Abstract Book

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68th Annual Cancer Symposium

Houston, Texas
March 25-28, 2015

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ABSTRACTS

Accepted for
PLENARY and PARALLEL
PRESENTATIONS

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**Background:** The DCIS Score (DS) was validated as a predictor of ipsilateral breast recurrence (IBR; DCIS or invasive) in 327 E5194 pts treated by breast-conserving surgery (BCS) without radiation (RT) (Solin, 2013). This Ontario population-based study of 3320 women with DCIS from 1994 to 2003 (Rakovitch, 2013) tested the DS as a predictor of IBR risk in a broader and more contemporary population of pts treated with BCS alone w/ and w/o clear margins (CM). **Methods:** Breast pathologists centrally reviewed all H&E slides. The DCIS Score was obtained by standardization quantitative RT-PCR using fixed paraffin embedded tumor. The pre-specified primary objective was to determine the relationship (HR:50 units) between the risk of an IBR and the continuous DS (using Cox models) in pts treated with BCS alone with ER+ tumors and CM (no ink on tumor). The association between the continuous DS in all patients with BCS alone w/ & w/o CM was explored. **Results:** Blocks were collected for 1751 pts (53% of parent cohort); 718 had BCS alone (N=571 w/CM). Median follow-up was 9.4 years. Among 718 pts w/BCS alone, 136 pts had an IBR (DCIS, N=57; invasive, N=80). Among 717 pts w/CM, 100 had IBR (DCIS,N=44; invasive, N=57). In the primary analysis, among 571 pts treated by BCS alone w/CM the continuous DS was significantly associated with IBR in ER+ pts (HR 2.26; 95%CI 1.41,3.59; P=0.001) and in all pts (HR 2.15;95%CI 1.43,3.22;P<=0.001). The DS was associated with invasive IBR (HR 1.78;95%CI 1.03,3.05;P=0.04); similar but non-significant results were noted in the ER+ subgroup (P=0.08). In multivariable analysis for IBR, the HR:50 units for the DS among pts treated w/BCS alone w/CM was 1.68 (95%CI 1.08,2.62;P=0.022) adjusting for multifocality, tumor size, subtype, and age. Among all 718 pts treated by BCS alone w/ and w/o CM, the DS was associated w/IBR, and the HR:50 units for the DS was 2.04 (95%CI 1.39,2.98; P<=0.001) adjusting for multifocality, tumor size, subtype, and age. **Conclusions:** The DCIS Score quantifies IBR risk for DCIS pts treated by BCS with or without CM. Integrating the DCIS Score with established risk factors can more accurately identify DCIS pts treated with BCS alone with low (<10%) or high (>25%) 10yr average IBR risk.

2  
**Targeted Axillary Dissection Improves Axillary Evaluation following Neoadjuvant Chemotherapy in Node Positive Patients**

A.S. Caudle,* W. Yang, E.A. Mittenдорf, D.M. Black, M. Gilcrease, I. Bedrosian, B.P. Hobs, R.P. Candelaria, G. Babiera, B.E. Dogan, M.J. Lim, L. Santiago, K.K. Hunt, S. Krishnamurthy, H.M. Kuerner. Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.

Breast cancer staging is enhanced by axillary ultrasound (US) and biopsy of abnormal lymph nodes. When clips are placed in nodes with metastases, they can be evaluated for response to neoadjuvant chemotherapy (NCT). The goal of this study was to determine if pathologic changes in clipped nodes reflect nodal response to NCT and if targeted axillary dissection (TAD), which includes sentinel lymph node dissection (SLND) in addition to selective localization and removal of marked nodes improves the accuracy of nodal assessment. **Methods:** A prospective study of patients with axillary metastases identified by US confirmed by needle biopsy with a clip placed in the node was performed. After NCT, patients underwent axillary lymphadenectomy (ALND) with x-ray of the axillary contents to identify the clipped node. The pathologic findings of the clipped node were reported separately from other nodes. Patients undergoing TAD had selective removal of the clipped node using US-guided marking of nodes with documented metastatic disease allows for selective removal of these nodes and improved pathologic evaluation for residual nodal disease. The FNR of SLND (11.6%) can be reduced (2.3%) by ensuring removal of the clipped node. TAD is technically feasible and allows for improved assessment of nodal response after chemotherapy.

3  
**The Impact of Health Insurance on Cancer Care in Disadvantaged Communities**

Z.M. Abdelsattar, S. Hendren, S.L. Wong, Department of Surgery, University of Michigan, Ann Arbor, MI.

**INTRODUCTION:** Individuals from disadvantaged communities are among millions of uninsured Americans who are gaining insurance under the Affordable Care Act. Whether health insurance can mitigate the effects of the social determinants of health in those communities for cancer care is unknown. **METHODS:** We linked the Surveillance, Epidemiology, and End Results (SEER) registries to US Census data for patients diagnosed with the 4 leading causes of cancer deaths between 2007-2011. SEER began collecting insurance data in 2007, and only released it this past year. We constructed a county-level composite measure using median household income, proportion of residents below the poverty level, and proportion of married couples. This measure was used to stratify patients into quintiles of social determinants, with the lowest quintile representing the most disadvantaged communities. Multiple logistic regression and Cox proportional hazard models were used to estimate associations and cancer-specific survival. **RESULTS:** A total of 468,564 patients aged 18 to 64 years were identified (Breast=208,639; Prostate=112,098; Lung=75,630; Colorectal=72,197). For all cancer types, patients from the most disadvantaged communities (median household income=$37,837; 21% below poverty level; 58% married) were more likely to present with distant disease (adjusted Odds Ratio [aOR]=1.16; P=0.001) and had higher cancer-specific mortality (aOR=1.25; P=0.001) than the least disadvantaged communities (median income=$76,785; 10% in poverty; 68% married). The effect of having health insurance on cancer-specific mortality was more pronounced in patients from the most disadvantaged communities (40% vs. 31% in relative survival benefit at 5 years; Figure). However, it did not fully mitigate the effect of social determinants of health (adjusted Hazard Ratio 0.70 vs. 0.56; P=0.001). **CONCLUSIONS:** Patients diagnosed with one of the leading causes of cancer deaths and are from socially disadvantaged communities, benefit most from health insurance coverage and access to care, thereby decreasing disparities in outcome. However, the disparities gap produced by social determinants of health cannot be fixed by insurance alone.
Despite the more pronounced benefit of health insurance in the most disadvantaged communities, cancer patients from the least disadvantaged communities still have better survival at 5 years.

**An Externally Validated Prognostic Multigene Expression Assay for Survival in Resected Colorectal Liver Metastases**


**Background** Recurrence free (RFS) and overall survival (OS) after resection of colorectal liver metastases (CRLM) are heterogeneous. Clinical risk scores (CRSs) are used to prognosticate RFS and OS but have limited accuracy, lack universal applicability, and rarely impact clinical decisions. We aimed to develop and externally validate a prognostic multigene expression assay after resection of CRLM. **Methods** We measured mRNA expression using an Illumina microarray on frozen tumor from 96 patients with completely resected CRLM between 2000-07 at Memorial Sloan Kettering Cancer Center (MSKCC). We created a 20-gene molecular risk score (MRS) using the supervised principal components method. We assessed the prognostic ability of chemotheraphy, three common CRSs (Fong, Nordlinger, Iwatsuki), and the MRS for RFS and OS using multivariate Cox regression. The prognostic ability of CRSs and the MRS was then assessed on mRNA expression measured on surgically resected tumors. **Findings** For OS in the Dutch validation cohort, MRS was the only independent prognosticator (low vs. high median 2 vs. 6 years; HR 3.6, Table 1) followed by adjuvant chemotherapy (HR 0.3, Table 1). MRS was also prognostic of RFS (HR 3.7, 95%CI 1.6-4.8, P<0.001). For OS in the MSKCC cohort, MRS was the strongest independent prognosticator (low vs. high MRS median 84 vs. 25 months; HR 4.2, Table 1). MRS was also prognostic of RFS (HR 1.6, 95%CI 1.2-2.4, P=0.04). The CRSs were not independently prognostic of OS in either dataset and only the Fong score was prognostic of RFS in the Dutch cohort (HR 1.6, 95%CI 1.1-2.6, P=0.02). **Interpretation** Compared to CRSs, the MRS is a more accurate, more broadly applicable, and an independent prognostic biomarker of RFS and OS in resected CRLM. This MRS is the first externally validated multigene assay to prognosticate outcomes in resected CRLM.

**Multivariate analysis of MRS, CRSs (Fong, Nordlinger, Iwatsuki), and adjuvant chemotherapy of OS.**

<table>
<thead>
<tr>
<th>CRS</th>
<th>HR</th>
<th>P-value</th>
<th>CR</th>
<th>HR</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fong Score Low</td>
<td>1.7</td>
<td>0.01</td>
<td>Fong Score High</td>
<td>1.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Fong Score Low</td>
<td>1.7</td>
<td>0.01</td>
<td>Fong Score High</td>
<td>1.2</td>
<td>0.01</td>
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Neoadjuvant and regional chemotherapy did not reach statistical significance on univariate analysis. HR = Hazard Ratio. ns = not significant. * = reference. NG = Nordic. MRS = Molecular Risk Score.

**5** Blockade of Inflammatory Monocytes is Effective in Pancreas Cancer: Results of a Phase Ib/II Trial in Borderline Resectable & Locally Advanced Disease


**Background** In pancreas cancer (PC), the tumor microenvironment (TME) is heavily infiltrated by CCR2+ inflammatory monocytes (IM) which are recruited from the bone marrow and infiltrate tumors to become tumor-associated macrophages (TAM). These TAMs suppress anti-tumor immunity, augment tumor growth and promote metastasis. Based on promising preclinical results, our group is conducting a Phase Ib/II trial of FOLFIRINOX + CCR2 inhibitor (PF-04136309) in patients with borderline resectable (BR) and locally advanced (LA) pancreas cancer. **Methods:** This ongoing phase Ib/II study includes a control group (FOLFIRINOX only; n=6), a dose de-escalation cohort (FOLFIRINOX+PF-04136309; n=6), and an expansion cohort at the rapid phase II dose (n=32). Standard dose FOLFIRINOX is administered every 2 weeks and PF-04136309 is dosed at 500 mg orally BID for 3 months. Pre- and post-treatment peripheral blood (PB), bone marrow (BM) and EUS-guided fine needle biopsies were analyzed by flow cytometry. Primary endpoint is partial response (PR) as defined by RECIST criteria and determined by a blinded radiologist. **Results:** Pre- and post- treatment specimen analysis reveals that CCR2 inhibition prevents IM egress from the BM leading to a significant reduction in circulating IM compared to FOLFIRINOX alone (p<0.01). At the primary tumor, TAMs were decreased and effector T-cells are increased (Fig 1). Currently, 24 patients who received FOLFIRINOX+PF-04136309 are evaluable (5BR, 19LA). Overall, 13 of 24 patients (54%) had PR. Subset analysis reveals PR in 4 of 5 (80%) patients with BR disease and 9 of 19 (47%) who presented with LA disease (Fig 2). Two patients who presented with LA PC were downstaged to resectability. No patients had disease progression. Median follow-up is 8 months and accrual will be completed soon. **Conclusions:** FOLFIRINOX+PF-04136309 effectively blocks recruitment of IM to the TME. Results of our ongoing clinical trial show a very promising response rate suggesting that this strategy may provide clinical benefit to PC patients. Updated response and survival results will be presented at the meeting.

**Fig 1.**

**Fig 2.**
6 Proteomic Features of Colorectal Cancer Predict Relapse-free Survival and Identify Tumor Subgroups Independent of Oncogenic Mutations  C. Clarke,* M. Lee, G. Manyam, Z. Jiang, D. Menter, G.J. Chang, S. Kopetz. Surgical Oncology, MD Anderson Cancer Center, Houston, TX.  

**Background:** The Cancer Genome Atlas Project (TCGA) utilized reverse-phase protein arrays (RPPAs) to identify critical protein markers and signaling pathways in colorectal cancers (CRC). Data from TCGA and an MD Anderson (MDACC) cohort suggest that CRCs cluster by proteomic features into distinct subsets that reflect the tumor’s functional state, and may provide more insight into the pathophysiology of CRC than established oncogenic mutations. We used RPPA to analyze the prognostic implications of the functional proteome in Stage 2/3 CRC an identify patterns of protein expression that drive tumorigenesis. **Methods:** Protein extraction was performed on 232 snap frozen stage 2/3 CRC samples from the MD Anderson Cancer Center. 163 validated proteins were analyzed by RPPA to identify predictors of tumor recurrence. Cox regression was used for univariate analysis with bootstrap validation, followed by inclusion of proteins with corrected p < 0.05 into multivariate model. Unsupervised hierarchical clustering was used to dichotomize samples by patterns of protein expression in both TCGA and MDACC cohorts. Proteins with highest discriminatory utility were identified by LIMMA in the discovery set and validated. Clinicopathological variables and mutation status were analyzed for correlation. Median follow up was 5 yrs. **Results:** 12 proteins were significant predictors of tumor recurrence on univariate analysis including key players in the energy balance/MTOR signaling pathway - AMPK, mTOR, PI3Kp85, FoxO3a. On multivariate analysis phospho-Bad, FoxO3a, HER3, and phospho-S6 remained significant. Clustering revealed dichotomization with Group 1 notable for high EMT (fibronectin, collagen VI, low E-cad), Group 2 high in Akt/MTOR pathway components (BRAF, HER2/3). There was no difference in MSI, KRAS, or BRF status between proteomic groups. **Conclusion:** Functional proteomic analysis has identified key proteins with prognostic importance in CRC, independent of known clinicopathological variables. CRCs can be classified into distinct subsets by proteomic features that reflect differences in cellular signaling independent of common oncogenic driver mutations.

**Multivariate Analysis**

<table>
<thead>
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<th>Variable</th>
<th>Protein Function</th>
<th>Hazard Ratio (HR)</th>
<th>Significance</th>
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<tbody>
<tr>
<td>Bad_pS112</td>
<td>Inhibits apoptosis</td>
<td>3.138</td>
<td>p &lt; 0.003</td>
</tr>
<tr>
<td>FOXO3a</td>
<td>Transcription factor modulating apoptosis and cell cycle</td>
<td>2.715</td>
<td>p = 0.036</td>
</tr>
<tr>
<td>HER3</td>
<td>Growth factor signaling, determines EGFR and HER2</td>
<td>0.312</td>
<td>p = 0.002</td>
</tr>
<tr>
<td>S6_pS240, S244 Cell cycle progression and mRNA translation</td>
<td>0.387</td>
<td>p &lt; 0.006</td>
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</tr>
</tbody>
</table>

7 Comprehensive Multiprotocol Biomarker Analysis of 313 Hepatocellular Carcinoma Identifies Potential Therapeutic Options  G.K. Abou-Alfa,* J.T. Miura,1 T. Gamblin,1 A.R. He,2 C. Ang,2 N.S. Yee,* 1. Medical College of Wisconsin, Milwaukee, WI; 2. Memorial Sloan Kettering Cancer Center, New York, NY; 3. Georgetown University Hospital, Washington, DC; 4. Penn State Hershey Cancer Institute, Hershey, PA.  

**Background:** Effective treatment strategies for hepatocellular carcinoma (HCC) remain limited. Identification of additional therapies remains paramount as currently available agents have resulted in marginal improvements in overall survival. **Methods:** 313 HCC samples were evaluated with a multiprotocol profiling approach (Caris Life Sciences, Phoenix, AZ), including gene sequencing (Sanger, NGS [N = 79]), protein expression (IHC) and gene amplification (ISH). **Results:** Biomarker changes of interest are shown in table below. TP53 was mutated in 28%, CTNNB1 in 23%, and BRCA2 in 20%; other gene mutation rates were < 5%. TP53-mutated tumors show significantly higher TOPO2A (89% vs. 39%, p < 0.0001), TS (70% vs. 32%, p = 0.0067) and RRM1 expression (40% vs. 12%, p = 0.017), implying high rates of proliferation and DNA synthesis. CTNNB1-mutated tumors showed significantly higher SPARC (67% vs. 21%, p = 0.0013) and AR expression (53% vs. 22%, p = 0.025). Primary HCC (N = 209) exhibited significantly higher PD-1 (89% vs. 33%, p = 0.01) and TS expression (35% vs. 13%, p < 0.0001) than metastatic (N = 105). Patient history/outcomes relative to biomarker status are being evaluated. **Conclusions:** These data suggest potential therapeutic targets, such as tyrosine kinase inhibitors, anti-PD1 agents, or PI3 kinase pathway inhibitors. Although no evidence shows that cytotoxic is effective in patients with HCC, immunotherapy, alkylation agents, fluoropyrimidines, anthracyclines, nab-paclitaxel, or taxanes (only by chemotherapeutically related). The protein changes associated with CTNNB1-mutated tumors suggest potential benefit of targeting WNT pathway in combination with nab-paclitaxel or anti-androgens. Immuno-modulatory agents may be a therapeutic option in primary HCC, based on the higher levels of PD-1. Multiprotocol tumor profiling reveals molecular heterogeneity HCC, similar overall to previous reports, and identifies different potential treatment options for molecular subtypes.

**Percentage of samples with change in protein expression, by IHC**

<table>
<thead>
<tr>
<th>High expression levels</th>
<th>Low expression levels</th>
</tr>
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<tbody>
<tr>
<td>08</td>
<td>52</td>
</tr>
<tr>
<td>52</td>
<td>56</td>
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<td>60</td>
<td>86</td>
</tr>
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<td>66</td>
<td>12</td>
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**Background:** Nonoperative management (NOM) of rectal cancer following clinical complete response (cCR) to neoadjuvant therapy is a non-standard approach. We reviewed our experience with NOM to evaluate safety and efficacy. **Methods:** A retrospective review of prospectively collected data between 2006 and 2014 was conducted. We compared patients completing neoadjuvant therapy for stage I to III rectal cancers who: a) achieved cCR and were treated with NOM, or b) underwent standard total mesorectal excision (TME) and achieved a pathologic complete response (pCR). Kaplan-Meier estimates and the log-rank test were used. **Results:** Seventy-three patients underwent NOM after cCR. From 369 rectal resections performed, 72 (20%) achieved pCR and form the comparison group. Median follow-up across both groups was 3.3 years. Rectal preservation was achieved in 56 (77%) of the patients treated with NOM. Of the 19 NOM patients with local recurrence, 18 were salvaged successfully with standard TME (n = 16) or local excision (n = 2) with one patient pending a salvage operation. No significant differences were noted in the number of distant recurrences between the NOM and pCR groups. Four-year disease-specific survival and overall survival between the two groups were not significantly different. **Conclusions:** In this highly selected group of patients with cCR to neoadjuvant treatment, NOM with surgical salvage of local tumor regrowth achieved local control in all patients. The oncologic outcome for NOM patients at 4 years was comparable to patients with pCR after rectal resection. These data continue to suggest that NOM does not compromise oncologic outcome, and that preservation of the rectum is achieved in a majority of patients.

BACKGROUND: The optimal treatment for patients with rectal cancer and synchronous resectable liver metastases is controversial. The current NCCN recommendation of pelvic radiation (XRT) to the rectal primary is systemically extrapolated from the non-metastatic setting. Our objective was to examine the impact of pelvic XRT on recurrence patterns. METHODS: Between 1999-2013, 623 rectal cancer patients with liver-only metastases was surgically evaluated for multimodality therapy of curative intent. 196 patients with SRLM (concomitant rectal and liver diagnoses) were reviewed for demographics, tumor, and treatment details. Disease recurrence/persistence and overall survival (OS) were analyzed. RESULTS: The median age at diagnosis was 53 years (interquartile range, IQR: 44-61). Rectal primary was clinically T3/4 or N+ in 133 (68%); unstaged/unknown in others; the median number of liver lesions per patient was 2 (IQR:1-4). 98 patients (50%) received pelvic XRT. R0 resection of rectal primary and liver metastases was achieved in 154 (79%) patients. Rectal operations included low anterior resection (99, 62%), coloanal anastomosis (25,16%), abdominal perineal resection (15,10%), total proctocolectomy (2, 1%) and posterior exenteration (1, 1%). After a median follow-up of 42 months, 109 (70%) patients reoccured, nearly all systemically (103, 94%). Six patients (4%) recurred locally (3 with and 3 without concomitant systemic recurrence). 2 did and 4 did not receive pelvic XRT (p=0.202). Among 42 patients with unresected persistent disease, 20 had an intact rectal primary. Palliative intervention was required in 4 (20%) patients (resection, endoscopic dilation, diverting ileostomy, stent). The 5-year OS was 58%. Neither pelvic XRT nor the site of recurrence correlated with OS. CONCLUSIONS: For rectal cancer patients with SRLM, excellent OS can be achieved with coordinated surgical resection and multi-modality therapy. Recurrent disease was predominantly systemic. Curative-intent oncologic resection of the rectal cancer performed in this setting provides excellent control of the primary site without the routine use of pelvic XRT.

Comparative Effectiveness of Primary Tumor Resection in Metastatic Colon Cancer: An Instrumental Variable Analysis Z. Alawadi, U. Phatak, C. Hu, C. Bailey, L. Kao, Y. You, G.J. Chang, 1. General Surgery, The University of Texas Health Science Center, Houston, TX; 2. The University of Texas MD Anderson Cancer Center, Houston, TX.

Background: Although the safety of chemotherapy without primary tumor resection (PTR) has been established, questions remain regarding potential survival benefit with PTR. The purpose of this study is to compare mortality with and without PTR among patients with unresectable metastatic colon cancer using nationwide hospital based cancer registry data. Methods: An observational study was conducted of patients with stage 4 colon cancer identified from the National Cancer Data Base (2003-2005). Patients who underwent metastectomy were excluded. Patient, treatment, and hospital data were analyzed. Multivariable Cox regression stratified by receipt of chemotherapy was performed to compare survival with and without PTR. To account for selection bias, propensity score weighting (PSW) and instrumental variable (IV) analyses, using hospital-level PTR rate as the instrument, were performed. In order to account for the potential bias associated with early comorbidity or disease burden associated deaths (survivor treatment bias), 1 year landmark analysis was performed. Results: A total of 14,399 patients met inclusion criteria and 6,735 patients were eligible for landmark analysis. PTR was performed in 38.2% of the total cohort and 73.8% of those at landmark. Using multivariable Cox regression analysis, PTR was associated with a significant reduction in mortality (HR 0.39; 95% CI 0.38-0.41). This effect persisted with PSW (HR 0.4; 95% CI 0.38-0.43). However, IV analysis showed a much smaller effect, (HR 0.88; 95% CI 0.83-0.93). While a smaller benefit was seen on landmark analysis using multivariable Cox regression (HR 0.6; 95% CI 0.55-0.64) and PSW (HR 0.59; 95% CI 0.54-0.64), IV analysis showed no improvement in survival (RR 0.97; 95% CI 0.87-1.06). Stratification by chemotherapy did not alter the results. Conclusions: Among patients with stage 4 colon cancer, PTR offered no survival benefit over chemotherapy alone when the IV method was applied at the 1 year landmark. Subject to selection and survivor treatment bias, standard regression analysis may overestimate the benefit of PTR. Future study should focus on identifying patients most likely to benefit from PTR.


Introduction: Metastatic spread of colorectal cancer (CRC) to the peritoneal cavity is common and difficult to treat, often resulting in malignant bowel obstruction. Chimeric antigen receptor (CAR)-T immunotherapy has shown great promise, and anti-CEA CAR-Ts have been used to target CRC. We previously reported on intrahepatic CAR-T infusion for CRC liver metastases, and now we hypothesize that intraperitoneal (IP) delivery of anti-CEA CAR-Ts would result in effective IP intratumoral delivery and limit tumor progression. Methods: We injected C57Bl/6 mice with 2.56e38CEA cells expressing luciferase. CAR-Ts were derived by transduction of activated splenocytes. Mice with established IP metastases (IPM) either remained untreated, received untransduced control T cells, or anti-CEA CAR-Ts on days 3 and 6 along with IP IL-2. We measured tumor burden by bioluminescence. Tumor and peritoneal lavage fluid were harvested on day 14 for analysis by flow cytometry. Results: CAR-Ts represented 8.4e1.6% of IPM and 12.3e2.4% of peritoneal fluid CD3+ T cells (p=0.52). Immunosuppressive FOXP3+ Treg accumulated in IP tumors, representing 25.1e3.5% of CD4+ T cells in IPM compared to 6.9e1.7% in lavage fluid (p=0.008). Expression of immunoinhibitory PD-1 was significantly higher among IPM CD4+ T cells (61.6e1.9%) compared to lavage (30.8e1.4%, p<0.001). Bioluminescence imaging demonstrated a significant decrease in tumor burden on day 12 in CAR-T treated mice compared with untreated mice (p=0.02). In contrast, injection of untransduced control T cells did not result in a significant decrease in tumor growth. The effects of IP CAR-T injections improved over time, with a 1.6-fold decrease in tumor burden compared with untreated mice at 1 week, and a 1.8-fold decrease by 2 weeks. There was a 2.7-fold decrease compared to mice treated with untransduced T cells and IL-2 by 2 weeks. Conclusions: IP infusions of anti-CEA CAR-T reduced growth of CRC IPM and IP IL-2 alone was likely partially responsible for this effect. Further preclinical study of IP CAR-T in combination with Treg depletion and PD-1 blockade is warranted, and subsequent phase I testing is planned.

Association of Surgical Site Infection with Survival and Receipt of Adjuvant Chemotherapy following Curative Resection for Non-metastatic Colon Cancer G.M. Barden, D.A. Anaya, G. Chen, L.T. Li, S. Mohammed, D.H. Berger, A. Artinayan, Surgery, Baylor College of Medicine, Houston, TX.

Background: Surgical site infections (SSIs) are common following curative resection for colon cancer and may be associated with worse survival. There is limited data elucidating the mechanism of this association. Our objective was to examine the impact of SSIs on overall-survival (OS) as well as receipt of adjuvant chemotherapy following radical colon cancer resection. We hypothesized that patients with SSIs would have decreased OS, in part secondary to decreased rates of administration of adjuvant chemotherapy. Methods:

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A retrospective study using merged VASQIP-VA Cancer Registry data (1999-2009) was conducted. We examined 9,946 patients (≥ 18y) who underwent radical resection for non-metastatic (stage III) colon cancer. Patients were stratified by presence of SSI. Kaplan-Meier and Cox-regression analyses were performed. Subgroup analysis by stage was performed. Results: SSI occurred in 1,340 (14%) patients. Patients with SSI were slightly younger (p=0.001), had worse functional status (p=0.002) and higher ASA scores (p=0.001). SSI was associated with worse OS in the entire cohort. On stratified analysis, the difference was only significant in stage III patients (median OS 29.3 vs. SSI 33 months, p=0.0001). In addition, stage III patients with SSI were significantly less likely to receive adjuvant chemotherapy (54% vs. 42% p=0.002). On multivariate analysis, both SSI and failure to receive adjuvant chemotherapy were independently associated with worse OS (Table 1). Conclusion: SSI after radical resection for colon cancer significantly decrease OS, predominantly in stage III patients. Although SSIs reduce the rate of administration of adjuvant chemotherapy, the impact of SSI on survival is not entirely mediated by failure to receive adjuvant therapy.

Effect of Surgical Site Infection on Overall Survival (OS) in Stage III Colorectal Patients, with and without Adjuvant Chemotherapy (1)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical Site Infection</td>
<td>1.59</td>
<td>[1.32-1.90]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Failure to Receive Adjuvant Chemotherapy</td>
<td>1.57</td>
<td>[1.33-1.85]</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

1. No significance in HR with unadjusted inclusion of failure to receive adjuvant chemotherapy.

13 Neoadjuvant Pelvic Perfusion Provides Symptom Control and may Facilitate Resection of Pelvic Recurrent Rectal Cancer

H.J. Wanebo, G. Begossi, J. Belliveau, E. Gustafson, I. Surgery, Landmark Medical Center, Bristol, Puerto Rico; 2. Alta Bates Medical Center, Oakland, CA.

Background: Isolated pelvic perfusion (IPP) may improve disease control and facilitate pelvic resection in selected high-risk patients with advanced recurrent rectal cancer by reducing painful tumor burden and lessening chances of recurrence. Methods: IPP was done in 42 patients with locally advanced previously irradiated rectal cancer, 26 as preoperative therapy and 16 for palliation. A comparative larger non-perfused group included 63 patients with pelvic resection only via abdominal sacral resection (ABSR) for recurrent rectal cancer. Isolated pelvic perfusion (IPP), with a pump oxygenator, (temp > 410c), delivered sequential (q 10 minutes) chemotherapy: - 5FU Citiplatin / Oxaliplatin 100/150mg/m2, Mitomycin 10mg/m2, for 60 minutes in 42 patients Results: Palliative IPP in 16 advanced rectal cancer patients resulted in significant relief (1 – 4 months) of narcotic resistant pain (in 70%). Pre-operative IPP in 26 locally advanced rectal cancer patients achieved a clinical path (CR) in 2 patients, and significant regression in 11 patients rendering them resectable. Seven had RO pelvic resections. Of 6 other patients, 4 refused surgery, 2 were medically excluded. Median survival was 30 months in 7 resected patients (all had RO resections) and 2 were 5 year survivors. This is compared to outcome in 63 patients having pelvic resection alone for recurrence: 57 % had RO resection (median OS = 36 months), 28% had R1 resection (median OS = 15 months) and 15% had R2 resection (marrow invasion) (median OS = 21 months). Conclusions: Neoadjuvant IPP may facilitate resection of advanced or (borderline resectable) recurrent rectal cancer by reducing tumor bulk and identifying therapeutic responders likely to benefit from major pelvic resection while excluding non-responders mostly likely to benefit from non-surgical therapy. The potential to induce regression and facilitate RO resection merits further exploration.

14 Factors associated with 60-day Readmission following Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy

K. Kelly, L. Cajas, J. Baumgartner, A.M. Lowy, Surgery, UCSD, La Jolla, CA.

Introduction: Readmission rates following surgery are subject to scrutiny in efforts to control health care costs. The aim of this study was to define the 60-day readmission rate following cytoreduction and HIPEC at a high volume center and to identify factors associated with readmission. Methods: Patients who underwent complete cytoreduction and HIPEC at a single-institution from August 2007 through June 2014 were identified from a prospectively maintained database. Multiple preoperative and operative factors were analyzed for their ability to predict 60-day readmission following surgery. Results: A total of 250 patients were identified. Forty patients (16%) experienced readmission within 60 days of surgery. The most common reasons for readmission were infection and obstructive symptoms. On univariate analysis of continuous variables, age, body mass index, peritoneal carcinomatosis index (PCI), serum albumin, estimated blood loss, number of anastomoses, number of visceral resections, and operative time were not associated with 60-day readmission (Table). Initial postoperative length of stay was longer for patients readmitted within 60 days (median 12 days versus 9 days, p=0.013). Of categorical variables analyzed, including gender, histology, HIPEC agent, intraoperative transfusion, individual procedures performed during cytoreduction, adjuvant systemic therapy, and postoperative morbidity, only Charlson comorbidity index (CCI) and postoperative transfusion of blood products were associated with 60-day readmission (33% of readmitted group received blood products versus 16% of those not readmitted, p=0.049). Conclusions: Few measurable variables are associated with readmission following cytoreduction and HIPEC. Patients with high CCI, prolonged initial hospital stay, and those who require transfusion of blood products in the postoperative setting may be at increased risk of readmission within 60 days. Earlier or more frequent follow-up for high-risk patients may reduce readmissions.

<table>
<thead>
<tr>
<th>Variable</th>
<th>All (N=250)</th>
<th>Readmitted (N=40)</th>
<th>No Readmission (N=210)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53 (20-86)</td>
<td>52 (25-79)</td>
<td>53 (20-86)</td>
<td>0.862</td>
</tr>
<tr>
<td>BMI</td>
<td>27.7 (18.4-48.0)</td>
<td>27.8 (18.6-44.0)</td>
<td>27.7 (18.7-43.0)</td>
<td>0.970</td>
</tr>
<tr>
<td>PCI</td>
<td>14 (0-29)</td>
<td>14 (0-26)</td>
<td>14 (0-27)</td>
<td>0.684</td>
</tr>
<tr>
<td>Anatomopathy (p/dL)</td>
<td>4.1 (2.9-5.2)</td>
<td>4.2 (3.1-5.1)</td>
<td>4.2 (2.9-5.2)</td>
<td>0.638</td>
</tr>
<tr>
<td>Length of Stay (days)</td>
<td>11 (4-45)</td>
<td>12 (3-34)</td>
<td>9 (1-45)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

15 Modern Era Adjuvant Chemotherapy is associated with Improved Survival in Patients with Stage II Colon Cancer

L. Casadan, M. Aklilu, D. Villenes, G. Raucher, S. Freels, A.V. Maker, I. University of Illinois at Chicago, Chicago, IL; 2. Cretoics Cancer Center at Advocate Illinois Masonic Medical Center, Chicago, IL.

Introduction: Patients are often selected for adjuvant therapy after resection of stage II colon cancer based on the presence of poor risk factors. However, the survival advantage of chemotherapy in this population is unclear and there remains variation in clinical practice. Methods: The National Cancer Data Base was analyzed for colon cancer patients treated 1998-2006. The primary outcome was overall survival (OS) stratified by receipt of adjuvant chemotherapy. Additional variables included patient high-risk features, age, multi-agent chemotherapy, and diagnosis after 2004 when oxaliplatin was approved for adjuvant therapy. Demographic and disease information was compared using the Pearson X² test and binary logistic regression, effect size with Cramer’s V/phi for categorical variables, and survival data with Cox regression. Proliferation score weighting was utilized to account for the possibility of selection bias. Results: Of 1,078,091 patients with colorectal cancer, 153,110 stage II colon cancer patients met inclusion criteria. Mean age was 72, 46% were male, 84% stage IIA (AJCC 6th ed.), 9% stage IIB, and 20% received adjuvant chemotherapy. Predictors of receiving treatment included age<65, male gender, community treatment facility, geographical location, non-Medicare insurance, education level, and diagnosis before 2004. All patient subgroups analyzed experienced improved OS with adjuvant chemotherapy regardless of the number of high-risk features, age, multi-agent chemotherapy, or adjustment for covariates. Median OS was 13.2 years in the chemotherapy group and 7.0 years in the no-chemotherapy group (p< 0.001). Median and 5-year OS was improved in both high and low-risk patients who received chemotherapy compared to those who did not with a median follow-up >5 years. Conclusions: This large-scale, highly powered study with long-term follow-up demonstrated that adjuvant chemotherapy was associated with a clinically relevant improvement in OS regardless of treatment regimen, patient age, or high-risk features in patients with resected stage II colon cancer. The results of this analysis warrant further prospective investigation.
A Novel Inhibitor of the β-catenin Pathway in Colorectal Cancers that Targets Colorectal Stem Cells to Prevent Endothelial-to-Mesenchymal Transition (EMT) and Migration

P. White,1,4 C. Subramanian,1 B.M. Timmermann,2 H. Zhang,3 M.S. Cohen,1 1. Department of Surgery, University of Michigan, Ann Arbor, MI; 2. Department of Medicinal Chemistry, The University of Kansas, Lawrence, KS.

Background: Cancer stem cells (CSCs) in colorectal cancer (CRC) contribute to tumor aggressiveness (invasion, metastasis) and drug resistance, yet no clinical therapies specifically target this cell population. Withanolides are novel anticancer drugs inhibiting the chaperone function of HSP90 by blocking CDC37 binding. As β-catenin and CSC markers (CD133 and Bmi-1) are clients of HSP90 chaperone function, we hypothesize that a novel potent withanolide, withanoligolide A-triacetate (WGA-TA), targets the β-catenin pathway and these key CSC functional proteins leading to effective removal of CSCs, tumor apoptosis, and decreased EMT and migration. Methods: Validated human CRC cell lines (SW480, SW620 and HCT116) were treated with WGA or its triacetate derivative, WGA-TA, at 1 to 5 μM concentrations for 24h. Expression levels of CSC marker CD133, and cell viability of treated cells were compared to controls by flow cytometry (FC). Proteins involved in CSC maintenance and EMT were assessed by Western blot. Migration and invasion was analyzed by Boyden chamber assays. Results: By FC, WGA-TA treatment of SW620 (CD133+ cell line) showed a dose-dependent reduction in live CD133+ (24% at 1 μM to 80% at 5 μM WGA-TA; p<0.02 vs control) with significant induction of apoptosis vs. controls across all cell lines confirmed by western blot for PARP cleavage (p<0.001). At 5 μM WGA-TA, β-catenin pathway proteins were significantly inhibited [Akt and Axin-2 by 85%, phospho-Akt by 90%, c-Myc by 70%, GSK3β by 55%, and p-GSK3β by 45%] as were CSC regulatory proteins Bmi-1 by 80% and EZH2 by 85% while the epithelial marker e-cadherin was increased by 800% (p<0.01 vs WGA and p<0.001 vs control). Finally at only 2.5 μM WGA-TA treatment, migration and invasion were reduced by >90% vs. WGA (p<0.02) and controls (p<0.01). Conclusions: WGA-TA represents a novel therapy for CRC that effectively targets tumor cells and the function of CRC stem cells. This targeted inhibition of key CSC and regulatory proteins including β-catenin, Bmi-1 and EZH2, lead to significantly decreased CSC EMT and invasion warranting future translational studies.

Serious postoperative Complications Affect Early Recurrence after Cytoadjuvant Surgery and HIPEC for Colorectal Peritoneal Carcinomatosis


Introduction. The prognosis of patients with peritoneally metastasized colorectal cancer has improved significantly with the introduction of cytoadjuvant surgery followed by hyperthermic intraperitoneal chemotherapy (CRS+HIPEC). Although a macroscopically complete resection is achieved in nearly every patient, recurrence rates are high. This study aims to identify risk factors for early recurrence, thereby offering ways to reduce its occurrence and improving the tools for optimal patient selection. Methods. All patients with colorectal peritoneal carcinomatosis referred to a tertiary referral hospital in the Netherlands between June 2007 and April 2013 were analysed retrospectively. Patient data were collected between patients with or without recurrent disease within 12 months after CRS+HIPEC. Results. A complete macroscopic cytoreduction was achieved in 96% of all patients treated with CRS+HIPEC. Forty-six of 133 patients (35%) developed recurrent disease within 12 months. A serious adverse event (SAE) grade 3 or higher after CRS+HIPEC was the only significant risk factor found for early recurrence (OR=2.3, p=0.046). Median survival in the early recurrence group was 19.3 months, compared to 43.2 months in the group without early recurrence (p=0.001). Patients with SAEs showed a reduced survival compared to patients who did not suffer such complications (median survival 22.1 vs. 31.0 months, respectively, p=0.02). Conclusion. Early recurrence after CRS and HIPEC is associated with a significant reduction in overall survival. This study identifies post-operative complications requiring intervention as the only significant risk factor for early recurrence, independent of the volume of peritoneal disease, highlighting the importance of minimizing the risk of post-operative complications.

Fluorescent Imaging Agent to Detect Cancer during Surgery

M.J. Whitley,1* D.M. Cardona,1 D.G. Blazer,2 E. Wang,3 R.A. Gremm,1 P.J. Mosca,1 J. Cahill,1 J.K. Mito,1 K.C. Cuneo,1 N. Larrier,1 E. O’Reilly,1 I. Spasojevic,1 R.F. Riedel,1 W.C. Eward,1 L.G. Griffith,2 M.G. Bawendi,1 D.G. Kirsch,1 B.E. Briggman,1 1. Duke University Medical Center, Apex, NC; 2. Massachusetts Institute of Technology, Cambridge, MA.

Introduction. Intra-operative detection of residual disease in the tumor bed can be used to decrease the risk of a positive surgical margin and reduce the rate of re-excision. LUM015 is an imaging agent containing a fluorophore and a quencher connected via a protease-sensitive peptide. Upon cleavage of the molecule by cathepsin proteases in the tumor, the quencher is released, allowing fluorescence to be detected. A phase I clinical trial was recently completed to test the safety of LUM015 in human patients with cancer. Methods. This open-label nonrandomized trial compared 3 dose cohorts (0.5, 1.0, and 1.5 mg/kg) of LUM015 in order to determine a safe dose of LUM015 that labels tumors in humans. Subjects with soft tissue sarcoma (STS) or breast cancer received IV LUM015 prior to surgical resection approximately 6 or 30 hours later. Safety evaluations were completed prior to, during, and after study agent delivery with the last adverse pharmacological activity (APA) assessment completed 30-35 days after surgery. Pharmacokinetic (PK) parameters were determined and quantitative fluorescence imaging of the resected tissues was performed. Results A total of 15 subjects (12 STS, 3 breast) completed the study without APA. Tumor to normal tissue fluorescence ratios ranged from 1 to 13 and tumor fluorescence was significantly higher than corresponding normal tissue from the same patient (p=0.0001). Furthermore, within the study population, the distribution of tumor fluorescence values was significantly higher than those recorded for fat or muscle (P=0.05). Tissue fluorescence appeared to be dose-independent across the 3 tested doses, but there was a trend for higher tumor fluorescence at 6 hours versus 30 hours post LUM015 injection. LUM015 plasma PK revealed a multiphasic concentration/time profile and linear dose-dependence, with only 2% of the administered probe remaining after 48 hours. Conclusion: LUM015 specifically labels tumors in human patients and all 3 doses were safe and tolerable. These findings support future studies coupling LUM015 with a novel intraoperative imaging device to detect residual cancer and guide surgical excision.

Background: Undifferentiated pleomorphic sarcomas (UPS) are a diagnosis of exclusion and present a diagnostic and therapeutic challenge. Therefore, identification of novel molecular markers is critical. The aim of this study was to correlate clinicopathologic variables, expression of tyrosine kinase receptors, and markers of cell cycle progression and survival with oncologic outcomes. Methods: A tissue microarray containing 219 UPS was constructed and analyzed by immunohistochemistry for protein expression. Staining results were correlated with clinicopathologic features and survival. Univariate and multivariate analyses were conducted to assess potential associations between expression of protein markers and overall survival (OS). Results: Of the 219 tumors examined, 179 (81.7%) were sporadic and 40 (18.3%) were radiation-associated (RAS) in patients with a median age of 61 years. 71.7% (n=157) of tumors were located in the extremity and the majority of those lesions were deep (86.8%; n=190). At a mean follow-up of 5.9 years, median OS was 8.9 years. Univariate analysis of clinicopathologic factors demonstrated reduced OS for patients with age >61 (p=0.001), RAS (p=0.0001) and tumor size >10cm (0.002). At the protein level, expression of low pEGFR (p=0.026), negative PTEN (p=0.001), positive IGFIR (p=0.049) and high AKT (p=0.026) were associated with reduced OS. PCNA, MET, PDGFRβ, MEK and pMEK were expressed strongly by >80% of the samples and were thus unable to be correlated with OS. An additional 13 commonly-mutated proteins were evaluated and were not found to be statistically significant for OS (Table 1). Multivariate analysis of OS of all clinicopathologic and protein variables with a p<0.1 demonstrated that age >61 (p=0.001), tumor size >10cm (p=0.038), low pEGFR status (p=0.019), and high pAKT expression (p=0.03) were associated with reduced OS. Conclusion: This study identifies several molecular markers and clinical factors associated with OS in patients with UPS. Further characterization of the markers may lead to improved understanding, diagnosis and development of targeted therapies in this sarcoma subtype.

20 The Use of Human Acellular Dermal Matrix (ADM) Seeded with Patient-autologous Fibroblasts to Cover Soft Tissue Defects in Irradiated Areas E. Roessner, M. Vitacolonna, M. Smith, J. Brune, P. Hohenberger, J. Dept of Surgery, Mannheim University Medical Center, University of Heidelberg, Germany, Div. of Surgical Oncology and Thoracic Surgery, Mannheim, Germany; 2. Deutsches Institut für Zell- und Gewebeersatz, Berlin, Germany.

Objective: Resection of large soft tissue areas causes defects and leave vital structures as vessel and nerves uncovered, requiring plastic surgery repair often in combination with artificial grafts. In irradiated (RT) areas no secondary wound healing can be expected. Degradation and infection is a constraint in engineered constructs. We developed a biological carrier composed of human allogeneic acellular dermis (ADM). Methods: Initially, a mouse model with defined resection of gluteus muscles +/- RT and replacement with ADM +/- fibroblast culture was used to determine wound breaking strength and MRI analysis of the graft incorporation. Human derived transplant recovered from screened consenting donors retain native extracellular matrix structure. Histology revealed normal appearance of the reticulized dermis, presence of laminin-6 and collagen-IV and typical collagen bundles of the papillary dermis and absence from donor cells. ADM was used as scaffold to be seeded with autologous fibroblasts offering a natural environment to expand. Human dermal fibroblasts were incubated in collagenase, filtered, centrifugated, resuspended, seeded, and populated the reticulized size of the ADM (density 15,700 cells/cm²). Results: ADM matrices were used up to a size of 10” by 12” in 57 patients who suffered from soft tissue sarcoma of the abdominal or chest wall, sternal tumors, breast radiation-induced sarcoma, or osteosarcoma. In 27 pts. the anatomical site had undergone significant RT (50.4 to 92 Gy total dose). Sites were abdominal wall (n=7), chest wall (n=7, plus titanium struts n=3), sternum/pericardium (n=4, struts n=3), recto-vesical space (n=4), extremities (n=5). Clinical results (median follow-up 29 mos): 24/27 grafts showed an uneventful ingrowth. There were two partial and one complete graft loss. Conclusion: ADM is an excellently suitable human scaffold with the potential for a revascularisation and wound integration. The results in heavily pretreated soft tissue areas were very satisfying with no long-term problems of shrinkage or displacement. ADM offers a tool to close wound defects even after prior radiation therapy.

21 Is less Really more for Retroperitoneal Sarcoma? A NSQIP Analysis of 1,018 Patients J.W. Harris,* D. Davenport, P.C. McGrath, C.D. Tseng. General Surgery, University of Kentucky, Lexington, KY.

Introduction: Due to high local recurrence rates of retroperitoneal sarcoma (RPS), some clinicians argue for balancing the surgical morbidity of aggressive concomitant organ resection (COR) and realistic tumor biology. The primary aim of this study was to identify which organ resections increase major morbidity (MM) and mortality in RPS resection. Methods: The National Surgical Quality Improvement Program (NSQIP) database was queried for radical resections of retroperitoneal tumors in 2005-2012. Years were grouped as 2005-08, 2009-10, and 2011-12 for trends. “Major” COR included the following: colon, small bowel, vasculature, pancreas, diaphragm, liver, spleen, stomach. Nonparametric tests were used to compare rates of 30-day MM and mortality for various COR. Multivariate models were used to analyze the impact of each COR on MM and mortality, adjusting for perioperative variables. Results: The 1,018 total patients represented just 0.07% of all general surgery procedures nationally. Major COR increased over the study period (51.6% vs. 76.8%, p=0.010) with low 30-day mortality (1.6%, no trend, p=0.812). 30-day MM was 18.8% (no trend, p=0.315). Univariate analyses showed the following COR were associated with MM: colon (p<0.001); small bowel, vascular, pancreas (all p<0.01); diaphragm, liver, spleen, stomach (all p<0.05). Nephrectomy did not increase MM or mortality. Multivariate analysis identified the following risk factors for MM: male gender (OR-1.48, p<0.001), lack of functional independence (OR-2.87, p=0.033), bilirubin>1mg/dL (OR-2.13, p=0.020), body mass index (kg/m²)(BMI <18.5, OR-2.92, p=0.034; BMI 35.1-40, OR-1.87, p=0.021), operative duration (per min, OR-1.003, p=0.001), any perioperative transfusion (OR-2.46, p<0.001), and colon resection (OR-1.73, p=0.003). Conclusions: In this national dataset, colon resection was the only COR independently associated with MM. While the oncologic value of aggressive COR remains under debate, MM is dependent on preoperative patient factors, longer operations, and transfusions needs, rather than most COR. When
clinically indicated, experienced RPS surgeons should not hesitate to perform COR to ensure a margin-negative resection.

22

A Meta-analysis of the Association between Radiation Therapy and Survival for Surgically Resected Extremity and Trunk Soft Tissue Sarcoma

Methods: A systematic review using a priori search, inclusion and exclusion criteria was conducted of Pubmed, Embase, Web of Science and Cochrane databases. Odds ratios for mortality at 5 years were calculated when possible from the raw data. Hazard ratios were used for studies reporting time to event data. A bias score was formulated for each study as the product of the margin status and tumor grade between the exposure and control groups. This score was used as a moderator in subgroup analyses, with a low score suggesting a low risk of bias and vice versa. Results: Initial search identified 527 studies, of which 18 studies met our selection criteria after screening. The pooled estimate of the odds ratio for mortality at 5 years in patients receiving radiation in all studies combined was 1.06 (95% CI 1.08-1.27), and was not significantly different from the null when studies at high and low risk for bias were analyzed separately. The pooled estimate for the hazards ratio for mortality was 0.81 (95% CI 0.68-0.95) in favor of a protective effect of radiation therapy compared to patients not undergoing radiation. This estimate was different for the one study at high risk of bias (HR 1.41; 95% CI 1.01-1.99) compared to the remaining studies which were collectively judged to be at low risk of bias (HR 0.68; 95% CI 0.58-0.82). Measures of heterogeneity were a Q statistic of 4.35 (p = 0.226) and an I² value of 31%. Significant publication bias was not seen. Conclusions: When studies reporting hazard ratios are considered, radiation therapy for surgically resected extremity and truncal STS confers a 19% improvement in mortality. Studies in which odds ratios are considered, radiation therapy for surgically resected extremity and truncal STS confers a 19% improvement in mortality. Studies in which odds ratios were calculated from event data and those judged to be at high risk of bias did not show the same benefit, likely due to confounding by indication.

23

The Effect of Neoadjuvant Therapy on Lymph Node Harvest for Patients undergoing Transhiatal Esophagectomy for Cancer

Background: Neoadjuvant therapy has been shown to negatively affect lymph node harvest in cancers such as colorectal and breast. For esophageal cancer, current recommendations suggest that retrieval of ≥15 nodes during esophagectomy is associated with better overall survival. However, most published studies have examined patients who have not undergone neoadjuvant therapy. It is unclear if neoadjuvant treatment affects lymph node harvest in esophageal cancer patients or if extended lymphadenectomy still provides a survival benefit. Methods: Data from a prospectively maintained database of esophagectomies performed for cancer (1999 – 2012) was analyzed. 349 patients had a transhiatal esophagectomy (THE) with standard lymphadenectomy after receiving neoadjuvant chemotherapy alone (CA) [n = 199], chemoradiotherapy (CRT) [n = 54] or no neoadjuvant therapy (NA) [n = 96]. Nodal harvest was recorded and overall survival was followed up to 5 years post-operatively. Results: Lymph node harvest did not decrease with neoadjuvant therapy and was actually greater in the CA group when compared to CRT and NA (14.6 ± 0.6 vs. 11.7 ± 0.9 vs. 11.4 ± 0.7, p = 0.01). Analysis of patients with <15 or ≥15 nodes in each group showed that the 1, 3 and 5 year survival rates were not statistically improved with greater lymph node harvest (Table). Additionally, patients were stratified according to a ratio of lymph node metastasis to total nodes examined of ≤0.2 versus >0.2 (a previously published poor prognostic factor). There was a significant survival advantage for all three groups with a ratio <0.2 (Table). Conclusions: In patients undergoing THE, neoadjuvant therapy did not have a deleterious effect on lymph node harvest. Retrieval of ≥15 lymph nodes, although previously shown to improve survival, did not affect outcome in the setting of neoadjuvant therapy. Having a greater ratio of positive to total lymph nodes harvested did portend a worse survival. The benefit of lymphadenectomy in patients undergoing neoadjuvant therapy may lie mostly within its ability to improve staging.
Sarcopenia is indirectly a component of frailty assessment, which predicted worse surgical outcomes in several studies. However, in this study low TPA was significantly associated with shorter operative time and less incidence of anastomotic leakage in esophageal patients. Further research is needed to confirm clinical significance of sarcopenia in patients with esophageal cancer.

