with positive margins was primarily a reflection of tumor characteristics and not socio-demographics, except for lack of insurance. After controlling for covariates, receipt of radiation significantlyimproved OS independent of all tumor features.

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Surgical Resection of Recurrent Leiomyosarcoma of the Retroperitoneum May be Beneficial N. Ikoma,* K.L. Watson, C.L. Roland, K.K. Hunt, J. Cormier, G.N. Mann, K. Torres, B. Feig. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: Leiomyosarcoma (LMS) in the retroperitoneum has a high propensity for both local and distant recurrence. The purpose of this study was to identify the role for surgery in the treatment of patients with localized recurrent disease. Method: We reviewed the medical records of patients with pathological diagnosis of LMS occurring in the retroperitoneum. Associations between clinicopathologic factors and local recurrence-free (LRFS), distant recurrence-free (DRFS), disease-specific (DSS), and overall (OS) survival outcomes were assessed using Log-rank and multivariate Cox regression methods. Results: 264 patients with pathologically confirmed retroperitoneal LMS were identified from our institutional tumor registry between 1994 and 2013. Median age was 56 years, and 53 patients (20.1%) were metastatic at presentation. Survival outcomes were evaluated in 176 patients who presented with localized disease and received R0/R1 surgical resection. Median follow-up time was 4.1 years (range, 0.1-28.8). 3-year DSS and OS were 89% and 88%, respectively. Variables associated with poor OS on multivariate analysis were age > 55 (HR 1.9, 95% CI 1.1-3.4; p = 0.028) and index tumor size ≥ 10 cm (HR 2.5, 95% CI 1.4-4.6; p = 0.003). Of those 176 patients, 100 (57%) patients developed a distant recurrence and 3-year DRFS was 52%. Fifty-three (27%) patients developed a local recurrence and 3-year LRFS was 76%. Positive margins (R1) was the only variable significantly associated with poor LRFS in univariate analysis (HR 3.3, 95%CI 1.5-7.4; p = 0.003). Of 53 patients who developed a local recurrence, 27 (51%) received additional resection, and repeat surgical resection was the only variable which showed a trend towards improved survival (3-year DSS, 69% vs 47%, HR 0.92, 95%CI 0.42-1.04, p=0.063). Conclusion: Although distant metastases are common, a significant percentage of patients with retroperitoneal LMS develop local recurrences. Surgical resection of recurrent disease may be beneficial in select patients. Further investigation is warranted to identify which patients with recurrent disease will benefit from surgical resection.

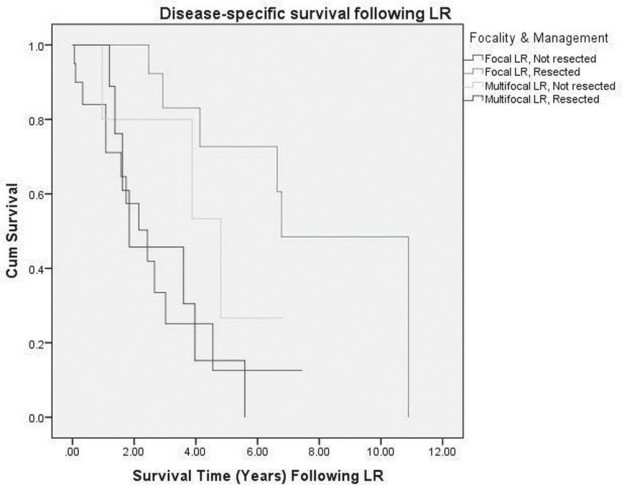

Table 1. Univariate analysis of factors associated with PFS and DSS

		PFS		DSS	
	N	5-year PFS Estimate (%)	p-value	5-year OS estimate (%)	p-value
Overall	87				
Disease spread					
Unifocal, single site	22 (25.3)	52	0.015	71	0.11
All others	65 (74.7)	18		48	
Duration of pre-operative TKI therapy	26 (29.9)	40	0.057	70	0.009
≤365 days	61 (70.1)	21		48	
>365 days					
Radiographic Response to TKI					
Stable	9 (10.3)	28	<0.001	80	<0.001
Progression only	17 (19.5)	14		62	
Regression only	22 (25.3)	55		86	
Regression & progression	36 (41.4)	0		25	
Pathologic viability					
≤50% viable	28 (32.2)	50.3	0.001	72.7	0.038
Mixed response	12 (13.8)	0.0		37.5	
>50% viable	17 (19.5)	0.0		45.2	
Not assessed	30 (34.5)				
Liver metastasis left *in situ*					
Yes					
No	15 (17.2)	0	<0.001	37	0.025
	72 (82.9)	33		59	

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Surgical Management of Patients with Recurrent or Intra-Abdominal Metastatic GIST Following Neoadjuvant Tyrosine Kinase Inhibitor Therapy: Who is Benefiting? C.L. Roland,* B. Bednarski, K. Watson, K. Torres, J. Cormier, G.N. Mann, W. Wang, A. Lazar, N. Somaiah, K.K. Hunt, B. Feig. *University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: The role of surgery for the treatment of patients with intra-abdominal metastatic/recurrent gastrointestinal stromal tumors (GIST) following tyrosine kinase inhibitor (TKI) therapy is unclear. The aim of this study was to identify patients who could potentially benefit from incorporating surgical resection in the multidisciplinary treatment plan. Methods: One hundred eight patients with metastatic (n=98) or recurrent (n=10) GIST who were treated with TKIs and surgical resection from 2002-2012 were identified. Patients that underwent resection with palliative intent (n=17) or treated for < 30 days (n=3) were excluded. Complete macroscopic resection was achieved in 87 patients and were included in the analytic cohort. Clinicopathologic features, treatment, and patient outcomes were analyzed. Univariate and multivariate analysis were used to determine independent risk factors for disease-specific survival (DSS) and progression-free survival (PFS). Results: Median age at diagnosis was 57 years. At a median follow-up of 108 months from surgical resection, median DSS was 73 months with a median PFS of 23 months. Factors on univariate analysis associated with improved 5-year PFS and DSS included: unifocal and single site disease, duration of TKI < 365 days, radiographic regression, and ≤ 50% viable tumor on pathologic evaluation (Table 1). Patients that underwent resection of peritoneal metastatic disease and did not undergo complete resection of the liver metastases (left in situ) had a reduced 5-year PFS (33% vs 0%, p<0.001) and DSS (59% vs 37%, p=0.025; Table 1). Tumor regression on radiographic imaging was associated with improved PFS (HR 0.37 [0.19-0.72]) and DSS (HR 0.24 [0.09-0.59]) on multivariate analysis. Conclusions: The management of patients with metastatic or recurrent GIST is complex and requires multidisciplinary treatment. Patients with unifocal/single site disease and radiographic evidence of tumor response to TKI therapy may achieve improved oncologic outcomes when complete surgical resection of all known disease is possible following treatment with systemic TKI.

P305

Effect of Intraoperative Radiotherapy in the Treatment of Retroperitoneal Sarcoma L.B. Wang,* D. McAneny, G. Doherty, T. Sachs. *Boston University School of Medicine, Boston, MA.*

Introduction Current NCCN guidelines for treatment of retroperitoneal sarcomas (RPS) endorse surgical resection, but the role of radiotherapy (RT) is less clear. We investigated the utilization and benefits of intraoperative RT (IORT) in the treatment of RPS. Methods We queried the Surveillance, Epidemiology & End Results (SEER) database (1988–2013) for the utilization of IORT and perioperative external beam RT (EBRT) in patients who underwent surgical resection of RPS. Groups were defined as follows: any IORT (aIORT), IORT alone (IORT-), IORT w/EBRT (IORT+) and preoperative and/or post-operative EBRT w/out IORT (EBRT). Demographics, tumor characteristics, extent of disease & survival were compared between groups. Results We identified 913 patients with RPS who underwent surgery and RT, of whom 65 (7.1%) had aIORT (51% IORT-, 49% IORT+). Liposarcoma (42%) and Leiomyosarcoma (31%) were the most common subtypes overall and in each group. Demographics were similar overall between aIORT and EBRT, but fewer aIORT patients were black (2% vs 11%; P=0.02). Mean size of tumors in patients receiving aIORT was no different than those receiving EBRT (17 vs 16 cm; P=0.47) but aIORT was more commonly used in patients with tumors > 20 cm than for smaller tumors (31% vs 20%; P=0.04). Tumor grade was not significantly different, although the EBRT group more commonly had no grade recorded (30% vs 9%; P=0.01). Mean survival was similar (aIORT 59.4 mo vs. EBRT 52.6 mo; P=0.34). aIORT was more often used in patients with tumor extension into adjacent tissues (75% vs. 56%; P<0.01). There was no difference in demographics, tumor characteristics, or survival between IORT+ and IORT- groups. In patients with liposarcoma (n=28) IORT+ demonstrated a survival benefit over IORT- (87 vs 34 mo; P=0.02) and EBRT (87 vs 55 mo; P=0.02) [Figure]. IORT- had worse survival than EBRT (34 vs 55 mo; P=0.02). Conclusions IORT was used infrequently for RPS, but generated equivalent outcomes as EBRT despite being utilized more often for larger tumors and those with peri-tumoral soft tissue invasion. Patients with the most common subtype of liposarcoma may benefit from combination IORT with adjuvant EBRT over other regimens.

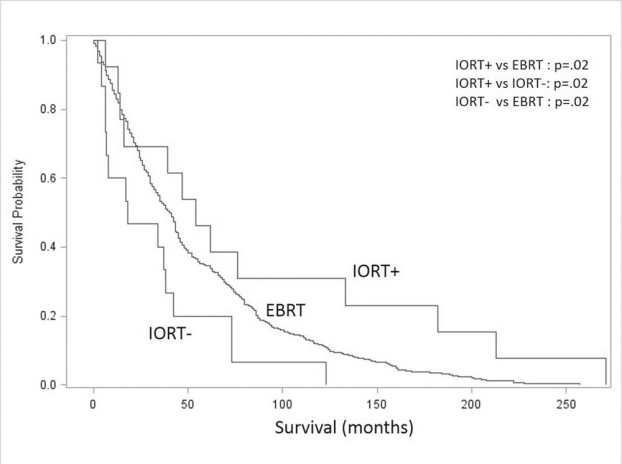

Figure: Kaplan-Meier Survival Estimates for patients in the SEER database (1988 – 2013) who underwent surgical resection of liposarcoma in combination with intraoperative radiation alone (IORT-), intraoperative radiation with adjuvant perioperative external beam radiation (IORT+) or adjuvant perioperative external beam radiation alone (EBRT).

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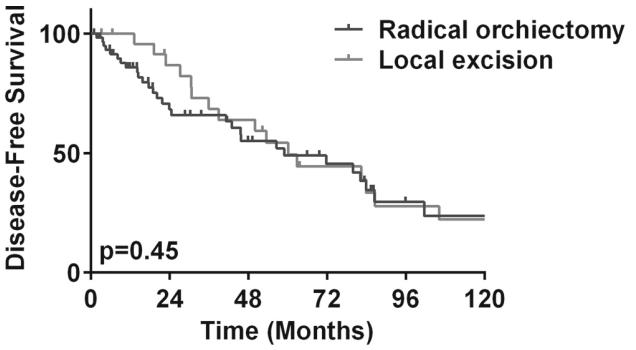
Inguinal Liposarcoma: Is Local Resection Alone Adequate?

T.E. Grotz,* K. Torres, A. Guadagnolo, W. Wang, N. Somaiah, G.N. Mann, J. Cormier, K.K. Hunt, B. Feig, C.L. Roland. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Background: Management of liposarcoma of the inguinal canal is complex, with surgical treatment options ranging from local resection to radical orchiectomy. We sought to evaluate the effect of the extent of surgical resection on oncologic outcomes in patients with liposarcoma of the inguinal canal. Methods: Between 1984 and 2014, 86 patients were diagnosed with primary well-differentiated (WDLPS; n=46) and dedifferentiated liposarcoma (DDLPS; n=40) of the inguinal canal. Patient, tumor and treatment variables were analyzed for associations with oncologic outcomes. Results: Median age was 58 years. Primary treatment consisted of local resection (LR) in 35 (41%) patients and radical orchiectomy (RO) in 51 (59%) patients. Negative margins were achieved in 10 (29%) patients that underwent LR and 17 (33%) RO patients (p=0.6). Of the 35 that underwent initial LR, 9 (26%) underwent re-resection with radical orchiectomy and additional tumor was identified in 7 (75%) and a negative margin achieved in 5 (71%). The remaining 26 patients had no evidence of residual disease after LR and were followed with close observation. The LR and RO groups were similar in regards to other prognostic factors. There was no significant difference between disease-free survival (DFS) or disease-specific survival (DSS) for those who underwent LR with observation vs. RO (DFS of 49 vs 49 months, respectively; p=0.45; Figure). At a median follow up of 83 months, 48 (56%) patients developed recurrent disease, most commonly in the inguinoscrotal area (62%) and retroperitoneum (31%). 14 (16%) patients were initially treated with radiation (4: LR; 10: RO). Radiation therapy was the only factor associated with improved 5-year DFS (70% vs 47%, respectively; p=0.02) on univariate analysis but lost significance on multivariate analysis. Tumor grade was associated with 5 -year DSS (WDLPS 94% vs. DDLPS: 74%; p=0.01). Conclusions: Liposarcoma of the inguinal canal has a high propensity for local recurrence, regardless of tumor grade, size, margin-status or resection-type. Our data supports close surveillance following local excision with no evidence of residual disease, as we found no benefit in DFS or DSS with aggressive re-resection.



P307

Adherence to Stage-Specific Treatment Guidelines for Stages IIA & IIB/III Extremity and Trunk Soft Tissue Sarcoma is Associated with Superior Survival

R.K. Voss,* J. Cormier, Y. Chiang, K. Torres, B. Feig, K.K. Hunt, G.N. Mann, C.L. Roland. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Background: The National Comprehensive Cancer Network (NCCN) has established evidence-based treatment guidelines for extremity and superficial trunk soft tissue sarcoma (STS), recommending margin-negative resection with or without radiation therapy (RT) for stage IIA disease (adherent IIA) and surgery plus RT with or without chemotherapy for stage IIB/III disease (adherent IIB/III). We sought to determine treatment adherence and associated survival outcomes for stages IIA and IIB/III STS. Methods: Stage IIA & IIB/III extremity and superficial trunk STS patients were identified in the National Cancer Data Base (2003-2011, n=28,115). Pediatric and bone sarcomas (n=10,591), patients not treated at the reporting hospital (n=943), and those with incomplete information (n=624) were excluded. The analytic cohort (n=15,957) was categorized by stage (IIA vs. IIB/III) and treatment group (adherent vs. non-adherent). Cox regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). Survival analyses were estimated after adjusting for gender, comorbidity score, type of treatment facility, and geographic region. Results: For stage IIA (n=5,734), 73% received guideline-adherent treatment. Adherent IIA patients had superior 5-year survival compared to non-adherent IIA (75.1% vs. 65.4%, p<0.01, Fig.1A), with a 48% higher risk of death for non-adherent IIA (HR 1.48 [95% CI: 1.32-1.67]). For stage IIB/III patients (n=10,223), 44% received guideline-adherent treatment which was associated with a superior 5-year survival compared to non-adherent IIB/III treatment (51.9% vs. 39.3%, p<0.01, Fig.1B). A 42% higher risk of death was associated with non-adherent IIB/III treatment (HR 1.42 [1.34-1.52]). Conclusion: Adherence to NCCN treatment guidelines is associated with improved survival for patients with stage IIA & IIB/III trunk and extremity STS. Further investigation to determine the reason for non-adherence to treatment guidelines is warranted to improve the delivery of care for patients with STS.

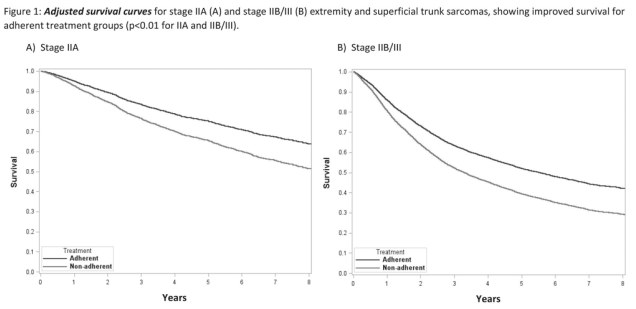


Figure 1: Adjusted survival curves for stage IIA (A) and stage IIB/III (B) extremity and superficial trunk sarcomas, showing improved survival for adherent treatment groups (p<0.01 for IIA and IIB/III)

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Differential miRNA Expressions Between Gastric and Metastatic Liver Gastrointestinal Stromal Tumors H. Kikuchi,* I. Iino, S. Miyazaki, Y. Ozaki, Y. Hiramatsu, M. Ohta, K. Kamiya, T. Sakaguchi, K. Hiroyuki. *Second Department of Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan.*

INTRODUCTION: Gastrointestinal stromal tumors (GIST), originating from the interstitial cells of Cajal (ICC) or their progenitor cells, are the most common mesenchymal neoplasm in the human digestive tract. The majority of GISTs have a gain-of-function mutation of the c-kit or PDGFRA gene in the ICC. Although tyrosine kinase inhibitors (TKIs) imatinib, sunitinib and regorafenib are effective for treating GISTs, resistance to TKIs often arises during therapy. In this era of TKIs, control of liver metastasis remains to be an important issue in the treatment of GISTs and mechanisms of liver metastasis need to be elucidated. In this study, we compared micro RNA (miRNA) expression profiles between gastric GISTs and metastatic liver GISTs to address mechanisms of GIST liver metastasis. METHODS: GIST cells were isolated from Formalin-fixed paraffin-embedded (FFPE) tissues of five gastric GISTs at low risk, five gastric GISTs at high risk and six metastatic liver GISTs surgically resected, and miRNA expression was analyzed using TaqMan miRNA array. None of the patients had received imatinib therapy before surgery. Protein expression of fascin-1 was immunohistochemically analyzed in primary gastric GISTs and metastatic liver GISTs. RESULTS: miR-122 was the most highly expressed in liver metastasis compared with primary gastric GISTs, consistent with our earlier papers that showed the overexpression of miR-122 and concomitant suppression of CAT1 in colorectal liver metastasis (Cancer Sci 104,624-30,2013). miR-133b, which has been reported to be downregulated in high-grade primary GISTs, was lower in liver metastasis. Protein levels of fascin-1, which has been reported as a negative target of miR-133, were higher in liver metastasis compared with primary gastric GISTs. CONCLUSIONS: In addition to the c-kit gene mutation, alterations of miRNA expression such as miR-122 and miR-133 play important roles in the metastatic process of gastric GIST

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Programmed Death Ligand-1 (PD-L1) Expression and Prognostic Value in Synovial Sarcoma K. Kozak, A. Szumera-Ciećkiewicz, A. Rembiszewska, A. Podgorska, H. Kosela-Paterczyk, J. Przybyl, A. Gos, T. Switaj, M. Wagrodzki, M. Prochorec-Sobieszek, P. Rutkowski.* *Departmnt of Soft Tissue/Bone Sarcoma and Melanoma, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Warsaw, Poland.*

Background: The interaction between PD-L1 expressed by tumor cells and its receptor PD-1 on activated T cells results in T cell suppression and inhibition of antitumor immune responses. Tumor PD-L1 expression has been associated with poor outcomes in many different cancer types. The aim of the study was to investigate the PD-L1 expression and correlation between PD-L1 expression and overall survival (OS) in one homogenous translocation-related sarcoma subtype -synovial sarcoma (SySa). Methods: We retrospectively analyzed formalin-fixed, paraffin-embedded tumor samples from 67 SySa patients treated at our institution between 04/1999 and 10/2011. Of the 67 samples, 38 (57%) were from primary tumor biopsies and 29 (43%) were metastatic lesions. PD-L1 immunohistochemistry (IHC) was performed using a rabbit polyclonal antibody (CD274, Cat No NBP1-76769, dilution 1/4000, NOVUS Biologicals, Cambridge, UK). A semiquantitative method for evaluation of PD-L1 IHC was applied. The combination of intensity (0-no staining; 1-weak, 2-intermediate and 3-strong staining) and proportion score (0: 0-10%, 1:11-33%, 2:34-66% and 3:>67%) was used for further analysis. The association between PD-L1 expression and OS was investigated using Kaplan-Meier curve and the log-rank test. Results: The median age was 38 years (range:17-60). Majority of patients (88%) had localized disease at the diagnosis. Median follow-up time for entire cohort was 67 months. Twenty three patients (34%) were still alive at the time of data analysis. The overall PD-L1 IHC staining positivity was 85% (1-3+). PD-L1 expression was observed at high percentage both in primary (89%) and metastatic tumors (79%). PD-L1 staining within tumor cells was associated with shorter median OS with borderline significance (83 months vs 108 months, p=0.1). Conclusions: This is the largest study evaluating PD-L1 expression in SySa. PD-L1 expression is present in the majority of synovial sarcoma and preliminary data implies to be a prognostic marker with PD-L1 expression associated with poorer outcomes. These findings may have implications for further studies with immunotherapy acting on PD-1/PD-L1 checkpoints in this type of soft tissue sarcoma.

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CT Scan as Single Modality, Cost-effective Surveillance Imaging for High-risk Extremity Soft Tissue Sarcomas A. Maciver,* L. Davis, K. Attwood, M. Wach, S. Singla, K. Salerno, N. Khushalani, J. Kane. *Roswell Park Cancer Institute, Buffalo, NY.*

INTRODUCTION Extremity soft tissue sarcomas (STS) that are large, deep, and high grade are "high risk" for both local recurrence (LR) and pulmonary metastases (PM). Chest CT is frequently used for lung surveillance, but MRI has been the "traditional" imaging modality for the primary site. We postulated that CT scan would be cost-effective surveillance imaging for both LR and PM. METHODS Retrospective review of "high-risk" extremity STS patients who underwent CT scan for surveillance of both the primary site and lungs. The standard surveillance imaging schedule was chest/extremity CT every 3 months for 2 years, every 6 months years 3-5, and annually until year 10. Patient/tumor demographics, treatment, and outcomes were analyzed. RESULTS 93 "high risk" extremity STS patients utilizing surveillance CT for both the primary site/chest were analyzed. Median age was 54 years (range 16-93), 55% male, and primary site was 78% lower limb/buttock/hip. "High risk" features included 65% tumors >5 cm (median size 6.2 cm), deep 77%, and 71% intermediate/high grade. Most common histologies were 28% liposarcoma, 14% undifferentiated pleomorphic sarcoma, and 14% leiomyosarcoma. Wide resection margins were definitively negative in 90%. Radiation was administered in 71% (47% preoperative, 24% postoperative) and 11% received chemotherapy. At a median followup of 50.5 months (range 0.4-122.3), estimated 5 year LR-free and distant recurrence-free survival were 70% and 71%, respectively. There were 14 LR in 11 patients. 11 LR were asymptomatic, only detected on surveillance CT. There was one "false positive" LR on CT. PM was identified on surveillance CT in 15 patients (15.5%). Interestingly, surveillance CT identified 5 incidental second primary malignancies. Using 2014 cost data, chest CT/extremity MRI for a 10 year surveillance would cost $64,969 per patient versus only $41,595 for combined chest/extremity CT. CONCLUSIONS Combined chest/extremity surveillance CT for high risk extremity STS reliably identified both LR and PM with very few "false positive" LR. Replacing MRI with extremity CT would result in a $23,000 cost savings per patient over a 10 year follow-up.

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Pathologic Fracture in Childhood and Adolescent Osteosarcoma: A Single Institution Experience L. Haynes,* S. Kaste, K. Ness, J. Wu, L. Ortega-Laureano, M. Bishop, M. Neel, B. Rao, I. Fernandez-Pineda. *St. Jude Children's Research Hospital, Memphis, TN.*

Introduction: Pathologic fractures occur in 5-10% of the pediatric osteosarcoma population and have historically been considered a contraindication to limb salvage. The purpose of this study was to describe the radiographic features and prognostic significance of pathologic fracture, and to examine its impact on local recurrence rates, functional outcomes and overall survival (OS). Methods: We retrospectively analyzed patients who presented to our institution from 1990-2015 with pathologic fracture at diagnosis or during neoadjuvant chemotherapy. We selected a control group of 50 osteosarcoma patients of similar age and gender without pathologic fracture from 1990-2015. Functional outcomes were scored using Musculoskeletal Tumor Society (MSTS) criteria. Chi square test was used for comparative analysis of groups. Results: Thirty-six patients presenting with 37 pathologic fractures form the study cohort. Of patients who received surgery, 18/34 (52.9%) patients with pathologic fracture underwent amputation, compared to 8/48 (16.7%) in the non-fracture group (p=0.007). Indications for amputation in fracture patients were tumor size (n=7), neurovascular involvement (n=6), and tumor progression during neoadjuvant chemotherapy (n=5). Only one patient (2.9%) in the pathologic fracture group who underwent limb salvage suffered a local recurrence. Of patients who received neoadjuvant chemotherapy, 25/34 (73.5%) fracture patients showed poor histological response, compared to 24/47 (51.1%) non-fracture patients. (p=0.044) There was no statistically significant difference in development of distant metastases or OS between the two groups. Functional outcomes were significantly lower (p-value=0.023) in pathologic fracture patients (MSTS median=17.5) than non-fracture patients (MSTS median=24). Conclusions: Radiographic features and clinical management of pathologic fractures were highly variable in this population. Pathologic fracture is not an indication for

amputation in pediatric osteosarcoma patients; limb salvage surgery can be performed without increased risk of local recurrence. Patients with pathologic fracture suffer worse functional outcomes, but show no decrease in OS.

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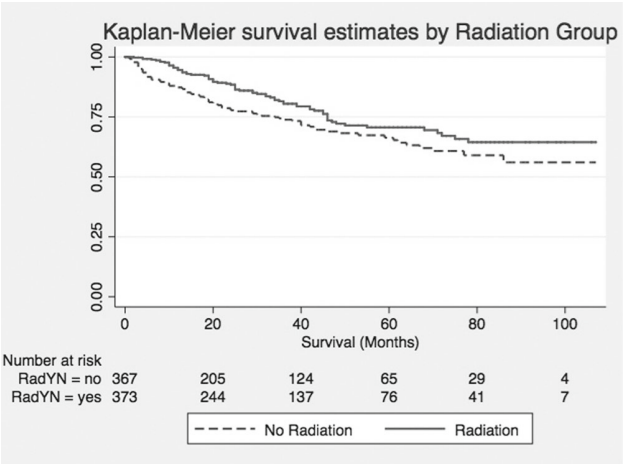
When Combined with Resection, Radiation Does Improve Survival in Retroperitoneal Sarcoma S. Dumitra,[1]* M. Raoof,[1] B. Lee,[1] W. Chow,[1] Y. Fong,[1] J.S. Barkun,[2] V. Trisal,[1] B. Paz.[1] *1. Surgical Oncology, City of Hope, Pasadena, CA; 2. McGill University, Montreal, QC, Canada.*

INTRODUCTION: Retroperitoneal sarcoma(RPS) remains a rare disease for which surgical resection is the cornerstone. Given high local recurrence rates, radiation is increasingly used for disease control but its impact on survival remains unknown. We propose a contemporary propensity score analysis of a large population database to answer this question. METHODS: This is a propensity matched study of a contemporary cohort of patients from the prospectively collected National Cancer Institute's SEER database (2004-2013). All patients older than 20 years with non-metastatic RPS undergoing resection were divided into radiation(R) and non radiation(NR) groups. Primary outcome was disease specific survival(DSS). Predictors of radiation treatment were identified using logistic regression and survival analysis was performed using Cox regression. RESULTS: A total of 1,197 met the inclusion criteria, 375(31.1%) in the R group and 822(68.7%) in the NR group. When compared to the NR group, those in R group were more likely to have higher grade and locally advanced disease but similar age and year of diagnosis. In the multivariate survival analysis R significantly improved DSS (HR 0.67 95%CI(0.51-0.91), p=0.006) as did older age at diagnosis, and tumor grade 1 (HR 0.24, 95%CI(1.16-0.36), p=0.000). Histologic type and regional disease negatively impacted survival while the extent of surgical resection had no effect on survival. Af ter propensity matching for all available variables, the survival advantage in the R group was even more pronounced (HR 0.59, 95%CI(0.43-0.82), p=0.002). Histologic type, high grade continued to negatively impact DSS while disease stage did not. CONCLUSION: In the absence of a randomized clinical trial, this is the largest study to date that provides robust evidence in support of radiation in resected RPS with a survival advantage. Patients with high-grade disease, unfavorable histology and locally advanced disease would benefit the most from radiation.



Surival is significantly higher in the radiation group (p=0.000) after propensity matching for all known variables.

P314

Disparities in Amputation Rates for Non-Metastatic Extremity Soft Tissue Sarcomas and the Impact on Survival T. Fischer,[1]* B. Lau,[1] M. Raval,[7] S. Vasudevan,[6] K. Gow,[2] E. Beierle,[3] J. Doski,[4] A. Goldin,[2] M. Langer,[5] N. Nuchtern,[6] L.J. Foshag,[1] M. Goldfarb.[1] *1. John Wayne Cancer Institute, Santa Monica, CA; 2. Seattle Children's, Seattle, WA; 3. Children's of Alabama, Birmingham, AL; 4. UT Health Science Center of San Antonio, San Antonio, TX; 5. Maine Medical Center, Portland, ME; 6. Texas Children's Hospital, Houston, TX; 7. Children's Healthcare of Atlanta, Atlanta, GA.*

INTRODUCTION: There are no definitive recommendations guiding amputation use in extremity soft tissue sarcomas (STS). This study explores disparities in amputation rates in a large cohort of patients with non-metastatic adult-type extremity STSs and the impact on survival. METHODS: Patients with non-metastatic adult-type extremity STS were identified from the 1998-2012 National Cancer Database. Factors relating to amputation were examined across all ages and separately in older (>40 years) and adolescent/young adults (AYA: ages 15-39). The impact on 10-year overall survival (OS) was also explored. RESULTS: Of 15,886 patients, only 4.65% had an amputation. AYAs had the most amputations (6.4%) compared to younger children (5.9%) and older adults (4.2%) (p<0.001). Patients most likely to receive an amputation had public insurance (OR:1.3, CI 1.08-1.58) and lived in the central states (OR:1.5, CI 1.2-1.86); less amputations were performed for those with the highest income (OR:0.8, CI 0.62-0.94) and treated at a community cancer center (OR:0.7, CI 0.62-0.90). As expected, those with increasing tumor grade and non-lipomatous histology had higher amputation rates. In AYAs, females were less likely to have an amputation (OR:0.6, CI 0.44-0.94) whereas in adults over 40, Hispanics had more amputations than whites (OR:1.7, CI 1.20-2.58). Having an amputation was an independent risk factor for death at 10 years, and this varied by age as the risk of death after amputation was significantly higher for AYAs than for older adults (HR:1.7, p<0.001). Additionally, treatment in eastern (HR:1.1, CI 1.07-1.03) or central states (HR:1.2, CI 1.04-1.25), lower income level, lack of private insurance, comorbidities and aggressive tumor features were all associated with decreased OS. Conversely, female gender (HR:0.8, CI 0.78-0.89) and treatment at the higher volume centers (>10 cases/year) (HR:0.8, CI 0.74-0.94) improved OS. CONCLUSIONS: Although amputations for non-metastatic adult-type extremity STS are rare, disparities exist across age groups, insurance and geography. Moreover, having an amputation is an independent risk factor for death, with the greatest impact in AYAs.

P315

Association of PD-L1 Expression and Prognosis in Angiosarcomas S. Bagaria,* S. Attia, M. Krishna, R. Joseph. *Surgery, Mayo Clinic, Jacksonville, FL.*

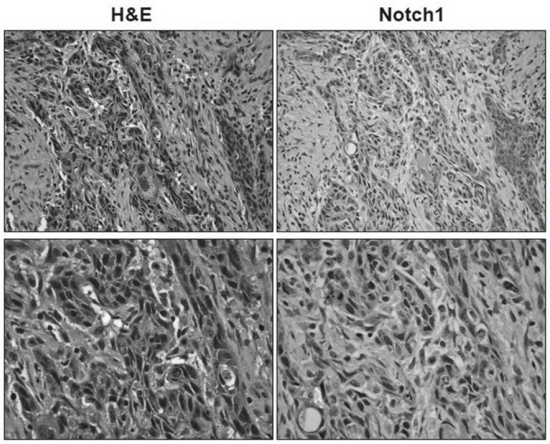
Introduction Angiosarcomas are vascular malignancies associated with a poor prognosis and chemotherapy resistance. Therefore, there is a critical need to develop novel therapeutic strategies, such as immunotherapy, for this patient population. Tumor expression of programmed death-ligand (PD-L1) plays a role in inhibiting the anti-cancer immune response. We investigated the expression of PD-L1 in angiosarcomas and correlated these findings with clinical parameters and outcomes. Methods We evaluated the immunohistochemical expression of PD-L1 and the presence of tumor infiltrating lymphocytes (TILs) in archived formalin-fixed paraffin-embedded angiosarcoma specimens. Tumors were considered PD-L1 positive if 5% of tumor cells expressed moderate staining intensity (≥2+). TILs were semi-quantitatively scored as brisk or non-brisk. We then correlated the expression of PD-L1 with TILs, clinical parameters and death due to angiosarcoma. Results Retrospective review identified 27 angiosarcoma patients treated at Mayo Clinic Florida between 1994 and 2012. Tumor PD-L1 expression and the presence of brisk TILs were noted in 5 (19%) and 6 (22%) specimens, respectively. It was noted that angiosarcomas that expressed PD-L1 were more likely to be cutaneous (80% vs. 68%; p<0.001), spindle-type (80% vs. 38%; p<0.001), and have brisk TILs (40% vs 20%; p<0.001). Patients with PD-L1 positive tumors were more likely to die from angiosarcoma than PD-L1 negative tumors (80% vs. 26%; p=0.015). Conclusion PD-L1 positive angiosarcomas are associated with the presence of brisk TILs, death from angiosarcoma, cutaneous primary, and spindle-type histology. This dataset is limited by its size and therefore, further work is necessary to confirm these findings and if confirmed provides a rationale for anti-PD1/PDL1 therapy in a subset of patients with angiosarcoma.