25 Complete Pathologic Response is Independent of the Timing of Esophagectomy and is Predictive of Improved Survival following Neoadjuvant Chemoradiation for Esophageal Cancer S. Singla,1,2* M. Kuukar,3 R.M. Alnajj3; W. Du,4 K. Attwood,5 H. Nava,6 S.J. Nurkin,7 B.W. Karges8; S. Hochholzer1,2.1 Surgical Oncology, Rutgers Park Cancer Institute, Buffalo, NY; 2. University at Buffalo, Buffalo, NY.

Introduction: The relationship of complete pathologic response (cPR) after neoadjuvant chemoradiation (nCRT) with the timing of esophagectomy is not well defined. We sought to determine if a delay in esophagectomy after nCRT would result in increased likelihood of cPR and therefore, improve survival. Methods: A single institution analysis of all patients treated with nCRT and esophagectomy between 2004 and 2014 was conducted. Patients were divided into two groups based on timing of surgery (<50 days (Early) and >50 days (Delayed)) from completion of nCRT. Patient and treatment characteristics were compared across using Wilcoxon rank sum and fisher’s exact tests. Survival outcomes were evaluated using standard kaplan-meier methods, with multivariate analyses utilizing cox-proportional hazards models. Results: 227 patients (M: 211, F: 16; median age, 61 years) were included in the study. 52 (23%) patients (early group) were compared to 175 patients (77%) (delayed group). The 2 groups were similar with respect to age, sex, comorbid conditions, ECOG status, location, grade and histology of tumor. Patients in the early group had a higher percentage of cPR (27% vs 19%, p=0.242). Amongst all cPR, response rate was statistically higher for squamous cell histology and tumors in mid esophagus. Patients in delayed group had a nonstatistical increase in the incidence of anastomotic leak, conduit necrosis, need for reoperation, and pulmonary complications. Median follow up was 52 months (range 2 months to 110 months). 3 year overall and recurrence free survival was similar in both groups based on timing of esophagectomy but was statistically higher for patients with complete pathologic response. On multivariate analysis, lower age, absence of signet cell histology, better ECOG status, lower length of stay and complete pathological response were independent predictors of improved overall survival. Conclusion: This analysis of a large cohort of patients with esophageal cancer undergoing trimodality therapy highlights that complete pathologic response is independent of the timing of esophagectomy.


Introduction: Esophagectomy is a procedure that is associated with significant morbidity, necessitating research in novel methods to minimize morbidity. Recently, an association between perioperative fluid administration and postoperative complications in patients undergoing major gastrointestinal abdominal surgery has been identified; however, studies focusing on esophagectomy have been limited primarily to transthoracic esophagectomy. Transhiatal esophagectomy is associated with shorter operative times, which may impact intraoperative fluid management. We sought to investigate the relationship of intraoperative fluid administration to perioperative outcomes in patients undergoing transhiatal esophagectomy. Methods: 211 patients who underwent transhiatal esophagectomy for esophageal carcinoma from 2000-2013 at a single tertiary university center were identified from a retrospective database. Clinical and pathologic variables were recorded and analyzed. Perioperative outcomes were compared, including complications per patient and complication severity (by Clavien-Dindo grade). Results: In the patient cohort, 84% were male, and the median age was 63 (range 40-82). 74% of patients underwent transhiatal esophagectomy for esophageal adenocarcinoma. Median length of stay was 9 days (range 5-107), and 27% of patients experienced major complications at 90 days (Clavien-Dindo grade of 3-5). Perioperative mortality was 1%. Univariate and multivariate analyses were performed comparing independent perioperative variables to the following outcomes: length of stay, 30-day mortality, complications per patient, major complications, and Clavien-Dindo grade. While a number of variables were associated with outcomes on univariate analysis (see Table), only intraoperative crystallloid administration and a history of smoking were significantly associated with complications per patient on multivariate analysis. Conclusion: Intraoperative fluid administration is associated with perioperative morbidity in patients undergoing transhiatal esophagectomy for esophageal carcinoma.

27 Identical MicroRNA Signatures of Adenocarcinoma and Squamous Cell Carcinoma Subtypes of Cancers of Different Organs R. Mallick,1* C. Jahansouz,1 E.D. Kannisto,2 S.K. Patnaik,2 1. University of Minnesota, Minneapolis, MN; 2. Roswell Park Cancer Institute, Buffalo, NY.

INTRODUCTION: Adenocarcinoma (AC) and squamous cell carcinoma (SCC) tumors of different organs have common features, such as glandular organization of cells in AC and keratinization in SCC, and expression of mucins in AC and P63 in SCC. MicroRNAs, ultra-short RNAs that act as genetic regulators, have been found to be useful biomarkers for a variety of purposes. Given the similarity of AC or SCC subtypes of tumors of different organs, we hypothesized that each of these subtypes is associated with a distinct microRNA expression profile regardless of the organ of origin of cancer, and that some of the histotype-related microRNAs may also be associated with squamous or adenomatous (columnar) histology of non-cancerous epithelia. METHODS: MicroRNA expression data was obtained from the Cancer Genome Atlas (TCGA) project for cervical (n = 74), esophageal (n = 22), and lung (n = 653) AC and SCC, and analyzed for differential expression. Published literature was reviewed for the differential expression of microRNAs in columnar epithelium of Barrett’s esophagus compared to normal, squamous esophageal epithelium. Squamous trans-differentiation of cultured normal human bronchial epithelial (NHBE) primary cells and BEAS-2B cell-line was induced in vitro with serum or transforming growth factor-b1 (TGF-b1) to identify changes in microRNAs that accompany the change in histology. RESULTS: A microRNA pattern distinctly associated with AC or SCC subtypes of cancer regardless of tumor site was identified. This pattern was also noted in a comparison of normal squamous and Barrett’s columnar esophageal epithelia (table), and partially observed during serum- or TGF-beta-1-induced squamous trans-differentiation of normal lung epithelial cells. CONCLUSIONS: These observations suggest that specific microRNAs play a universal role in the generation or maintenance of squamous or adenomatous histologies in both cancerous and normal epithelial cells. These microRNAs can be useful for the development of methods to identify AC and SCC subtypes of cancer and for our understanding of their genesis.

Log2(fold-change) values of histology-associated microRNAs

<table>
<thead>
<tr>
<th>MicroRNA</th>
<th>Cervix</th>
<th>SCC vs. AC</th>
<th>Normal vs. Barrett’s esophagus</th>
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<tr>
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<td>miR-944</td>
<td>5.0</td>
<td>5.2</td>
<td>4.6</td>
</tr>
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</table>

Table. Univariate analysis of perioperative variables and outcomes *p<0.05 on multivariate analysis
28 Prognostic Value of Combined Clinical and Pathologic Staging Variables in Predicting Local-regional Recurrence following Neoadjuvant Chemotherapy for Breast Cancer M. Teshome,* S. Tucker, K.K. Hunt, E.A. Mittendorf, Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.

Background We previously defined and validated a novel scoring system incorporating the American Joint Committee on Cancer (AJCC) clinical stage, final AJCC pathologic stage, estrogen receptor status and nuclear grade (CPS+EG score). The CPS+EG score is associated with breast cancer specific survival outcomes in patients treated with neoadjuvant chemotherapy (NCT). The current study was undertaken to determine if the CPS+EG score could stratify patients with respect to local-regional recurrence (LRR).

Methods Patients receiving NCT between January 1997 and December 2005 were included. The current study was undertaken to determine if the CPS+EG score is associated with breast cancer specific survival outcomes in patients treated with neoadjuvant chemotherapy (NCT). The current study was undertaken to determine if the CPS+EG score could stratify patients with respect to local-regional recurrence (LRR).

Results A total of 1736 patients treated with neoadjuvant chemotherapy were identified. BCT and mastectomy followed by postmastectomy radiation therapy (PMRT), was also recorded. A multivariate analysis that included CPS+EG score and local therapy was performed to evaluate for association with LRR. Results A total of 1736 patients treated with neoadjuvant chemotherapy were identified. BCT was performed in 659 (38%), mastectomy in 330 (19%) and mastectomy + PMRT in 747 (43%). At a median follow up of 51 months (range 4 – 113), the crude incidence of LRR was 117 (6.7%). Freedom from LRR at 5 years ranged from 87-97% by clinical stage, 86-97% by pathologic stage and 72-99% by CPS+EG score (figure). On multivariate analysis, CPS+EG score and type of surgery were independently associated with LRR, with increased risk among patients with CPS+EG scores of 2 or greater (HR 3.63, 95% CI 1.64-8.05) or mastectomy alone (HR 2.20, 95%CI 1.43-3.39). Risk was further increased in patients with CPS+EG scores of 4 or higher (HR 3.04, 95% CI 2.03-4.54) or 6 (HR 2.95, 95% CI 1.40-6.23).

Conclusion The CPS+EG scoring system better stratifies patients with respect to LRR after NCT than presenting clinical or final pathologic stage. For patients with CPS+EG scores >4, PMRT decreases the likelihood of LRR after mastectomy.


Introduction: We have demonstrated a dramatic loss of anti-HER2 CD4 T-helper type 1 responses (Th1resp) in HER2+ invasive breast cancer (IBC) pts compared with healthy controls. Pathologic complete response (pCR) to neoadjuvant trastuzumab/chemotherapy (T/C) confers an improved prognosis in HER2+ IBC. We examined differences in anti-HER2 Th1resp between pCR and pCR pts following neoadjuvant T/C. Methods: Th1resp were generated from PBMCs pulsed with 6 HER2 class II peptides by measuring IFN-γ production via ELISPOT, and compared between HER2+ IBC groups. Th1resp metrics were anti-HER2 responsivity, no. of reactive peptides (repertoire), and cumulative response across 6 peptides (spots/10⁶ cells). Th1resp of IBC pts (n=11) receiving neoadjuvant HER2-pulsed dendritic cell vaccination were analyzed pre-post-immunization. Results: The study comprised 77 pts. Depressed anti-HER2 Th1resp in untreated HER2+ IBC pts (n=21) – assessed by responsivity, repertoire, or cumulative response – did not improve in T/C-treated IBC pts (n=56, p>0.05); however, HER2 vaccination significantly restored responsivity (18 vs 91%, p=0.004), repertoire (0.3 vs 3.7, p=0.001), and cumulative response (29.7 vs 162.8, p<0.001). Among T/C-treated pts, neoadjuvant T/C (n=31; 55.4%) was associated with higher repertoire (1.5 vs 0.7, p=0.05), but not cumulative response or responsivity, compared with adjuvant T/C (n=25). While pCR (n=13) and pCR (n=18) pts did not differ across pCR clinical characteristics, pCR pts were more likely to have ER_ tumors (69 vs 28%, p=0.03). pCR pts demonstrated dramatically higher responsivity (92% vs 33% vs 38%, p=0.002), repertoire (3.3 vs 0.2 vs 0.6, p<0.001), and cumulative response (155.7 vs 18.7 vs 33.5, p<0.001) vs pCR and untreated pts. This disparity was not attributable to pCR pts’ immune incompetence or increase in suppressive (Treg/MDSC) populations, but associated with shifts in IFN-γ/IL-10-producing phenotypes (Fig). Conclusion: Restored anti-HER2 Th1resp strongly correlate with pCR after neoadjuvant T/C. In high-risk pts, augmenting Th1 immunity via neoadjuvant HER2 vaccination may improve pCR rates and long-term outcomes.

30 TFAP2C Regulates Luminal Breast Cancer Growth through EGFR and is a Target for Vandetanib J. De Andrade,* J.M. Park, T. Wu, A. Lorenzen, M. Kulak, P. Spanheimer, R.J. Weigel. Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA.

Background: TFAP2C regulates luminal breast cancer development in part through RET; however additional mechanisms of action remain unaccounted. We sought to identify these mechanisms and to characterize treatment response through TFAP2C. Methods: Gene knockdowns (KD) were created in several luminal breast cancer cell lines using siRNA or shRNA. Profiling was performed by western blot, IHC, qPCR, MTT, and ChIP-seq. Nude mice tumor xenografts were created using MCF-7 inoculations. Statistical comparisons were made by t-test and log-rank. Results: Transient TFAP2C KD in MCF-7 and BT-474 reduced in vitro proliferation (19%, 48%, p<0.01). This was again demonstrated in vivo as stable TFAP2C KD in MCF-7 resulted in reduced mean xenograft volume at 16 days (840 mm³ vs 52.5 mm³, p=0.013) and 30% reduced Ki67 staining (p<0.01). TFAP2C KD resulted in decreased expression of EGFR in MCF-7, BT-474, and ZR-75-1 at both the mRNA and protein levels. This is due to direct transcriptional regulation as several TFAP2C binding peaks are found within the EGFR gene by ChIP-seq. mRNA and protein levels. This is due to direct transcriptional regulation as several TFAP2C binding peaks are found within the EGFR gene by ChIP-seq. Methods: A. Lorenzen, J.M. Park,* R.J. Weigel. Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA.

Abstracts: Plenary and Parallel Sessions S15
S16 Abstracts: Plenary and Parallel Sessions

Surgery, University of Pennsylvania, Philadelphia, PA.

J. Datta
cell (DC) vaccine shown to induce immune and clinical responses in HER2pos
HER-2 Pulsed Dendritic Cell Vaccination Augments HER-2
vandetanib (mean 7.9% reduction, p = NS). KD of RET or EGFR, but dual RET and EGFR KD eliminated the effect of vandetanib (mean 7.9% reduction, p < 0.01). While still significant, vandetanib’s effects were blunted in cells with KD of RET or EGFR, which contributes to growth and sensitivity to vandetanib independent of RET. Vandetanib may be a viable novel chemotherapeutic agent in luminal breast cancer, and RET and EGFR may serve as molecular markers for response to vandetanib.

HER-2 Pulsed Dendritic Cell Vaccination Augments HER-2

31

Immunity and Clinical Response Regardless of Injection Route in DCIS
Surgery, University of Pennsylvania, Philadelphia, PA.

Methods: Patients with HER2+ DCIS (n=37), or incidentally discovered Stage I invasive breast cancer at surgery (n=10), received 6 weekly injections either in groin nodes (IN), affected breast (B) or both (IN/B) prior to surgery. CD4 T-cell responses were detected by IFN-γ production to 6 HER2 Class II peptides by ELISPOT, and CD8 T-cell responses to one HLA-A2 peptide by ELISA. A positive response was defined as at least a two-fold increase in IFN-γ secretion pre- to post-vaccination. Four measures were analyzed: 1) overall response rate, 2) cumulative peptide response, 3) response repertoire (i.e. no. of responding peptides), and 4) fold-change pre- to post-vaccination. Results: Forty-three of 47 (95.7%) patients mounted a CD4 T cell response post-vaccination. There was no significant difference in overall CD4 response rate (94% vs. 94% vs. 83%, p=0.55), cumulative response (272.6 vs. 194.4 vs. 188.2, p=0.22), peptide response repertoire (3.4 vs. 2.9 vs. 2.8, p=0.54) or fold-change in response (5.6 vs. 4.0 vs. 5.0, p=0.71) between IN, B or IN/B injection routes, respectively. Seventeen of 19 (73.7%) HLA-A2+ patients mounted a CD8 T cell response post-vaccination. No significant difference in overall CD8 response rate (60% vs. 83% vs. 75%, p=0.67) or CD8 peptide response rate (4,488 vs. 7,494 vs. 6,052, p=0.66) was observed between IN, B or IN/B, respectively. Subgroup analysis of DCIS patients revealed a trend toward stronger CD4 cumulative responses in the IN group, but this did not reach statistical significance (304.1 vs. 208.3 vs. 171.6, p=0.13). There was no difference in complete pathologic response between vaccination routes (29.4% vs. 22.2% vs. 16.7%, p=0.70). Conclusion: HER-2 pulsed DC1 vaccination induces both strong T cell responses and clinical response in patients with DCIS and early invasive breast cancer supporting further clinical development.


Abstracts: Plenary and Parallel Sessions

1. Women’s Oncology, Women & Infants Hospital, Providence, RI; 2. MD Anderson, Houston, TX; 3. Alpert Medical School of Brown University, Providence, RI; 4. Brown University, Providence, RI; 5. Greater Baltimore Medical Center, Baltimore, MD; 6. Pennsylvania Hospital, Philadelphia, PA.

Objectives: The treatment of breast cancer has been shown to be associated with a decline in sexual function. While many studies have evaluated effects of systemic agents on sexuality, few have examined the role of surgery. With...
increasing rates of mastectomy and advances in reconstructive techniques, we sought to evaluate the impact of the modality of breast surgery on survivors’ sexual function. Methods: A survey including 7 investigator generated questions with the validated Female Sexual Function Index (FSFI) was administered to women who underwent breast cancer surgery at an academic oncology program from 2000-2012. We examined the association between the surgical modality and women’s responses with specific survey responses and the overall FSFI score. The Kruskal-Wallis test was used to analyze FSFI scores and Chi-square or Fisher’s exact test were used for categorical data. Results: 268 patients completed the survey. 67.9% underwent lumpectomy (L), 20.5% mastectomy with reconstruction (MR), and 11.6% mastectomy alone (M). Women who had L were significantly more satisfied with their chest appearance than MR (80.8% vs. 67.3%, p = 0.04), M (80.8% vs. 48.4%, p = 0.0004). Median FSFI scores were similar among modalities (L: 28.1, MR: 27.5, and M: 26.5, p = 0.9). However, patients who were more satisfied with their chest appearance had significantly better sexual function than those who were not (29.1 vs 22.0, p = 0.0001). Though the treated breast was equally a part of intimacy for L and MR patients (62.3% and 66%, p = 0.9), those who were treated with L reported more breast specific pleasure than those who had undergone MR (52% vs 28.6%, p = 0.007). Conclusion: While the surgical approach does not impact a woman’s overall survival, the modality of breast cancer surgery can impact self-satisfaction and consequently sexual function. The treated breast can be part of intimacy similarly for L and MR patients, yet L patients are almost twice as likely to experience breast specific pleasure. By helping patients select the surgical modality most likely to lead to personal satisfaction and fulfillment, breast surgeons have a unique opportunity to contribute to improved survivorship outcomes.

34 The Incidence of Adjacent Synchronous Invasive Carcinoma and/or DCIS in Patients with Lobular Neoplasia on Core Biopsy: Results from a Prospective Multi-institutional Registry (TBCRC 020) F. Nakhlis,* L. Gilmore, R. Gelman, T.A. King, L. Bedrosian, K. Ludwig, H. E. Hwang, S. Wiley, C. Hudis, J. Iglchlan, E. Lawler, N. Ryabin, M. Goldstein, B. Schmitt, J. Bracamontes and W. Ross. Memorial Sloan Kettering Cancer Center, Boston, MA; 2. Mount Auburn Hospital, Cambridge, MA; 3. Dana Farber Cancer Institute, Boston, MA; 4. Memorial Sloan Kettering Cancer Center, New York, NY; 5. MD Anderson Cancer Center, Houston, TX; 6. Indiana University Purdue University Indianapolis, Indianapolis, IN; 7. Georgetown University Medical Center, Washington, DC; 8. Duke University Medical Center, Durham, NC; 9. Beth Israel Deaconess Medical Center, Boston, MA.

Background Lobular neoplasia (LN) is a spectrum of atypical proliferative lesions that includes atypical lobular hyperplasia (ALH) and lobular carcinoma in situ (LCIS). The need for excision of LN identified on core biopsy (CB) is controversial, with 0-50% reported rates of upgrade to cancer. We conducted a prospective multi-institutional trial through the Translational Breast Cancer Research Consortium (TBCRC 020) to determine the frequency of invasive cancer and/or DCIS following excision of LN diagnosed by CB of a mammographic abnormality. Methods Following a CB diagnosis of LN, patients underwent wire guided excision; upgrades to invasive cancer and/or DCIS at excision were recorded. Both the core and the excisional biopsy underwent central pathology review at DF/HCC. All cases had BI-RADS scores of 4 or less and showed radiologic-pathologic concordance. Confidence intervals were calculated using the binomial. The study was conducted initially at the Dana Farber/Harvard Cancer Center (DF/HCC) and since 2012 expanded to TBCRC sites. Results Of 79 registered patients, 2 were unable to have surgery and 77 had surgery as planned (median age 51 yrs, range 27-82). Core biopsies were available for central pathology review in 76 cases and LN was confirmed in 74; in 1 case no LN was seen in the CB and in 1 invasive carcinoma was seen (which had not been found by original pathology examination). Two patients had upgrades on excision (upgrade rate 2.6%, 95% CI 0 – 9%); 1 invasive cancer and 1 DCIS (grade 2, estrogen receptor positive). On central pathology review, the case upgraded to a grade 1 invasive tubular carcinoma was found to have invasive tubular carcinoma in the initial CB. If this case is excluded from analysis, one of 76 patients (with LCIS on CB) had an upgrade at excision (upgrade rate 1.3%, 95% CI 0 – 7%). Conclusions In this prospective multi-institutional study of patients with LN on CB we found an upgrade rate to invasive cancer or DCIS of 1.3%. Our evidence supports surveillance rather than excision in patients with LN on CB with radiologic-pathologic concordance.

35 Circulating Tumor Cells after Neoadjuvant Therapy in Stage I-III Triple-negative Breast Cancer C. Hall, B. Laubacher, A. Anderson, M. Karthade, H.M. Kuether, S. DeSnyder, A. Luci,* Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.

Background: Triple negative breast cancer (TNBC) is characterized by a lack of estrogen and progesterone receptor and HER-2 gene overexpression/amplification. Because of the absence of these receptors, TNBC patients are not candidates for targeted therapies. Circulating tumor cells (CTCs) can be identified in 25% of stage I - III breast cancer patients, and the identification of a 1 CTC predicts outcome. The aim of this study was to determine if CTCs present after neoadjuvant chemotherapy (NACT) predicted worse outcome in Stage I - III TNBC patients. Methods: We evaluated 48 patients with stage I - III TNBC 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 CellSearch® System (Janssen) and were defined as nucleated cells lacking CD45 but expressing cytokeratins (CK) 8, 18, or 19. The presence of 1 CTC meeting morphological criteria for malignancy was considered a positive result. Log-rank test and Cox regression analysis were applied to establish the association of circulating tumor cells with progression-free and overall survival. Results: Median follow-up was 24 months and mean age was 53 years. Thirty patients (69%) had >2cm tumors, 41 (87%) were nuclear grade 3, and 33 (69%) had positive axillary lymph nodes. One or more CTC was identified in 27% of patients. CTC presence was not associated with primary tumor size, high nuclear grade, or axillary lymph node positivity (P=NS for all). Detection of one or more CTCs predicted decreased progression-free survival (log-rank P=0.004, HR = 7.9, 95% CI, 1.53 to 41.02), but not overall survival (log-rank P=0.08, HR = 4.24, 95% CI, 0.70 to 25.57). Conclusions: One or more CTCs present after completion of NACT predicted relapse in TNBC patients. This information would be helpful in future clinical trial design to assess adjuvant treatments for TNBC patients who are at risk for relapse after completing NACT.

Complete Axillary Response in Breast Cancer Patients after Neoadjuvant Treatment Correlates with Overall Survival S. Diaz-Botero,† M. Espinoza-Bravo,† V. Rodrigues Gonçalves,† A. Esguerra-Colmenarejo,† V. Peg,‡ J. Perez,‡ J. Cortes,‡ I.T. Rubio,† 1. Breast Surgical Oncology Unit - Hospital Universitario Vall d’Hebron - Universidad Autonoma de Barcelona, Barcelona, Spain; 2. Pathology Department - Hospital Universitario Vall d’Hebron - Universidad Autonoma de Barcelona, Barcelona, Spain; 3. Department of Medical Oncology - Vall d’Hebron Institute of Oncology (VHIO), Barcelona, Spain.

INTRODUCTION: Neoadjuvant chemotherapy (NAC) has been regarded as an equally effective option when compared to adjuvant therapy. Different descriptions of pathologic complete response (pCR) to NAC have been reported that includes the breast and axilla or just the breast. The objective of
this study was to determine the impact of site of response on overall survival (OS) and disease free survival (DFS) across different molecular subtypes of breast cancer after neoadjuvant treatment. METHODS: From a prospective maintained database, records from 357 patients who received NAC from 2004 to 2011 were reviewed. Patients who classified in 4 groups depending on the site of response to treatment as per ct ypT(yN0), breast CT (BrpCT) (ypT+yn+), axilla CT (AxpCT) (ypT+yn+ and no pCT (ypT+n+) to determine the association between response to NAC and OS. RESULTS: Mean follow up was 50.8 months (range 1.6 - 117.2). 178 patients (49.8%) were N1-N2 at diagnosis. CT was achieved in 82 patients (23%), BrpCT in 15 patients (4.2%), AxpCR in 112 patients (31%) and no pCT in 148 patients (41.4%). Of the 357 patients, 280 were classified by molecular subtypes, being triple negative (TN) 55 (15.4%), HER2-positive 36 (10%), Luminal HER2-positive 25 (7%), Luminal B HER2-negative 96 (26.9%) and Luminal A 68 (19%). HER2-positive and TN tumors had statistically significant higher rates of pCT (55% and 33% respectively). Patients with TN tumors had a hazard ratio (HR) of OS of 13.35 (95%, CI 3.48-51.05). Achieving pCT predicted a favorable OS and DFS. The 4 year OS for pCT vs BrpCT vs AxpCR and no pCT was 96.9%, 64.9%, 87.8% and 85.18% respectively. (p<0.002) Patients with BrpCT had a HR of OS of 11.94. (95% CI 1.99 - 71.70) Patients who did not respond in the axilla (ypN1) had a HR of DFS of 2.48 (95%, CI 1.47-4.19). Multivariate analysis showed that molecular subtypes and AxpCR were predictors of OS and DFS (p<0.001, p=0.001). CONCLUSIONS: Patients who achieved an axillary CT after NAC have a better OS than patients who had a breast CT. Further studies on treatment for residual disease in the axilla may be considered in non-responders.

37 Results of a Phase Ib Trial of Combination Immunotherapy with HER2-derived Peptide Vaccine GP2+GM-CSF and Trastuzumab in Breast Cancer Patients G.T. Clifton, S.E. Stassen, K.L. Arrington, S. Ponniah, J.M. Greenz, E.J. Schneible, V. Gall, E. Peoples, E.A. Mittendorf, 1. Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX; 2. Henry M. Jackson Foundation, Bethesda, MD; 3. Uniformed Services University of Health Sciences, Bethesda, MD; 4. Sam Houston, TX.

Introduction: Recurrence of breast cancer remains a significant clinical problem. The effectiveness of cancer vaccines in decreasing recurrence rates is under investigation. Preclinical data shows that trastuzumab increases the susceptibility of tumor cells to lysis by vaccine-generated CD8+ T cells suggesting potential benefit of a combination immunotherapy strategy. The current trial was undertaken to demonstrate the safety of this approach. Methods: Clinically disease-free, HLA-A2/A3+, HER2 over-expressing breast cancer patients were enrolled in a dose-escalation trial evaluating 5 dosing cohorts. Patients received six inoculations of monthly intradermal GP2 + GM-CSF administered concurrently with their standard of care trastuzumab. Local and systemic toxicity was monitored. Cardiac ejection fraction (EF) was measured at baseline (BL) and during treatment. Immunologic responses were monitored in-vivo by measuring the orthogonal mean of local reaction (LR) and in-vitro using IFN-gamma ELISPOT assay. Results: 17 disease-free breast cancer patients were vaccinated. All patients completed the series without dose-limiting or grade 3-5 local or systemic toxicity. The median cardiac EF was 60% at BL and remained 60% during treatment. The optimal biologic dose was determined to be 1000mcg of GP2 + 250mcg of GM-CSF based on safety and immunologic response. Mean ELISPOT response to GP2 increased from 47 +/- 19 at BL to 144 +/- 60 (p = 0.13) after vaccination. Mean LR increased significantly from BL at all inoculation timepoints indicating an immunologic response to vaccination. Mean LR at initial inoculation was 28 +/- 10 mm and increased to 68 +/- 8 mm at the final inoculation (p = 0.01). Conclusion: The GP2+ GM-CSF vaccine is safe and well tolerated when given concurrently with trastuzumab in clinically disease-free, HER2 over-expressing breast cancer. Vaccination is immunologically active and sequential trastuzumab and vaccination has shown clinical promise in a randomized phase 2 trial. Further evaluation of HER2 peptide vaccination administered concurrently with trastuzumab is warranted.


Background: Eighty percent of patients with pancreatic ductal adenocarcinoma (PDAC) will die within five years following resection plus adjuvant gemcitabine (Gem) due to the eventual outgrowth of occult metastatic cells. We hypothesized that adjuvant therapy with the MEK inhibitor trametinib would inhibit the outgrowth of occult liver metastases in a murine preclinical model. Methods: Liver metastases were harvested from two patients with PDAC, tumor cell lines were established, transduced with luciferase, injected into the spleens of immunocompromised mice to generate microscopic liver metastases, then the primary tumors were removed via splenectomy. Growth kinetics and tumor burden in the liver were measured during treatment with bioluminescent imaging and time to progression (TTP), progression-free survival (PFS), and overall survival (OS) were determined. Results: Trametinib (0.3 mg/kg oral daily) significantly prolonged OS in mice vs. control (tumor 608, MS: 114 vs. 43 days, p<0.001, Fig 1A; tumor 366, MS: not reached vs. 167 days, p=0.0488, Fig 1B). In vivo target validation demonstrated that trametinib significantly reduced tumor levels of phosphorylated ERK and reduced expression of the ERK-responsive gene DUSP6. In a randomized preclinical trial, following resection of the primary tumor, mice were randomized to: 1) control, 2) adjuvant Gem (100 mg/kg IP, every 3 days) x 7 days followed by surveillance, or 3) adjuvant Gem followed by trametinib (0.3 mg/kg daily). Sequential Gem followed by trametinib resulted in a significant decrease in metastatic cell outgrowth (Fig. 1C,D), and increased TTP and PFS (Fig. 1E,F). Conclusions: In a randomized preclinical murine trial using patient-derived liver metastases from PDAC, the adjuvant regimen of sequential Gem followed by trametinib inhibited occult metastatic cell outgrowth in the liver and increased PFS compared to adjuvant Gem alone. An adjuvant trial of sequential Gem followed by trametinib is being planned in patients with resected stage I-III PDAC.
Minimally Invasive Pancreatoduodenectomy does not Improve Use or Time to Initiation of Adjuvant Chemotherapy in Patients with Pancreatic Adenocarcinoma

**INTRODUCTION:** The modifiable variable best proven to improve survival following resection of pancreatic adenocarcinoma is the addition of adjuvant chemotherapy. A theoretical benefit of minimally invasive pancreatoduodenectomy is faster postoperative recovery, with the potential for greater use and earlier initiation of adjuvant therapy. **METHODS:** The 2010-2011 National Cancer Data Base was queried for all patients undergoing pancreatoduodenectomy for pancreatic adenocarcinoma. Subjects were classified by surgical approach: minimally invasive versus open pancreatoduodenectomy (MI-PD, O-PD). Baseline demographic and clinicopathologic variables were compared between groups. The independent effect of surgical approach on the use and timing of adjuvant chemotherapy was estimated using multivariable logistic and linear regression analysis. **RESULTS:** In total, 5,851 subjects were identified: 844 MI-PD (14%) and 5,007 O-PD (86%). Patients who underwent O-PD had lower comorbidity scores, lower grade tumors, and were less likely to be treated at an academic center; otherwise there were no baseline differences between groups (Table 1). In both the MI-PD and O-PD groups, only 50% of patients received adjuvant chemotherapy, initiated at a median 51 vs. 54 days postoperatively (p<0.17). Following multivariable adjustment, surgical approach was not independently associated with either use (OR 0.98, p=0.78) or time to initiation (1.8 days, p=0.11) of adjuvant chemotherapy. Only younger patient age (OR 1.23, p<0.01), insurance status (OR 1.79, p<0.01), higher income (OR 1.31, p<0.01), higher tumor stage (OR 3.11, p<0.01), and presence of lymph node metastases (OR 1.36, p<0.01) were independently associated with the use of adjuvant chemotherapy. **CONCLUSIONS:** At a national level, minimally invasive pancreatoduodenectomy does not appear to result in greater use or earlier initiation of adjuvant chemotherapy. As sur-geons and institutions continue to gain experience with this complex procedure, it will be important to revisit this benchmark as a justification for its increasing use in patients with pancreatic cancer.

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**Table 1: Baseline characteristics of patients undergoing pancreatoduodenectomy**

<table>
<thead>
<tr>
<th>Variable</th>
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<th>p-value</th>
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<td>66 ± 11</td>
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<td>Sex</td>
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<tr>
<td>Female</td>
<td>2,539 (49.9%)</td>
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<tr>
<td>Male</td>
<td>2,458 (50.1%)</td>
<td>417 (49.4%)</td>
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<td>Race</td>
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<td>0.67</td>
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<tr>
<td>Asian</td>
<td>116 (2.3%)</td>
<td>25 (3.0%)</td>
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<tr>
<td>Black</td>
<td>498 (10.0%)</td>
<td>79 (9.4%)</td>
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<tr>
<td>White</td>
<td>4,288 (85.6%)</td>
<td>724 (85.8%)</td>
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</tr>
<tr>
<td>Other</td>
<td>64 (1.3%)</td>
<td>10 (1.2%)</td>
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<tr>
<td>Charlson/Deyo Comorbidity Score</td>
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<td>0</td>
<td>3,291 (65.7%)</td>
<td>512 (60.7%)</td>
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<td>1</td>
<td>1,564 (27.1%)</td>
<td>276 (32.7%)</td>
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<tr>
<td>≥2</td>
<td>370 (7.4%)</td>
<td>56 (6.0%)</td>
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<td>Tumor Size (cm; mean ± SD)</td>
<td>3.4 ± 2.5</td>
<td>3.5 ± 5.0</td>
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<td>Tumor Grade</td>
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<td>414 (49.5%)</td>
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<td>High/Undifferentiated</td>
<td>1,612 (31.6%)</td>
<td>309 (36.5%)</td>
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<td>AJCC Stage</td>
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<tr>
<td>I</td>
<td>894 (17.9%)</td>
<td>145 (17.2%)</td>
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<tr>
<td>II</td>
<td>4,113 (82.1%)</td>
<td>699 (82.8%)</td>
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<td>Insurance Status</td>
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<td>21 (2.5%)</td>
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<td>812 (97.5%)</td>
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<td>Annual Income</td>
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<td>3,243 (64.9%)</td>
<td>541 (64.1%)</td>
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<td>&lt;$35,000</td>
<td>1,415 (30.4%)</td>
<td>258 (30.6%)</td>
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<td>Hospital Type</td>
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<td>Academic/Research Program</td>
<td>3,204 (64.1%)</td>
<td>623 (73.8%)</td>
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<tr>
<td>Comprehensive cancer program</td>
<td>1,701 (34.0%)</td>
<td>214 (25.4%)</td>
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<tr>
<td>Community cancer program</td>
<td>93 (1.9%)</td>
<td>7 (0.8%)</td>
<td></td>
</tr>
</tbody>
</table>
42
Outcomes of a Clinical Pathway for Borderline Resectable Pancreatic Cancer O.M. Rashid,1,* J.M. Pimiento,1 P. Nguyen,1 G. Springer,1 S. Hoff,1 R. Shridhar,1 R.L. Johnson,2 K. Illing,1 strong,2 M.P. Malafa,1 J. H. Lee Moffitt Cancer Center, Tampa, FL; 2. University of South Florida, Tampa, FL.

Introduction: While multimodality therapy for borderline resectable pancreatic adenocarcinoma (BPA) is advocated, treatment regimens vary by institution without a standardized approach supported by prospective randomized data. We implemented a multidisciplinary multimodality clinical pathway (CP) for the management of BPA and examined outcomes to investigate optimal therapy. Methods: From January 1, 2006 to December 31, 2013 BPA patients as defined by the NCCN and AHPBA consensus guidelines were prospectively managed along CP. Pancreatectomy rate, margin status, pathologic response, disease free (DFS), disease specific (DSS), and overall survival (OS) were retrospectively examined. Standard statistical methods and Kaplan-Meier survival analysis were used for statistical comparison. Results: 121 patients were classified as BPA and 101 entered CP. Of those who entered CP, 94 (93.1%) completed neoadjuvant chemoradiation (NT). Of those who entered CP, 55 (54.5%) underwent pancreatectomy, with R0, R1 and R2 rates of 96.4% (53), 3.6% (2), and 0%, respectively. Of those who underwent pancreatectomy, 22 (40%) required vascular reconstruction with R0, R1 and R2 rates of 95.5% (21), 4.5% (1), and 0%, respectively. Pathologic response (grade IIa-IV) to treatment was seen in 81.8% (45), with a 14.5% (10) complete response rate (21), 4.5% (1), and 0%, respectively. Results: Among 394 patients, SN detection rate was 99% (392 of 394). Of 38 patients with lymph node metastasis, 92% (35 of 38) was positive of SN metastasis, and accuracy of nodal evaluation of metastasis was 99% (391 of 394). Function-preserving gastrectomy was performed in 33% (129 of 394) patients. Operations performed were, proximal gastrectomy in 64 patients (50%), pylorus-preserving gastrectomy or segmental gastrectomy in 53 patients (41%), and partial gastrectomy in 10 patients (8%). Of all the patients who underwent function-preserving gastrectomy, 67 patients (53%) underwent laparoscopic surgery. No local recurrence nor metastasis has been observed in patients who underwent function-preserving gastrectomy. Discussion: Based on SN concept function-preserving gastrectomy is safely performed in early gastric cancer patients. Recently, we developed non-exposure endoscopic wall inversion surgery (endoscopic full-thickness resection performed in laparoscopy and endoscopy cooperative surgery) as partial gastrectomy in patients with SN-negative, and starting clinical study to validate this new promising procedure.

Figure 1: Median disease specific survival for patients who underwent pancreatectomy (N=55) was 43 months (95%CI:25.7-60.3) versus 14 months (95%CI:10.9-17.1) for the non-pancreatectomy group (N=46), p=3.5x10^-13.
New Circulating Biomarker for Patients with Metastatic Pancreatic Ductal Adenocarcinoma  
R. Marayati,1,2* R.L. Whittlesey,2 L.A. Williams,2 S. Herrera Loeza,1 R.A. Moffitt,1 J. Yeh,3 1. UNC Lineberger Comprehensive Cancer Center, Chapel Hill, NC; 2. UNC Department of Genetics and Lineberger Comprehensive Cancer Center, Chapel Hill, NC; 3. UNC Department of Epidemiology and Lineberger Comprehensive Cancer Center, Chapel Hill, NC; 4. UNC Departments of Surgery and Pharmacology and Lineberger Comprehensive Cancer Center, Chapel Hill, NC.

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive disease characterized by early invasion and metastasis, for which there are limited diagnostic tools and minimal effective therapies. Circulating tumor cell (CTC) burden has been shown to be prognostic in patients with metastatic disease. We aimed to identify novel biomarkers of CTCs that have potential clinical use for patients with metastatic PDAC (mPDAC). Methods: Microarray data was analyzed from 154 primary and 30 metastatic PDAC patients. After IRB approval, CTCs and hematopoietic cells were isolated from blood samples from a prospective cohort of 20 PDAC and 4 non-PDAC patients using density gradient centrifugation followed by CD45 microbead selection. Quantitative real-time PCR was used for gene expression validation. Overall survival (OS) was assessed using the log-rank test. Results: We identified 67 genes differentially overexpressed in mPDAC tumors compared to primary PDAC and normal tissues. Expression of these genes was evaluated in a panel of 11 pancreatic cancer cell lines and in blood samples from 3 non-PDAC patients. We found that connexin 31 (GJB3), a gap junction protein, was undetectable in blood samples from non-PDAC patients but had high expression in all pancreatic cancer cell lines. We then validated GJB3 expression in blood samples from 20 PDAC patients including 5 patients with localized, 7 with locally advanced, and 8 with metastatic PDAC, as well as 3 non-cancer patients and 1 patient with a cancer other than PDAC. GJB3 expression was higher in samples from patients with mPDAC compared to patients with localized PDAC (p=0.016). In an analysis of 131 patients with resected PDAC tumors, patients with high tumor expression of GJB3 had a shorter median OS (15 mos vs. 24 mos, p=0.031). Conclusions: Our results suggest that GJB3 is associated with metastasis as patients with higher GJB3 expression have a worse outcome. GJB3 is found selectively in blood samples from patients with mPDAC and thus is a potential circulating biomarker for mPDAC. Further analysis in a larger cohort of patients will be done to establish the use of GJB3 as a prognostic circulating biomarker.

Desmoplastic Stroma Differences in Metastatic Pancreatic Cancer

R.J. Torphy,1,3 S.R. Cader,2 K.E. Volmar,1 J. Yeh,3 1. University of North Carolina School of Medicine, Chapel Hill, NC; 2. University of North Carolina-Rex Healthcare, Raleigh, NC; 3. University of North Carolina School of Medicine Department of Surgical Oncology, Chapel Hill, NC.

A hallmark of pancreatic cancer is its abundant desmoplastic stroma (DS) that has been described as contributing to tumor progression and is presumed to be a barrier to drug delivery. This has led to an interest in therapeutically targeting DS in pancreatic cancer. While it is widely accepted that there is abundant DS in primary tumors and that modulation of the stroma may alter tumor growth, little is known about the significance of this stroma at metastatic sites. The aim of this study was to evaluate the presence of DS at both primary and metastatic sites. Tissue microarrays were prepared from formalin-fixed paraffin-embedded tissue sections using a 2 mm punch. The arrays contained 270 samples with triplicate cores of normal, primary and metastatic tissue from 15 metastatic pancreatic cancer patients. Tumor epithelium (TE) and desmoplastic stroma (DS) were digitally annotated by a pathologist and quantified using Aperio Spectrum WebScope. Triplicate cores were averaged prior to statistical analysis. Overall tumor cellularity was 28% (± 21%) in primary tumors compared to 54% (± 35%) in metastatic sites. The ratio of TE/DS was 0.95 (± 0.8) in primary tumors compared to 5.1 (± 4.3) in metastases (t-test, p=0.001). There were significant differences in TE/DS ratios between primary tumors and solid organ, lymph node, and peritoneal metastases (ANOVA, p=0.001). Solid organ metastases (e.g. lung and liver) had the highest TE/DS ratio of 7.8 (± 2.7), followed by lymph node metastases, TE/DS ratio of 5.8 (± 4.8). Interestingly, peritoneal metastases had the most abundant DS and were most similar to the primary tumor with a TE/DS ratio of 0.4 (± 0.2). Ours results confirm the abundant presence of DS in primary pancreatic tumors. However, we show that the degree of DS varies depending on the route of metastatic spread (peritoneal=lymphatic=hematogenous). The degree of DS at distant metastatic sites is limited compared to the primary tumor, suggesting that the role of DS at these sites may be limited. The relative low abundance of DS compared to TE in solid organ and lymph node metastases raises concern for the utility of targeting stroma in regionally and distant metastatic pancreatic cancer.

Importance of preoperative CA 19-9 Levels in Patients with Localized Pancreatic Cancer Treated with Neoadjuvant Therapy


Background: The prognostic importance of preoperative CA 19-9 levels in pancreatic cancer (PC) is controversial. The association of neoadjuvant therapy, preoperative CA 19-9 and survival in patients (pts) with localized PC is unclear. Methods: CA 19-9 levels were measured prior to therapy (baseline) and after neoadjuvant therapy prior to surgery (preop) in pts with resectable and borderline resectable (BLR) PC. CA 19-9 levels were classified as normal or elevated based on a cutoff of 36 U/mL. Pts were grouped by their baseline and preop CA 19-9 levels. Results: CA 19-9 was evaluable in 225 pts prior to any treatment; 97 (43%) were resectable and 128 (57%) were BLR. Baseline CA 19-9 was normal (GrpA) in 53 (24%) and elevated in 172 (76%). Of the 172 pts with elevated baseline CA 19-9, 60 (35%) had a normal preop CA 19-9 (GrpB), 85 (49%) had a decreased but elevated preop CA 19-9 (GrpC); and 27 (16%) had an elevated baseline and increased preop CA 19-9 (GrpD). No differences were observed in preop CA 19-9 grouping and clinical stage. Completion of all neoadjuvant therapy including surgery occurred in 164 (73%) of the 225 pts; 41 (77%) of 53 GrpA, 52 (87%) of 60 GrpB, 59 (69%) of 85 GrpC, and 12 (44%) of 27 GrpD pts (P < 0.001). Of the 164 pts who completed all therapy, node positive disease was present in 11 (27%) of 41 GrpA, 11 (21%) of 52 GrpB, 27 (46%) of 59 GrpC, and 5 (42%) of 12 GrpD pts (P =0.03). Median survival of all 225 pts was 24 months (mo); median survival for Grps A, B, C, and D was 34, 45, 20, and 17 mo, respectively (P = 0.0004). Median survival for the 164 pts who completed all therapy including surgery was 37 vs. 11 mo for the 61 pts who were not resected. Conclusions: Preop CA 19-9 level after neoadjuvant therapy was a powerful predictor of outcome; a normal level (Grps A&B), even if elevated prior to neoadjuvant therapy (Grp B), was associated with a superior survival as compared to those whose preop CA 19-9 remained elevated. This data has important implications for treatment sequencing, pts selection for surgery, and the use of postoperative systemic therapy.
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Prediction of Stage II/III Gastric Cancer Patients who were Rescued by postoperative Adjuvant Chemotherapy by CDO1 Gene Promoter Hypermethylation K. Yamashita,* A. Emia, H. Ushiku, H. Moriya, K. Hosoda, H. Mieno, N. Katada, S. Kikuchi, M. Watanabe. Surgery, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan.

(Background) Cysteine dioxygenase 1 (CDO1) involves cysteine metabolism, and regulates intracellular cysteine and reactive oxygen species (ROS). We have recently identified CDO1 gene hypermethylation in human cancer, and shown that it is characterized by advanced gastric cancer. In this study, we describe clinical potential of CDO1 methylation for patient selection of S1 adjuvant chemotherapy. (Patients and Methods) We performed Q- MSP for CDO1 methylation level (TaqMethV) in 321 stage II/III primary gastric cancer tissue. The patients underwent curative surgery followed by postoperative S-1 chemotherapy (S-1 group; n=167) or curative surgery (surgery alone group; n=154) between 2000 and 2010. (Results) Mean CDO1 TaqMethV was 36.4, and CDO1methylation is significantly higher than that in the corresponding normal tissues (AUROC=0.81; p<0.0001). (2) Log-rank plot analysis revealed that the higher CDO1 methylation level was, the poorer prognosis in stage II/III gastric cancer. More importantly, CDO1 hypermethylation may predict chemotherapeutic benefits of stage II/III gastric cancer with postoperative adjuvant chemotherapy, which could save the patients who have to undergo chemotherapy that would not be beneficial to improve survival.

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CALM Study: A Phase II Study of a Novel Oncolytic Immuno-therapeutic Agent, CVA21, Delivered Intratumorally in Patients with Advanced Malignant Melanoma R.H. Andtbacka,1,* B. Curti,2 H. Kaufman,3 G.A. Daniels,4 J.J. Nemunatitis,5 E.L. Spitter,6 S. Hallmeyer,7 J. Lutzky,7 S. Schultz,1 E.D. Whiteman,4 K. Zhon,4 J.J. Nemunatitis,5 S. Zani, Jr.6 Background: CVA21, an oncolytic immunotherapy, is a bio-selected oncolytic strain of Coxsackievirus A21 (CVA21) that preferentially infects ICAM-1 expressing tumor cells, resulting in cell lysis and a systemic anti-tumor immune response. Methods: The CALM study investigated the efficacy and safety of intratumoral (IT) CVA21 in 57 pts with treated or untreated unresectable Stage III/IV M1c melanoma. Pts received up to 3 x 108 TCID50 CVA21 IT injection was detected in >85% of pts. The most common patient side effects observed were Gr 1 local injection site reactions, fatigue, chills and fever. There were no Gr 3 or 4 product-related AE's. Preliminary analysis identified a possible serum cytokine signature of elevated levels of IL-8 and γ-IFN linked to systemic tumor response. Conclusions: Intralesional CVA21 is a promising novel oncolytic immunotherapeutic agent with limited toxicity and robust responses in both injected and non-injected lesions in pts with advanced melanoma. The effectiveness of CVA21 warrants additional investigation as a monotherapy and in combination with other targeted immunotherapies.