P316

Nuclear Notch1 Expression is Associated with Treatment Failure and Predicts Prognosis in Patients with Esophageal Squamous Cell Carcinoma Y. Kita,[1]* S. Naganuma,[2] H. Nakagawa,[3] H. Okumura,[1] Y. Uchikado,[1] T. Arigami,[1] K. Sasaki,[1] K. Tanoue,[1] I. Omoto,[1] K. Baba,[1] S. Mori,[1] Y. Uenososno,[1] Y. Mataki,[1] Y. Kijima,[1] K. Mamura,[1] S. Natsugoe.[1] *1. Department of Digestive Surgery, Kagoshima University, Kagoshima, Japan; 2. Department of Pathology, Kochi Medical School, Nangoku, Kochi, Japan; 3. Abramson Cancer Center, Perelman School of Medicine, Philadelphia, PA.*

Introduction: Notch signaling is involved in cell fate decisions and tumorigenesis. Ligand stimulation of a cell surface Notch receptor triggers enzymatic cleavages, resulting in translocation of the intracellular domain of Notch into the cell nucleus to act as a transcription factor. Yet, the consequences of Notch activation are context dependent. The roles of Notch signaling in the pathogenesis of esophageal squamous cell carcinoma (ESCC) remain elusive. Methods: Surgically resected primary tumors and adjacent normal mucosa from patients with ESCC (n=152) were analyzed by immunohistochemistry using two kinds of antibodies. Results: Both antibodies detected Notch1 expression on serial sections with specific signals. Notch1 expression appeared to be heterogeneous within single tumors. Moreover, Nuclear Notch1 was detected in a small subset of cancer cells displaying spindle-shaped cell morphology consistent with epithelial-mesenchymal transition (EMT) as corroborated by concurrent expression of ZEB1, a marker of EMT. Present in 75 out of 140 ESCC cases (54%), nuclear Notch1 was categorized into three classes distinguished by a differential expression pattern and cellular localization: type I (Fig.1), a focal expression in the tumor invasive fronts at the stromal interface (49/75); type II, a patchy expression within tumor nests (39/75); and type III, a focal expression within superficial lesions (14/75). 25 cases showed multiple types concurrently. Interestingly, type I (49/140, 33%) only was associated with poor 5-year survival (P=0.01), tumor depth (P=0.01), lymphatic and venous invasion (P=0.003) and distant metastasis (P=0.002). Moreover, type I only was observed among tumors expressing nuclear Notch1 (7/12, 58%) from patients who received neoadjuvant therapy Conclusions: Morphological evaluation of ESCC tissues reveals heterogeneous Notch1 expression, ranging from loss of expression to activation within a single tumor. Nuclear expression of the activated form of Notch1 found in the tumor invasive fronts may contribute to disease progression, providing a molecular and clinical insight in the pathobiology of ESCC.

Figure 1



Pattern1: nuclear N1(+) cells are seen in narrow trabecular nests at invasive lesion. Majority of cells in these nests are de-differentiated.

P317

Timing of Esophagectomy After Neoadjuvant Chemoradiation Therapy Affects Clinically Significant Anastomotic Leak Rates S. Roh,[1]* M. Iannettoni,[2] J. Keech,[1] P. Gruber,[1] R. Weigel,[1] K. Parekh.[1] *1. University of Iowa Hospitals and Clinics, Iowa City, IA; 2. East Carolina University Brody School of Medicine, Greenville, NC.*

Introduction Neoadjuvant chemoradiation therapy (CRT) for esophageal cancer is used routinely to decrease the tumor burden prior to esophagectomy as well as increase long term survival. The optimum timing for surgery after completion of CRT remains unclear. The goal of this study was to study the effect of timing of esophagectomy after CRT on postoperative anastomotic leaks. Methods We reviewed all patients who underwent esophagectomy for esophageal cancer between January 2000 and December 2013 at our institution. Patients were evaluated for clinically significant leaks (defined as neck wound infection requiring jejunal feeds and/or parenteral nutrition) during the postoperative period. Patients were categorized into 3 groups based on timing of esophagectomy after CRT (no CRT, ≤30 days, >30 days). Statistically significant difference in development of anastomotic leaks was calculated among the patient groups using Chi-square test. Results A total of 326 esophagectomies were performed for esophageal cancer using transhiatal (n=295), Mckeown (n=22), or Ivor Lewis (n=9) techniques. 322 anastomoses were assessed for leaks. 38 developed leaks and 284 did not develop leaks. 13(12%) leaked in the no CRT group, 9(7%) leaked in the ≤30 days group, and 16(19%) leaked in the >30 days group (p=0.029). For subgroup analysis, the anastomotic leak rate reached statistically significant difference between the ≤30 days group and >30 days group (p=0.026) (Table 1). The median length of stay for the patients who had no leak was 7 days. Anastomotic leak significantly increased the median length of stay in the hospital to 21.5 days. The 30-day operative mortality for patients without leak was 6/284(2.1%) and patients with leak was 3/38(7.8%) (p=0.075). Conclusion Esophagectomy within 30 days after neoadjuvant CRT results in lower anastomotic leak rates. Anastomotic leak increases length of stay in the hospital, however, there was no statistically significant difference in operative mortality between patients with and patients without leak. Our practice has evolved to perform esophagectomy within 4 weeks after completion of neoadjuvant CRT.

Table 1

Timing of neoadjuvant CRT	n	With anastomotic leak	Chi-square p-value	Pairwise comparison	Tukey adjusted p-value
No neoadjuvant treatment	106	13 (12%)	0.029	No CRT vs. ≤30 days	0.338
≤30 days prior to surgery	131	9 (7%)		No CRT vs >30 days	0.425
>30 days prior to surgery	85	16 (19%)		≤30 days vs. >30 days	0.026

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Transthoracic Anastomotic Leak After Esophagectomy: No Longer a Catastrophe C.E. Ryan,[1]* A. Paniccia,[2] R. Meguid,[2] M.D. McCarter.[2] *1. University of South Florida Morsani College of Medicine, Tampa, FL; 2. University of Colorado Hospital, Aurora, CO.*

Introduction: Leaks from intrathoracic esophagogastric anastomosis are thought to be associated with higher rates of morbidity and mortality than leaks from cervical anastomosis. We challenge this assumption, and hypothesize that there is no significant difference in mortality based on the position of the esophagogastric anastomosis. Methods: A systematic literature search was conducted using PubMed and Embase databases on all studies published between January 2000 and June 2015 comparing transthoracic (TTE) and transhiatal (THE) esophagectomies. Studies that used alternate reconstruction approaches were excluded. Outcomes analyzed were leak rate, leak-associated mortality, overall 30-day mortality, and overall morbidity. Meta-analyses were performed using Mantel Haenszel statistical analyses on studies that reported on leak rates of both approaches. Nominal data are presented as frequency and interquartile range (IQR); measures of the association between treatments and outcomes are presented as odds ratio (OR) with 95% confidence interval (CI). When the CI does not include 1, data are considered significantly different. Results: Twenty-one studies (including 3 randomized controlled trials) were included comprising of 7167 patients (54% TTE). THE approach yields a higher anastomotic leak rate (12%; IQR: 11.6% - 22.1%) than TTE (9.8%; IQR: 6.0% - 12.2%) (OR: 0.56 [0.34-0.92]), without any difference in leak-associated mortality (7.1% TTE vs. 4.6% THE; OR: 1.83, [0.39-8.52]). There was no difference in overall 30-day mortality (3.9% TTE vs. 4.3% THE; OR: 0.86, [0.66-1.13]) and

morbidity (59.0% TTE vs. 66.6% THE; OR: 0.76, [0.37-1.59]). Discussion: Transthoracic esophagectomy is associated with a lower leak rate and does not result in higher morbidity or mortality than transhiatal esophagectomy. The previously assumed higher rate of transthoracic leak-associated mortality is overstated, thus allowing surgeon discretion and other factors to influence the choice of thoracic versus cervical esophagogastric anastomosis.

P319

Does Minimally Invasive Esophagectomy Provide a Benefit Over Open Esophagectomy? A Study of the National Inpatient Sample

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Introduction: Esophagectomy is the standard treatment for resectable esophageal cancer. However, open approaches to esophagectomy carry high postoperative complications. Minimally invasive esophagectomy (MIE) has been attempted, with the intent of lowering postoperative morbidities. The aim of this study is to identify trends in the use of MIE and compare postoperative outcomes between open and minimally invasive techniques. Methods: Patient data was collected from the National Inpatient Sample (NIS), the largest publically available all-payer inpatient care database in the United States. All patients that received an esophagectomy from 2010-2012 were included. Patients were placed into two groups: open esophagectomy and MIE. MIE was defined as laparoscopic or robotic. Univariate and multivariate analysis was performed. Results: A total of 2,429 patients were identified, with 221(9.1%) in the minimally invasive group. No clear yearly trends were identified. The average age for the cohort was 62 and approximately 20% of the group were women. The demographics of the open and minimally invasive groups were comparable in terms of age, race, and sex. Over 88% of all esophagectomies were performed in teaching hospitals. Median length of stay was lower for MIE on univariate analysis (10 versus 11 days, $p<0.0008$) but on multivariate analysis (MV) this became a non-statistically significant trend ($p<0.08$). Total charges were statistically significantly higher for MIE on MV ($151,381 versus $125,416, $p=0.01$). There was a trend toward lower mortality in the MIE group on MV (3.6% versus 0.5%, $p=0.08$). Total complication rates were similar between the two groups (38% in open versus 40% in MIE). Conclusions: MIE is a new technology that may offer shorter length of stay and lower mortality compared to open esophagectomy. The overall benefit remains small possibly due to the complexity of the case and the potential complications that are not placated by technique. As surgeons become more facile more research will need to be done to see if the benefit to MIE increases.

P320

Effectiveness of Repeat Positron Emission Tomography Scan in Accurately Detecting Disease Progression After Neoadjuvant Chemoradiation for Esophageal Cancer

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Introduction Our group published that for patients with esophageal cancer (EC) treated with neoadjuvant chemoradiation (nCRT), a post-nCRT PET-CT was 91.7% predictive of residual disease. The aims of this study were to determine the positive predictive value (PPV) of PET-CT in accurately detecting disease progression (DP) after nCRT and stratify false positives into clinically useful categories. Methods This is a single institution retrospective study of EC patients treated with nCRT from 1/2005 to 12/2012 who underwent both pre- and post-nCRT PET-CT scans prior to esophagectomy. Results A total of 283 patients were treated with nCRT, of which 258 (91.2%) had both a pre- and post-nCRT PET-CT. On the post-nCRT PET-CT, 64 patients (24.8%) were found to have new findings concerning for DP. Of these patients, 10 (15.6%) had truly positive findings of new metastatic disease (6 biopsy proven). In 1 patient, a new primary malignancy (papillary thyroid cancer) was found. A total of 208 patients proceeded with surgery: 163 (78.4%) had no DP and 45 (21.6%) had false positive new findings of DP. The PPV of post-nCRT PET-CT for the detection of DP was 18.2%. The most common sites of false positive results were the lung (28.3%), liver (26.4%) and bone (13.2%). The work-up of the 53 patients (82.3%) with false positive post-nCRT findings included biopsy (24.6%) and additional imaging (45.2%) such as high resolution CT/MRI. Negative biopsy was confirmed through percutaneous approach (7 patients), surgery (2 open and 1 laparoscopic), endobronchial ultrasound (2), endoscopic ultrasound (1) or mediastinoscopy (1). There were no peri-procedural complications resulting from biopsy. Figure 1 summarizes these results. Conclusions Post-nCRT PET-CT is a valuable tool in assessing response to nCRT. However, in cases where new findings concerning for DP are detected, PET-CT often leads to a high proportion of false positives and subsequent investigational work-up. Post-nCRT PET-CT most frequently raises suspicion in the common metastasis sites of EC, but its low PPV should be thoughtfully considered when evaluating new findings.

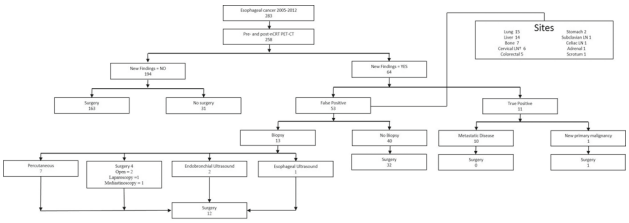

Figure 1: Flow diagram of inclusion criteria and outcomes for patients with esophageal cancer who had neoadjuvant chemoradiation (nCRT) with both pre- and post-nCRT PET. †LN = lymph node.

P321

Pre-Neoadjuvant Therapy Clinical Staging Predicts Overall Survival in Esophageal Cancer Patients with Pathologic Complete Response

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BACKGROUND Pathologic complete response (pCR) to neoadjuvant therapy is presumably associated with favorable outcomes in patients (pts) with esophageal cancer, but reported survival rates vary. This study evaluates patterns of recurrence after curative esophagectomy and identifies factors predictive of recurrent disease and overall survival (OS) in patients with pCR. METHODS An IRB-approved, retrospective review of a prospective esophageal cancer database was conducted. Patient demographics, perioperative data, and outcomes were examined. Recurrences were classified as locoregional (LR) or systemic. Cox regression model and Kaplan–Meier (KM) plots were used for survival analysis. RESULTS 837 pts with invasive esophageal cancer treated at a single institution from 1994 to 2013 were identified. 176 pts underwent neoadjuvant therapy followed by surgery and had pCR. Of these, 93.7% had adenocarcinoma and 6.3% had squamous cell cancer. Mean age was 56.6 and most pts were white (96.6%) males (79.5%). Median follow up was 42.6 months. 95 pts were treated before 2007 and 81 after. Most pts (85%) underwent transthoracic esophagectomy. All 176 pts received chemotherapy and radiation; dose-specific information was available on 144 pts, of whom most received 50.4 Gy (45%). 170 pts had recurrence data available: 39 (22.9%) had recurrent disease at a mean of 18.3 months; 5 (2.9%) with LR and 34 (20%) with systemic disease. On multivariate analysis, when evaluating patient demographics, pretreatment stage, type of surgery, type of chemotherapy, and number of lymph nodes resected, only pretreatment stage was associated with recurrence ($p=0.04$). Median time to recurrence was 26.3 months for LR disease and 10.9 months for systemic disease ($p=0.3$). KM estimates determined that pre-treatment stage and time of treatment (<2007 or ≥ 2007) were predictive of improved OS ($p <0.01$, $=0.03$). CONCLUSIONS The incidence of disease recurrence in pts who experience pCR is low. The pretreatment stage and time of treatment were independent predictors of improved OS. Enhancing treatment strategies to maximize pCR would improve outcomes in pts with esophageal cancer.

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Is Chemical Pyloroplasty Necessary for Minimally Invasive Esophagectomy?

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Introduction: Many centers routinely employ botulinum toxin for chemical pyloroplasty in minimally invasive esophagectomies (MIE) as prophylaxis against delayed gastric emptying. There is limited data to support this practice, however, and no previous studies have compared botulinum toxin injection to no pyloric intervention in patients treated with a combined laparoscopic/

thoracoscopic approach. We hypothesized that chemical pyloroplasty does not improve outcomes in these patients. Methods: We queried all patients undergoing MIE from 9/2009-6/2015 at our institution. We excluded 3 patients who underwent surgical pyloric drainage. Delayed gastric emptying was defined as inability to tolerate a soft diet by post-operative day 10 without other clear reasons for this, and corroboration of diagnosis by esophagogram or upper endoscopy. Clinical information was compared using Student's t-test, chi-square analysis, and Mann-Whitney U test where appropriate. Results: We identified 71 patients treated with MIE; 35 with chemical pyloroplasty treated from 9/2009-1/2014, and 36 without pyloric intervention from 2/2014-6/2015. Groups were statistically similar in age, gender distribution, T-stage, percent receiving neo-adjuvant therapy, body mass index, pre-operative weight loss, pre-operative serum albumin, and pre-operative placement of feeding tubes (all $p>0.05$). There were 3/35 (8.6%) patients who had chemical pyloroplasty that developed delayed gastric emptying in the post-operative period, compared to 2/36 (5.6%) patients with no pyloric intervention ($x^2=0.25$, $p=0.62$), which was not statistically different. There were also no significant differences between groups for development of anastomotic leak (8/35 vs 5/36, $p=0.33$), or 30-day mortality (3/35 vs 2/36, $p=0.62$). Patients with chemical pyloroplasty did, however, have longer hospitalizations (median 13 vs 10 days, $p=0.009$). Conclusions: In a well-matched cohort study with historical control, use of botulinum toxin for chemical pyloroplasty in MIE was not associated with improved outcomes when compared to no pyloric intervention. Absence of evidence for this additional step suggests that it should not routinely be employed.

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Accuracy of Clinical Staging with EUS for Early Stage Esophageal Cancer: Are We Denying Patients Beneficial Neoadjuvant Therapy? C. Luu,* N. Garcia-Henriquez, J.B. Klapman, C.L. Harris, K. Almhanna, S. Hoffe, J.M. Pimiento, J. Fontaine. *Moffitt Cancer Center, Tampa, FL.*

Introduction: Esophagectomy alone has been considered the standard of care for early stage esophageal cancer (EC) while neoadjuvant therapy is now standard for locally advanced disease. The choice of treatment therefore hinges on accurate locoregional staging by endoscopic ultrasound (EUS). Our objective is to evaluate the accuracy of EUS performed in a high-volume tertiary cancer center in clinical stage T1N0 (cT1N0) and T2N0 (cT2N0) esophageal cancer patients undergoing esophagectomy without neoadjuvant therapy. Methods: A retrospective review of the esophageal cancer database at a single institution was performed. Patients with cT1N0 and cT2N0 esophageal cancer based on EUS undergoing esophagectomy without neoadjuvant treatment were evaluated. Patient demographics, tumor characteristics, and treatment were reviewed. Surgical pathology was compared to EUS staging. Results: Between 2000 and 2015, 139 patients were identified. There were 25 (18%) female and 114 (82%) male patients. The tumor location included the middle 1/3 of the esophagus in 11 (8%) and lower 1/3 and gastroesophageal junction in 128 (92%) patients. Eighty-one percent of patients had adenocarcinoma, 9% had squamous cell carcinoma, 9% had Barrett's dysplasia, and 1% had mixed histology. Clinical staging were as follows: 110 (79%) patients had cT1N0 and 29 (21%) patients had cT2N0 tumors. For the entire cohort, preoperative EUS matched the final surgical pathology in 76/139 patients for an accuracy rate of 53%. Twenty-nine patients (21%) were under-staged by EUS; of those, 19 (14%) had unrecognized nodal disease. This included 12/109 (11%) of cT1N0 and 7/29 (24%) of cT2N0 patients. Conclusions: The accuracy of preoperative EUS staging in early esophageal cancer remains sub-optimal. Interestingly, a significant proportion (24%) of cT2N0 EC patients were found to have positive lymph nodes on surgical pathology, and perhaps these patients could have benefitted from neoadjuvant therapy. In light of these findings, the current management of cT2N0 esophageal cancer should be reconsidered.

	Total # of patients	Under-staged by N stage	Under-staged by T stage
EUS stage			
T1N0	110	12	12
T2N0	29	2	7
Total	139	14	19

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Anti-Inflammatory Effect of Alpha-Lypoic Acid Derivative on Acute Lung Injury Y. Shoji,[1]* H. Takeuchi,[1] K. Fukuda,[1] R. Nakamura,[1] T. Takahashi,[1] N. Wada,[1] H. Kawakubo,[1] T. Miyasho,[2] Y. Kitagawa.[1] *1. Surgery, Keio University, School of Medicine, Tokyo, Japan; 2. Rakuno Gakuen University, Emonbetsu, Japan.*

Backgrounds Acute lung injury (ALI) is one of the most critical early complications after surgery, especially esophagectomy. Because of the high invasiveness of thoracolaparotomy, the reported incidence of respiratory complication is up to 30%, highest rate among all gastrointestinal surgeries. In order to prevent ALI after esophagectomy, we focused attention on the anti inflammatory effect of Alpha – Lypoic Acid Derivative DHLHis – Zn (ALA). Methods ALI model rats were developed by intra – tracheal administration of lipopolysaccharides (LPS) against Sprague-Dawley rats (male, 8th age in weeks). ALA was administrated intraperitoneally in 2-hour advance of LPS administration (ALA group). In the control group, phosphate buffered saline (PBS) was administrated instead of ALA. Four hours after LPS administration, peripheral blood drawing, bronchoalveolar lavage (BAL), and lung tissue collection were investigated in both groups. Number of cells, number of neutrophil, and cytokine concentration of peripheral blood and BAL fluid (BALF), and pathological findings of the lung tissues were estimated. Results Numbers of cases were ALA group; 11, control group; 11, respectively. There were no significant differences in the peripheral blood cell count in both groups. Numbers of cells and neutrophils of the BALF was significantly lower in the ALA group than in the control group ($p < 0.001$). When we investigated the cytokine concentration of the BALF cyclopaedically, levels of IL1a, IL1b, IL2, IL4, IL5, IL6, IL10, IL12, IFNγ, and TNFα were significantly lower in the ALA group than in the control group ($p < 0.05$). NF-kB p65 subunit concentration of the BALF investigated by enzyme – linked immunosorbent assay (ELISA) was significantly lower in the ALA group than in the control group ($p < 0.001$). There was no apparent difference in the pathological findings of the lung tissue in both groups. Conclusion ALA inhibited elevation of cell numbers, neutrophil numbers, and various inflammatory cytokine levels of the BALF in LPS induced ALI model rats. The mechanism of action of ALA is suggested to be inhibition of NF – kB signaling pathway. ALA is suggested to be a new prophylactic agent for ALI.

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Near-Infrared Intraoperative Molecular Imaging Identifies Mesothelioma During Pleurectomy J. Keating,* J. Predina, S. Nims, O. Venegas, S. Singhal. *Surgery, University of Pennsylvania, Philadelphia, PA.*

Background: Extrapleural pneumonectomy or pleurectomy/decortication are surgical treatment options for selected patients with malignant pleural mesothelioma (MPM). If macroscopic complete resection is obtained, these procedures are associated with prolonged survival. We hypothesized that near-infrared (NIR) intraoperative molecular imaging using systemic indocyanine green would localize to pleural mesothelioma implants and improve resection. Methods: AB12 tumors were established in mice (N=56) via intrapleural injection. Next, we performed a thoracotomy on 8 mice each day for 7 days following tumor initiation. Traditional visualization and NIR intraoperative molecular imaging were used to localize tumor nodules. Tumor fluorescence was measured using tumor-to-background ratio (TBR) and tumors were biopsied for H&E and fluorescence microscopy. Next, three patients with MPM were enrolled in a proof-of-principal clinical study using NIR imaging for tumor localization during pleurectomy. Results: On post-injection days 1 through 3, no pulmonary tumors were discovered by traditional inspection or molecular imaging. On days 4 and 5, of the nodules confirmed to be tumor on H&E, 43% were discovered by traditional inspection, whereas molecular imaging discovered 86%. The mean tumor size was 0.95 mm (IQR 0.72-1.18) with a mean TBR of 3.1 +/- 0.2. On days 6 and 7, larger tumors with a mean size of 1.95 mm (IQR 1.87-2.20) were localized with both traditional inspection (75%) and fluorescent imaging (100%). Mean TBR of these tumors was 3.1 +/- 0.2. Overall, tumor detection using molecular imaging was significantly more sensitive than traditional inspection alone (85% vs. 55%, p-value <0.01). All patients had biopsy proven malignant mesothelioma that was markedly fluorescent during thoracotomy and pleurectomy with a mean in vivo TBR ranging from 3.1 to 3.6. Conclusions: Systemic indocyanine green localizes to pleural mesothelioma, and NIR intraoperative imaging aids tumor localization and resection in a murine model. A larger clinical trial is underway to investigate the impact of NIR intraoperative imaging on patient survival.

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Small Caliber Covered Self Expanding Metal Stents in the Management of Malignant Dysphagia S. Kucera,[1] J. Barthel,[3] R. Shridhar,[2] C.L. Harris,[4] J.B. Klapman,[4] K. Meredith.[1]* *1. Florida State University, Sarasota, FL; 2. Florida Hospital, Orlando, FL; 3. Florida Digestive Health System, Largo, FL; 4. Moffitt Cancer Center, Tampa, FL.*

Background: Use of large caliber (≥ 18 mm body diameter) self expanding metal stents (SEMS) for management of malignant dysphasia is associated with substantial adverse event (AE) and mortality rates (MRs). We sought to determine dysphagia response, stent migration rates, and AE and MRs, for small caliber covered SEMS (sccSEMS) with body diameters (BDs) between 10 - 16 mm in malignant dysphagia. Methods: We identified 31 patients underwent direct endoscopic placement of 50 sccSEMS. Patients were monitored for change in dysphagia score (DS), stent migration, AEs, and death. Results: The cohort consisted of 23 (74%) men and 8 (26%) women with a median age of 64 years (35 - 87 years). Esophageal adenocarcinoma (AC) was present in 19 (61%) patients and squamous cell carcinoma (SCCA) in 12 (39%) patients. Of the patients with SCCA, 2 tumors were located in the proximal esophagus, 7 in the mid-esophagus and 3 in the distal esophagus. All 19 ACs were located in the distal esophagus. The AJCC clinical stages at time of sccSEMS placement were: 1 (3%) Stage II, 8 (26%) Stage III, and 22 (71%) Stage IV. The initial pre-stent lumen diameter was less than 8 mm in 77% (24/31) of patients. The initial pre-stent lumen diameter was equal to 9 mm in 1 patient (3%), equal to 10 mm in 4 patients (13%), and equal to 11 mm in 2 patients (6%). The median pre-stent tumor length was 5.0 cm (interquartile range 4.0 – 7.0 cm). Dysphagia score improved in 30 of 31 patients (97%). The median DS decreased from 3 to 2 ($p < 0.0001$). The median effective duration of first sccSEMS placement was 116 (95% CI: 75-196) days. Major and minor AE rates were 6.5% and 19.4% respectively. No stent related deaths were encountered. The overall migration rate was 36% (18/50). The anticipated migration rate was 45.7% (16/35) and the unanticipated migration rate was 13.3% (2/15) ($p = 0.052$). Positive effective clinical outcome occurred in 93.5% (29/31) of cases. Conclusions: In malignant dysphagia, direct endoscopic sccSEMS placement provided acceptable dysphagia control and migration rates with substantial reductions in stent related AEs and MRs compared to those reported for large caliber SEMS.

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Readmission After Robotic Ivor Lewis Esophagectomy: Earlier Discharge, Increased Readmissions? A.I. Salem,[2] M.P. Doepker,[4] R. Shridhar,[3] K. Almhanna,[4] S. Hoffe,[4] K. Meredith.[1]* *1. Florida State University, SMH Campus, Sarasota, FL; 2. University of Wisconsin, Madison, WI; 3. University of Central Florida, Florida Hospital Orlando, Orlando, FL; 4. Moffitt Cancer Center, Tampa, FL.*

Background: Readmissions after esophagectomy are costly and incidence can be as high as 25%. The robotic assisted approach has potential benefits of earlier discharge compared to conventional techniques, however it is unclear what impact an earlier discharge will have on readmission rates. We sought to examine the impact of early discharge on readmission rates with robotic approaches. Methods: A retrospective review of all patients undergoing robotic assisted Ivor Lewis esophagectomy (RAIL) from 2009-2015 was conducted. Clinicopathologic factors and surgical outcomes were recorded and compared. We then compared outcomes to a historical cohort from the Surveillance, Epidemiology, and End Results-Medicare data (2002 to 2009). Length of stay, 30-day and 90-day readmissions, and mortality were determined. All statistical tests were two-sided and a p-value <0.05 was considered statistically significant. Results: We identified 147 patients who underwent RAIL. There were 78.9% (116) male with an average age 66 ±10 years. Adenocarcinoma was the predominant histology in 86% (126) patients, 9.52% (14) patients had squamous cell histology, and 4.76% (7) patients had other histology. Neoadjuvant therapy was administered to 77.6% (114) patients. In the SEER database 1,744 patients with esophageal cancer underwent esophagectomy: 80% of patients (1,390) were male, with a mean age of 73 years; 71.8% of tumors (1,251) were adenocarcinomas, and 38% of patients (667) received neoadjuvant therapy. Median length of stay was 13 days, 30-day mortality was 8.8% (158 patients), and 90 day mortality was 17.9% (302) compared to median LOH of 9 days, 30-day mortality of 0.6% (1) and 90-day mortality of 1.4% (2)% in the robotic cohort, $p<0.0001$, $p=0.007$, and $p<0.0001$. Readmission rates at 30 and 90 days were 18.6% (212) and 31.3% (356) in the SEER patients, and 3.4% (5) and 5.4% (8) in the robotic cohort $p=0.001$ and $p<0.001$. Conclusion: RAIL is a safe surgical technique that provides an alternative to conventional approaches to esophageal resection. Patients undergoing RAIL had lower mortality rates and LOH. Despite the lower LOH, RAIL was associated with lower 30 and 90-day readmissions.

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The Effect of Neoadjuvant Therapy on the 30-Day Morbidity and Mortality of Esophagectomy for Esophageal Cancer: A Multicenter Study M. Sabra,* C.R. Smotherman, Z.T. Awad. *University of Florida, Jacksonville, FL.*

Objective This study used a multi-center database to evaluate the impact of neoadjuvant therapy on the thirty day morbidity and mortality following esophagectomy for esophageal cancer. Methods The American College of Surgeons National Quality Improvement Program database was queried for 2005–2012 for patients who had esophagectomy for esophageal cancer. Patients were divided into two groups: neoadjuvant therapy (chemotherapy, radiation therapy, or both) and esophagectomy only. The two groups were described using counts and percentages for categorical variables, and medians and interquartile ranges (IQR) for continuous variables. Differences between the groups were considered significant at p-value < 0.05. Results The neoadjuvant group had 548 patients (38%), and the esophagectomy only group had 898 patients (62%). Patients in the neoadjuvant group were younger (median=63 years, IQR 56; 70) compared to patients in the esophagectomy group (median=65 years, IQR 58; 72) (p=0.0001). More white patients (96%) were in the neoadjuvant group compared to the esophagectomy group (92%) (p=0.01). The total length of stay was shorter in the neoadjuvant group (median=11 days, IQR 8; 17) compared to the esophagectomy only group (median 12, IQR 9; 18) (p=0.02). The neoadjuvant group had a lower rates of sepsis (8% vs. 13%, p. 0.004) and acute renal failure (0.4% vs. 2%, p. 0.013), and a higher rate of pulmonary embolism (3% vs. 1%, p=0.04). The difference in rates of reoperation, readmission, stroke, cardiac arrest, MI, surgical site and deep organ infections, anastomosis failure, blood transfusions, DVT, septic shock, pneumonia, UTI, and respiratory failure were not statistically significant (all p>0.08). The thirty day mortality rates were not different between the neoadjuvant group (22 deaths, 4.0%) and the esophagectomy group (34 deaths, 3.8%) (p=0.83). Conclusion Neoadjuvant therapy before esophagectomy for esophageal cancer does not have a negative impact on the thirty-day morbidity and mortality of the operation, albeit a small increase in the rate of PE. .

Post operative complications

Complication	Esophagectomy only (n=898, 62%)	Neoadjuvant therapy (n=548, 38%)	P-Value
Length of total hospital stay*	12 (9;18)	11 (8;17)	0.020a
Days from Operation to Death*	17.5 (10;22)	15 (10;22)	0.724a
Days from Operation to Discharge*	11 (9;18)	11 (8;17)	0.104a
Reoperation	16 (12)	17 (17)	0.314b
Readmission	20 (17)	11 (11)	0.218b
Stroke	5 (0.6)	3 (0.5)	0.982c
Cardiac Arrest	18 (2)	11 (2)	0.997b
Myocardial Infarction	11 (1)	5 (0.9)	0.581b
Superficial surgical site infection	87 (10)	62 (11)	0.324b
Deep Incisional SSI	27 (3)	13 (2)	0.476b
Organ Space SSI	46 (5)	33 (6)	0.465b
Wound Disrupt	15 (2)	12 (2)	0.479b
Graft/ Flap Failure	3 (0.3)	0 (0)	0.294c
Post-operative blood transfusion	75 (8.4)	63 (11.5)	0.098c
DVT Requiring Therapy	27 (3)	25 (5)	0.077b
Pulmonary Embolism	11 (1)	15 (3)	0.036b
Sepsis	118 (13)	45 (8)	0.004b
Septic Shock	75 (8)	47 (9)	0.881b
Pneumonia	168 (19)	83 (15)	0.083b
Urinary Tract Infection	39 (4)	15 (3)	0.118b
Acute Renal Failure	17 (2)	2 (0.4)	0.013b
Unplanned Intubation	149 (17)	84 (15)	0.526b
Failure to wean ventilation	152 (17)	82 (15)	0.326b

Data is counts (percentages), unless otherwise specified
*median (IQR); IQR=25th percentile; 75th percentile; **includes 'At rest' and 'Moderate exertion';
a-Wilcoxon rank-sum test; b-Pearson Chi-square test; c-Fisher's Exact test

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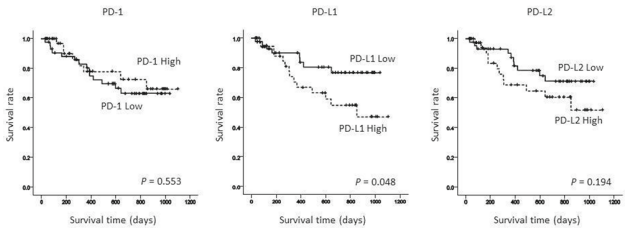
The Concentration of PD-L1 in the Peripheral Blood is a Prognostic Biomarker for Esophageal Squamous Cell Carcinoma Y. Akutsu,* N. Hanari, K. Murakami, M. Kano, A. Usui, H. Suioto, M. Takahashi, Y. Matsumoto, R. Otsuka, H. Matsubara. *Chiba University, Chiba, Japan.*

Introduction: Programmed cell death-1 (PD-1) and its ligands (PD-L1 and PD-L2) play important roles in the immune system and evasion of cancer from the immune system. Here, we determined the serum concentrations of PD-1, PD-L1, and PD-L2 in patients with esophageal squamous cell carcinoma (ESCC) and evaluated the applicability of these molecules as prognostic markers. Material and Methods: Blood samples were collected from 85 patients with histologically proved ESCC. Serum levels of PD-1, PD-L1, and PD-L2 were measured using enzyme linked immunosorbent assays. Correlations between serum PD-1/PD-L1/PD-L2 concentrations and tumor depth, lymph node status, number of lymph node metastases, organ metastasis status, or disease stage were assessed. The patients were divided into groups according to the levels of PD-1, PD-L1, and PD-L2, with high and low concentration cut-offs based on the median. Five-year survival rates according to clinicopathological characteristics were calculated. Results: Tumor depth of T3/T4 ($p = 0.014$); lymph node positivity ($p = 0.003$); positivity of distant metastases ($p = 0.001$); stages II, III, and IV ($p = 0.001$); and serum concentration of PD-L1 ($p = 0.048$) were potential prognostic factors. The 5-year survival rate in patients with high concentration of PD-L1 was 47.0%, which was significantly lower than that in patients with low PD-L1 concentration (76.8%). A similar tendency was observed for PD-L2 concentration. The 5-year survival rate of patients with high concentration of PD-L2 was 51.9%, whereas that in patients with low PD-L2 concentration was 71.1%. Therefore, high PD-L2 expression may predict poor survival in patients with ESCC, although statistical significance was not achieved ($p = 0.194$). In contrast, survival did not differ in patients with high and low PD-1 concentrations ($p = 0.553$). Conclusion: Our study demonstrated the usefulness of measuring PD-L1 concentrations in the blood to predict prognoses in patients with ESCC. The immune checkpoint mechanism is critical for development of a new modality for next-generation therapies. Therefore, further investigations are required to investigate these possibilities.