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Background: MILND is a novel approach to inguinal lymphadenectomy. SAFE-MILND (NCT01500304) is a multi-center, phase I/II clinical trial evaluating the safety and feasibility of MILND for patients with melanoma in a group of surgeons newly adopting the procedure. Methods: 13 melanoma surgeons from 10 institutions without any previous MILND experience completed specialized training including didactic lectures, participating in a hands-on cadaveric lab and being provided an instructional DVD of the procedure. Assessment of the learning curve for MILND was performed by a composite score derived from the following variables: number of lymph nodes identified, operative time, EBL and complications. Results: 30 day outcomes are available for 72 of the 77 MILND procedures performed to date. The median number of lymph nodes pathologically reported (SLNB + MILND) was 12 (IQR 8-14) and the median operative time was 184 minutes (IQR 131-223); neither was related to surgeon case number. There have been 10 (13%) conversions secondary to: advanced disease (4), intraoperative injury (2), lack of progression (2), bleeding (1), hypercarbia (1). 9 of the 10 conversions occurred in a surgeon’s first 5 cases. The first 5 cases made up 47 of the 77 cases. 9 (19%) of these 47 “early” cases were converted. Conversely, only 1 (3%) of the 30 cases that happened after the “early” stage was converted to an open procedure. MILND score showed improvement over time secondary to fewer conversions. 30 day complications are listed in the table and no grade 4 or 5 adverse events were observed. Conclusions: Following a structured training program, high volume melanoma surgeons adopted a novel surgical technique with low morbidity and an acceptable number of lymph nodes as an early oncologic surrogate. Wound complications occurred at a lower frequency and grade compared with historical controls using the open approach. Operative time and number of lymph nodes were not related to case number suggesting a high volume surgeon can transition to a new approach well with appropriate education; however, conversion rates decreased with time, possibly secondary to better patient selection.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wound Infections</td>
<td>1 (1%)</td>
<td>7 (9%)</td>
<td>6 (8%)</td>
<td>14 (19%)</td>
</tr>
<tr>
<td>Seroma</td>
<td>3 (6%)</td>
<td>3 (6%)</td>
<td>11 (15%)</td>
<td>15 (20%)</td>
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<tr>
<td>Anaemia</td>
<td>7 (13%)</td>
<td>1 (1%)</td>
<td>8 (11%)</td>
<td>16 (21%)</td>
</tr>
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<td>1 (1%)</td>
<td>1 (1%)</td>
<td>2 (3%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Hematoma</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>2 (3%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Interscapular Skin Injury</td>
<td>5 (9%)</td>
<td>2 (3%)</td>
<td>7 (10%)</td>
<td>14 (19%)</td>
</tr>
<tr>
<td>Wound Dehiscence</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>2 (3%)</td>
<td>4 (5%)</td>
</tr>
<tr>
<td>Interscapular Skin Necrosis</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Interscapular Hemorrhage</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Syncope</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Peripheral Sensory Neuropathy</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>1 (1%)</td>
<td>3 (4%)</td>
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</table>
Lower Risk of Visceral/Bone Metastasis (VM) in Patients with Stage IIB/C/IVM1a Melanoma Treated with Talimogene Laherparepvec (T-VEC) versus GM-CSF in OPTiM (NCT007697044)


Background: Patients with stage IIB/C/IVM1a melanoma are at high risk of developing VM. T-VEC is an HSV type I-derived oncolytic immunotherapy that selectively replicates in tumors & produces GM-CSF to enhance systemic antitumor immune responses. In OPTiM, a randomized phase 3 trial in 436 patients with unresected melanoma with regional or distant metastases, T-VEC improved durable response rate (DRR; response lasting continuously for ≥6 months [m]; primary endpoint) vs GM-CSF (16% vs 2%, p<0.0001). In the primary overall survival (OS) analysis, median OS was 23.3 m with T-VEC vs 18.9 m with GM-CSF (HR=0.79, 95% CI=0.62-1.00; p=0.051). In exploratory analyses, DRR for stage IIB/C/IVM1a melanoma was 25% with T-VEC vs 18% with GM-CSF (p=0.175). For stage IIB/IVM1a, the OS benefit was 9.9 months vs 4.4 months (HR=0.59, 95% CI=0.40-0.88, p=0.001). Here we report the effect of T-VEC vs GM-CSF on the risk to develop VM in patients with stage IIB/C/IVM1a melanoma. Methods: OPTiM data for stage IIB/C/IVM1a melanoma at baseline was analyzed retrospectively to identify investigator-reported visceral sites of disease during the study. Results: Of 225 patients with stage IIB (8%), IIC (22%), and IVM1a (27%) melanoma, 152 (68%) received T-VEC and 73 (32%) GM-CSF. Median followup was 33.4 m with T-VEC vs 21.5 m with GM-CSF. VM developed in 22 patients with T-VEC vs 10 with GM-CSF. The risk of VM was lower with T-VEC than with GM-CSF (unadjusted HR=0.63, 95% CI=0.42-0.94; log-rank p=0.046) with VM-free survival at 6, 9, and 12 m of 92%, 80%, and 71%, respectively, with T-VEC vs 86%, 73%, and 53%, respectively, with GM-CSF. After adjusting for imbalances in age ≥50 (87% with T-VEC vs 81% with GM-CSF), stage IIIB/C (54% vs 45%), ECOG PS 0 (74% vs 70%), 12-week line of treatment (55% vs 51%), and tumor burden (median 7.8 cm² vs 7.1 cm²), the HR for the T-VEC effect in a multivariate analysis was 0.45 (95% CI=0.29-0.69). Conclusion: Compared to GM-CSF, T-VEC-treated patients with stage IIB/C/IVM1a unresected melanoma had a 37% lower risk of VM. T-VEC should be further investigated in its ability to decrease the risk to develop VM in patients with stage IIB/C/IVM1a melanoma.


Introduction- Although sentinel lymph node biopsy (SLNB) is accurate in experienced hands, false negatives (FN) occur. Previous attempts to identify such patients have shown limited benefit; however, several immunotherapies like cytokine therapies and checkpoint inhibitors have shown promise. Unfortunately, these immunotherapies are effective in only a small number of patients (pts), are non-specific and often toxic. We investigated a non-toxic and active specific form of immunotherapy, our dendritic cell vaccine (DV), in late stage melanoma pts in a phase I/IIa trial. METHODS Autologous tumor and dendritic cells are fused, and sorted to create a DV for each stage IV melanoma pt. In the phase I, 10 pts were vaccinated every 3mos with doses of 0.5-1×10⁹ DV. IL-2 was initiated on day 1 after vaccination, and increased from 3-9MIU/m²/day as tolerated for 5 days. In the phase IIa, 15 pts were vaccinated with doses from 0.25-1×10¹⁰ DV every 6 wks up to 6 inoculations. IL-2 (3MIU/m²/day) was given on days 1, 3, and 5 after vaccination. RESULTS In the combined phase I/IIa trials (n=25), there were no grade 3-5 toxicities. There was a 24% pCR, and a 32% overall survival (OS) rate at 5 yrs. The median OS was 16.1 mos compared to a historical 5.5 mos. An increase in OS (75% vs 23.8%, p=0.0065) was seen in pts with stage IV resected disease (n=4) versus all other pts (28% vs 50%) (p=0.0016). Comparing phase I and Ila, there were no differences in pt characteristics (all p>0.1) yet median OS of phase I pts was 8.7 mos vs 21.5 mos for phase II pts. There was a higher dose of IL-2 and higher DV dose (710,983 vs 402,540 dendrimers (p=0.0006)) in the phase I but more frequent dosing and higher mean number of inoculations (3 vs 2.5 p=0.27) in the phase Ila. CONCLUSIONS The dendritic cell vaccine potentially provides a clinical benefit without toxicity. There was an apparent dose response for inoculation number but not dose of the DV. Patients with resected stage IV disease benefited most. We have initiated a phase IIb trial in stage III/IV (resected) melanoma pts in the adjacent setting to prevent recurrence.
ulceration, and cervical SLNB. **Conclusion-** With long-term follow up, male gender and primary site (head/neck, leg) were associated with FN SLNB. This may represent technical challenges of SLNB or biologic behavior in areas with increased in-transit disease. FN SLNB was an independent predictor of worse MSS in melanomas <4mm in thickness, but this survival difference did not become apparent until after 2 to 3 years of follow up. This may indicate that any possible benefit of completion node dissection in SLNB metastasis patients may require extended follow up to identify.

**Table 1. Demographics and Tumor Characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
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<th>True Negative</th>
<th>True Positive</th>
<th>Predict (p&lt;.05)</th>
</tr>
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<tbody>
<tr>
<td>Age, years (range)</td>
<td>50.1 ± 16.1</td>
<td>56.6 ± 16.1</td>
<td>33.5 ± 16.1</td>
<td>0.447</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>64 (72.5%)</td>
<td>1495 (90.5%)</td>
<td>298 (60.5%)</td>
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<td>Primary Site</td>
<td>Arm</td>
<td>10 (10.4%)</td>
<td>309 (19.8%)</td>
<td>70 (14.4%)</td>
</tr>
<tr>
<td>Leg</td>
<td>Head/Neck</td>
<td>23 (24.6%)</td>
<td>470 (31.5%)</td>
<td>138 (27.7%)</td>
</tr>
<tr>
<td>Tumor</td>
<td>T1</td>
<td>20 (21.3%)</td>
<td>934 (58.6%)</td>
<td>203 (41.3%)</td>
</tr>
<tr>
<td>Extension, mm (Range)</td>
<td>&lt;1mm</td>
<td>12 (12.8%)</td>
<td>235 (15.0%)</td>
<td>57 (12.7%)</td>
</tr>
<tr>
<td>1-4mm</td>
<td>15 (15.6%)</td>
<td>589 (38.4%)</td>
<td>118 (25.7%)</td>
<td>0.007</td>
</tr>
<tr>
<td>&gt;4mm</td>
<td>Unknown</td>
<td>0 (0%)</td>
<td>83 (5.4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Ulceration</td>
<td>No</td>
<td>50 (55.7%)</td>
<td>1993 (129.2%)</td>
<td>347 (72.8%)</td>
</tr>
<tr>
<td>Maln</td>
<td>7 (7.6%)</td>
<td>87 (5.6%)</td>
<td>16 (3.2%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Clark level</td>
<td>I/II</td>
<td>2.1 (2.5)</td>
<td>437 (28.5%)</td>
<td>177 (37.5%)</td>
</tr>
<tr>
<td>III</td>
<td>18 (20.5%)</td>
<td>737 (49.1%)</td>
<td>138 (29.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IV</td>
<td>50 (55.7%)</td>
<td>1805 (116.1%)</td>
<td>323 (69.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ulcer</td>
<td>Yes</td>
<td>19 (21.5%)</td>
<td>839 (54.0%)</td>
<td>148 (31.4%)</td>
</tr>
<tr>
<td>Nodal</td>
<td>No</td>
<td>50 (55.7%)</td>
<td>1993 (129.2%)</td>
<td>347 (72.8%)</td>
</tr>
<tr>
<td>Sentinel Lymph Node Biopsy</td>
<td>Yes</td>
<td>21 (23.7%)</td>
<td>525 (34.4%)</td>
<td>143 (29.6%)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>0</td>
<td>57 (65.8%)</td>
<td>197 (127.4%)</td>
<td>37 (7.9%)</td>
</tr>
</tbody>
</table>

**Figure 1: Melanoma-Specific Survival by SN Group**

**54 Molecular Characterization of the Immune Profile in the Sentinel Lymph Node in Melanoma**


**Introduction:** The sentinel node (SN) has become the standard diagnostic tool for staging melanoma. With the recent development of several potent immunotherapies we hypothesized that the early immune events in melanoma may first be seen in the SN. **Methods:** Eighty-one SN from 79 patients were analyzed. Most patients were male (M:F, 2:1) and average age at diagnosis was 62 years. Median follow up was 48 months for patients alive at last contact. NLR was stratified as high or low, relative to the median of 2.73. There were no differences in median NLR with respect to tumor site, ulceration, clinical or pathologic nodal status, or pathologic stage. However, increasing age, male sex and greater tumor thickness were associated with high NLR. High NLR was strongly associated with poorer OS. Median OS was 58.8 versus 103.2 months for patients with high NLR versus low NLR, respectively (p<0.001).

In a multivariable analysis of survival including nodal status, tumor depth, ulceration, age and gender, high NLR remained an independent predictor of worse OS (OR 1.24, 95%CI 1.00 – 1.53, p<0.05). **Conclusions:** Increased preoperative peripheral blood NLR is independently associated with decreased overall survival in patients with stage III-II melanoma. It remains unclear whether this represents another prognostic factor, or a possible opportunity for therapeutic intervention.
56 Molecular Characterization of Cutaneous Melanoma for the Surgical Oncologist: Insights from the Cancer Genome Atlas Program W.R. Burns,1,5 I.R. Watson,1 C. Wu,1 R.A. Scolyer,2 L. Chin,1 J. Ger-shenwald,2 1. The University of Texas MD Anderson Cancer Center, Houston, TX; 2. Melanoma Institute Australia, Sydney, NSW, Australia; 3. The University of Texas MD Anderson Cancer Center, Houston, TX; United States, on behalf of the Melanoma TCGA Project, Bethesda, MD.

Introduction: As our understanding of the molecular and immunologic underpinnings of melanoma continues to improve, patient care continues to rapidly evolve. The NIH-funded Cancer Genome Atlas (TCGA) Program is an international team science effort that catalogs molecular alterations of multiple cancers. In 2009, melanoma was included in this effort; here we provide initial insights from this collaborative study for the surgical oncology community. Methods: Comprehensive DNA, RNA, and protein-based molecular analyses were performed on 333 primary cutaneous melanomas and metastases acquired from 331 patients in IRB-approved protocols at 14 international centers through the melanoma TCGA project. Most biospecimens (80%) were from regional or distant metastases, including those with no known primary. Pathologic immune infiltration was also assessed. Integrative analyses of molecular data with well-annotated clinicopathologic information were performed to identify molecular alterations with potential biological and clinical relevance. Results: In addition to confirmation of several previously described significantly mutated genes in melanoma (BRAF, NRAS, CDKN2A, TP53, and PTEN), additional novel aberrations were identified in this large cohort; all were classified into genomic subtypes based on the mutation status of 3 genes involved in the MAPK pathway (BRAF, RAS, and NF1) or a 4th subtype (triple wild-type) in which none of these 3 genes were mutated. Clustering analysis of RNA-seq data identified 3 subgroups categorized by patterns of immune, keratin, and melanocyte differentiation markers. Tumors in the immune subgroup were similarly found to have greater immune infiltration on pathologic review; these patients also had a more favorable prognosis. Conclusions: The melanoma TCGA project demonstrates that comprehensive molecular profiling can be performed at an international level and the power of team science. Future studies involving this rich dataset and team infrastructure will likely provide additional insights into melanoma biology that may inform integrated prognostic/predictive models and advances in personalized therapy.

57 Risk Factors for Positive Deep Pelvic Nodal Involvement in Patients with Palpable Groin Melanoma Metastases: Can Extent of Surgery be Minimized? C.M. Oude Ophuis,1,6 A.J. Akkooi,2 B. Van der Hiel,2 B. Van der Wielen,2 H.J. Hoekstra,1 M.G. Niebling,4 H.J. Bonenkamp,4 H.H. De Wilt,5 S. Koljenovic,4 D.J. Grünhagen,5 K. Verhoef,1 1. Erasmus MC Cancer Institute - University Medical Center Rotterdam, Rotterdam, Netherlands; 2. Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, Netherlands; 3. University Medical Center Groningen, Groningen, Netherlands; 4. Radboud University Nijmegen Medical Center, Nijmegen, Netherlands.

Introduction Patients with palpable melanoma groin metastases are a subgroup with poor prognosis. There is debate whether a combined (CGD) superficial (SGD) and deep groin dissection is necessary or if SGD alone is sufficient. This study analyses risk factors for positive deep pelvic node involvement.

Methods We performed a retrospective multicenter cohort study, concerning 291 therapeutic CGDs from four tertiary centers in the Netherlands (1992-2013). Patients were selected based on complete pathology reports and pre-operative imaging. Analyzed imaging modalities were: CT scan with/without separate PET, and PET combined with low dose CT (PET-CT). Analyzed risk factors included sex, age, location of primary, histology, Breslow thickness, ulceration, Clark level, number of total and positive inguinal nodes, inguinal lymph node ratio (LNR) and positive deep pelvic nodes on imaging.

Results After exclusion of patients without imaging, 210 CGDs remained. Median age was 57 years, 55% was female, median follow-up was 20 months (inter quartile range (IQR) 10-44 months). Median Breslow thickness was 2.10mm (IQR 1.4-3.3mm), 24% was ulcerated. Eleven patients had a history of negative sentinel node. Positive deep pelvic nodes were present in 35% of CGDs, one patient had no positive inguinal nodes. Number of positive inguinal nodes was significantly lower among patients without positive deep pelvic nodes: median 1 node (IQR 1-2) versus 3 nodes (IQR 1-4) with involved deep nodes (p<0.001). LNR was significantly lower for patients without involved pelvic nodes; median 0.17 (IQR 0.10-0.25), vs 0.33 (IQR 0.14-0.52) for patients with positive deep pelvic nodes (p<0.001). There was a linear association between number of positive inguinal nodes and presence of positive deep pelvic nodes. Combination of negative imaging, < 3 positive inguinal nodes and LNR ≤ 0.30 could accurately predict the absence of deep nodal involvement in 88%. Conclusion Patients with negative preoperative imaging, <3 positive inguinal nodes and inguinal LNRs ≤ 0.30, have a very low incidence of positive deep pelvic nodes.
was 32.8% after subareolar injection, 64.2% after periareolar and 67.2% after peritumoral injection. LM in a two-day protocol was successful in 64.3%, versus 48.8% in a one-day protocol (P=0.016). Conclusion: This is the largest series describing repeat SNB in recurrent breast cancer. Repeat SNB is technically feasible and provides staging information, leading to changes in management. Aberrant drainage is observed in 48.9% of patients. Technical success is achieved more often when more Tc-99 is injected and when LM is performed in a two-day protocol. Subareolar Tc-99 injection appears inadequate. At the SSO in March 2015, we expect to update our results of >500 inclusions.

Table 1. Univariate (UVA) and multivariate (MVA) analyses of factors associated with skin flap necrosis after mastectomy with reconstruction

<table>
<thead>
<tr>
<th>Factor</th>
<th>UVA OR (95% CI)</th>
<th>p-value</th>
<th>MVA OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Neerosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=606</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking (current or past never)</td>
<td>1.61 (1.01-2.56)</td>
<td>0.05</td>
<td>1.81 (1.08-3.05)</td>
<td>0.03</td>
</tr>
<tr>
<td>Previous breast reduction</td>
<td>3.14 (0.92-10.71)</td>
<td>0.07</td>
<td>4.14 (1.04-16.45)</td>
<td>0.04</td>
</tr>
<tr>
<td>Nipple sparing mastectomy</td>
<td>3.34 (1.85-5.95)</td>
<td>&lt;0.01</td>
<td>4.62 (1.34-15.15)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Time to incision to specimen removal (hr)</td>
<td>1.19 (1.07-1.33)</td>
<td>&lt;0.01</td>
<td>1.20 (1.07-1.35)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sharp dissection (vs cautery)</td>
<td>2.20 (0.95-1.73)</td>
<td>0.06</td>
<td>4.16 (1.43-12.04)</td>
<td>0.01</td>
</tr>
<tr>
<td>Previous breast augmentation</td>
<td>2.60 (0.97-7.99)</td>
<td>0.06</td>
<td>4.34 (1.66-11.31)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=604</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate or Severe Neerosis</td>
<td>N=58*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nipple sparing mastectomy</td>
<td>3.99 (1.77-8.99)</td>
<td>&lt;0.01</td>
<td>4.02 (1.20-13.70)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Specimen size (per 100 gm)</td>
<td>1.010 (1.01-1.20)</td>
<td>0.03</td>
<td>1.24 (1.20-3.83)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BMI*</td>
<td>1.08 (1.02-1.14)</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes*</td>
<td>5.77 (1.66-17.95)</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*does not include expander size ^excluded from MVA by backwards selection

The Protrusion Protein Polo-like Kinase 4 (PLK4) Enhances Cancer Invasion K. Kazazian,\(^{1*}\) R. Xu,\(^{2}\) C. Rosario,\(^{3}\) O. Brashavitskaya,\(^{2}\) F. Zli,\(^{2}\) C.J. Swallow,\(^{4}\) 1. General Surgery, University of Toronto, Toronto, ON, Canada; 2. Lunenfeld-Tanenbaum Research Institute, Toronto, ON, Canada.

Metastasis remains the most common cause of death following resection of primary breast, pancreas or colon cancer, high expression of the putative oncogene PLK4 in these cancers predicts aggressive behavior and resistance to therapy. Our objective is to understand the mechanism(s) of PLK4’s oncogenic effect in order to therapeutically modulate the pathways/networks that facilitate metastatic capacity. We hypothesize that PLK4 enhances cancer cell invasion and metastasis by regulating cytoskeletal dynamics and cell polarity. Methods/Results: During a genome-wide screen for secondary alterations in PLK4-related tumors, we identified an unexpected correlation between PLK4 status and motility gene expression. Cancer cell spreading and protrusion formation were facilitated by increasing active PLK4 with Flag-PLK4 transfection (p<0.001 vs. Flag and kinase-dead controls, n=6), while PLK4 knockdown using siRNA had a suppressive effect (p<0.01, n=4). Rescue experiments confirmed phenotype specificity for the siRNA target gene. Development of cell polarity and migration towards a wound were impaired with PLK4 knockdown (p<0.05, n=3), and PLK4 was found at a previously undescribed location: the protrusions of migrating cells. PLK4 siRNA transfected cancer cells showed a depletion of protrusional PLK4 and decreased invasion through Matrigel in a transwell assay. Interrogation of a panel of genes revealed a signature consistent with mesenchymal to epithelial re-programming upon PLK4 knockdown in cancer cells that have previously undergone EMT. Interaction proteomics identified novel PLK4 interactors, including the RhoA GEF ArhGEF10, suggesting involvement in regulation of cytoskeletal dynamics. The breast cancer line MDA MB-231 has been engineered for stable PLK4 knockdown using shRNA with recapitulation of the transient PLK4 suppression phenotypes observed in vitro, and a xenograft invasion/metastasis model in NOD/SCID mice is underway. Conclusions: PLK4 localizes to the protrusions of motile cancer cells and enhances spreading, migration, invasion and development of polarity. This supports the pursuit of PLK4 inhibitors for use in patients experiencing cancer progression on conventional chemotherapy.

Skin Flap Necrosis (SFN) after Mastectomy with Reconstruction (M+R): A Prospective Study C.B. Matsen,\(^{2,3}\) B. Mehra,\(^{2}\) A. Eaton,\(^{2}\) D. Capko,\(^{2}\) K.J. Van Zee,\(^{2}\) H.S. Cody,\(^{2}\) M. El Tamer,\(^{2}\) G. Pilitas,\(^{2}\) L. Sclafani,\(^{2}\) M. Morrow,\(^{2}\) 1. Surgery, University of Utah, Huntsman Cancer Institute, Salt Lake City, UT; 2. Memorial Sloan Kettering Cancer Center, New York City, NY.

Introduction: SFN after M+R can increase cost and impact cosmesis. Retrospective studies report variable definitions of necrosis, event rates, and predictors. Given these limitations, we conducted a prospective single-institution study to define the rate of SFN after M+R and to identify potentially modifiable factors. Methods: After IRB approval, we prospectively collected 30 patient and surgeon level factors in 606 consecutive mastectomies with 8-wk follow-up. There were no exclusions. SFN was defined as mild (no intervention, healed at 8 wks), moderate (clinic debridement, healed at 8 wks), or severe (OR debridement, implant loss, or not healed at 8 wks). Uni- and multivariate (MVA) analysis was performed. Significant factors associated with flap necrosis are shown in the table. On MVA, expander size was associated with any necrosis (OR 1.17, 95%CI 1.02-1.34, p=0.03), but not mod/severe necrosis. Conclusion: Modifiable factors had limited impact on SFN. Severe SFN was infrequent, but strongly associated with NSM even among experienced surgeons. Patients opting for NSM should be educated regarding the risk of both nipple and flap necrosis. In patients with multiple factors increasing the risk of SFN, removal of additional skin to ensure viability may be prudent.
defined as an interlimb volume difference of >10% by VD when compared to baseline (with or without an abnormal L-Dex). Change in L-Dex was plotted against change in VD at 3 and 6 months; correlation was assessed using Pearson correlation. RESULTS: Median follow-up was 13.5 months. Over the study period, 165 patients had 625 follow-up measurements. Twenty-four developed preclinical lymphedema; 4 progressed to lymphedema while 20 have remained asymptomatic at a median follow-up of 8 months. In total, 10 patients developed lymphedema requiring treatment. Evaluating all time points, of 15 abnormal VD measurements, 9 were abnormal by L-Dex. Of 54 abnormal L-Dex measurements, 9 were abnormal by VD. 565 measurements were normal by both methods. There was no clear correlation between change in VD and change in L-Dex at 3 months (R=0.32) or at 6 months (R=0.14).

CONCLUSIONS: VD and bioimpedance demonstrated poor correlation with inconsistent overlap of measurements considered abnormal. Of patients considered to have preclinical lymphedema, few progressed to lymphedema. Further studies are needed to understand the clinical significance of preclinical lymphedema as defined by bioimpedance.
rates. Abnormal nodes were seen on 7%, 25%, and 30% of mammograms, US, and MRIs, respectively. While abnormal lymph nodes on mammogram or US were associated with a significant increase in ALND, 68-73% of women with abnormal axillary imaging had <3 positive SLNs and did not require ALND. Among 10 patients with >2 abnormal LNs on imaging, only 2 required ALND. Conclusion: Among clinically node-negative patients with abnormal axillary imaging, 71% did not meet criteria for ALND and were spared further surgical morbidity. Abnormal nodes on US, MRI, or mammogram in clinically node-negative patients are not reliable indicators of the need for ALND. Axillary imaging in this population is not cost-effective.

### Table 1

<table>
<thead>
<tr>
<th>Imaging Modality</th>
<th>Number of patients (N)</th>
<th>Number of images reviewed (%)</th>
<th>ALND</th>
<th>Spared ALND</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No LNs done</td>
<td>183</td>
<td>195 (81%)</td>
<td></td>
<td></td>
<td>0.005</td>
</tr>
<tr>
<td>0 abnormal LNs</td>
<td>181</td>
<td>21 (12%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any abnormal LNs</td>
<td>61</td>
<td>18 (30%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>182</td>
<td>43 (70%)</td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
</tbody>
</table>

### Validation of the ACOSOG Z11 Trial Criteria: A Matched Cohort Analysis on 637 Women

**Background** The ACOSOG Z0011 (Z11) trial has been criticized for possibly selecting patients with favorable tumors at low risk of axillary recurrence. In order to assess for possible selection bias, we compared the features of the patients in Z11 to another large non-selective sentinel lymph node (SLN) study from the same time period (1997-2004).

**Methods** The University of Louisville Breast Cancer Sentinel Lymph Node study (ULSLN), prospectively enrolled patients with T1-T3, N0 tumors for SLN biopsy followed by axillary dissection (AD). A subset of SLN positive patients from this database that met Z11 eligibility criteria was compared to the AD arm of Z11. T-test and chi square test were used to assess the differences between the two studies and to determine factors related to the risk of increased tumor burden (≥4 positive nodes) in the axilla. Results: 637 patients in the ULSLN study had T1-T2 tumors treated with lumpectomy and at least one positive sentinel lymph node. Of these, 576 patients had ≥2 positive nodes and met Z11 criteria to avoid AD. When compared, both groups were well balanced in terms of T stage (p=0.47), total number of positive lymph nodes (p=0.94) and percentage of non-SLN involvement (27.3% Z11 vs. 30.4% ULSLN, p=0.31). ULSLN had more ductal carcinomas and less of other tumor types (p=0.02). Ninety percent of patients (576/637) in ULSLN could have been spared from AD, according to Z11 criteria. On subset analysis, patients with T2 tumors and 2 positive SLN had an increased risk of having ≥4 involved lymph nodes, compared to those with T1 tumors and one positive SLN (35.0% vs. 12.5%, P=0.01, OR 3.76 [1.87-7.57 95% CI]). Conclusion: The similarities between cohorts in these two studies suggest that the AD arm of Z11 represents the majority of patients undergoing breast conservation with one to two positive SLN, and not only those with favorable features. Our study confirms that approximately 30% of these patients have non-SLN metastases. Patients with T2 tumors and 2 positive SLN have a threefold increased risk of extensive axillary nodal tumor burden and may be considered for AD or adjustment of radiation therapy plans, as some Z11’s critics suggest.

### Comparison of the Z11 axillary lymph node dissection arm with the University of Louisville Breast Cancer Sentinel Lymph Node study subset of lumpectomy with 1 to 2 positive SLN.

<table>
<thead>
<tr>
<th>Number of Patients</th>
<th>Median age</th>
<th>T stage n(%)</th>
<th>T stage n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACOSOG/Z11</td>
<td>418</td>
<td>56</td>
<td>418</td>
</tr>
<tr>
<td>ULSLN</td>
<td>576</td>
<td>55</td>
<td>576</td>
</tr>
<tr>
<td>p-value</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

**Introduction:** Volatile Organic Compounds (VOCs) that are indicative of disease state are found in the exhaled air. The aim of this study was to identify Breast Cancer Characteristic VOCs patterns and to evaluate the accuracy of Breast Cancer detection utilizing a novel VOCs analysis system. Methods: Breast samples of 79 Breast Cancer Patients, biopsy proven, prior to treatment and of 65 healthy women were collected at our breast clinic. Samples were transferred for analysis. The Patients exhaled breath into breath kits with sorbent capsules to absorb VOCs. Capsules were mounted on a fast Gas Chromatography device for 10 minutes analysis. The chromatographic data from all samples
was then analyzed by a novel algorithm to identify the VOCs clusters that are breast cancer biomarkers. Study was approved by the Institutional Review Board, all subjects have signed written informed consent. RESULTS: A total of 41 biomarkers has been detected, yielding 85% sensitivity and 86% specificity, cross validated by a delete-1 jackknifing, with p value < 0.0001. Test sample with at least one biomarker is diagnosed as breast cancer positive. 17 biomarkers were non-invasive, simple and low cost test, with 85% sensitivity and 86% specificity. The described method has the potential to become a screening tool for early detection of breast cancer.

68
Quantitative High Throughput Screening Identifies Carfilzomib as an Effective Anticancer Agent for Adrenocortical Carcinoma

K. Auffarth,1,∗ M. Boufraqech,1 E. Li-Chittenden,1 Y. Zhang,2 M. Shen,2 K. Gaskin,1 L. Zhang,2 E. Kebebew,1 1. Endocrine Oncology, National Cancer Institute, Washington, DC; 2. National Center for Advancing Translational Sciences, Bethesda, MD.

Background: Adrenocortical Carcinoma (ACC) is a rare malignancy with high mortality. Currently there is no effective therapy for ACC. Drug repurposing for cancer treatment is an emerging concept for identifying clinically approved drugs, especially for rare/orphan cancers. The aim of the present study was to use a quantitative high throughput drug screening (qHTS) approach to identify and validate novel therapeutic agents with anticancer effects in ACC. Methods: qHTS of 3,282 clinically approved drugs and pharmacologically active small molecules was performed in 2 ACC cell lines (SW13, and BD140A) using cell proliferation, apoptosis, and three-dimensional multicellular tumor spheroids (MCTS) assays. In vivo xenograft tumor model of ACC in nude mice was conducted to confirm in vivo findings. Results: We identified 60 active agents by qHTS. Carfilzomib, a second generation proteasome inhibitor, was one of the most active agents in ACC cells. The ACC cell lines were treated with different concentrations of Carfilzomib (1.13 nM–126.5 μM), well below the clinically achievable plasma concentration (5.9 μM). Carfilzomib treatment significantly inhibited cellular proliferation (70–98% at day 6), which was dose and time dependent, in all 3 cell lines. This effect was observed at concentrations up to 1000-fold lower than the achievable plasma concentration in humans. Carfilzomib treatment also induced caspase-dependent apoptosis (p<0.0001) and inhibited tumor spheroid growth compared to vehicle. In the xenograft model of ACC, Carfilzomib significantly inhibited tumor growth by weeks 3, 4, and 5 (p<0.03) (N=16 tumors/group). Carfilzomib treated mice had significant weight loss compared to control (p<0.01). However, no mice experienced toxicity-related mortality. Conclusions: Carfilzomib shows promising anticancer effects in preclinical studies of ACC and warrants further investigation in clinical trials for ACC.

69
Wide Inter-institutional Variation in Performance of a Molecular Classifier for Indeterminate Thyroid Nodules


INTRODUCTION: The Afirma Gene Expression Classifier (GEC) is used to assess risk of malignancy in indeterminate thyroid nodules (ITNs) classified as Bethesda Category III/IV. GEC performance is dependent on an institution’s prevalence of malignancy in ITNs. Our objective was to analyze the performance of the GEC at 2 institutions with high volume thyroid cytopathology but differing prevalence of malignancy. METHODS: We examined the performance of the GEC at 2 neighboring institutions, a comprehensive health system (MSBI), and a tertiary-referral cancer center (MSC), with differing prevalence of malignancy in ITNs. Retrospective analysis of all ITNs evaluated with the GEC at Memorial Sloan Kettering Cancer Center (MSC; n=944) or Mount Sinai Beth Israel (MSBI; n=64) in New York, NY. We have previously calculated the prevalence of malignancy in ITNs as 30–38% (MSK) and 10–19% (MSBI). Surgical pathology was correlated with GEC findings for each nodule. Positive and negative predictive value (PPV, NPV) were estimated using Bayes Theorem. RESULTS: Patient and nodule characteristics were similar at MSK and MSBI: mean age 49 vs. 57y, 66% vs. 75% female; median nodule size 1.7 vs 2.4 cm. The GEC benign call rate was 38% (MSK) and 50% (MSBI). Of GEC-benign nodules, 8% (MSK) and 16% (MSBI) underwent surgery; all were benign on surgical pathology. At the time of analysis, 60% (MSK) and 50% (MSBI) of GEC-suspicious nodules had undergone surgery. The PPV of a GEC-suspicious result was 57.1% (95%CI 41.0–72.3) at MSK and 6.3% (95%CI 0.2–30.2) at MSBI. The estimated NPV was 86.9% (MSK) and 95.9% (MSBI). CONCLUSION: The performance characteristics (benign call rate, PPV and NPV) of a diagnostic test with given sensitivity and specificity are dependent on the prevalence of disease in the population. We observed wide variation in benign call rate, PPV and NPV of the GEC, comparable to predicted values based on prevalence (Figure). Depending on practice setting, the implications of a benign or suspicious GEC result may differ. Knowledge of the prevalence of malignancy in ITNs at a particular institution is critical to the reliable clinical interpretation of GEC results.

70
Role of Adrenal Vein Sampling in Primary Hyperaldosteronism with Non-localizing Imaging


Background: Adrenal Vein Sampling (AVS) is a non-invasive, simple and low cost test, with 85% sensitivity and 86% specificity, The described method has the potential to become a screening tool for early detection of breast cancer.
the 54 NL patients with a lateralizing gradient on AVS, 45 (83.3%) underwent laparoscopic adrenalectomy at our institution. Adrenal adenomas were found on histopathology in 95.6% (n=43) of patients who underwent surgery. The median tumor size was 1.0 cm (IQR 0.7-1.5 cm). Conclusion: In this study, AVS changed management in a significant minority of L patients, and successfully identified unilateral PHA in the majority of NL patients. Small adenomas were common in the NL group. AVS can identify surgically curable PHA which is missed by cross-sectional imaging, and therefore is essential for all patients with non-localizing imaging.

### Table 1: Characteristics of patients with primary hyperaldosteronism (PHA) and non-localizing imaging who underwent successful adrenal vein sampling (AVS)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Unilateral gradient on AVS (n=51)</th>
<th>No gradient on AVS (n=39)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>35 (64.3)</td>
<td>22 (56.4)</td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>19 (35.7)</td>
<td>17 (43.6)</td>
<td>0.391</td>
</tr>
<tr>
<td>Presence of extra-adrenal mass</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No adrenal mass (%)</td>
<td>40 (74.2)</td>
<td>33 (84.6)</td>
<td></td>
</tr>
<tr>
<td>Bilateral adrenal masses (%)</td>
<td>13 (24.2)</td>
<td>6 (15.4)</td>
<td></td>
</tr>
<tr>
<td>Non-localizing, NOS (%)</td>
<td>1 (1.9)</td>
<td>0 (0.0)</td>
<td></td>
</tr>
<tr>
<td>Lateralization index*</td>
<td>12.2 (10.0)</td>
<td>1.0 (0.8)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Lateralization index was defined as the higher aldosterone to cortisol ratio divided by the lower aldosterone to cortisol ratio. Abbreviations: PHA – Primary hyperaldosteronism; AVS – Adrenal vein sampling; SD – Standard deviation; NOS – Not otherwise specified.

### 71

**Role of Octreotide Scan in Localization of Intra-abdominal Neuroendocrine Tumors**


**Introduction**

Neuroendocrine tumors (NETs) are most often small and slow-growing. Identifying these lesions is often difficult, especially in early stages of the disease. Cross-sectional imaging (CT or MRI) is frequently performed in the evaluation of this disease, but the relative additional value of octreotide scan in these patients is not well defined. Methods: A retrospective cohort study was performed using our prospectively maintained institutional neuroendocrine surgery registry inclusive of carcinoid and pancreatic neuroendocrine tumors (1997 -2011). Patients were identified with a NET who had both pre-operative octreotide scan (OS) and cross-sectional imaging (CS). Comparisons in sensitivity of imaging modalities were performed using Wilcoxon ranksum test, Fisher’s exact test and Chi square test as appropriate. Results: Out of 116 patients with NET undergoing surgical resection, 60 patients underwent both pre-operative OS and CS and were included for study. At least one suspected NET (primary or metastatic) was more commonly identified by CS (N=53, 88.3%) as compared to OS (N=46, 76.7%), p<0.05. Moreover, CS was able to detect lesions in 10 of 14 patients (71.4%) with negative OS imaging. Lesions in these 10 patients were identified on surgical exploration in the pancreas (N=5), liver (N=4) and small bowel (N=1). Conversely, OS was able to detect lesions in 4 of 7 patients (57.1%) with negative CS imaging. Of these 4 patients, 3 had tumors in the small bowel and one in the cecum. Mean size of small bowel tumors was 2.67 cm. Among patients with liver metastases identified at surgery (N=19), sensitivity of OS and CS were 68.4% and 89.4% respectively (p<0.05). In patients with liver lesions identified by both CS and OS, the mean number of liver metastases identified were fewer in OS (1.2) versus CS (2.7) group (p=0.01). Conclusion: Cross-sectional imaging identifies the large majority of NET and appears to have particular utility for tumors in the liver and pancreas as compared to octreotide scan. OS may have adjunct role in identifying small bowel carcinoids in a subset of patients with small bowel tumors otherwise radiographically occult by cross-sectional imaging.

### 72

**Does the Addition of Adjuvant Intraoperative Post-dissection Tumor Bed Chemotherapy during GI Neuroendocrine Tumor Debulking Benefit Patients?**


**Background:** Midgut neuroendocrine tumor (NET) patients are often diagnosed at an advanced stage with extensive mesenteric lymph node and liver metastasis. The only treatment for potential cure and durable results is resection with extensive debulking. However, even with the most elegant surgical dissection/resection, macro and microscopic residual disease at the tumor resection bed remains a distinctive possibility. We hypothesize that local application of 5-florouracil (5-FU) within tumor bed would eliminate the microscopic residual disease post operatively. Methods: Surgical records of 188 consecutive patients who underwent extensive cytoreductive surgeries for stage IV, small bowel NETs with boggly mesenteric lymphadenopathy between 2003-2012 were reviewed. 85 Patients who had 5-Florouracil saturated gelfoam strips secured into their mesenteric resection defects served as the study group (n=85) with one hundred three patients who did not receive such intra-operative chemotherapy as the control (n=103). Survival from the time of diagnosis, postoperative morbidity and mortality between the two groups were collected and compared. Results: Mortality rates at immediate, 30, 60 and 90 days post operative period were 3; 0; 1; 0; and 0; 2; 0; 4 respectively for study and control group. Minor complications (Clavien-Dindo Grade I and II) at 30, 60 and 90-day postoperative period were 12; 0; 1 and 5; 5 respectively. Major complications (Grade III and IV) at the same time intervals were 2; 0; 2 and 2; 0; 4 respectively for study and control groups. Most of all, the mean survival from time of histological diagnosis for the study patients was 210 months (17.5 years) as compared to 177 months (14.7 years) for the control group with a difference of 33 months (2.75 years). Conclusion: Intra-operative tumor resection bed chemotherapy is a safe adjuvant without any discernible toxicity. Furthermore, it might provide survival benefit to midgut NET patients with extensive mesenteric lymphadenopathy undergoing extensive cytoreductive surgery without additional procedure related complications.

![Application of 5 FU treated gelfoam to post dissectional tumor bed.](image)

### 73

**Impact of Multifocality in the Management of Small Bowel Neuroendocrine Tumors**

A. Gangi,*, E. Siegel, N. Mann, S. Lo, L. Jamil, M. Choi, A. Hendlir, N. Nissen, S. Colquhoun, R. Yu, E. Wolin, F. Amersi, J. Surgery, Cedars-Sinai Medical Center, Playa Vista, CA; 2. University of Louisville, Louisville, KY.

**BACKGROUND:** Neuroendocrine tumors (NET) account for 30% of small bowel neoplasms. Appropriate localization and surgical resection leads to improved outcomes. Our objective was to evaluate the incidence of multifocality in primary small bowel NET in addition to determining the utility of double balloon enteroscopy (DBE) in the management of these patients. METHODS: Retrospective review of a database identified 178 patients with primary small bowel NET diagnosed between 2006 and 2013. Final analysis included only those patients who underwent pre-operative and surgical inter-
vention at our institution. RESULTS: 107 patients met study criteria. Of these, 48% were male with an average age of 61.04 years. 59 patients had a primary NET in the ileum (55.1%), 23 patients mid small bowel lesions (21.5%), and 21 patients with duodenal primaries (19.6%). Pre-operatively 8 patients underwent capsule endoscopy and 49 patients had a DBE. Of those patients who underwent DBE, 24 (49%) had additional lesions, of which 13 patients (54%) had these lesions confirmed as NET on biopsy. Fifteen (63%) patients who had additional lesions on DBE had a primary tumor in the ileum. Sixty one patients (57%) underwent laparotomy and 21 patients (19.6%) underwent laparoscopic resection. Twenty five patients (23.4%) had liver cytoreductive surgery at the time of resection. Average primary tumor size was 2.6 cm. A majority were well differentiated (91.7%), and most had a Ki-67 of el al (49.5%). 77% of patients had adrenocortical metastases. 43 (40%) patients had multifocal disease, of which 28 (65%) had a primary lesion in the ileum. Of the patients who had DBE, 30 patients had additional NET lesions on final path. Of these 30, 10 patients had negative findings on DBE and 20 had additional lesions identified on DBE, of which 12 had NET identified on DBE biopsy specimens. At a median follow up of 21 months, 90.6% patients were alive: CONCLUSIONS: Small bowel NET tumors have a high incidence of multifocality. DBE proved valuable in the detection and diagnosis of multifocal NET. Incidence of multifocality was higher in those patients with positive DBE findings. Use of DBE in patients with NET could guide preoperative planning.


Introduction: Size ≥ 4 cm has traditionally guided increased suspicion of malignancy and need for adrenalectomy. Cross-sectional imaging features can also provide reliable characterization. Our study objective was to compare imaging features and mass size for accuracy in diagnosing adrenal malignancy.

Methods: Data were retrieved for a consecutive series of 112 patients who had adrenocortical adenoma from 1/1/8-14. Pheochromocytomas were excluded due to well-recognized imaging features. Malignancy, imaging features were classified as indeterminate if HU >10 was seen on noncontrast CT scan or no loss of signal on out-of-phase imaging was present on chemical-shift MRI. Indications for adrenocortical adenoma included hormonal hypersecretion, presence of indeterminate imaging features, and/or mass size ≥ 4 cm. Results: Of 113 resected adrenals, 37% were functional and 1 patient had bilateral adrenocortical adenoma. Histologic malignancy was diagnosed in 17.7% (20/113) of adrenergens, and included 3 adrenocortical carcinomas, 1 epitheloid liposarcoma, 1 lymphoma, 1 malignant nerve sheath tumor arising from the adrenal gland, and 14 adrenal metastases. Malignant adrenal masses were more common in older patients (mean 60.13y v. 51.1+1.4y, p=0.01), and were larger on preoperative imaging (mean 5.3+3.2cm v. 3.9+2.4cm, p=0.03). All 20 malignant adrenal masses had indeterminate imaging features. In predicting malignancy, the sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV) of indeterminate imaging features was 100%, 57%, 100% and 33%, respectively. Mass size ≥ 4 cm was less predictive with a sensitivity, specificity, NPV, and PPV of 55%, 61%, 86%, and 23%, respectively. If size ≥ 4 cm had been used as the sole criterion, nearly half of malignancies (9/20, 45%) would have been missed including 8 metastases and an adrenocortical carcinoma. Conclusion: In resected adrenal incidentosomes, the presence of indeterminate imaging features was a more sensitive criterion for malignancy than mass size (100% v. 55%) and predict malignancy with equivalency specificity (57% v. 61%). Regardless of mass size, adrenocortical adenoma should be strongly considered when indeterminate imaging features are present.

Lymphoscintigraphy Concordance with Intraoperative Findings from Sentinel Lymph Node (SLN) Biopsy with 18F-FLT Tilmancet in Clinically Node-negative (cN0) Head and Neck Squamous Cell Carcinoma Patients (HNSSC) D. Chepeha,1 A. Agrawal,2 F.J. Civانتos,3 S.Y. Lai,1 J. Otolaryngology, University of Toronto - Princess Margaret Hospital, Toronto, ON, Canada; 2. The Ohio State University, Columbus, OH; 3. University of Miami Hospitals and Clinics, Miami, FL. 4. MD Anderson Cancer Center, Houston, TX.

INTRODUCTION: SLN biopsy has been shown to be a suitable alternative to full lymph node dissection in cN0 early-stage breast cancer and melanoma (ACOSOG Z0011, NSABP B-32, MSLT-1). SLN biopsy has been extensively studied and has recently been added to the NCCN clinical practice guidelines (v1.2014) for early oral cavity cancer. A phase 3, prospective, multi-institutional, open-label, single arm trial assessed 18F-FLT Tilmancet, a CD206 receptor-targeted radiopharmaceutical, for intraoperative identification of SLNs in cN0 intraoral or cutaneous HNSCC patients (ClinicalTrials.gov/ NCT00913296). METHODS: This trial enrolled 101 patients with clinically T1-T4, N0, M0 HNSSCC. Patients received 50 μg (18F-FLT Tilmancet) radio-labeled with either 0.5 mCi (same-day) or 2.0 mCi (next-day), followed by lymphoscintigraphy, tumor resection, SLN biopsy, and planned elective neck dissection (END). All excised tissues were evaluated for tissue type and tumor presence. The primary endpoint of the study was the false negative rate (FNR) associated with 18F-FLT Tilmancet-identified SLNs relative to the pathology status of non-SLNs. Exploratory endpoints included the success of preoperative lymphoscintigraphy and its agreement with intraoperative SLN findings. RESULTS: 100% of the 85 patients injected with 18F-FLT Tilmancet (79 intraoral, 6 cutaneous HNSCC) were imaged preoperatively with planar lymphoscintigraphy and/or SPECT/CT. Table 1 summarizes the lymphoscintigraphy results. Notably, 95.2% of patients had agreement between their preoperative (by imaging) and intraoperative (by handheld probe) findings. CONCLUSIONS: High concordance between preoperative lymphoscintigraphy and intraoperative SLN findings using 18F-FLT Tilmancet confirms the utility of preoperative imaging in planning and conducting SLN biopsy. These findings are comparable to previously presented imaging data with 18F-FLT Tilmancet in breast cancer and melanoma studies and demonstrate the clinical utility of 18F-FLT Tilmancet for lymphoscintigraphy.

Summary of Lymphoscintigraphy Results

<table>
<thead>
<tr>
<th>Injected population (n)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoscintigraphy performed, yes (n, %)</td>
<td>85 (100%)</td>
</tr>
<tr>
<td>Intra-op re-treatment population (n)</td>
<td>83</td>
</tr>
<tr>
<td>Hot spot located with lymphoscintigraphy? Yes (n, %)</td>
<td>77 (92.8%)</td>
</tr>
<tr>
<td>Patient also had at least 1 hot SLN intraoperatively (n, %)</td>
<td>77 (100%)</td>
</tr>
<tr>
<td>Ne (n, %)</td>
<td>6 (7.2%)</td>
</tr>
<tr>
<td>Patient had no SLN intraoperatively (n, %)</td>
<td>2 (33.3%)</td>
</tr>
<tr>
<td>Patient had at least 1 hot SLN intraoperatively, n (%)</td>
<td>4 (66.7%)</td>
</tr>
<tr>
<td>Total agreement between lymphoscintigraphy and SLN findings (%)</td>
<td>99.2%</td>
</tr>
</tbody>
</table>


Introduction: Common questions by cancer patients include “Will I die from this cancer?” and “Will this scan find cancer?” A published survival curve can help answer these questions at the time of initial treatment. But after that point in time, the correct probabilities shift as the DFI (disease free interval) since surgery increases. Methods We present a Bayesian model of post-surgical sarcoma risk which dynamically updates the survival curves in Kattan et al. (2002) for DFI, and provides time-dependent probabilities to answer the questions above and more. To examine risk perceptions, we asked a survey sample of 306 adults from the general population to estimate the remaining lifetime risk and scan risk when randomly assigned to realistic cancer scenarios differing in lifetime risk (20%, 50%, 80%) and DFI (6 mo, 2 yr, 5 yr). Results The model shows us that the risk of a given scan detecting a return or spread of cancer is actually very low, because that scan covers only a fraction of the remaining lifetime. Figure 1 illustrates this contrast using the overall sarcoma risk of .40 from Kattan et al. On average, survey respondents overestimated the remaining lifetime risk compared to the model probability (mean overestimation = .122, p <.001), and even more so as the DFI increased. They also vastly overestimated the probability that a scan will show cancer (mean overestimation = .319, p<.001). Many respondents appear to think that the risk for one scan is similar to the remaining lifetime risk. Reactions from focus groups of sarcoma patients suggest that they have similar misperceptions. A survey of similar patients is in progress to assess this more systematically. Conclusion Follow-up appointments and scans provide natural points in time to update disease risks. Currently, physicians have no systematic way to adjust the original survival curve for DFI. These appointments are extremely stressful for patients because a scan result could show that the cancer is back. Our method for determining these time-dependent (and declining) risks could help physicians to decrease patients’ emotional distress and better manage their risk perceptions.
A Simple preoperative Risk Scale Accurately Predicts perioperative Mortality following Gastric Resection for Malignancy C.R. Harnsberger,1,2 H.F. Fuchs,3 R.C. Broderick,3 G.R. Jacobsen,3 B.J. Sandler,3 D.C. Chang,4 K. Kelly,5 S. Horgan,6 1. University of California, San Diego, Department of Surgery, Center for the Future of Surgery, San Diego, CA; 2. Massachusetts General Hospital, Harvard Medical School, Department of Surgery, Codman Center, Boston, MA.

Purpose: Gastric resection is a primary treatment modality in management of patients with gastric cancer, but can be accompanied by significant mortality in certain populations. We sought to create a simple risk scale that can be used at the bedside to predict perioperative mortality of gastric resection for malignancy using preoperative patient and hospital factors. Methods: The Nationwide Inpatient Sample (NIS) database was used to create a risk scale. Adult patients were included if they had a diagnosis of gastric cancer and underwent a potentially curative partial or total gastrectomy as identified by ICD-9 codes. Multivariate logistic regression analyses were used to create a predictive model of perioperative mortality, and subsequently to construct a risk scale. Results: From 1998-2011, a total of 24,538 patients were included. The overall perioperative mortality rate was 5.5%. Independent patient predictors of mortality incorporated in the risk scale included male gender, age ≥75 years, and comorbid disease (cardiovascular, pulmonary, renal, and hepatic); hospitals that performed ≥25 gastric resections for cancer per year was a protective factor. The calibration revealed a good agreement between observed and expected mortality at each risk score. Sensitivity and specificity for each score were calculated, and thereby low-risk populations (score<6) and high-risk populations (score ≥6) were defined. Mortality in patients with a score of 0-5 ranged from 1.3-4.5% compared to 6.0-23.1% in patients with a score of 6-11. (Figure 1) Conclusion: This simple preoperative risk scale may accurately predict perioperative mortality following gastric resection for cancer while accounting for patient and hospital factors, and is clinically useful for preoperative patient counseling.

Figure 1: Risk Scale Properties in Gastrrectomy for Gastric Cancer

78 Oncology-led Clinical Documentation Improvement Program Beneficial for Physicians and Hospital A.J. Ward,1 J.M. McLoughlin,2 J.M. Lewis,3 J.L. Bell,4 C.T. La Charité,5 K.D. Gray,6 1. Surgical Oncology, University of Tennessee Medical Center Cancer Institute, Knoxville, TN; 2. University of Tennessee Medical Center Cancer Institute, Knoxville, TN.