Figure 1



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Survival Rates After Surgery for Stage-3A (N2) Non-Small Cell Lung Cancer with Induction Versus Adjuvant Chemotherapy +/- Radiation Therapy E.M. Toloza,* T. Tanvetyanon, D. Chen, A. Chiappori, B. Creelan, T. Dilling, J. Fontaine, J. Gray, M. Pinder-Schenck, L. Robinson, E. Haura, C. Stevens, C. Williams, S. Antonia. *Thoracic Oncology, Moffitt Cancer Center, Tampa, FL.*

Introduction: Stage-3A (N2) NSCLC patients (pts) who have induction therapy (chemotherapy + radiation therapy [chemo+XRT]) then surgery have improved survival compared to pts who have surgery alone. However, survival of stage-3A NSCLC pts who have induction therapy then surgery have not been compared to survival of pts who have adjuvant therapy after surgery. Methods: Of pts treated for NSCLC at our institution from 1986 through 2010, we identified pts with clinical stage-3A (cStage3A) NSCLC and had surgery without or with induction chemo+XRT or who were pathologic stage-3A (pStage3A) and had adjuvant chemo+XRT. Kaplan-Meier survival curves for these 3 groups were compared, with significant differences at $p<0.05$ by Chi Square test, with Log Rank (Mantel-Cox), Breslow (Generalized Wilcoxon), and Tarone-Ware pairwise comparisons. Results: From 1/1986 to 12/2010, of 2760 pts who were treated for primary lung cancer at our institution, with 437 pts were cStage3A at diagnosis. Another 52 pts were not cStage3A at surgery, but were then pStage3A. Of these 489 pts, 192 had curative resection, of which 56 pts had surgery alone (SURG), 43 pts had surgery after induction therapy (NEOADJ), and 93 pts had surgery then adjuvant therapy (ADJ). Kaplan-Meier survival for SURG was worse than that for either NEOADJ ($p=0.03$) or ADJ ($p=0.005$), while NEOADJ and ADJ had similar survival ($p=0.90$). Median survival was 17.9+3.1 mon (95%CI = 11.6-23.9 mon) for SURG, 37.2+6.2 mon (95%CI = 25.0-49.5 mon) for NEOADJ, and 40.9+5.3 mon (95%CI = 30.5-51.3 mon) for ADJ. Survival for NEOADJ chemo-alone pts was better than for SURG pts ($p=0.031$), while that of NEOADJ chemo+XRT pts was similar to SURG survival ($p=0.488$). Survival for ADJ chemo-alone pts was better than for SURG pts ($p=0.007$), while that of ADJ chemo+XRT pts was similar to SURG survival ($p=0.163$). Conclusions: Stage-3A NSCLC pts have improved survival with either induction or adjuvant therapy compared to surgery alone. Patients with induction or adjuvant chemo alone, but not those with induction or adjuvant chemo+XRT, have improved survival compared to surgery alone.

Study	Treatment	No. of Pts	Median Survival (mon)	3-Yr Survival (%)	5-Yr Survival (%)
Pass, et al (1992)	Chemo + Surg Surg + RT	13 14	28.7 15.6	42 18	- -
Rosell, et al (1994 [1998])	Chemo + Surg(RT) Surg(RT)	30 30	26 [22] 8 [10]	30 0	- -
Roth, et al (1994 [1998])	Chemo + Surg Surg	28 32	21 14	[43] -	36 15
Elias, et al (1997)	Chemo + Surg-RT Surg-RT	23 24	19 23	- -	- -
Depierre, et al (1999)	Chemo+Surg+Chemo Surg	187 186	36 26	49 41	- -
This Study (2015)	Neoadj + Surg Surg + Adj Surg	37 93 56	37.2 40.2 17.4	53 55 35	- - -
This Study (2015)	Chemo + Surg Chemo/RT + Surg Surg + Chemo Surg + Chemo/RT Surg	19 17 48 36 46	45.6 24.2 47.6 34.3 17.7	68 32 60 44 33	- - - - -

Comparison of median survival and survival rates among studies that compared surgery alone to induction therapy plus surgery versus surgery plus adjuvant therapy.

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Protein Arginine Methyltransferase 5 Promotes Peritoneal Metastasis of Gastric Cancer Cells K. Ezaka,* M. Kanda, D. Shimizu, C. Tanaka, D. Kobayashi, N. Iwata, S. Yamada, T. Fujii, G. Nakayama, H. Sugimoto, M. Koike, M. Fujiwara, Y. Kodera. *Department of Gastroenterological Surgery (Surgery II), Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan.*

Background: Identification of novel gastric cancer (GC)-related molecules is necessary to improve management of patients with GC in both diagnostic and therapeutic aspects. Protein arginine methyltransferase 5 (PRMT5) is implicated in diverse cellular and biological processes. The aim of this study was to clarify whether PRMT5 has overt oncogenic function in the context of GC and whether it represents a novel diagnostic and therapeutic target. Methods: Global expression profiling of GC cell lines and siRNA experiments were conducted to determine the effect of PRMT5 expression on phenotype of GC cells. We evaluated the association of PRMT5 mRNA levels in 179 patients' tissue with clinicopathological factors. Results: Differential expression of PRMT5 mRNA by GC cell lines correlated positively to levels of GEMIN2, STAT3 and TGFB3. Knockdown of PRMT5 reduced the proliferation, invasion and migration of GC cells. The mean expression level of PRMT5 mRNA was significantly higher in 179 GC tissues compared with those in the corresponding adjacent normal tissues. PRMT5 mRNA levels was independent from tumour depth, differentiation and lymph node metastasis, whereas it was associated significantly exclusively with peritoneal lavage cytology. In multivariate binomial logistic analysis, high PRMT5 mRNA expression was identified as an independent risk factor of positive peritoneal lavage cytology (hazard ratio, 3.90, $P = 0.003$). Patients with high levels of PRMT5 mRNA were more likely to survive for shorter times compared with those without. Conclusion: PRMT5 acts as an oncogene that enhances the malignant phenotype of GC cells. PRMT5 expression in gastric tissues may represent a promising biomarker for patient stratification, and PRMT5 may be considered as a potential target of therapy of GC.

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The Non-T Cell-Inflamed Tumor: A Model for Pancreatic Cancer K.B. Skowron,[1]* W. Zheng,[1] J.P. Namm,[2] B. Burnette,[1] Y. Fu,[1] R.R. Weichselbaum,[1] M.C. Posner.[1] *1. University of Chicago Medicine, Chicago, IL; 2. Loma Linda University Health, Loma Linda, IL.*

Introduction: A limitation for immune therapy in pancreatic cancer is the lack of anti-tumor T cell infiltration. Few models mimic the interaction of the immune system with the tumor microenvironment. We report a pancreatic cancer model which mirrors the clinical state and allows for testing of immunologic agents. Methods: A pancreatic tumor cell line expressing the strong antigen SIY in suspension is injected intradermally into OT-1 T cell receptor transgenic (relatively T cell deficient) mice. Tumors are excised, divided into 1-2mm fragments, and implanted subcutaneously into immune-competent C57Bl/6 mice. Tumors are treated with radiation (IR, 25Gy), SIY cellular vaccine, and combination treatment. The tumor is assessed for growth, removed along with the draining lymph nodes and spleen, and T cell infiltration is quantified. Results: Tumors established from suspension of Panc02-SIY cells demonstrate IR-sensitivity and high antigen response as seen by proliferation of SIY-specific CD8+ T cells. Tumors from transplanted tumor fragments are resistant to IR. Very few SIY-specific T cells are detected in untreated fragment-bearing mice (tumor, draining lymph node or peripheral blood). Neither vaccination nor irradiation alone induce an antigen-specific T cell response, as is noted clinically in pancreatic cancer patients. However, a combination of vaccination and IR produces a T cell response which approaches the tumor-naïve, vaccinated positive control. This increased antigen-specific T cell activation peaks at day 7 (%SIY-specific/CD8 T cells: 5.4 for IR+vaccine compared to 1.4 for IR only, 1.7 for vaccine only, and 1.2 for control, $p<0.01$ for all). Tumor growth is restricted by the combination treatment (Figure 1, day 21 mean volume 2266 mm^3 versus 4151 mm^3 for IR alone and 7141 mm^3 for control, $p<0.05$ and <0.01, respectively). Conclusions: Our tumor fragment system models the non-inflamed tumor microenvironment observed clinically in pancreatic cancer. IR and vaccine alone are insufficient to induce a T cell response, however together can lead to T cell immunity and control of tumor growth. These results implicate CD8+ cytotoxic T cells in the response to IR and potentially other cytotoxic agents.

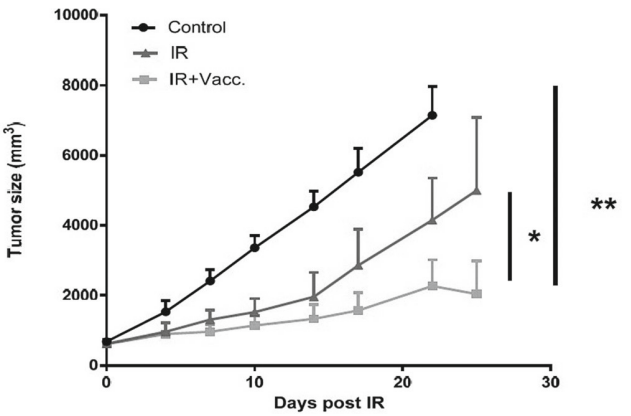

Figure 1. Growth curves demonstrate improved control of tumor growth with the combination of vaccine and irradiation over control or irradiation alone.

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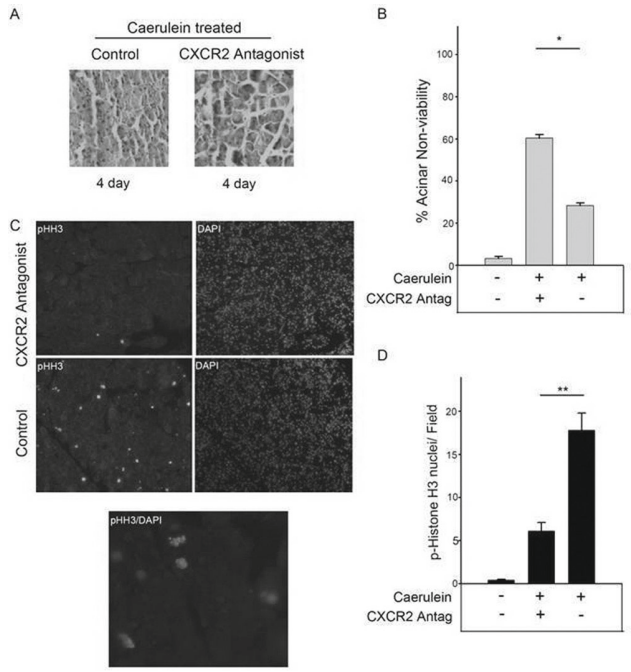
Role of Myeloid Derived Suppressor Cells in the Inflammatory Response of Pancreatitis and Pancreatic Cancer N.E. Cieza Rubio,* R. Heimark, T. Jie. *Surgery, University of Arizona, Tucson, AZ.*

Introduction: Tumor-infiltrating myeloid-derived suppressor cells (MDSCs), are important mediators of a tumor-permissive microenvironment that contributes to tumor growth and could account for the limited success of immunotherapeutic strategies. MDSCs suppress adaptive immunity by blocking T cell activation, inducing Treg accumulation, and inhibiting natural killer cell cytotoxicity against tumor cells. Aim: We investigated the roles of MDSCs in the regeneration of the exocrine pancreas associated with acute pancreatitis and the progression of acinar to ductal metaplasia. Results: Acute pancreatitis was induced in wild type and $P48^{+/Cre}$;LSL-$KRAS^{G12D}$ mice using caerulein and an early influx of MDSCs into the pancreas was observed flow cytometry and immunocytochemistry. Numbers of Gr1(+)CD11b(+) MDSCs increased over 20-fold in pancreata of mice with acute pancreatitis to account for nearly 15% of intrapancreatic leukocytes and have T cell suppressive properties. This marked accumulation of MDSCs returned to normal values within 24 hours of the insult in wild type mice; however, in the oncogenic KRAS mice, MDSCs levels remained elevated. When intrapancreatic MDSCs were depleted by administration of a CXCR2 antagonist (SB265610) in wild type mice the severity of acinar damage was increased. This was also accompanied by a delayed regeneration determined morphologically and with the mitotic immunomarker phospho-histone H3. Isolated intrapancreatic MDSCs from treated mice induce naïve acinar cells to undergo acinar ductal metaplasia when co-cultured in collagen 3D cultures. Purified splenic MDSCs failed to induce the phenotypic transdifferentiation. Conclusion: MDSCs are required for adequate pancreatic regeneration in wild type mice with acute pancreatitis and their persistent elevation in oncogenic KRAS mice is not only associated with immune-evasion, but may also function as direct enhancer of malignant proliferation.



Intrapancreatic MDSCs depletion delays acinar regeneration.

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γδ T-Cells Support Pancreatic Oncogenesis by Inducing αβ T Cell Exhaustion D. Daley,* L. Tomkoetter, C. Zambirinis, N. Akkad, R. Narayanan, G. Miller. *Department of Surgery, New York University School of Medicine, New York, NY.*

Pancreatic ductal adenocarcinoma (PDA) is invariably associated with a robust immune infiltrate which can have divergent influences on disease by either combating cancer growth via antigen-restricted tumoricidal immune responses or by promoting tumor progression via induction of immune suppression. However, determinants governing the regulation of the balance between immunogenic and suppressive T cell responses in cancer remain unclear. We evaluated the effects of deletion or depletion of γδT Cells in PDA on tumor size, survival, peri-tumoral fibro-inflammation, and epithelial transformation. The immune infiltrate within the pancreatic TME was assessed and characterized using immunohistochemistry, flow cytometry and western blotting in human and murine tissue. We found that a uniquely-activated γδT cell population constitutes ~50% of tumor-infiltrating T cells in human PDA and is associated with advanced disease. Recruitment and activation of γδT cells is contingent on CCL2-CCR2 signaling. γδT cell deletion, depletion, or blockade of recruitment were protective against PDA and resulted in increased infiltration, activation, and Th1-polarization of PDA-infiltrating αβT cells. Further, whereas $CD4^+$/$CD8^+$ T cells were dispensable to outcome, they became

indispensable for tumor-protection upon γδT cell ablation. PDA-infiltrating γδT cells express high PD-L1 and Galectin-9 and negate adaptive anti-tumor immunity by engagement of their respective checkpoint receptors. Blockade of PD-L1 and Galectin-9 had anti-tumor efficacy only in γδT cell-competent hosts suggesting that γδT cells are primary sources of exhaustion ligand expression. We describe a role for intra-tumoral γδT cells as central mediators of αβ T cell exhaustion in cancer and implicate novel γδT-αβT cell cross-regulation. Our studies suggest that targeting γδT cells is an innovative approach for experimental therapeutics in human PDA.

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Increased RhoA Activity Predicts Worse Overall Survival in Patients Undergoing Surgical Resection for Diffuse-Type Gastric Adenocarcinoma K.K. Chang,* S. Cho, C. Yoon, J.H. Lee, D.J. Park, S. Yoon. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Several studies have reported a high rate of RHOA mutations in the Lauren diffuse-type gastric adenocarcinoma (GA) but not in intestinal-type GA. The aim of this study was to determine if RhoA activity is prognostic for overall survival (OS) in patients with resectable GA. Methods: Retrospective review was performed of a prospective database of GA patients who underwent potentially curative resection between 2003 and 2012 at a single institution. Tissue microarrays were constructed from surgical specimens and analyzed for phosphorylated RhoA, a marker of inactive RhoA signaling. OS was estimated by the Kaplan-Meier method and compared using the log-rank test. Results: One-hundred thirty-six patients with diffuse GA, 129 patients with intestinal GA, and 23 patients with mixed-type GA were examined. High RhoA activity was significantly associated with earlier T status and increased lymphatic invasion and was not associated with age, gender, N status, vascular invasion, or perineural invasion. The proportion of high RhoA activity was higher in diffuse tumors than intestinal tumors. In patients with diffuse GA, high RhoA activity was associated with significantly worse OS when compared to low RhoA activity (five-year OS 52.5% vs. 81.0%, p = 0.017). This difference in OS was not observed in patients with intestinal GA (five-year OS 83.9% vs. 80.5%, p = 0.612). Conclusions: Increased RhoA activity is predictive of worse OS in patients with diffuse GA who undergo potentially curative surgical resection. Along with the findings from genomic and molecular profiling studies, these results suggest RhoA may be a novel therapeutic target in diffuse GA.

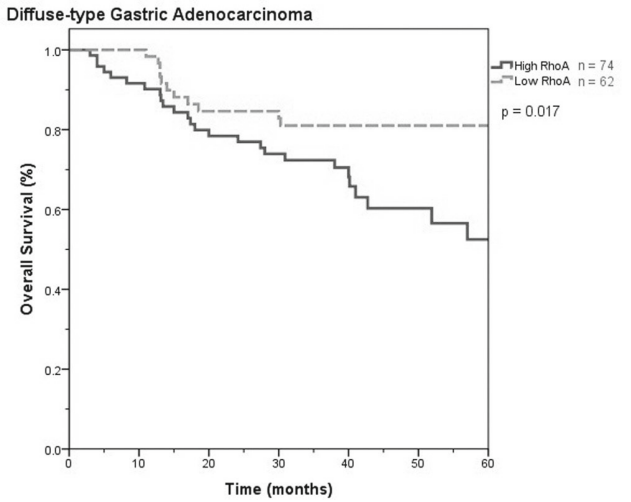

Figure. Kaplan-Meier survival curves of overall survival stratified by RhoA activity in patients with diffuse-type gastric adenocarcinoma.

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Symptomatic Presentation as a Predictor of Recurrence in Gastroenteropancreatic Neuroendocrine Tumors: A Single Institution Experience Over 15 Years G.G. Baptiste,* L.M. Postlewait, C.G. Ethun, N. Le, M.R. McInnis, M.C. Russell, J.H. Winer, D.A. Kooby, C.A. Staley, S.K. Maithel, K. Cardona. *Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA.*

Background The prognostic implications on outcomes of symptomatic presentation of gastroenteropancreatic (GEP) neuroendocrine tumors (NETs) remains unclear. Methods Patients who underwent curative-intent resection of nonfunctional, well-differentiated GEP NETs from 2000-2014 at a single institution were analyzed. Patients were classified as symptomatic if clinical symptoms were present at diagnosis. Primary end points were distant recurrence-free survival (DRFS) and overall survival (OS). Results A total of 339pts were identified, of which 208pts (61%) were symptomatic at presentation. Symptomatic presentation was associated with younger age at presentation (55vs59yrs, p=0.001), higher tumor grade (38vs21%, p=0.027), LVI (58vs33%, p<0.001), PNI (53vs30%, p=0.002), and advanced disease (T3/T4/N1/M1 63vs44%, p=0.002), but not tumor size (2.6vs2.5cm, p=0.74). Symptomatic presentation was associated with decreased DRFS (Fig1) but not OS. When accounting for race, tumor size, positive resection margins, presence of metastatic disease, and positive lymph nodes on multivariate analysis (MVA), symptomatic presentation remained independently associated with reduced DRFS (HR 3.51, p=0.007). On subgroup analysis of patients only with advanced disease (T3/T4/N1/M1), symptomatic presentation was still associated with decreased 3-yr DRFS (67vs79%, p=0.012), but not OS. On MVA, symptomatic presentation persisted as an independent factor associated with decreased DRFS in patients with advanced disease (HR 2.89, p=0.014). Conclusions Symptomatic presentation of GEP NETs is associated with more aggressive pathologic features and worse DRFS than incidentally diagnosed NETs irrespective of tumor size. As our armamentarium of therapeutic agents for NETs expands and improves, trials assessing the value of adjuvant therapy for advanced GEP NETs are needed, and symptomatic presentation may be considered as one inclusion criterion. Following resection, symptomatic presentation should be taken into account when planning follow-up strategies, as these patients may require closer surveillance than their incidentally diagnosed counterparts.

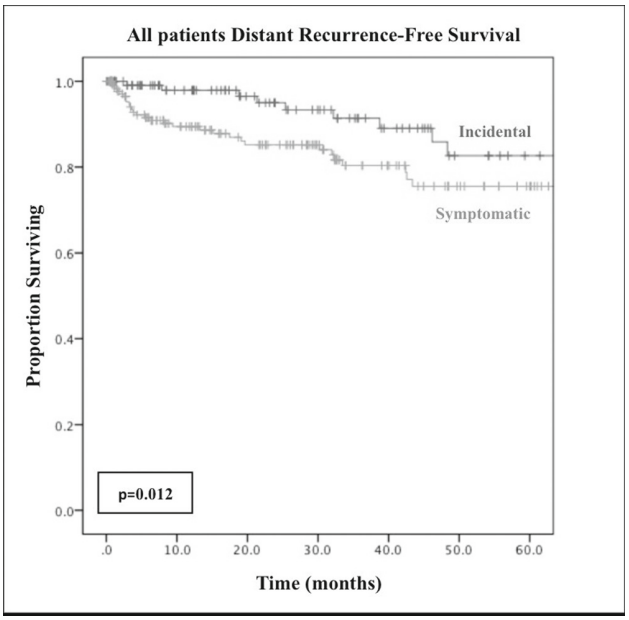

Figure 1. Kaplan-Meier analysis of distant recurrence-free survival of gastroenteropancreatic NET patients stratified by presentation (n=119 for incidentally diagnosed patients and n=182 for symptomatic patients, p=0.012, log-rank test). The 3-yr DRFS for incidentally diagnosed and symptomatic patients was 91% and 80%, respectively.

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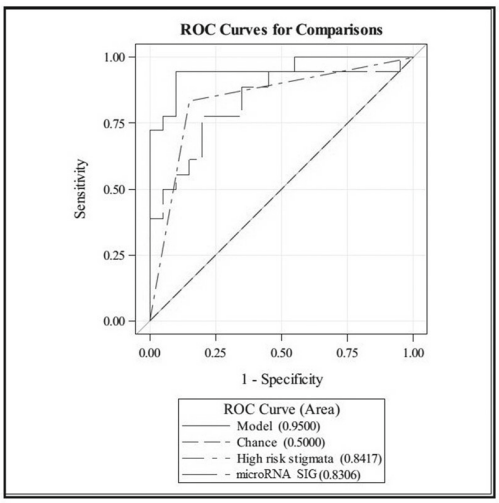
Noninvasive Markers Can Predict Malignant Intraductal Papillary Mucinous Neoplasms of the Pancreas S.T. Orcutt,* J.P. Wey, J.W. Choi, D. Chen, L. Chen, M.P. Malafa. *Surgery, Moffitt Cancer Center, Tampa, FL.*

Background: Despite guidelines to preoperatively distinguish malignant from benign intraductal papillary mucinous neoplasms (IPMN), many patients undergo invasive testing and morbid pancreatic resection but ultimately have benign disease on pathology. A blood-based microRNA signature (SIG, including miR-200a-3p, miR-1185-5p, miR-33a-5p, miR-574-4p, and miR-664b) has been shown to preoperatively discriminate malignant from benign IPMN, with expression lower in malignant IPMN. This study was designed to develop a model to improve preoperative prediction of IPMN pathologic status combining imaging markers and SIG values. Methods: An institutional database was used to identify patients undergoing resection for IPMN (2006-2011) with preoperative computed tomography (CT) scans and SIG values. CTs were read by a single radiologist blinded to pathology to assess predetermined radiographic features. The outcome was malignant pathology (MP, invasive carcinoma and high-grade dysplasia) vs. benign pathology (BP, low- and moderate-grade). Results: Of 38 eligible patients, 20 (53%) had MP and 18 (47%) had BP. 72% with MP had main pancreatic duct (PD) involvement vs. 20% with BP, p=0.003. Median cyst size was higher in the MP group (3.9 vs. 2.8cm), p=0.018. 83% of those with MP had ≥1 "high-risk stigmata" (PD size≥10mm, enhancing solid component, or obstructive jaundice), vs. 15% of those with BP (p<0.001), yet ≥1 "worrisome" feature (acute pancreatitis, PD size 5-9mm, cyst size>3cm, thickened enhanced cyst walls, or non-enhanced mural nodules) was not associated with malignancy (p=0.734). SIG was significantly lower in the MP group, p<0.001. Multivariate logistic regression analyses revealed that high risk stigmata and SIG retained significance (43.0 [4.64-398.8], p=0.001 and 0.30 [0.10-0.86], p=0.026, respectively). The area under the receiver operating characteristic curve resulted in 0.950 for the model with both variables, compared to 0.841 and 0.836 for each variable independently. Conclusions: Combining high-risk stigmata from preoperative CT scans with a blood-based miRNA genomic classifier may improve the ability to noninvasively predict IPMN status preoperatively.

Figure 1. Area under the receiver operator characteristic (ROC) curve for the model (high risk stigmata and the microRNA signature SIG), chance, high risk stigmata only, and SIG only.



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Impact of Minimally Invasive Gastrectomy on Use and Time to Adjuvant Chemotherapy for Adenocarcinoma C. Gonczy,* M. Adam, D. Blazer, D. Nussbaum. *Advanced GI/Surgical Oncology, Duke University Hospital, Durham, NC.*

Objective: There is high level evidence that adjuvant chemotherapy improves outcomes in patients with resectable gastric cancer. Minimally invasive approaches (MIS) to treatment of patients with gastric adenocarcinoma have continued to see increased utilization, and it has been previously shown that MIS approaches lead to fewer complications and shorter hospital stays, however, its impact on adjuvant therapy remains unclear. We hypothesized that MIS procedures may improve time to initiation and utilization of adjuvant chemotherapy and its subsequent oncologic benefits compared to open gastrectomy. Methods: Adult patients in the National Cancer Database (NCDB) who underwent surgery for high-risk gastric adenocarcinoma (T3 or T4 tumors, positive margins, or those who received neoadjuvant chemotherapy) between 2010-12 were included. Patients with metastatic disease were excluded. Patients were stratified based on type of procedure, and analyzed using multivariable regression modeling. Primary endpoints were time to initiation and utilization of adjuvant chemotherapy. Results: 8338 patients met criteria, with 6548(79%) in the open surgery group and 1790(21%) in the MIS group. Patients undergoing MIS had smaller tumors, lower stage disease, and fewer lymph node metastases (all p<0.01). Use of MIS increased by 44% from 481 cases in 2010 to 692 cases in 2012. After adjusting for the differences in patient characteristics, patients undergoing MIS were significantly more likely to undergo adjuvant chemotherapy (OR 1.19, 95% CI 1.047-1.361) and time to initiation of adjuvant therapy was slightly earlier than those in the open group (-4%, p=0.05). MIS was also associated with shorter hospital stays without concomitant increase in rate of readmission. Adjusted survival was similar regardless of surgical approach, but use of adjuvant chemotherapy was associated with improved survival (HR 0.78, 95% CI 0.70-0.86, p<0.01). Conclusions: In this national database review, MIS for gastric adenocarcinoma appears to be associated with shorter hospital stays and more frequent utilization of adjuvant chemotherapy as compared to open surgery.

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C6 Ceramide Potentiate Chemotoxicity of Gemcitabine Against Chemo Resistant Pancreatic Cancer Cell Lines H. Wanebo,[1]* A. Liss,[2] W. Bowen.[3] *1. Surgical Oncology, Roger Williams Medical Center, Providence, RI; 2. Pancreatic Cancer Laboratory, MGH, Boston, MA; 3. Brown University, Providence, RI.*

INTRODUCTION: Pancreatic cancer is a highly chemo-resistant malignancy with 5% overall survival, and limited treatment options with chemotherapy (Gemcitabine) and surgical resection possible in <20% of patients with post resection survival of only 15-20% OBJECTIVE: Our studies suggest potential value of C6 Ceramide as a chemo enhancing biologic in therapy of chemoresistant pancreatic cancer. C6 Ceramide is an active sphingomyelin end product that has the major biologic function of inducing apoptosis in cells compromised or damaged by injury or malignancy, and appears to have potential value in therapy of malignancy. We and others have demonstrated C6 Ceramide inhibition of pro survival (AKT/PI3K/mTOR) and KRAS mutant pathways, which promote pancreatic cancer growth and metastases. METHODS/MATERIALS: Cell lines obtained from 4 freshly cultured pancreatic cancers, and 3 well established cancer cell lines (ATCC) were cultured in 96 well plates, 4000 cells/well, and were treated at 24 hours with Gemcitabine in 0.9% NaCl (1,2,5,10 ug/ml), alone and with C6 Ceramide in DMSO (2.5, 5.0, 10 ug/ml) and two liposomal formulations of C6 Ceramide: (galloyl) DPC6: D0PC: C6 Ceramide (0.5, 1.0,2.0 ug/ml), and (pegylated) 180 PEG 2PE: D0PC: C6 Ceramide (0.5, 1.0, 2.0 ug/ml), and included vehicle controls. Cell viability was assessed by resazurin assay, 48 hour post drug infusion. RESULTS: As noted in Figure 1, the effect of treatment on freshly cultured cell lines (722, 1108, 1312, and 1513) showed marked cell growth inhibition with combination C6 Ceramide and Gemcitabine (cell death 60-80%). This result was also replicated in all of the 3 ATC based cells (long term cultured). CONCLUSION: C6 Ceramide appears to potentiate chemotoxicity of Gemcitabine against all (freshly cultured and long term cultured) pancreatic cancer cell lines, suggesting clinical value in continued development of C6 Ceramide as an anti-cancer biologic.

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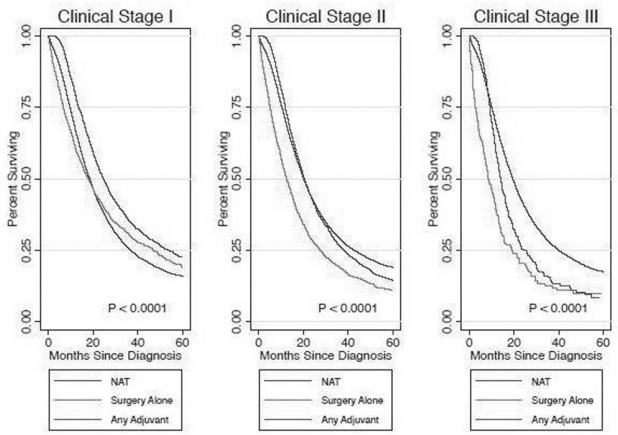
Survival Impact of Neoadjuvant Therapy in Resected Pancreatic Cancer K.A. Mirkin,* C. Hollenbeak, J. Wong. *Surgical Oncology, Penn State Medical Center, Hershey, PA.*

Background: Pancreatic cancer carries a dismal prognosis, with surgical resection and adjuvant therapy offering the only hope for long-term survival. In recent years, neoadjuvant therapy (NAT) has been employed to optimize outcomes. This study evaluates the impact of NAT on survival in patients with resected stage I-III pancreatic cancer. Methods: The National Cancer Data Base (2003-2011) was analyzed for patients with clinical stage I-III resected carcinoma of the pancreas who underwent NAT or surgery-first +/- adjuvant

therapy. Univariate statistics were used to compare characteristics between groups. Analysis of variance and Kaplan Meier analyses were used to compare median survival for each clinical stage of disease. Multivariate analyses were performed using a Cox proportional hazards model. Results: 16,122 patients who underwent NAT and 16,869 patients who underwent surgery-first were included. Patients who underwent NAT tended to be younger, covered by private insurance, have a higher median income, greater comorbidities, higher clinical stage disease, and undergo a whipple. Additionally, NAT patients had a greater number of positive regional lymph nodes (9 vs. 6, respectively), although a similar number of nodes retrieved, and higher pathological stage disease. In patients with clinical stage I disease, adjuvant therapy was associated with improved median survival than NAT and surgery-alone (24.8, 18.5, 17.9 months, p<0.0001, respectively). However, in stage II, adjuvant therapy and NAT offered similar median survival, which was improved over surgery-alone (20.5, 20.1, and 12.4 months, p<0.0001, respectively). In stage III, NAT had improved median survival compared to the other groups (19.6, 14.2, 8.6 months, p<0.0001, respectively). In the multivariate survival analysis, patients who received NAT had a 22% lower hazard of mortality up to 5 years as compared to adjuvant therapy (p<0.0001). Conclusion: Neoadjuvant therapy in advanced stage pancreatic cancer confers a survival benefit and may allow more patients to undergo surgery; NAT appears to offer similar survival as adjuvant therapy in early stage pancreatic cancer.



P341

Vaccination Enhances Anti-tumor Immunity in Pancreatic Adenocarcinoma Following Repolarization of the Tumor Microenvironment with CCR2 Blockade D.R. Cullinan,[1]* T. Nywening,[1] R. Panni,[1] B. Belt,[2] R.C. Fields,[1] W. Hawkins,[1] D.C. Linehan.[2] *1. Surgery, Washington University in Saint Louis, Saint Louis, MO; 2. University of Rochester Medical Center, Rochester, NY.*

Introduction: Pancreatic adenocarcinoma (PC) is infiltrated with tumor associated macrophages (TAM) that establish an immunosuppressive microenvironment. CCR2 inhibitor (CCR2i) blocks tumor mediated recruitment of bone marrow derived TAM and facilitates an adaptive anti-tumor immune response in both pre-clinical models and a recently completed phase Ib trial using FOLFIRINOX+CCR2i in human PC. Here we present the rationale for combining immunostimulatory therapies with CCR2i in order to enhance the effector capabilities of tumor infiltrating lymphocytes in PC. Methods: A tissue microarray (TMA) from resected PC at Washington University (St. Louis, MO) was constructed under IRB approval. For murine studies animals were injected orthotopically in the tail of the pancreas with $2.5x10^6$ syngeneic PC cells (KCKO). Transduction of KCKO cells with a lentivirus expressing murine GM-CSF (Gene Target, Inc) allowed for the establishment of a whole cell vaccine (GVAK) that expressed GM-CSF by ELISA. CCR2i (Tocris) was given at 10 mg/kg SQ BID. Monoclonal αCD8 antibody (BioXCell) was used for depletion studies. Results: $CD14^{Hi}$ TAM: $CD8^{Low}$ T-cell ratio conveyed worse survival following resection in human PC patients. Conversely, $CD14^{Low}$: $CD8^{Hi}$ was protective (Fig 1A). To test the hypothesis that CCR2 blockades anti-tumor activity is mediated by the adaptive immune system we performed CD8 depletion experiments in tumor bearing animals receiving CCR2i. Targeting TAM at the primary site requires the presence of CD8+ T-cells, as the efficacy of CCR2 blockade was lost following CD8 depletion (Fig 1B). Repolarization of the tumor microenvironment (TME) with CCR2i monotherapy was effective in reducing tumor burden, but this impact was further enhanced in the setting of vaccination (Fig 1C). Within the TME we found evidence of enhanced effector T-cell function with an increase in CD69+, CD44+ effector T-cells (Fig 1D). Conclusion: Thus far vaccination has not provided durable patient responses in PC. Therapies targeting the immunosuppressive TME are an attractive treatment modality to enhance vaccination and facilitate anti-tumor immunity in PC.

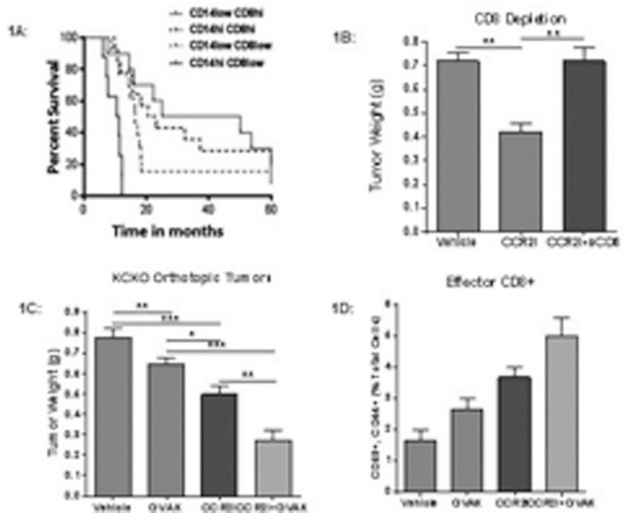


Fig 1A: The CD14+ TAM–CD8+ ratio predicts PC patient survival. Patients with predominant CD14Hi/CD8Low infiltrate in the tumor had a significantly reduced overall survival compared to all other groups (p <0.01). Fig 1B: CD8 depletion in the murine model results in loss of CCR2i efficacy (p<0.01). Fig 1C and 1D: Addition of vaccination (GVAK) to CCR2i lead to decreased tumor size (p= 0.01) and increased effector CD8+ T-cells (p<0.05) compared to CCR2i alone in a murine model.

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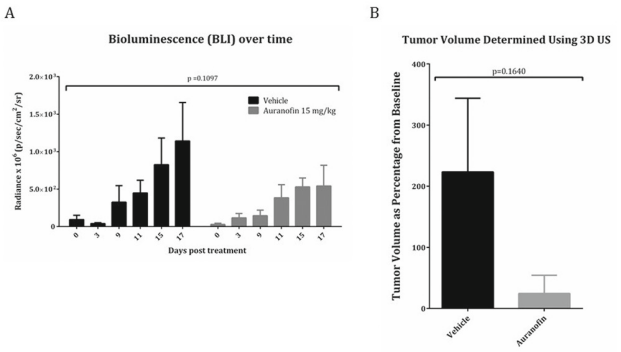
Auranofin Prevents Progression of Human Pancreatic Ductal Adenocarcinoma M.V. Rios Perez,* D. Roife, B. Dai, Y. Kang, X. Li, M. Pratt, J.B. Fleming. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: Auranofin, an FDA anti-rheumatic agent shown to have anticancer properties for lung and ovarian cancer has never been studied for pancreatic cancer. We hypothesize that Auranofin may prevent pancreatic ductal adenocarcinoma (PDAC) progression by induction of apoptosis. Methods: We performed in vitro and in vivo studies using human PDAC cell lines and patient-derived xenografts (PDX) to assess Auranofin anticancer activity. Sensitivity to the compound was determined based on IC_{50}s. Western blot assay was used to interrogate mechanisms of apoptosis, autophagy, and resistance. Two PDAC orthotopic mouse models were designed to determine optimal dose (survival), and antitumor effect (non-survival) in vivo. Results: We found more than half of PDAC cell lines (10/18) to be sensitive to Auranofin based on IC_{50}s below 5μM. Ex vivo tissue growth inhibition greater than 44% was observed for 13 PDX tissue cases treated with 10 μM Auranofin. Treatment with low-dose Auranofin (0.5-1μM) was found to induce PARP cleavage and LC3B expression among sensitive cell lines when compared to control (0.1% DMSO). High Txnrd1 and low Nrf2 expression was observed for resistant cell lines. Survival study using MiaPaCa-2 Luc+ showed 15mg/kg IP as the optimal dose due to absence of gross solid organ metastasis up to 13 weeks post-treatment (median survival 8 and 12, respectively; p=0.0953). Non-survival study using MDA-Patc53 Luc+ showed a decreased tumor bioluminescence (p=0.1097) and a 9-fold decrease in mean tumor progression from baseline (p=0.1640) 3 weeks post-treatment (Ref. Figure 1). Conclusions: We have demonstrated that Auranofin prevents PDAC progression using two animal models. In vitro studies suggest apoptosis and autophagy as possible mechanisms of action, and Txnrd1 as a biomarker of resistance. This study altogether demonstrates

both primary and metastatic antitumor effect of Auranofin for PDAC, which could represent an advantageous therapeutic approach for a broad selection of patients in both neoadjuvant and adjuvant settings.

Figure 1



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The Mechanisms Acquiring Drug Resistance through the Exosome-Mediated Cell-Cell Interaction in Pancreatic Ductal Adenocarcinoma M. Mikamori,* D. Yamada, H. Eguchi, H. Ogawa, T. Asaoka, T. Noda, H. Wada, K. Kawamoto, K. Gotoh, M. Mori, Y. Doki. *Osaka University, Suita-shi, Osaka, Japan.*

[Introduction] Pancreatic ductal adenocarcinoma (PDAC) is a lethal neoplasm. Gemcitabine (GEM) is a key anticancer drug, but we have often experienced the cases acquiring drug resistance. The interaction among cancer cells will play a dominant manner in acquiring drug resistance, and the exosome is recently emerging as a cell-cell interaction tool. Our aims are to investigate the factors which may induce exosome, and to evaluate the induced-exosome function to PDAC cells. [Materials and Methods] For investigating the candidate factor involving GEM resistance, we employed GEM-resistant cells. Clinical-resected specimen or corresponding blood are used for evaluation value of candidate factor. Exosome amount is counted by Bradford method, and the function is evaluated with exposure of the isolated-exosome on PDAC cells. Furthermore, to clarify whether the factor brings chemo-resistance to PDAC cells by itself or via exosome function, we inhibited exosome secretion by transducing siRAB27B. [Results] GEM resistant cells secrete significantly high number of exosome, and the exosome exposure brings GEM resistance. The transcriptome analysis between parental cells and GEM-resistant cells were performed. miR-155 was one of the top 5 gene in the ranking of GEM-resistant/ parental cells expression, and miR-155 overexpression increases the number of exosome and leads GEM resistance. The exosome derived from the cells overexpressing miR-155 bring GEM-resistance, and siRAB27B transfection decreases the exosome secretion and ameliorates induction of GEM resistance even in the cells overexpressing miR-155. We checked the miR-155 expression of tumor cells in resected specimen, miR-155 expression was a significant prognostic factor in overall survival ($p<0.001$) or disease free survival ($p=0.001$). The expression level of miR-155 in exosome isolated from blood serum was significantly correlated with miR-155 expression in each corresponding resected specimen. [Conclusion] The present results suggested that miR-155 have responsible for exosome secretion inducing GEM resistance in PDAC, indicating this mechanism will be a treatment target to control PDAC.

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Adjuvant (AD) Radiotherapy (RT) Does Not Improve Outcomes Following Pancreaticoduodenectomy (PD) for Pancreatic Adenocarcinoma (PDA): A Margin-Stratified Analysis L. Ocuin,[1]* J. Miller,[1] M. Zenati,[1] J. Steve,[1] A. Singhi,[2] S. Burton,[3] N. Bahary,[4] D. Bartlett,[1] M. Hogg,[1] H. Zeh III,[1] A. Zureikat.[1] *1. Division of Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA; 2. Department of Pathology, University of Pittsburgh Medical Center, Pittsburgh, PA; 3. Department of Radiation Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA; 4. Division of Hematology/ Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: The role of RT following PD for PDA remains controversial due to ambiguity in the definition of R0/R1 margin status in existing clinical trials. Recent data suggest that increased margin clearance (MC) is associated with improved survival after PD for PDA, however the role of adjuvant radiotherapy (ADRT) in patients with known MC is undefined. We sought to analyze the influence of ADRT on outcomes of PD for PDA based on MC data. Methods: We retrospectively identified 326 patients with MC data (in mm) who underwent PD between 2002-2014. Recurrence-free (RFS) and overall survival (OS) was determined by Kaplan-Meier analysis. Hazard ratios (HR) were calculated by Cox multivariate regression analysis on significant variables. Results: Mean age was 68yrs and 55% were male. Median follow-up was 21mos (IQR 12-34mos). ADRT was administered to 87 patients (27%). Median RFS and OS for the entire cohort was 14mos and 25mos. On univariate analysis, ADRT was not associated with improved median RFS (13 vs 14mos;p=NS) or OS (23 vs 27mos;p=NS), but increasing MC was associated with prolonged median RFS [10 (0mm) vs 13 (0-1mm) vs 23mos (>1mm);$p<0.02$ for all pairs] and OS [16 (0mm) vs 23 (0-1mm) vs 40mos (>1mm);$p<0.01$ for all pairs]. After controlling for sex, BMI, neoadjuvant therapy, LVI, PNI, lymph node ratio>0.2, tumor size>2.5cm, and adjuvant chemotherapy, increasing MC was independently associated with improved OS [HR 0.680;p=0.034 (0-1mm); HR 0.451;$p<0.001$ (>1mm), compared to 0mm]. Patients were subsequently stratified into 3 groups based on MC [0mm (n=73); 0-1mm (n=118); >1mm (n=135)]. ADRT was administered less frequently to patients with greater MC [0mm (n=29; 41%); 0-1mm (n=36; 31%); >1mm (n=22; 16%);$p<0.001$]. Even when stratified by MC, ADRT was not associated with improved RFS [10 vs 9mos (0mm); 13 vs 12mos (0-1mm); 21 vs 23mos (>1mm);p=NS for all pairs] or OS [16 vs 18mos (0mm); 24 vs 23mos (0-1mm); 33 vs 42mos (>1mm);p=NS for all pairs]. Conclusions: ADRT is not associated with improved RFS or OS following PD for PDA regardless of MC. The use of RT following PD for PDA should be re-examined.

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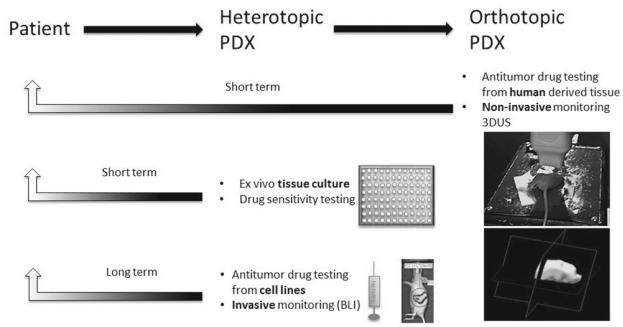
Noninvasive Monitoring of Patient-Derived Orthotopic Xenograft: An Optimal System for Rapid In Vivo Testing M.V. Rios Perez,* M. Pratt, Y. Kang, J.B. Fleming. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: Heterotopic patient-derived xenografts (PDX) have been used to assess response to therapy however they underrepresent the role of tumor microenvironment and rarely develop metastasis, both of which are overcome by orthotopic models. Fluorescent orthotopic mouse models require invasive measures to determine tumor bioluminescence. Ultrasonography (US) is a cost-effective, non-invasive imaging technique that has been used in genetically engineered mouse models of pancreatic cancer for a three-dimensional (3D) acquisition of tumor volume which allows rapid and safe in vivo drug testing. We intend to demonstrate that this technique allows rapid real time monitoring of in vivo response to therapy using patient-derived orthotopic xenograft (PDOX) of pancreatic ductal adenocarcinoma (PDAC). Methods: A non-survival study using PDOX was designed with control (n=5) and treatment (n=5) groups. Weekly 3D US images were obtained pre and post-treatment over 4 weeks. Tumor growth curves were generated to monitor progression of disease. Metastatic burden was determined during necropsy. Results: One mouse was excluded from control and treatment groups due to baseline tumor size exceeding 300mm^3 and drug toxicity, respectively. Pre-treatment average tumor volumes for control and treatment groups were (36±12)mm^3 and (34±12) mm^3, respectively. No difference was found in average tumor growth over time between groups (p=0.9120). A 20% tumor regression was observed per group. Both groups exhibited gross metastasis to spleen, peritoneum, and omentum. Liver, periportal metastasis and local extension to the gastrointestinal and genitourinary system were present on the treatment group. Conclusions: This

study describes a rapid technique for in vivo drug response by using 3D US to monitor PDOX; failure of response to therapy correlated with metastatic burden observed. PDOX regression could be explained by tumor heterogeneity. PDOX models, as challenging as they could be, remain to be necessary in vivo models to show therapeutic response to human PDAC, which could be easily monitored using 3D US imaging.

Figure 1



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A Multicenter Study of 349 Pancreatic Mucinous Cystic Neoplasms: Preoperative Risk Factors for Adenocarcinoma L.M. Postlewait,[1]* C.G. Ethun,[1] M.R. McInnis,[1] N. Merchant,[2] A. Parikh,[3] K. Idrees,[3] C.A. Isom,[3] W. Hawkins,[4] R.C. Fields,[4] M. Strand,[4] S. Weber,[5] C.S. Cho,[5] A.I. Salem,[5] R.C. Martin,[6] C. Scoggins,[6] D. Bentrem,[7] H.J. Kim,[8] J. Carr,[8] S. Ahmad,[9] D. Abbott,[9] G. Wilson,[9] D.A. Kooby,[1] S.K. Maithel.[1] *1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Division of Surgical Oncology, Department of Surgery, University of Miami, Miami, FL; 3. Division of Surgical Oncology, Department of Surgery, Vanderbilt University Medical Center, Nashville, TN; 4. Department of Surgery, Washington University School of Medicine, St. Louis, MO; 5. Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 6. Division of Surgical Oncology, Department of Surgery, University of Louisville, Louisville, KY; 7. Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL; 8. Division of Surgical Oncology, Department of Surgery, University of North Carolina, Chapel Hill, NC; 9. Division of Surgical Oncology, Department of Surgery, University of Cincinnati Cancer Institute, Cincinnati, OH.*

Background: Pancreatic mucinous cystic neoplasms (MCN) are defined by presence of ovarian stroma per WHO 2000 classification. Given their malignant potential, current guidelines recommend resection. However, there are limited data on the preoperative risk factors for adenocarcinoma (AC) and high grade dysplasia (HGD) occurring in the setting of an MCN. Methods: MCN resections from 2000-2014 at the 8 institutions of the Central Pancreas Consortium were included. Patients with and without AC/HGD were compared. Primary aims were to determine preoperative risk factors for AC/HGD in an MCN and to assess outcomes of MCN-associated AC. Results: Of 1667 resections for pancreatic cystic lesions, 349 patients (21%) had an MCN with 52 (15%) having MCN-associated AC/HGD. Male gender (29 vs 8%; p<0.001), pancreatic head/neck location (39 vs 13%; p<0.001), increased MCN size (7.2 vs 4.6 cm; p=0.004), radiographic presence of a solid component/mural nodule (54 vs 20%; p<0.001), and duct dilation (43 vs 12%; p<0.001) were associated with AC/HGD compared to benign MCN. All of these factors persisted as independent predictors of MCN-associated AC/HGD (Table). AC/HGD was not associated with presence of radiographic septations or preoperative cyst fluid analysis (CEA, amylase, or mucin presence). Median CA19-9 for patients with AC/HGD was 210 vs 15 U/ml for those without (p=0.001). In the 44 patients with AC, 41 (93%) had lymph nodes harvested with nodal metastases in only 14 (34%). Median FU for patients with AC was 27 mos. AC recurred in 12 patients (27%) with a 3-yr RFS of 59%. OS for patients with MCN-associated AC was 64% at 3 yrs. Conclusions: Adenocarcinoma or high grade dysplasia is present in 15% of resected pancreatic mucinous cystic neoplasms. Pre-operative factors associated with AC/HGD in an MCN include male gender, pancreatic head/neck location, larger MCN, presence of a solid component/mural nodule, and duct dilation on imaging. MCN-associated AC appears to have decreased nodal involvement and increased recurrence-free and overall survival compared to typical pancreatic ductal adenocarcinoma.

Multivariate Regression Model of Factors Associated with High Grade Dysplasia and Adenocarcinoma in Mucinous Cystic Neoplasms (MCN)

Variable	Odds Ratio	95% Confidence Interval	p-value
Male gender	3.72	1.21-11.44	0.022*
Head/Neck location	3.93	1.43-10.81	0.008*
Radiographic size	1.17	1.08-1.27	<0.001*
Radiographic solid component or mural nodule	4.54	1.95-10.57	<0.001*
Radiographic pancreatic duct dilation	4.17	1.63-10.64	0.003*

*p<0.05

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Predicting Response to Neoadjuvant Chemoradiotherapy in Esophageal Cancer by Textural Features Derived from Pretreatment FDG-PET Scans J. Beukinga,[1] J. Hulshoff,[1] M. Sijtsema,[1] S. van Dijk,[1] K. Muijs,[1] H. Burgerhof,[1] G. Kats,[1] R. Slart,[1] K. Slump,[2] V. Mul,[1] J. Plukker.[1]* *1. Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands; 2. University of Twente, Enschede, Netherlands.*

Introduction 18-F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) is currently the imaging method of choice in assessing response of neoadjuvant chemoradiotherapy (nCRT) in esophageal cancer (EC) patients. PET/CT derived texture analysis is potentially more useful than common PET/CT measurements in response assessment and might also be of predictive value in different cancer types. The aim of this study was to develop a model to predict response to nCRT in EC based on pretreatment FDG-PET derived textural features in combination with clinical parameters. Patients and Methods We reviewed 80 locally advanced EC patients who underwent pretreatment FDG-PET/CT and radiation planning CT scans between 2009 and 2015. Patients received nCRT according to the CROSS regimen (carboplatin/paclitaxel/41.4Gy) followed by esophagectomy. We analyzed 7 clinical, 16 geometry-based, and 87 different texture features derived from pretreatment FDG-PET images of the radiotherapy gross tumor volume. Ordinal logistic regression analysis was performed to construct a prediction model for treatment response, which was pathologically classified in complete, partial and no response on the Mandard tumor regression grade (1 vs. 2-3 vs. 4-5). The performance of this model was estimated by comparison with clinical outcome. Results Pathologic examination revealed 16 (20.0%) complete, 46 (57.5%) partial, and 18 (22.5%) non- responders. Response analysis yielded the following independent predictive textural features: SUV_{min}, small zone low gray level emphasis, and contrast; and the independent predictive clinical parameters: nodal stage, endoscopic tumor length, and gender. The model has a sensitivity/specificity, positive/negative predictive value, and accuracy of 69%/97%, 85%/93%, and 91% for the prediction of complete response and 61%/79%, 46%/88%, and 75% for non-response, respectively. Conclusion The prediction model constructed in this study, shows a good overall performance level in predicting response to nCRT in EC patients, but requires further external validation and refinement before it can be used for clinical decision making.

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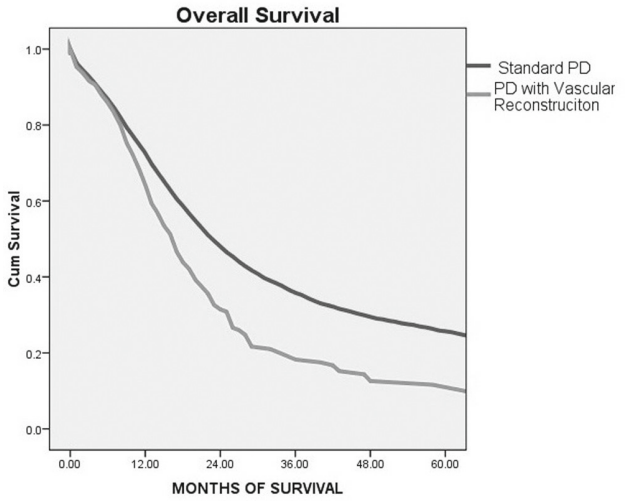
Pancreaticoduodenectomies with Venous Reconstruction Do Worse than Standard Pancreaticoduodenectomies B. Goldner,* F. Tozzi, L. Melstrom, S. Warner, G. Singh. *Surgical Oncology, City of Hope National Medical Center, Duarte, CA.*

Introduction: Locally advanced disease requiring pancreaticoduodenectomy (PD) with venous reconstruction is a controversial topic that is often determined by careful patient selection. There are numerous published single institution, but sparse multicenter studies, demonstrating the safety and efficacy of PD with venous reconstruction. The goal of this study is to evaluate survival outcomes in patients who underwent a PD with our without venous reconstruction utilizing a large statewide database. Methods: The California Cancer Registry (CCR) was used to obtain data on all PD performed from 2000-2011. This data was merged with Office of Statewide Planning and Development data to obtain inpatient hospitalization data. ICD-09 codes were used to identify all PD with or without venous reconstruction. Data was

obtained on demographics, disease process, surgery, hospitalization statistics, and survival. Venous reconstruction was divided into venous segmental resection with reconstruction (VSR) and primary repair of the vein with a patch (PR). Survival was analyzed using Kaplan-Meier Survival analysis (KM). Results: Data were obtained on 5,228 patients who underwent PD, 3.7% (161) underwent venous reconstruction (148; 2.8% VSR and 43; 0.8% PR). A significant overall survival difference between PD and all vascular reconstruction was observed (23 months vs 17 months respectively, $p<0.001$) (Figure 1). Further analysis revealed no significant difference in survival between standard PD and PD with PR (median 21 months; $p=0.2$). However, there was a significant survival advantage of PD compared to PD with VSR (21 vs 16 months respectively, $p<0.001$). Evaluation of length of stay and complications revealed no difference ($p=0.07$ and $p=0.8$) between PD and vascular reconstruction. . Conclusions: Venous reconstruction in PD is associated with worse survival compared to PD alone. Interestingly, patients who had a PR had a better survival than VSR alone. Overall survival for all comers of vascular reconstruction remains inferior which reinforces the biology of disease as an important predictor of outcomes as well as shorter segment portal vein involvement conferring improved survival.



Overall survival for pancreaticoduodenectomies (PD) with and without vascular reconstruction.

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The Role of mTOR Inhibitors in Targeting a Putative Cancer Stem Cell-like Population in Esophageal Cancer D. Wang,* R. Chiu, J. Plukker, R. Coppes. *Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands.*

Introduction: Despite modern advances in the treatment of esophageal cancer (EC), using neoadjuvant chemoradiotherapy (CRT) and esophagectomy, most patients face poor outcome. Growing evidence indicates that cancer stem cells (CSCs) might contribute to the poor prospects. CSCs are usually resistant to CRT and ultimately can generate a new tumor. The mammalian target of rapamycin (mTOR) pathway is associated with cancer stemness. However, its role in EC CSC-like populations needs to be elucidated. Here, we investigate the role of the mTOR pathway on the stemness of a putative CSC-like population. Methods: Previously, we identified a putative CSC-like population (CD44+/CD24-) in EC cell lines and in tumor biopsy from EC patients. qPCR was used to measure the expression of mTOR in CD44+/CD24- CSC-like population of OE21 squamous cell carcinoma and OE33 adenocarcinoma cell lines compared to controls, that consisted of solid tumors generated from the same cell lines obtained from xenografts. mTOR inhibitors rapamycin and torin-1 were used to see their effect on CD44+/CD24- expression and sphere formation. Results: mTOR expression was 2-fold up-regulated in the OE33 CD44+/CD24- CSC-like population compared to control. Furthermore, in OE21 this up-regulation was 1.9-fold. Surprisingly, inhibiting the mTOR pathway with rapamycin enhanced OE33 CD44+/CD24- expression compared to its control ($p=0.01$). In pilot experiments this effect was dose dependent and cells treated with rapamycin formed more spheres than control. Rapamycin did not alter the expression of CD44+/CD24- in OE21. Inhibiting the mTOR pathway with Torin-1 enhanced OE21 CD44+/CD24- expression by 1.2-fold compared to control (N=2). In another pilot experiment Torin-1 treated cells were able to form more spheres compared to control. Torin-1 did not have an effect on the expression of CD44+/CD24- in OE33. Conclusion: These findings indicate that inhibiting the mTOR pathway may enhance CSC-like properties in EC. Additional research needs to be done to further support this hypothesis and elucidate the mechanism in this process. Furthermore, the effect of mTOR pathway inducers in EC need to be explored.

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Functional Screens for Gene Drivers of Pancreatic Cancer N. Villafane,* Y. Tsang, W. Fisher, G. Van Buren, K. Scott. *Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX.*

Introduction: Identifying early cancer biomarkers and genes responsible for promoting progression is of extreme importance in cancer research. This is especially true for pancreatic ductal adenocarcinoma (PDAC), which often presents with advanced metastatic disease. Like other cancers, PDAC genomes are made up of key "driver" events critical to pathogenesis, but also numerous biologically-neutral "passengers" inherent to unstable cancer genomes. We aim to identify functional drivers of pancreatic ductal adenocarcinoma among gene aberrations reported by The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC). Targeting such driver aberrations or their molecular pathways offers great hope of improving patient outcomes. Methods: We leveraged our High-Throughput Mutagenesis and Molecular Barcoding (HiTMMoB) platform enabling gain of function annotation of genes found amplified in PDAC through: 1) a robotics-driven platfom of more than 32,000 sequence-verified open reading frames and 2) a molecular barcoding approach facilitating cost-effective detection of driver events following pooled genetic screens. Amplified gene pools were delivered to a human pancreatic epithelial cell line engineered with doxycycline-inducible $KRAS^{G12D}$ to identify those that function with or without oncogenic KRAS to drive tumor growth in mice. Results: We generated a list of gene amplifications in PDAC by combining data provided by the International Cancer Genome Consortium (33 tumors) and The Cancer Genome Atlas (185 tumors). Data analysis revealed a hightly-vetted list of 311 amplified gene candidates with copy number ≥ 5 (GISTIC q-value ≤ 0.075). Screening these candidates as gene pools revealed potent drivers of pancreatic cancer tumorigenesis, including axon guidance pathway genes such as SEMA4A, a transmembrane member of the semaphorin family of proteins known to signal through Rho GTPases and other Ras-related molecules. Conclusion: Our functional screening technologies have revealed high priority targets to enroll in mechanistic biology studies and drug development programs with the goal of developing personalized treatment strategies critically needed for pancreatic cancer patients.

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EUS Complements CT in Predicting SMV/PV Resection in Patients with Borderline Resectable Pancreatic Carcinoma E.S. Glazer,* O.M. Rashid, J.B. Klapman, C.L. Harris, P.J. Hodul, J.M. Pimiento, M.P. Malafa. *Surgical Oncology, Moffitt Cancer Center, Tampa, FL.*

Introduction: Clinical guidelines recommend pancreatic CT scan (CT) for staging vascular involvement in patients with pancreatic cancer (PC). Although endoscopic ultrasound (EUS) has been demonstrated to be highly effective in venous staging of PC, its role when combined with CT is poorly defined. We evaluated the utility of EUS in addition to CT in staging PC. We hypothesized that EUS complements CT in identifying SMV/PV tumor involvement as measured by the requirement for SMV/PV resection. Methods: We reviewed our database (2006-13) of patients with borderline resectable PC who went to surgery with curative intent. Inclusion criteria were: pre-operative staging with CT scan, EUS, PET scan, & CA 19-9 levels, as well as completion of neoadjuvant chemotherapy & radiation. Results: We identified 62 patients with 74% of tumors located in the pancreatic head. 97% of patients underwent R0 resections. The average age was 65 ± 9 years; 60% were male. Patients were classified as borderline resectable by EUS alone in 29%, CT alone in 23%, and both modalities in 48% of patients, respectively. 34 patients required SMV/PV resection (24 required grafts); EUS identified 88% of these patients pre-operatively while CT scan identified 68%. EUS identified 11 patients who required vein resection that CT did not identify while CT identified 4 patients that EUS did not identify. EUS had higher sensitivity & specificity than CT

in identifying patients requiring venous resection (see Table). On multivariate logistic regression analysis, a positive EUS was predictive of vein resection ($P < 0.02$) but CT scan findings, PET scan findings, tumor size, & CA19-9 values were not predictive (each $P > 0.1$). In margin negative resected patients, median survival was longer when both CT and EUS identified borderline status compared to only 1 modality (43 months vs 23 months, $P < 0.05$). Conclusions: In this group of patients, EUS complemented CT in identifying patients requiring SMV/PV resection. EUS predicted this treatment in 29% of patients that CT alone would not have identified. This observation supports the use of EUS in addition to CT scan for the vascular staging of patients with PC.

Venous Resection in Patients with Borderline Resectable Pancreatic Carcinoma

	EUS	CT
Sensitivity	0.88	0.67
Specificity	0.35	0.25
PPV	0.62	0.52
NPV	0.71	0.39

PPV: Positive Predictive Value. NPV: Negative Predictive Value.

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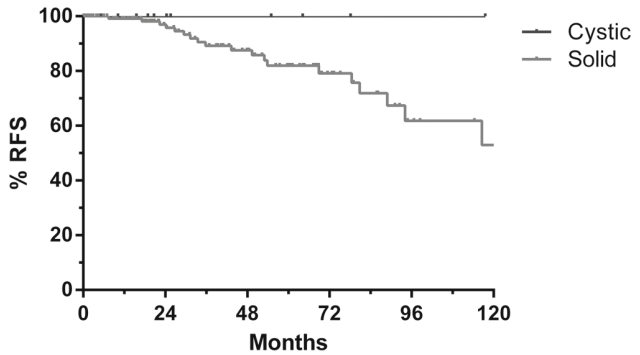
Pancreatic Neuroendocrine Tumors: Degree of Cystic Component Influences Prognosis J. Cloyd,* K.E. Kopecky, J.A. Norton, B.C. Visser, W. Park, G.A. Poultsides. *Stanford University, Stanford, CA.*

Introduction: Although most pancreatic neuroendocrine tumors (PNET) are solid, approximately 10% are cystic. Some studies have suggested that cystic PNETs are associated with a more favorable prognosis. Methods: A retrospective review of all patients with PNETs who underwent surgical resection between 1999 and 2014 at a single academic medical center was performed. PNETs were classified into the following categories based on radiographic features and gross pathology: purely cystic, mostly (>50%) cystic, mostly (>50%) solid, and purely solid. Clinicopathologic characteristics and recurrence free survival (RFS) were assessed between groups. Results: 214 patients met inclusion criteria: 8 purely cystic, 7 mostly cystic, 15 mostly solid and 184 purely solid. Significant differences were found in a step-wise fashion among the four groups in tumor size (1.5 ± 0.5, 3.0 ± 1.7, 3.7 ± 2.6, 4.0 ± 3.5cm, $P<0.05$), LN positivity (0%, 0%, 27%, 34%, $p<0.001$), intermediate or high grade (0%, 17%, 20%, 31%, $p<0.05$), synchronous liver metastases (0%, 14%, 20%, 26%, $p=0.07$) and need for pancreaticoduodenectomy (0%, 0%, 7%, 25%, $p<0.05$). Among patients presenting without metastatic disease, 10 year RFS was 100.0% in purely/mostly cystic tumors versus 53.0% in purely/mostly solid patients, however this difference did not reach statistical significance (Figure). Conclusion: PNETs demonstrate a spectrum of biologic behavior and increasing cystic morphology is associated with more favorable clinicopathologic features and prognosis. No cases of purely cystic PNETs were associated with synchronous liver or LN metastasis, intermediate or higher grade, recurrence or death due to disease. Further research should determine whether these tumors may be safely observed and forgo formal resection.