Object: Successful Clinical Documentation Improvement (CDI) programs may improve relative clinical outcomes and maximize hospital DRG-related reimbursement. Lack of physician champions remains a key obstacle to successful implementation. Because the case mix index (CMI) of surgical oncology inpatients ranks among the highest nationally, surgical oncologists may be the ideal group to lead CDI implementation. This abstract reports the success of a CDI pilot program implemented by a surgical oncology division. Methods: After appropriate CDI training, a physician extender conducted audits and updates of all inpatient diagnoses for four surgical oncologists, from November 2012 to May 2014. Diagnoses were listed as either present on admission or occurring during the inpatient stay. CMI, average risk of mortality and average severity levels of 489 inpatients during this study period were compared to 482 inpatients from March 2011 to October 2012, during which no intentional CDI improvement activities were performed. Results: Audits and updates of all diagnoses related to surgical admission significantly increased the departments CMI, average risk of mortality, and average patient severity level. CMI increased from 2.38 to 2.59 (p<0.001), the average risk of patient mortality increased from 1.88 to 2.07 (p<0.001), and the average patient severity level increased from 2.32 to 2.54 (p<0.001). The rise in CMI corresponded with a $728,830 relative increase in hospital reimbursement. Conclusions: CDI may be the most important next step for physicians in the era of pay for performance, bundled payments, and dwindling operating margins. Compliance with such programs creates a win-win healthcare environment where practitioners and hospital leaders can benefit. Training post graduates and physician extenders in CDI can curtail the added time commitment required by individual physicians. Added hospital reimbursement related to improved documentation may be a point of negotiation with the hospital for new hires and equipment.

79 Prolonged Venous Thromboprophylaxis following Major Abdominal and Pelvic Cancer Surgery: A Meta-analysis and Systematic Review V. Chakravorty,* R. Chamberlain, St. Barnabas Medical Center, Livingston, NJ.

Introduction: Deep vein thrombosis (DVT) is a potentially fatal complication following any major abdominal or pelvic cancer surgery, and malignancy further increases the risk of DVT. Current DVT prophylaxis guidelines for patients undergoing major abdominal/pelvic procedures recommend thromboprophylaxis (TP) be continued until hospital discharge, and its efficacy in decreasing DVT risk is well established. More recent data suggests that a substantial percentage of DVT events occur post-discharge, and whether prolonged post-discharge DVT prophylaxis should be continued remains controversial. This study represents a meta-analysis of all published randomized controlled trials (RCTs) investigating prolonged DVT prophylaxis following major abdominal and pelvic surgery for malignancy. Method: A comprehensive search of PubMed, Google Scholar, and the Cochrane and the NIH Registry of clinical trials assessing duration of TP with low molecular weight heparin (LMWH) following major abdominal and pelvic cancer surgery was performed with studies identified from 2002 to 2014. Outcomes analyzed included DVT, and bleeding events during the study period. Results: 4 trials involving 1,538 patients evaluated 4- vs. 1-week of post-operative TP using LMWH and were included in the meta-analysis. The risk of DVT was decreased by 53.3% in patients receiving 4-weeks of TP vs. 1-week (RR 0.447, CI 0.246-0.818; p=0.352). No significant difference in the risk of bleeding (p=0.077) was observed. Conclusion: 4 weeks of TP is associated with significantly decreased risk of DVT following major abdominal and pelvic surgery (53.3%) with no increased risk of bleeding complications compared with 1-week of TP. In patients undergoing major abdominal and pelvic cancer surgery, which are not at prohibitive risk of bleeding, 4-weeks of TP post-operatively should be adopted as standard of care. Additional studies looking specifically at VTE-related mortality and incidence of pulmonary embolism are required as this data is currently limited or non-existent.
164 were diagnosed with invasive breast carcinoma. 260 patients in the RDU group were investigated, resulting in 154 diagnoses of invasive carcinoma. Lesion characteristics were not significantly different between groups. Patients visiting the RDU had fewer visits for biopsies (92% in RDU group with single visit for biopsy vs. 78% in non-RDU group, p<0.0001). For patients with invasive disease, the RDU group had a significantly shorter wait time from initial consultation to delivery of diagnosis (mean 2.1 vs. 16.7 days; p=0.0001) and a greater probability of receiving neoadjuvant chemotherapy (37% vs. 24%, p=0.0106). Overall time from referral to management remained statistically unchanged (mean 53 (RDU) vs. 50 days (non-RDU), p=0.3860). Conclusions: Introduction of a RDU appears to decrease wait times to definitive diagnosis but not to treatment initiation, suggesting that obstacles to care delivery for breast cancer patients may occur at several points in the diagnostic trajectory. Multi-pronged efforts to reduce system-related delays to treatment are needed.


Background: While the literature is replete with findings underscoring the issue of elderly (≥ 65 years) into surgical oncology trials, little is known about the attributes and outcomes of older individuals who do enroll in these trials. A deeper understanding of these trends will inform future designs of elderly surgical oncology trials. To bridge this gap, Z901101 was conducted as a pooled analysis of 21 ACOSOG studies aimed at assessing variations in attributes and outcomes of older adults who do enroll in surgical oncology trials. Study design: 12,367 participants in breast, gastrointestinal, thoracic or other studies that had reached target accrual, closed, or were nearly closed were included. Logistic regression analyses were used to assess the impact of older age on: adverse events (AEs) and trial completion: 1) across all 21 protocols, 2) therapeutic trials only, 3) and within each disease site. Results: 36% of ACOSOG participants were ≥65 years. Of these, 90% completed participation in their protocols and 28.6% experienced ≥3 AEs. Older participants were more likely to experience AEs ≥ grade 3 (25% vs. 36%, p <0.001). Older participants in breast trials experienced higher AEs (OR 1.3, p=0.11) than their younger counterparts but were as likely to complete their trial (OR 1.2, p=0.75). Evaluation of older participants in GI trials experienced higher AEs (OR 1.5, p=0.003) and lower rates of trial completion (OR 0.5, p<0.001). Similar patterns were also observed in participants ≥70 years. Conclusion: In this pooled analysis of 12,367 participants in ACOSOG trials, older age continues to impact patterns and outcomes of enrollees overall and within-disease sites. Findings highlight the need for targeted interventions to augment enrollment of older adults especially in non-breast trials to broaden the benefits of cancer clinical trials to the aging population of the US.

82 Minor Complications are not Minor: The Effect of postoperative Complications on Early Patient Satisfaction with their Surgeon L. Selby,*, A. Scott, S.M. Jhanwar, V.E. Strong, A.L. Pusic. Memorial Sloan Kettering Cancer Center, New York, NY.

Introduction: Post-operative complications are commonly graded according to the Clavien–Dindo classification, a clinician reported outcome scale. The BREAST-Q, a patient reported outcome instrument, measures multiple outcomes and patient satisfaction with quality of life following breast surgery. The objective of this retrospective cross-sectional study was to investigate the impact of complications on patient satisfaction following breast cancer surgery. Methods: At our institution, patients undergoing breast surgery routinely complete the BREAST-Q at multiple post-operative time points. Surgical complications are prospectively recorded and graded according to our institution’s surgical secondary events database, a modified Clavien–Dindo classification. Grade 1 and 2 complications are classified as minor. Patients were included in this study if they completed the BREAST-Q at least once following mastectomy and tissue expander insertion. Student’s t-test was used to analyze differences in BREAST-Q score between groups. Results: Since 2010, 1,558 patients underwent either therapeutic or prophylactic mastectomy with tissue expander insertion and completed the BREAST-Q at least once post-operatively. A total of 284 patients (18%) had at least one documented complication, 82 of whom (29%) had multiple documented complications. The majority of documented complications were Grade 1 (47%) or Grade 2 (19%). Mastectomy skin flap necrosis was the most common complication (10%), followed by cellulitis (4%) and hematoma (3%). Patients with an early post-operative complication reported significantly lower satisfaction with their surgeon six weeks post-operatively than patients who did not suffer a complication (78 vs 83, MID = 4, p = 0.05). Discussion: Complications, even those considered minor by clinicians, can have a significant negative impact on patient-reported outcomes. Our study highlights the importance of considering both clinician and patient-reported outcomes in quality metrics. Understanding both perspectives may provide important insights for preoperative patient education, postoperative care and quality improvement.

83 Does Surgical Palliation Improve Quality of Life Outcomes at the End of Life? A. Falor,* V. Sun,* D. Smith,* D. Luyimbizi,* L. Uyeno, G. Singh, V. Trisal. 1. City of Hope, Duarte, CA; 2. Virginia Tech Carillion School of Medicine, Roanoke, VA; 3. Kaiser Permanente Hawaii, Honolulu, HI.

Background: Surgical palliation seeks to relieve suffering and improve quality of life (QOL) for patients with terminal malignancies. A previous review of our experience demonstrated that short hospital stays and low morbidity are achievable when surgical interventions are selectively used. The purpose of this analysis was to examine not only clinical but QOL outcomes of patients who underwent palliative procedures at an NCI-designated comprehensive cancer center. Methods: Surgical case logs from January 1 to December 31, 2011 were retrospectively reviewed for procedures performed in patients whose 5-yr survival was less than 5%. Cases were selected in which the goal of the operation was improvement of QOL and relief of symptoms. Data regarding procedures (primary diagnosis, type and number of procedures), clinical outcomes (length of stay, readmissions), and QOL (symptom relief, Karnofsky Performance Score - KPS) were extracted from patient medical records. Data were tabulated using descriptive statistics. Preoperative and postoperative
mean endpoints were compared with ANOVA tests. Results: In 2011, 247 procedures were performed for palliation (11.9%) on 202 patients. The most common diagnoses were large intestine (11%), lung (9%), stomach (9%) and breast (9%) cancer. The majority of patients (83%) underwent a single palliative procedure. The most common indications were dysphagia (13%) and pain (10%). Postoperatively, only 3% presented to urgent care within 30 days. Pain scores (0-10) were significantly improved postoperatively (mean difference 1.2, p<0.0001) and performance status was unchanged following surgical palliation (preoperative/postoperative KPS between 80-100 78% versus 70%, p=0.39). Conclusions: Surgical palliation can play an important role in managing difficult to control symptoms in terminal cancer patients. Palliative surgery should be considered an option in end of life care in carefully selected patients to maintain QOL. Prospective studies are warranted to identify valid and feasible methods of assessing QOL outcomes in surgical palliation, and to further quantify its specific role in symptom management at the end of life.


Introduction Current literature addressing the treatment of neuroendocrine tumors is conflicting. This is especially true with regards to extent of resection, inclusion of lymphadenectomy, and non-operative management of small tumors. Methods The National Cancer Data Base (NCDB) was queried for patients who underwent surgical resection for pancreatic neuroendocrine tumors between 1998 and 2011. Extent of resection, tumor characteristics, lymph node positivity, margin status and overall survival were analyzed using Chi Square and Cox Proportional Hazards Regression. Results 2,735 patients were identified. Multivariate survival analysis was performed on 1,800 patients with complete data. Overall median survival for the analyzed cohort was 9.83 years. Regional lymph node positivity, involved surgical margins, male sex, increased tumor size, older age, and undergoing a pancreaticoduodenectomy were predictive of decreased overall survival. A reduced survival model showing only the significant effects is summarized in the table below. Positive margin rates for enucleation were 21%, versus 14% in other surgical procedures. The overall incidence of patients with lymph nodes positive for metastatic disease in the cohort was 51%. In the subset of patients with tumors < 1 cm, 27% had positive lymph nodes; in the lowest risk group with grade 1 tumors < 1 cm, 24% had positive nodes. Conclusions Patients undergoing resection of pancreatic neuroendocrine tumors should be offered lymphadenectomy, including those undergoing enucleation and those with small tumors. The incidence of lymph node involvement in low grade tumors < 1 cm brings the role of observation of these small tumors into question.

85 Results from a Prospective Hepatocellular Cancer (HCC) Screening Program in 7,120 Chronic Hepatitis C Virus (HCV)-infected Patients S.A. Curley,1* M. Leonigto,2 V. Albino,2 A. Palai,2 A. Amore,1 M. Piccirillo,2 V. Granata,3 A. Petrelli,3 F. Izzo,3 I. Surgery, Baylor College of Medicine, Houston, TX; 2. Istituto Nazionale Tumori, Naples, Campania, Italy.

Prospective trials in chronic hepatitis B virus-infected patients have shown reduced mortality from HCC due to increased rates of diagnosis of subclinical, resectable disease. We performed this prospective trial in HCV-infected patients to determine if their survival rates are improved by diagnosing more patients with early stage, surgically-treatable disease. Methods: 7,120 HCV-positive patients were registered and screened prospectively for HCC from 1993-2003 with serum alpha-fetoprotein (AFP) measured and ultrasonography (US) performed every 6 months. These screening studies continued through 2008. All patients had core liver biopsies to assess HCV-related liver injury. An elevated serum AFP and/or liver mass on US led to further computed tomography or magnetic resonance imaging and tumor biopsy. All patients with HCC were biopsy-proven. Results: Pathologic grading of the core liver biopsies showed that mild chronic active hepatitis was present in 4,058 (57%), severe chronic active hepatitis in 1,780 (25%), and cirrhosis in 1,282 (18%) of the patients. HCC was diagnosed in 612 of the 7,120 patients (8.6%), however, 606 were in the 1,282 patients with cirrhosis (47%, P<0.001 compared to non-cirrhotics). Prospective screening led to diagnosis of early stage HCC (TNM stage I or II) in 419 of the 612 patients (68%). Potentially curative treatment (resection, thermal ablation, or transplantation) was performed in all 419, while the remaining 193 (32%) were diagnosed with advanced disease and received trans-arterial chemoembolization and/or systemic chemotheraphy. Among the 419 HCC patients treated with curative intent, 5-year overall survival rate by Child-Pugh class was 26% for A, 14% for B, and 11% for C. There were no 5-years survivors in the 193 patients diagnosed with more advanced stage disease. Conclusions: The group of chronic HCV-infected patients who should be screened for HCC is those with cirrhosis. While screening this group led to diagnosis of subclinical, surgically-treatable disease in 68% of patients, the 5-year overall survival rate was only 21%, indicating a need for effective adjuvant and anti-viral therapy.

86 A Phase II Study of Bavituximab and Sorafenib in Advanced Hepatocellular Carcinoma (HCC) A. Yopp,* H. Zhu, J. Mansour, A. Singal, Y. Arriaga, S. Beg, Surgery, UT Southwestern Medical Center, Dallas, TX.

Background: Bavituximab is a first-in-class immunomodulator targeting phosphatidylserine (PS), a membrane lipid externalized on tumor and endothelial cells. Preclinical and phase I studies demonstrated that sorafenib upregulates PS externalization and can be given safely with bavituximab. We thus evaluated the safety and clinical activity of bavituximab plus sorafenib in HCC. Methods: Patients with locally advanced or metastatic HCC deemed ineligible for curative therapy with no previous systemic treatment, ECOG score 0-2, Child Pugh score A or B7 received bavituximab, 3 mg/kg IV weekly, and sorafenib, 400 mg PO BID until disease progression or intolerable toxicity. 38 patients were accrued providing a power of 80% and two-sided significance level of 10% to show an 8.2 month time to progression compared to historical control, 5-5 months. Secondary endpoints included safety and tolerability, 4-month progression free survival, overall survival, and response rates. Correlative studies using tissue from pre- and post-treatment tumor biopsies included IHC analysis of regulatory, cytotoxic, and helper T cells in addition to macrophage infiltrates. Results: 38 patients were accrued, 7 still on treatment. Patient characteristics: median age: 60.5 years, male 74%, HCV: 79%, Black: 47%/Hispanic: 29%/White: 21%, previous treatment 37%, and metastases: 6.8 months (95% CI 3,10). Four month PFS is 76% and there are no partial or complete responses. Treatment related adverse events were observed in 53% of patients, one grade 3 (GI bleed), four grade 2 (DVT, anorexia, diarrhea, and infusion reaction). Most common grade 1 events were diarrhea (16%), fatigue (16%), and anorexia (16%). Six patients had tissue analyzed pre- and post-treatment, 2 of 6 demonstrated increase tumor infiltration of CD4+, CD8+, and macrophages with a corresponding decrease in Tregs. Conclusions: Bavituximab and sorafenib were well tolerated in patients with advanced HCC. When compared with historical controls, combination therapy demonstrated an
improvement in TTP and PFS at four months. Combination therapy increases immune tumor infiltrates.

Comparing perioperative Processes of Care in High- and Low-mortality Centers Performing Pancreatic Surgery

**Objective**: There is wide variation in outcomes following pancreatic cancer resection. The mechanisms underlying this variation are poorly understood. We hypothesize that by comparing high and low mortality hospitals, we may identify differences in processes of care that impact outcomes. Identifying these factors may help direct future quality improvement efforts.

**Methods**: From 1,279 hospitals submitting data to the NCDB, we sampled the extremes of 30-day mortality for major cancer resection - 30 high mortality hospitals (HMH) and 19 low mortality hospitals (LMH) were included in the study. We conducted on-site chart reviews during 2006-07, sampling up to 150 cancer resection cases from each center. Data were abstracted on patient and tumor characteristics, as well as perioperative processes of care and outcomes. All cases of pancreatic cancer sampled during this period were included in our analysis.

**Results**: The HMH cohort had a 11.6% mortality rate among 67 patients; compared to 1.5% among 202 patients in the LMHs. Patients in the HMHs had worse ASA classification (20.9% ASA Class 4 vs 2.0%, p<0.001) and greater comorbidity burden (55.3% with ≥1 comorbidity vs 39.6%, p<0.037). The operations took significantly longer (353.9 min vs 313.7 min, p=.05), had higher average blood loss (1203.7 mL vs 881.6 mL, p<0.04), and patients were more likely to undergo transfusion (70.2% vs 41.1%, p<0.001). There were differences in anesthetic care, with lower levels of invasive monitoring (76.1% vs 93.1%, p<0.001) and lower use of epidural pain management (22.5% vs 62.9%, p<0.001). HMHs had higher rates of postoperative ICU admission (85.1% vs 53.9%, p<0.001). Both cohorts had similar rates of perioperative VTE prophylaxis, antibiotic administration, and beta blockade continuation.

**Conclusion**: High and low mortality hospitals both have high rates of compliance with commonly measured processes of care variables; however HMHs performed worse in other processes of care including anesthetic monitoring, blood product administration, and resource utilization. Future efforts targeting these areas may benefit patients undergoing pancreatic cancer resection.

Adjuvant Chemotherapy and Radiation Therapy Improves Survival for Patients with Extrahepatic Cholangiocarcinoma

**OBJECTIVES**: Because no randomized data exist to guide decision-making for adjuvant therapy in patients with extrahepatic cholangiocarcinoma (EHC), we used a prospective, multi-center dataset to identify associations between adjuvant therapy and improved survival. METHODS: The American College of Surgeons National Cancer Data Base (NCDB) was used to identify patients with resected EHC (pathologic stage I-3) between 1998-2006 (n=8,741). We compared three groups: surgery only (S, n=5,766), surgery plus adjuvant chemotherapy (AC, n=450), and surgery plus adjuvant chemotherapy and radiation therapy (ACR, n=1,918). Univariate analysis and Cox regression were used to determine how patient demographics, provider characteristics, and tumor-specific variables were associated with receipt of adjuvant therapy and overall survival. RESULTS: Patients who received adjuvant treatment were more likely to be younger (median age- S: 70, AC: 65, ACR: 44.6%; p<0.001), of the highest income quartile ($>46,000- S: 38.4%; AC: 43.0%; ACR: 44.6%; p<0.001), and treated at a community cancer center (S: 43.0%; AC: 50.9%; ACR: 52.9%; p<0.001). These patients were also more likely to have positive lymph nodes (S: 34.8%; AC: 69.4%; ACR: 63.3%; p<0.001), positive surgical margins (S: 6.4%; AC: 8.5%; ACR: 11.6%; p<0.001), and pathologic stage 3 disease (S: 21.5%; AC: 37.6%; ACR: 37.9%; p<0.002). Multivariate analysis of the entire cohort showed improved survival with ACR (HR 0.84, 95%CI 0.76-0.92). In subset analysis, patients with positive lymph nodes had improved survival with ACR (HR 0.63, 95%CI 0.54-0.74) whereas patients with node-negative disease did not (HR 1.08, 95%CI 0.87-1.33). The survival benefit was independent of margin status (RO: HR 0.88, 95%CI 0.78-0.98; R1: HR 0.65, 95%CI 0.53-0.80). CONCLUSION: This national analysis suggests that adjuvant chemotherapy and radiation therapy may improve survival for patients with EHC, particularly for high-risk patients with positive lymph nodes. Until randomized clinical trials are conducted, these may be the best available data to guide adjuvant therapy for resected EHC.

National Trends in Resection of Cystic Lesions of the Pancreas

**Introduction**: Cystic lesions of the pancreas (CLP) are being identified with increasing frequency. Management of asymptomatic CLP is controversial, but recent guidelines recommend a selective approach to resection. We sought to investigate recent national trends in resection of CLP in the elderly.

**Methods**: This retrospective cohort study used national Medicare claims data to identify all patients 65 years and older undergoing pancreatic resection for neoplasm from 2001-2012. We then identified all patients undergoing resection for CLP. Hospitals were stratified into quintiles of pancreatic resection volume. We used Cuzick’s test for trend to examine changes in demographics, surgical indications, and outcomes over time.

**Results**: Of 55,959 pancreaticectomies performed during the 12-year period, 2,109 (3.8%) were for CLP. Patients undergoing resection for CLP were younger (median age 72 y.o. vs. 74 y.o. for other indications, P<0.001) and more likely female (59.6% female, vs. 51.5% female for other indications, P<0.001). Type of CLP resection was distal pancreaticectomy in 59%, Whipple in 26%, total pancreatectomy in 4%, and other partial pancreatectomy in 11% (P=0.3 for trend). The proportion of resections performed for CLP more than doubled during the period, from 2.1% in 2001, to 4.6% in 2012 (P<0.001, Figure). This increase was mirrored across all age groups (65-74 years: 2.4% to 4.7%, P=0.001; ≥75 years:1.8% to 4.4%, P<0.001) and across all hospital volume quintiles (very low volume: 2.1% to 4.6%, P=0.002; very high volume: 1.9% to 3.8%, P<0.001). The proportion of CLP with a diagnosis of malignancy was 16% and did not vary significantly over time (P=0.1 for trend). Although overall complication rates did not vary (17.7%, P=0.7 for trend), operative mortality for CLP resection improved from 9.2% in 2001 to 3.2% in 2012 (P=0.003 for trend), paralleling improvements in mortality of pancreatic resection for other indications (9.6% vs 4.6%, P<0.001).

**Conclusion**: The proportion of pancreaticectomies performed for CLP has doubled during a recent 12-year period, despite concurrent updated guidelines recommending a selective approach to resection. These trends persist in all age groups, and across hospital volumes.
and rectal cancer (RC). In this cohort we examined the evolution of management and outcomes over time to identify key determinants of potential cure.

**METHODS:** Between 1999-2013, 623 rectal cancer patients with liver only metastases were evaluated with curative intent. 196 patients had synchronous RC with resectable LM. Three time periods were defined *a priori*: 1999-2003, 2004-2008, and 2009-2013. Records were reviewed for demographics, tumor, and treatment details. Overall survival (OS) was analyzed by Kaplan-Meier methods.

**RESULTS:** Treatment sequences were: 98 (50%) primary first (“Classic”), 43 (22%) combined resections (“Combined”), and 55 (28%) liver first (“Reversed”). The median number of LM was significantly higher in “Reversed” vs. “Combined” (3 [1-75] vs. 1 [1-11]; p=0.006). Patients treated with “Reversed” vs. “Classic” approach increased over time: years 1999-2003: 3 (6%) vs. 39 (75%) patients; 2004-2008: 26 (35%) vs. 34 (46%); and 2009-2013: 26 (37%) vs. 25 (36%). 154 patients were rendered disease free after completion of all treatment sequences. 42 patients failed to achieve R0 with the most common sites of failure being liver (27) vs. rectum (9) and other distant sites (6). The significant increase in the use of “Reverse” approach over time managing patients with increased disease burden, led to a significantly improved 5-year OS: 2009-2014 = 61% vs. 1999-2008 = 49% (p<0.001). Failure to render R0 resulted in a poor 5-year-OS of 11%

**CONCLUSION:** The adoption of a “reversed” approach over time allows RC patients with higher disease burden of resectable synchronous LM to be rendered R0 which is associated with cure. This tailored sequencing of a liver-focused approach has contributed to an improved 5-year OS that approaches stage III disease patients.

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**Chemotherapy for Surgically Resected Intrahepatic Cholangiocarcinoma: Lymph Node Status Influences Treatment Efficacy**


**Background:** High rates of recurrence following surgery (S) for intrahepatic cholangiocarcinoma (ICC) have prompted treatment strategies that incorporate chemotherapy (CT). However the benefit of CT remains poorly defined. The present study sought to determine the survival impact of CT for surgically resected ICC. **Methods:** Patients with non-metastatic ICC that underwent surgery were identified from the National Cancer Database (1998-2011) and stratified by receipt of CT. Survival outcomes between treatment cohorts were analyzed following propensity score modeling using the greedy matching algorithm. **Results:** A total of 2,751 patients were identified (median age: 64 years, 51% female); 985 (35.8%) received CT. Younger age, tumor size > 5cm, advanced tumor stage, R1/R2 surgical margins, and lymph node metastasis were all independently associated with receipt of CT (p<0.05). Median number of lymph nodes examined was 2 (IQR: 1-5). However, lymph node evaluation was not formally conducted in 34% (Nx: n=925) of the collective cohort. Following propensity matching, there was no difference in median OS between patients receiving CT compared to S alone (Figure: 23 vs 20 months, p=0.09). When stratified by lymph node status, CT demonstrated a significant improvement in median OS among N1 patients (19.8 vs 10.7 months, p=0.0001). In contrast, patients with N0 disease derived no benefit from CT (29.4 vs 29 months, p=0.33). **Conclusion:** The use of CT was associated with a survival benefit only for ICC patients with nodal metastasis. Assessment of lymph nodes at the time of surgical resection is critical when attempting to identify a subgroup of patients best suited for CT.
ABSTRACTS

Accepted for
VIDEO PRESENTATIONS

68th Annual Cancer Symposium
Society of Surgical Oncology
March 25–28, 2015
Houston, Texas
The Modified Keystone Flap

Radical Resection of Abdominal Wall Desmoid Tumor with Reconstruction using Posterior Component Separation and Mesh Implantation

V2

Radical Resection of Abdominal Wall Desmoid Tumor with Reconstruction using Posterior Component Separation and Mesh Implantation

K. Choong,* J. Blatnik, Y. Novitsky, J. Ammor. University Hospitals Case Medical Center, Cleveland, OH.

While the resection of abdominal wall desmoid tumors is not uncommon, the options for reconstruction are historically limited. These include component separation and/or placement of mesh either as an underlay, overlay, or interposition. All of these methods have their shortcomings and associated complications. Recent advances in ventral hernia repairs and abdominal wall reconstruction warrant further discussion regarding reconstructive options. We present a case of a 29 year old female with a large abdominal wall desmoid tumor encompassing the majority of her right rectus muscle and encroaching into the lateral abdominal wall musculature. Following radical resection, abdominal wall reconstruction was performed using the posterior component separation technique in addition to bilateral transversus abdominis releases. Polypropylene mesh was implanted in the extraperitoneal space after the posterior components were reconstructed. The technical aspects of this repair will be highlighted. We believe this to be a durable reconstruction option after radical resection of abdominal wall tumors.

V3

Total Laparoscopic Pancreatoduodenectomy: A Single Institutional Experience

A. Paniccia,* R.D. Schultick, B.H. Edil. Department of Surgery, University of Colorado, Anschutz Medical Campus, Aurora, CO.

Introduction: Laparoscopic pancreaticoduodenectomy (LTPD) with a video of the technique we have developed and the clinical as well as oncologic outcomes obtained with this technique. Methodology: Retrospective review of all cases consecutively performed by two operators between January 2013 and May 2014 at The University of Colorado. Results: Twenty patients underwent TLPD and conversion to open procedure was required in 2 cases (10%). Median age at diagnosis was 55.4 years (IQR 42.8-66.5). Operative characteristics and postoperative complications are summarized in table 1. The operative time decreased from 353 minutes (IQR 320-421) in the first 10 cases to 323.5 minutes (IQR 272-379) in the second 10 cases (r²=0.67; p=0.012). The estimated blood loss decreased from 300 mL (IQR 330-400) in the first 10 cases to 200 mL (IQR 100 – 500) in the second 10 cases (r²=0.85; p=0.544). Conclusion: Laparoscopic Pancreatoduodenectomy is a challenging, operation, which is not done in a high volume at most centers. We present our initial experience as a new laparoscopic pancreas program. Our experience shows that oncologic outcomes are acceptable in terms of margin and lymph node harvest. Minimally invasive pancreas surgery can be done safely with comparable complications rates to the traditional open approach and with no mortality. The perioperative outcomes are similar to the traditional approach and long-term benefits are likely comparable to those seen with other laparoscopic abdominal operations.

Table 1. Operative characteristics and postoperative complications

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>N = 20</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>SURGICAL MARGIN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative R0</td>
<td>20 (100%)</td>
<td></td>
</tr>
<tr>
<td>NUMBER OF NODES HARVESTED</td>
<td>16.5 (13.205)</td>
<td></td>
</tr>
<tr>
<td>OPERATIVE TIME (min)</td>
<td>340 (100.3-381.5)</td>
<td></td>
</tr>
<tr>
<td>FBL (ml)</td>
<td>300 (175–450)</td>
<td></td>
</tr>
<tr>
<td>PANECKETIC FISTULA GRADE</td>
<td>19 (50%)</td>
<td></td>
</tr>
<tr>
<td>Grade A</td>
<td>7 (35%)</td>
<td></td>
</tr>
<tr>
<td>Grade B</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Grade C</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>DELAYED GASTRIC EMPTYING (DGE)</td>
<td>8 (40%)</td>
<td></td>
</tr>
<tr>
<td>I&amp;O ORAL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade A</td>
<td>3 (15%)</td>
<td></td>
</tr>
<tr>
<td>Grade B</td>
<td>4 (20%)</td>
<td></td>
</tr>
<tr>
<td>Grade C</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>BILE FLEAK</td>
<td>3 (15%)</td>
<td></td>
</tr>
<tr>
<td>PSEUDOANEURYSM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Esophageal artery</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal artery</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>CHEST FLEAK</td>
<td>1 (5%)</td>
<td></td>
</tr>
<tr>
<td>SURGICAL SITE INFECTION (SSI)</td>
<td>5 (20%)</td>
<td></td>
</tr>
<tr>
<td>ISS FV6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superficial</td>
<td>2 (10%)</td>
<td></td>
</tr>
<tr>
<td>Electrical</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Organ Space</td>
<td>3 (15%)</td>
<td></td>
</tr>
<tr>
<td>I&amp;O (days)</td>
<td>12 (9 - 16)</td>
<td></td>
</tr>
<tr>
<td>MORTALITY (0 days)</td>
<td>4 (20%)</td>
<td></td>
</tr>
<tr>
<td>READMISSION (30 days)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

V4

Use of Pedicled Omental Flap in Minimally Invasive Robotic-assisted Ivor-Lewis Esophagogastrectomy

G. Wu,* D.J. Raz, J. Kim,2 J.Y. Kim,4 1. Thoracic Surgery, City of Hope National Medical Center, Duarte, CA; 2. Surgical Oncology, City of Hope National Medical Center, Duarte, CA.

INTRODUCTION: Esophagogastric anastomotic leak, especially intrathoracic, confers high morbidity and mortality in patients after esophagogastrectomy for esophageal cancer. Omental reinforcement of the esophagogastric anastomosis (EGA) has been reported to decrease leak and stricture rates. We present a video of the minimally invasive technique of pedicled omental flap (POF) creation, transfer, and reinforcement of the EGA. METHODS: We performed minimally invasive robotic-assisted Ivor-Lewis esophagogastrectomy on a 65-year-old female who received neoadjuvant chemoradiation for locally advanced distal esophageal adenocarcinoma. The patient was placed in supine position and the abdomen was entered laparoscopically. The omental flap was harvested with a pedicle originating from the right gastroepiploic artery. Following creation of the gastric conduit, the POF was secured to the gastric conduit with suture. The abdominal esophagus was completely mobilized and laparoscopy was concluded. The patient was then placed in left lateral decubitus position and the chest was entered thorascopically. The abdominal esophagus was pulled into the chest and the POF attachment to the gastric conduit was released. Using robotic assistance, the thoracic esophagus was dissected and transected at the level of the azygos vein. An EGA was created using a circular stapler. After a negative leak test and endoscopic examination of the anastomosis, the POF was wrapped around the EGA and secured to the adjacent pleura with suture. RESULTS: The patient had an unremarkable hospital course and was discharged on postoperative day 7 on tube feeds. She passed an outpatient contrast swallow study and diet was advanced. Final pathology revealed a 1.6 cm poorly differentiated (G3) adenocarcinoma of the esophagogastric junction with negative margins and 0 of 19 positive lymph nodes (pT3N0M0, stage IIA). CONCLUSION: We demonstrated the creation, transfer, and securing of a POF around an EGA during minimally invasive robotic-assisted Ivor-Lewis esophagogastrectomy which may help to prevent anastomotic leak and decrease the chance of stricture.
Total Laparoscopic Spleen Preserving Distal Pancreatoectomy for pNETs in a Young Patient with MEN1

L. Schwarz, N. D. Perrier, J. B. Fleming, M. H. Katz, J. E. Lee, T. A. Aloia, J. Vauthney, C. Conrad, Department of Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX.

Background: MEN1 patients requiring resection of neuroendocrine tumors (pNET) are frequently young, active patients in whom a minimal access approach minimizes perioperative morbidity and splenic preservation decreases the risk for post-splenectomy sepsis. Laparoscopic spleen preserving distal pancreatectomy can be performed with removal (Warshaw Technique) or preservation of the splenic vessels, the later having a higher rate of successful splenic preservation. Patients: This is an active, 16 year old Jehovah’s Witness with trifocal non-functioning neuroendocrine tumors in the proximal body and tail of the pancreas as part of MEN1 syndrome. Technique: This video demonstrates patient and trocar positioning as well as operative tactics for a laparoscopic distal pancreatectomy with preservation of splenic vessels. Intraoperative ultrasound is crucial in assessing pNETs’ relation to critical vessels, pancreatic duct, and to exclude synchronous lesions. The video focuses on safe laparoscopic creation of the retropancreatic tunnel and dissecting the pancreas off the splenic vessels using novel energy devises to control direct on safe laparoscopic creation of the retropancreatic tunnel and dissecting the pancreas off the splenic vessels using novel energy devises to control direct

V6

Robotic Prophylactic Total Gastrectomy

R. Kirks, R. Seshadri, P.D. Lorimer, R.Z. Swan, D.A. Iannitti, J.B. Martinic, General Surgery, Carolinas Medical Center, Charlotte, NC; 2. Levine Cancer Institute, Charlotte, NC.

Background: Patients with a family history of Diffuse Hereditary Gastric Cancer syndrome (DHGC) are typically referred for prophylactic total gastrectomy early in life, prior to the development of gastric neoplasm. Total gastrectomy with esophagegajunal anastomosis has historically been performed laparotomically but advances in laparoscopy make this procedure attainable through minimally-invasive techniques. Introduction: We present a 51yo M with a strong family history of gastric cancer and lobular carcinoma of the breast. He had been found to harbor a mutation in the CDH1 gene. Prior to surgical consultation, the patient had been found to have a gastric ulcer which was negative for malignancy on endoscopic biopsy. We elected to proceed with a robotic total gastrectomy with esophagegajunal anastomosis. Methods: After trocar placement and abdominal exploration, the stomach was mobilized and dissection below level of the tumor with adequate margins, gastrointestinal, Sunnyvale, CA, USA) proceeding with total mesorectal dissection with the patient tolerated the procedure well and was discharged 6 days later following an upper GI series that demonstrated the absence of an anastomotic leak. Conclusion: We present a minimally-invasive approach for total gastrectomy, highlighting the feasibility of this approach. Performing this procedure via a robotic approach achieves adequate lymph node harvest, decreases the morbidity of the procedure, and promotes early recovery.

V7

Robotic-assisted Low Anterior Resection with Use of Fluorescence Imaging to Assess Proximal Bowel Transection Site and Anastomosis Perfusion

T. El Amadiel, A. Webb, G. Balch, M. Choti, P.M. Polanco, University of Texas Southwestern Medical Center, Dallas, TX.

Introduction: Anastomotic leak after low anterior resection (LAR) for rectal cancer can lead to prolonged length of stay, increased cost, local recurrence and mortality. Ischemia and technical aspects are the main factors related to anastomotic leaks. Indocyanine green fluorescence (ICG-F) imaging with near-infrared (NIR) technology has been described as a useful tool to assess tissue and intestinal perfusion. Our goal is to present a video that describes our Robotic Assisted LAR (RA-LAR) technique and the use of ICG fluorescence imaging in the assessment of intestinal perfusion and location of the ideal proximal transection site. Methods: A 54 year-old man that underwent neoadjuvant therapy (NAT) with 5400 rads of external radiation and 5-FU chemotherapy for a T3N1M0 rectal adenocarcinoma at 8 cm from anal margin. Six weeks after completion of NAT he underwent a (RA-LAR) Technique/Results: Patient is positioned in lithotomy followed by lighted ureteral stent placement, pneumoperitoneum creation and trocar placement. Laparoscopic medial to lateral mobilization of the left colon is performed with high dissection and stapling of IMA. Robotic arms are then docked (Du Vinci Si, Intuitive Surgical, Sunnyvale, CA, USA) proceeding with total mesorectal dissection with nerve sparing technique using hook cautery and vessel sealer. After complete mobilization and dissection below level of the tumor with adequate margins, division of distal rectum is performed with laparoscopic linear stapling device. 10mg of IV ICG is then injected and NIR fluorescence imaging is used to assess proximal bowel perfusion marking the level of ischemia and transection. Robotic arms are undocked followed by exteriorization of specimen, bowel transection and and placement of EEA anvil via a 2cm suprapubic incision. EEA stapler anastomosis is completed under laparoscopic guidance followed by proctoscopy and insufflation test. Conclusion: ICG–F during RA-LAR may be a useful tool for tissue perfusion assessment and potentially minimize anastomotic leak rate. Further validation of this technology is necessary to better define its clinical application.

LBV1

A Minimally Invasive Technique to Obtain Optimal Tumor Margins in Anatomically Confined Locations using a Contoured Stapler


Introduction: The use of linear endo-staplers to excise tumors and maintain a consistent oncologic margin often requires multiple staple fires, various and sometimes awkward stapler angles, and crossing staple lines. These resections can be further complicated when tumors are in anatomically confined locations near critical structures where linear resection of additional non-involved parenchyma would be detrimental or have functional consequences. Thus, there are unique oncologic situations where a customized curved resection would be advantageous. Methods/Results: Though the contoured stapler has traditionally been used and marketed for rectal resection, in this video we demonstrate its applicability in unique oncologic situations. Gastric GISTs approximating the pylorus can be challenging to approach laparoscopically and often require a distal gastrectomy to excise with an adequate margin without narrowing the gastric outlet. The technique demonstrated enables dissection of the tumor from the pylorus and contouring resection without the need for an anastomosis. For tumors near the ileocecal valve, the technique demonstrated enables contoured resection ofecal tumors without impinging on the ileum or the need for an anastomosis. For tumors in the pancreas, pancreatectomy can be performed as oncologically indicated with an increased margin around the tumor compared to a linear staple fire. In addition, the ability to excise small endophytic and exophytic gastric GISTs with a single contoured staple fire is demonstrated. Conclusion: The techniques demonstrated in this video were created to use a contoured endo-stapler in a non-traditional way to simplify and customize minimally invasive oncologic resections, optimize margins, minimize crossing staple lines, and limit costs by reducing the number of staple loads in unique anatomical locations.
LBV2

Approach to the Porta Hepatis during Cytoreductive Surgery: Technical Considerations

N. Aydin,* V. Milovanov, A. Sardi. Surgical Oncology, Mercy Medical Center, Ellicott City, MD.

Peritoneal carcinomatosis has always been considered uniformly fatal resulting in intestinal obstructions and eventually leading to a fatal outcome with progression of the disease. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy has become an important option for patients with peritoneal carcinomatosis. The completeness of cytoreduction determines survival. Frequently, the porta hepatis and the lesser sac are massively involved by tumor. Encauscement of the portal triad, lesser omentum, retroperitoneal vena cava, duodenum and the stomach is frequently seen. The proximity to major portal structures as well as the retroperitoneal vena cava makes this dissection challenging. In this video clip, we aim to display the critical technical steps to do a safe portal dissection which constitutes an important part of cytoreductive surgery.

LBV3

A Role for Minimally Invasive Approaches to Cytoreductive Surgery and Hyperthermic Intra-peritoneal Chemotherapy in Super Morbidly Obese Patients

D. Luzinavicius,1,* M.A. White,2 M. Waskabayashi,2 B. Lecj1. Surgery, Carilion Clinic, Roanoke, VA; 2. City of Hope National Medical Center, Duarte, CA.

Introduction: This case illustrates the value of minimally invasive techniques in the treatment of pseudomyxoma peritonei in a super morbidly obese patient while preserving strict oncologic principles. The patient is a 58-year-old female with a BMI of 60 and multiple related co-morbidities, referred to us with a diagnosis of mucinous neoplasm of the appendix. The diagnosis was made during a planned operation for a laparoscopic sleeve gastrectomy. The case was aborted after the surgeon found a significant amount of mucinous material in the right upper abdomen and pelvis, along with an ulcerated lesion in the appendix. An appendectomy was performed along with peritoneal biopsies. Pathology results confirmed mucinous deposits on the appendiceal stump. This case illustrates the value of minimally invasive techniques to treat this rare entity in carefully selected patients.

Methods: Following a staging work-up negative for any further disease, the patient was taken to the operating room for cytoreductive surgery with hyperthermic intra-peritoneal chemotherapy (HIPEC) using Mitomycin C. Given the potential for increased morbidity associated with an open procedure in a morbidly obese patient, we decided to attempt the procedure laparoscopically. To address her BMI, we planned on completing a sleeve gastrectomy.

Outcome: She ultimately underwent a laparoscopic extended right hemicolectomy, pelvic peritonectomy, bilateral salpingo-oophorectomy, HIPEC and sleeve gastrectomy with omentectomy in a safe manner while preserving all necessary oncologic principles. Her completeness of cytoreduction score was 0, indicating no visible disease (CC-0). Her post-operative course was uneventful.

Conclusion: This case illustrates a potential value for a minimally invasive approach to cytoreductive surgery and HIPEC for peritoneal malignancies in carefully selected patients.

LBV4

Minimally Invasive Total Gastrectomy in the Setting of CDH-1 Mutation


Introduction: CDH-1 mutation results in a genetic disorder predisposing to gastric carcinoma and is an indication to perform prophylactic total gastrectomy at an early age. Total gastrectomy with roux-en-y esophagojejunostomy is feasible with a laparoscopic approach. The patient was positioned supine on the operating table, and five laparoscopic ports were placed. The gastrocolic ligament was divided, and the greater curvature mobilized by dividing the short gastric vessels. The first portion of the duodenum was then divided with a linear stapler. The gastroplastic vessels were divided with a vascular load. Next, the lesser curve was dissected up to the right crus. A window was created posterior to the esophagus, which was divided with a linear stapler. The jejunum was divided 30 cm distal to the ligament of Treitz. After measuring 75 cm of roux limb, a side-to-side jejunojejunostomy was created. The jejunum was divided 30 cm distal to the ligament of Treitz. A 10 mm flat Jackson Pratt drain was placed posterior to the anastomosis. The specimen was extracted, and trocars were removed under direct vision. The fascia and skin incisions were then closed.

Results: R0 laparoscopic total gastrectomy with roux-en-y esophagojejunostomy with D1 lymphadenectomy for hereditary diffuse gastric cancer was successfully completed. Postoperatively, the patient recovered well and was discharged on post-operative day six. The pathology revealed pylipolN0 poorly differentiated type intramuscular signet ring cell carcinoma with 27 lymph nodes negative for malignancy. Conclusion: Prophylactic laparoscopic total gastrectomy is a safe and effective approach for patients with CDH-1 mutation. This case highlights the need to perform early prophylactic gastrectomy in this patient population. In addition, it offers the numerous benefits of a minimally invasive approach.

LBV5

Robotic-assisted Laparoscopic Marsupialization of Esophageal Duplication Cyst

LBV6

Laparoscopic Total Gastrectomy

A. Chawla,* J. Ammori. Surgery, Case Western Reserve University, Cleveland, OH.

Laparoscopic total gastrectomy for gastric cancer is becoming an increasingly utilized procedure performed at high volume tertiary care centers. Our patient is a 44-year-old male who presented with an upper GI bleed and subsequent endoscopy revealed a 5 cm polyp found to have high-grade dysplasia. We demonstrate our technique and steps involved in performing a laparoscopic total gastrectomy. The procedure begins with the placement of four working ports. The omentum is detached from the transverse colon opening up the lesser space. Next, the posterior attachments of the stomach are taken down and dissection is undertaken in the direction of the gastroplastic vessels which are transected after freeing up all lymphatic tissues along with the specimen. Next, the omental attachments to the greater curvature of the stomach are taken down towards the spleen and the short gastric vessels are encountered and transected. In the lesser space, the pars flaccida of the gastrohepatic ligament is incised and dissected superiorly to the right crus. The phrenoesophageal ligament is taken down with meticulous dissection and mobilization of the esophagus into the lower mediastinum. Next, the first portion of the duodenum is transected. The stomach is retracted anteriorly enabling isolation of the left gastric vessels which are then transected. Next, the distal esophagus is transected and the specimen is removed after extending the left upper quadrant incision. 60 cm distal to the ligament of Treitz, a jejunoj-jejunal anastomosis is performed with a stapled technique. The proximal jejumum is transected in preparation for the esophagojejunostomy. A transorally inserted anvil is inserted and an esophagostomy is made within the staple line where the anvil is brought into place. The EEA stapler is placed through a proximal jejunal enteroctomy just distal to the ligament of Treitz. This is brought into the abdomen through the LUQ using a single incision port. The spike and anvil are mated and a circular anastomosis is made. The enterotomy is closed and a leak test is performed using esophagostroduodenoscopy guidance with direct visualization of the anastomosis. Final pathology demonstrated high-grade dysplasia with all margins free of dysplasia.

LBV7

Surgical Placement of Novel 3D Tissue Marker during Lumpectomy


Accurately targeting the lumpectomy site by the radiation oncologist remains one of the important quality improvement opportunities in breast cancer care. The development of a three dimensional tissue marker has facilitated accurate targeting of whole breast and partial breast irradiation for breast
cancer. The 3-D tissue marker is positioned in the breast at the same location that the excised tumor was located. By so doing, communication between the surgeon and the radiation oncologist is facilitated. The surgeon who may have removed peripheral tissue that does not contain cancer on their path towards the site of the tumor, can avoid excess in the radiation field by placing the 3-D tissue marker at the specific site of the tumor and avoid dissection planes that contain only benign tissue. Some of these planes are extra tissue that is inadvertently removed while approaching a non-palpable image localized target. This video demonstrates the placement of this novel 3-D tissue marker combined with an oncoplastic closure.
P1
Early postoperative Complications of Breast Conservation Surgery versus Simple Mastectomy with Implant Reconstruction: A NSQIP Analysis of 11,645 Patients

A. Chatterjee,1 B. Piye,2 J.F. Nigrin,2 J. Tehou,1 B. Czernecki,1 C. Fisher,1 J. Surgery, University of Pennsylvania, Drexel Hill, PA; 2. Dartmouth Hitchcock Medical Center, Lebanon, NH.

Introduction: There has been little studied in regards to early postoperative outcomes comparing breast conservation surgery (BCS) and simple mastectomy (SM) with implant reconstruction. This information would guide treatment strategy, facilitate decision-making, and improve a surgeon’s ability to provide informed consent to patients requiring treatment. Our goal was to compare early postoperative outcomes in patients having BCS versus SM with implant reconstruction for early stage breast cancer patients. Methods: The NSQIP database was analyzed from 2009-2012. Patients were selected that underwent either BCS or SM with implant reconstruction with sentinel lymph node biopsy (SLNB) performed at the same time. Exclusion criteria included axillary lymph node dissection, prior radiation therapy, and concurrent autologous tissue reconstructive surgery. We compared both pre-operative co-morbidity differences and postoperative complication rates in each group using chi square tests, two sample t-tests and odds ratios. Results: Our criteria yielded a total of 11,645 patients with 9,571 patients undergoing BCS and SLNB and 2,074 undergoing SM with implant reconstruction and SLNB(1834 with tissue expanders and 240 with direct implant). Baseline co-morbidity conditions were statistically different for BCS versus SM: Age (61.7 vs 53.5), hypertension (47.0% vs 25.6%), BMI (29.6 kg/m^2 vs 27 kg/m^2), coronary artery disease (1.3% vs 0.6%), COPD status (2.4% vs 1.0%), and diabetes (11.7% vs 5.9%). Table 1 demonstrates significantly higher overall complications in the simple mastectomy with reconstruction group largely due to higher wound complications, infection, and bleeding rates than the BCS group. Conclusion: Compared to simple mastectomy with implant reconstruction, breast conservation surgery has fewer overall early post-operative complications with regards to wound complications and infection despite a significantly higher rate of pre-existing co-morbid conditions.

P2
Avoidance of Sentinel Lymph Node Biopsy: Can Molecular Profiling of Primary Breast Tumors Predict Lymph Node Status?

C. Shriver, M. Hueman, R. Ellsworth.* Clinical Breast Care Project, Murtha Cancer Center, Windber, PA.

Introduction: Identification of a gene expression signature in primary breast tumors that could classify patients by lymph node status would allow patients to avoid the potential morbidities of surgical staging of the lymph nodes. Attempts to identify such a signature have to date been unsuccessful. Because breast tumor intrinsic subtypes have unique molecular characteristics and different sites of metastasis, molecular signatures for lymph node involvement may vary by subtype. Methods: Gene expression data was generated from HG U133A 2.0 arrays for 135 node positive and 210 node negative primary breast tumors. Intrinsic subtype was assigned using the BreastPRS (Signal Genetics). Differential expression analysis was performed using one-way ANOVA (Partek) using lymph node status as the variable using a False-discovery rate <0.05, >1.5-fold change to define significance. Results: By subtype of the primary tumor, Luminal A were most common (51%) followed by basal-like (27%), HER2-enriched (14%) luminal B (7%) and normal-like (1%). Basal-like and luminal A tumors were less likely to have metastatic lymph nodes (35% and 37%, respectively) compared to luminal B or HER2-enriched (52% and 51%, respectively). No differentially expressed genes associated with lymph node status were detected when all tumors were considered together or within each subtype. Conclusions: Gene expression patterns from the primary tumor are not able to predict lymph node status. Although the primary breast tumor may influence tumor cell dissemination, once metastatic cells enter the lymphatics it is likely that characteristics of the lymph node microenvironment, such as establishment of a pre-metastatic niche and release of pro-survival factors, determine which cells are able to colonize. The inability to utilize molecular profiles from the primary tumor to determine lymph node status suggest that other avenues of investigation, such as how systemic factors like diminished immune response or genetic susceptibility contribute to metastasis, may be critical in the development of tools for non-surgical assessment of lymph node status.