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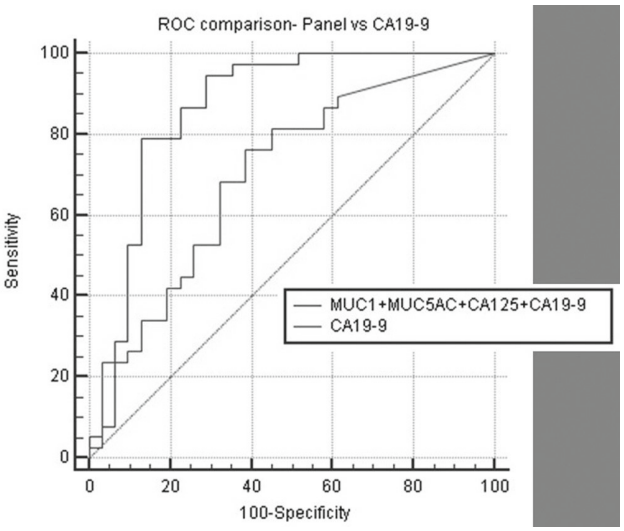
Diagnostic Potential of Mucins in Pancreatic Juice for Pancreatic Cancer A. Patel,* S. Kaur, L. Smith, C. Are, S. Batra. *Surgery, University of Nebraska Medical Center, Omaha, NE.*

Introduction: Pancreatic juice remains an underutilized resource for diagnosing pancreatic cancer. Mucins are high molecular weight glycoproteins differentially upregulated in pancreatic cancer, and we hypothesize that their profile in pancreatic juice may have diagnostic potential. Methods: Pancreatic juice was obtained during endoscopy from non-healthy non-pancreatic control (NHPC, n=57), chronic pancreatitis (CP, n=23), and pancreatic cancer (PC, n=23) patients. Sandwich ELISA was used to detect MUC1, MUC4, MUC5AC, CA125, and CA19-9. Kruskal-Wallis test and Wilcoxon rank sum test for group and pairwise comparison was done with $p<0.05$ as significant. Logistic regression with ROC curve modeling of log transformed data was done for each biomarker individually and in combination to determine odds ratio (OR), sensitivity (SN), and specificity (SP) for PC. Results: PC vs NHPC: MUC5AC had the best individual performance for diagnosing PC with an OR= 2.78 (95% CI=1.51-5.13), AUC= 0.81, and optimal SN/SP of 0.83 and 0.67, respectively. CA125 was increased in PC with an OR=2.31 (95% CI=1.4-4.0), AUC=0.73, and optimal SN/SP of 0.88 and 0.67. CA19-9 was increased in PC with an OR= 1.5 (95% CI= 1.2-1.8), AUC=0.76, and optimal SN/SP of 0.73 and 0.70. A combination of MUC1, MUC5AC, CA125, and CA19-9 outperformed all individual markers and had the largest AUC (0.89) with optimal SN/SP of 0.84 and 0.79. PC vs CP: MUC1 concentration in PC was significantly less than CP with an OR= 0.21 (95%CI=0.088-0.49), AUC= 0.82, and optimal SN/SP of 0.87 and 0.78. PC vs NHPC+CP: MUC1 was decreased significantly in PC with an OR=0.65 (95% CI=0.44-0.96), AUC=0.69, and optimal SN/SP of 0.87 and 0.63. CA125 was increased in PC with an OR= 1.64 (95%CI=1.1-2.4), AUC=0.66, and optimal SN/SP of 0.67 and 0.64. CA19-9 was increased in PC with an OR= 1.32 (95%CI=1.1-1.6), AUC=0.68, and optimal SN/SP of 0.63 and 0.67. A combination of MUC1, MUC5AC, CA125, and CA19-9 had an AUC=0.86 with optimal SN/SP of 0.87 and 0.77 for PC (Fig.1). Conclusion: MUC1, MUC5AC, CA125, and CA19-9 combination provides a significantly improved diagnostic panel compared to any individual marker in pancreatic juice for detecting malignancy.



AUC comparison between the biomarker panel vs CA19-9 for distinguishing between PC and NHPC+CP in pancreatic juice. AUC of the panel was 0.86, which is significantly improved ($p<0.05$) compared to the AUC of CA19-9 (0.68).

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Effect of Incorporation of Pretreatment Serum Carbohydrate Antigen 19-9 into AJCC Staging for Pancreatic Adenocarcinoma M.A. Healy,* L.A. Herrel, S.L. Wong. *Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: Carbohydrate Antigen 19-9 (CA19-9) is often obtained as part of the diagnostic workup for pancreatic adenocarcinoma. However, it

is unclear to what extent pretreatment levels of CA19-9 are associated with long-term survival estimates. We sought to evaluate whether prognostication of overall survival is affected by inclusion of CA19-9 into the American Joint Committee on Cancer (AJCC) TNM staging system. Methods: Using the American College of Surgeons National Cancer Data Base, we performed a retrospective study of 118,970 patients diagnosed with pancreatic cancer from 2009 through 2012. We stratified each AJCC stage into groups of patients with (>37 U/mL) and without (<= 37 U/mL) elevated pretreatment CA19-9 levels. We then analyzed survival using Cox proportional hazards regression. Median follow-up was 21.4 months. Results: Out of 56,535 patients with CA19-9 recorded, 16,522 (29.2%) had normal pretreatment CA19-9 and 40,013 (70.8%) had elevated pretreatment CA19-9. Elevated CA19-9 was independently associated with risk of mortality (HR 1.63; 95% CI, 1.59 – 1.67; P < 0.001). At each stage, patients with elevated CA19-9 fared worse when compared to their same stage counterparts with normal levels (Stage I: HR 2.27; 95% CI, 2.06 – 2.50; P < 0.001; Stage II: HR 1.51; 95% CI, 1.43 – 1.59; P < 0.001; Stage III: HR 1.34; 95% CI, 1.24 – 1.45; P < 0.001; Stage IV: HR 1.34; 95% CI, 1.29 – 1.39; P < 0.001). Conclusion: Elevated pretreatment CA19-9 is associated with worse survival in patients with pancreatic cancer, independent of AJCC TNM stage. Inclusion of CA19-9 resulted in substantial changes in survival estimates, with elevated CA19-9 portending a worse prognosis for patients at the same stage as other patients with a normal CA19-9 level. This pretreatment measure could improve prognostication in the AJCC staging system and should be considered during treatment planning and risk stratification.

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Multivisceral Resection for Gastric Cancer is Associated with Increased Morbidity and Mortality A.U. Friedrich,* E. Rouanet, K. Dinh, G.F. Whalen, J. LaFemina. *Surgery, University of Massachusetts, Southborough, MA.*

INTRODUCTION: In the setting of locally advanced disease during gastrectomy for gastric cancer, multi-visceral resection may be required to achieve negative margins. It is unclear if this is associated with higher rates of postoperative complications. We aim to determine if multivisceral resection in the setting of gastrectomy impacts perioperative outcomes. METHODS: The American College of Surgeons (ACS) National Surgical Quality Improvement Project (NSQIP) database was analyzed for all patients undergoing gastrectomy for gastric cancer between 2005 and 2012. RESULTS: 3832 patients were identified who underwent gastrectomy for gastric cancer, 354 (9.2%) of which had multi-visceral resection. The most commonly resected organs were the spleen (50%), colon (31%), pancreas (25%) and liver (14%). Multivisceral resection was associated with a longer length of stay (15.8 vs 11.8 days, p<0.001) and increased risk of multiple complications within 30 days. Among these were wound complications, such as superficial site infection (RR 1.6, 95% CI 1.1-2.4), wound infection (RR 2.0, 95% CI 1.0-3.7), deep organ space infection (RR 2.9, 95% CI 2.2-3.8), and wound dehiscence (RR 3.7, 95% CI 2.1-6.6); risk of respiratory complications such as pneumonia (RR 2.1, 95% CI 1.6–2.9), failure to wean from a ventilator (RR 1.9, 95% CI 1.3-2.6) and reintubation (RR 2.0, 95% CI 1.4-2.8); as well as severe systemic complications, such as postoperative sepsis (RR 2.3, 95% CI 1.7–3.0), septic shock (RR 2.8, 95% CI 2.0–4.0), acute renal failure (RR 2.5, 95% CI 1.1-5.8), cardiac arrest (RR 3.0, 95% CI 1.5-6.0) and major bleed with transfusion requirement (RR 2.1, 95% CI 1.7–2.8). Patients who underwent multivisceral resection also had higher risk of reoperation (RR 1.9, 95% CI 1.4-2.6). Overall mortality within 30 days was increased 2.6-fold (95% CI 1.8-3.7, p<0.001). CONCLUSION: In this analysis of a national cohort of gastric cancer patients, resection of adjacent organs was associated with a significant higher 30-day morbidity and mortality. This increased risk associated with a multivisceral approach should thus be considered carefully when attempting a margin-negative resection.

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Resident Liver Macrophages Suppress Outgrowth of Occult Liver Metastases and Prolong Survival in a Preclinical Mouse Model of Pancreatic Cancer T. Newhook,* J.M. Lindberg, S.J. Adair, S. Nagdas, J. Parsons, T.W. Bauer. *Surgery, University of Virginia, Charlottesville, VA.*

Background: Most patients will die of metastatic disease following resection of pancreatic ductal adenocarcinoma (PDAC), likely due to presence of occult liver metastases at time of resection. We hypothesized that macrophages in the liver microenvironment act to suppress the outgrowth of occult metastatic PDAC cells. Methods: Liver metastases were harvested from two patients with PDAC, tumor cell lines established, transduced with firefly luciferase, injected into the spleens of nude (T-cell deficient) mice to generate liver metastases, then primary tumors were removed. Outgrowth of occult liver metastases was measured with bioluminescent imaging following pretreatment with clodronate (to ablate macrophages) vs. control. Livers were harvested for H&E and macrophage staining, mouse cytokine array, and FACS analysis of macrophages. Experiments were repeated in nude vs. NOD scid gamma (NSG) mice (deficient in B- and T-cells, macrophages, dendritic cells, NK cells) and tumor outgrowth and survival were compared. Results: There was a robust increase in macrophage chemo-attractant cytokines in the liver 48 and 72 hours post-injection of PDAC cells. H&E sections demonstrated abundant macrophages surrounding tumor cells in the liver. Macrophage ablation with clodronate significantly decreased time to outgrowth of occult metastases (14 vs. 28 days in control; Fig.1A). FACS analysis revealed a lower ratio of resident macrophages ($F4/80^{hi}$ $CD11b^{low}$) to infiltrating monocytes and neutrophils ($F4/80^{low}$ $CD11b^{hi}$) in livers of clodronate-treated mice, whereas control mice exhibit a constant ratio (Fig.1B). Histologic analysis confirmed absence of macrophages at sites of tumor metastasis in clodronate mice (Fig.1C). Tumor outgrowth and survival in macrophage-deficient mice (NSG mice) was similar to that in clodronate-treated mice. Conclusions: In a preclinical model of occult liver metastasis from PDAC, resident liver macrophages inhibit tumor progression and prolong survival of mice. Further elucidation of the tumor cell-macrophage interaction in the metastatic niche may lead to new therapeutic strategies for PDAC.

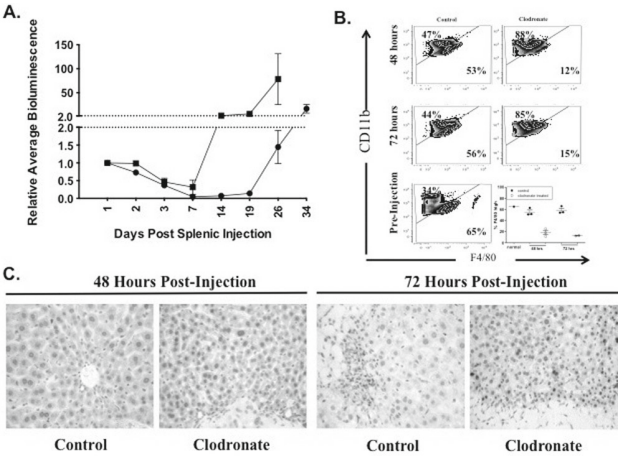

Figure 1. Resident macrophages in the liver are essential for suppression of metastatic PDAC disease progression. A. Macrophage ablation with clodronate significantly decreased time to outgrowth of occult metastases (14 vs. 28 days in control; ■Clodronate ●Control). B. FACS analysis revealed a lower ratio of resident macrophages ($F4/80^{hi}$ $CD11b^{low}$) to infiltrating monocytes and neutrophils ($F4/80^{low}$ $CD11b^{hi}$) in livers of clodronate-treated mice, whereas control mice exhibit a constant ratio. C. Immunohistochemical analysis staining for F4/80 confirmed absence of macrophages at sites of tumor metastasis in clodronate mice relative to control mice.

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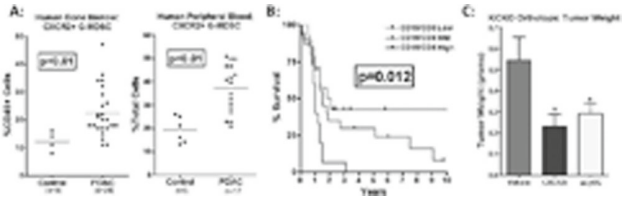
Targeting Granulocytic Myeloid Derived Suppressor Cells Promotes Anti-Tumor Immunity in Pancreas Adenocarcinoma T. Nywening,[1]* B. Belt,[2] R.C. Fields,[1] W. Hawkins,[1] D.G. Denardo,[1] P. Goedegebuure,[1] D.C. Linehan.[2] *1. Surgery, Washington University, St. Louis, MO; 2. University of Rochester Medical Center, Rochester, NY.*

Pancreas adenocarcinoma (PC) is a lethal malignancy with poor prognosis. Granulocytic myeloid derived suppressor cells (G-MDSC) are recruited by PC and critical in shaping the immune privileged tumor microenvironment (TME). We report that mobilization of these cells from the bone marrow has prognostic implications in human PC. Furthermore, targeting G-MDSC restores anti-tumor immunity in pre-clinical models. Human bone marrow, blood, and tumor was collected under an IRB approved protocol. A tissue microarray (TMA) from resected PC patients was analyzed for immune infiltrate. Mice were injected orthotopically with $2.5x10^6$ syngeneic PC cells (KCKO, KPC). CXCR2 inhibitor (Tocris) was given IP twice daily. Tumor burden was assessed by bioluminescence (BLI) and weight. Flow cytometry, real time PCR, and IHC was performed on collected specimens. G-MDSC express the chemokine receptor CXCR2 and are elevated in the bone marrow

and blood of patients with PC (Fig 1A). Furthermore, increased G-MDSC in both compartments also correlates with one-year survival in human patients. PC has elevated expression of the CXCR2 ligands CXCL5 and CXCL8 relative to normal tissue. Tumor infiltrating G-MDSC are abundant and vastly outnumber effector CD8+ T-cells with the ratio of the populations correlating with survival in resected PC patients (HR=0.44; Fig 1B). In a murine model, both Ly6G depletion and CXCR2 inhibitor (CXCR2i) results in a reduction of G-MDSC and tumor burden (Fig 1C). Assessment of local factors reveals a repolarization of the TME, which correlates with an increase in activated CD8+ T-cells. Additionally markers of cytolytic function, including perforin and granzyme B were elevated following CXCR2i. Using a T-cell reporter model ($Nur77^{GFP}$) confirmed CD8+ TIL are activated in the absence of G-MDSC. To demonstrate that G-MDSC blockade requires effector T-cells we performed CD8 depletion and found that CXCR2i efficacy was lost. CXCR2+ G-MDSC are recruited from the bone marrow in human PC and have prognostic implications. CXCR2 inhibitors are in clinical trials for non-malignant indications and may have translational value in restoring anti-tumor immunity.



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Irreversible Electroporation for the Treatment of Locally Advanced and Unresectable Pancreatic Cancer: One Institution's Experience K.E. Poruk,* L. Rosati, J.M. Herman, K. Hirose, T.M. Pawlik, J. He, C. Wolfgang, M.J. Weiss. *Department of Surgery, Johns Hopkins School of Medicine, Baltimore, MD.*

Background: Surgery offers the best opportunity for prolonged survival for pancreatic adenocarcinoma (PDAC), but few patients are amenable to resection at diagnosis. Irreversible electroporation (IRE) provides a novel method of treatment for locally advanced or unresectable pancreatic tumors without distant metastases. We describe our experience with IRE for locally advanced and unresectable PDAC. Methods: Between January 2012 and July 2015, 38 patients received IRE for treatment of a primary pancreatic tumor or augmentation of margins after resection. Fisher's Exact Test was used to calculate differences between cohorts, and survival was calculated by Kaplan-Meier method. Results: IRE was the primary treatment of the pancreatic tumor for 17 patients (45%) while IRE was used to augment close margins at resection in the remaining patients. All patients received neoadjuvant chemotherapy, and 35 (92%) underwent preoperative radiation therapy. Twenty-three patients (68%) had fiducials placed for radiation prior to surgery, including 13 patients (87%) undergoing in-situ IRE. Mean time from tumor diagnosis to surgery was 10.2 months (3.8-20 months). Post-operative complications occurred in 22 patients (58%), primarily those undergoing margin augmentation after resection (P=0.02). Among in-situ IRE patients, there was no difference in post-operative complications for patients with fiducials (P=0.99). Thirty day post-operative mortality was 0%. Median overall survival for the entire cohort was 23.4 months and tended to be longer after margin augmentation (16.3 mo vs. 26.8 mo, P=0.08). Tumor recurrence was seen in 16 patients (76%) after margin augmentation. Six patients (35%) had distant tumor progression after primary IRE, with only one patient having isolated local progression. Conclusion: Irreversible electroporation appears to be a safe and effective option for treatment of PDAC, including patients with preoperative fiducials. Median survival after in-situ IRE is improved compared to historical survivals with chemoradiation alone. Careful consideration is needed to choose patients with stable disease who may potentially benefit from IRE.

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Disparities in the Utilization of Multimodal Therapy for Gastric Cancer: Exploring the National Cancer Data Base K. Jaap,* R. Erwin, M. Fluck, J. Dove, M. Hunsinger, J. Wild, T. Arora, M. Shabahang, J. Blansfield. *Surgical Oncology, Geisinger Medical Center, Danville, PA.*

Introduction: Multiple studies have shown benefit from combined modality therapy for gastric cancer. However, access to multimodality care may be limited for some of the population. This study aims to examine disparities in the use of systemic therapy in gastric cancer, identify predictive factors for systemic therapy and examine overall survival (OS) benefit from multimodal therapy compared with surgery alone. Methods: Patients with gastric cancer staged IB-III from 2005-2011 were identified using the National Cancer Database and were placed into two categories: surgery alone or systemic therapy plus surgery. Statistical analysis was performed to identify predictors of systemic therapy. OS was analyzed by Kaplan-Meier methods. Results: A total of 9637 gastric cancer patients were identified. Most underwent surgery and systemic therapy (70%). This percentage increased from 62% to 76% from 2005-2011 ($p<0.01$). Several predictors for systemic therapy were identified on multivariate analysis. Patients receiving systemic therapy tended to be younger ($p<0.0001$) and male (OR 1.15; 95% CI 1.02-1.29). Patient race and insurance coverage appeared to play a significant role in determining systemic therapy ($p<0.01$ and $p<0.0001$ respectively). Whites underwent systemic therapy in 72% of cases versus 65% in non-whites while privately insured patients received systemic therapy in 83% of cases compared with 73% in non-insured patients. Local earning strata played a significant role as patients from lower-earning economic areas were more likely to receive surgery alone when compared to the most affluent regions ($p=0.002$). Systemic therapy showed an advantage in OS over surgery alone (HR 0.72; 95% CI 0.68-0.77). Conclusions: For the management of gastric cancer, systemic therapy in combination with surgery clearly shows an OS benefit versus surgery alone. There exists a national discrepancy in equivalent access to systemic therapy for older, non-white, lower socioeconomic patients and patients without insurance. As the Affordable Care Act may change access to health insurance, studies may need to readdress differences in disparities in the future.

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Trends and Predictors of Multimodal Therapy for Gastric Cancer Using the National Cancer Data Base R. Erwin,* N. Molacek, M. Fluck, J. Dove, M. Hunsinger, J. Wild, T. Arora, M. Shabahang, J. Blansfield. *Surgical Oncology, Geisinger Medical Center, Danville, PA.*

Introduction: Multiple studies have shown benefit from combined modality therapy for gastric cancer. However, timing of each modality is controversial. This study aims to examine trends in the use of systemic therapy in gastric cancer, identify predictive factors for neoadjuvant and adjuvant therapy and examine overall survival (OS) benefit from multimodal therapy compared with surgery alone. Methods: Patients with gastric cancers staged IB-III from 2005-2011 were identified using the National Cancer Database and were placed into three categories: 1. surgery alone, 2. neoadjuvant treatment plus surgery, 3. surgery with adjuvant therapy. Statistical analysis was performed to identify predictors of neoadjuvant therapy. OS was analyzed by Kaplan-Meier methods. Results A total of 9637 gastric cancer patients were identified for analysis with the majority of patients receiving a combination of surgery and systemic therapy (70%). This percentage increased from 62% to 76% from 2005-2011 ($p<0.01$). The dominant reason for the increase was neoadjuvant therapy rose from 28% to 49%, while those receiving adjuvant therapy dropped from 35% to 27% and surgery alone dropped from 37% to 24%. Several predictors of neoadjuvant versus adjuvant therapy were identified using multivariate analysis. Tumor location in the gastric cardia was a strong predictor of neoadjuvant therapy ($p<0.0001$). Treatment at an academic center was also a strong predictor of neoadjuvant treatment ($p<0.001$). Patients receiving neoadjuvant therapy tended to be younger ($p<0.0001$), male (OR 1.15; 95% CI 1.01, 1.33), white ($p<0.0001$). Neoadjuvant was utilized less in patients with clinical stage I tumors ($p<0.0001$). An OS advantage was seen in those receiving systemic therapy versus surgery alone ($p<0.01$), but no OS advantage when neoadjuvant therapy was compared with adjuvant therapy. Conclusions: Systemic therapy use for gastric cancer rose dramatically since 2005, largely due to increased neoadjuvant use. As neoadjuvant therapy becomes more prevalent it is offering more patients the opportunity to have multimodality therapy for gastric cancer which improves patients overall survival.

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Is Preoperative Chemoradiation Necessary for Borderline Resectable Pancreatic Cancer (BRPC)?: Clinical and Surgical Outcomes Associated with Neoadjuvant FOLFIRINOX Alone in BRPC

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Introduction: BRPC is now recognized as a distinct clinical entity in which neoadjuvant therapy is recommended to increase the likelihood of margin-negative (R0) resection. However, there is no consensus regarding the optimal treatment paradigm for such pts, including the respective roles of chemotherapy and radiation (RT). Methods: A retrospective chart review of BRPC pts at a single tertiary care referral center treated with neoadjuvant FOLFIRINOX over a 4-year period who then underwent surgical resection was conducted. Data analyzed included baseline pt characteristics, toxicity profiles, radiographic and serum CA19-9 response, perioperative complication rate, R0 resection rate, and frequency and patterns of recurrence. Results: Of 26 BRPC pts, 22 received neoadjuvant FOLFIRINOX therapy alone w/o RT. Abutment of the SMV (n=9, 40.9%), SMA (n=4, 18.2%), CHA (n=4, 18.2%), and narrowing of the SMV (n=4, 18.2%) were the most common vascular involvement with 9 (40.9%) pts having both arterial and venous involvement. Median baseline CA19-9 level was 278.5 U/ml. Pts received a median of 9 treatment cycles (range, 4-12). Radiographic response was categorized as shrinkage (n= 11, 50%), stable (n=9, 40.9%), or progression (n=2, 9.1%). The Whipple procedure was the most common operation performed (n=17, 77.3%), with 12 pts (54.5%) undergoing vascular reconstruction. R0 resection rate was 86.4%, with 15 (68.2%) having negative lymph nodes. Best pathologic response was pathological complete response. Clavien-Dindo complication rate: Grade 0 (25.9%), Grade I (11.1%) Grade II (44.4%), Grade IIIa (14.82%). With a median f/u time of 22.1 months, 8 pts (36.4%) have progressed, inc 7 (87.5%) with distant disease, with a median PFS of 22.5 months. Conclusion: This is one of the largest series to report on the use of neoadjuvant chemotherapy alone, without RT, in BRPC pts. FOLFIRINOX therapy alone in carefully selected pts is associated with high R0 resection rates and favorable clinical and surgical outcomes.

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A Multi-Institutional Analysis of Duodenal Neuroendocrine Tumors: Tumor Biology Rather than Extent of Resection Dictates Prognosis

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Introduction: Duodenal neuroendocrine tumors (NETs) are rare neoplasms and their management is poorly defined. As such, we sought to evaluate the management and outcomes of patients undergoing resection of duodenal NETs. Methods: Using a multi-institutional database, 132 patients who underwent curative-intent resection for duodenal NETs between 1998 and 2015 were identified. Data on clinical characteristics, comorbidities, procedural details, as well as recurrence-free survival (RFS) were collected and analyzed. Results: Median age was 63 years and most patients were male(52.3%). Two-thirds(66.7%) of patients had symptomatic disease. Most patients presented with abdominal pain(47.8%), while 17(19.3%) patients presented with GI bleeding/anemia. Lesions were located in first/second(94.5%) or third/fourth(5.5%) portion of the duodenum. Median tumor size was 1.7 cm. Local surgical resection(LSR) was performed in 55(42.0%) patients, while 47(35.9%) patients underwent pancreaticoduodenectomy(PD) and 29(22.1%) underwent an endoscopic resection(ER). Most patients had an R0 surgical margin(88.4%)(LSR, 88.7% vs. PD, 95.7% vs. ER, 71.4%; P=0.02). Among patients who had at least one lymph node examined(n=86), 49(57.0%) had a metastatic lymph node; lymph node metastasis were more common among patients with tumors ≥2cm(OR=3.21, P=0.02). Median length-of-stay was longer for PD(11 days) versus LSR(7 days)(P <0.001). PD patients had more complications(LSR, 52.7% vs. PD, 63.8% vs. ER, 6.9%; P<0.001). 3- and 5-year RFS was 80.1%, and 69.6%, respectively (site of recurrence: locoregional, n=8 vs. distant, n=14). Factors associated with worse RFS included tumor grade(moderate-to-poor: HR=4.12) and presence of metastasis at diagnosis(HR=5.66)(both P<0.05). PD versus LSR versus ER approach was not associated with RFS (P>0.05). Conclusion: Recurrence of duodenal NETs was dependent on tumor biology rather than procedure type. PD was associated with a longer hospital stay and higher risk of perioperative complications. For patients with tumors <2cm, LSR or ER may be appropriate with PD reserved for larger lesions and those not amenable to a more local approach.

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Going the Extra Mile: Improved Survival for Pancreatic Cancer Patients Traveling to High-Volume Centers

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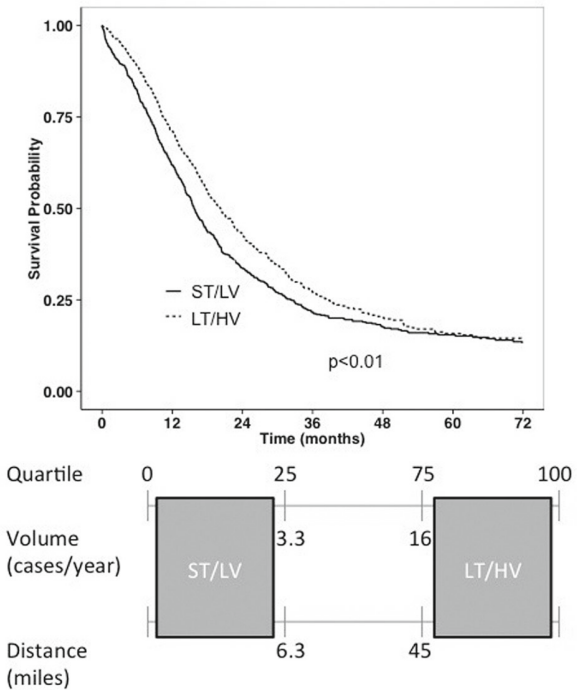
Background: Although outcomes for pancreaticoduodenectomy (PD) are superior at high-volume institutions, not all patients live in proximity to major medical centers. Theoretical advantages for undergoing surgery at a local facility exist. The purpose of this study was to compare outcomes following PD for patients treated at local, low-volume centers and those that traveled to high-volume centers. Methods: The 1998-2012 National Cancer Data Base was queried to identify patients with T1-3N0-1M0 pancreatic adenocarcinoma that underwent PD. Travel distances from patients' homes to treatment centers were calculated by Haversine method. Overlaying the upper and lower quartiles of travel distance with that of institutional volume established two cohorts (Figure): short travel/low volume (ST/LV) and long travel/high volume (LT/HV). Overall survival was evaluated using multivariable linear regression. Results: Of 7,086 PD patients, 773 were classified as ST/LV and traveled ≤ 6.3 (median 3.2) miles to centers performing ≤3.3 PDs yearly, and 758 were classified as LT/HV and traveled ≥ 45 (median 97.3) miles to centers performing ≥16 PDs yearly (p<0.01). LT/HV patients were more frequently white, had higher T- and N-stage disease, and were more often treated with neoadjuvant therapy (p <0.05). LT/HV patients had lower rates of positive margins (20.5% vs. 25.9%, p=0.01) and improved lymph node harvest (16 vs. 11 nodes, p<0.01). Moreover, LT/HV patients had shorter hospitalizations (9 vs. 12 days, p<0.01) and lower 30-day mortality (2.0% vs. 6.3%, p<0.01). Despite having more advanced disease, LT/HV patients had superior unadjusted median survival (20.3 vs. 15.7 months; Figure). After adjustment, travel to a high-volume center remained associated with reduced hazard of long-term mortality (HR 0.75, p<0.01). Conclusion: Despite a perceived "travel burden," patients who sought care at high-volume centers had significantly improved perioperative outcomes, short-term mortality, and overall survival compared to patients treated at local, low-volume centers. These data support efforts to centralize care to highly experienced centers for patients undergoing PD.



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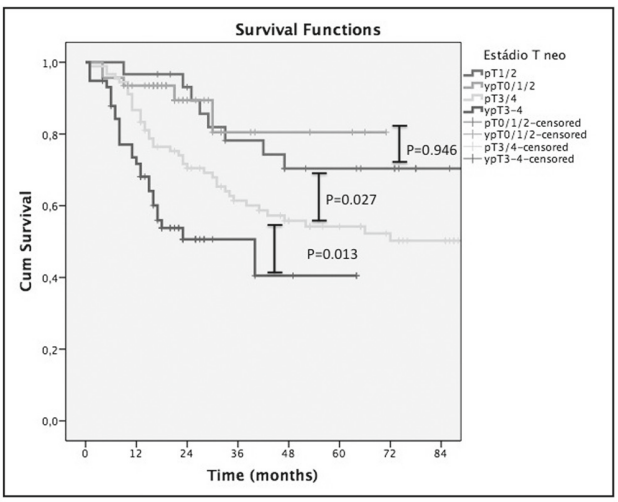
Early and Long-term Outcomes of Gastric Cancer Patients Treated with Neoadjuvant Chemotherapy and D2-Lymphadenectomy: A Comparative Study W.L. da Costa,* F.J. Coimbra, H.S. Ribeiro, A.L. Diniz, A.L. de Godoy, I.C. de Farias, A.M. Cury, V.H. de Jesus, H.C. Freitas, V. Martins, R.C. Fogaroli, F.A. Soares, M.F. Begnami. *Abdominal Surgery, A. C. Camargo Cancer Center, Sao Paulo, Brazil.*

BACKGROUND: Multimodality treatment in gastric cancer is standard of care nowadays, although controversy remains regarding the best scheme, particularly with D2-lymphadenectomy. The aim of this study was to describe early and long-term outcomes of gastric cancer patients who had neoadjuvant chemotherapy in comparison to those who received surgery and adjuvant treatment. METHODS: This is a retrospective study from a prospectively-collected database of a single cancer center from 2000 to 2013. Exclusion criteria were tumors of the gastric stump, concomitant esophagectomy and intraperitoneal chemotherapy use. Only resected cases were analysed. The study comprised 224 patients, 104 in the neoadjuvant group (NAC) and 120 in the adjuvant one (S + ADJ), 95 of them treated with chemoradiotherapy. RESULTS: The groups matched for age, gender, tumor site and preoperative staging. The NAC group had more intestinal-type tumors and more ASA 3/4 patients. Overall morbidity was 30.8% and mortality was 1.3%. Neoadjuvant treatment was associated with more blood transfusion, higher operative time and overall postoperative complications, but multivariate analysis demonstrated that the only independent factor for morbidity was blood transfusion (HR – 3.01; 95% CI 1.54-5.87; P=0.001). Overall 5-year survival was 57.0% in the NAC group and 58.3% in the S + ADJ one. Subjects who received neoadjuvant treatment had significant downstaging in T-category and N-category, which were independent prognostic factors for survival, along with multivisceral resections. Also, patients with ypT1-2 tumors had similar survival in comparison with the ones who had surgery first and pT1-2 lesions; on the other hand, those with ypT3-4 had the worst survival result. The same pattern was observed regarding N-category, with ypN0-1 lesions having similar survival to pN0-1 ones and ypN2-3 the worst numbers. CONCLUSION: Neoadjuvant chemotherapy in gastric cancer patients treated with D2-lymphadenectomy was associated with acceptable morbidity outcomes and had a marked impact on survival, as downstaging was related to very good prognosis and lack of it with the worst outcomes.



Overall survival of gastric cancer patients by depth of invasion pT1-2 and pT3-4 tumors - Surgery + adjuvant treatment group ypT0-1-2 and ypT3-4 tumors - Neoadjuvant chemotherapy group

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Development of a Prognostic Gene Expression Profile (GEP) Signature in Patients with Localized Esophageal Cancer (EC) Receiving Preoperative Chemoradiation (CTRT) D. Giugliano,* P. Cotzia, D. Levine, J. Palazzo, E. Rosato, A. Berger. *General Surgery, Thomas Jefferson University, Philadelphia, PA.*

Introduction: The standard of care for loco-regional EC is neoadjuvant CTRT followed by surgery. It is known that ~30% of EC patients will exhibit extreme resistance to neoadjuvant CTRT, which is associated with poor survival outcomes compared with those who exhibit more favorable responses. The current study was designed to develop a prognostic GEP signature that accurately predicts survival in EC patients. Methods: Twenty-four patients treated at our institution were enrolled in an IRB approved study. Archived formalin-fixed paraffin-embedded EC biopsy specimens were macro-dissected and RT-PCR analysis of 96 candidate genes was performed. Unsupervised hierarchical clustering (UHC) and predictive modeling methods were used to identify genes with prognostic potential. Kaplan-Meier survival analysis was performed for the predicted risk groups and cross-validation was carried out to assess the reliability of the identified signatures. Results: Five of the 96 genes exhibited minimal expression changes and were established as control genes. UHC analysis of the remaining 91 genes separated the 24 EC cases into two distinct clusters (A and B) associated with overall survival (OS), and identified 24 genes that were significantly differentially expressed between the clusters ($p<0.05$). Partial least squares predictive modeling using the 24 genes resulted in accurate differentiation of samples from cluster A and cluster B. Thirty iterations using 10-fold cross-validation resulted in an average accuracy of 97% and AUC of 0.99. Kaplan-Meier analysis showed significantly different 3-year OS rates of 29% and 73% for cluster A and B, respectively ($p<0.01$). The 24 prognostic genes are felt to regulate apoptosis, cell adhesion, epithelial differentiation, and hypoxia responses. Conclusions: We report the initial discovery of a GEP signature able to accurately predict OS for a cohort of 24 EC patients. Identification of EC patients' risk offers an opportunity to employ personalized treatment strategies to high risk patients who are more likely to exhibit resistance to pre-operative CTRT.