P3
Impact of Consensus Guidelines by Society of Surgical Oncology/American Society for Radiation Oncology on Margins for Breast Conservation Surgery in Stages I and II Invasive Breast Cancer

A. Chung,* A. Gangi, F. Amersi, S. Bose, X. Zhang, A.E. Giuliano. Surgery, Cedars Sinai Medical Center, Los Angeles, CA.

Introduction: The purpose of this study was to evaluate the impact of the release of consensus guidelines on margins in breast conserving surgery (BCS) on re-excision rates. Methods: A review of a prospectively maintained database of patients with operable invasive breast cancer treated with BCS at our institution was conducted. Patients were divided into 2 groups: 1) those diagnosed from July 1, 2011-July 31, 2013 (prior to release of the guidelines) and 2) those diagnosed from February 1, 2014 - July 31, 2014 (after release of guidelines). Groups were evaluated with respect to patient and tumor characteristics, re-excision rates and reasons for re-excision. A positive margin was defined as presence of ink on tumor; close margin was determined based on the surgeon’s discretion. Results: A total of 814 cases of BCS were performed during the specified time periods: 599, group 1; 215, group 2. Re-excision rates were significantly reduced after release of the consensus guidelines (p=0.03). In group 1, 122/599 (20%) had re-excisions: 10 for close invasive margins, 33 for positive invasive margins, 70 for positive or close DCIS margins, 8 for positive invasive and DCIS margins, and 1 for missed tumor. In group 2, 33 for positive invasive margins, 70 for positive or close DCIS margins, 12 for positive or close DCIS margins. Re-excisions were performed based on the consensus guidelines in 29/31 (94%) of cases. There were more grade 3 tumors in group 1 compared to group 2 (p=0.04). There was no significant difference between the 2 groups with respect to age, tumor size, histology, or nodal status. Conclusions: The consensus guidelines on margins were adopted in 94% of patients who underwent BCS and resulted in a significant reduction in re-excision rates.
P4

Introduction: The 21 gene assay (ODX) Recurrence Score (RS) result quantifies the likelihood of distant recurrence in early-stage, node-negative, estrogen receptor positive (ER+) breast cancer patients (pts). RS is stratified as low risk (<18), intermediate, or high risk (>30). We examined pts that had RS directed adjuvant treatment and subsequent locoregional recurrence (LRR) to identify factors associated LRR. Methods: An IRB-approved, retrospective review of a prospective ODx database was conducted. ODx use was based on NCCN guidelines or physician discretion. Data collected included: demograph-ics, clinical-pathologic features of incident breast cancer and LRR, surgery, margin status, RS, adjuvant treatment, and outcomes. LRR was defined as breast cancer presenting in the ipsilateral breast or axilla after RS result directed multimodal therapy. Comparisons of pts with at least 4 years of follow up were made with Wilcoxon Rank Sum Test. Results: 606 pts had ODx as part of their initial treatment plan from 2004-2012. 191 pts had 4+ years of follow up; 5 pts had LRR within that timeframe. 60% of LRR pts had breast conservation of which 40% required additional surgery for margin clearance. Higher RS result (p=0.009), younger age (p=0.0007), pre/peri-menopausal status (p=0.017), higher mitoses (p=0.027), and lower percentage ER score (p=0.003) were significantly associated with LRR. Pt. declined endocrine therapy was higher in pts with LRR (p=0.016) but, when taken, endocrine therapy length was not significant. No pts with a low risk RS had LRR. Between the 2 groups, there was no significant difference in median tumor size, surgery type, use of or recommendations for adjuvant radiation or chemotherapy. Conclusion: RS results have been shown to predict distant recurrence. Our data suggests that younger pts, tumors with lower ER expression, higher proliferative markers, and intermediate to high RS result (>18) on ODx are associated with LRR. Although not typically used for LRR, ODx RS result may impact adherence to endocrine therapy recommendations and surveillance/follow-up for LRR in select pts.

<table>
<thead>
<tr>
<th>Variable (median)</th>
<th>LRR Pts (5)</th>
<th>No LRR Pts (136)</th>
<th>P value</th>
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<tr>
<td>Age (years)</td>
<td>42</td>
<td>58</td>
<td>0.0007</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
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<td>1.45</td>
<td>0.023</td>
</tr>
<tr>
<td>ER (%)</td>
<td>70</td>
<td>95</td>
<td>0.0129</td>
</tr>
<tr>
<td>Endocrine treatment (months)</td>
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<td>31</td>
<td>0.85</td>
</tr>
<tr>
<td>Follow up (years)</td>
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<td>4.97</td>
<td>0.25</td>
</tr>
<tr>
<td>Chemotherapy Declined (pts)</td>
<td>1</td>
<td>11</td>
<td>0.237</td>
</tr>
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</table>

P5
Interaction between CD47 and SIRPA in BM and in PB Predicts Poor Prognosis in Breast Cancer Subtypes M. Nagahara,* M. Mom,† H. Miki,‡ S. Takayama,† K. Inoue,† M. Ito,† K. Sakurai,‡ 1. Surgical Oncology, Tokyo Medical and Dental University, Tokyo, Japan; 2. Osaka University, Osaka, Japan.

Introduction: Focused on CD47 expression in bone marrow (BM) and peripheral blood (PB), we found the correlation between breast cancer subtypes and CD47 expression, which may indicate important implications for prognostic factor. Moreover, CD47 expression is strongly correlated with SIRPA expression in both the BM and PB of breast cancer and it indicates that the poor prognosis of breast cancer with high expression of CD47 is due to an active CD47/SIRPA signaling pathway in circulating cells. Experimental Design: Quantitative real-time PCR was used to evaluate CD47 mRNA and SIRPA mRNA expression in BM and in PB from 452 cases of breast cancer. Results: In Her2 enriched patients with high CD47 expression in BM and PB, survival was significantly poorer compared to patients with low CD47 expression. Furthermore, high CD47 expression group in Her2 enriched of multivariate analysis showed significance as an independent variable for poorer prognosis in DFS (BM: P = 0.002; PB: P = 0.01) and in OS (BM: P =0.02; PB: P =0.008). On the other hand, in triple negative patients with high CD47 expression in BM, survival was significantly poorer compared to patients with low CD47 expression group. CD47 expression was strongly correlated with SIRPA expression in both the BM and PB of breast cancer patients (BM: P < 0.0001; PB: P < 0.0001). In particular, CD47 expression was more strongly correlated with SIRPA expression in luminal types (Spearman correlation: 0.88). Conclusions: Overexpression of CD47 in BM correlated with the recurrence in Her2 enriched and triple negative subtypes. CD47 high expression may indicate the potential capacity to relapse after surgical operation. It can be inferred from the association between CD47 and cancer stem cells that ITC would elude the immune system by taking advantage of activation and initiation of CD47’s signal transduction cascade, resulting in inhibition of phagocytosis. CD47 is an useful prognostic biomarker for predicting survival of Her2 enriched and triple negative subtypes in breast cancer. High expression of CD47 in luminal types could be used as an index of therapeutic effect marker.

P6

Introduction HER2 overexpression accounts for 20% of breast cancers. The poor prognosis historically associated with HER2 overexpression has sig-nificantly improved with the addition of HER2-targeted therapy to standard chemotherapy. Our objectives were: 1) to evaluate if HER2 amplification is associated with different clinicopathological features, and 2) to determine if amplification affects recurrence-free survival (RFS) after standard treatment. Methods We retrospectively analyzed 153 patients with HER2+ breast cancer who had surgery at our institution from 2002-2010. Determined by recursive partitioning, a HER2/CEP17 ratio of 7.2 predicted survival. We compared demographics, surgery and systemic treatment, pathology, and RFS in patients with ratio ≤ 7.2 versus > 7.2. Results Of HER2+ cases, 63 (39%) had a HER2/CEP17 ratio ≤ 7.2. Median follow-up was 75 months. Most patients (71%) received standard systemic treatment with chemotherapy and trastuzumab. There was no difference in age, race, menopausal status, and family history of breast cancer between groups. Compared to lower amplification tumors, those with a high level were associated with decreased PR positivity (47.8% vs. 68.3%, p=0.01), increased Ki67 (median 33% vs. 25%, p=0.03), and smaller size (T1 52.2% vs. 30.2%, p=0.02). There was no difference in tumor differ-entiation/grade, ER status, lymphovascular invasion, nodal stage, and type of surgery or systemic treatment. In multivariate classification tree survival analysis, ratio ≤ 7.2 and positive nodal status were independent predictors for recurrence/death. Tree modeling identified the highest risk group for recur-rence/death to be patients with node positive disease and ratio 5.6-7.2 (n=8, HR=12.2, p<0.01). Conclusion Ours is the first analysis, albeit in a small set of patients, to suggest that low HER2 amplification is associated with an increased risk of recurrence/death even when controlling for pathologic and treatment variables. Since high amplification was associated with an increased median Ki67, these patients may have a better response to systemic treatment and an improved RFS. Larger dataset analysis is needed to better define the effect of HER2 amplification in HER2+ breast cancer.
Rehabilitation Needs in the Breast Cancer (BC) Survivorship Population: A Prospective Observational Study

Introduction: Despite less invasive treatment options for BC, morbidity of surgical procedures remains high. Data from the ACOSOG Z0010 trial recently cited the incidence of lymphedema to be 10.5% at 1 year and upper quarter morbidity higher than expected among patients who received less aggressive axillary management. Adding to this data, we conducted a prospective study to examine the impact of early rehabilitation for BC patients.

Methods: We enrolled 120 women undergoing either breast conservation surgery (BCS) or mastectomy, receiving objective and subjective rehabilitation assessments preoperatively, early postoperatively and during surveillance of one year at a public hospital. Symptoms and/or functional limitations were identified and patients meeting pre-determined criteria were referred for further interventions. We measured the true incidence of morbidity and the impact of early intervention and identified factors contributing to postoperative morbidity using multivariate analyses.

Results: To date, 108 patients have undergone surgical intervention with BCS (57%) and sentinel lymph node biopsy (58%) being the most common. Seventy percent of patients have undergone whole breast irradiation (WBI). Forty-two patients (35%) have required physical therapy interventions. These patients had a mean number of 8 lymph nodes removed compared to 6 in the non-intervention group. There was no statistically significant difference between the two groups in type of surgical procedures.

Conclusions: A significant proportion of patients were found to have impairments that warranted early rehabilitation, supporting the underestimation of the true incidence of morbidity and demonstrating that early intervention may decrease the overall burden of morbidity.

### Table 1

<table>
<thead>
<tr>
<th>Mean Age</th>
<th>Intervention</th>
<th>No Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean 57.9 (SD 8.86)</td>
<td>34.9 (SD 7.6)</td>
<td>32.4 (SD 9.3)</td>
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<tr>
<td>Rate of intervention with condition</td>
<td>2.68 (37.9%)</td>
<td>23.69 (38.3%)</td>
</tr>
<tr>
<td>P value</td>
<td>0.977</td>
<td>0.035</td>
</tr>
<tr>
<td>Pre-op exercise</td>
<td>12/34 (35.3%)</td>
<td>20/37 (54.1%)</td>
</tr>
<tr>
<td>Neoadjuvant chemotherapy</td>
<td>26/71 (36.6%)</td>
<td>15/56 (26.8%)</td>
</tr>
<tr>
<td>Lymphedema vs. mastectomy</td>
<td>27/58 (46.6%)</td>
<td>7/24 (29.2%)</td>
</tr>
</tbody>
</table>
Factors associated with Increasing Mastectomy Rates in Early Stage Breast Cancer Patients: Report from a Single Institution and Population-based Database

Introduction: Over the last decade, increased mastectomy rates have been reported in the treatment of early-stage breast cancer. The aims of this study were to examine trends in mastectomy rates at our institution and a population-based database and to compare differences between the cohorts. Methods: Patients with stage 0-II breast cancer diagnosed from 2000 to 2012 were identified from our institution (CC cohort, n=14,638) and the SEER database (SEER cohort, from 2000-2011, n=503,451). Mastectomy rates by year of diagnosis were evaluated and multivariable logistic regression models were built to identify clinicopathologic factors that predicted mastectomy as the treatment choice. Results: The proportion of patients treated with mastectomy decreased from 46.3% to 39.1% between 2000 and 2005 in the CC cohort (P=0.003) and from 42.0% to 37.3% in the SEER cohort (P<0.0001). Subsequently, mastectomy rates increased to 48.1% in the CC cohort (P=0.001) by 2012 and to 40.0% in SEER by 2011 (P=0.0001). Multivariable analysis demonstrated that patients with younger age (<50), stage II vs. stage I, high grade tumor, and lobular histology were more likely to choose mastectomy in both SEER and CC cohorts. In the CC cohort, patients with contralateral breast cancer were also more likely to undergo mastectomy. Those patients undergoing bilateral mastectomy and choosing reconstruction increased each year in both CC and SEER cohorts. Patients undergoing bilateral mastectomy increased from 12.8% in 2005 to 21.5% in 2012 in the CC cohort (P=0.001) and from 12.4% to 26.0% in 2011 in SEER. Patients choosing reconstruction increased from 60.5% in 2005 to 70.9% in 2012 in the CC cohort (P<0.0001) and from 12.4% to 26.0% in 2011 in SEER (P<0.0001). Conclusions: Our study shows that there was a decrease in mastectomy rates from 2000 to 2005, subsequently mastectomy rates consistently increased from 2005-2012 /2005-2011 in both cohorts. Increased rates of bilateral mastectomy and the decision to undergo contralateral prophylactic mastectomy likely contributed to the increased mastectomy rates in both cohorts.

Health Disparity or Bad Biology? An Analysis of Triple-negative Breast Cancer Patients in an Urban Academic Hospital

INTRODUCTION: 10-25% 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. Reviews suggest TNBC may represent a higher proportion of tumors in African Americans and present at a later stage. The objectives of this study is to examine the demographics of a population of patients with TNBC. METHODS: The Commission on Cancer registry tumor database was queried according to receptor status. Patient demographics were analyzed. Stage of tumor, lymph nodes, and metastases were assessed. Analyses using the Chi-Square test were conducted (www.vassarstats.net). RESULTS: Breast cancer tumors were identified in the database (n=3267), and complete receptor data was available for 1238 tumors. 1028/1238 (83%) of the tumors were non-TNBC, while 210/1238 (17%) were TNBC. There were more women less than 40 years of age in the TNBC group (p=0.018). Women were more likely to be black in the TNBC group (p<0.0001). TNBC tumors were more likely to be classified as grade III (p<0.0001). There were more patients presenting with American Joint Commission on Cancer (AJCC) stage I cancer in the non-TNBC group (p<0.0001), and more women presenting with AJCC stage II cancer in the TNBC group (p<0.0001). There was no significant difference in the proportion of women that were uninsured or Medicaid patients. There was significant difference in the proportion of patients that were residents of Illinois counties with less than $25,000 median household income between the non-TNBC and TNBC patients. There was no significant difference in time from diagnosis to the time of first contact at treating institution. CONCLUSION: TNBC is more common among African-American and younger women, but TNBC is not more common among poor patients below the poverty level or without insurance. This suggests an actual difference in tumor biology with TNBC patients, and not simply a health disparity.

Comparison of Patient Demographics and Tumor Characteristics between Triple Negative Tumors and Non-Triple Negative Tumors

Anti-HER2 CD4+ Th1 Responses can be Restored in DC1 Vaccinated Breast Cancer Patients

INTRODUCTION: HER2+ breast cancer (BC) pts with residual disease following neoadjuvant therapy have an anti-HER2 T-helper type 1 (Th1) cell immune deficit and a significant risk of recurrent disease. We measured Th1 responsivity to HER2-pulsed type 1 dendritic cell (DC1) vaccination, and investigated strategies for in vitro expansion of HER2-specific Th1 cells derived from vaccinated pts, for potential adoptive T-cell transfer. METHOD: HER2+ BC pts (n=4) received adjuvant HER2-pulsed DC1 vaccines. Pre-vaccination Th1 responses were compared with post-vaccination and 3-month responses. Responses were generated from CD4+ T-cells co-cultured with HER2-pulsed DCs (post-vaccination), or unexpanded PBMCs pulsed with 6 HER2 Class II peptides (3 mo), by measuring IFN production via ELISPOT. In vitro, HER2-specific CD4+ T-cells were generated by co-culture with HER2-pulsed DC1s and expanded using IL-2 alone or IL-2/7/15. These HER2-specific cells were subsequently expanded via anti-CD3/CD28 stimulation. Fold expansion was defined as: (dT-cells post expansion/dT-cells pre expansion); specificity was measured by antigen specific IFN production by ELISA. RESULT: Compared to pre-vaccination responses, all pts demonstrated >2-fold increase in anti-HER2 IFNpos Th1 responses to ≥1 peptide post-vaccination; cumulative responses improved (153 post vs 73 pre SFC/106; p=0.007). Of evaluable pts at 3 mo follow-up (n=2), anti-HER2 response rate (100% post vs 0% pre; p=NA) and cumulative response (113.4 post vs 11.7 pre SFC/106; p=0.02) improved. In vitro, HER2-specific Th1 expansion was significantly better when stimulated with IL-2/7/15 (p<0.0001) compared with IL-2 alone. Subsequent stimulation via anti-CD3/CD28 resulted in an addtional 4-fold expansion. CONCLUSION: HER2-pulsed DC1 vaccination in HER2+ pts with residual disease boosts anti-HER2 Th1 immune responses. Post-vaccination, in vitro expansion of anti-HER2 Th1 cells may be used for adoptive transfer as a supplemental strategy in resurrecting the anti-HER2 CD4+ Th1 immune response.

Abstracts: Poster Presentations S47
Excising Additional Margins at Initial Breast-conserving Surgery (BCS) Reduces the Need for Re-excision: A Report of a Randomized Prospective Study in a Public Hospital

Introduction: Margin status is an important prognostic factor for local recurrence after BCS for breast cancer (BC). Our previous retrospective review showed that shave margins taken at the time of initial surgery reduces the positive margin rate. We designed a prospective randomized trial to stratify which patients benefit from additional shave margins.

Methods: Seventy-six patients with Stage 0–III BC were randomized to BCS or BCS with resection of additional margins (BCS+M). Tumor margins were classified as negative (>2 mm for ductal carcinoma-in-situ (DCIS); >1 mm for invasive ductal carcinoma (IDC)) based on guidelines at the time of accrual. Data were analyzed using multivariate analyses.

Results: Seventy-six patients with Stage 0–III BC were randomized from 2009–2012. Mean age was 59.6 years and median follow up was 39.5 months (26–56 months). Clinical characteristics are summarized below. Overall, 21 patients (27.6%) had positive margins: 14 had undergone BCS and seven BCS+M (p=0.005). Nineteen of the 21 patients with positive margins had DCIS on final pathology, regardless of the operative approach (OR=7.56, 95% CI=1.52, 37.51). Documentation of the 21 patients with positive margins had DCIS on final pathology, regardless of the operative approach (OR=7.56, 95% CI=1.52, 37.51). Documentation of the 21 patients with positive margins had DCIS on final pathology, regardless of the operative approach (OR=7.56, 95% CI=1.52, 37.51). Documentation of the 21 patients with positive margins had DCIS on final pathology, regardless of the operative approach (OR=7.56, 95% CI=1.52, 37.51).

Conclusion: Taking an additional 5 margins at the time of initial excision resulted in a reduction in positive margin rate among all patients. This approach may be beneficial for patients with limited resources for adequate follow-up or additional surgery. Regardless of the surgical approach, patients with positive margins should have re-excision based on a higher recurrence rate.
Independent Predictors of Omitting Post-Mastectomy Radiation Therapy in Breast Cancer Table 1. Patients with Neoadjuvant Chemotherapy, 2010-2011.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Facility Type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community</td>
<td>1.67</td>
<td>1.34-2.09</td>
<td>&lt;0.001</td>
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<tr>
<td>Academic</td>
<td>1.31</td>
<td>1.13-1.51</td>
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<td>Facility Location</td>
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<td>East South Central</td>
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<td>1.28-2.94</td>
<td>0.002</td>
</tr>
<tr>
<td>West South Central</td>
<td>2.23</td>
<td>1.51-3.29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pacific</td>
<td>2.23</td>
<td>1.53-3.27</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I (TNM)</td>
<td>1.70</td>
<td>1.47-1.96</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subtype</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triple Negative</td>
<td>1.21</td>
<td>1.02-1.45</td>
<td>0.03</td>
</tr>
<tr>
<td>HR/ ER Positive</td>
<td>1.25</td>
<td>1.06-1.49</td>
<td>0.01</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductal</td>
<td>1.34</td>
<td>1.07-1.67</td>
<td>0.01</td>
</tr>
<tr>
<td>Insurance Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>1.45</td>
<td>1.16-1.80</td>
<td>0.001</td>
</tr>
<tr>
<td>Age</td>
<td>1.82</td>
<td>1.33-2.48</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

For Adjusted for facility type, facility location, income, insurance status, clinical stage, tumor subtype, histology, grade, comorbidity index, age, and race.

**P17**

Trends in Tumor Characteristics among DCIS Patients: A Population-based Analysis of 130,229 Patients M. Worni,1,* M. D. Ryser,2 U. Guller,1 R. A. Greenup1, S. E. Hwang1, J. Duke University Medical Center, Durham, NC; 2. Duke University, Durham, NC; 3. Department of Medical Oncology, Cantonal Hospital, St. Gallen, Switzerland.

**Background**

The introduction of mammography screening in the US has led to a significant increase in the incidence of ductal carcinoma in situ (DCIS). However, changes in tumor characteristics over time and potential associations with treatment have not been well characterized. **Methods**

The Surveillance, Epidemiology, and End Results registry was queried for DCIS diagnoses from 1991 to 2011. Trends in tumor characteristics (tumor size, tumor grade, and estrogen receptor (ER) status) were analyzed using Cochrane Armitage trend test and their impact on treatment choice was assessed using multivariable adjusted logistic regression. **Results**

In total, 130,229 DCIS cases were identified. Among patients with known tumor grade, a significant increase in high-grade tumors was reported from 35.2% (n=1,195, 1991-96) to 44.5% (n=18,716, 2007-11) (p<0.001). Among patients with known tumor size there was a significant decrease in tumors of sizes ≤15mm, from 82.1% (n=7,636, 1991-96) to 66.6% (n=24,045, 2007-11) (p<0.001). The fraction of individuals tested for estrogen receptor status increased from 18.9% (n=2,644, 1991-96) to 85.0% (n=40,685, 2007-11) (p<0.001). Surgery type and radiation were tested for estrogen receptor status increased from 18.9% (n=2,644, 1991-96) to 52.6% (n=40,685, 2007-11) (p<0.001). Among patients with known tumor grade, a significant increase in the incidence of ductal carcinoma in situ (DCIS). However, changes in tumor characteristics over time and potential associations with treatment have not been well characterized. **Conclusion**

Between 1991 and 2011, there was increased reporting of tumor characteristics in SEER, with a trend towards increased incidence of high tumor grade, larger tumor size, and positive ER status. There is evidence of increased tailoring of surgery and radiation treatment over time based upon tumor features, although marked treatment variations persist, even among the lowest risk and highest risk DCIS.

Association of tumor characteristics with treatment choice from 1991 to 2011 (XRT: radiation therapy)

<table>
<thead>
<tr>
<th>Tumor grade</th>
<th>Unilateral mastectomy</th>
<th>Bilateral mastectomy</th>
<th>Lumpectomy with XRT</th>
<th>Lumpectomy without XRT</th>
<th>No surgery/XRT</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2,342 (15.9)</td>
<td>493 (3.3)</td>
<td>2,714 (46.0)</td>
<td>1,358 (23.6)</td>
<td>785 (13.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>III/IV</td>
<td>12,120 (27.2)</td>
<td>2,813 (6.5)</td>
<td>11,502 (45.0)</td>
<td>7,319 (28.7)</td>
<td>4,043 (15.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Unknown</td>
<td>8,523 (26.8)</td>
<td>808 (2.6)</td>
<td>11,366 (35.7)</td>
<td>5,902 (32.1)</td>
<td>4,043 (22.1)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**P18**


**Background**

Utilization of breast MRI has increased dramatically in recent years, and there is ongoing debate regarding the role of MRI in patients with breast cancer. Guidelines for MRI use in newly diagnosed breast cancer patients have not been established, and ordering patterns vary widely. We investigated patterns of MRI ordering by healthcare providers in the setting of newly diagnosed breast cancer patients. **Methods**

We reviewed all newly diagnosed breast cancer patients presenting for surgical management at a single tertiary care breast center from January 2011 through December 2013 were reviewed. Cases were evaluated for the use of pre-operative MRI, and medical specialty of the ordering provider was determined. Patients who presented to a specialized breast center with MRI already completed were compared to those who had MRIs ordered by their treating breast surgeon. **Results**

A total of 423 women with newly diagnosed breast cancer underwent MRI during the study period. In this group, 253/423 patients (60%) presented to our institution with an MRI already completed. Of MRIs performed prior to presentation, 73% were ordered by a primary care provider, and 27% were ordered by a breast specialist seen previously. Race was a significant predictor of having an MRI before presentation to a breast center (64% of Caucasians, 41% of African-Americans, 25% of Asians, and 65% of Hispanic patients, p<0.001). Women with commercial insurance were significantly more likely to have an MRI completed before presentation than those with Medicaid (62% vs 37%, p<0.002). Age, family history of breast cancer, genetic testing, breast density, mode of diagnosis, and biopsy pathology were not significant factors in determining whether a patient underwent MRI prior to presentation to a breast surgeon. **Conclusion**

In our experience, many MRIs performed in newly diagnosed breast cancer patients were ordered by non-breast specialists as part of their patient’s initial work-up. Socioeconomic disparities exist in MRI utilization prior to presenting to a breast specialist. Further research is needed to develop guidelines for breast MRI use in newly diagnosed cancer patients.
P19

Axillary Ultrasound Predicts Lymph Node Metastatic Burden in Invasive Ductal Carcinoma

R. Jackson,* C. Mylander, M. Rosman, K. Sawyer, L. Tafra. Anne Arundel Medical Center, Annapolis, MD.

INTRODUCTION: Use of axillary ultrasound (AUS) in the preoperative assessment of breast cancer is controversial. Given the ACOSOG Z0011 trial results, some suggest that abnormal AUS may assign patients to unnecessary axillary node dissection (AND). Conversely, clinical trials are underway to investigate AUS to replace sentinel node biopsy (SNB) for axillary staging in patients without clinically evident lymphadenopathy. The goal of this study was to assess the utility of AUS to predict nodal disease burden, and to examine differences in AUS performance by cancer type. METHODS: From an institutional database, all newly diagnosed invasive breast carcinomas in 2011 with both preoperative AUS and surgical axillary staging were identified. Exclusion criteria were palpable lymphadenopathy, previous axillary surgery, or neoadjuvant chemotherapy. AUS findings, categorized as suspicious vs. not suspicious, were correlated with the number of axillary nodal metastasis from surgical pathology (SNB and/or AND). RESULTS: 119 cancers were included: 91 (76%) were invasive ductal carcinoma (IDC), 15 (13%) were invasive lobular carcinoma (ILC), 12 (10%) were mixed IDC/ILC, and 2 (2%) were other invasive carcinomas. 32 (27%) had a suspicious AUS (Table). 25% (n=8) of those with suspicious AUS had ≥3 positive nodes, compared to 5% (n=4) of those with normal AUS (p=0.006). Suspicious AUS was more sensitive for ≥3 positive nodes in IDC or mixed tumors (88%) than in pure ILC (25%). Among 72 IDC/mixed tumors with normal AUS, only 1% (n=1) had ≥3 positive nodes, whereas among 13 pure ILCs with normal AUS, 23% (n=3) had ≥3 positive nodes (p=0.011). CONCLUSIONS: Compared to patients with normal AUS, patients with suspicious AUS were more likely to have a higher nodal disease burden than patients included in the ACOSOG Z0011 trial. AUS was 88% sensitive in predicting high nodal disease burden in IDC, but performed poorly in ILC. This supports the idea that, beyond prognostic value, SNB may not be beneficial in IDC with negative AUS. Negative AUS should be interpreted cautiously in ILC. Prospective studies of AUS as a sole staging modality should be powered for subgroup analysis by cancer type.

Table. N stage, by axillary ultrasound results.

| Category Assessed | 0 | 1 | 2 | 3 | 4 | 5-
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal AUS Ultrasound</td>
<td>61 (85%)</td>
<td>9 (14%)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Suspicious AUS Ultrasound</td>
<td>17 (57%)</td>
<td>6 (20%)</td>
<td>3 (10%)</td>
<td>3 (10%)</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Percent are calculated by row. 2 non-IDC, non-ILC invasive carcinomas with normal AUS/0 axillary nodal metastasis are not included in table.

P20

LCIS, Race and Age: 10-year Cancer Specific Survival after a Diagnosis of Lobular in situ Disease

I.M. Lizarraga,* M.C. Schroeder, S.L. Sugg, R.J. Weigel, E. Chrischilles, A. Thomas. University of Iowa Hospitals and Clinics, Iowa City, IA.

BACKGROUND Lobular carcinoma in situ is generally considered a marker of increased risk for future breast cancer rather than malignant disease. The influence of a first diagnosis of LCIS on subsequent breast cancer specific survival has never been examined. We examined 10-year survival trends for women diagnosed with LCIS and compared them by age and race. METHODS Female patients with microscopically confirmed breast cancers reported to the Surveillance, Epidemiology and End Results (SEER) Program between 1988 and 2011 were identified. The crude probability of various measures of mortality was estimated using SEER*Stat (expected survival by year, age and race). Survival outcomes for LCIS were compared with DCIS and with adjusted AJCC 6th stage I-III breast cancers. Analyses were stratified by age (<50 and ≥50) and race (white and black) and time period: 1988-1999 and 2000-2012. RESULTS In white women in both age groups and black women ≥50y, LCIS was not associated with increased probability of 10-year breast cancer specific mortality (BCSM) during either time period (table). From 1988-1999, this finding was the same for black women <50y. However, from 2000-2011 the probability of BCSM in this group increased 3 fold to 2.49% (statistically different from zero, p<0.05). This is comparable to the BCSM of DCIS in this age group during the same time period (p<0.052). Additionally, relative survival (RS; observed divided by expected) was statistically less than 100% in black women <50y in both time periods, while in white women with LCIS, RS was 100%. In contrast, BCSM and RS for stage I-III invasive cancer in both black and white women at all ages has improved between the two time periods, with black women <50y experiencing a greater improvement than those ≥50y. There have been no statistically significant changes to survival over time for DCIS. CONCLUSION From 2000-2011, a diagnosis of LCIS in black women ≤50y was associated an increased risk of BCSM, in contrast with older black women and white women of all ages. This worrisome trend denotes a significant increase in risk of death from breast cancer for young black women with LCIS compared to the previous decade.

Table 1. Estimated 10-year relative survival* and cause-specific death by race, age, stage, and time period.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Age (y)</th>
<th>Race</th>
<th>N</th>
<th>Relative survival (RS)</th>
<th>Breast cancer specific death</th>
<th>N</th>
<th>Relative survival (RS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCIS</td>
<td>≤50</td>
<td>≥50</td>
<td>White</td>
<td>58%</td>
<td>98.9%</td>
<td>98.9%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Black</td>
<td>1.23%</td>
<td>1.23%</td>
<td>1.23%</td>
<td>1.23%</td>
<td>1.23%</td>
<td>1.23%</td>
<td>1.23%</td>
</tr>
<tr>
<td>DCIS</td>
<td>≤50</td>
<td>≥50</td>
<td>White</td>
<td>86.4%</td>
<td>99.7%</td>
<td>99.7%</td>
<td>99.7%</td>
</tr>
<tr>
<td>Black</td>
<td>2.02%</td>
<td>2.02%</td>
<td>2.02%</td>
<td>2.02%</td>
<td>2.02%</td>
<td>2.02%</td>
<td>2.02%</td>
</tr>
<tr>
<td>BCSM</td>
<td>≤50</td>
<td>≥50</td>
<td>White</td>
<td>63.4%</td>
<td>63.4%</td>
<td>63.4%</td>
<td>63.4%</td>
</tr>
<tr>
<td>Black</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
</tr>
<tr>
<td>RS</td>
<td>≤50</td>
<td>≥50</td>
<td>White</td>
<td>92.3%</td>
<td>92.3%</td>
<td>92.3%</td>
<td>92.3%</td>
</tr>
<tr>
<td>Black</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
<td>1.69%</td>
</tr>
</tbody>
</table>

*Statistically different from 0 or 100% (p<0.05). 
*Relative survival is observed divided by expected survival (adjusted by age, race, and year).

P21

Metaplastic Breast Cancer is Resistant to Standard Breast Cancer Treatment Modalities


Introduction: Metaplastic breast cancer (MBC) is a variant of invasive breast cancer (BC), comprising less than 1% of all BCs. Guidelines state that MBC should be treated like other invasive BC. The natural history and response to treatment of MBC is poorly understood. Further insight into this rare disease is necessary to determine if currently utilized treatments are effective. Methods: Institutional databases were reviewed to identify MBC cases treated from 1995-2012. Cases were divided into MBC subtypes: pure epithelial, mesenchymal, or mixed epithelial/mesenchymal. BC-free survival (BCFS) and overall survival (OS) was calculated by Kaplan-Meier analysis stratified by MBC subtype. Results: 100 cases of MBC were identified. The median age at diagnosis was 56 years (range 30-83). 57% of patients pre-
sented with Stage II disease. Patient and tumor characteristics are listed in Table 1. Hormone-receptor (HR) and HER2 status were as follows: 7% HR+/HER2-, 81% HR-/HER2-, 1% HR-/HER2+, and 11% HR/HER2 unknown. Breast conservation was attempted in 64 patients; 10 of whom converted to mastectomy. Neoadjuvant chemotherapy was used to downstage 8 patients with locally advanced MBC; 3 converted from mastectomy to lumpectomy and 5 progressed on treatment, ultimately requiring mastectomy; there were no complete pathologic responses. At the median follow-up of 5.4 years (range .09 to 15.9), there were 28 recurrences: 16 distant, 8 local-regional (LRR), and 7 LRR plus distant. All patients with LRR had chest wall or ipsilateral breast tumor recurrences. In patients who developed distant metastases, 20 had visceral metastases, 2 had bony metastases, 1 had both, and 16 patients have died of disease. 5-yt BCFS and OS were 0.73 (95% CI 0.63-0.81) and 0.77 (95% CI 0.67-0.85), respectively, and did not vary by MBC subtype. Conclusion: Among 100 cases of MBC, we observed a high rate of LRR, lack of response to neoadjuvant chemotherapy, and poor BCFS regardless of metastatic subtype. These data suggest that current treatments for BC are less effective for MBC and alternative therapeutic strategies should be investigated.

Clinicopathologic features of patients with metaplastic breast cancer

<table>
<thead>
<tr>
<th>Clinicopathologic feature</th>
<th>No=100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologic tumor size</td>
<td></td>
</tr>
<tr>
<td>≤2 cm</td>
<td>43</td>
</tr>
<tr>
<td>&gt;2mm and ≤5 cm</td>
<td>46</td>
</tr>
<tr>
<td>&gt;5 cm</td>
<td>9</td>
</tr>
<tr>
<td>Pathologic axillary lymph node status</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>24</td>
</tr>
<tr>
<td>Negative</td>
<td>74</td>
</tr>
<tr>
<td>Unknown</td>
<td>5</td>
</tr>
<tr>
<td>Metaplastic subtype</td>
<td></td>
</tr>
<tr>
<td>Pure epithelial (squamous, adenoepithelial)</td>
<td></td>
</tr>
<tr>
<td>Mesenchymal (spindle cell, myoepithelial, chordoid, oncocytic, carcinoisocellular, matrix-producing)</td>
<td>26</td>
</tr>
<tr>
<td>Mixed epithelial/mesenchymal</td>
<td>29</td>
</tr>
<tr>
<td>Metaplastic NOS</td>
<td>4</td>
</tr>
<tr>
<td>Local therapy</td>
<td></td>
</tr>
<tr>
<td>Lumpectomy</td>
<td>54</td>
</tr>
<tr>
<td>With radiation therapy</td>
<td>44</td>
</tr>
<tr>
<td>Mastectomy</td>
<td>46</td>
</tr>
<tr>
<td>With radiation therapy</td>
<td>13</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>86</td>
</tr>
<tr>
<td>No</td>
<td>12</td>
</tr>
</tbody>
</table>

The proportion of patients with positive nodes did not differ between groups. **Discussion** While this study is limited by its retrospective nature, delays of up to 60 days were not associated with worse outcomes. A selection bias for earlier surgery based on worrisome radiographic or clinical findings likely explains the seemingly worse prognosis for stage II patients treated with early surgery. This study should reassure patients and surgeons that modest delays do not adversely affect breast cancer outcomes.

**P23**

**Trends in Income, Race and Ethnicity Disparities in Guidelines for Breast Conserving Therapy** J.L. Patrick,* J.M. Feinglass, S.A. Khan, Northwestern University, Chicago, IL.

NCCN guidelines for treatment of breast cancer recommend treatment with breast-conserving therapy (BCT) for early stage breast cancer, without positive margins (PM) and use of whole breast radiotherapy (RT). We analyzed trends in guideline adherence by income, education, race and ethnicity from the National Cancer Data Base (NCDB) 1998-2011. **Methods** Women with stage I and stage II breast cancer (T1N0 or T1N1, n=346,034) were identified from 1123 hospitals. Chi square tests of differences by race and ethnicity and quartiles of patients’ zip code income and education were used to test the significance of differences in guideline adherence. Random effects logistic regression, adjusted for nesting of patients within hospitals, was used compute odds ratios for disparities controlling for patient demographic and clinical characteristics and hospital type and region. **Results** BCT disparities remained similar for non-Hispanic whites (79.9-87.3%), Blacks (80.0-85.7%) and Hispanics (79.1-85.2%) and increased between the highest versus lowest zip code income and education quartiles. Among BCT patients, PM disparities between non-Hispanic whites (7.6-3.7%), and Blacks (9.3-4.5%) and Hispanics (11.6-4.6%) and across income and education quartiles improved. No RT disparities improved for Blacks (24.7-20.5%) and Hispanics (27.0-22.0%) but not between income and education quartiles. Regression results for all years indicated that white-Black BCT differences were non-significant, but Hispanics had 13% lower likelihood of BCT; highest and lowest income quartiles differed by 5-7%. PM was higher for Blacks and Hispanics (16%, 8%) but did not differ by income and education. Hispanics and low income patients were less likely to receive RT while Blacks were more likely and education differences were non-significant. **Conclusion** There was a mixed pattern of progress in reducing guideline disparities. Other risk factors such as older age, insurance status, region and hospital type were more significant than zip code socioeconomic status, race and ethnicity. These results are conservative to the extent that the NCDB reflects higher quality of care than non-participating hospitals.

**P22**

**Timing of Breast Cancer Surgery; How Much does it Matter?**

S. Mansfield,* M. Abdel-Rasoul,2 A.M. Terando,3 D. Agnese,3 1. Department of General Surgery, The Ohio State University, Columbus, OH; 2. Center for Biostatistics, The Ohio State University, Columbus, OH; 3. Division of Surgical Oncology, The Ohio State University, Columbus, OH.

**Introduction** Patients do not plan for a diagnosis of breast cancer, often occurring at inconvenient times. Previous commitments and surgeon availability may influence scheduling. Most want surgery as soon as possible, while others would rather delay care. Lengthy delays may lead to cancer growth and metastasis, however, the impact of modest delays is lacking in the literature. The aim of this study was to evaluate the impact of delays in surgery on outcomes, including disease-free survival (DFS) and nodal status (NS). **Methods** The cancer registry from one academic cancer hospital was retrospectively reviewed to identify patients with ductal carcinoma in situ (DCIS), invasive ductal carcinoma (IDC), and invasive lobular carcinoma (ILC) treated between 1990 and 2009. Time from initial biopsy to surgical resection was calculated. Patients were grouped into early (ES, 0-21 days), intermediate (IS, 22-42 days), and late (LS, 43-63 days) surgery. Groups were evaluated for differences in NS at the time of surgery and DFS for each cancer stage separately. Chi-squared or Fisher’s exact tests were used to compare proportion of patients with positive nodes and DFS was compared using age-adjusted Cox Proportional Hazards Models. **Results** A total of 3874 patients were identified for analysis (Figure 1). There were no LS patients in the DCIS cohort. DFS was not affected by timing of surgery for DCIS (p=0.31, HR=1.94, CI 0.54-6.98) or stage I invasive cancers (p=0.053, ES vs IS: HR=1.54, CI 1.04-2.28; ES vs LS: HR=0.87, CI 0.51-1.49). In stage II cancers, ES was associated with worse DFS (p = 0.0004, ES vs IS: HR=1.58, CI 1.22-2.03; ES vs LS: HR=1.85, CI 1.14-2.99).

**Figure 1. Group descriptions.**

**P24**


**Introduction.** After curative treatment for breast cancer, some patients experience a contralateral lymph node recurrence (CLNR). The prognosis remains of CLNR unclear. According to the AJCC TNM classification, contralateral nodes are considered distant disease. However, aberrant lymph drainage after previous surgery is common, as described in lymphoscintigraphy studies. This might indicate that CLNR is a regional rather than a distant event. This...
study aimed to systematically review the literature to determine the prognosis of CLNR. Methods. PubMed (including MEDLINE) was searched until July 2014. Articles were included if they reported on CLNR with or without ipsilateral breast tumor recurrence (IBTR), in cohorts or individual patients, as well as repeat sentinel node (SN) studies reporting on patients with positive contralateral nodes. Exclusion criteria were synchronous contralateral breast cancer and distant events. Patient and tumor characteristics were extracted, as well as follow-up data if available. Results. 24 articles were included in the analysis, describing 48 patients, of which follow-up was available for 23. Of these 23 patients, 13 had an isolated CLNR, 4 IBTR and clinically detected CLNR, and 6 IBTR with a positive repeat SN. Time to CLNR was longer for CLNR with IBTR than for isolated CLNR. Axillary treatment was described for 38/48 patients and consisted of ALND for 34, resection of affected nodes for 1, and radiotherapy for 1 patient. For 27/48 patients, information on adjuvant therapy was available: 21/27 received chemotherapy. Mean follow-up after CLNR was 50.3 months. Overall survival (OS) and disease-free survival (DFS) after CLNR were 82.6% and 65.2% respectively at last follow-up. Conclusion. Although described in a highly selected population with heterogeneous characteristics, DFS and OS after CLNR were not consistent with distant disease. Furthermore, most patients received regional and systemic treatment, suggesting a curative intent. Combined with the fact that aberrant contralateral drainage is a well-established phenomenon, this indicates that CLNR could be considered a regional event. This should be confirmed with prospective data.

P25 Predictors of 30-day Readmission after Mastectomy: A Multi-institutional Analysis of 21,271 Patients I. Chow, P.J. Hanwright, N.M. Hansen, S.N. Leilabadi, J.Y. Kim, Northwestern University, Chicago, IL.

BACKGROUND: Recent healthcare legislation has made unplanned hospital readmission an important metric of health care quality and current efforts center on reducing this complication in order to avoid fiduciary penalties. There is currently a paucity of data delineating risk factors for readmission following mastectomy. METHODS: The 2011 and 2012 National Surgical Quality Improvement Program (NSQIP) dataset was retrospectively queried to identify patients who underwent mastectomy. Multivariate logistic regression modeling was used to identify risk factors for readmission. RESULTS: Of 21,271 patients meeting inclusion criteria, 1,190 (5.59%) were readmitted. The most commonly cited reasons for readmission included surgical site complications (32.85%), infection (27.72%), and venous thromboembolism (4.39%). The readmitted cohort demonstrated significantly more comorbidities and post-operative complications. The complications most associated with readmission were either infectious or venous thromboembolic. Independent predictors of readmission included BMI, cardiovascular disease, a history of a bleeding disorder, inpatient hospitalization, prior surgery, and skin-sparing mastectomy. Significantly, concurrent breast reconstruction and bilateral mastectomy were not independent predictors of readmission. CONCLUSIONS: This is the first study of readmission rates after mastectomy. Awareness of specific risk factors for readmission, particularly those that are modifiable, may serve to identify and manage high risk patients, aid in the development of pre- and postoperative clinical care guidelines, and ultimately improve patient care.

P26 Importance of Hospital Volume and Treatment Facility on Early-stage Breast Cancer R.A. Greenup, K. Houck, D. Sarma, A. Mackey, J.A. Sosa, J. Peppercorn, R. Blitzblau, E. Hwang, Duke University Medical Center, Durham, NC.

INTRODUCTION: Hospital volume and treatment facility correlate with clinical outcomes among patients with rare malignancies. Treatment facility type was associated with risk of death, with significantly lower 5-year mortality among women treated at academic/research (OR: 0.764 95% CI: 0.73-0.797) and comprehensive community cancer centers (OR: 0.861 95% CI: 0.830-0.895) when compared to community cancer programs. Increased 5-year mortality was seen in women treated at the lowest volume centers (stage I, OR: 1.199{1.221-1.375}; stage II, OR: 1.233{1.139-1.314}; stage III, OR: 1.273{1.145-1.422}. Hospital volume or facility type did not impact risk of death in stage IV patients. Private insurance correlated with improved 5-year mortality when compared to Medicare (OR: 2.550, 95% CI: 12.475-2.628), Medicaid (OR: 1.885, 95% CI: 1.780-1.997) or other (OR: 1.392, 95% CI: 1.313-1.476) coverage. CONCLUSIONS: Among women with early stage breast cancer, treatment at higher volume and academic/research or comprehensive community cancer centers was associated with improved overall survival. Referral to multidisciplinary specialty centers may benefit women with breast cancer.


Background: Lymph node ratio (LNR) has been shown to be a better prognostic factor for disease specific survival (DFS) and overall survival (OS) than the number of positive nodes. Calculation of residual cancer burden is labor intensive and thus we were interested in determining whether the burden of regional nodal disease could by itself offer additional prognostic information.

Methods: Patients who underwent definitive surgery after receiving neoadjuvant endocrine or chemotherapy were identified through the hospital based Breast Imaging Registry. Lymph node ratios for patients with node positive disease were calculated based on previously published classifications: low 0.01-0.2, intermediate 0.21-0.65, and high >0.65. Additionally, we searched for other cut-off points that could better apply to this cohort of patients. Kaplan-Meier log-rank test was used for survival analysis. Results: A total of 105 node negative and 92 node positive cases were identified from 2003 to 2010. The total number of lymph nodes examined ranged from 2 to 40, median 13. LNR range for the entire group was 0.03-1.0, median 0.22. For the low LNR group (N=42) the range of positive nodes was 1 to 4, for the intermediate group (N=32) 1 to 13, and for the high group (N=18) 2 to 25. In the node negative patients, the 3-year DFS and OS were 94% and 98%, respectively. For node positive patients, the 3-year DFS and OS were 66% and 77%, respectively. Percentage of patients alive by LNR subgroup were: Low: 79% (6-128 months, median 55 months); Intermediate 56.2% (9-127 months, median 52 months); High 55.6% (6-95 months, median 49 months). Three- and 5-year OS for patients with LNR <0.5 was 78.1% and 69.9%, and for LNR >0.5, 52.2% and 39.8%, respectively (p=0.02). Conclusion: LNR of 0.5 was found to discriminate for survival in patients after neoadjuvant systemic therapies. This differs from the LNR categories defined for patients who had surgery first. Further validation in a larger dataset is warranted. 1. Vinh-Hung V, Verkooijen HM, Fioretta G, et al. Lymph node ratio as an alternative to pN staging in node-negative breast cancer. J Clin Oncol 2009;27:1062-1068.


Introduction. Magnetic resonance imaging (MRI) is gaining popularity in the preoperative management of breast cancer patients. However, the role of this modality remains controversial. We aimed to study the effects of preoperative MRI (pMRI) on surgical management of breast cancer patients.

Methods. This retrospective study included 765 subjects with breast cancer treated operatively at the Cedars Breast Clinic of the McGill University Health Centre. Results. Between those who underwent pMRI (MRI group, N=307) and those who did not (no-MRI group, N=458), there were no significant differences (p=0.254) in the proportions of total (20.5% vs 17%) versus segmental mastectomies (79.5% vs 83%). Patients in the MRI group were significantly more likely (p=0.002) to undergo contralateral skin sparing surgery (12% vs 5.5%, respectively). Similar results were obtained in a multivariate regression analysis.
adjusting for confounders, with the proportions of contralateral breast operations significantly higher in the MRI group (OR=2.25, p=0.007). pMRI had no significant effect on the proportion of total re-excisions (7.5% vs 8.7%) in either univariate (p=0.540) or multivariate analysis (p=0.552). No significant differences (p=0.099) were observed in the type of re-excision (total vs segmental mastectomy) between the groups. Conclusions: pMRI does not have a significant impact on the type of post-mastectomy breast surgery but is associated with an increase in contralateral operations. Similarly, pMRI does not change the proportion of re-excisions or the type of the re-excision performed. This study demonstrates that pMRI has little impact on the surgical management of breast cancer and its value as an adjunct in the pre-operative workup of recently diagnosed breast cancer patients needs to be re-evaluated.

P29 Survival Post-neoadjuvant Chemotherapy in Breast Cancer: Validation of the MD Anderson Cancer Center Nomogram

S. Shaitelman, C. Loveland-Jones

Background In 2005, MD Anderson Cancer Center (MDACC) released their data on survival after neoadjuvant chemotherapy (NACT) for breast cancer, through which a nomogram was created for predictions based on tumor characteristics. We applied our institutional data to this nomogram to confirm its reliability and potentially further its applicability to modern chemotherapy regimens. Methods This is a retrospective study of patients undergoing NACT from 2006-2009 at Levine Cancer Institute. Data points for validation included chemotherapy regimen, final pathological tumor size, histologic type and grade, hormone status, nodal involvement, and outcomes of overall (OS) and disease free survival (DFS). Receiver operating characteristic curve analysis was used to evaluate discrimination for the nomogram. Calibration was assessed by comparing nomogram-predicted probabilities of 5-year DFS and 5-year Kaplan-Meier DFS estimates. Results 200 patients were identified for analysis. The following were excluded: 66 patients with insufficient data, 22 patients with inflammatory cancer or metastatic disease at presentation, 1 male patient, and 3 patients with concurrent primary malignancies. 108 patients (77 anthracycline based and 31 non-anthracycline) were evaluated by the MDACC nomogram calculator. 24% of the total cohort experienced a pathological complete response. Five-year survival of the cohort was 76.9%. Median DFS was not reached. The anthracycline-based group, a discrimination rate of 0.74 was found between survival predicted by the nomogram and our actuarial data. When expanded to include the non-anthracycline-based group, similar results were found (AUC 0.69). Conclusion This study demonstrates the generalizability of the MDACC NACT breast cancer nomogram to an independent cohort. A positive correlation was found not only in the originally described cohort but also in the MDACC NACT breast cancer nomogram to an independent cohort.