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Pancreaticoduodenectomy for Metastatic Pancreatic Neuroendocrine Tumor R. Williams,[1]* N. Sich,[2] T. Clancy,[1] J. Wang,[1] C. Pezzi,[2] S. Ashley,[1] R. Swanson.[1] *1. Surgical Oncology, Dana-Farber/Partners Cancer Care, Boston, MA; 2. Abington Jefferson Health, Abington, PA.*

Background: The optimal management of metastatic pancreatic neuroendocrine tumor (PNET) is controversial, with some advocating aggressive surgical resection and others a more conservative approach. The objective of this study was to define the role of pancreaticoduodenectomy (PD) in the treatment of patients with metastatic PNET utilizing a large, multi-institutional patient cohort. Methods: We analyzed 4,667 patients diagnosed with metastatic PNET in the National Cancer Data Base from 1998 to 2012. Thirty- and 90-day mortality was calculated for patients undergoing PD compared to patients managed without resection of the primary tumor. Kaplan-Meier and Cox regression models were used to assess the effect of relevant clinicopathologic and treatment factors on survival. Results: Approximately 1/5 of patients with metastatic PNET (970, 20.8%) underwent surgical resection of the primary tumor, with 351 (7.5%) undergoing PD and almost 1/2 of these (184, 52.4%) combined with resection of extrapancreatic disease (PD+). In the no primary resection (NPR) group, 185 (5%) had resection of extrapancreatic tumor (NPR+). Compared to NPR, PD patients were more likely to be younger (45% age <55 vs. 32.9%), privately insured (64.4% vs. 48.9%), treated in an academic medical center (71.2% vs. 47.2%), and less likely to have received chemotherapy (25.9% vs. 48.6%), $p<0.001$ for all. Thirty- and 90-day mortality rates, respectively, were 1.4% and 4.3% after PD and 7.6% and 19.2% for NPR. Median survival times in months were: NPR only 14.5, NPR+ 24.9, PD only 67.9, and PD+ 93.2. Overall 5- and 10-year survival rates, respectively, were 57% and 37% with PD, and 19% and 8% with NPR. On multivariable analysis, PD remained an independent predictor of improved survival (HR 0.41, 95% CI 0.33-0.50). Conclusion: PD is associated with a significant long-term survival advantage and minimal postoperative mortality in patients with metastatic PNET. Resection of the primary and resection of extrapancreatic disease each improved survival but seemed to have an additive effect when combined. PD, preferably with resection of metastatic disease, should be considered in patients with metastatic PNET when possible.

Survival in Patients with Metastatic PNET Treated with Pancreaticoduodenectomy Versus No Resection of the Primary Tumor

	NPR (n = 3687)		PD (n = 351)	
	NPR only	NPR+	PD only	PD+
Number of patients (%)	3502 (95%)	185 (5%)	167 (47.6%)	184 (52.4%)
30-day Mortality (%)	7.6		1.4	
90-day Mortality (%)	19.2		4.3	
Median survival (months)	14.5	24.9	67.9	93.2
OS at 5 Years (%)	19		57	
OS at 10 Years (%)	8		37	

NPR = No primary resection,
NPR+ = No primary resection but resection of extra pancreatic disease,
PD = Pancreaticoduodenectomy,
PD+ = Pancreaticoduodenectomy with resection of extra pancreatic disease,
OS = Overall survival

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Oncologic Outcomes of Patients with Resectable Pancreatic Adenocarcinoma Treated with Neoadjuvant Gemcitabine-Based Chemoradiation: A 10-Year Experience R.J. Louie,[1]* M.V. Hill,[1] S.J. Liu,[1] D. Caba-Molina,[2] J.J. Judkins,[1] B.I. Zaki,[1] J.J. Shatzel,[1] K. Mody,[3] J.M. Pipas,[1] K.C. Hourdequin,[1] G.H. Ripple,[1] G.H. Tsongalis,[1] M.J. Tsapakos,[1] J.B. Mills,[1] M. Lisovsky,[1] A.A. Suriawinata,[1] C.V. Angeles,[1] T.A. Colacchio,[1] J.E. Sutton Jr.,[1] S.R. Gordon,[1] T.B. Gardner,[1] R.J. Barth Jr.,[1] K.D. Smith.[1] *1. General Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, NH; 2. University of Chicago, Chicago, IL; 3. Mayo Clinic, Jacksonville, FL.*

Neoadjuvant therapy for borderline resectable pancreatic ductal adenocarcinoma (PDAC) patients is gaining wide spread acceptance as standard-of-care, but is still controversial for resectable PDAC. We aim to evaluate the patterns of recurrence and survival for resectable PDAC treated with gemcitabine-based neoadjuvant chemoradiation. Retrospective cohort study of all patients with biopsy-proven PDAC treated at our institution from January 1, 2004-December 31, 2013. We reviewed images and stratified patients according to 2009 AHABPA/SSAT/SSO resectability guidelines and collected patient demographics, clinical-pathologic variables and outcome endpoints. R1 margin was defined as tumor cells ≤ 1 mm to the margin. Patterns and timing of recurrence were determined per review of surveillance imaging. Statistics were performed using STATA. We identified 452 patients with biopsy-proven PDAC. Excluding patients with metastatic (102), borderline resectable (171) and locally advanced (70) disease, 109 patients had resectable PDAC at diagnosis. We identified metastatic disease in 5 patients (6%) of 84 patients who underwent diagnostic laparoscopy at the time of diagnosis. 73 of 79 patients completed neoadjuvant therapy (92%). Restaging imaging identified distant progression in 7 patients (10%) and no cases of local progression. Of the 60 patients explored with curative intent, 52 patients had a complete resection, with R0 margins in 37 patients (71%). Within 5 years, 29 patients recurred: local recurrence (LR) in 8 patients (15%), with LR only in 2 patients and both local and distant recurrence in 6 patients. 13 patients were alive and disease-free with a median follow-up of 42.5 months. Median overall survival was 25 months with 37.4% predicted 5-year survival. Gemcitabine-based neoadjuvant chemoradiation is feasible and may improve oncologic outcomes for patients with resectable PDAC. Benefits include identification of patients who would not benefit from surgery-up-front, no local progression through neoadjuvant therapy, a high complete resection rate and low incidence of local recurrence.

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Distal Pancreatectomy for Benign and Low-grade Malignant Tumors: The Importance of Spleen Preservation on Short-term Postoperative Outcomes. A Systematic Review and Update Meta-analysis F. Pendola,* R. Gadde, C. Ripat, R. Sharma, O. Picado, L. Lobo, D. Sleeman, N. Merchant, A. Livingstone, D. Yakoub. *University of Miami, Miami, FL.*

BACKGROUND: The value of spleen preservation with distal pancreatectomy (DP) for benign and low grade malignant tumors remains unclear. The aim of this study was to evaluate the short term postoperative clinical outcomes in patients undergoing DP with splenectomy (DPS) or spleen preservation (SPDP). METHODS: Online database search of PubMed, MEDLINE, EMBASE, SCOPUS, COCHRANE, and GOOGLE SCHOLAR was performed (2000 – Present); key bibliographies were reviewed. Studies comparing patients undergoing DP with either DPS or SPDP, and assessing postoperative complications were included. Relative risks with the corresponding 95% confidence intervals (CI) by random effects models of pooled data were calculated. Study quality was assessed using STROBE criteria. RESULTS: Out of 68 studies, 19 studies met our selection criteria. These included 1652 patients in total; 521 underwent SPDP while 1131 underwent DPS. Median age was 63 years. Meta-analysis of included data showed that there was no significant difference between the two groups in operative time. SPDP patients had significantly less operative blood loss (SMD -0.42; 95% CI -0.78 to -0.07, P = 0.01), shorter duration of hospitalization (SMD -2.26, 95% CI -3.74 to -0.79, p = 0.002), lower incidence of fluid collection and abscess (RR 0.69; 95% CI 0.47 – 0.99; p = 0.04), lower incidence of postoperative splenic and portal vein thrombosis (RR=0.35; 95% CI 0.22 – 0.57, p <0.001) and lower incidence of new onset postoperative Diabetes (RR 2.10, 95% CI 1.00 to -4.42, p = 0.05) and lower incidence of POPF (RR=0.95; 95% CI 0.65 – 1.40, P = 0.80, though didn't reach statistical significance). Further subgroup analysis of studies that used ISGPF criteria showed that DPS patients had increased POPF Grade B/C (RR=1.35; 95% CI 1.08 – 1.70, P = 0.01). All included studies reported 0% 30-day mortality in both groups. CONCLUSIONS: SPDP for benign and low grade malignant tumors is feasible with shorter hospital stay and less postoperative complications compared to DPS. Randomized controlled trials are needed to examine long term outcomes of SPDP.

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Palliative Pancreaticoduodenectomy for Metastatic Pancreatic Adenocarcinoma is Associated with Excessive Postoperative Mortality R. Williams,[1]* N. Sich,[2] J. Wang,[1] C. Pezzi,[2] T. Clancy,[1] S. Ashley,[1] R. Swanson.[1] *1. Surgical Oncology, Dana-Farber/Partners Cancer Care, Boston, MA; 2. Abington Jefferson Health, Abington, PA.*

Background: National Cancer Data Base (NCDB) data shows that pancreaticoduodenectomy (PD) can be performed in high volume centers with <2% 30-day and 4% 90-day mortality rates (MR) (Ann Surg Oncol 21:4059, 2014). In recent years there has been an ongoing debate about the role of palliative PD. We examined PD for adenocarcinoma to determine whether outcomes supported this approach for selected stage 4 patients. Methods: We identified NCDB patients with stage 4 pancreatic adenocarcinoma from 1998 to 2012. 30- and 90-day MR and survival were determined for stage 4 patients undergoing PD and compared to the non-operative group (NOG). Results: Of 118,761 patients diagnosed with metastatic pancreatic adenocarcinoma, 1583 (1.3%) had a PD. 30- and 90-day MR were 6.2% and 17%, respectively, compared with 21.4% and 47.1% for the NOG. Median survival time was 9.3 months for the PD group vs. 2.9 months for the NOG. For PD, 1-, 2-, and 3-year survival was 39.7%, 17.4%, and 9.4%, respectively, vs. 11.5%, 3.3%, and 1.6% in the NOG. Conclusion: PD is performed in 1.3% of patients with stage 4 pancreatic adenocarcinoma. Even in this highly selected cohort, 30- and 90-day MR were much higher than the acceptable rates in most published series. The 90-day MR was triple the 30-day MR. Although there may be a subset of stage 4 patients that derives a survival benefit, before palliative PD can be recommended: (1) the mortality rate for PD in this group needs to be improved, and (2) more research is needed to better define this cohort.

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Pancreatic Neck/Body Benign and Low Grade Malignant Tumors: Is Central Pancreatectomy Better than Distal Pancreatectomy? An Update Meta-analysis F. Pendola,* R. Gadde, C. Ripat, R. Sharma, O. Picado, L. Lobo, D. Sleeman, N. Merchant, A. Livingstone, D. Yakoub. *University of Miami, Miami, FL.*

BACKGROUND: Pancreatic endocrine and exocrine dysfunction as well as POPF remain unresolved complications of pancreatic surgery. Central pancreatectomy (CP) has been an alternative technique to distal pancreatectomy (DP) to preserve pancreatic parenchyma. The aim of this update meta-analysis was to reevaluate the short term postoperative clinical outcomes in patients undergoing both methods. METHODS: Online database search of PubMed, MEDLINE, EMBASE, SCOPUS, COCHRANE, and GOOGLE SCHOLAR was performed (2000 – Present); key bibliographies were reviewed. Studies comparing patients undergoing (CP) and (DP) for pancreatic neck and body

tumors, assessing postoperative pancreatic outcomes were included. Pooled relative risk with the corresponding 95% confidence interval (CI) by random effects models were calculated. Study quality was assessed using STROBE criteria. RESULTS: The search strategy yielded 97 studies, of which 15 studies met our selection criteria. All studies were retrospective and included a total of 1088 patients; 454 underwent CP while 634 underwent DP. Median age was 49.3 years. Female/male ratio was 2 to1. Meta-analysis of included data showed that CP patients had a significantly lower incidence of pancreatic endocrine insufficiency (RR 0.22; CI 0.14-0.35 p<0.001; N= 1080 patients), significantly lower incidence of pancreatic exocrine insufficiency (RR 0.31; CI 0.19-0.50 p<0.001; N= 676 patients) and lower incidence of Post-Operative Pancreatic Fistula (POPF) (RR 1.56; CI 1.5-2.11 p=0.004; N= 1080 patients); as compared to DP patients. There was no significant difference between CP and DP when comparing operative blood loss, Length of Stay (LOS), overall morbidity, and abdominal abscess formation. CONCLUSIONS: CP for benign and low grade malignant pancreatic neck/body tumors appears to preserve exocrine and endocrine functions of the pancreas and has less incidence of POPF than DP. Prospective randomized controlled trials are necessary to consolidate these results and compare long term outcomes and survival between the two techniques.

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Lymph Node Status and Patterns of Recurrence Following Pancreaticoduodenectomy for Pancreatic Ductal Adenocarcinoma

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Introduction: Positive lymph node (LN) status is an established negative prognostic factor in PDAC patients, yet its role in predicting recurrence patterns is not well documented. We evaluated whether LN status affects patterns of recurrence in a relatively large and homogenous cohort of surgically treated PDAC patients. Methods: Prospectively accrued data was analyzed for PDAC patients who underwent pancreaticoduodenectomy (PD) with curative intent at our institution between 1995 and 2015. Of them, 281 patients had recurrence data and 260 had complete recurrence pattern data. Recurrence free survival (RFS), and pattern of recurrence were analyzed in relation to nodal status and lymph node ratio (LNR). Results: Of the 281 patients evaluated, 147 (52%) had LN metastasis (N1). Of them, LNR>0.3 was documented in 41 (28%). With a median follow-up of 17 months, 205 patients (73%) experienced recurrence. Median RFS was shorter in N1 vs. N0 patients, 11.5 vs. 16 months, respectively (p=0.012). Multivariate analysis identified N1 status as an independent prognostic factor for recurrence, (HR 3.47, p=0.0002). Of the 260 patients with complete recurrence pattern data, 127 patients (49%) had local recurrence, 91 (35%) nodal recurrence, and 192 patients (74%) had distant recurrence. Only 67 patients (26%) presented with isolated loco-regional recurrence. Isolated local recurrence occurred in 10% of N1 patients vs. 17% of N0 patients (p=0.27), whereas distant recurrence was insignificantly more common in the N1 vs. N0 group of patients, 75% vs. 72.3% (p=0.62), respectively. Neither LNR nor number of positive lymph nodes added discriminative information related to pattern of recurrence within the N1 group of patients. Conclusion: Our data confirms the prognostic value of LN status in surgically treated PDAC patients, mostly affecting RFS. However, it shows no predominant pattern of recurrence associated with either LN status or LNR. The results imply that both N1 status and high LNR are markers for advanced systemic rather than loco-regional disease. It is possible that pre-operative identification of extensive nodal disease justifies neoadjuvant systemic therapy.

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Peritoneal Carcinomatosis of Gastric Cancer: The Microenvironment as a Potential Target for Therapy

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Introduction: Omental spread is a common and lethal event in gastric carcinoma patients. Increasing data suggest that the omentum is an active metabolic tissue that secretes numerous pro-tumorigenic cytokines. Of them, chemokines play an important role in cancer progression and metastasis. We evaluated the potential role of CXCl5 in gastric cancer peritoneal metastasis. Methods: A non-targeted proteomic approach was used to study the omental proteome. Human gastric carcinoma cell lines, efficient in generating malignant omental carcinomatosis and ascites in nude mice upon i.p. inoculation and conditioned medium (CM) of non-cancerous human omental cells, incubated for 24h were utilized for all in-vitro and in-vivo experiments. Results: An in-vivo experiment showed increased gastric cancer tumor growth when cancer cells were co-cultured with human omentum CM as compared to subcutaneous human fat CM (p<0.05). Omental CM increased gastric cancer cellular growth and decreased chemotherapy-induced apoptosis. Moreover, it enhanced migration, invasion, and angiogenic capacities. Several chemokines were identified within the omental proteome. Of them, CXCl5 was predominantly expressed by the omentum as compared to subcutaneous fat (6.15 fold change; p= 0.024). AGS and SNU16 cells expressed CXCR2 mRNA at high levels and demonstrated strong migratory responses to its ligand CXCl5. CXCl5 enhanced proliferation, activating the PI3K/Akt signaling pathway in AGS cells. Utilizing an anti-CXCR2 antibody, we effectively reduced tumor growth and ascitic fluid formation in nude mice inoculated with SNU16 cells. Conclusion: Our findings suggest that the omentum is an active player in gastric cancer carcinomatosis. The data imply that the CXCR2/CXC15 axis plays an important role in the development of peritoneal spread. Hence, CXCR2 may be a potential therapeutic target for peritoneal carcinomatosis of gastric cancer.

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Erasing Site-specific Variation in Pancreatic Cancer Survival

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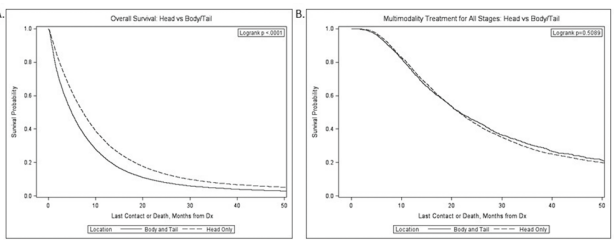
Introduction: It is generally accepted that pancreatic adenocarcinoma of the body/tail has worse survival than tumors of the head, in part due to lack of symptomatology and advanced stage at presentation. Here we perform a large database comparison of survival and treatment for tumors in the head and body/tail. Methods: The National Cancer Data Base was queried for patients with adenocarcinoma from 2003-2012. Tumor location, AJCC clinical stage, and treatment regimen were noted. Patient demographics were analyzed by $\chi 2$ test. Survival data was analyzed using Kaplan-Meier curves. Differences in survival by tumor location and treatment received were determined by log-rank tests. Multimodality therapy is defined as surgery plus chemotherapy and/or chemoradiotherapy in any sequence. Results: Of the 118,742 patients identified, 80,204 (67.5%) and 38,538 (32.5%) had tumors arising in the head and body/tail, respectively. Body/tail tumors were more likely to be diagnosed at stage IV disease (68.8% vs 36.6%, p<0.0001). Treatments received differed significantly (p<0.0001), with body/tail tumors being more likely to have no treatment (34.3% vs 31.8%) and less likely to undergo resection (9.4% vs 19.8%). Overall survival was worse for body/tail tumors, with median survival of 4.9 vs 7.3 months (p<0.0001). However, when analyzed by stage, overall survival was better in the body/tail group for those with potentially resectable (stage I/II) disease and conversely, in the head group for advanced (stage III-IV) disease (p<0.0001). Furthermore, for those with potentially resectable disease who underwent surgery or multimodality treatment a survival benefit for the body/tail location was present (p=0.0001 and p=0.0241, respectively). No survival difference was noted for those with advanced disease undergoing surgery or multimodality therapy. Conclusion: The worsened prognosis for body/tail pancreatic cancers disappears for patients receiving multimodality treatment. In addition, patients with potentially resectable body/tail tumors demonstrate a survival advantage when treated with cancer-directed therapy, suggesting that early detection and aggressive treatment are key to survival in body/tail pancreatic cancer patients.



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Overall Survival After Surgical Resection of Diffuse Type Gastric Adenocarcinoma is Equivalent in Caucasians and Asians

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Introduction: Numerous studies suggest that the biology of gastric adenocarcinoma (GA) is more aggressive in Caucasians than Asians. Since Lauren diffuse type GA is more genomically stable and possibly less influenced by environment, we hypothesize that Caucasian and Asian patients with diffuse GA would have similar overall survival (OS). Methods: We queried prospectively-maintained gastric cancer databases at Memorial Sloan Kettering Cancer Center (MSKCC) and Seoul National University Bundang Hospital (SNUBH) for patients undergoing potentially curative resection for diffuse GA between 1998 and 2011. Patient receiving neoadjuvant treatment and Asian patients treated at MSKCC were excluded. Results: A total of 183 Caucasian MSKCC and 1252 Asian SNUBH patients were included. MSKCC patients were older, more commonly female, and had higher BMI. MSKCC patients had more distal tumors with more frequent vascular and perineural invasion. The mean number of examined nodes was 25 for MSKCC patients and 50 for SNUBH patients. There was no difference between MSKCC and SNUBH patients in 5-yr OS for stage I patients (91% vs. 91%, p=0.828), but stage II and III patients from MSKCC had significantly worse 5-yr OS (61% vs. 81%, p=0.009, and 22% vs. 43%, p<0.001, respectively), possibly due to stage migration. On univariate analysis, significant predictors of OS included age, tumor size, tumor location, vascular invasion, perineural invasion, T status, N status, and race (all p<0.001). On multivariate analysis, independent predictors of OS included age, vascular invasion, T status, and N status; race was not an independent predictor. Conclusions: Race (Caucasian vs. Asian) is not independently associated with OS for patients undergoing potentially curative resection of diffuse type GA.

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Indeterminate Nodules in Pancreatic Adenocarcinoma: Are CT Scans of the Chest Necessary?

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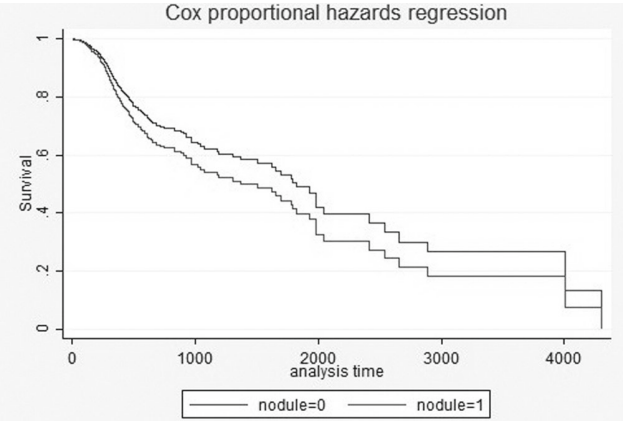
Introduction: There is no consensus guideline on the use of chest imaging in pancreatic ductal adenocarcinoma (PDAC) patients. While chest imaging is recommended for a metastatic workup, there are no specifications on the frequency or type of imaging to obtain. Prior work has described the significance of indeterminate pulmonary nodules (IPNs) in patients undergoing resection of PDAC. We sought to determine if the presence of IPNs impact overall survival or predict lung first metastases in both resected and non-resected patients with PDAC. Methods: Institutional retrospective clinicopathologic data was collected for patients diagnosed with PDAC, who also underwent a staging chest CT scan between 1998-2014. IPN was defined as ≥1 well-defined non-calcified lung nodule(s) less than or equal to 1 cm in diameter. Time to overall survival (OS) was our main outcome measure and assessed using univariate and multivariate Cox regression. Lung first metastasis was our secondary outcome measure and assessed using univariate and multivariate logistic regression. Outcome measures were risk adjusted using demographic and oncologic patient level data. Results: Of the 1062 patients diagnosed with PDAC who underwent a staging chest CT scan, 657 (61.9%) patients with indeterminate nodules were identified. No significant demographic or clinical differences (all p > 0.05) were found between patients with versus those without IPNs. There was no difference in median overall survival in patients with nodules (14.1 months) compared to those without nodules (16.4 months, p=0.09). No radiographic criteria of IPNs (including number, size, and calcification) was associated with overall survival. Lung-first metastasis (LFM) developed in 18.5% of patients with nodules vs. 15.0% of patients with no nodules (p=0.57). Conclusions: Overall survival in both resected and non-resected PDAC patients was not impacted by the presence of IPNs. Furthermore, the presence of indeterminate lung nodules on staging CT scans are not predictive of developing lung metastases as the first site of metastatic disease. Frequent and routine chest CTs for staging of patients with pancreatic cancer may be of little clinical utility.



P378

Outcomes of Surgical Intervention in Gastric Carcinoid Disease

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Background: Gastric carcinoids are rare entities, representing 8.7% of all gastrointestinal carcinoids. Although this disease is often stratified into subtypes with differing clinical courses and prognoses, the prognosis is generally improved by surgical resection. We evaluated the outcomes of patients with gastric carcinoids in a large cancer registry. Methods: We queried the California Cancer Registry (CCR), merged with the California Office of Statewide Health Planning and Development (OSHPD) database, for all patients with a diagnosis of gastric carcinoid disease. Demographic, clinicopathologic characteristics, surgical treatment, and outcomes were analyzed. Results: Among the 1,012 patients who met our criteria, 64% had localized disease (644), 9.4% (95) had regional disease and 13.4% (133) had distant metastases. Most of these patients underwent gastric surgery (56.7%, n=574 vs 43.2%, n=438). Surgery at the primary site conferred a survival advantage in patients with local and regional disease (regional disease: 27 months with surgery vs 5 months without, p=0.007; local disease: median survival was not reached, p<0.0001). Patients who underwent resection of the primary tumor and any hepatic metastases showed a similar median survival to patients without hepatic metastases (26 vs 27 months, p=0.8). Conclusions: Although the biology of the disease is the most significant predictor of overall outcome, aggressive surgical intervention, including resection of the primary tumor and any metastatic disease in the liver, should be offered when it is technically feasible. Surgical intervention in patients with hepatic metastases results in a survival similar to surgically managed patients without distant disease.

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Pancreatic Neuroendocrine Tumors (PNETs): Survival Analysis Comparing Surgical Resection Versus Non-Surgical Management

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BACKGROUND: The optimal management of PNETs remains controversial. This study aims to compare survival of patients with PNETs undergoing either surgical resection or non-surgical management. METHODS: A comprehensive search of MEDLINE, EMBASE, PubMed, SCOPUS and the Cochrane database was conducted (2006-present). All studies for patients with PNETs comparing surgical with non-surgical management were included. The STROBE checklist was used for quality assessment of included studies. Pooled risk ratios (RR) along with 95% confidence intervals (CI) for overall survival (OS) at 1, 3, and 5 years were calculated. RESULTS: Our search strategy yielded 759 studies, out of which 10 studies met our inclusion criteria. Overall, 10 studies with 3,008 PNET patients were included; 1,420 underwent resection and 1,588 underwent non-surgical management. Meta-analysis showed statistically significant improved OS in patients undergoing resection compared with non-surgical management at 1 (RR= 1.281, CI: 1.064 – 1.542, p = 0.009), 3 (RR= 1.837, CI: 1.594 – 2.117, p < 0.001), and 5 years (RR= 2.103, CI: 1.50 – 2.945, p < 0.001). Subgroup analysis of patients with nonfunctioning PNETs also showed significantly improved OS in the resection group at 1 (RR= 1.240,

CI: 0.778 – 1.975 p = 0.366), 3 (RR= 1.847, CI: 1.477–2.309, p < 0.001), and 5 years (RR= 1.767, CI: 1.068 – 2.924, p = 0.027). Subgroup analysis of patients with PNETs ≤ 2 cm in size, all of which were nonfunctioning, also showed improved survival in the resection group at 1 (RR= 1.177, CI: 0.441 – 3.147 p = 0.745), 3 (RR= 1.695 CI: 1.269 – 2.264, p < 0.001), and 5 years (RR= 2.210 CI: 1.749 – 2.791 p < 0.001). In patients with tumors <2cm, regardless of lymph node status or histological grade, resection of the primary tumor was still associated with improved OS regardless of histological grade and whether nodes were positive or not. CONCLUSION: Surgical resection of PNETs is associated with improved OS compared with non-surgical management. The improved OS with surgical resection is seen in patients with non-functional tumors, tumors > or < 2cm and regardless of lymph node status of histologic grade.

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The Value of Endoscopic Ultrasonography in a PET/CT Upfront Model in Staging Esophageal Cancer with Respect to Treatment Decision J. Hulshoff,[1]* H.E. de Boer,[1] W. Noordzij,[3] W.B. Nagengast,[4] H.M. Dullemen,[4] V. Mul,[2] J. Plukker.[1] *1. University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands; 2. University of Groningen, University Medical Center Groningen, Department of Radiation Oncology, Groningen, Netherlands; 3. University of Groningen, University Medical Center Groningen, Department of Nuclear Medicine and Molecular Imaging, Groningen, Netherlands; 4. University of Groningen, University Medical Center Groningen, Department of Gastroenterology and Hepatology, Groningen, Netherlands.*

Introduction: The optimal sequence of endoscopic ultrasonography (EUS) and positron emission tomography with computed tomography (PET/CT) in esophageal cancer (EC) is a matter of debate. The use of EUS with eventual fine needle aspiration (FNA) after PET/CT seems to increase the efficacy of curative intended neoadjuvant or definitive chemoradiotherapy. Retrospectively, we assessed the impact of EUS in the PET/CT upfront model on the treatment decision making in EC patients. Patients and Method: In the period 2009 to 2015, 298 EC patients were staged with hybrid PET/CT or PET with CT, and EUS if applicable, in a non-specific order to assess curability (T1-4a,N0-3M0). We determined the feasibility of EUS and whether the initial or additional EUS changed the primary decision suspicious incurable (T4b and M+) into curable disease or added extra nodal information leading to up/downstaging or exhibit suspected nodes at different lymph node stations. In addition, we assessed if EUS changed the radiation area (i.e lymph nodes >3.5 cm from the defined radiation target volumes) in the PET/CT "upfront model". Results: EUS was complete in 185 (62.1%) and incomplete due to stricture from a relative obstructing tumor in 59 (19.8%) patients. Fifty-four patients (18.1%) did not receive EUS because of stenosis (n=46; 15.4%), patient dependant reasons (n=4; 1.3%) or other reasons (n=4; 1.3%). EUS after hybrid PET/CT or PET with CT (n=244) gave additional information in 166 patients (68.0%); it changed the curability in 4 (1.6%), lead to nodal up and downstaging in respectively, 81 (33.2%) and 27 (11.1%) patients, changed the number of or lymph node station of suspected lymph nodes in an additional 58 patients (n=23.8%), and FNA gave additional information in 34 (13.9%) patients. EUS after PET/CT "upfront" changed the treatment plan in 90 patients (36.9%), including alteration in the radiation field (86; 35.2%) and curability (4; 1.6%). Conclusion: EUS gave additional information after PET/CT "up front" and altered the radiation field in about one third of the EC patients, suggesting a better yield of "EUS on indication" after PET/CT upfront.

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Smoking Results in Distinct Alterations in Gene Expression and Upregulation of Protein Sialylation in Pancreatic Cancers M.G. Mullen,* T. Newhook, S.J. Adair, E.M. Blais, A. Michaels, J.A. Papin, J. Parsons, T.W. Bauer. *Surgery, University of Virginia, Charlottesville, VA.*

Background: Pancreatic ductal adenocarcinoma (PDAC) is a highly lethal malignancy with poor response to chemotherapy. Smoking is the most well-established risk factor for PDAC; however, the impact of smoking on molecular signaling in PDAC has not been elucidated. We hypothesized that gene expression is different in PDAC tumors resected from smokers compared with non-smokers. Methods: Pancreatic cancers from 24 patients (AJCC Stage I-IV) were harvested and grown orthotopically in mice. Gene expression profiling was performed on these early passage tumors. Gene expression patterns and biologic pathway analyses were performed comparing tumors resected from smokers and non-smokers. Genes within enriched pathways were further investigated in The Cancer Genome Atlas (TCGA). Results: Gene expression profiling was performed on 24 PDAC tumors, 12 (50%) of which were resected from patients with a history of smoking. Survival was similar in the smokers vs. non-smokers. Tumors resected from smokers were significantly enriched (q-value < 0.05) for increased expression in pathways related to glycolipid biosynthesis and JAK/STAT signaling. The gene that contributed most to the enrichment of glycolipid metabolism was ST3GAL1, a sialyl-transferase that is also amplified in 12% of PDAC patients from TCGA data. Additionally, ST3GAL1 amplification was found to be positively correlated with patient pack-years smoking history (Pearson's r=0.304; Fig. 1), confirming the potential role for this gene in the pathogenicity of PDAC within smoking populations. Conclusions: Smoking is a major risk factor for PDAC. Tumors resected from smokers demonstrate unique upregulation of genes involved in protein sialylation and other crucial metabolic pathways. Although survival between smokers and non-smokers is similar, smoking results in distinct PDAC tumor biology, and further investigation may lead to novel targets for therapy in patients with PDAC.

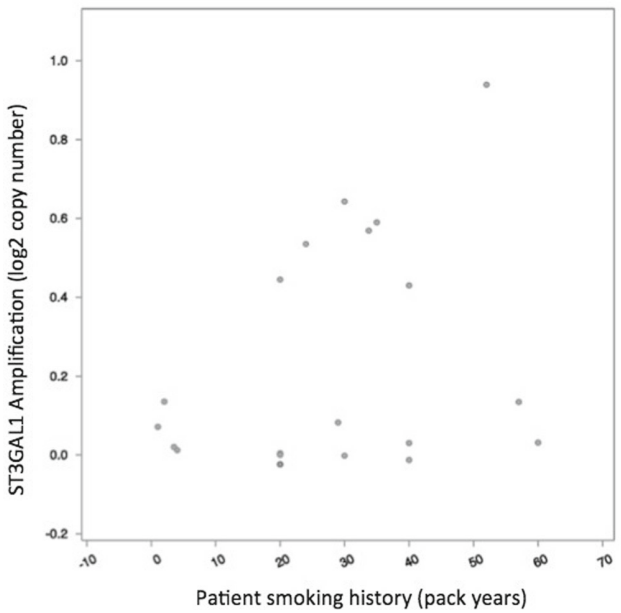

Figure 1 – ST3GAL1 copy number in PDAC patient tumors positively correlates with smoking history (Pearson's r = .304).

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Regional Therapy for Isolated Peritoneal Metastases from Small Bowel and Upper Gastrointestinal Malignancies D. Magge,* J.F. Pingpank, S. Ahrendt, M. Holtzman, H. Zeh III, A. Zureikat, D. Bartlett, M.A. Choudry. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: Well-selected patients with isolated peritoneal metastases (PM) from cancers of the appendix, colon and ovaries have benefited from the addition of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemoperfusion (HIPEC) to standard systemic chemotherapy. We hypothesized that this multidisciplinary approach would benefit select patients with PM from small bowel and upper gastrointestinal (UGI) malignancies. Methods: From a prospectively maintained database, we analyzed clinicopathologic, perioperative and oncologic outcomes in 81 consecutive patients undergoing CRS-HIPEC for PM from small bowel/UGI cancers. Kaplan-Meier survival curves and multivariate Cox-regression models identified prognostic factors effecting survival. Results: CRS-HIPEC was performed for PM from small bowel (19), esophageal (5), gastric (38), pancreatic (4), and hepatobiliary (15) cancers. CRS-HIPEC was performed for synchronous PM in 58% and metachronous PM in 42% of patients. Preoperative systemic chemotherapy was

administered in 70% of patients. The median peritoneal cancer index was 9 and complete CRS was achieved in 74 patients (CC-0/no macroscopic residual disease= 56; CC-1/residual tumor nodules<2.5 mm= 18). Major morbidity (Clavien-Dindo grades 3-4) occurred in 23 patients (28%), while 30-day mortality rate was 1%. After a median follow-up time from surgery of 41 months, median overall survival (OS) was 13 months (1- and 3-year OS: 53% and 17%). Median OS for patients with small bowel, esophageal, gastric, pancreatic and hepatobiliary cancers was 14, 12, 10, 26, and 12 months, respectively. Cox-regression analysis revealed significant association between overall survival and presence of preoperative symptoms (p=0.04), CC-score (p=0.04), number of visceral anastomoses (p=0.04), major postoperative morbidity (p=0.007), and adjuvant chemotherapy (p=0.05). Conclusions: CRS-HIPEC was associated with limited survival benefit overall in patients with peritoneal metastases from small bowel/UGI cancers. However, a subgroup may derive long-term survival benefit, without excessive treatment-associated morbidity, with this multimodality approach.

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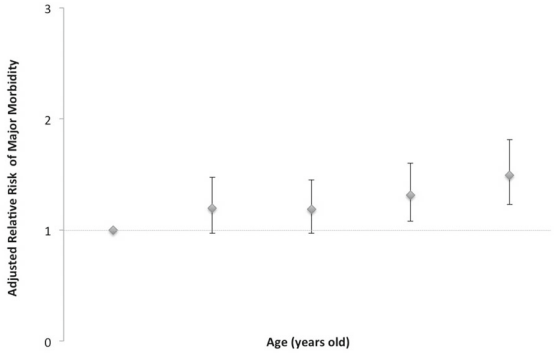
Does Age Matter in Morbidity Following Gastric Cancer Resection? An ACS-NSQIP Analysis T.D. Hamilton,[2]* A.L. Mahar,[3] A.B. Nathens,[1] P. Karanicolas,[1] C. Law,[1] N. Coburn,[1] J. Hallet.[1] *1. Surgery, Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada; 2. Vancouver General Hospital, Vancouver, BC, Canada; 3. Queen's University, Kingston, ON, Canada.*

Introduction: Evidence on short-term outcomes for gastric cancer (GC) resection in elderly patients is limited by small samples from single-institutions. Patient selection remains challenging. We sought to examine the association between advanced age and short-term outcomes of gastrectomy for GC. Methods: Using multi-institutional data from the ACS-NSQIP, we identified patients undergoing gastrectomy for GC (2007-2013). Primary outcome was 30-day major morbidity. Outcomes were compared among age categories (<65, 65-70, 71-75, 76-80, >80 years old [yo]). Univariable and multivariable regression was used to estimate the morbidity risk associated with age. Results: Of 3637 patients, 60.6% were elderly (>65 yo). Major morbidity increased with age, from 16.3% (<65yo) to 20.8% (65-70yo), 20.7% (71-75yo), 21.5% (76-80yo), and 24.1% (>80yo)(p<0.001). This was driven by higher respiratory and infectious events. Peri-operative 30-day mortality increased from 1.2% (<65yo) to 6.5% (>80yo) (p<0.0001). After adjusting for relevant clinical variables, age was independently associated with morbidity in the 76-80yo (RR 1.31, 95% CI 1.08-1.60) and >80yo (RR 1.49, 95% CI 1.23-1.81) groups. The magnitude of effect of pre-operative variables associated with morbidity in elderly patients (>65yo) did not change when considering higher age cut-offs (70, 75, and 80yo). A predictive model including age, gender, body mass index, functional status, extent of surgery, cardiovascular, respiratory, and diabetes comorbidities was created. Assuming adverse pre-operative characteristics, predicted morbidity increased by 18.6% in 75-80yo and 27.5% in >80yo (compared to <65yo) for total gastrectomy, and by 11.6% and 17.2% for sub-total gastrectomy. With optimal pre-operative characteristics, it increased by 5.1% in 75-80yo and 7.6% in >80yo for total gastrectomy, and by 11.5% and 17.1% for sub-total gastrectomy. Conclusions: Advanced age beyond 75yo was independently associated with increased morbidity after GC resection. The magnitude of this impact is modulated by pre-operative characteristics. Indication for resection in elderly GC patients should be revised according to age-specific morbidity risk



	<65	65-70	71-75	76-80	>80
Number of patients	1434	481	567	604	551
Relative Risk	Reference	1.19	1.18	1.31	1.49
95% Confidence Interval	Reference	0.97-1.47	0.97-1.45	1.08-1.60	1.23-1.81

Adjusted for gender, body mass index, pre-operative respiratory and cardiovascular comorbidities, diabetes, weight loss, and extent of surgery.

Figure. Adjusted relative risk of major morbidity based on age category.

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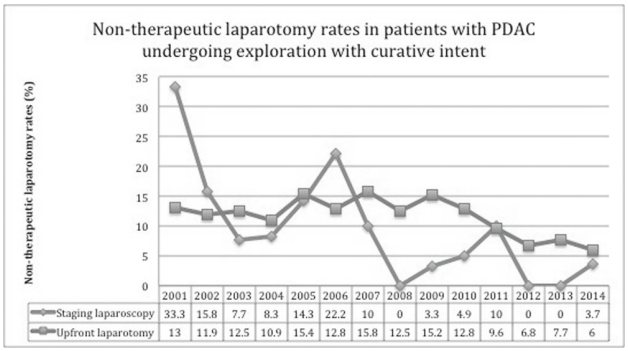
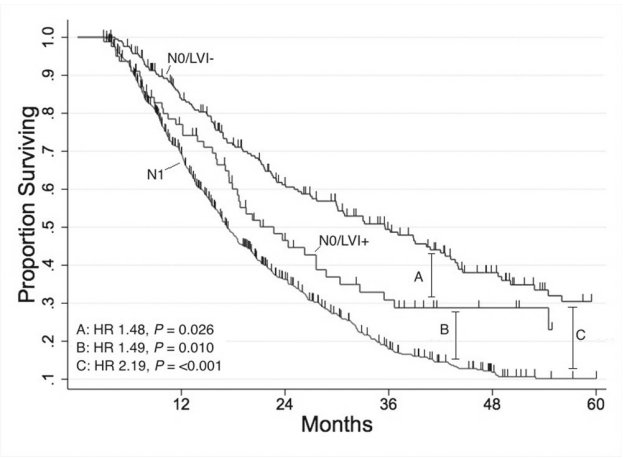
The Role of Staging Laparoscopy in Patients with Pancreatic Adenocarcinoma: Withstanding the Test of Time? Z. Fong,* W. Mehtsun, K. Lillemoe, A. Warshaw, C. Fernandez-del Castillo, D.C. Chang, C.R. Ferrone. *Surgery, Massachusetts General Hospital, Natick, MA.*

Introduction: Staging laparoscopy has been hypothesized to reduce non-therapeutic laparotomy (NTL) rates by detecting radiographically occult metastases in patients with pancreatic adenocarcinoma (PDAC). However, recent advances in imaging and increasing use of neoadjuvant therapy puts its contemporary utility in question. Methods: We compared patients with PDAC who underwent staging laparoscopy versus upfront laparotomy with curative intent from 2001 to 2015. The primary outcome, NTL, was defined as laparotomy without resection secondary to metastatic disease. The cohort was stratified by time periods for when exploration was performed: group 1 (2001-2008) and group 2 (2009-2015). Results: In 929 patients with head and body/tail PDACs explored with curative intent, 309 patients underwent staging laparoscopy. The overall NTL rate was 9.5% (12.4% in time group 1 vs 6.7% in time group 2, p=0.003). The NTL rate was lower in the staging laparoscopy group when compared the upfront laparotomy group (6.8% vs 10.8%, p=0.049). When stratified by time periods, staging laparoscopy had similar NTL rates with the upfront laparotomy group in time frame 1 (11.2% vs 12.9%, p=0.624), but had lower NTL rates in time group 2 (3.4% vs 8.6%, p=0.029). After adjusting for preoperative CA 19-9 level, tumor resectability and location, staging laparoscopy was associated with lower NTL rates in both time period 1 (OR 0.351, p=0.025) and time period 2 (OR 0.169, p=0.007). Patients who were unresectable secondary to radiographically occult metastatic disease who underwent staging laparoscopy had a shorter length of hospitals stay (1.8 days vs 5.6 days, p=0.007) and were more likely to receive chemotherapy (94.3% vs 89.6%, p=0.05). Patients who underwent staging laparoscopy were also associated with a shorter time to receipt of chemotherapy (20.2 days vs 38.6 days, p<0.0001). Conclusion: The overall NTL rate is 9.5%, with lower rates in the contemporary time frame likely secondary to improved imaging. Despite the overall decrease in NTL rates, staging laparoscopy was still associated with lower NTL rates when compared to upfront laparotomy in both time frames.



Non-therapeutic laparotomy rates in patients with PDAC undergoing exploration with curative intent.



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Lymphovascular Invasion: An Underappreciated Prognostic Factor in Pancreatic Cancer J. Epstein,[1]* G. Kozak,[2] Z. Fong,[3] W. Jiang,[4] H. Lavu,[2] C.R. Ferrone,[3] K. Lillemoe,[3] C. Yeo,[2] C. Fernandez-del Castillo,[3] J. Winter.[2] *1. Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA; 2. Thomas Jefferson University Hospital, Department of Surgery, Philadelphia, PA; 3. Massachussetts General Hospital, Department of Surgery, Boston, MA; 4. Thomas Jefferson University Hospital, Department of Pathology, Philadelphia, PA.*

Introduction: Despite the fact that lymphovascular invasion (LVI) is routinely reported in pathologic reports of resected pancreatic ductal adenocarcinomas (PDA), this feature remains poorly characterized as a prognostic factor. Methods: We performed a multi-institution analysis of patients who underwent a pancreatectomy for PDA at Thomas Jefferson University Hospital and Massachusetts General Hospital between 2003 and 2014. Pathology reports were used to document LVI. Patients who either expired or were lost to follow-up in the 90-day post-operative period were excluded. Overall survival (OS) analyses were performed using Cox proportional hazard tests. Results: 1074 patients had resected PDA with a median overall survival of 20.1 months and a 5-year survival rate of 15.3%. LVI was identified in 582 specimens (54.4%) while nodal metastases were observed in 752 (69.8%). We observed substantial overlap between LVI and nodal metastases in resected specimens, which was likely a result of a common biologic mechanism: 84.7% of patients with LVI also had nodal disease (P = <0.001). This interplay was further evident in the observation that LVI was more commonly identified in routine histologic review in patients with increased numbers of lymph node metastases (OR 1.14, P = <0.001), reflecting greater lymphatic disease burden. In a multivariate model including pathologic features except nodal metastases, LVI was an independent predictor of survival (HR= 1.32, P = 0.001). Patients without lymph node metastases were stratified according to LVI status, and LVI- PDA patients proved to have a more favorable overall survival than LVI+ PDAs in the N0 subgroup (median 36 vs. 21 mo, P = 0.026). Both subgroups had superior survival to patients with N1 disease (17 mo, P = 0.010 and P = <0.001, respectively). Conclusion: Microscopic lymphatic channels likely provide the conduit for regional lymph node metastases, accounting for a strong association between LVI and nodal disease. LVI is an independent adverse prognostic factor for PDA, based largely on the findings that LVI-, N0 cancers had favorable survival, and that reported LVI proved to be a surrogate marker for high lymphatic disease burden.

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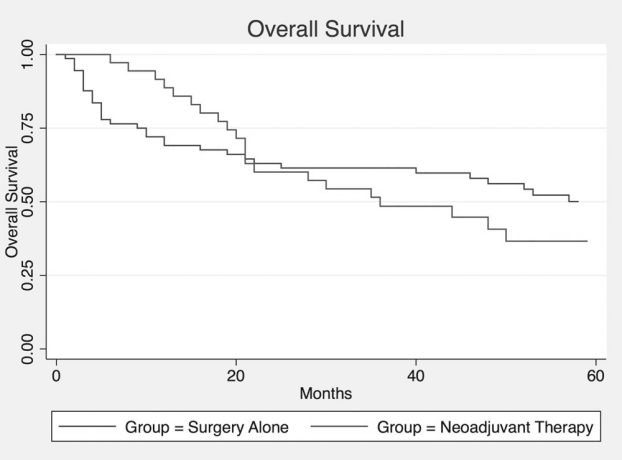
Neoadjuvant Chemoradiotherapy Versus Surgery in Gastric and Gastroesophageal Junction Cancer: A Single Institutional Review D. Baltrusaitis,* H. Cheng, R. Rajeev, T. Gamblin, K. Turaga, F. Johnston. *Surgery, Medical College of Wisconsin, Milwaukee, WI.*

Introduction: Debate surrounds the optimal use of neoadjuvant therapies to supplement surgery in patients with gastric and gastroesophageal junction cancer. Current data suggest equivocal results in patients receiving neoadjuvant chemoradiation therapy (CRT). We aimed to report the results of this treatment paradigm in our institution. Methods: Patients with gastroesophageal (GE) junction (Siewert I to III) or gastric adenocarcinoma undergoing neoadjuvant CRT followed by planned surgical resection and those undergoing surgery first approaches at our institution between 1996 and 2015 were reviewed. Descriptive analyses were performed. Safety, overall survival (OS), and disease free survival (DFS) were estimated. Results: One hundred twelve patients were identified. Thirty-seven (33%) were grouped into the neoadjuvant therapy (NT) arm and 75 (67%) were grouped into the surgery alone (SA) arm. Median age was 67 years (SA) vs 60 years (NT) (p <0.05). Among NT patients, 15 (40.5%) patients received induction chemotherapy followed by CRT before surgery, 21 (56.8%) patients received CRT alone before surgery, and 1 (2.7%) patient received chemotherapy followed by radiotherapy before surgery. Twenty-nine (78%) NT patients had tumors located in the GE junction compared to 39 (52%) SA patients. Patients with more advanced AJCC stage were significantly more likely to receive NT (p=0.02). There was no difference in length of stay, 30 and 60-day morbidity or mortality between the groups, and surgical quality markers (number of resected lymph nodes, margin status). Recurrence was more common among patients receiving NT (p=0.046). Lymph node metastasis was more common within the SA group. The median 5-year OS was 50% for SA and 37% for NT, respectively (p = 0.47). Multivariate cox-regression analysis yielded a hazard ratio of 2.30 (0.86-6.17, p=0.097) for NT compared to SA. Conclusion: Preoperative CRT was well tolerated in comparison to surgery alone with acceptable rates of morbidity and mortality. There is no difference in survival between the groups. Further study comparing equivalent groups of neoadjuvant CRT to surgery alone is needed.



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Time to Initiation of Adjuvant Chemotherapy Does Not Impact Survival in Resected Pancreatic Cancer K.A. Mirkin,* C.S. Hollenbeak, J. Wong. *Department of Surgery, Penn State Hershey Medical Center, Hershey, PA.*

Background: Pancreatic cancer carries a grim prognosis. Surgical resection followed by adjuvant chemotherapy is standard of care, but little is known about the temporal relationship of chemotherapy initiation and survival. This study analyzed the impact of time to initiation of adjuvant chemotherapy on survival in patients with resected pancreatic cancer. Methods: The National Cancer Data Base (2003-2011) was retrospectively reviewed for patients with clinical stages 1-3 resected pancreatic carcinoma. Time to chemotherapy was stratified at the 12-week post-operative timepoint. Univariate statistics, Kaplan-meier estimates, and Cox proportional hazard modeling were performed. Results: 5,205 patients underwent surgery-only, while 4,050 underwent surgery and adjuvant chemotherapy. The majority of the adjuvant group (N=3,144, 78%) initiated chemotherapy by 12 weeks post-operatively, while 906 (22%) started after 12 weeks. Patients who received chemotherapy >12 weeks tended to be older, have more co-morbidities, receive treatment at academic centers, and undergo whipple procedures. In all pathologic disease stages, adjuvant chemotherapy conferred a significant survival benefit over surgery-alone ($p < 0.0001$). However, there was no significant overall survival benefit for patients receiving adjuvant chemotherapy before 12 weeks as compared to after ($p = 0.85$). When stratified by pathological stage, there was still no significant survival benefit for earlier initiation of chemotherapy (<= vs. > 12 weeks): stage I, $p = 0.16$, stage II, $p = 0.12$, stage III, $p = 0.38$. After controlling for patient, disease, and surgery characteristics, patients who received adjuvant chemotherapy after 12 weeks had a 31% lower odds of mortality at 5 years, while those who initiated it before 12 weeks had a 34% lower odds ($p <0.0001$, $p<0.0001$ respectively), versus surgery-alone. Conclusion: Earlier initiation of adjuvant chemotherapy does not significantly impact long-term survival in patients with resected pancreatic cancer. However, because adjuvant chemotherapy confers a survival benefit over surgery-only, delayed chemotherapy should be offered when appropriate.

Median Survival (Months)

Pathological Stage	Surgical Resection Alone	Adjuvant Chemotherapy <=12weeks	Adjuvant Chemotherapy >12weeks	P-value	P-value (Surgical Resection Alone Excluded)
Stage I	30.68	41.72	49.48	<0.0001	0.1558
Stage II	12.78	21.13	19.71	<0.0001	0.1169
Stage III	8.25	13.7	14.19	0.0035	0.3841
Stage IV	5.91	12.42	16.76	<0.0001	0.6571
All Stages	14.36	21.95	21.26	<0.0001	0.8461

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The Necrosome Promotes Pancreatic Oncogenesis via CXCL1 and Mincle-Induced Immune Suppression G. Werba,* L. Seifert, S. Tiwari, N. Ly, D. Daley, A. Torres Hernandez, R. Barilla, G. Miller. *Surgery, NYU Langone Medical Center, New York, NY.*

Introduction: Disruption of apoptosis is a basic modality cancer cells exploit for survival. However, the role of programmed necrosis in the life cycle of pancreatic ductal adenocarcinoma (PDA) is uncertain. Here we report that the principal components of the necrosome, RIP1 and RIP3, are highly expressed in pancreatic ductal adenocarcinoma (PDA) and are further upregulated by chemotherapeutics. Methods: We evaluated the effects of deletion orblockade of the necroptosis pathway in pancreatic cancer on tumor size and survival, peritumoral fibroinflammation, and epithelial transformation. We utilized p48Cre;KrasG12D(KC) mice as our murine PDA oncogenesis model and crossed KC with RIP3-/- and Mincle-/- mice to create a knockout pancreatic cancer mouse model. Alternatively, we challenged wildtype mice with orthopic injection of the cancer cell line FC1242 into the pancreas. Components of the necroptosis pathway and the immune infiltrate within the pancreatic TME were assessed and characterized using immunohistochemistry, flow cytometry and western blotting in human and murine tissue. Results: Blockade of the necrosome in vitro promoted cancer cell proliferation and induced an aggressive oncogenic phenotype in transformed pancreatic epithelial cells. Conversely, in vivo RIP3 deletion or RIP1 inhibition was protective against oncogenic progression and was associated with the development of a highly immunogenic myeloid and T cell phenotype within the tumor microenvironment (TME). The immunesuppressive infiltrate associated with intact RIP1/RIP3 signaling was contingent on necroptosisinduced CXCL1 expression whereas CXCL1 blockade was protective against PDA. Moreover, we found that the necroptotic byproduct SAP130 was highly prevalent in PDA and Mincle – its cognate receptor – was upregulated in tumorinfiltrating myeloid cells. Mincle ligation powerfully promoted oncogenesis whereas Mincle deletion was protective against tumorigenesis and phenocopied the immunogenic reprogramming of the TME characteristic of RIP3 deletion. Conclusion: Our work describes a novel RIP1/RIP3–Mincle axis as a critical regulator of peritumoral immune suppression and PDA progression.

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HER Family Receptor Expression in Esophagogastric Tumorigenesis B.L. Ecker,* L. Taylor, P.J. Zhang, E.E. Furth, G.G. Ginsberg, B.J. Czerniecki, R. Roses. *University of Pennsylvania, Philadelphia, PA.*

Introduction: Over-expression of receptor tyrosine kinases, including members of the HER family, have prognostic and therapeutic significance in invasive esophagogastric carcinoma. HER family expression patterns in premalignant gastroesophageal lesions have not been well characterized. Methods: Retrospective formalin-fixed paraffin-embedded tissue samples of esophageal biopsy specimens from 72 patients with Barrett's esophagus with either low-grade dysplasia (LGD) (n=32) or high-grade dysplasia (HGD) (n=59) were analyzed for HER1, HER2 and HER3 expression by immunohistochemistry (IHC). Overexpression was defined by 3+ staining pattern or 2+ staining in ≥10% of tumor cells. Immunophenotype was correlated with histologic and clinical features. Results: Median patient age was 65 (IQR 60-73); 80.6% of patients were male and 86.1% of patients were Caucasian. The rate of HER overexpression was 15.6%, 3.4% and 32.6% for HER1, HER2 and HER3, respectively. HGD was associated with an increased rate of HER1 overexpression (22.4% vs. 3.1%, p=0.016), HER2 overexpression (5.3% vs. 0.0%, p=0.187) and HER3 overexpression (45.6% vs. 9.4%, p<0.001), compared to LGD. Focuses of invasive esophageal adenocarcinoma were associated with dysplastic lesions in 14 cases (19.4%). There was an absolute increase in HER overexpression in HGD lesions associated with carcinoma compared to those without evidence of invasion (HER1: 36.4% vs. 29.4%, p=0.665; HER2: 66.7% vs. 26.8%, p=0.144; HER3: 38.1% vs. 21.7%, p=0.235). Conclusions: HER1-3 expression in premalignant lesions of the gastroesophageal junction is correlated with degree of dysplasia. These data provide rationale for the application of therapeutics which target the HER family-associated pathways in an early disease setting to prevent disease progression.

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Lymph Node Evaluation and Survival After Curative Resection of Small Bowel Adenocarcinoma B.L. Ecker,* M.T. McMillan, L.E. Kuo, L. Ruffolo, D.L. Fraker, J. Drebin, G. Karakousis, R. Roses. *University of Pennsylvania, Philadelphia, PA.*

Introduction: The presence of lymph node (LN) metastasis in patients with small bowel adenocarcinoma (SBA) is associated with poor prognosis. The threshold number of lymph nodes required for adequate surgical staging is not clearly defined. Methods: Resected AJCC pathologic stage I-III SBA patients (n=4,332) were identified in the National Cancer Data Base (1998–2011). Logistic regression analysis identified covariates associated with LN metastasis in the overall cohort. The influence of extent of LN evaluation on overall survival (OS) was analyzed using the log-rank test and Cox proportional hazards modeling for increasing LN cutpoints. Results: Lymph node metastases were present in 1,952 patients (45.1%). Factors associated with nodal involvement included younger patient age (≤65 years: OR 1.18, 95% CI 1.01-1.39, p=0.041), male gender (OR 1.19, 95% CI 1.05-1.36, p=0.010), duodenal location (OR 1.33, 95% CI 1.15-1.53, p<0.001), increasing T-classification (T3: OR 3.25, 95% CI 2.61-4.04, p<0.001; T4: OR 4.94, 95% CI 3.93-6.22, p<0.001), poorly differentiated histology (OR 1.83, 95% CI 1.60-2.10, p<0.001), and increasing number of LNs examined (6-10 LN: OR 1.63, 95% CI 1.37-1.94, p<0.001; 11-15 LN: OR 1.96, 95% CI 1.63-2.37, p<0.001; 16-20 LN: OR 1.97, 95% CI 1.59-2.45, p<0.001; >20 LN: OR 2.26, 95% CI 1.83-2.80, p<0.001). In patients without known nodal involvement, increasing LN identification was associated with a decreased risk of death (6-10 LN: HR 0.82, 95% CI 0.70-0.97, p=0.011; 11-15 LN: HR 0.73, 95% CI 0.60-0.89, p=0.002; 16-20 LN: HR 0.51, 95% CI 0.39-0.66, p<0.001; >20 LN: HR 0.64, 95% CI 0.50-0.82, p<0.001). The identification of at least 15 LN in duodenal SBA (HR 0.59, 95% CI 0.44-0.78, p<0.001) and 5 LN in jejunoileal SBA (HR 0.66, 95% CI 0.53-0.81, p<0.001) were the strongest predictors of OS in patients without known nodal metastases. Conclusions: Increasing LN identification is associated with improved survival for SBA patients without known LN metastases. The role of adjuvant therapies in patients with "inadequate" LN identification is an area for further investigation.

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Differences in Pancreatic Surgery Management and Techniques: A Nationwide Multi-Institutional Survey M.U. Butt,* H. Osman, H. Aderianwalla, R. Hellums, S. Furlough, D. Jeyarajah. *Surgery, Methodist Dallas Medical Center, Dallas, TX.*

Introduction: Hospitals identified as high volume centers for pancreatic surgery have lower perioperative mortality rates. Most of these high volume centers in the United States (US) have dedicated fellowship training programs and are sponsored by Americas Hepato-Pancreato-Biliary Association (AHPBA) and society of surgical oncology (SSO) fellowship programs. Our aim was to determine whether there was any differences in pancreatic surgery management and techniques specifically identifying how the specimen margin was inked and assessed. Methods: This survey targeted program directors (PD's) participating in the 18 AHPBA and 22 SSO accredited fellowships. Results: The response rate was 83% for AHPBA PD's (15/18) and 50% for SSO PD's (11/22). Fifty or more pancreaticoduodenectomies were done in 100% of AHPBA programs compared to 73% SSO programs. Routine diagnostic laparoscopy was performed in 53% vs 60% ; AHPBA vs. SSO (AvS). Most common method of pancreas reconstruction was duct to mucosa without stent; 53% vs 60% (AvS). Interrupted absorbable suture was the most common method for bile duct anastamosis; 70% for both groups. Seventy percent placed drains and nasogastric tube in both groups. More than 70% removed drain based on amylase level in both groups. Majority cases were done open. Majority converted <10% of their robotic cases to open, and when they did usually it was due to inability to progress (100% for SSO). Interestingly in pancreaticoduodenectomies 40% of SSO PD's sent no margin for frozen section compared to 21% for AHPBA PD's. Superior mesenteric artery margin was specifically inked in more than 80% of whipple specimens. The margin was inked mostly by surgeons (46%) in the AHPBA groups compared to pathologist PA (60%) in the SSO group. Conclusion: Our data shows AHPBA and SSO training programs have similar technical approach and management strategies to pancreatic surgery. There were significant differences in how the specimen was handled for frozen section and inking of the margin throughout both groups. Standardized protocols should be developed for optimal specimen handling.

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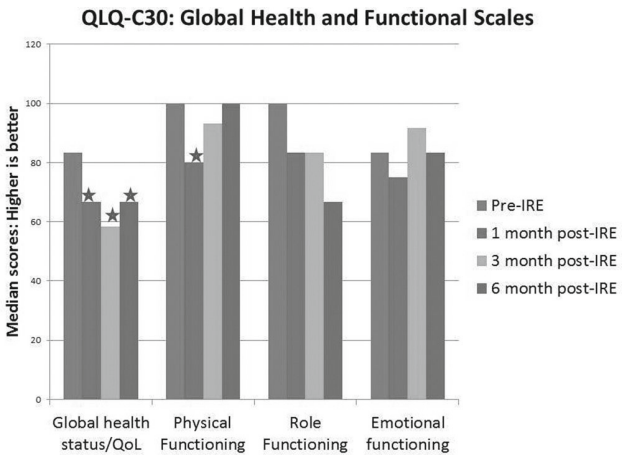
Quality of Life Following Treatment of Locally Advanced Pancreatic Cancer by Irreversible Electroporation J.W. Rostas,* R.C. Martin. *General Surgery, University of Louisville, Louisville, KY.*

Purpose: To determine the effect of irreversible electroporation (IRE) on self-reported health-related quality of life (QoL) in patients with locally advanced pancreatic cancer (LAPC). Patients and Methods: Prospectively collected data was reviewed in patients undergoing IRE for un-resectable LAPC. HRQoL was assessed by 3 self-reported survey instruments, the European Organization for Research and Treatment of Cancer QLQ-C30, a global rating of change (GRoC) scale, and the Edmonton Symptom Assessment System (ESAS). Baseline assessments were performed prior to evaluation by the physician performing the IRE, and at 1, 3, and 6 months post-procedure. Results: Thirty-seven patients (median age 61 years, range 27-78) with un-resectable LAPC of the head/neck, body and tail received IRE. Thirty-six patients (97%) had some form of previous therapy (one patient refused all previous therapies), with 24 (65%) having previous multi-modal therapies. All patients received a complete IRE treatment, as defined by at least 90 pulses delivered. Completed pre-procedure, 1-month, 3-month and 6-month post-procedure evaluations were obtained from 37, 34, 34, and 30 patients, respectively. One patient was excluded for further analysis due to the lack of at least one follow-up questionnaire. Throughout the 6 month follow-up patient reported stable scores in the key functional scores on QLQ C30: physical, role and emotional. Patients self-reported overall QoL was significantly lower at initial follow-up and then remained stable per QLQ C30, and was similar to EORTC reference values for Stage III/IV pancreatic cancer (median 58.3). GRoC scores reflected improvement in QoL and well-being during the entire follow-up period. ESAS scores improved on long term follow-up. Conclusion: IRE is well tolerated in the treatment of LAPC. IRE has been proven to be a safe and effective option for carefully selected patients with LAPC. IRE should be considered early in the multidisciplinary management of LAPC, to allow increased implementation and therefore lead to improved rates of local control.



Reported diminished overall QoL with subsequent stablilization over the follow-up period. Key functional scores remained stable throughout the follow-up period.

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The Effect of Treatment Facility Type on Overall Survival in Surgically Treated Pancreas Cancer A. Paniccia,* P.W. Hosokawa, W. Henderson, R. Schulick, B.H. Edil, M.D. McCarter, C. Gajdos. *University of Colorado, Aurora, CO.*

Introduction: Several factors have been described as having a significant effect on survival in surgically treated pancreatic adenocarcinomas (PDAC). We sought to evaluate the effect of facility type, including academic medical centers (AMC), comprehensive community cancer programs (CCCP), and community cancer programs (CCP), on overall survival using the National Cancer Data Base (NCDB). Methods: A nationwide retrospective cohort-study was conducted using the NCDB. Selected cohort included all histologically proven PDAC who underwent pancreatic surgical resection aimed at removal of the primary tumor between January 1998 and December 2006. Median

follow-up was 15.9 months (8.5-31.8).A Cox proportional hazards survival model was used to examine factors associated with risk of mortality.Results: Of the 22 229 patients identified, the majority of patients were treated at AMC (n=10 875), followed by CCCP (n=9 062), and CCP (n=1 292). Patients treated at AMC were significantly more likely to have a higher histologic tumor grade, median number of lymph nodes examined, rate of positive lymph nodes, income and educational status. The three groups were similar in terms of tumors size and rate of negative surgical margins. Patients treated at AMC were more likely to receive postoperative chemotherapy or radiation and had a longer median overall survival compared with CCCP and CCP (16.9 vs. 15.2 vs. 13.2 months, respectively; p<0.001, [Figure 1]).Multivariable analysis suggested that treatment received at AMC was associated with a 19% and a 13% increase likelihood of survival compared to CCP and CCCP after controlling for known predictors of overall survival including: lymph node positivity ratio (positive over harvested), surgical margins status, tumor grade, age, tumor size, pathologic stage, use of chemotherapy or radiation, and income quartile (C-index= 0.87). Conclusions: Patients with surgically resected PAC treated at AMC have significantly longer survival compared to CCCP and CCC despite worse histological grade and higher number of positive nodes. Amongst other factors, facility type remained a significant variable predicting overall survival in multivariable analysis.

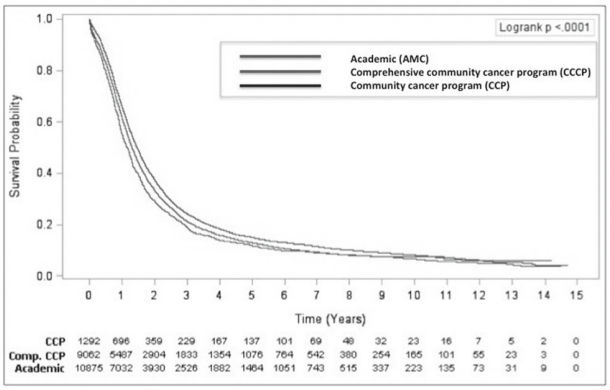

Figure 1. Kaplan-Meier of overall survival stratified by treatment facility type.

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Patient-derived Xenograft (PDX) Models are Indispensable for Newly Discovered Patient Subtypes of Pancreatic Adenocarcinoma (PDAC) C. Becker,[2]* R. Marayati,[1] R.A. Moffitt,[1] K.E. Volmar,[3] J. Yeh.[1] *1. Lineberger Comprehensive Cancer Center, UNC-Chapel Hill, Chapel Hill, NC; 2. Department of Surgery, UNC-Chapel Hill, Chapel Hill, NC; 3. UNC Rex Healthcare, Raleigh, NC.*

Two newly identified PDAC tumor subtypes, basal and classical, have important biologic and clinical implications. Patients with basal subtype tumors have a worse survival and may derive greater benefit from adjuvant therapy. To date, no cell line of the classical subtype has been identified suggesting that existing cell lines are inadequate for preclinical studies. Furthermore, the stromal component of PDAC, absent in cell lines, has important prognostic value. Our aim was to determine what preclinical models best exemplify the new PDAC subtypes. RNAseq was performed on 37 PDX tumors (PDXtu) from de-identified resected PDAC patients. Histologic features were reviewed by a blinded expert. Faster PDXtu growth rate was associated with decreased recurrence free survival (p=0.01) in patients after surgery, suggesting that PDXtu are a good surrogate for disease aggressiveness. In patients with resected PDAC, 71% (n=89) had classical vs 29% (n=36) basal subtype tumors. PDXtu recapitulated the prevalence of classical (80%, n=27) and basal (20%, n=7) tumor subtypes with near complete correlation between matched PDAC and PDX tumors (ρ=0.847). Importantly, stroma was present in PDXtu of both subtypes. Mean stroma percentage was 28.0% (n=27) in classical and 37.2% (n=7) in basal PDXtu. Similar to our findings of increased extracellular mucin in classical subtype tumors in patients (p=0.042), classical PDXtu had a higher amount of extracellular mucin. Mean extracellular mucin was 22.6% (n=27) in classical and 4.6% (n=7) in basal PDXtu (p=0.50). 81% (n=22) of classical PDXtu had >10% extracellular mucin compared to only 14% (n=1) of basal PDXtu (x^2=19.174, p<0.001) Our results show that PDX models are the only known preclinical model to fully represent newly discovered patient tumor subtypes. The prognostic implications and histological features of patient PDAC subtypes are retained in PDX. PDX models will be critical for the preclinical evaluation of subtype specific treatment response and future selection of subtype specific therapies. Further study of the PDX stroma will be required for the development of stroma-targeted therapies.