P30 Disparities in the Use of Post-mastectomy Radiation Therapy for Inflammatory Breast Cancer


Abstracts: Poster Presentations

Significant disparities exist with respect to which IBC patients receive PMRT. As use of PMRT for IBC has increased over time, it continues to be underused in a large number of patients despite its positive impact on recurrence and survival. Significant disparities exist with respect to which IBC patients receive PMRT. The reasons for these disparities are unknown but may include poor access to care and lack of physician knowledge regarding indications for PMRT in IBC. Further investigation is warranted.

Figure 1. Predictors of Underuse of PMRT for IBC: Multivariate Analysis Results

<table>
<thead>
<tr>
<th>Patient Factors</th>
<th>Insurance Status</th>
<th>Factor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private</td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Not insured</td>
<td></td>
<td>0.85</td>
<td>0.65 - 1.00</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td></td>
<td>0.87</td>
<td>0.72 - 1.05</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td></td>
<td>0.69</td>
<td>0.60 - 0.80</td>
<td></td>
</tr>
<tr>
<td>Other government</td>
<td></td>
<td>1.23</td>
<td>0.63 - 2.39</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td>0.82</td>
<td>0.57 - 1.17</td>
<td></td>
</tr>
</tbody>
</table>

Annual Income ($)

<table>
<thead>
<tr>
<th>Tumor Factors</th>
<th>Nodal Status</th>
<th>Treatment Factors</th>
<th>Chemotherapy Use</th>
<th>Factor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
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<tr>
<td>≥ 30,000</td>
<td>N3</td>
<td></td>
<td>Yes</td>
<td>1.00</td>
<td>0.68 - 0.97</td>
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</tr>
<tr>
<td>&lt; 30,000</td>
<td>N2</td>
<td></td>
<td>No</td>
<td>0.15</td>
<td>0.12 - 0.20</td>
<td></td>
</tr>
</tbody>
</table>

P31 Comprehensive Exploration of Phenylbutyrate (PB) Sensitivity

Phenylbutyrate (PB) is a drug that has been safely used in patients with hyperammonemia, and also harbors deoxyadenosine deaminase (DADA) activity which exhibits anti-tumor activity. In this study, we comprehensively searched for prediction gene markers of PB sensitivity using expression microarray in breast cancer. (Materials and Methods) We first investigated sensitivity of 7 breast cancer cell lines, identified both sensitive and resistant cell lines, and compared expression profile of genes with Affymetrix expression microarray harboring 54,675 genes. Candidate genes associated with PB sensitivity were finally identified and functionally validated using gene transfection experiments. (Results) 1 Breast cancer cell lines that are sensitive for PB were selected as CRL and MDAMB453 in which proliferation was decreased by 80% by PB treatment as compared with the control, while MDAMB231, triple negative breast cancer cell, was resistant to PB. (2) Comprehensive gene expression profiles compared mRNA expression of MDAMB231 cells against CRL and MDAMB453. As a result, Rab25, TFAP2B, and ESR1 over-expressions were recognized exclusively in CRL and MDAMB453. Using the National Cancer Database, female patients who underwent mastectomy for non-metastatic IBC from 1998 to 2011 were identified. Univariate and multivariate analysis were performed. This study demonstrates that pMRI has little impact on the surgical management of breast cancer and its value as an adjunct in the pre-operative workup of recently diagnosed breast cancer patients needs to be re-evaluated.
P32

Introduction: The benefit in overall survival and progression-free survival of surgical treatment of the primary tumor in metastatic breast cancer has not yet been clearly defined; a less explored topic is the benefit that would provide the addition of postmastectomy radiation therapy in this group of patients. Method: This is a retrospective study of patients with complete local treatment in metastatic breast cancer. To define the eligibility for surgery, was considered patients with resectable tumor, some clinical response to primary chemotherapy and low risk metastatic disease; and the addition of postmastectomy radiation therapy depends on characteristics of the primary tumor and nodal status (tumors more than 5 cm, AJCC T4 tumors and more than three positive lymph nodes). Based on treatment, patients were divided into three groups: 1.-chemotherapy alone, 2.- chemotherapy + surgery, 3.- chemotherapy + surgery + radiation therapy. The impact of local management in overall survival and progression-free survival was evaluated. Results: A total of 140 patients were included, with a median age of 53.4±14 years old. At diagnosis, 62% had metastases at one anatomical site; 49% bone metastases, 20% soft tissue, 14% lung and 17% other sites. 79 patients were in group 1, 31 in group 2 and 30 in group 3. The probability of 18 months survival was 68%, 79% and 90% respectively; the 18 months disease-free survival was 35%, 52% and 68% respectively for each group. The probability of survival at 18 months was 91% for luminal A, 75% for luminal B, 52% for Her 2 + and 42% for triple negative tumors. At comparative analysis, significant difference in overall survival and disease free survival was observed in favor of those patients who received chemotherapy + surgery + radiation therapy. Conclusions: The overall survival and disease-free survival at 18 months in selected patients with metastatic breast cancer is higher when multimodality treatment based in chemotherapy + surgery + radiation therapy is used. Long surveillance and further studies are necessary to confirm this data.

P33
Effect of Topical Microporous Polysaccharide Hemosphere on Wound Drainage Following Mastectomy: A Prospective Randomized Trial. L.P. Suarez-Kelly, W.H. Pasley, R. Rudolph. Surgery, Memorial Health-University Medical Center, Savannah, GA.

INTRODUCTION: Seroma formation is the most common complication after mastectomy and places patients at risk of associated morbidities. Microporous polysaccharide hemosphere (MPH) consists of hydrophilic, plant based polysaccharide particles and used as an absorbable hemostatic agent. Studies have shown that polysaccharides accelerate the healing process. MPH may promote wound healing and prevent seroma formation. Study done evaluating MPH and seroma formation after mastectomy with axillary dissection in rats showed a statistically significant decrease in seroma volume. Our aim is to evaluate the effects of topical MPH on wound drainage following mastectomy. METHODS: Prospective randomized single-blinded clinical trial of patients undergoing mastectomy for the treatment of breast cancer. MPH was applied to the surgical site in the study group and no application was performed in the control group. RESULTS: Fifty patients were enrolled, eight were excluded due to noncompliance. Forty-two patients were evaluated, control (n=21) vs MPH (n=21). No difference was identified on assessment of these two groups regarding patient demographics, tumor stage, number of total drain days, total drain output, number of clinic visits, or postoperative complication rate. On a subset analysis, body mass index (BMI) was identified as an independent factor for wound drainage. Analysis evaluating BMI less than 30 vs BMI greater than 30 revealed a statistical difference in mean drain days in simple mastectomy without sentinel lymph node biopsy (8.2 vs 15.3; p=0.036) and mean total drain output (496.5 vs 716.9 ml; p=0.046). Analyses evaluating BMI less than 30 vs MPH and BMI greater than 30 vs MPH revealed no statistical difference. CONCLUSION: No statistical difference was demonstrated in the amount of wound drainage or seroma formation related to the use of MPH. BMI greater than 30 has statistically significant increase in wound drainage, but does not appear to be related to MPH use. Unlike the data presented in the animal model, MPH does not reduce wound drainage or seroma formation in patients undergoing mastectomy for the treatment of breast cancer.

P34

Background: Neoadjuvant chemotherapy (NAC) can decrease tumor size and facilitate breast conserving surgery (BCS). Traditionally, wire localization (WL) has been used to guide excision of non-palpable lesions after NAC. Radioactive seed localization (RSL) is an alternative technique that has, in some studies, resulted in smaller resections with equivalent, or superior, negative margin rates. The use of RSL after NAC has not been well-studied. We hypothesize that RSL will result in equivalent re-excision rates and resection volume when compared to WL after NAC. METHODS: All cases of BCS after NAC at our institution were retrospectively reviewed between 2009 and 2011 for WL (n=72) and 2011 and 2013 for RSL (n=66). Patient and tumor characteristics were recorded. Re-excision of margins at the time of initial operation and need for second surgery due to positive or close (<2mm) margins were assessed. Surgical specimen volumes were compared. RESULTS: Patient characteristics were comparable between groups. The WL group had a significantly higher proportion of luminal tumors than did the RSL group. T stage before and after NAC was comparable (Table 1). Re-excision of margins at initial surgery and need for second surgery due to close/positive margins did not differ between patients treated with WL and RSL (29% vs. 33%, p= 0.59 and 16% vs. 10%, p= 0.30 respectively). Surgical specimen volume was comparable (mean 98 cm³ WL vs. 94 cm³ RSL, p= 0.76). There were significantly more complete responders (no residual invasive or in-situ disease) in the RSL group (22% WL vs. 45% RSL, p= 0.013). However, among partial responders (n= 56 WL, n=36 RSL), there remained no differences in re-excision rate, second surgery for close/positive margin rate or surgical specimen volumes (p = 0.87, 0.81 and 0.31 respectively). CONCLUSION: Among patients treated with BCS after NAC, tumor localization method (wire vs. radioactive seed) had no effect on surgical specimen volume or the need for re-excision or second surgery due to close/positive margins. RSL is a safe and effective alternative to WL when used in breast conserving surgery after NAC.
# P35

Are We Failing to Treat? Trends in the Omission of XRT after Lumpectomy for Breast Cancer in the United States C. Minimi, J.M. Feinglass, K.Y. Bilimoria, J. Strauss, N. Rydzewski, N.M. Hansen. Surgery, Northwestern Memorial Hospital, Chicago, IL

**Background:** Radiation therapy (XRT) has been the standard of care for DCIS and breast cancer, but recent studies suggest that XRT may be omitted in certain populations. Our objective was to examine trends in adjuvant XRT use in patients undergoing lumpectomy for DCIS or invasive breast cancer. **Methods:** From the NCDB, 540,040 lumpectomies at 1123 hospitals were identified from 1998-2011. Changes in XRT use over time were explored using random effects logistic regression analyses, adjusting for patient demographics, tumor characteristics, and hospital type. **Results:** XRT was used in 61.6% of patients with DCIS and 80% of patients with invasive cancer. The proportion of patients receiving XRT in both groups increased from 1998-2011 (DCIS: 57.1% to 64.4%; invasive: 78.0% to 80.8%; P=0.001 for both). However, in adjusted analyses, lumpectomy patients treated in 2010-2011 were less likely to receive XRT than those treated in 1998-2000 (DCIS: OR 0.87, 95% CI 0.83 to 0.91; invasive: OR 0.92, 95% CI 0.89 to 0.94; P=0.001). Compared to 1998-2000, in 2010-2011, the elderly were less likely to receive XRT (DCIS: OR 0.91, 95% CI 0.84 to 0.99; invasive: OR 0.69, 95% CI 0.66 to 0.72; P<0.001) as were patients<40 with DCIS (OR 0.57, 95% CI 0.41 to 0.80). Although a greater proportion of patients received XRT in both groups increased from 1998-2011 (DCIS: OR 0.87, 95% CI 0.83 to 0.91; invasive: OR 0.69, 95% CI 0.66 to 0.72; P<0.001) as were patients<40 with DCIS (OR 0.57, 95% CI 0.41 to 0.80). A greater proportion of patients received XRT in 2010-2011 than in1998-2000, changes in hormonal therapy use over the study period resulted in a lower likelihood of XRT in 2010-2011 in adjusted analyses. After the 2002 approval of the MamoSite device, the proportion of patients receiving accelerated partial breast irradiation increased significantly (DCIS: 0.6% to 6.1%, P=0.001; invasive: 1.3% to 7.4%, P<0.001). **Conclusion:** When adjusted for covariates, XRT use among breast cancer patients undergoing lumpectomy decreased from 1998-2011. Omission of XRT may be reasonable in selected populations, but the overall decrease in adjuvant XRT use in patients with invasive cancer undergoing lumpectomy is concerning and could reflect inappropriate extrapolation of studies supporting selective XRT omission. The reasons for the omission of guideline-recommended XRT merit further investigation.

<table>
<thead>
<tr>
<th>Clinicopathologic Factors in Wire Localized versus Radioactive Seed Localized Patients</th>
<th>WIL</th>
<th>n (% category)</th>
<th>RSL</th>
<th>n (% category)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td>Mean</td>
<td>55</td>
<td>54</td>
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</tr>
<tr>
<td>Range</td>
<td>39 - 86</td>
<td>26 - 89</td>
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<td>0.16</td>
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<td><strong>Race</strong></td>
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<tr>
<td>Caucasian</td>
<td>67 (92)</td>
<td>57 (86)</td>
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</tr>
<tr>
<td>African-American</td>
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<tr>
<td>Other</td>
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<td><strong>Histology</strong></td>
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<td>ILC</td>
<td>3 (5)</td>
<td>1 (2)</td>
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<td><strong>Clinical T stage: Pre-therapy</strong></td>
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<td></td>
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<td>0.91</td>
</tr>
<tr>
<td>T1</td>
<td>18 (25)</td>
<td>13 (20)</td>
<td></td>
<td></td>
<td></td>
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<td>T2</td>
<td>41 (62)</td>
<td>45 (69)</td>
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<tr>
<td>T3</td>
<td>7 (10)</td>
<td>6 (9)</td>
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<tr>
<td>T4</td>
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<tr>
<td><strong>Clinical T stage: Post-therapy</strong></td>
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<td>T0</td>
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<td>T1</td>
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</tr>
<tr>
<td>T2</td>
<td>21 (29)</td>
<td>14 (21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>1 (1)</td>
<td>0 (0)</td>
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<tr>
<td><strong>Tumor Phenotype</strong></td>
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<tr>
<td>Triple-Positive</td>
<td>21 (29)</td>
<td>21 (32)</td>
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<tr>
<td>HER2-enriched</td>
<td>14 (20)</td>
<td>22 (33)</td>
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<tr>
<td>Luminal</td>
<td>37 (51)</td>
<td>23 (35)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Clinical T stage determined radiographically. **Triple Negative = Estrogen/Progesterone/HER2 negative HER2-enriched = Estrogen/Progesterone negative, HER2 positive Luminal = Estrogen and/or Progesterone positive, HER2 negative*
size and limited nodal disease. Further studies are needed to evaluate the benefit of PMRT in TN patients who do not fit traditional indications.

P38
Baseline MRI for Breast Cancer Patients Receiving Neoadjuvant Chemotherapy Leads to Additional Biopsies and Unnecessary Costs

Introduction: Utilizing data from the California Cancer Registry, we identified 100 consecutive women treated for locally advanced breast cancer. We included patients diagnosed with unilateral, non-recurrent breast cancer who received a baseline MRI at the onset of neoadjuvant chemotherapy. At our institution, a baseline breast MRI has an average cost of 8,765 USD and an MRI guided breast biopsy is 13,762 - 15,261 USD. Results: Median age at time of diagnosis was 50.57 years. The majority of patients were Caucasian (72%), Asian (18%), Hispanic (1%), African American (1%) and Native American (1%). Thirty-four patients were hormone receptor positive, HER2 negative, 36 were HER2 positive and 28 were triple negative. Baseline MRI identified contralateral findings in 35 patients. Twenty-four of these patients received a contralateral biopsy, of which 83.3% required MRI guidance. The majority of contralateral biopsies were benign (87.5%), 2 were invasive, and 1 was DCIS.

Discussion: There was no association between index tumor biology and the incidence of contralateral MRI findings or pathology. Patients with a triple negative index tumor were least likely to have a contralateral biopsy (p = 0.039) and patients with a triple positive index tumor were most likely to have bilateral surgery (p = 0.006). A contralateral biopsy, regardless of the pathology finding, resulted in a significant increase in the occurrence of bilateral partial mastectomy (p = 0.005) and a trend towards bilateral surgery (p = 0.15).

Conclusions: We estimate that $876,500 USD were spent to obtain 100 baseline MRIs, which lead to 24 contralateral biopsies, at an additional cost of $316,292 USD. Overall, baseline MRI detected clinically relevant contralateral pathology in only 3/100 patients (3%). In the current climate of healthcare cost consciousness, future efforts will need to focus on identifying ways to limit unnecessary biopsy through improvements in MRI specificity. A more selective approach to using MRI could help ensure effective resource allocation. Until then, surgeons must remain cognizant that a contralateral biopsy, regardless of the pathology finding, has the potential to influence their surgical decision making.

<table>
<thead>
<tr>
<th>Biopsy Type</th>
<th>Contralateral Biopsy (n=24)</th>
<th>No Contralateral Biopsy (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilateral</td>
<td>52% (12/23)</td>
<td>19% (15/78)</td>
</tr>
<tr>
<td>Unilateral</td>
<td>47% (12/25)</td>
<td>90% (69/76)</td>
</tr>
</tbody>
</table>

P39
A Prospective Study of Preoperative BRCA Status Determination and Surgical Choice
M. Howard-McNatt, S. Isom, G. Hurt, K.I. Votanopoulos, E.A. Levine. Surgery, Wake Forest School of Medicine, Winston-Salem, NC.

BRCA 1 and 2 positive breast cancer patients often opt for contralateral prophylactic mastectomy (CPM). Some women with breast cancer who test negative for the mutation still opt for CPM. We sought to understand the factors before and after genetic testing that contribute to a breast cancer patient’s decision to have a CPM despite being BRCA negative. METHODS: This is a prospective study utilizing demographic and qualitative questionnaires for stage 0 to III female breast cancer patients. Data collection after initial diagnosis of breast cancer was performed prior to genetic testing and surgery, and six months following surgery. Only women who tested BRCA negative and chose a CPM were included in the 6 month survey. RESULTS: From 2010 until 2014 one hundred women were prospectively enrolled. The median age was 45 years. There was no difference as to race, age, education, marital status, parity or family history between women who chose a lumpectomy, mastectomy, or CPM at the initial survey. Women who chose CPM presented at a higher stage (p=0.012). Women with DCIS chose a lumpectomy over other forms of surgery (p=0.042). Women with a breast MRI trended to have a CPM (p=0.056). A BRCA mutation was found in nine women. Twenty-six women after negative genetic testing and surgery chose CPM. Compared to women who did not have a CPM (p=0.0157) and had invasive ductal carcinoma (p=0.05). Twelve women who initially chose a unilateral mastectomy changed their surgery to CPM after genetic testing (p=0.0023). The reasoning for their choice that did not change postoperatively, was to be around for their children, while the reason to be around for their partner decreased (p=0.014). Eighty percent of the women were satisfied with their choice. CONCLUSION: This is the first prospective study looking at genetic testing, surgical choice and CPM. BRCA negative women were more likely to have a CPM if they presented at a higher stage and initially chose a unilateral mastectomy. Preoperative genotyping resulted in a significant change in a woman’s surgical choice. Patients need to be educated about the role of CPM and genotyping as part of their surgical decision making.

P40
Complication Rates in Early Stage Breast Cancer Patients Treated with Single Lumen versus Multi-lumen Brachytherapy Catheters

Introduction: Recent retrospective and Medicare claims-based studies have demonstrated higher complication rates in breast cancer patients treated with single lumen (SL) brachytherapy catheters compared to whole breast irradiation (WBI). Most patients receiving brachytherapy in the current era are treated with multi-lumen (ML) balloon catheters, due to the theoretical dosimetric advantages. However, data evaluating local toxicity with ML brachytherapy catheters is lacking. We compared local toxicity between patients treated with SL versus ML catheters. METHODS: Between January 2004 and December 2011, 301 patients with early stage breast cancer were treated with breast conserving surgery and balloon-based brachytherapy at our institution. Of the 306 cancers, 223 were treated with SL catheters and 83 with ML catheters. Complication rates were assessed using Kaplan-Meier curves with log-rank. RESULTS: Median follow-up for the entire cohort was 5.22 years; with a median follow-up of 6.21 years for the SL group and 3.53 years for the ML group. SL catheter patients were more likely to be estrogen receptor negative (p=0.01) and more likely to receive systemic therapy (p=0.04) compared to ML patients; otherwise the groups were similar. Four-year incidence of any complication was similar in patients treated with SL vs. ML catheters (66.2% vs. 59.7%, p=0.98; respectively). There was no difference in 4-year incidence of infectious skin complications (10.6% vs. 9.9%, p=0.94), abscess (1.4% vs. 0%, p=0.29), telangiectasia (7.4% vs. 14.4%, p=0.14) and breast pain (11.6% vs. 12.4%, p=0.81) between the SL and ML groups. Four-year incidence of seroma (41.4% vs. 42.0%, p=0.86) and fat necrosis (30.6% vs. 30.2%, p=0.50) was also similar in patients treated with SL vs. ML catheters.

An increasing incidence of seroma formation and fat necrosis was noted in both treatment groups out to 5 years. CONCLUSION: Multi-lumen catheters do not provide a statistically significant decrease in complication rates compared to single lumen catheters. Both types of brachytherapy leave patients at significant risk for seroma and fat necrosis, long after the radiation ends.

P41
A Simple Intervention to Relieve Chest Wall Pain due to Post-mastectomy Pain Syndrome

Introduction: Post-mastectomy pain syndrome (PMPS) is chronic pain persisting beyond the normal healing period. It is common (30-70%) and often debilitating. Many patients are never treated and current therapies are ineffective. Although PMPS encompasses a number of conditions, we believe the majority of cases arise from damage to the T4 and T5 sensory nerves as they exit the chest wall; these nerves are damaged when the adjacent blood vessels are cauterized during surgical removal of the breast. We report on a series of patients treated with a simple intervention using established pain management...
techniques for perineural infiltration to achieve pain relief due to nerve damage. **Methods:** Starting in January 2011, we treated patients presenting with characteristic neuropathic pain, often described as chest wall pain aggravated by wearing a bra. Each patient had exquisite point tenderness located along the infra-mammary fold, either below the nipple or at the mid-axillary line. These trigger points correlate with the egress of the T4 and T5 cutaneous branches and were thus targeted for injection. We injected a 2 mL mixture of equal parts 0.5% bupivacaine and 4 mg/mL dexamethasone. Patients were prospectively surveyed for resolution of pain. **Results:** Forty injection sites were treated in 26 patients. All patients experienced immediate relief upon injection. A single injection was effective in resolving the pain for 24 sites (60%), 10 sites achieved resolution with a second injection (25%) and one site required three injections (2.5%). This resulted in an overall treatment success rate of 87.5%. There were no observed complications. **Conclusion:** Perineural infiltration with a combination of bupivacaine and dexamethasone is a safe, simple, and effective treatment option for chronic neuropathic pain with trigger point tenderness along the infra-mammary fold after breast surgery. This technique should be added to the armamentarium of all surgeons who perform breast surgery. Healthcare providers should routinely screen their patients for the presence of PMPS as there is a treatment option available with the ability to achieve rapid and dramatic results.

**P42**

Left-sided Breast Radiation does not Result in Increased Long-term Cardiac-related Mortality among Women undergoing Breast Conserving Surgery G. Wright,1,2 J. Driane,3 H.L. Sobel,7 M.H. Chung,3 1. GRMEP/Michigan State University, Grand Rapids, MI; 2. Michigan State University College of Human Medicine, Grand Rapids, MI; 3. Spectrum Health Medical Group, Grand Rapids, MI.

**Introduction:** Standard therapy following lumpectomy for breast cancer has included adjuvant whole-breast radiotherapy. Recent long-term studies have suggested a possible association between left-sided radiotherapy and long-term cardiac-related mortality. **Methods:** The SEER database was queried for female breast cancers diagnosed from 1990-1999, with follow-up data through November 2013. Subjects who underwent lumpectomy and adjuvant external beam radiation were included for study. Staging was extrapolated to AJCC 7th ed. based on tumor characteristics. These subjects were divided into groups based on the laterality for performance of univariate analysis. The primary outcome measure was the rate of cardiac-related mortality over time. A Cox regression model was constructed to analyze overall, disease-specific, and tumor grade, or stage. Factors impacting survival on multivariate analysis included: age, race, AJCC stage, ER/PR status, and grade. Left-sided cancer was not associated with poorer survival for any of the metrics. Fifteen-year overall survival and disease-specific survival were 63.0% and 86.5% for left-sided breast cancers and 63.1% and 86.5% for right-sided disease (p=NS). Rate of cardiac mortality at 5-, 10-, and 15-year follow-up were 1.6%, 4.3%, and 7.4% for left-sided cancers and 1.5%, 4.4%, and 7.7% for right-sided cancers, respectively (p=NS).

**Conclusion:** In this large population-based study, women receiving left-sided external beam radiation for breast cancer did not have a resultant increase in cardiac-related mortality. The potential association of left-sided radiotherapy and ischemic heart disease warrants further study.

**P43**

FOXC1 Mediates the Basal Phenotype in BRCA1-mutant Breast Cancer J. Johnson,* M. Choi, B. Han, Y. Qu, F. Dadmanesh, X. Zhang, B. Karlan, A.E. Giuliano, X. Cui, F. Amersi. Surgery, Cedars-Sinai Medical Center, Los Angeles, CA.

**Introduction:** Germline mutations in BRCA1 and BRCA2 are associated with basal-like breast cancer (BLBC) and luminal subtype cancer, respectively. The forkhead box transcription factor FOXC1 is overexpressed specifically in BLBC, predicts worse prognosis, and has been implicated as a regulator of BLBC cell function. We sought to demonstrate the clinicopathologic and biological significance of FOXC1 expression in BRCA-mutant breast cancer. **Methods:** Institutional database review identified 37 BRCA1 and 35 BRCA2-mutant breast cancers from 1995 to 2013. Immunohistochemical staining was performed on paraffin-embedded tissue sections using a monoclonal FOXC1 antibody. Luciferase assays were performed after cotransfection of breast cancer cell lines with FOXC1 promoter luciferase reporter, β-galactosidase internal control, and either BRCA1 or control plasmids. Proliferation assays were performed using control and FOXC1 knockout SUM149 BRCA1-mutant cells. FOXC1 qRT-PCR was performed on breast cancer cells following transfection with BRCA1 or control plasmids. **Results:** Among 37 BRCA1 cancers, 20/23 basal and 1/14 luminal tumors were FOXC1 positive by IHC. Among 35 BRCA2 cancers, 5/5 basal and 1/30 luminal tumors were positive. FOXC1 expression was associated with younger age (42.9±13.3 vs. 50.7±13.5, p=0.006), higher tumor grade (p<10-4), increased Ki67 (50.9±21.9 vs. 19.9±13.6, p<10-4), ER/PR-, basal subtype, but fewer lymph node metastases (0.1±0.5 vs. 2.6±5.6, p<10-4). There was a trend toward increased locoregional recurrence (3/27 vs 0/45, p=0.0512). No difference in overall or disease-free survival was seen. Immunoblotting showed that FOXC1 is expressed in BLBC and BRCA1-mutant cell lines but is absent in luminal cells. Transient expression of BRCA1 repressed FOXC1 promoter activity and FOXC1 mRNA levels. FOXC1 knockout in BRCA1-mutant cells significantly decreased proliferation. **Conclusion:** FOXC1 expression predicts the BLBC subtype in BRCA1/2 cancers. FOXC1, which is overexpressed in BRCA1-mutant cell lines, is essential for BRCA1-mutant breast cancer cell growth and is repressed by wildtype BRCA1. These results suggest FOXC1 is a critical mediator of the basal phenotype in BRCA1-mutant breast cancer.

**Abstracts: Poster Presentations S57**

**Left-sided Breast Radiation does not Result in Increased Long-term Cardiac-related Mortality among Women undergoing Breast Conserving Surgery G. Wright,1,2 J. Driane,3 H.L. Sobel,7 M.H. Chung,3 1. GRMEP/Michigan State University, Grand Rapids, MI; 2. Michigan State University College of Human Medicine, Grand Rapids, MI; 3. Spectrum Health Medical Group, Grand Rapids, MI.

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**Conclusion:** In this large population-based study, women receiving left-sided external beam radiation for breast cancer did not have a resultant increase in cardiac-related mortality. The potential association of left-sided radiotherapy and ischemic heart disease warrants further study.
P44
Implications of New Lumpectomy Margin Guidelines for Breast-conserving Surgery: Changes in Re-excision Rates and Predicted Rates of Residual Tumor
A.L. Merrill,* S.B. Coopey, R. Tang, M.P. Maureen, M.C. Specht, K.S. Hughes, M.A. Gadd, B.L. Smith, General Surgery, Massachusetts General Hospital, Boston, MA.

Background: 2014 guidelines endorsed by the SSO, ASBS and ASTRO advocate “no tumor on ink” as the new margin standard for breast conserving surgery. We used our lumpectomy margins database to predict the effect of these new guidelines on rates of positive margins, re-exciusions, and extent of residual tumor in the lumpectomy cavity. Methods: We performed retrospective review of lumpectomies for invasive breast cancer at our institution from 2004-2006. We excluded patients with neoadjuvant therapy, pure DCIS or incomplete margin data. We applied new (“no tumor on ink”) and old (≥2 mm) margin guidelines and compared rates of positive margins and re-excision. Rates of residual tumor found on re-excision for “tumor on ink” versus tumor <2mm from the margin, but “not on ink”, were determined. Results: 437 women undergoing lumpectomy from 2004-2006 for invasive breast cancer met eligibility criteria. Median age was 55 yrs (range 29-91). 86% had invasive ductal carcinoma (IDC), 12% invasive lobular carcinoma (ILC) and 2% IDC and ILC. Using a ≥2mm margin standard, 36% of lumpectomies had positive margins compared with 19% using new guidelines (p<0.0001), 97% of patients received radiation and 88% received systemic therapy. The observed local recurrence rate in our cohort was 4.3% at 55 mo median follow-up using ≥2mm margin guidelines. 77% of patients with “tumor on ink” had residual disease found at re-excision. 50% of those re-excised for margins <2mm had residual disease (p=0.0013), but would not have been re-excised with new guidelines. Residual tumor was more common in re-excisions for DCIS <2mm from a margin than in those for invasive cancer <2mm from a margin (53% vs. 40%), although this was not statistically significant. Conclusions: Use of new lumpectomy margin guidelines would have reduced re-operation for breast-conserving therapy by half in our patient cohort. However, residual disease was present in many patients who would not have been re-excised with the new guidelines. Long-term follow-up of local recurrence rates is needed to determine if this increase in residual disease is clinically significant.

P45
Breast Reconstruction Risk Assessment (BRA) Score for Surgical Site Infections: Comparing Risk Models based on TOPS and NSQIP

Introduction: Risk calculators for surgery and its complications have recently come into common clinical use. Our group previously formulated a risk schema for individualized risk of surgical complications in the setting of breast reconstruction. This Breast Reconstruction Risk Assessment (BRA) Score drew from both the Tracking Operations and Outcomes for Plastic Surgeons (TOPS) and National Surgical Quality Improvement Program (NSQIP) database to create an online risk calculator for patients and surgeons alike (BRAScore.org). However, the two databases yielded different models with different predictions for surgical site infection (SSI). The goal of this study was to compare the two models. Methods: Sixteen patient scenarios representing every permutation of four demographic/comorbid characteristics were put into the BRA Score interface to compare SSI risk as predicted by the TOPS model and the NSQIP model. Additionally, the TOPS risk model was fitted to the data from which the NSQIP model was derived in order to determine accuracy and goodness of fit. Results: The sixteen patient scenarios yielded similar predictions of risk from both models, with discrepancies ranging from 0.72% and 8.14%. In all scenarios, the TOPS model predicted a greater risk of SSI for prosthetic, pedicled TRAM, and latissimus-based reconstruction. In contrast, the TOPS model predicted a lower risk of SSI than the NSQIP model for microvascular reconstructions. The TOPS model, when applied to NSQIP data, had adequate goodness of fit, as measured by a c-statistic of 0.664 (95% CI 0.641-0.687). It also had good accuracy, as measured by the Brier score of 0.036, with values closer to 0 representing better accuracy. Discussion/Conclusion: This study provides, with some limitation, an external validation of the TOPS-based BRA Score for surgical site infection. It reveals the NSQIP and TOPS risk models to be qualitatively concordant, with some differences attributable to patient populations and differences inherent to the two databases. External validation of both risk models on the same cohort will ultimately reveal which is superior.

P46
Pleomorphic Invasive Lobular Carcinoma: An Aggressive Variant?

INTRODUCTION: Pleomorphic invasive lobular carcinoma (PLC) is a relatively recent formally recognized rare variant of invasive lobular carcinoma thus it’s clinical course and best management practice’s have not been fully established. PLC has been characterized by worse disease free survival, advanced stage at presentation, large tumor size, lymphovascular invasion, higher rates of regional and distant metastasis, however the literature is limited to small case series. We report our institutions experience with PLC and classic invasive lobular carcinoma. METHODS: Retrospective chart review of lobular carcinoma cases from 2008 to 2013 was completed. Clinical and pathologic data was collected on 136 ILC cases and 25 PLC cases. Median follow-up was 30 months. A Fisher exact test was used for statistical analysis. RESULTS: PLC patients presented with more regional metastasis warranting AXL’D’s, had a worse histologic grade, were more likely to have a mastectomy, and less likely to be estrogen positive when compared to classic lobular invasive carcinoma. PLC patients presented at more advanced stages and had a higher mortality (ILC 3.6% v PLC 20% P = 0.009). See Table 1. CONCLUSION: There is accumulating evidence that pleomorphic lobular carcinoma is a more aggressive variant of invasive lobular carcinoma and our results concur. PLC compared to ILC presents at a more advanced stage with a propensity for axillary metastasis resulting in significantly more mastectomies, ALND’s, and systemic therapies.
Abstracts: Poster Presentations

**P47**

Acceptance of Adjuvant Chemotherapy in Patients with Early Stage Breast Cancer


Surgical Oncology, City of Hope, Azusa, CA.

The role of systemic chemotherapy (CT) in early-stage, ER-positive, Her-2 negative (Her2-) breast cancer remains an area of active investigation. The decision to recommend CT is multifactorial, influenced by both the biology of disease and patient characteristics. Despite physician recommendations, some patients decline CT. We sought to identify patient factors leading to refusal of adjuvant CT in an NCI-designated Comprehensive Cancer Center. A single-institution dataset was collected from the National Comprehensive Cancer Network Outcomes database and used to identify breast cancer patients diagnosed from 2005-2011 with primary, unilateral, T1-T2, N0, ER+, Her2- disease. Patients with neoadjuvant CT or had <180 days of follow-up post-pre-sentation were excluded. Patient and clinical characteristics were analyzed for associations with physician recommendation for CT and patient acceptance of treatment. A multivariable logistic regression model was utilized. 329 eligible patients were identified. CT was recommended in 191 patients (58.1%) and was not in 138 (41.9%). Patients < age 50 (Odds ratio [OR]=3.9, 95% Confidence Interval [CI] 1.2-12.7), higher T-stage (OR=6.69, 95% CI 3.31-13.5), and higher Oncotype DX scores (OR=11.2, 95% CI 4.5-27.9) were more likely to receive a recommendation for CT. Among patients who received a recommendation for CT, 71 (37.1%) refused. Patients < age 50 (OR=20.9, 95% CI 2.5-172.0), higher T-stage (OR=3.4, 95% CI 1.3-8.7), Oncotype DX score >31 (OR=3.1, 95% CI 1.3-295.0), privately insured (OR=8.2, 95% CI 1.9-34.7), and of Hispanic ethnicity (OR=5.2, 1.6-16.8) were more likely to accept CT. Patient acceptance was not influenced by education level (p=0.71), employment status (p=0.17), nor existing comorbidities (p=0.89). Physician recommendations to receive CT for the treatment of early-stage ER+, Her2- breast cancer varied only by aggressive tumor biology and patient age. Patient acceptance of the CT recommendation varied by similar factors, but also by ethnicity and insurance status. This may be explained by cultural or social factors not well-understood or not overcome by physician guidance. Further study is needed to understand this disparity.

**P48**

Features of Triple-negative Breast Cancer (TNBC): Analysis of 38,813 Cases from the National Cancer Data Base (NCDB)

M. Plasilova,* B. Hayse, B.K. Killelea, N.R. Horowitz, A.B. Chagpar, D.R. Lannin. Yale University School of Medicine, The Breast Center-Smilow Cancer Hospital at Yale New Haven, New Haven, CT.

Background: Triple negative breast cancer is considered to be an aggressive subtype without good therapeutic targets. The aim of this study was to determine the features of TNBC using the largest database available. Methods: All patients with invasive breast cancer and known molecular subtype diagnosed in 2010-2011 were identified from the NCDB. Patients with and without TNBC were compared with respect to demographics, tumor features, and probability of lymph node metastases. Results: TNBC was present in 38,628 out of 295,801 (13%) female patients compared to 185 out of 3,136 (6%) male patients (p=0.001). The incidence ranged from 10.8% in New England to 15.8% in the east south central US (p=0.001). There were characteristic racial differences with the highest rates for the Black population (23.7%), Asian Indian (15.6%), American Indian (14.6%), Pakistani (14%) and Korean patients (13.5%); intermediate rates for White patients (11.6%), Chinese, Japanese or Vietnamese patients (11%); and the lowest rate in Filipino patients (8.9%). As seen in Figure A, younger patients had a higher rate of TNBC than older patients but this varied by race. The incidence of TNBC also varied by histology and was 15% in infiltrating ductal, 2% in infiltrating lobular, 76% in metaplastic, 56% in medullary, 26% in inflammatory carcinoma. There was no difference between TNBC and non-TNBC in the percent of positive nodes; 10,768/33,620 (32.0%) vs. 71,649/226,070 (31.7%, p=0.22), even though TNBCs were significantly larger than non-TNBC (mean 3.2 cm vs. 2.5 cm, p=0.001) and more frequently poorly differentiated (79.7% vs. 25.8%, p<0.001). When stratified by tumor size, TNBC had significantly fewer positive nodes (p<0.001; see figure B). Furthermore, on multivariable analysis controlling for tumor size and grade, TNBCs were roughly half as likely to be node positive than non-TNBCs (OR: 0.59; 95% CI: 0.57 – 0.60). Conclusion: TNBC has distinct features regarding age, gender, geographic and racial distribution. Compared to non-TNBC, TNBC is larger and higher grade, but less likely to have lymph node metastases.

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**Table 1. Clinical and pathologic characteristics of patients with ILC and PLC**

<table>
<thead>
<tr>
<th></th>
<th>ILC</th>
<th>PLC</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>136</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Average age</td>
<td>63.4</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Average size(cm)</td>
<td>2.32</td>
<td>2.43</td>
<td></td>
</tr>
<tr>
<td>LN+</td>
<td>29 (21%)</td>
<td>11 (44%)</td>
<td>0.023</td>
</tr>
<tr>
<td>Stage I</td>
<td>76 (58%)</td>
<td>8 (32%)</td>
<td>0.031</td>
</tr>
<tr>
<td>Stage II</td>
<td>30 (23%)</td>
<td>11 (44%)</td>
<td>0.026</td>
</tr>
<tr>
<td>Stage III</td>
<td>13 (10%)</td>
<td>5 (20%)</td>
<td></td>
</tr>
<tr>
<td>Stage IV</td>
<td>6 (5%)</td>
<td>1 (4%)</td>
<td></td>
</tr>
<tr>
<td>Bilateral BCa</td>
<td>7 (5%)</td>
<td>4 (16%)</td>
<td></td>
</tr>
<tr>
<td>ER+</td>
<td>135 (99%)</td>
<td>21 (84%)</td>
<td>0.002</td>
</tr>
<tr>
<td>PR+</td>
<td>109 (80%)</td>
<td>16 (64%)</td>
<td></td>
</tr>
<tr>
<td>Her2+</td>
<td>5 (4%)</td>
<td>3 (12%)</td>
<td></td>
</tr>
</tbody>
</table>

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**Age Distribution of Diagnosis in Early Stage TNBC-Breast Cancer**

- Age of Diagnosis: 30-34 vs. 50-54
- Stage of Diagnosis: 1 vs. 2
- Oncotype DX Score: 10-20 vs. 20-29
- Performance Status: 0 vs. 1-2
- Race: Asian, Hispanic, African American
- Ethnicity: Other vs. Caucasian

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**Associations with Receipt of Adjuvant Chemotherapy in Early Stage TNBC-Breast Cancer**

- Age of Diagnosis: 30-34 vs. 50-54
- Stage of Diagnosis: 1 vs. 2
- Oncotype DX Score: 10-20 vs. 20-29
- Performance Status: 0 vs. 1-2
- Race: Asian, Hispanic, African American
- Ethnicity: Other vs. Caucasian

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**P48**

Features of Triple-negative Breast Cancer (TNBC): Analysis of 38,813 Cases from the National Cancer Data Base (NCDB)

M. Plasilova,* B. Hayse, B.K. Killelea, N.R. Horowitz, A.B. Chagpar, D.R. Lannin. Yale University School of Medicine, The Breast Center-Smilow Cancer Hospital at Yale New Haven, New Haven, CT.

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P49
Failure of a Breast Density Notification Law to Impact the Screening of Women with Dense Breasts

Introduction: In 2009, Connecticut passed a dense breast notification law, which increased screening ultrasounds and the breast cancer detection rate. In 2011, Texas enacted a similar law (termed Henda’s Law), which differed in its recommendation to imaging facilities and insurance coverage of additional imaging. In this study, our aim was to identify any differences in the rate and selection of various supplemental breast imaging modalities after passage of the law.

Methods: A retrospective study was performed at a university hospital in Texas. Data of women with dense breasts and a normal mammogram was reviewed for one year before (9/1/2010 – 8/31/2011) and one year after (7/1/2013 – 6/30/2014) implementation of the density law. Results: In the pre-law group, 12,099 women were identified as mammographically normal and 4414 (36.5%) of these women had dense breasts. 6.6% (n=289) of these dense breast women underwent additional imaging, with 3.8% (n=168) receiving ultrasound and 2.7% (n=121) receiving MRI. In the post-law group, 17,272 women were identified as mammographically normal and 5617(32.5%) of these women had dense breasts. 5.1% (n=285) of these dense breast women underwent additional imaging, with 2.1% (n=120) receiving ultrasound, 1.5% (n=86) receiving tomosynthesis mammogram, and 1.5% (n=88) receiving MRI. Among those with additional imaging, the biopsy rate was 1% (n=3) in pre-law and 3.4% (n=10) in post-law group (p=0.05). No cancers were detected in the pre-law group, with 1 cancer detected in the post-law group. In the post-law group, the availability of tomosynthesis mammogram as an option may have led to the decreased rate of supplemental MRI and ultrasound examinations. Conclusion: Unlike the Connecticut bill, the breast density law in Texas failed to increase the utilization rate of additional imaging, which may be due to differences in the language of the law and lack of a legal provision for insurance coverage. Use of a validated algorithm for additional imaging may improve both the efficacy of this law and the overall breast cancer detection rate in the future.

P51
The Influence of Breast Cancer Subtype on the Prognosis of Young Breast Cancer Patients in China
L. Tang,1,* X. Jin, H. Yang, Y. Fu, G. Di, Z. Zhuang,2 Z. Shao,1 H.R. Chang,1 J. Yan, R. Rao,1 A.M. Leitch.1 1. Shanghai Cancer Center, Fudan University, Shanghai, China; 2. Shanghai First Maternity and Infant Hospital, Shanghai, China; 3. Revlon/UCCLA Breast Center, David Geffen School of Medicine, University of California, Los Angeles, CA.

Background: Young breast cancer has been associated with poor prognosis. The purpose of this study is to evaluate the different characteristics and prognoses among different subtype groups of young breast cancer patients.

Patients and methods: The study included 4670 operable young breast cancer patients in Shanghai Cancer Database between 2003 and 2012. Among them, 1360 patients were <40 years old and 3110 were 40-50 years old. The characteristics, overall survival and disease-free survival were compared between the young breast cancer and those in the next age group 40–50. Results: The median follow-up was 54 months. In comparison with 40-50 years old patients, young breast cancer patients presented a higher percentage of breast cancer family history, higher tumor grade, more vessel invasion and higher Ki67 index (P<0.05) and were more likely to experience death (P=0.001) and relapse (P<0.001). The distribution of the subtypes was similar between the two age groups. In younger group, the 5 year disease-free survival and overall survival were 74% and 89%. The luminal B subtype young breast cancer patients presented a lower disease-free survival (69% vs. 80%, 79% and 75%, P<0.05) but a similar overall survival (88% vs. 90%, 90% and 89%, P<0.05) in comparison with luminal A, triple negative and Her2 over-expression groups. In a multivariate analysis, age 39 or younger was an independent predictor for disease-free survival (P<0.05) but not for overall survival. Lymph node positivity (HR=2.14 95%CI=1.05-5.03, P<0.03) and higher T stage (HR=2.14 95%CI=1.05-5.03, P<0.03) were predictive of disease-free survival in young breast cancer patients. Luminal B subtype had a trend to be a risk factor (HR=1.03, 95%CI=0.99 to 1.09, P=0.06) in young breast cancer patients. Conclusions: Characteristics of breast cancer are more aggressive in Chinese young breast cancer patients. The luminal B subtype may have a negative effect on their prognosis which should be validated further.

P52
Factors Affecting Completion of Adjuvant Chemotherapy in Early Stage Breast Cancer
S.A. Reyes,1,* K. Fei,2 R. Franco,3 T.A. King,4 N.A. Bickell,1 1. Memorial Sloan-Kettering Cancer Center, New York, NY, 2. Mount Sinai School of Medicine, New York, NY.

Introduction: Despite the survival benefit associated with adjuvant chemotherapy (CT) in early stage breast cancer (BC), many women do not complete treatment. The purpose of this study is to identify factors associated with failure to complete adjuvant CT in stage I-IIa BC patients.

Methods: The study sample was obtained from a multi-center parent study designed to evaluate the use of patient assistance programs in early stage BC patients requiring adjuvant therapy. Patients with stage I-IIa BC undergoing surgery from 10/06-9/09 were asked to complete a baseline needs assessment survey and a 6 month follow-up survey assessing their experiences with care, health status, social support, self-efficacy, and treatment beliefs. Patients who initiated adjuvant CT and completed the 6 month survey formed our study cohort. Comparisons were made between patients who completed adjuvant CT and those that did not. Results: Of 198 patients in the cohort, median age was 53yrs (28-86yrs); median tumor size 1.8cm (0.3-6.7cm). 50 patients (25%) had triple negative BC. 13 patients (7%) failed to complete adjuvant CT. Patient age, education, insurance, HER2 status, tumor size, surgery type, presence of comorbidities, instrumental social support, self-efficacy, fatalism and treatment associated side effects did not differ between patients who did and did not complete CT. On multivariate analysis, African-American race (OR 5.4), medicaid insurance (OR 4.6), poor body image (OR 11.2), and presence of comorbidities (OR 5.8) were significant. (Table) Conclusions: In this multi-center, early stage BC cohort, African-American race, medicaid insurance, presence of co-morbid-ities and poor body image were significantly associated with failure to complete adjuvant CT. Poor body image, a potentially modifiable risk factor, demonstrated the strongest association. These data suggest that strategies to identify and address patient perceptions may improve rates of compliance with adjuvant CT recommendations.
Severity of Acute Pain after Axillary Lymphadenectomy and Primary Reconstruction with a Tissue Expander in Breast Cancer Patients

N. Besic,* B. Strazisar, A. Perhavec. Surgical Oncology, Institute of Oncology, Ljubljana, Slovenia. (S61)

Background: Axillary lymphadenectomy and breast reconstruction are painful surgical procedures. Our aim was to evaluate severity of pain and consumption of analgesics after axillary lymphadenectomy and breast reconstruction with a tissue expander. Methods: Breast cancer patients (age 25-84 y., mean 54 y.) surgically treated with lymphadenectomy (N=60) and/or immediate breast reconstruction with a tissue expander (42 unilateral and 18 bilateral) were randomised into local anaesthetic group (0.25% levobupivacaine-flow rate 2 mL/hour/expander) and standard group (continuous intravenous infusion of piritramide, metoclopramide and metamizole). All patients were on oral analgesics after the day of surgery and received 100 mg of diclofenac, 2,600 mg of paracetamol and 300 mg of tramadol per day. Whenever needed, patients from both groups could get an intravenous bolus of piritramide. Pain was measured at rest and during activity using the standard visual analogue scale (VAS) score. Mean VAS score was calculated from 8 and 6 measurements on the day of surgery and on the following days, respectively. Results: Pain was more severe during activity than at rest. Patients had more severe pain after bilateral reconstruction in comparison to unilateral reconstruction or axillary lymphadenectomy (Table 1). Consumption of piritramide during the first day after the surgical procedure was higher after bilateral reconstruction than after unilateral reconstruction or lymphadenectomy (24 vs. 17 vs. 2 vs. 1 mg, respectively; p<0.0001). Consumption of piritramide was higher in the standard group compared to the local anaesthetic group (24 mg vs. 9 mg; 13 mg, respectively; p<0.0001). Chronic pain after 3 months was reported after bilateral and unilateral reconstruction and axillary lymphadenectomy in 33%, 28% and 44%, respectively (p = 0.49). Conclusions: Patients experience pain after surgical procedure despite pain treatment. Pain after bilateral primary reconstruction with a tissue expander is more severe than after unilateral reconstruction or axillary lymphadenectomy. Wound infusion of a local anaesthetic reduces acute pain resulting in a smaller consumption of opioids.

Table 1. VAS score after axillary lymphadenectomy, reconstruction with unilateral and bilateral tissue expander.

<table>
<thead>
<tr>
<th></th>
<th>VAS Score After Axillary Lymphadenectomy</th>
<th>Unilateral Reconstruction</th>
<th>Bilateral Reconstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
<td>Mean (95% CI)</td>
</tr>
<tr>
<td>Recovery Room - At Rest</td>
<td>2.18 (1.74-2.62)</td>
<td>3.23 (2.52-3.93)</td>
<td>5.12 (3.94-6.29)</td>
</tr>
<tr>
<td></td>
<td>p = 0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recovery Room - During Activity</td>
<td>2.87 (2.56-3.37)</td>
<td>3.93 (3.24-4.64)</td>
<td>5.88 (4.59-7.18)</td>
</tr>
<tr>
<td></td>
<td>p = 0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day of Surgery</td>
<td>2.00 (1.67-2.34)</td>
<td>2.86 (2.63-3.08)</td>
<td>4.42 (3.57-4.87)</td>
</tr>
<tr>
<td></td>
<td>p = 0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1st Postoperative Day</td>
<td>2.20 (1.88-2.52)</td>
<td>2.63 (2.37-2.88)</td>
<td>3.41 (2.57-3.90)</td>
</tr>
<tr>
<td></td>
<td>p = 0.0001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2nd Postoperative Day</td>
<td>2.16 (1.78-2.53)</td>
<td>2.21 (1.99-2.45)</td>
<td>3.11 (2.67-3.56)</td>
</tr>
<tr>
<td></td>
<td>p = 0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P54

The Feasibility of Performing a Preference-tolerant Randomized Controlled Trial of Personalized versus Annual Breast Cancer Screening


Introduction: Breast cancer screening costs 8-10 billion dollars annually, generates 4.3 million false-positive recalls and 526,000 false-positive biopsies annually and results in a rate of overdiagnosis of 19%. A better approach to breast cancer screening is needed. We believe that a personalized approach to screening will be better and have designed a trial to test personalized screening against annual screening. Personalized screening involves calculating a five-year breast cancer risk based on comprehensive genomic testing, exposures, family history, comorbidities and breast density and uses this risk to assign ages to start and stop screening, a frequency of screening and a screening modality. In this study we report on the feasibility of performing a personalized screening trial. Methods: All women getting their mammograms at the University of California participate in the Athena Breast Health Network and complete an Athena Health Questionnaire. 500 women from Athena who agreed to participate in future research were sent an electronic survey consisting of ten questions that assessed the feasibility of conducting a randomized controlled trial of personalized versus annual screening. Results: 224 women responded to the survey in 10 days. Of the 224 women who responded, 66% indicated that they were either very likely or somewhat likely to agree to be randomized, whereas, 20% were not likely or not at all likely and 15% were neutral or undecided. If given a choice of which arm they would participate in, 46% would choose the personalized screening arm, 28% would choose the annual screening arm and 23% would not have a preference. 94% would be comfortable having a genetic test to determine their risk of developing breast cancer. Conclusions: The time has come to compare personalized screening to annual screening in the setting of a clinical trial and to settle the screening debate. The majority of women surveyed would be willing to be randomized in a trial of this nature. In January of 2015, we will initiate a pilot study in preparation for a large randomized controlled trial of personalized versus annual breast cancer screening.

*Correspondence to: C.K. Thompson, University of California San Francisco, San Francisco, CA.
P55
Concordance of Clinical and Pathologic Staging in Breast Cancer: Report from the National Cancer Data Base

S. Singh,1 E. Liederbach,2 C. Wang,2 C. Pesce,2 D.J. Winchester,2 K. Yao.2 1. Department of Surgery, The University of Chicago, Chicago, IL; 2. Department of Surgery, NorthShore University HealthSystem, Evanston, IL; 3. Center for Biomedical Research Informatics, NorthShore University HealthSystem, Evanston, IL.

Introduction: In 2008, the Commission on Cancer required clinical staging prior to treatment. However, concordance between clinical (cStage) and final pathologic stage (pStage) for breast cancer has not been well characterized. We hypothesized that patient and tumor factors may be associated with discordant staging. Methods: Using the National Cancer Data Base, we identified 457,903 female patients with AJCC cStage 0-II breast cancer who underwent surgery without neoadjuvant therapy from 2008-2011. Upstage was defined as change to any higher pStage; downstage was similarly defined. Results: There were 91,199 (19.9%) cStage 0; 229,813 (50.2%) cStage I; 97,583 (21.3%) cStage II; 12,620 (2.8%) cStage III; and 26,688 (5.8%) patients with unknown cStage. Overall, 15.7% of patients were upstaged, 2.8% were downstaged and 81.5% had no change in stage. For cStage 0, 1, and II disease, 12.7, 18.2 and 19.4% were upstaged, respectively. Of overall upstaged patients, the change in cStage was the result of a T-category upstage in 34.2%, N-category upstage in 46.4% and both T and N upstage in 19.4%. On multivariate analysis (table), patients were more likely to be upstaged if they were <50 years of age (young), of Black race, had ILC or mixed IDC/ILC histology, T3 tumors, grade 2, Her2+ phenotype or lymphovascular invasion (LVI). On subgroup analysis, 23.9% of young patients were upstaged; 45.1% with LVI were upstaged; and 27.3% with Her2+ tumors were upstaged. All of young patients, 36.3% of those with ILC or mixed IDC/ILC were upstaged. Additionally, 32.1% of young patients with Her2+ tumors were upstaged. Nearly twice as many upstaged patients had completion mastectomy after breast conservation surgery compared to those with no change in stage (10.0% vs 5.7%, p<0.001). Similarly, twice as many upstaged patients received adjuvant chemotherapy compared to those with no change in stage (59.3% vs 28.0%, p<0.001). Conclusion: Discordant staging occurs in 16% of patients. Patients <50 years, of Black race, with lobular or mixed histologies, larger tumors, Her2+ tumors, and/or LVI should be advised pre-operatively of potential upstaging and its treatment implications.

Summary of independent predictors of upstaging on adjusted analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤50 years</td>
<td>1.17</td>
<td>1.18 - 1.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black race</td>
<td>1.07</td>
<td>1.02 - 1.12</td>
<td>0.002</td>
</tr>
<tr>
<td>ILC histology</td>
<td>1.10</td>
<td>1.03 - 1.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mixed IDC/ILC histology</td>
<td>1.32</td>
<td>1.25 - 1.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>T3</td>
<td>2.69</td>
<td>2.50 - 2.88</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tumor grade 2</td>
<td>1.17</td>
<td>1.00 - 1.38</td>
<td>0.001</td>
</tr>
<tr>
<td>Her2+ status</td>
<td>1.21</td>
<td>1.16 - 1.26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVI</td>
<td>2.23</td>
<td>2.16 - 2.29</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P56
Axillary Staging after Neoadjuvant Chemotherapy (NAC) for Breast Cancer (BC): A Pilot Study Combining Sentinel Lymph Node Biopsy (SLB) with Radioactive Seed Localization (RSL) of Pre-treatment Positive Axillary Lymph Nodes (LN+).

P. McAuliffe,1 P. Bach,1 E. Liederbach,2 C. Pesce,2 D.J. Winchester,2 K. Yao.1 1. Department of Surgery, NorthShore University HealthSystem, Evanston, IL; 2. NorthShore University HealthSystem, Evanston, IL;

Background: False negative (FN) rates upon excision of LN+ nodes following SLB vary widely. The risk of discordant staging following NAC is unknown. We hypothesized there would be an increased risk of discordance following NAC. Methods: A retrospective review of a single-institution prospectively maintained tumor registry from May 2013 to June 2014 was performed to identify pts with percutaneous biopsy proven LN+ BC who received NAC and had RSL of the LN+ combined with SLB at surgery. All LN+ were marked with a radiopaque clip prior to initiation of NAC to facilitate RSL localization post-NAC. Demographics and surgical outcomes were evaluated. Results: Twenty eight pts with biopsy proven LN+ prior to NAC were cN0 at end of treatment. Mean age was 51. Stage at diagnosis was IIA-IIIB. 27/28 pts had ducal cancer: 10 triple negative and 16 HER2+ phenotypes. All had dual tracer SLB and RSL of the LN+. Number of nodes retrieved with RSL/SLB combination was 1-11. 27/28 LN+ were successfully excised with RSL, and 15/28 showed chemotheraphy related changes. Presence of isolated and/or dye in the LN+ was noted for 21/28 pts. In 19/21 pts, the LN+ was also a sentinel node. 18 pts had no residual disease in the LN+, or in the other excised lymph nodes. 10 had persistent axillary disease. All pts who remained node positive had persistent disease in the LN+. Conclusion: RSL of the LN+ combined with SLB is a promising approach for axillary staging after NAC in pts who become cN0. In this pilot study, LN+ status after NAC predicted axillary status, suggesting that localization and excision of the LN+ may be sufficient for restaging following NAC. A larger sample is needed to confirm these preliminary findings.

Patient Demographics and Pathologic Characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean±S, stage 50-70</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>1 (24%)</td>
</tr>
<tr>
<td>IIA</td>
<td>14 (50%)</td>
</tr>
<tr>
<td>IIB</td>
<td>6 (21%)</td>
</tr>
<tr>
<td>IIIA</td>
<td>5 (17%)</td>
</tr>
<tr>
<td>IIIIB</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Luminal</td>
<td>16 (57%)</td>
</tr>
<tr>
<td>HER2 positive</td>
<td>10 (36%)</td>
</tr>
<tr>
<td>Triple negative</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Biopsy proven positive lymph node at diagnosis</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Involved Ductal Cancer</td>
<td>27 (97%)</td>
</tr>
<tr>
<td>Involved Lobular Cancer</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Pathologic stage of lymph nodes at surgery</td>
<td>1 (10%)</td>
</tr>
<tr>
<td>LN+ (RSL)</td>
<td>18 (64%)</td>
</tr>
<tr>
<td>Additional excised lymph nodes</td>
<td>18 (64%)</td>
</tr>
</tbody>
</table>

P57
Knowledge Deficits and Concern about Contralateral Breast Cancer Risk: A Prospective Study

E. Diego,1 E. Liederbach,1 K. Sepucha,1 J. Tilburt,1 S. Rabbitt,1 I. Bedrosian,2 I. Surgery, NorthShore University HealthSystem, Evanston, IL; 2. NorthShore University HealthSystem, Evanston, IL;

Background: Little is known about newly diagnosed breast cancer patients’ concern and knowledge levels of contralateral breast cancer risk (CBC) at the time of initial evaluation. Methods: A 17 item survey was administered to 58 newly diagnosed breast cancer patients at the time of surgical consultation. The survey utilized multiple choice questions about concern for CBC, risk of CBC and how bilateral mastectomy (BM) affects outcomes. Results: Ten (17%) of the patients were ≤50 years old and 48 (83%) were >50yo. Forty-three (74%) patients were White, 26 (44.8%) had at least one relative with breast cancer and 50 (86%) were Stage 0-III. When asked about the risk of CBC, 40% stated they were very concerned about developing cancer in the other breast, 43% somewhat concerned and 16% not concerned. When asked which women with breast cancer live longer, a lumpectomy, unilateral mastectomy or bilateral mastectomy, 40% stated they were very concerned about developing cancer in the other breast, 43% somewhat concerned and 16% not concerned. When asked which pigs with breast cancer live longer, a lumpectomy, unilateral mastectomy or BM; 7% stated BM, 10% lumpectomy, 2% unilateral mastectomy and 29% were unsure. Of those very concerned about CBC risk, 65% answered incorrectly, compared to 35% incorrect among those who were somewhat or not concerned about contralateral risk (p=0.026). Fifty percent had incorrect perceptions about the impact of BM on the risk of cancer coming back in the body. Eighty-one percent were incorrect in assessing their CBC risk at five years and 76% did not know that BM is associated with more complications then unilateral mastectomy. When patients were asked to rank how important certain factors were in deciding what type of surgery they wanted, improve/extend my survival ranked the highest and reducing the chance of having cancer in the other breast ranked second (Table 1). Fourty percent stated that a BM would have a positive effect on their overall appearance. Conclusion: In this prospective study, many newly-diagnosed breast cancer patients report
a high degree of concern about CBC risk but over half of patients have one or more knowledge deficits about CBC risk and how BM affects outcomes. Future studies of interventions are warranted to identify effective strategies to better inform patients about CBC risk.

Table 1. Ranking of Factors in Deciding What Type of Surgery to Have at Time of Surgeon Consultation.

<table>
<thead>
<tr>
<th>FACTOR</th>
<th>Average Answer (Scale 0-10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improves/extends my overall survival</td>
<td>8.3</td>
</tr>
<tr>
<td>Reduce the chance of having cancer in the other breast</td>
<td>8.1</td>
</tr>
<tr>
<td>Doctor recommendation</td>
<td>8.1</td>
</tr>
<tr>
<td>Post of mind</td>
<td>7.8</td>
</tr>
<tr>
<td>Desire to have both breasts look the same after surgery</td>
<td>5.3</td>
</tr>
<tr>
<td>My family history</td>
<td>5.1</td>
</tr>
<tr>
<td>Avoid future mammograms</td>
<td>3.8</td>
</tr>
<tr>
<td>Avoid future biopsies</td>
<td>3.6</td>
</tr>
</tbody>
</table>

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Using Quantitative ER to Predict the Likelihood and Timing of Distant Recurrence of Breast Cancer

M. Gage, C. Mylander, K. Sawyer, C. Tran, L. Tafral, I. Walter Reed National Military Medical Center, Bethesda, MD; 2. Anne Arundel Medical Center, Annapolis, MD.

Objective: It is widely accepted that ER positive breast cancers have better prognosis and lesser risk of early distant recurrence (DR) relative to ER negative tumors, however, does prognosis improve as the quantitative score of ER increases? The answer could impact long-term screening, and possibly adjuvant treatment regimens, of our breast cancer patients. We sought to investigate if there was indeed a relationship between the quantitative value of ER and the rate of distant recurrence (RoDR). Methods: A retrospective review was conducted on DR patients initially diagnosed with stage I-III breast cancer from 1/2002 through 12/2008. Records were reviewed for quantitative ER score. The frequencies of these characteristics were compared to two groups of stage I-III non-recurrence patients to determine odds ratios (OR): (D1) prospectively collected dataset of cases diagnosed between 2011-2013 (n=596), and (D2) retrospectively collected matched-pair by year dataset of cases diagnosed between 2002-2008 (n=548). Results: Of 107 DR patients evaluated, 37 (35%) recurred within 2 years, 29 (27%) between 2-4 years, and 41 (38%) after 4 years. Quantitative ER groups were divided into the following: 0%, 1-10%, 11-64%, 95-90%, and greater than 90%. The groups with the highest recurrence rates within 2 years of diagnosis were ER 0% (OR 5.1, 3.2) followed by ER 1-10% (OR 1.2, 1.9). For recurrences after 4 years, however, the highest recurrence rates were within the ER 65-90% group (OR 4.6, 1.2), with ER 0% tumors demonstrating decreased rates (OR 0.5, 0.3). ER>90% consistently demonstrated low recurrence rates within our study. Conclusion: Our study demonstrated that ER negative tumors consistently recur earlier, while tumors with ER ranging from 65-90% tend to recur later, after 4 years. There were very few ER<90% tumors significantly recurrent in our study. It cannot be assessed if these tumors are unlikely to recur at all, or if they tend to recur after 6 or more years. Quantitative ER score may be a means of distinguishing quiescent tumors from more initially aggressive tumors, and possibly of identifying luminal subtypes and tailoring screening regimens more appropriately.

Odds Ratios of Timing of Distant Recurrences of Breast Cancer by Quantitative ER Ranges

<table>
<thead>
<tr>
<th>Recurrence&lt;2 Years</th>
<th>D1 OR 0.00</th>
<th>D2 OR 0.00</th>
<th>Recurrence 2-4 Years</th>
<th>D1 OR 0.00</th>
<th>D2 OR 0.00</th>
<th>Recurrence&gt;4 Years</th>
<th>D1 OR 0.00</th>
<th>D2 OR 0.00</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER&gt;90%</td>
<td>0</td>
<td>2.22</td>
<td>0.00</td>
<td>2</td>
<td>1.37</td>
<td>0.00</td>
<td>2</td>
<td>1.57</td>
</tr>
<tr>
<td>ER 65-90%</td>
<td>16</td>
<td>2.22</td>
<td>1.59</td>
<td>12</td>
<td>2.13</td>
<td>0.57</td>
<td>37</td>
<td>4.6</td>
</tr>
<tr>
<td>ER 11-64%</td>
<td>0</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
<td>0.00</td>
</tr>
<tr>
<td>ER 1-10%</td>
<td>2</td>
<td>1.19</td>
<td>1.85</td>
<td>3</td>
<td>2.28</td>
<td>3.54</td>
<td>2</td>
<td>3.08</td>
</tr>
<tr>
<td>ER 0%</td>
<td>19</td>
<td>5.10</td>
<td>3.23</td>
<td>11</td>
<td>3.77</td>
<td>2.39</td>
<td>2</td>
<td>0.48</td>
</tr>
<tr>
<td>Total</td>
<td>37</td>
<td>29</td>
<td>41</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

OR: Odds Ratio; D1: Dataset 1: Prospectively Collected Dataset of Patients Diagnosed Between 2/2011-6/2013 (n=596); D2: Dataset 2: Retrospectively Collected Dataset, Match-Paired By Year, of Patients Diagnosed Between 2002-2008 (n=548)

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Introduction: Reoperative SLNB is feasible in patients with local recurrence (LR) of invasive breast cancer, but it is uncertain if this procedure affects either treatment decisions or outcome. Here we ask whether axillary restaging (vs. none) at the time of LR after previous SLNB affects the rate of subsequent events: axillary failure (AF), non-axillary recurrence (NAR), distant metastasis (DM) or death. Methods: Under IRB waiver, we queried our institutional database for patients treated surgically for invasive breast cancer with negative SLNB (1997-2001) who had an ipsilateral breast tumor recurrence (IBTR) or chest wall (CW) recurrence as a first event. We excluded patients with gross nodal disease at the time of LR. Cumulative events were estimated using competing risks methodology and were compared across groups using Gray’s test. Results: Of 1529 patients with negative SLNs at initial surgery, 86% (66) had an IBTR (83) or CW recurrence (5) with clinically negative regional nodes. 46 (52%) were treated with and 42 (48%) without axillary surgery. Primary tumor characteristics were similar between groups although time to LR was shorter in the no-axillary-surgery group (median 3.7 vs. 6.4 years, p<0.05). All patients in the axillary-surgery group and 81% of patients in the no-axillary-surgery group had surgical excision of their LR. The frequency of radiation and systemic therapy (chemotherapy, hormonal and anti-HER2) was similar between groups. At a median follow-up of 4.2 years from the time of LR, there were no statistically significant differences in the rates of subsequent AF, NAR, DM or death (Table). Conclusions: Among breast cancer patients with LR and clinically negative nodes, we find no significant association between reoperative axillary surgery and either treatment of LR or outcome. Our results coupled with the CALOR trial indicating a benefit for chemotherapy after LR, suggest that axillary restaging is not required for breast cancer patients with LR and clinically negative nodes, but our sample size is insufficient to exclude small differences, particularly in nodal recurrence.

Clinical Characteristics and Outcome of Patients Treated With and Without Axillary Surgery at the Time of First LR

<table>
<thead>
<tr>
<th>Treatment variable</th>
<th>Axillary surgery for LR (N=66)</th>
<th>No axillary surgery for LR (N=42)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation to CW for LR</td>
<td>3(7%)</td>
<td>6(15%)</td>
<td>0.295</td>
</tr>
<tr>
<td>Chemotherapy for LR</td>
<td>16(26%)</td>
<td>9(23%)</td>
<td>0.234</td>
</tr>
<tr>
<td>Hormonal therapy for LR</td>
<td>27(50%)</td>
<td>17(44%)</td>
<td>0.661</td>
</tr>
<tr>
<td>Anti-HER2 therapy for LR</td>
<td>1(2%)</td>
<td>1(2%)</td>
<td>1.000</td>
</tr>
<tr>
<td>5-year outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Axillary failure</td>
<td>0(0%)</td>
<td>4(11%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Non-axillary recurrence</td>
<td>0(0%)</td>
<td>6(15%)</td>
<td>0.252</td>
</tr>
<tr>
<td>Distant metastases</td>
<td>5(15%)</td>
<td>7(17%)</td>
<td>0.034</td>
</tr>
<tr>
<td>Death</td>
<td>1(4%)</td>
<td>1(4%)</td>
<td>0.672</td>
</tr>
</tbody>
</table>

P60

Sentinel Node Biopsy in Patients with Ductal Carcinoma in situ on Core Biopsy: Standard Care or Overtreatment? L.M. Van Roozendael, M. Klinkert, B. De Vries, L.J. Strobbe, C. Wauters, E. Rutgers, J. Wesseling, M.L. Smidt, I. Surgical Oncology, Maastricht University Medical Center, Maastricht, Netherlands; 2. Canisius-Wilhelmina Hospital, Nijmegen, Gelderland, Netherlands; 3. Netherlands Cancer Institute, Amsterdam, North-Holland, Netherlands.

Background: For patients with the diagnosis of ductal carcinoma in situ on core biopsy, a sentinel node biopsy is advised in case of a mastectomy, or in case of a risk factor for conversion to invasive breast cancer at final diagnosis. In invasive breast cancer, more and more trials are conducted with the purpose of safely minimizing invasive axillary staging and treatment. Ductal carcinoma in situ, so far, escaped from this trend, as the decision to perform a sentinel node biopsy still depends on the risk of invasive breast cancer instead of the risk of nodal metastases or recurrence. We aimed to investigate the incidence of sentinel node metastases in patients with the preoperative diagnosis of ductal carcinoma in situ on core biopsy. Methods: Patients diagnosed with ductal carcinoma in situ on core biopsy, from 2004 (one center) or 2008 (two centers) till 2013, were identified and included from the PALGA database. Clinical, radiological and pathological characteristics were recorded. Results: A senti-
nel node biopsy was performed in 358 of 753 included patients. The sentinel node was negative in 90%, showed pN0i+ in 5%, pN1mi in 4%, and pN1 in 2%. Final pathology results after excision showed solely ductal carcinoma in situ in 83%, and in 17% also invasive breast cancer (Figure 1). In patients with solely ductal carcinoma in situ, the sentinel node biopsy was performed in 258 patients, and showed pN0 in 93%, pN0i+ in 4%, pN1mi in 2%, and pN1 in 0.4%. In patients with also invasive breast cancer, the sentinel node biopsy was performed in 100 patients, and showed pN0 in 80%, pN0i+ in 6%, pN1mi in 8%, and pN1 in 6%. **Conclusion:** Seventeen percent of patients with the preoperative diagnosis of ductal carcinoma in situ at core biopsy were finally diagnosed with invasive breast cancer. Regardless of the conversion rate, micro or macrometastases were detected in 5.6% of patients undergoing sentinel node biopsy (2.7% of all 753 patients). Therefore, standard sentinel node biopsy in this patient population seems rather overtreatment than proper care.

**Results of the sentinel lymph node biopsy (SLNB)**

<table>
<thead>
<tr>
<th>Case Type</th>
<th>Number of Patients</th>
<th>Multiple Wire</th>
<th>Single Wire</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Recurrence</td>
<td>156 months</td>
<td>100 months</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Dissect Metastasis</td>
<td>4</td>
<td>2</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Extra Imaging</td>
<td>0</td>
<td>3 (19%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Additional Biopsy</td>
<td>7 (9%)</td>
<td>11 (6%)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>0</td>
<td>3</td>
<td>NS</td>
<td></td>
</tr>
</tbody>
</table>

**P62 Healthcare Costs Reduced after Incorporating the Results of the American College of Surgeons Oncology Group (ACOSOG) Z11 Trial into Clinical Practice**

**Background:** The ACOSOG Z11 trial showed no survival or local recurrence benefit from axillary lymph node dissection (ALND) for patients with 1-2 positive sentinel lymph nodes (SLN) treated with breast conservation for tumors < 5 cm. The aim of this study was to evaluate changes in the use of ALND and frozen section (FS) and the impact on cost. **Methods:** We reviewed clinically node negative breast cancer patients treated with lumpectomy and SLN biopsy who met Z11 criteria from 2007 to July 2013. We compared axillary nodal management data between pre and post Z11 cohorts. Billing information was extracted for all hospital, surgical, and pathology costs related to the patients’ surgical intervention: SLN Only, ALND and FS. Cost refers to all billing charges prior to reimbursements rendered by third party payers.

**Results:** Eight hundred patients underwent breast conservation therapy: 504 in the pre Z11 and 296 in the post Z11 cohort. Sixty-seven patients (13.5%) in the pre Z11 era and 34 patients (12.5%) in post Z11 group had 1-2 positive SLN. The use of ALND significantly decreased from 78% to 21% (p < 0.001) after the publication of the ACOSOG Z11 data. Intraoperative FS use decreased from 95% to 66% (p < 0.015). FS sensitivity was 57%. The mean overall cost per patient for SLN Only and SLN+ALND was $41,059 and $50,999 respectively (p < 0.001). The incorporation of Z11 data into surgical practice resulted in an overall mean cost savings of $368,466 from 2011 to July 2013. By omitting FS, there was a $2,283/patient (53%) reduction in the mean pathology costs from $4,319/patient to $2,037/patient, which translated into a cost savings of $203,187 by performing 29% fewer FS. If FS was completely eliminated in the 192 Post Z11 patients for whom it was performed, an additional $438,336 of pathology cost savings could have been achieved as well. **Conclusions:** ACOSOG Z11 significantly impacted the axillary management and subsequently healthcare costs in SLN positive patients. FS is a costly and unreliable tool which should play a minimal role in patients undergoing lumpectomy and SLN biopsy for small breast cancers.

**P61 Long-term Outcomes of Multiple Wire Localization for Breast Cancer: Multiple Wires do not Increase Recurrence, Unplanned Imaging or Biopsies**

**Introduction:** We previously reported that breast conservation is possible for most breast cancer patients with mammographic lesions large enough to require multiple localizing wires solary excision. We now report long term rates of local recurrence, additional imaging and biopsy in lumpectomy patients requiring multiple vs. single wire localizations to assess the safety of breast conservation for large mammographic lesions. **Methods:** We retrospectively reviewed patients undergoing wire localized lumpectomies in our institution from 5/2000-11/2006. Rates of in-breast tumor recurrence, metastasis, additional diagnostic imaging, and biopsy were compared for patients requiring multiple localizing wires for excision and for matched single wire controls. **Results:** 153 patients underwent multiple wire lumpectomy and 190 controls underwent single wire lumpectomy for breast cancer. Median age was 56 (range: 27-92) years. Median follow up was 156 mo (range 1-192 mo) in multiple wire patients post lumpectomy and was 100 mo (range 1-228 mo) in single wire. In the multiple wire group 33 (22%) had DCIS, 8 (5%) had IDC, 50 (33%) had both DCIS and IDC, 2 (1%) had ILC and 60 (39%) had mixed type. In the single wire group 55 (29%) had DCIS, 23 (12%) had IDC, 86 (45%) had both DCIS and IDC, 7 (4%) had IDC and 19 (10%) had mixed type. There were 3 local recurrences in multiple wire patients and 2 in single wire patients. All local recurrences were treated with mastectomy and remain alive and NED. Four multiple wire and 4 single wire patients developed metastatic disease and there were 3 deaths, all in single wire patients. Additional diagnostic imaging was required in 32 (21%) of multiple wire and 36 (19%) of single wire cases. Ipsilateral biopsy occurred in 7 (5%) of multiple wire cases and 11 (6%) of the single cases. **Discussion:** There is no increase in local recurrence, additional imaging or diagnostic biopsies in breast cancer patients whose lesions are large enough to require multiple localizing wires for excision. Breast conservation is a safe alternative to mastectomy in patients with large mammographic lesions.

**P63 Outcomes with Contralateral Axillary Nodal Metastases in Breast Cancer**

**Background:** Contralateral axillary metastases (CAMs) in breast cancer are rare. While classified as distant metastases, the prognosis may be more similar to that of regional recurrences. The goal of this study was to evaluate oncologic outcomes in patients with CAMs and the effect of different therapeutic approaches. **Methods:** This is a retrospective review of patients treated for isolated CAM from 1984-2014. Patients were identified from prospective breast surgical, medical oncology, and radiation oncology databases. Patients
presenting with AJCC 7th Edition Stage I and II breast cancer who did not receive neoadjuvant chemotherapy were included. Data collected included demographics, tumor size, lymph node status, utilization of chest CT within six months of diagnosis, imaging findings, need for additional workup, and identification of metastatic disease. Descriptive statistics were used for analysis. From 1998-2012, 3321 patients were diagnosed with Stage I and II breast cancer. Of these, 2062 (62.1%) were clinically Stage I and 1259 (37.9%) were Stage II on initial evaluation. Two hundred twenty seven (11%) Stage I patients and 457 (36.3%) Stage II patients received chest CT. Of these patients, 187 (27.3%) were found to have pulmonary nodules (Table 1). Pulmonary nodules measured ≤5 mm for 131 (70%) patients, 5-10mm for 6 (3.2%) patients, and ≥10mm for 46 (24.7%) patients, 11-20mm for 6 (3.2%) patients, and ≥20mm for 4 (2.1%) patients. Patients undergoing chest CT for staging subsequently underwent a mean of 2.34 (range 0-16) additional chest CTs in follow-up. Of all patients undergoing chest CT for staging, only 9 (1.3%) were ultimately diagnosed with pulmonary metastases (Table 1). Patients were diagnosed with pulmonary metastases an average of 25 months (range 0-97) after initial staging chest CT. A significant percentage of Stage I and II breast cancer patients underwent unnecessary chest CT as part of their initial workup. Nearly one-third of these patients were found to have pulmonary nodules, but only 1.3% eventually developed pulmonary metastases. Adherence to NCCN guidelines will reduce the excessive use of CT chest imaging.

**P65**

**Over-utilization of Chest Computed Tomography in Stage I and II Breast Cancer Patients**

B.Z. Dull,* A. Linkugal, J. Margenthaler, A. C. Y. Surgical Oncology, Washi ngton University, St. Louis, MO.

The National Comprehensive Cancer Network (NCCN) guidelines recommend clinical Stage I and II breast cancer patients undergo chest computed tomography (CT) for metastatic workup only if pulmonary symptoms are present. Despite this, many asymptomatic early stage breast cancer patients undergo chest CT. The aim of this study was to assess the utilization and results of chest CT in clinical Stage I and II breast cancer patients at an NCCN member institution. A prospectively maintained database of breast cancer patients was queried to identify patients treated between 1998 and 2012. All patients with concurrent distant metastases, locoregional relapse, or contralateral breast primaries were excluded. Medical records were reviewed for clinicopathologic features, treatment information, and survival data. Kaplan-Meier curves and log-rank tests were used to assess survival differences. **Results:** Forty-two patients were included with mean 43 month follow-up (range 4-283). Eighty-six percent (36/42) initially presented with node positive disease. The primary tumor was classified as T1 in 4 (10%) cases, T2 in 6 (14%), T3 in 3 (7%), and T4 in 29 (69%) cases with 26 (62%) patients diagnosed with inflammatory breast cancer (IBC). Twenty (48%) patients were diagnosed with CAM with their initial breast cancer diagnosis. In the remaining 22 patients, the median time to development of CAM was 15 months (range 0-79.4). Synchronous CAM was more common with IBC (17/26, 65.4%) than in non-IBC (3/16, 18.8%) (p<0.005). CAM was treated with chemotherapy in 98% (41/42), surgery in 50% (21/42), and radiotherapy in 50% (21/42). Median overall survival (OS) for the entire cohort was 31.0 months with median time to progression (TPP) of 11.5 months. Patients treated with surgery had prolonged median TTP (19.1 vs. 7.8 months, p=0.001) with a trend toward improved OS (41 vs. 24 months, p=0.11). **Conclusion:** Patients with CAM often have a history of advanced breast cancer. Patients with IBC are more likely to present with synchronous CAM than others. While a retrospective review of treatment results is prone to selection bias, the data suggests that CAM patients treated with surgery have improved outcomes and should be considered for this approach.

**P66**

**Contralateral Prophylactic Mastectomy in Young Women with Breast Cancer: A Population-based Analysis of Predictive Factors and Clinical Impact**

A. Bouchard-Fortier,* N. Baxter, X. Camacho,1* A. Bouchard-Fortier, X. Camacho,1 A. Bouchard-Fortier,1 X. Camacho,1 M. Quan,1 J. Surgical Oncology, University of Calgary, Calgary, AB, Canada; 2. St. Michael’s Hospital, Toronto, ON, Canada; 3. Institute of Clinical Evaluative Sciences, Toronto, ON, Canada.

The objectives of the present study were to describe factors predictive of CPM in young women (<35 years old) with invasive breast cancer and evaluate its impact on survival, in a large population based cohort. **Methods:** All women diagnosed with invasive breast cancer aged ≤35 from 1994 – 2003 treated with mastectomy were identified from the Ontario Cancer Registry. Patient demographics, complete tumor and treatment characteristics were abstracted from primary chart review. Cox proportional hazard regression was performed to assess factors associated with performance of CPM and its effect on recurrence and overall survival, performance of CPM was modeled as a time varying co-variate. The models were controlled for known predictors including age, tumor size, nodal status, ER/PR, LVI, histologic grade, systemic therapy and adjuvant radiation. **Results:** There were 628 women identified. Of these, 101 underwent a contralateral mastectomy (16.1%), of which 87 were prophylactic (13.9%). On multivariable analysis, factors predictive of CPM were node positive status (HR: 1.96, 95% CI [1.13 – 3.40]; p-value = 0.017), negative estrogen receptor status (HR: 2.06, 95% CI [1.10 – 3.88]; p-value = 0.025) and initial BCS with reexcision (HR: 2.87, 95% CI [1.67 – 4.93]; p-value = 0.0001). A median follow up of 11 years, no significant difference in relapse-free survival was observed in women undergoing CPM compared to those who did not (HR: 0.60, 95% CI [0.36 – 1.00]; p-value = 0.05). **Conclusions:** Performance of
CPM in young women with invasive breast cancer did not result in a significant survival benefit, compared to those without CPM. Factors found to be predictive of performance of CPM were negative lymph node status, negative estrogen receptor status and initial BCS with re-excision. Further studies are needed to determine if a subset of young women might benefit from CPM.

P67

Introduction: The need for axillary lymph node dissection (ALND) is determined by the number of positive sentinel nodes (SLNs), rather than the presence of any involved nodes in patients (pts) who meet ACOSOG Z11 eligibility criteria. We sought to determine if adoption of Z11 criteria was associated with removal of an increased number of SLNs. Methods: Upon retrospective review of a prospective database of breast cancer pts treated at our institution between 2006 and 2013, we identified 5227 pts who were eligible and elected to undergo breast conserving surgery; 2374 pts were treated pre-Z11 and 2853 pts post-Z11 (after 8/2010). Clinical-pathologic factors were collected to determine variables associated with number of SLNs removed. Univariate analysis, controlling for surgeon, was performed using linear regression to identify variables associated with removal of more SLNs. Significant variables were included in a multivariable model. Results: Among 4635 pts, 51% were treated pre-Z11. In the pre-Z11 group, factors associated with removal of an increased number of SLNs were patient age > 60 years, did not differ between groups. Median tumor size was similar in both groups: 1.1 (0.05-5.0cm) in pre-Z11 and 1.2 (0.1-5.2cm) in the post-Z11 group. The mean number of SLNs excised in the pre-Z11 pts was 2.8 compared to 2.9 in the post-Z11 pts (p=0.015). 4 lymph nodes or more were removed in 601 (25%) pre-Z11 pts compared to 838 (29%) post-Z11 pts (p=0.001). Factors associated with the removal of more SLNs on multivariate analysis were young age (<50 years), median tumor size (p=0.0004). Z11 criteria were not strongly associated with removal of more SLNs (p=0.47). ALND was performed in 372 (79%) node positive pre-Z11 pts compared to 68 (16%) node positive post-Z11 pts (p=0.0001). Conclusion: Since adoption of the Z11 criteria, we found the mean number of SLNs removed was very similar, with a significantly fewer number of pts undergoing ALND for positive SLNs. We noted a significant slight shift in the removal of ≥4 SLNs, likely ensuring the identification of pts who would benefit from ALND. Overall, the Z11 criteria were not associated with a clinically significant increase in number of SLNs removed; further study is warranted into factors associated with removal of additional SLNs, such as young age and tumor size.

P68

Background: With increased mammographic screening, the incidence of ductal carcinoma in situ (DCIS) has been reported to have markedly increased. However, there is limited information about demographic differences in women diagnosed with DCIS vs. invasive breast cancer (IBC). The objective of this study is to provide a comprehensive population based review of the factors associated with the diagnosis of DCIS. Methods: Using the National Cancer Database (NCDB), we conducted a review of demographic trends in the diagnosis of DCIS compared with IBC. Logistic regression analysis was used to assess the multivariable relationship between subject demographics, clinical characteristics, and DCIS diagnosis probability. Results: Between 1998-2011, 90,671 women were diagnosed with DCIS and 1,531,922 women with IBC. The proportion of women with DCIS increased from 2.6% in 1998 to 9.6% in 2009 and thereafter remained stable at approximately 9% (p value <.0001). Compared with women over the age of 70, younger women were more likely to be diagnosed with DCIS than with IBC (p value <.0001). Compared to white women, African American and other minority populations were more likely to have a diagnosis of DCIS (OR 1.12 [95% CI 1.10-1.15] and OR 1.17 [95%CI 1.13-1.22] respectively). Patients with private insurance were almost twice as likely to be diagnosed with DCIS compared with uninsured patients (OR 1.80 [95%CI 1.71-1.90]). DCIS diagnosis was more likely in those with the highest education level and highest median income (OR 1.04 [95%CI 1.01-1.07] and OR 1.16 [95%CI 1.13-1.20] respectively). Among facility types DCIS rates were highest rates in academic programs and among facilities located in the east south central region of the U.S. (OR 1.16 [95%CI 1.13-1.19] and OR 1.27 [95%CI 1.22-1.32]). Conclusion: The proportion of breast cancer patients diagnosed with DCIS has significantly increased over the last 15 years. We find variability across different demographic populations in the increasing incidence of DCIS that may relate to differences in uptake of mammographic screening programs. Our finding of race based differences also suggests biologic heterogeneity of this disease.

P69

Introduction: Breast cancer survivorship has improved significantly over the last 20 years. Few studies have evaluated the health-related quality of life (HRQOL) for long-term survivors of breast cancer. The current study investigates factors associated with poor HRQOL among long-term breast cancer survivors. Methods: Using the Surveillance, Epidemiology, and End-Result registry and the Medicare Health Outcome Survey linked database, breast cancer patients surviving > 5 years were identified. Patients with a VR12 physical (PCS) or mental (MCS) component score 10 points lower than the median PCS/ MCS score were categorized as having poor HRQOL. Univariate and multiple variable analyses were used to identify predictors of poor HRQOL. Results: 937 resected breast cancer patients (median age 77, median follow-up 15.6 yrs) were identified. The majority of patients were white (77%) and Stage I (60%). Median time from diagnosis to HRQOL survey was 9.5 yrs. Median PCS was 36 (IQR 20) with 217 (23%) with poor PCS. Median MCS was 54 (IQR 15) with 226 (24%) with poor MCS. Predictors of poor PCS included age, no home ownership, smoker, >2 comorbidities, inability to perform > 2 of 6 activities of daily living (ADLs), and modified or radical mastectomy (all p < 0.05). Predictors of poor MCS included age, no home ownership, income less than $30k per year, no high school education, smoker, >2 comorbidities, and inability to perform > 2 of 6 ADLs (all p < 0.05). Tumor characteristics including tumor type, stage, size, and lymph node ratio did not predict poor HRQOL. After adjusting for SES, comorbidities, ADLs, and time from diagnosis to survey, modified or radical mastectomy was independently associated with poor PCS (OR 3.6, 1.2-10.6 95% CI, p =0.02). After adjusting for smoking status, SES, and time from diagnosis to survey, > 2 comorbidities (OR 1.6, 1.0-2.5 95%CI, p =0.044) and inability to perform >2 of 6 ADLs (OR 3.7, 2.3-5.9 95% CI, p < 0.01) were independent predictors of poor MCS. Conclusion: For long-term survivors of breast cancer, modified or radical mastectomy has a lasting impact on physical HRQOL; however, mental HRQOL is dependent on comorbidities and ADLs.

P70

Introduction: MICA is an innate ligand for natural killer cells and activated T cells. Here we investigate whether MICA expression in nonmalignant breast lobules varies between histologically normal and abnormal lobules with fibrocystic change. Methods: Archived breast tissue samples were obtained from 141 age-matched women with differing levels of breast cancer risk: 47 normal women with no clinical breast disease from the Komen Tissue Bank (KTB), 47 women with benign breast disease (BBD) and later cancer (cases), and 47 women with BBD but no cancer (controls). Cases and controls were matched on year of biopsy and follow-up. Consecutive sections were stained for MICA and H&E. Up to 10 lobules in each sample were characterized by H&E for epithelial abnormality (normal, nonproliferative, proliferative, atypia). MICA staining was quantitated digitally by pixel analysis and reported on a per lobule basis by positive pixel percent (PPP) (positive pixels/total pixels)x100. Statistical analysis was performed using linear mixed effects regression on the rank transformed PPP to account for correlations among multiple lobules from the same sample. Results: Among 141 women (median age 53, range 35-79), 1278 lobules were evaluated. Overall, 699 lobules (55%) were normal and the remaining 579 (45%) exhibited fibrocystic changes. Among fibrocystic lobules, 329 (57%) had nonproliferative changes, 226 (39%) had...
epithelial proliferation, and 24 (4%) had atypical hyperplasia. Median MICA PPP was 7.4 (range: 0-68) and did not differ significantly by risk group (p=0.09). However, fibrocystic lobules showed significantly lower median CD56+ PPP compared to normal lobules (6.3 vs 8.0, p<0.0001). **Conclusions:** Breast lobules with fibrocystic changes show less MICA expression, raising a question of possible immune suppression induced by early epithelial abnormalities. Better understanding is needed of the immune microenvironment in premalignant breast tissues.

**P71**

**Limited Efficacy of preoperative Magnetic Resonance Imaging in Breast Cancer Patients**


**Introduction:** Literature regarding the benefits of preoperative magnetic resonance imaging (MRI) on surgical outcomes in women with breast cancer is equivocal, highlighting the need for additional studies. The aim of this study was to determine the effect of preoperative MRI on the treatment of breast cancer patients. **Methods:** Using a retrospective cohort design, female patients surgically treated for breast cancer were sorted into MRI or non-MRI cohorts and evaluated, using bivariate and multivariate statistics. Prophylactic surgeries and neoadjuvant patients were excluded. **Results:** Four-hundred and two patients presented for breast surgery between June 2009 and April 2013, with 150 (37.3%) receiving a preoperative MRI. Compared to those not receiving MRI, the MRI group was significantly younger, 55.5 to 70 years (p<0.0001), and showed a significantly longer time until surgery; 43 to 26 days (p<0.0001). The MRI group also showed a significantly higher proportion of patients receiving a total mastectomy; 46.7% to 35.3% (p=0.0244). Analyzing only partial mastectomy patients in both groups, the MRI group showed statistically similar outcomes with respect to margin positivity (4% to 7.1%, p=0.1983) and re-operation rates (8.7% vs 10.7%, p=0.5071). Multivariate (MV) analyses revealed that MRI did not change total mastectomy rates (OR 1.28 [95% CI 0.80-2.05]; p=0.30), margin positivity (OR 0.36 [95% CI 0.10-1.36]; p=0.13), or re-operation rates (OR 1.4 [95% CI 0.53-3.75]; p=0.50). MRI did significantly increase time until surgery on MV analysis (OR 0.53 [95% CI 0.43-0.66]; p=0.0001). **Conclusion:** This study demonstrates that preoperative MRI use for breast cancer patients did not improve margin control and did not decrease re-operation rates, but did significantly lengthen time until surgery. These findings suggest a more judicious use of preoperative MRI in breast cancer patients.

**P72**

**Contralateral Breast Cancer: Is the Second Cancer Worse?**


**a.** The past decade has seen an increase in the use of contralateral mastectomy (CPM), in many instances without specific medical indication. There have also been studies suggesting improved survival with the use of CPM. However, in order for CPM to prevent death, metachronous cancers in the opposite breast should be more ominous than the index cancer. We set out to compare the features of contralateral events to the index tumors to determine how often these cancers were worse and what impact that would have on disease management and overall survival. **b.** We conducted a retrospective review of a prospectively maintained database and identified 161 women with DCIS or Stage I-II breast cancer who experienced a contralateral breast cancer (CBC) from 1998 to 2009. Patient characteristics and those of the index and metachronous CBC (~6 month interval from index) were described in terms of stage, grade, histology, receptor status, size, and nodal status. Continuous variables compared via the signed-rank test; categorical variables compared via McNemar’s test. The mean age of the patient population was 54±12 (median and range: 33-86) at the time of initial diagnosis. The mean time to CBC was 6 years ±5 (mean and range: 5 ± 0.26). 73.13% of CBCs were detected by mammography while only 48.75% of the index tumors presented in this manner (p value < 0.0001). The histology of the index tumor was found to be DCIS in 34.18% of patients, compared to 38.61% of CBCs, while the fraction of invasive cancers was the same for both. The size of the index tumor was 18 mm ± 17 (15(1,150)) and the contralateral 16 mm ±16(11(0,80)). The rate of nodal positivity was similar between index tumors and CBC (14% and 16% respectively). A significantly higher percentage of second tumors were found to be ER/PR+ when compared to the initial cancer 72.67% vs 62.11%, respectively. In our population, we were unable to find any significant differences in the index and metachronous contralateral tumors that would result in poorer prognosis from a CBC. These results do not support the premise that a CBC will pose a more significant hazard of breast cancer death than the index tumor, or that CPM will confer a significant survival advantage.

**P73**

**Pilot Study of a Passive Non-radioactive Infrared-activated and Radar-detected Marker to Localize Non-palpable Breast Lesions**

C.E. Cox,* M. Themar-Geck,* R. Pratt,* M. Jung, J. King, S.C. Shivers,1* 1. University of South Florida Morsani College of Medicine, Tampa, FL. 2. The Breast Care Center at Florida Hospital Tampa, Tampa, FL.

**Background:** The standard preoperative technique for localizing non-palpable breast lesions is wire localization (WL). Radioactive seed localization is an alternative approach that addresses some of the disadvantages of WL, but has considerable regulatory requirements for handling radioactive materials. The Surgical Guidance System (SGS) is an FDA-cleared medical device that utilizes passive non-radioactive infrared-activated and radar-detected technology to provide real-time guidance during excisional breast procedures. We conducted a pilot study to determine the safety and efficacy of the SGS in localizing and directing the removal of non-palpable breast lesions during excisional biopsy or lumpectomy. **Methods:** After a feasibility study in resected breast tissues ex vivo, IRB approval was granted for women with a non-palpable breast lesion requiring localization for excision. Using mammographic or ultrasound guidance, the SGS tissue marker was placed percutaneously up to 7 days prior to the scheduled excision. The surgeon used the SGS hand piece to locate the marker, which was removed along with the surrounding breast tissue. The SGS console provides audible feedback of marker proximity to the hand piece. Successful marker placement, localization and retrieval were the primary endpoints. **Results:** A total of 6 pts have been enrolled in the study to date. Markers were successfully placed with mammographic guidance in 5/5 pts and with ultrasound guidance in 1/1 pts. Markers were placed an average of 3.8 days (range 1-8 days) before surgery. The intended lesion and marker were successfully removed in 6/6 pts. Of the pts in which final pathology is currently available, the margins were in clear in 4/4 pts, although one pt was recommended for re-excusion due to close margins (1 mm). Marker migration did not occur. No adverse events occurred. **Conclusions:** The preliminary data show the SGS to be a safe and effective tool for the localization of non-palpable breast lesions. Ongoing accrual to this pilot study will validate these findings with enrollment of 50 pts in total in the next 60 days at up to 4 additional sites.

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**Specimen radiograph showing the SGS marker (right) and biopsy clip (left).**
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Oncotype DX in Bilateral Synchronous Primary Invasive Breast Cancer M. Gunthner-Biller,* M. Stempel, S. Patel, T. King, Memorial Sloan Kettering Cancer Center, New York, NY.

Introduction Oncotype DX predicts response to chemotherapy in early stage estrogen receptor (ER) positive breast cancer. Synchronous bilateral breast cancers frequently share the same ER status yet may differ in other histopathologic features. We sought to examine concordance rates of Oncotype DX testing in women presenting with bilateral ER positive invasive breast cancer. METHODS Institutional databases were reviewed to identify patients with multiple Oncotype scores (RS) and synchronous bilateral invasive breast cancer. Patient demographics, tumor and treatment characteristics, and RS were obtained from the medical record. Oncotype scores were stratified by risk group (RS<18, low; RS 18-30, intermediate; RS>30, high). RS were considered discordant if they reflected different risk groups. Comparisons were made between cases with concordant and discordant RS. RESULTS From Jan 2005-2014, 3976 patients had Oncotype DX testing. Bilateral RS were available for 43 pts with synchronous bilateral ER+ Her2 negative breast cancer; median age 58yrs (42-84yrs). Among 86 tumors tested, 63 (73%) were low risk, 20 (23%) were intermediate risk and 3 (3%) were high risk by RS. Scores were concordant in 29(67%) pts (Table). Patients with concordant RS were slightly older, median age 62yrs vs 56yrs (p=ns). Histologic subtype differed in 8/29 (28%) concordant cases and 4/14(29%) discordant cases. There were no differences in tumor size or median levels of ER expression. Median levels of PR expression were higher and more similar in concordant cases, 80% for bilateral cancers respectively, and 55% and 75% for bilateral cancers in discordant cases. Among discordant cases, all patients with at least 1 high risk RS and 6/12 patients with at least 1 intermediate risk RS received chemotherapy. Conclusion Among women with synchronous bilateral ER+ Her2 negative breast cancer, Oncotype DX scores were concordant in 67% of cases. Concordance rates may be higher in older women or among those with comparable levels of PR expression, however this requires testing in a larger sample. These data do suggest that testing of both tumors should be considered in patients who are candidates for adjuvant chemotherapy.

<table>
<thead>
<tr>
<th>Oncotype DX RS tumor 1</th>
<th>Oncotype DX RS tumor 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low RS n=27</td>
<td>Low RS n=36</td>
</tr>
<tr>
<td>25 (93%)</td>
<td>27 (96%)</td>
</tr>
<tr>
<td>Intermediate n=13</td>
<td>Intermediate n=7</td>
</tr>
<tr>
<td>9 (69%)</td>
<td>4 (56%)</td>
</tr>
<tr>
<td>High RS n=3</td>
<td>High RS n=7</td>
</tr>
<tr>
<td>2 (67%)</td>
<td>1 (13%)</td>
</tr>
</tbody>
</table>

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INTRODUCTION: The routine use of preoperative MRI in breast cancer is controversial, as several studies have shown that the addition of preoperative MRI does not reduce the re-excision rate for patients undergoing breast conserving therapy (BCT). We sought to determine if surgical outcomes, such as margin positivity and rates of re-excision, were reduced in patients for whom MRI estimates of the tumor size were discordant with the final pathologic measurements obtained from excised surgical specimens. METHODS: A retrospective cohort study of breast cancer patients evaluated with preoperative breast MRI prior to surgical treatment at the McGill University Health Centre (MUHC) between January 2006 and January 2012 was performed. Pertinent radiologic, pathologic, and operative information, including margin positivity and re-excision status, was abstracted from medical records. RESULTS: In the 317 patients with invasive ductal or lobular carcinoma who underwent breast MRI prior to surgery, mean pathologic tumor size was 1.88 cm (95% CI 1.77 - 2.03 cm) and did not significantly differ from the mean radiologic size of 1.90 cm (95% CI 1.74 – 2.02 cm, p=0.90). MRI was concordant within 5 mm of final pathologic size in 57% of the patients, whereas it underestimated 23% of cases and overestimated 20% of cases. Ductal carcinoma in situ (DCIS) diagnosed on preoperative core needle biopsy was associated with MRI overestimation of the tumor size (70.0 vs. 17.2%, p < 0.0001). Positive margins were present in 55 (21.9%) of BCT cases, and MRI underestimation of the final tumor size was associated with increased presence of positive margins (34% vs 19%, p=0.032) and need for re-excision (21.3% vs. 7.8%, p=0.013) compared to cases where the MRI was concordant or overestimated the final tumor size.

CONCLUSION: Radio-pathologic discordance with underestimation of tumor size by greater than 5 mm on preoperative MRI correlates with increased rates of positive margins and need for re-excision.

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False Negative Rate (FNR) and Negative Predictive Value (NPV) from 3-year Outcome Study after Sentinel Lymph Node Biopsy (SLNB) with [99mTc] Tilmanocept in Clinically Node-negative (cN0) Breast Cancer and Melanoma Patients J. Kim,* J.K. O’Donnell, Division of Surgical Oncology, Department of Surgery, Case Western Reserve University, Cleveland, OH.