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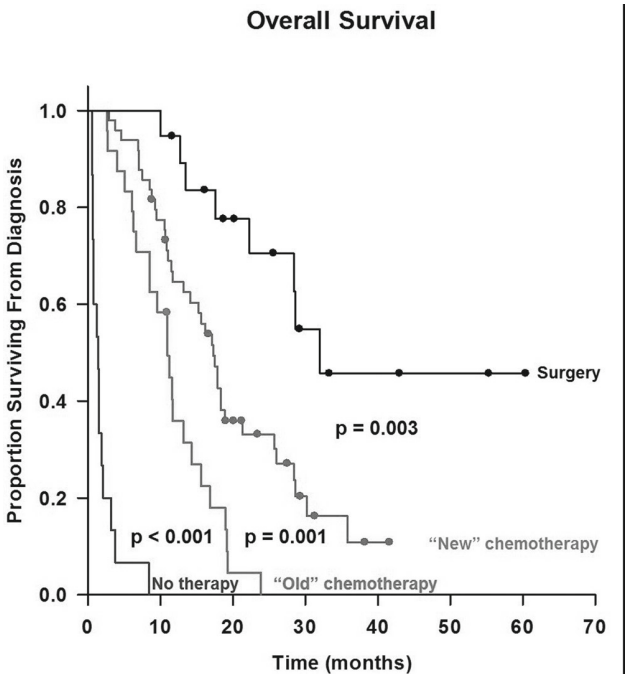
FOLFIRINOX and Gemcitabine/nab-Paclitaxel Demonstrate Improved Survival in Locally Advanced Unresectable Pancreatic Adenocarcinoma F. Bednar,* L. Ocuin, J. Steve, M. Zenati, S. Winters, M. Hogg, N. Bahary, H. Zeh III, A. Zureikat. *Surgery, University of Pittsburgh, Pittsburgh, PA.*

Introduction: Locally advanced (LA) unresectable pancreatic adenocarcinoma (PDA) historically portends a poor prognosis with a median OS of 9-11 months. Recently, 2 multi-drug regimens - FOLFIRINOX and gemcitabine/nab-paclitaxel – have proven effective in the metastatic setting. We hypothesized that use of these regimens in the LA setting may improve survival. Methods: A retrospective review of a single institution's cancer registry of all consecutive LA (unresectable) PDA patients between 2010 and 2014 was performed. LA status was verified by review of the triphasic, pancreas protocol CT scan at diagnosis using the 2015 NCCN criteria for resectability. Patients were divided into 4 groups: Group 1 = no therapy, Group 2 = "old" gemcitabine or 5-FU-based chemotherapy (CTX), Group 3 = "new" CTX (FOLFIRINOX and/or Gem/nab-paclitaxel), and Group 4 = resection after downstaging. Demographic, tumor related variables, and treatment outcomes were analyzed. Results: LA disease was verified in 107 consecutive patients. Median age was 69 years (range 36-92) and 50.5% were male. Median follow-up was 13.2 months (range 0.6-60.4). Median OS for Groups 1 (n=15), 2 (n=24), 3 (n=49), 4 (n=19) was 1.4, 11, 17.3, and 32 months respectively (p<0.001, Figure). On Cox multivariate regression (adjusted for age, sex, anatomic variables, and CA19-9 level at diagnosis), radiation (HR 0.44, p=0.003), older CTX (HR 0.16, p=0.007), newer CTX (HR 0.10, p=0.001), use of 2 or more lines of CTX (HR 0.16, p=0.022), CA19-9 decrease by >50% with any line of therapy (HR 0.31, p<0.001) and surgery (HR 0.28, p=0.002) were all significant predictors of OS in this cohort. On multivariate analysis between groups 2 and 3, newer CTX compared to older CTX (HR 0.490, p=0.02) and radiation (HR 0.510, p=0.015) provided an OS benefit. Conclusion: Compared to older CTX regimens, FOLFIRINOX and Gemcitabine/nab-paclitaxel improve survival in verified LA PDA patients. For the subset that ultimately undergoes resection, survival outcomes rival those of historically published resectable cohorts.



Overall survival from the time of diagnosis for locally advanced pancreatic cancer patients without any therapy (n=15), with "old" chemotherapy (n=24), with "new" chemotherapy (n=49), and those that have undergone a curative resection (n=19).

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Factors Leading to Omission of Adjuvant Therapy After Pancreaticoduodenectomy: An Argument Against a Surgery-First Approach B. Xia,* D. Vikrom, N. Levinsky, D. Habib, D.J. Hanseman, J.M. Sutton, G. Wilson, M. Smith, K. Choe, J.J. Sussman, S. Ahmad, D. Abbott. *University of Cincinnati, Cincinnati, OH.*

Introduction: Sequencing therapy for patients with peri-ampullary malignancy remains controversial. Surgery-first proponents allude to clinical trial data (ESPAC 3, RTOG 9704) with high rates of multi-modality completion, though contemporary data detailing off-trial, 'real-world' adjuvant therapy rates are incomplete. We sought to define patients who fail to receive adjuvant therapy, a subset of patients who might benefit most from neoadjuvant therapy (NT). Methods: We identified 226 patients who underwent pancreaticoduodenectomy (PD) for peri-ampullary malignancies between 1999 and 2015; patients receiving NT were excluded. Medical records were retrospectively reviewed, and predictors of failure to receive adjuvant therapy were identified by univariate and multivariate analyses. Overall survival (OS) was compared for subsets of patients, including those with early recurrence (within 6 months). Results: There were 115 male and 111 female patients, with a median age of 66.4 years (IQR 57-74). 78.6% of patients received adjuvant therapy, and median OS for patients who did and did not complete adjuvant therapy were 28.1 vs 13.8 months, p=0.11). The most common reasons for omission of adjuvant therapy were poor performance status (35.7%), patient refusal (28.5%) and complication after surgery (21.4%). Univariate predictors of failure to undergo adjuvant therapy were age, Charlson Comorbidity Index, operative transfusion, re-operation, length of stay, and readmissions (all $p<0.05$). Age persisted as a significant predictor on multivariate analysis (p=0.01). 33 (15%) patients had early recurrence, 22 of which received systemic therapy following recurrence. Patients who failed to receive adjuvant therapy and/or developed early recurrence had significantly worse OS than all other patients (12.5 vs 30.7 months; $p<0.01$). Conclusions: Approximately one-third of surgery-first patients undergoing PD at our institution did not receive adjuvant therapy and/or demonstrated early recurrence. This substantial subset of patients may not benefit from PD, and patient selection through NT can optimize outcomes for patients with peri-ampullary malignancies.

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Yield of Staging Laparoscopy in Gastric Cancer N. Ikoma,* E. Elimova, M.M. Blum, J.A. Ajani, Y. Chiang, K. Fournier, P. Mansfield, B. Badgwell. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: The purpose of this study was to identify clinicopathologic factors associated with the identification of peritoneal disease in patients with gastric cancer and to compare the yield of laparoscopy over time. Methods: The medical records of 7,404 patients with gastric or gastroesophageal adenocarcinoma presenting to our institution (1/1995 to 12/2012) were reviewed to identify patients who underwent diagnostic laparoscopy as a staging procedure before treatment. Associations between clinicopathologic factors and peritoneal disease were examined with chi square and logistic regression analysis. The yield on laparoscopy was stratified according to time. Results: We identified 880 patients who underwent staging laparoscopy for gastric adenocarcinoma. Excluded patients included those with recurrent gastric cancer, those who underwent prior chemotherapy and/or radiation therapy, those with known distant metastatic disease (except for equivocal radiological findings), and those who underwent procedures not for staging purposes, leaving 711 patients in this study: 43.5% with gastroesophageal junctional tumors, 72.9% with poorly differentiated adenocarcinoma, and 53.0% with signet ring cell morphology. Endoscopic ultrasound (EUS) most commonly identified T3 (83.9%) and N-positive (66.4%) tumors. As results of laparoscopy, 148 patients (20.8%) were found to have macroscopic peritoneal carcinomatosis. Among 514 macroscopically negative patients who had peritoneal lavage cytology analysis, 68 (13.2%) were found to have positive. Of the 711 study patients, 42 (5.9%) had other unexpected clinically important findings (e.g., distant metastasis, cirrhosis). Multivariate analysis showed a high positive rate of laparoscopy in patients with poorly differentiated pathology, linitis plastica, or equivocal CT scan, after adjusting race, signet ring cell, and tumor location. The yield of laparoscopy did not change over time when divided into three 6-year periods (p=0.58). Conclusions: Laparoscopy remains an important staging procedure to evaluate for peritoneal spread when considering treatment or surgery, even in the current era of high-quality imaging evaluation.

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Outcomes of Neoadjuvant Chemotherapy Versus Chemoradiation Among Patients with Resected Pancreatic Head Adenocarcinoma J. Franko,[1]* H. Hsu,[1] P. Thirunavukarasu,[2] C.D. Goldman.[1] *1. Surgery, Mercy Medical Center, Des Moines, IA; 2. MD Anderson Cancer Center, Houston, TX.*

BACKGROUND: Increasing use of neoadjuvant therapy in pancreatic cancer has been reported. We compared patterns of practice and outcomes of neoadjuvant chemotherapy (nCHT) versus chemoradiation (nCRT) among pancreatic cancer pts receiving pancreaticoduodenectomy. METHODS: National Cancer Data Base pancreatic head adenocarcinoma patients (pts) diagnosed between 2003 and 2011 treated by nCHT or nCRT followed by pancreaticoduodenectomy. Backward elimination logistic and Cox regression models were used. Primary outcome measures were 30-day and 90-day postsurgical mortality and overall survival; adjusted odds (aOR) & hazard ratios (aHR) and 95% confidence intervals (CI) are reported. RESULTS: In all 1,432 pts received neoadjuvant treatment with nCHT (n=523) or nCRT (n=909). Odds of 30-day mortality were influenced by age (aOR 1.03, CI 0.99-1.06,p=0.077), average annual resection volume of facility (aOR 0.98, CI 0.97-1.00, p=0.135), and household income quartile (aOR 1.94, CI 0.97-3.90, p=0.060), but not by delivery of RT, comorbidities, gender, insurance status or facility type. Odds of 90-day mortality were influenced by age (aOR 1.03, 1.01-1.05,p=0.004), household income quartile (aOR 1.37, CI 0.87-2.16, p=0.171), and delivery of nCRT (aOR 1.69, CI 1.04-2.74, p=0.032), but not by average annual resection volume of facility, comorbidity, gender, insurance status or facility type. Survival odds were influenced by age (aHR 1.01, CI 1.00-1.02, p=0.001), margin status (aOR 1.50, CI 1.27-1.77, $p<0.001$), ypN status (aHR 1.45, CI 1.26-1.68), $p<0.001$), adjuvant CHT (aHR 0.81, CI 0.69-0.94, p=0.006), and nCRT (aHR 1.21, CI 1.04-1.40, p=0.012). On average pts with nCHT as compared to nCRT lived longer (median OS 26.4 vs. 24.2 months, p=0.001; actuarial 3 yr 58% vs 49%, and 5 year survival 30% vs 14%). CONCLUSIONS: There is no detectable difference in early outcome (30-day postsurgical mortality) among pancreaticoduodenectomy pts treated with nCHT or nCRT. Trend toward a more favorable long-term outcome (30-day postsurgical mortality and overall survival) among those with nCHT without radiation is noted. Further studies with more detailed data sources are needed.

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Actual 5-Year Long-term Nutritional Outcomes After Curative Gastrectomy in Gastric Cancer Patients D. Park,* K. Kim, D. Park, Y. Park, S. Ahn, H. Kim. *Surgery, Seoul National University Bundang Hospital, Seongnam-si, Gyeonggi-go, Korea (the Republic of).*

Introduction We aimed to evaluate the long-term nutritional results, rarely reported, after curative gastrectomy in gastric cancer patients. Methods The prospectively collected medical records of 658 patients who underwent radical gastrectomy with curative intent for gastric cancer from January 2008 to December 2009 and had no recurrence were reviewed retrospectively. All patients were followed up for 5 years. Nutritional statuses were assessed by body weight, serum hemoglobin, total lymphocyte count (TLC), protein, albumin, cholesterol, and Nutritional Risk Index (NRI). Results The ratio of male to female was 1.8:1 and the mean age was 58.3 (20-83) years. Distal gastrectomy (DG) was performed in 569 (86.5%) patients and total gastrectomy (TG) in 89 (13.5%) patients. There were three types of reconstruction after distal gastrectomy such as Billroth I (n=403, 70.8%), Billroth II (n=112, 19.7%), and Roux-en-Y (n=54, 9.5%) anastomosis. Comparing DG with TG, TG group showed lower body weight, hemoglobin, protein, albumin, cholesterol levels, TLC, and NRI than DG group on the first postoperative year ($P<0.05$), and also lower hemoglobin level and NRI on the fifth year after surgery ($p<0.05$). According to the reconstruction types after DG, Roux-en-Y group had lower protein and cholesterol levels than Billroth I and II groups on the first and fifth years after gastrectomy, respectively ($P<0.05$). Furthermore, comparison of patients who received adjuvant chemotherapy after gastrectomy with patients who underwent gastrectomy alone showed that hemoglobin, protein, albumin, cholesterol levels, TLC, and NRI were lower in the patients with adjuvant chemotherapy than in the patients with gastrectomy only on the first year after surgery ($P<0.05$). Conclusions The present study suggests that patients undergoing TG, DG with Roux-en-Y anastomosis, or adjuvant chemotherapy after surgery should be cautioned not to be malnourished on the first year after surgery and TG patients should be monitored for malnutrition and anemia for 5 years.

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Cojugated Bile Acid Promote the Proliferation of Pancreatic Cancer via Sphingosine 1-Phosphate Receptor H. Aoki,[1] M. Aoki,[1] E. Katsuta,[1] L.J. Fernandez,[1] P. Mukhopadhyay,[1] C. Barnett,[2] S. Spiegel,[1] K. Takabe.[1]* *1. Surgical Oncology, Virginia Commonwealth University, Richmond, VA; 2. University of Colorado, Denver, CO.*

Introduction: There have been numerous publications regarding the clinical benefit of bile drainage in obstructive jaundice, however, the mechanism of bile acid signaling on pancreatic cancer biology has not been thoroughly investigated. We have recently published that conjugated bile acids (CBAs) binds to sphingosine 1-phosphate receptor 2 (S1PR2), and it activate nuclear Sphingosine kinase 2 that regulate gene expression. Indeed, it was reported that CBAs promote growth of cholangiocarcinoma through S1PR2. Thus, we hypothesized that CBAs from obstructive jaundice aggravate the pancreatic cancer progression via S1PRs. Method: Expression of S1P receptors in murine (panc02-luc) and human (MiaPaca-2, AsPC-1, BxPC-2, Panc-1) pancreatic cancer cell lines were determined by real-time RT-PCR. Cells were treated with CBAs with or without JTE-013 (S1PR2 antagonist) and viable cells were quantified using WST-8. Panc02-luc cells were implanted in the left lobe of the liver of C57/Bl6 mice with or without obstructive jaundice, created by left and middle bile duct ligation with cholecystectomy. Tumors were harvested on day 18. Result: Hielarchial cluster analysis of pancreatic adenocarcinoma in The Cancer Genome Atlas (N=183) demonstrated that S1PR2, S1PR5 and SphK1 gene expressions have strong positive correlations. Among 5 S1P receptors, S1PR2 is dominantly expressed in panc02-luc and AsPC-1 cells. S1PR2 and S1PR5 are expressed in MiaPaca-2 and BxPC-3 cells. TCA (Taurocholate) promote the cell proliferation of pancreatic cancer cells. TCA-mediated cell growth was inhibited by JTE-013, but JTE-013 alone was also found to be growth inhibitory even in the absence of CBA. The tumors in obstructive jaundice group were significantly larger by bioluminescence measurement and weight. Conclusion: Conjugated bile acid signaling via S1PR2 promotes pancreatic cancer cell growth. Obstructive jaundice aggravated pancreatic cancer, and further study is warranted to investigate the possibility of targeting S1PR2 as a potential new therapeutic for pancreatic cancer treatment.

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Diagnosed in the Emergency Department: The Impact of Presenting Location on Outcomes for Gastric Cancer Patients I. Solsky,* B. Rapkin, P. Friedmann, P. Muscarella, H. In. *Surgery, Montefiore Medical Center, Bronx, NY.*

INTRODUCTION The impact of location of diagnosis on outcomes has been poorly defined for gastric cancer (GC) patients. Using detailed clinical data from a large urban academic center, we aimed to examine differences in outcomes based on location of diagnosis. METHODS Data from all gastric adenocarcinoma patients diagnosed and treated at a single academic medical center over five years (2009-2013) was analyzed. Demographics, treatment, and outcomes of patients treated non-emergently after diagnosis in the emergency department (ED) was compared to that of patients diagnosed in other locations. Cox regression was used after adjusting for potential confounders to estimate the Hazard Ratio (aHR) for mortality given a GC diagnosis in the ED. RESULTS Of the 273 patients identified with GC, 54% were diagnosed in the ED. Of these, 8% required surgery on the same admission and were excluded from analysis. Compared to patients presenting to non-ED settings, those in the ED group were more likely to be older and male but of similar race and insurance status. They presented with later cancer stages (stage IV: 50% vs. 24%, $p<0.05$) and with larger tumors (>=5cm: 21% vs. 15%, $p<0.05$). While both groups reported comparable rates of symptoms at presentation (82% vs. 74%, ns), patients in the ED group were more likely to have anemia or bleeding (51% vs 24%, $p<0.05$) and less likely to have pain or GI symptoms. After adjusting for patient and tumor factors, GC diagnosis after ED presentation was associated with an increased mortality risk (aHR 2.4; 95% CI: 1.1-5.3). CONCLUSIONS In our study, more than half of GC patients were diagnosed after presenting to the ED. After accounting for tumor factors, diagnosis in the ED was associated with a 2.5 fold increase in mortality risk. Diagnosis in the ED should be considered a marker of poor outcomes for GC. These findings may be related to unaccounted patient-level factors such as poor health behaviors or systems-level factors such as lack of patient navigation or multi-disciplinary cancer care. The non-specific symptoms of the ED group underscore the need to develop cancer detection methods that do not rely on symptomatology.

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Race is a Risk for Lymph Node Metastasis in Early T Stage Gastric Cancer N. Ikoma,* E. Elimova, M.M. Blum, J.A. Ajani, Y. Chiang, K. Fournier, P. Mansfield, B. Badgwell. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction Frequency of lymph node metastasis based on depth of tumor penetration (T stage) is not well described in Western countries, and its association with race/ethnicity has been barely investigated. The purpose of this study was to identify clinicopathologic factors associated with the frequency of lymph node metastases. Methods The medical records of 8,260 patients with gastric or gastroesophageal adenocarcinoma presenting to our institution (1/1995 to 12/2013) were reviewed to identify those who underwent surgical resection without neoadjuvant therapy. Associations between clinicopathological variables and lymph node metastasis were tested with chi-square and logistic regression analysis. Results We identified 225 patients who underwent upfront gastrectomy with a pathological diagnosis of gastric adenocarcinoma. Patients who had previously undergone gastrectomy were excluded (n=7), leaving 218 patients in this study, including 115 (53%) Caucasian and 19 (9%) African-American. Tumor locations included 25 (12%) in the esophagogastric junction and 105 (48%) in the antrum. Of the 218 study patients, 122 (56%) underwent extended lymph node dissection (>D1), and 144 (66%) had more than 15 lymph nodes examined. Lymph node metastasis rates were 10.0%, 34.4%, 43.5%, 73.2%, and 95.0% in T1a, T1b, T2, T3, and T4, respectively. On univariate analysis, variables associated with lymph node metastasis in early T stage (T1 or T2) tumors were submucosal invasion, tumor size more than 5 cm, lymphovascular invasion, and African-American race. Multivariate analysis showed higher risk of lymph node metastasis associated with lymphovascular invasion (OR 4.97, 95% CI 1.82-13.57; $p<0.01$) and African-American race (OR 10.3, 95% CI 1.97-53.81; $p=0.02$). Cases with more than 15 lymph nodes examined had a higher rate of lymph node metastasis (OR 3.31; $p=0.03$). Conclusions We observed high lymph node metastasis rates compared with those reported in Eastern literature, and we found that race is a risk factor for lymph node metastasis in early T stage gastric cancer. Caution is needed when applying evidence from Eastern countries to racially diverse Western countries.

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Staging Laparoscopy is Essential to Accurately Stage Gastric Cancer in Hispanic and African American Patients I. Nassour,* H. Hirsch, A. Yopp, M.A. Choti, J. Mansour, S. Wang, M. Porembka. *University of Texas Southwestern, Dallas, TX.*

Background: Staging laparoscopy (SL) detects occult metastases not visible on cross sectional imaging. Previous studies have shown SL to improve the accuracy of radiographic staging in gastric cancer patients. However, Hispanic (HS) and African American (AA) patients are underrepresented in these studies. Methods: We performed a retrospective review of a prospectively maintained database to identify patients with gastric cancer treated with curative intent at University of Texas Southwestern Medical Center from 2008-2015. Patients with no evidence of metastatic disease on cross-sectional imaging and who subsequently underwent SL were included. Clinicopathologic, demographic, and treatment data were collected and analyzed using student t-test and Chi square analysis. Results: We identified 122 patients with radiographically resectable gastric cancer. HS (N=44, 36%) and AA (N=32, 26%) comprised the majority of the cohort compared to Caucasian (CS N=28, 23%), Asian (AS N=11, 9%), and patients from miscellaneous ethnicities (N=7, 6%). HS and AA presented at an earlier age (HS 56.5 years, AA 59.5, CA 64.5, AS 63; p = 0.03[IN1]) and were more often noted to have locoregional disease characterized by bulky nodal disease or T3/T4 primary tumor (HS 79.5%; AA 68.7%; CS 60.7%, AS 45.4%; P[IN2] =0.06). SL was performed in 89% of patients. HS were most often found to harbor occult metastatic disease on SL which altered management (HS N=16, 45%; AA N=6, 22%; CS N=7, 35%; AS N=3, 50%; P=0.03[IN3]). Conclusion: SL is essential to accurately stage patients of all ethnic backgrounds undergoing surgery for GC. HS and AA gastric cancer patients present more often with locoregional and metastatic disease as compared to CS and AS. Although environmental or socioeconomic factors may account for this observation, additional studies are necessary to determine the contribution of underlying biology to aggressive disease.

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Inflammation Induced by Sphingosine Kinase of the Host Aggravates Pancreatic Cancer Peritoneal Carcinomatosis H. Aoki, M. Aoki, P. Mukhopadhyay, C. Barnett, S. Spiegel, K. Takabe.* *Surgical Oncology, Virginia Commonwealth University, Richmond, VA.*

Introduction: Prognosis of pancreatic cancer patients with peritoneal carcinomatosis (PC) is particularly poor with median survival of only 6 weeks. Sphingosine-1-phosphate (S1P), a bioactive lipid mediator produced by sphingosine kinase 1 (SphK1) and sphingosine kinase 2 (SphK2), plays critical roles in many aspects of cancer progression. We have recently published that S1P link inflammation and cancer in colitis-associated cancer progression. Given the fact that inflammation is known to be essential for establishment and progression of PC, where cancer cells need to adhere to the peritoneum and form a nodule, we hypothesized that S1P levels regulated by SphK1 and SphK2 in the host animal may have different mechanism in promoting progression of pancreatic cancer PC. Methods: Murine pancreatic adenocarcinoma panc02-luc cells were intraperitoneally injected into SphK1 wild type (WT) or knockout (KO), or SphK2 WT or KO mice to generate PC model. Tumor burden was quantified using bioluminescence imaging. Survival was assessed by Kaplan-Meier analysis. PC nodules were harvested 14 days after injection and analyzed. The proliferation was assessed by Ki-67 staining and apoptosis was evaluated by TUNEL assay. We also compared mRNA expression by RT-PCR. Results: The longer survival was determined in SphK1 KO mice. Panc02-luc cells developed significantly less tumor burden both in bioluminescence imaging and tumor weight. Histologically, less inflammatory cell infiltration and less cancer cell proliferation were observed in tumor of SphK1 KO mice. However no difference was determined in apoptosis between SphK1 KO and WT mice tumor. These results suggest that host S1P generated by SphK1 promotes PC progression by stimulation of proliferation of cancer cells. Interestingly, SphK2 KO mice developed less tumor burden, longer survival with elevated CD4 and CD8 lymphocyte infiltrates in PC. Conclusion: Our results implicate an intriguing possibility that S1P levels in the host may have different mechanisms in promoting progression of pancreatic cancer PC depending upon its levels.

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Field Change in Synchronous and Metachronous Squamous Cell Carcinomas: The Two Face Janus of Susceptibility C. Ong,[1]* N. Shannon,[1] Q. Tan,[1] F. Chong,[2] K. Koh,[1] K. Li,[1] S. Tan,[2] M. Teo,[2] K. Soo,[2] G. Iyer.[2] *1. Singapore General Hospital, Singagpore, Singapore; 2. National Cancer Centre Singapore, Singapore, Singapore.*

Background The concept of field change (FC) was first described more than 50 years ago. In head and neck squamous cell cancers, FC is believed to be the scientific basis underlying multiple primary tumour formation. In this study, we aim to examine the patterns of genomic events that define FC which predispose to synchronous versus metachronous tumours. Methods Using next generation sequencing technology, we performed exome sequencing of synchronous or metachronous tumours along with adjacent normal mucosa to identify mutations (n=6 and 4 respectively). Copy number profiling was performed for all tumours and normal mucosa. Integrative genomic analysis was performed to identify the genomic patterns which define FC Results In metachronous tumours (n=3), a total of 678/103 somatic mutations were identified in tumours and adjacent normal mucosal respectively. 58 (8.6%) of all mutations were present in all samples (normal and tumour), highlighting a common FC which tumours arose from. Interestingly, the mutational and copy number profiles of synchronous tumours are grossly divergent. 23 common somatic mutations were identified in adjacent normal while 671 mutations were identified in the synchronous tumours (n=3). Intriguingly, only 13 (1.9%) somatic mutations were shared in all samples (normal and tumour). Using integrative analysis and Sanger sequencing, we identified and validated 2 key tumour suppressors that are inactivated via germline mutations with subsequent loss of heterozygosity (LOH) in all synchronous tumour samples. All normal samples retained the normal allele. Conclusion Using exome sequencing and copy number profiling of multiple tumour samples with matched normal mucosa, we have demonstrated 2 distinct models of field change. The first model supports the conventional definition of FC; with all areas of mucosa sharing a significant amount of altered genomic burden; tumour formation then occurs spatially and temporally. The second model is potentiated by germline mutations of small number of key tumour suppressors. Tumour formation is then initiated with LOH of the second allele with tumour formation occurring spatially.

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Tumour Markers in CRS-HIPEC Patients: An Analysis of 157 Patients in a Single Institution M. Chee,[1]* W. Ong,[2] M. Teo.[2] *1. Singapore General Hospital, Singapore, Singapore; 2. National Cancer Centre, Singapore, Singapore.*

Introduction Raised pre-op & persistently raised post-op tumour markers (TM) are thought to connote a poorer prognosis. There is currently no guideline on when to measure TM post cytoreductive surgery & hyperthermic intraoperative chemotherapy (CRS-HIPEC) to determine disease response to surgery. This study examines the time to normalisation (TTN) of TM & the prognostic value of a normalised CEA, CA125 & CA19-9 in patients with peritoneal carcinomatosis (PC) who had raised pre-op TM & underwent CRS-HIPEC. Method 157 patients with PC from appendiceal (n=29), colorectal (n=51), ovarian (n=58) & other (n=19) cancers, underwent CRS-HIPEC at the National Cancer Centre Singapore from Jan 2001-April 2014. Raised TM were defined as: CEA>5ug/L, CA125>35ug/L, CA19-9>37ug/L. Post-op TM levels were determined at multiple time-points. The cut-off for normalisation was taken at POD 30. Standard survival analysis techniques were applied. Results CEA, CA125 & CA19-9 were raised pre-op in 40%, 40% & 30% of patients respectively. Among patients with raised pre-op TM, the median TTN was 7 days for CEA, 90 days for CA125 & 6 days for CA 19-9. Patients with raised pre-op CEA which did not normalise post-op had worse overall survival (OS) (HR 1.48; 95% CI 0.30–7.41) & disease-free survival (DFS) (HR 1.28; 95% CI 0.40–4.13) as compared to patients with normalised post-op CEA. Similar survival outcomes were observed for CA19-9 (OS: HR 1.80; 95% CI 0.30–10.88; DFS: HR 3.25; 95% CI 0.80–13.16). In contrast, patients with raised pre-op CA125 which did not normalise post-op had better OS (HR 0.78; 95% CI 0.25–2.48) & DFS (HR 0.92; 95% CI 0.38-2.22) than those with normalised post-op CA125. Conclusion This study demonstrates interesting differences in the TTN of the different TM in PC patients who underwent CRS-HIPEC. While not statistically significant, the 48% & 80% increase in the risk of death for patients with raised post-op CEA & CA19-9 are noteworthy. A raised pre-op CA125 was more commonly observed in patients with ovarian cancer with PC, and its normalisation might have limited prognostication

value given that many patients with ovarian cancer required and received pre & post-op chemotherapy.

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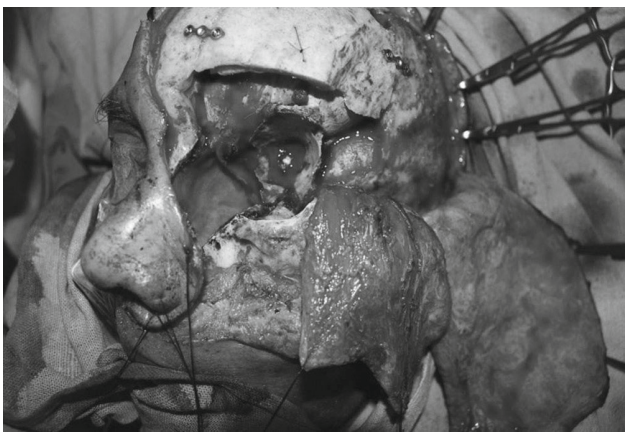
Clinical Profile, Treatment Patterns and Outcomes in Locally Advanced and Recurrent Orbital Tumors from a Tertiary Care Cancer Centre S. Deo, N. Shukla, S. Kumar, V. Kumar,* S. Bakshi, S. Pathy, S. Thulkar. *All India Institute of Medical Sciences (AIIMS), New Delhi, Delhi, India.*

Introduction: Orbital tumors constitute a rare and heterogeneous group of neoplasms arising from the orbital or peri-orbital contents. Majority of these patients are seen and managed by ophthalmic surgeons but patients with advanced and recurrent tumors require multidisciplinary management in a comprehensive cancer centre. We present our experience of managing 72 loco-regionally advanced orbital tumors at a tertiary cancer centre in north India. Methods: A retrospective analysis of prospectively maintained computerized database was done to identify patients undergoing surgery for orbital tumors between 1997 and 2015. An analysis of clinical spectrum, types of surgical resections, adjuvant therapy details and long-term outcomes was performed. RESULTS: Seventy-two patients underwent exenteration during the study period of which 42 were males and 30 were females. Mean age of the cohort was 53.2 years (range 18–85 years). In total, 41 patients had prior sub-optimal interventions of which 38 had a local tumour excision and 12 received previous radiotherapy. Eyelids were the most common site for primary neoplasm and sebaceous cell carcinoma was the most common histopathology. Total orbital exenteration was performed in 57 patients and Extended orbital exenteration in 15 patients. Neck dissection was performed in 44(61%) patients of which 29(66%) had metastatic lymph nodes. In most of the patients, reconstruction was done by temporalis muscle flap. Margin negative resection was achieved in 62(86%) patients. Total 34 (47%) patients received adjuvant radiotherapy for positive margin or metastatic lymph nodes. During follow-up 18 recurrences (25%) were observed(17 loco-regional & 2 distant). Conclusion: Orbital tumors constitute a heterogeneous group of head & neck malignancies. A significant number of patients present with loco-regionally advanced disease requiring orbital exenteration. Aggressive surgical resection with lymph nodal clearance and postoperative radiotherapy results in optimal long term outcomes.



Anterior cranio facial resection

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Multimodality Therapy for Peritoneal Metastases from Epithelial Ovarian Cancer D. Magge,* J.F. Pingpank, M. Holtzman, S. Ahrendt, H. Zeh III, D. Bartlett, M.A. Choudry. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: Peritoneal metastases frequently occur in advanced epithelial ovarian cancer (EOC) despite optimal therapy (surgical resection, intravenous chemotherapy, with or without intraperitoneal chemotherapy). We initiated a multimodality approach, including cytoreductive surgery (CRS), hyperthermic intraperitoneal chemoperfusion (HIPEC) and systemic chemotherapy, with the hypothesis that this approach would provide long-term survival with acceptable morbidity. Methods: From a prospectively maintained database, we analyzed clinicopathologic, perioperative and oncologic outcomes in 103 consecutive patients undergoing CRS-HIPEC for PM from EOC. Kaplan-Meier survival curves and multivariate Cox-regression models identified prognostic factors effecting survival. Results: CRS-HIPEC was performed as first-line therapy in 52% and at time of disease recurrence in 49% of patients. Systemic chemotherapy was given preoperatively in 44% and postoperatively in 69% of patients. Median prior surgical score (PSS) was 2, with 5 patients undergoing prior CRS-HIPEC. Median peritoneal carcinomatosis index was 11 and complete CRS was achieved in 94 patients (CC-0/no macroscopic residual disease= 73; CC-1/residual tumor nodules <2.5 mm= 21). Intraperitoneal drug used was mitomycin C or cisplatin in 85 and 18 patients, respectively. Major postoperative morbidity (Clavien-Dindo grades 3-4) occurred in 14 patients (14%), while 30-day mortality rate was 3%. After median follow-up time from surgery of 66 mos, disease progressed in 62 patients, with a median progression-free survival of 11 mos. Median overall survival (OS) was 22 mos (1- and 3-year OS: 82% and 31%). In a multivariate Cox-regression model, Karnofsky performance status (p=0.031), PSS (p=0.01), CC-score (p=0.015), number of visceral anastomoses (p=0.001), and lack of neoadjuvant or adjuvant chemotherapy (p=0.005) were independent predictors of poor survival. Conclusions: Multimodality treatment is an effective and potentially curative option for select patients with peritoneal metastases from EOC. Long-term survival can be achieved in well-selected patients, without excessive morbidity and mortality, at experienced centers.

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