INTRODUCTION: SLNB has been shown to be a suitable alternative to full lymph node dissection in cN0 early-stage breast cancer and melanoma (ACOSOG Z0011, NSABP B-32, MSLT-1). A phase 3, prospective, multi-institutional, open-label, single arm trial assessed receptor-targeted [99mTc]tilmanocept for intraoperative identification of SLNs in cN0 breast cancer and melanoma patients (ClinicalTrials.gov/NC100671918). A 3-year follow-up study was conducted to assess recurrence and survival outcomes following SLNB, FNR and NPV are reported here. METHODS: Following participation in the [99mTc]tilmanocept phase 3 trial, voluntary enrollment in the follow-up study was open to patients with (pN+) or without (pN0) SLN metastases. Recurrence and survival data were collected at 6 to 36 months after primary tumor excision and SLNB. The primary endpoint was the regional (i.e., draining lymph node basin) recurrence-free rate after SLNB with [99mTc]tilmanocept. Exploratory endpoints included calculation of FNR and NPV from the regional recurrence data. RESULTS: Of 169 patients completing the Phase 3 trial and eligible for the follow-up study, 109 (64 breast cancer, 45 melanoma) completed at least 1 follow-up visit. By 36 months, the pathology status was known for 89 patients. Table 1 summarizes 3-year regional recurrence results and the calculated diagnostic performance metrics. Overall, FNR was 5.6% and NPV was 98.6% for the two tumor types combined. CONCLUSIONS: Low FNR and high NPV in patients with breast cancer and melanoma after 3 years indicate [99mTc]tilmanocept accurately identifies SLNs and is likely predictive of pathological staging. These findings are comparable to previously published outcome data and demonstrate the clinical utility of [99mTc]tilmanocept for SLNB.

| Summary of 3-year regional recurrence results and diagnostic performance metrics |
|----------------------------------------|------------------|------------------|
| Breast Cancer N=57                      | Melanoma N=32     | Combined N=89     |
| Cumulative regional recurrence-free rate (derived from Kaplan-Meier curve), % (n) |                  |
| pN0 patients, n (%)                    |                  |
| 100% (6)                               |                  |
| pN+ patients, n (%)                    |                  |
| 97.4% (41)                             |                  |
| False negative (FN) patients, n        |                  |
| 13                                     |                  |
| False positive (FP) patients, n        |                  |
| 4                                       |                  |
| False negative (FN) patients, n        |                  |
| 0                                      |                  |
| False positive (FP) patients, n        |                  |
| 1                                       |                  |
| FNR                                     |                  |
| 0.01 (3)                               |                  |
| NPV                                     |                  |
| 99.0% (159)                            |                  |
| Negative predictive value, % (TN/(TN+FN)) |                  |
| 99% (4444)                             |                  |
| 96.4% (4272)                           |                  |

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INTRODUCTION: The routine use of preoperative MRI in breast cancer is controversial, as several studies have shown that the addition of preoperative MRI does not reduce the re-excision rate for patients undergoing breast conserving therapy (BCT). We sought to determine if surgical outcomes, such as margin positivity and rates of re-excision, were reduced in patients for whom MRI estimates of the tumor size were discordant with the final pathologic measurements obtained from excised surgical specimens. METHODS: A retrospective cohort study of breast cancer patients evaluated with preoperative breast MRI prior to surgical treatment at the McGill University Health Centre (MUHC) between January 2006 and January 2012 was performed. Pertinent radiologic, pathologic, and operative information, including margin positivity and re-excision status, was abstracted from medical records. RESULTS: In the 317 patients with invasive ductal or lobular carcinoma who underwent breast MRI prior to surgery, mean pathologic tumor size was 1.88 cm (95% CI 1.77 - 2.03 cm) and did not significantly differ from the mean radiologic size of 1.90 cm (95% CI 1.74 – 2.02 cm, p=0.90). MRI was concordant within 5 mm of final pathologic size in 57% of the patients, whereas it underestimated 23% of cases and overestimated 20% of cases. Ductal carcinoma in situ (DCIS) diagnosed on preoperative core needle biopsy was associated with MRI overestimation of the tumor size (70.0 vs. 17.2%, p < 0.0001). Positive margins were present in 55 (21.9%) of BCT cases, and MRI underestimation of the final tumor size was associated with increased presence of positive margins (34% vs 19%, p=0.032) and need for re-excision (21.3% vs. 7.8%, p=0.013) compared to cases where the MRI was concordant or overestimated the final tumor size.

CONCLUSION: Radio-pathologic discordance with underestimation of tumor size by greater than 5 mm on preoperative MRI correlates with increased rates of positive margins and need for re-excision.
underwent re-excision and 27/125 (21.6%) underwent completion mastectomy. Following initial re-excision, an additional 15/533 (2.8%) patients underwent a second margin re-excision, and 1 (0.2%) underwent a third. Overall, 59/533 (11.0%) total patients and 49/167 (29.3%) patients with positive or close margins eventually underwent completion mastectomy. On reoperation, residual cancer was found with equal frequency when comparing cases with positive (57.7%) and <1mm margins (58.9%) (p=NS) (see table). When 2 or more margins were <1mm or positive, residual cancer was found on re-excision in 37/50 (74%) cases as opposed to 36/75 (48%) with only one <1mm or positive margin (p=0.003). After controlling for other clinicopathologic factors positive margins and <1mm margins were equally likely to be associated with residual disease. **Conclusion** While current guidelines define an adequate margin as “no ink on tumor”, in this series of lumpectomy cases, residual cancer was equally as likely to be found with <1mm margin as a positive margin found at original surgery. Multiple positive or close margins was a significant predictor of residual disease. Further study is needed to better define indications for additional surgery in patients with very close margins.

**Positive and close margins in 533 lumpectomies for invasive breast cancer**

<table>
<thead>
<tr>
<th>Number of cases</th>
<th>Cases with 2 or more involved margins</th>
<th>Reoperations</th>
<th>Number of completion mastectomies</th>
<th>Residual cancer found on reoperation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive margins</td>
<td>167/533 (31.3%)</td>
<td>40/157 (25.5%)</td>
<td>62/147 (42.9%)</td>
<td>38/43 (88.4%)</td>
</tr>
<tr>
<td>closest &lt;1mm margin</td>
<td>111/533 (20.8%)</td>
<td>36/111 (32.5%)</td>
<td>77/111 (67.2%)</td>
<td>47/77 (61.0%)</td>
</tr>
<tr>
<td>Combined positive and close margins</td>
<td>167/533 (31.3%)</td>
<td>40/157 (25.5%)</td>
<td>62/147 (42.9%)</td>
<td>38/43 (88.4%)</td>
</tr>
</tbody>
</table>

### P78

**Augmentation of Adoptive Cellular Immunotherapy for Breast Cancer with Decitabine**

**K. Terracina,1 L. J. Graham,1 K.K. Payne,1 M.H. Manjili,2 H.D. Bear,1 1. Department of Surgery, Virginia Commonwealth University and Massey Cancer Center, Richmond, VA; 2. Department of Microbiology and Immunology, Virginia Commonwealth University and Massey Cancer Center, Richmond, VA.**

**Introduction:** Resistance of cancers to immunotherapy can result from silencing of tumor antigens, which may be dependent on gene methylation. Tumors can also increase myeloid derived suppressor cells (MDSC) that inhibit T cell responses. We hypothesized that increasing expression of immunogenic tumor antigens with the DNA methyltransferase inhibitor decitabine could increase the efficacy of T cell immunotherapy.

**Methods:** HER-2 and MHC Class I expression were measured using flow cytometry. Cancer testis antigens (CTA) were measured by qRT-PCR. Stimulation of T cells by 4T1 cells, either untreated or treated with decitabine, was assessed using an IFN-γ gene release assay. MDSCs were quantified with flow cytometry. Adoptive immunotherapy (AIT) in vivo was studied in 4T1 tumor-bearing Balb/c mice.

**Results:** Treatment of 4T1 cells with decitabine in vitro increased both HER-2 (Mean Fluorescence Intensity [MFI] 2,109 vs. 1,186) and MHC Class I expression (MFI 11,666 vs. 4,670). Four out of six murine CTAs demonstrated increased expression after treatment with decitabine. Stimulation of IFN-γ gene release from tumor-sensitized T cells was significantly higher with decitabine-treated 4T1 cells versus control 4T1 cells (13,400 pg/mL vs. 3,748 pg/mL, p=0.02).

Decitabine treatment of 4T1 tumor bearing mice also resulted in statistically significant decreases in MDSCs in spleens (210x10^6 vs 22x10^6, p=0.006), livers (2.6% vs 1.1%, p=0.001), and blood (22% vs 21%, p=0.005). Decitabine in combination with AIT resulted in a significant decrease in 4T1 tumor size compared to AIT alone (66.7 vs 6.1 mm^2 on day 24), and longer survival to humane endpoint (mean 48 vs 30 days, p<0.05).

**Conclusions:** Decitabine increased expression of tumor antigens and antigen presentation molecules in 4T1 cells. Decitabine treated 4T1 cells stimulated greater IFN-γ gene release from tumor-sensitized lymphocytes, implying increased immunogenicity. Along with the impressive decrease in MDSC burden, these effects result in a significant augmentation of the therapeutic efficacy of AIT. Decitabine may have a role in combination with existing and emerging immunotherapies for breast cancer.

### P79

**Changes in Practice Patterns for Completion Axillary Node Dissection in a Population-based Breast Cancer Cohort before and after the Dissemination of ACOSOC Z11 Results**

S.D. Cornacchi,1 M. Simunovic,1 L. Thabane,1 M. O’Brien,2 B. Strang,1 S.D. Mukherjee,2 D. Bhattacharyya,1 N. Hodgson1 1. Surgery, McMaster University, Hamilton, ON, Canada; 2. University of Toronto, Toronto, ON, Canada.

**Introduction** Sentinel node biopsy (SNB) is the mainstay of axillary staging in breast cancer (BC). Prior to 2011, a completion axillary node dissection (cALND) was routinely performed in patients with a positive SNB. Since the publication of ACOSOG Z11 there has been a trend towards omission of cALND. This study examines changes in surgical management of the axilla in South-Central Ontario before and after the publication of Z11.

**Methods** Consecutive cases undergoing SNB for invasive BC were reviewed at 12 hospitals. Data were collected for a 16-month time period (TP1) before Z11 publication (May 2009-Aug 2010) and afterwards (TP2) (Mar 2011-June 2012). Cases with surgery for recurrence, in situ or benign disease or receiving neo-adjuvant therapy were excluded. Data were collected on tumour factors, surgeon volume, type of hospital, type of breast and nodal surgery, number of positive SLNs, size of SLN metastases (micro- or macro) and cALND rate. Cases were categorized by whether they met Z11 eligibility criteria or not.

There were 620 cases with SLNB in TP1 and 774 in TP2 and SNB success rate was 97% and 99% respectively. The rate of positive SNB was 24% for TP1 (n=148) and 26% for TP2 (n=199). For cases meeting Z11 criteria, cALND rate decreased from 74% (TP1) to 49% (TP2) (p<0.01) and cALND rate varied across hospitals from 56%-100% at TP1 and from 14%-100% at TP2. cALND rate for cases with macromets decreased after Z11 (81% to 58%, p<0.01). For cases not meeting Z11 criteria, the cALND rate decreased from 74% (TP1) to 49% (TP2) (p<0.01) and cALND rate varied across hospitals at TP1 and from 46%-100% at TP2. Physicians at academic hospitals, surgical oncologists and higher volume surgeons (+4 cases/month) were more likely to omit cALND at TP2 for patient that met Z11 criteria.

**Conclusion** We observed a reduction in cALND rate in our region with variation across hospitals demonstrating that surgeons generally accepted the conclusions of Z11 and modified their practice accordingly with variation seen for different practice location, surgeon volume and specialization.

### P80

**The Impact of Obesity on Costs for Mastectomy**

S.X. Sun,1 C. Hollenbeak, A.M. Leung. Surgical Oncology, Penn State Hershey Medical Center, Hummelstown, PA.

**Background:** Obesity is a growing epidemic affecting 34.9% of adults in the United States. In an era of rising health care costs and the need to provide more cost effective and efficient care we sought to determine the economic impact of obesity on resource utilization in patients undergoing mastectomy for breast cancer. We hypothesized that obesity would result in more costly care.

**Methods** A retrospective analysis was done on all female patients with...
age greater than 18 undergoing mastectomy from 2004-2010 for breast cancer using the National Inpatient Sample (NIS). The main outcome variables were cost, length of stay, and complications. The key independent variable was obesity as coded by ICD-9. Additional independent variables included the 30 comorbidities defined by the Elixhauser Comorbidity index. We analyzed the association of obesity with cost, length of stay, and complications using multivariable regression models. Then to control for bias due to covariate imbalance, propensity score matching was performed. Results: 49,985 women over age 18 with breast cancer undergoing mastectomy were identified. Of these, 2,897 patients (5.80%) were identified as obese. In regression analyses obese patients had significantly higher costs ($0.0001) but not longer lengths of stays or higher overall complications. Propensity yieded 2,076 obese patients and 2,076 non-obese comparison patients. The cost for obese patients continued to be higher at an additional $1,734.65 cost per patient ($0.0001), but was not significantly associated with longer length of stay or higher overall complications in the matched comparison group. Conclusion: The cost for mastectomy was 18% higher for obese versus non-obese patients, even when matched for other patient factors. In addition these higher costs were not due to longer lengths of stay or higher overall complications. A CPT modifier may be warranted for mastectomies performed on obese patients to ensure appropriate reimbursement for surgical complexity related to caring for obese patients.

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Risk of Axillary Recurrence in Breast Cancer Patients with a Negative Sentinel Node Biopsy (SNB) who do not Receive Radiation: Implications for Partial Breast Irradiation (PBI)
M. McEvoy,1,4 A.G. Fiedler,1 A.L. Merrill,1 S.B. Coopey,1 M.C. Specht,1 K.S. Hughes,1 M.A. Gadd,1 M. Golshan,2 D.L. Smith,1 J. Breast Surgical Oncology, Massachusetts General Hospital, Boston, MA; 2. Brigham and Women's, Boston, MA.

Introduction: Axillary recurrence after a negative SNB is rare, potentially due to standard use of whole breast irradiation (RT) that includes much of the axilla. Concern exists that axillary failures will increase with PBI, which does not cover the axilla. We analyzed patients undergoing mastectomy-SNB to determine axillary recurrence rates for a negative SNB without RT. Methods: We retrospectively reviewed simple mastectomies at our institutions in 1998-2005. Patients with negative SNB or SNB with isolated tumor cells (ITCs) who did not receive radiation or axillary dissection were identified. Prophylactic mastectomies were excluded. Results: Among 340 patients who underwent mastectomy-SNB, 305 (90%) SNBs were negative and 35 (10%) contained ITCs. Median age at diagnosis was 50 years (range 39-82 yrs). Median follow up was 134 months (range 1-180 mo). 176 patients had invasive cancer and 164 had only intraductal cancer (DCIS). A mean of 2 SLN and 5 total nodes were removed in the mastectomy specimen (SLN and non-SLN). 139/176 (80%) of patients with invasive cancer and 49/164 (30%) with DCIS received systemic therapy. Mean duration of endocrine therapy was 6 years. Overall, only 3 patients (0.9%) had axillary recurrences. There were no axillary recurrences in patients with ITC's. In 2 patients with axillary relapses at 56 and 28 mo, the initial diagnosis was Grade 3 DCIS with negative SNBs; one ER+PR-HER2-, the other ER-PR+HER2-; neither had received tamoxifen. The third relapse was at 77 mo in a BRCA2 carrier with a 1mm grade 2 ER+PR-HER2- invasive ductal cancer with 3 years of endocrine therapy without chemotherapy. All 3 recurrences were treated with axillary lymph node dissection, systemic therapy, and radiation. Axillary dissections showed 6/7, 13/20 and 3/11 positive nodes, respectively. All three are NED 78, 96 and 67 months respectively. Conclusions: Risk of axillary failure is very low in SNB(-) mastectomy patients who do not receive radiation, suggesting that axillary failure rates will be low in SNB(-) patients who undergo lumpectomy and PBI.

PD-L1 expression has been associated with response to immunotherapy with checkpoint inhibitors. The over-expression of PD-L1 in newly diagnosed and metastatic cancer is not well documented. Methods: We performed array-based comparative genomic hybridization (aCGH) on surgical tumor samples from patients with solid tumors. Nuclei from distinct populations of tumor cells underwent DNA based flow sorting for aCGH analysis. DNA gene amplification and deletions were identified. The focus of this evaluation was the PD-L1 gene on chromosome 9 which is amplified in a subset of lymphomas. Results: Tumor samples from 315 subjects were evaluated including triple negative breast cancer (TNBC) n=45, HER2+ breast cancer n=10, ER+Her2- breast cancer n=8, pancreatic adenocarcinoma n=150 (including 30 liver metastases), colorectal carcinoma n=68, and glioblastoma n=34. High level (log.ratio $\geq 1$) amplification on chromosome 9 was identified in 13/45 (29%) of TNBC, 1/10 (10%) HER2+ breast cancer, 2/68 (3%) colorectal cancers, and 1/34 (3%) glioblastomas. A moderate level (log.ratio <1 < 0) of amplification was found in 18/45 TNBC, 17/68 colorectal cancers, and 11/34 glioblastomas. Interestingly, no amplification was found in the pancreatic or ER+ breast cancers. Only 9 TNBC showed no amplification. To determine other genes consistently co-amplified with PD-L1, a shortest region of overlap was identified. This 77 kb region showed that Jak2 (a member of the tyrosine kinase family, involved in cytokine signaling) and PD-L2 (another PD-1 ligand) are consistently co-amplified with PD-L1. Conclusion: We identified a focal amplification of chromosome 9 involving PD-L1, PD-L2, and Jak2 in a multiple solid tumors, and notably in a high proportion of TNBCs. Further validation of a larger dataset is being performed along with investigation into whether PD-L1 amplification results in functional changes. These results suggest that targeted checkpoint blockade may be useful for these patients.

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PD-L1 Gene Amplification in Triple-negative Breast Cancer: Implications for Immunotherapy

Introduction: PD-L1 and PD-L2 are immune regulatory molecules that limit the duration and level of the T-cell response. Tumor cells can block the immune response by expressing PD-L1 and inhibiting T-lymphocytes.
nodal status, use of neoadjuvant or adjuvant chemotherapy, type of surgery, post-mastectomy radiation, hormonal therapy, timing of reconstruction and rates of genetic testing were similar between groups. Median survival for the BRCA1/2 carriers and non-carriers was 41 and 40.5 months, respectively. No difference in overall survival was present between groups (p=0.98). Conclusion: BRCA4 mutations were frequently detected in a young, predominantly Hispanic population. These mutations correlated with more aggressive disease, however, no difference in overall survival was demonstrated at short-term follow-up.

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Background: Reconstruction of partial lumpectomy defects with reduction mammoplasty techniques can improve aesthetic outcomes and patient satisfaction. It can also allow for larger resections without compromising cosmesis. However, one concern with the significant tissue rearrangement is the increased risk for future biopsies or the inability to follow patients mammographically. We report on the post-operative mammographic findings and subsequent recommendations for biopsy in oncoplastic mammoplasty patients compared with lumpectomy alone. Methods: We performed a retrospective review of 98 patients from 2001 to 2009 who underwent partial mastectomy with oncoplastic reduction mammoplasty (49 patients) compared to an age-matched cohort of lumpectomy alone (49 patients). Mammography reports at 6 months, 1, 2, and 5 years post-operatively were reviewed for Breast Imaging Reporting and Data System (BI-RADS) scores, predominant findings, and recommendations for subsequent imaging or biopsy. Results: There was no significant difference in abnormal mammographic findings between the oncoplastic and lumpectomy cohorts at 6 months, 1, 2 and 5 years (p>0.05). Biopsy rates over the five year period did not differ significantly between the two cohorts (11 (22%) in the lumpectomy cohort, 15 (31%) in the oncoplastic cohort, p=0.25). Overall cancer-to-biopsy ratio was 18% (2 of 11) in the lumpectomy cohort and 33% (5 of 15) in the oncoplastic cohort (p=0.65). Conclusions: Although substantial tissue rearrangement is performed at the time of oncoplastic mammoplasty, our results demonstrate no increased incidence of post-operative mammographic abnormalities and recommendation for biopsy when compared to lumpectomy alone. These results support the incorporation of this technique as a way to optimize outcomes for breast conservation.

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Background: Axillary staging is an essential component of breast cancer management but there is ongoing debate regarding the need for sentinel lymph node (SLN) staging prior to neoadjuvant chemotherapy (NEO). Methods: Our study cohort included 417 NEO patients (pts) undergoing comprehensive, multidisciplinary evaluation, 1996-2014. Pre-NEO axillary node status was assessed by clinical exam and ultrasound with FNA biopsy in cases of abnormal appearing nodes. A definitive pre-NEO SLN biopsy was performed if the clinical work-up was neg. Pts with node-pos disease before NEO underwent a post-NEO axillary lymph node dissection at time of definitive surgery. Results: Median patient age was 49; mean tumor size was 4.17 cm. 98 pts (23.5%) had documented pre-NEO node neg axillary status. Of the 319 pre-NEO node pos pts, 194 (60.5%) had their axillary disease confirmed by FNA and 71 (22.3%) were found to have pre-NEO SLN mets following a neg imaging work-up, yielding a clinical/imaging false neg rate of 22.2%. At completion of NEO, 171 partial (53.6%) and 101 complete clinical response (24.2%) were observed. Mean residual tumor size was 1.61. 114 (35.7%) had no residual axillary disease post-NEO. Median f/u was 2 yrs (range 0.25-18 yrs). 100 pts (24%) recurred, with median time to recurrence 3.2 yrs (range 0.25-12 yrs). In the pre-NEO node neg there were 4 local and 4 distant recurrence (4.2%). Of 114 pts downstaged from node pos to neg there were 6 local (6.3%) and 13 distant (13.8%) recurrences (Graph 1). Locoregional radiation was associated with fewer local recurrences in the downstaged patients from 20% to 5%. The 160 persistently pos node positive pts had 22 local recurrences (13.8%) and 40 distant (25%) recurrences. Conclusion: Our experience suggests that comprehensive histopathologic staging of the axilla prior to NEO is prognostically valuable. Definitive SLN biopsy is necessary for patients with negative axillary ultrasound evaluation. Distinguishing pts that are downstaged to node-neg from node-neg at presentation identifies a cohort for whom more aggressive locoregional treatment and systemic therapy may be warranted.

Distant recurrence by Pre-NEO nodal status.

P86
Comparison of Intraoperative Specimen Mammography to Standard Specimen Mammography: A Randomized Trial C.L. Miller,* S.B. Coopey, E.A. Rafferty, M.A. Gadd, B.L. Smith, M.C. Specht. Massachusetts General Hospital, Boston, MA.

Background: During wire-localized excisions, standard specimen mammography (SSM) is performed to confirm presence of the target and evaluate margins. SSM can be time-consuming due to specimen transport and radiologist interpretation time. Intra-operative specimen mammography (ISM) is an alternative that allows surgeons to view images in the operating room (OR). We compared operative and interpretation times for SSM and ISM in a randomized cohort. Methods: Women undergoing wire-localized excision for breast cancer or imaging abnormality were randomized to SSM or ISM. For SSM the specimen was imaged in the radiology department. Surgeons could not see the images and relied on radiologists’ verbal description of target lesion and margins. For ISM the specimen was imaged using the ISM device and interpreted by the surgeon, then sent to radiology for SSM. Interpretation time was measured from specimen leaving the OR until radiologist call for SSM and time from specimen placement in the ISM device until surgeon interpretation for ISM. OR and interpretation times were compared between arms. Concordance between ISM and SSM for target and margin interpretation was evaluated. Results: 72 patients were randomized, 36 ISM and 36 SSM. 1 ISM patient underwent SSM only and was analyzed as intention to treat. Median OR and procedure times were similar between arms, 68 (29-180) and 48.5 (17-138) minutes for ISM, 74 (35-177) and 54 (17-40) minutes for SSM (p=0.68, p=0.72 respectively), likely since specimens in both groups traveled to radiology for SSM. Median
interpretation time and time from procedure start to interpretation was shorter for ISM compared to SSM. Conclusions: For ISM compared to SSM, 1 (5.2-6.0) and 19 (6-41) minutes for ISM, 9 (4-18) and 31 (16-60) minutes for SSM (p=0.0001 for both). Among specimens with ISM and SSM, concordance between ISM and SSM was 100% (35/35) for target and 93% (14/15) for margins in patients undergoing lumpectomy. Conclusions: Although randomized trials for lumpectomy did not show additional benefit, SSM significantly reduced interpretation times while accurately identifying the target. This could result in decreased operative costs resulting from shorter total OR and procedure times with use of ISM.

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Presence of Circulating Tumor Cells and Disseminated Tumor Cells does not Predict Site of Recurrent or Metastatic Disease
S.M. DeSnyder,†, A. Lucci, S.M. DeSnyder, C. Hall, M. Kueker, A. Anderson, A. Lucci. Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.

Introduction: Published studies have shown the presence of micrometastasis, including circulating tumor cells (CTCs), circulating blood and disseminated tumor cells (DTCs), bone marrow, predicts outcomes in patients with breast cancer. However, no studies have examined if the site (bone versus blood marrow) of micrometastasis predicts recurrent disease or site of distant metastasis. The purpose of this study was to assess if patients with CTCs and DTCs have a predilection for local recurrence or specific metastasis sites. Methods: A total of 623 patients with clinical stage I-III breast cancer seen at a single tertiary care center provided consent to participate in an IRB-approved study involving collection of blood (7.5 ml x 2 tubes) and bone marrow (5 ml x 2 tubes) at the time of surgery for their primary breast cancer. CTCs were identified using the CellSearch™ System (Janssen). CTCs were defined as nucleated cells lacking CD45 and expressing CK 8, 18, or 19. The presence of 1 or more cells per 7.5 ml of blood was defined as a positive result. DTCs were identified by an anti-cytokeratin (CK) antibody cocktail (AE1/AE3, CAM5.2, MNF 116, CK8 and 18) following cytoospin. A positive result was defined as the presence of 1 or more cells per 5 ml of bone marrow. Patients who developed metastasis were compared to determine if CTCs or DTCs predicted recurrent disease or site of distant metastasis at the median follow-up of 48 months. Metastasis sites included bone, brain, lung, and liver as well as recurrent local disease. There was no significant difference in recurrent local disease or site of distant metastasis between patients with CTCs, DTCs, and neither. Conclusions: CTCs and DTCs do not have a predilection for specific sites of distant metastasis or recurrence. This supports the hypothesis that microscopic disease is dynamic and can circulate and metastasize to different organs.

P88
Combined Chemotherapy and Radiation are associated with Improved Overall Survival for Metastatic Breast Cancer

Background Metastatic breast carcinoma is a rare form of breast cancer and predictors of survival have not been definitively determined. Our aim was to determine which factors predict overall survival (OS) for this rare breast cancer using a national database. Methods A retrospective review of the National Cancer Data Base from 1998-2006 was conducted of all patients with Stage I-II metastatic breast cancers. After controlling for age, co-morbidities, race, insurance status, facility type and location, grade, tumor size, nodal status, receptor status, and regional and systemic therapies, predictors of 5-year OS were identified using Kaplan-Meier estimates and Cox hazard model analysis. Results 2,449 patients met study criteria. 1,207 (49%) of patients had T2 tumors, 1,752 (72%) were N0, and 1,607 (66%) had poorly/undifferentiated tumors. 1,119 (46%) underwent lumpectomy and 1,330 (54%) underwent mastectomy. 1,448 (59%) received chemotherapy (CT), 1,174 (48%) received radiation (RT), and 223 (9%) received hormonal therapy (HT). The 5-year OS for the entire cohort was 70% with a median follow-up time of 69 months. The 5-year OS for patients who received CT alone was 66% vs 77% for chemotherapy + radiation (CRT) (p=0.0004); there was no difference in the 5-year OS between patients who received RT only (74%) and those who received CRT (p=0.243). Factors independently associated with an increase in mortality on Cox hazard modeling were older age, Native American/Alaskan race, higher co-morbidity scores, larger tumors, and nodal metastases. CRT and chemotherapy + radiation + hormonal therapy (CRTH) were independently associated with improved OS (CRT: HR 0.70, 95% CI [0.530, 0.935], p=0.015; CRTH: HR 0.47, 95% CI [0.254, 0.879], p=0.018) compared to patients who received no additional therapy. CT alone, radiation + hormonal therapy, and radiation + hormonal therapy did not independently predict survival. Conclusions Patients with metastatic breast cancer had an improved 5-year overall survival following surgical resection when treated with combined regional and systemic therapy.

P89
A Comparison of Treatment Outcomes for Patients with Close or Positive DCIS Margins after Mastectomy for Early Stage Breast Cancer
M. Freyvogel,*, C. O’Rourke,*, S. Valente,‡ A. Fanning,*, J. Dietz,‡ 1. University Hospitals Case Medical Center, Westlake, OH; 2. Cleveland Clinic Foundation, Cleveland, OH.

Introduction: With constant improvements in breast cancer screening, ductal carcinoma in situ (DCIS) represents up to 25% of newly diagnosed breast cancers. Positive margin status is a known factor for local recurrence after breast conservation, however, the significance after mastectomy is unclear. Our aim was to identify the impact on local control of a positive DCIS margin after mastectomy. Methods: We performed a retrospective chart review of all patients who had mastectomy for pure DCIS or DCIS with a T1 invasive component over a 10 year period. Patients were categorized into 4 groups based on margin status: positive, <1mm, 1-2mm and >2mm. Positive margins were excluded from analysis. Adjuvant therapy including surgical re-excision, radiation, endocrine therapy and chemotherapy was recorded, as well as local and distant recurrence. Results: A total of 629 mastectomies from 603 patients were eligible for analysis. Eleven (1.75%) mastectomies had a positive DCIS margin, 43 had a margin <1mm, and 22 had a margin of 1-2mm. Sixteen patients received postmastectomy radiation, including 8/11 with a positive DCIS margin and 3/43 with a margin <1mm. Median follow-up was 5 years (0.5-13 years). There were 27 total recurrences, 17 local and 10 distant. Of 254 patients with pure DCIS, the overall recurrence rate, both local and distant was 2.76% (7/254). There were no recurrences among any patients with a positive DCIS margin, or with a margin <1mm. Interestingly, of the 27 recurrences, 26 had a margin >2mm and 1 had a margin of 1-2mm. None of the patients who received postmastectomy radiation developed a recurrence. In addition, none of the patients who developed a recurrence received postmastectomy radiation. Conclusions: Positive DCIS margins after mastectomy is found infrequently. Positive and close DCIS margin status does not appear to be directly related to recurrence, particularly for patients receiving postmastectomy radiation.

P90
Expression of HER-2 Receptor is not associated with Worse Outcomes in Breast Cancer: An 18-year Prospective Follow-up
K.J. Rosso,* E. Karamanos, D.S. Nathanson. General Surgery, Henry Ford Hospital, Grosse Pointe Woods, MI.

Introduction: Before anti-HER-2/neu targeted therapy, HER-2 amplification was an independent predictor of overall survival and time to relapse in patients with breast cancer. We hypothesized that the use of HER2-directed systemic therapies changed the prognosis of HER2-positive patients to that of HER-2 negative patients. Methods: From a prospective database of breast cancer patients undergoing sentinel lymph node biopsy (SLNB) from 1994 to 2013 HER-2/neu status was dichotomized as positive or negative. Other demographics included histologic type, grade, ER/PR status, age, location of the tumor and molecular class. Outcomes included survival, evidence of positive SLN, recurrence of the tumor, distant metastases and diagnosis of a second primary tumor. A multivariate analysis was performed to adjust for differences at p < 0.05 from the bivariate analysis between the two groups. Results: Of 2,067 patients, 385 patients were HER2 positive for 326 and negative for 1,741 patients. HER-2/neu positive patients were more likely to present with a G3 histologic grade (48% vs. 23%, p < 0.001), invasive ductal carcinoma (91% vs. 85%, p=0.002) and less likely to have positive ER and PR receptors (65% vs. 82%, p<0.001 and 54% vs. 76%, p<0.001). After adjusting for differences, HER-2/neu status did not change long term mortality, positive SLN, local or distant metastases or development of a second primary [AOR (95% CI), adj.] p= 0.82 (0.53, 1.24), p = 0.343; 1.06 (0.65, 1.73), p = 0.809; 1.35 (0.79, 2.31),
**P91**

**Overall Survival in Patients with a Re-excision following Breast Conserving Surgery compared to those without in a Large Population-based Cohort**

**E.L. Vos,1* A. Jager,1 K. Verhoef,1 A. Voogd,2 L.B. Koppert1 1. Surgery, Erasmus MC Cancer Institute, Rotterdam, Zuid-Holland, Netherlands; 2. Comprehensive Cancer Centre South, Eindhoven, Netherlands.**

**Introduction:** The aim was to investigate the overall survival of invasive breast cancer patients with primary breast conserving surgery (BCS) followed by re-excision compared to those with primary BCS only. Which is interesting since the Dutch re-excision indications are less stringent compared to other European and Northern American countries (SSO/ASTRO guideline). Methods: Retrospective analyses in women <75 years with breast cancer stage pT1-T3 treated by BCS and radiotherapy between 1999-2012 from a population-based database. The national guideline recommends to reserve re-excision for invasive tumors showing ‘more than focally positive’ margin since 2002. Patients were divided into ‘primary BCS only’, ‘re-excision by BCS’, and ‘re-excision by mastectomy’. In multivariable Cox regression analysis was adjusted for patient and systemic treatment characteristics. Results: A total of 11,695 patients were included of which 2,156 (18.4%) underwent re-excision. Median time of follow-up was 61 months (IQR 26-101). The 5-year overall survival rates in the ‘primary BCS only’, ‘re-excision by BCS’, and ‘re-excision by mastectomy’ group were 92%, 95%, and 91%, respectively. The 10-year overall survival rates were 81%, 82%, and 79%, respectively (P=0.20). After multivariable analyses no significant association was observed between use of and type of re-excision and overall survival. Conclusions: The overall survival of breast cancer patients with a re-excision did not significantly differ from the survival of women who underwent primary BCS only. Avoiding re-excision only for those tumors showing ‘more than focally positive’ resection margin appears safe, supposing long-term safety of the recent SSO/ASTRO guideline that more cautiously recommended re-excision for tumors showing ‘ink on tumor’.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>HER 2 neg (-) (n = 1,714)</th>
<th>HER 2 neg (+) (n = 526)</th>
<th>p-value</th>
<th>AOR (95% CI)</th>
<th>adj-p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive SLN</td>
<td>290 (16.9)</td>
<td>33 (6.3)</td>
<td>0.033</td>
<td>1.00 (0.65, 1.53)</td>
<td>0.909</td>
</tr>
<tr>
<td>Recurrence</td>
<td>82 (4.7)</td>
<td>21 (4.0)</td>
<td>0.187</td>
<td>1.04 (0.55, 1.95)</td>
<td>0.907</td>
</tr>
<tr>
<td>Second Primary</td>
<td>210 (12.1)</td>
<td>34 (6.5)</td>
<td>0.402</td>
<td>1.05 (0.57, 1.95)</td>
<td>0.839</td>
</tr>
<tr>
<td>Mortality</td>
<td>114 (6.5)</td>
<td>32 (6.1)</td>
<td>0.035</td>
<td>1.35 (0.76, 2.31)</td>
<td>0.276</td>
</tr>
</tbody>
</table>

**P92**

**The Impact of Neoadjuvant Chemotherapy on Anxiety in Breast Cancer Patients**


**Background:** Neoadjuvant chemotherapy is gaining favor in the treatment of breast cancer. This approach gives patients and providers additional information about how breast tumors respond to therapy. More knowledge could make patients less anxious. The aim of this study was to determine if patients had less anxiety after neoadjuvant chemotherapy than patients following adjuvant chemotherapy. Methods: 429 patients were surveyed regarding quality of life, specifically anxiety symptoms, following adjuvant and neoadjuvant chemotherapy. Patients answered questions about their perceived anxiety 30 days following treatment and long term. Results: 170 patients responded to the survey. 57 of respondents (33%) had neoadjuvant chemotherapy (NAC) and 113 (66%) adjuvant chemotherapy (AC). NAC chemotherapy patients were significantly younger (P=0.001). While overall there were no statistically significant differences in responses endorsing anxiety between NAC and AC groups, younger NAC patients (30-50 years old) had less anxiety long-term following treatment than AC patients (P=0.001). Other NAC patients (>50) trended towards more anxiety (0.08). This was especially true of patients aged 60-69, who were more anxious than those who had undergone adjuvant chemotherapy (0.001). There were no differences in anxiety between NAC and AC patients based on stage at diagnosis. Conclusions: Younger breast cancer patients were less anxious after neoadjuvant chemotherapy, while older patients, specifically patients age 60-69, experienced more long-term anxiety when compared to age matched peers who had adjuvant chemotherapy. These differences have implications for education and information provided to specific populations of patients prior to therapy.

**P93**

**Predictors of Tamoxifen Use in Women with Estrogen-receptor Positive DCIS**


**Background:** Tamoxifen (Tam) use in estrogen-receptor positive (ER+) ductal carcinoma in-situ (DCIS) has been shown to reduce the incidence of both non-invasive and invasive locally- recurrent and contralateral breast cancer. There is variability in recommendations for Tam by providers and acceptance of Tam by patients with ER+ DCIS. Few studies have evaluated the factors associated with Tam use in ER+ DCIS. Methods: The California Cancer Registry was queried for female patients diagnosed with ER+ DCIS and treated with lumpectomy or unilateral mastectomy from 2000-2011. Patient demographics and clinical characteristics were analyzed for association with Tam use in ER+ DCIS. Results: A total of 4,442 (79.0%) patients underwent lumpectomy and 1,177 (21.0%) underwent unilateral mastectomy. Of the total cohort, 1,803 (32.1%) patients were treated with Tam, and the remaining 469 (8.3%) were recommended Tam but administration was not documented. Performance of lumpectomy predicted Tam compared to mastectomy (OR=2.05, 95% CI 1.78, 2.36). Asian/Pacific Islanders were more often recommended Tam when compared to whites (OR = 1.31 95% CI: 1.13, 1.52). Other races did not show significant differences in Tam when compared to whites. Patients younger than 70 were more often recommended Tam (age 18-49: OR = 1.42 95% CI 1.17, 1.72; age 50-69: OR = 1.54 95% CI: 1.30, 1.821). Managed care/HMO/PPO patients were more often recommended Tam when compared to Medicare (OR = 1.21 95% CI: 1.03, 1.42). Other insurance types, reconstruction, and marital status were not significant. Conclusions: Despite current guidelines, utilization of Tam after DCIS remains low, having been recommended to 40% of ER+ DCIS patients and utilized by less than one-third. While reconstruction and marital status have no impact on predicting Tam use, significant predictors include lumpectomy as opposed to unilateral mastectomy, Asian race, younger age, and managed care insurance. Further work is merited to understand patterns of Tam usage in patients with DCIS.
P94
Local Recurrence and Metachronous Contralateral Breast Cancers Diagnosed at a Community-based Regional Cancer Program over a 10-year Period: Patterns and Practice P.A. Soriano,1,2 L. Whitaker,2 N. Neubauer,2 J. Varady,2 W. Wisbeck,2 D. Little,2 W. Wang,1 P. Jiang,1 S.R. Martinez,1 The Everett Clinic and Providence Cancer Partnership, Everett, WA; 2. Providence Cancer Partnership, Everett, WA.

Background: Factors that contribute to breast cancer local recurrence (LR) as opposed to metachronous contralateral breast cancer (MCBC) are largely unknown. Our aim was to identify differences in tumor and treatment-related factors that may influence LR and MCBC. Methods: The Cancer Registry data of a Commission on Cancer approved community based cancer program was used to identify women diagnosed with secondary breast events (LR or MCBC) from 2002 to 2012. Patients were categorized as having LR or MCBC. We assessed patient, tumor, and treatment-related factors as univariate predictors of LR or MCBC using Fisher’s exact test. Variables assessed included patient race/ethnicity, primary tumor histology, tumor grade, hormone receptor and HER-2/neu overexpression status, type of primary surgery, and use of chemotherapy, hormonal therapy, and radiation therapy. Results: Between 2002 and 2012, 51 patients experienced secondary breast events, including 6 LR (11.8%) and 45 MCBC (88.2%). The median time to any secondary breast event was 39 months. On univariate analysis, differences were noted between LR and MCBC with respect to tumor histology (P=0.05), tumor grade (P=0.03), estrogen receptor expression (P=0.008), progesterone receptor (PR) expression (P=0.02), and use hormonal therapy in patients that were PR positive (P=0.05). Conclusion: The majority of secondary breast events noted in our patient population were MCBCs. This indicates that potential ways to improve rates of MCBC may involve more robust contralateral breast screening. Tumor and treatment-related factors were identified that may modulate the risk for MCBC and LR.

P95

Background: BRCA mutation carriers are at increased risk of developing breast cancer (BC). Optimal BC surveillance has been well characterized in BRCA mutation carriers without a personal history of BC undergoing bilateral prophylactic mastectomy. In this study, we sought to determine the accuracy of preoperative imaging in this high risk population, in addition to correlating pre-operative imaging as a predictor of outcome. Methods: Retrospective chart review of a prospectively maintained database identified 82 patients who were found to carry a germline mutation in BRCA-1 or BRCA-2 who underwent bilateral prophylactic mastectomies at an academic Breast Center between 2006 and 2013. Patient, imaging, and pathology characteristics were evaluated. Results: Of the 82 BRCA mutation carriers, 76 had preoperative imaging (mammogram or MRI) and were included for analysis. Median age was 39.5 years (range: 23-66). 54 (71%) patients were BRCA-1 carriers and 22 (29%) were BRCA-2 carriers. Sixty five (86%) patients had either a preoperative mammogram (n=32; 42%) or MRI (n=51;67%) within 6 months of surgery. 48 (63%) patients had both a mammogram and MRI. 64 patients (84%) had bilateral skin sparing mastectomies; 35 patients (46%) underwent sentinel node (SN) procedures. 54 (71%) patients had benign pathology, although preoperative imaging identified abnormalities in only 10 (19%) patients. 11 (14%) patients had ADH/ALH of which 10 (91%) had no corresponding imaging abnormality. 11 (14%) patients had either DCIS or invasive cancer on final pathology and 7 (9%) of these patients had no imaging abnormalities. There were no positive SNs. Conclusions: Pre-operative mammogram and MRI did not detect all the BC or atypical proliferative lesions seen in this high risk group of patients. Preoperative imaging for patients with BRCA mutations does not correlate with their final histopathology. This data suggests that preoperative imaging may not be useful for surgical planning in this patient population.

P96
Can Twitter Social Media be an Effective Tool for Breast Cancer Survivor Support and Education? D.J. Attai,1,4 J. Landerkeszer,1 J.M. Schoger,1 A.C. Staley,1 M.S. Cowher,1 J. Surgery, David Geffen School of Medicine at UCLA, Burbank, CA; 2. Gunderson Health System, LaCrosse, WI; 3. Cleveland Clinic, Cleveland, OH; 4. Women With Cancer, The Woodlands, TX; 5. Akari Health, Charlestown, MA.

Background: Despite their reported benefits, approximately 60% of women do not attend breast cancer support groups (SG). Many online resources for support exist, but information regarding the effects of participation is lacking. We report the results of a Twitter breast cancer support community participant survey. Methods: The Breast Cancer Social Media (#BCSM) Twitter support community began in July 2011. IRB approval with waiver of informed consent was obtained for a de-identified survey which was posted online for two weeks. Results: There were 206 respondents, with a median age of 45-54. 93% were female. 74% of respondents were from the United States. 92% were Caucasian. 83% had completed a 4-year college degree. 69% had been treated for breast cancer. 14% reported having metastatic breast cancer. 81% of respondents reported increased overall knowledge about breast cancer. Percentage of respondents noting increased knowledge in specific areas included: 86% survivorship, 80% metastatic breast cancer, 70% cancer types and biology, 66% clinical trials and research, 56% treatment options, 56% breast imaging and 54% genetic testing and risk assessment. 31% reported that participation led them to seek a second opinion or bring additional information to the attention of their treatment team. 73% reported plans to increase their outreach and advocacy efforts as a result of participation. Levels of reported anxiety before and after participation were analyzed. 29 of 43 patients (67%) who initially reported “high or extreme” anxiety reported “low or no” anxiety after participation, a statistically significant difference. (p=0.001). Also, no patients initially reporting “no or low” anxiety prior to participation reported an increase to “high or extreme anxiety” after participation. Conclusions: Many online breast cancer patient resources exist, but data has been lacking regarding benefits of participation. This study demonstrates that breast cancer patients’ perceived knowledge can be increased and that anxiety can be decreased by participation in an online SG.

P97
Implementing a Radioactive Seed Localization Program in Breast Cancer Surgery: A Multidisciplinary Approach D. Black,1* J. Wagner,1 R.F. Hwang,1 S.M. Desnyder,1 F. Ames,1 T. Yoburn,1 N. Wipf,1 S. Gollhar,1 F. Mercier-Bernstam,5 B.E. Dogan,1 M. Dryden,1 W. Yang,1 E. Rohren,1 M. Gilcrease,1 H.M. Kuerner,1 K.K. Hurst,1 A.S. Caudle,1 A.A. Cauley,1 Surgical Oncology, MD Anderson Cancer Center. Houston, TX; 2. University of Kansas Medical Center, Kansas City, KS.

Background: Radioactive iodine seed localization (RSL) is an alternative to wire localization (WL) to guide breast conserving surgery (BCS). Benefits of RSL compared to WL include improved patient comfort, less risk of dislodgment, and efficient operative scheduling. RSL requires a multidisciplinary approach, and efficient operative scheduling. RSL compared to WL include improved patient comfort, less risk of dislodgment. Results: There were 206 respondents, with a median age of 45-54. 93% were female. 74% of respondents were from the United States. 92% were Caucasian. 83% had completed a 4-year college degree. 69% had been treated for breast cancer. 14% reported having metastatic breast cancer. 81% of respondents reported increased overall knowledge about breast cancer. Percentage of respondents noting increased knowledge in specific areas included: 86% survivorship, 80% metastatic breast cancer, 70% cancer types and biology, 66% clinical trials and research, 56% treatment options, 56% breast imaging and 54% genetic testing and risk assessment. 31% reported that participation led them to seek a second opinion or bring additional information to the attention of their treatment team. 73% reported plans to increase their outreach and advocacy efforts as a result of participation. Levels of reported anxiety before and after participation were analyzed. 29 of 43 patients (67%) who initially reported “high or extreme” anxiety reported “low or no” anxiety after participation, a statistically significant difference. (p=0.001). Also, no patients initially reporting “no or low” anxiety prior to participation reported an increase to “high or extreme anxiety” after participation. Conclusions: Many online breast cancer patient resources exist, but data has been lacking regarding benefits of participation. This study demonstrates that breast cancer patients’ perceived knowledge can be increased and that anxiety can be decreased by participation in an online SG.
had re-excision segmental mastectomy and 12 (2.6%) underwent mastectomy. Conclusions: RSL in BCS is a safe approach for surgical management of breast cancer presenting with focal or extensive imaging findings. A RSL program can be successfully implemented with a multidisciplinary team.

P98 Prospective Trial of Breast MRI versus Ultrasound (US) for Evaluation of Response to Neoadjuvant Chemotherapy S.J. Gonzalez,* B. Mooney, H. Lin, J. Kiluk, C. Laronga, M.C. Lee. Surgical Oncology, H. Lee Moffitt Cancer Center, Tampa, FL.

Introduction: Preoperative imaging to assess response to neoadjuvant chemotherapy in breast cancer is routine, but no standard imaging modality is accepted. Our hypothesis is that ultrasound (US) is not inferior to MRI evaluating response to neoadjuvant treatment. Methods: A single institution, IRB-approved, prospective trial of primary invasive ductal breast cancer patients receiving neoadjuvant chemotherapy enrolled women from 9/2008-9/2012. Two and 3-dimensional (3D) US, and MRI images of pre- and post-neoadjuvant tumors were obtained. Skin involvement or inadequate images were excluded. Results on imaging were then compared to surgical pathology and were evaluated by non-parametric Wilcoxon Signed-Rank test. US to MRI agreement was determined by the Kappa coefficient, and predictive values were also analyzed. Estrogen receptor (ER), progesterone receptor (PR), and Her2neu subgroups were compared by Kruskal-Wallis test. ER/PR staining <5% were considered negative; Her2neu status was determined by in-situ hybridization. Results: Forty-two patients enrolled; 39 had evaluable data. Four patients were Her2neu positive, 17 (46%) had triple-negative tumors. Among eleven (28%) with complete pathologic response (pCR), ultrasound correctly predicted pCR in 6 (54.5%), compared to 8 (72.7%) by MRI, showing a substantial agreement between the US to MRI in predicting pCR (kappa=0.62). In terms of predictive value, MRI had the lowest positive predictive value (PPV=57%), compared to the 2D (75%) and 3D (63%) US in predicting pCR. The corresponding negative predictive values (NPV) were 88%, 84% and 81%, respectively. Furthermore, the false positives of pCR had an error of up to 1.6 cm³, for the MRI, and 1 cm³ for the 2D (75%) and 3D US, respectively. There was no significant difference between 2D and 3D US modalities. Similarly, there was no significant difference in volume estimation of pathology between the imagine tests evaluated, even after stratified by receptor status. Conclusion: The estimation of residual tumor by US is non-inferior to MRI in evaluation of residual tumor burden after neoadjuvant breast cancer therapy, including prediction of pCR.

MRI and US showing a breast tumor. The 2D and 3D US showed no difference in volumetric evaluation. Similarly, the MRI image displayed shows the similarities of these tests to evaluate breast lesions.


Key words: lobular intraepithelial neoplasia, atypical lobular hyperplasia, lobular carcinoma in situ, upstaging, core needle biopsy, excision, surgical management Background: Breast lobular intraepithelial neoplasia (LIN) includes lobular carcinoma in situ (LCIS) and atypical lobular hyperplasia (ALH). These are often incidental findings, and the management of LIN remains controversial. The objective of this study was to define the rate of upstage after diagnosis of LIN on core needle biopsy, and to assess the clinical, radiological and pathologic factors that are associated with upstaging. Methods: A retrospective review was performed, including 50 women diagnosed with either LIN NOS (not otherwise specified), ALH or LCIS breast lesions on core needle biopsy at the Cedars Breast Centre of the McGill University Health Center between 2000 and 2012. Results: Excisions were performed in 56 (70%) cases. The cohort included 46 cases of ALH (57%), 22 LIN NOS (28%), and 12 LCIS (15%). Upstaging of the lesion was documented in 15.2% (7/47) of ALH, 13.6% (3/22) of LIN NOS and 40% (4/10) of LCIS lesions. The total proportion of upstaged lesions constituted 25% (14/56). Of the upstaged lesions, 42.9% (6/14) were upstaged to DCIS, 14.3% (2/14) to pleomorphic LCIS, 14.3% (2/14) to invasive ductal carcinoma, 21.4% (3/14) to invasive lobular carcinoma, and 7.1% (1/14) to invasive mammary carcinoma. The upstaging associated with LCIS was 40.0%, compared to 13.6% associated with LIN NOS and 15.2% with ALH. Mammographically-defined calcifications, prior breast cancer, age at biopsy, as well as both biopsy and surgical pathology results were not found to be associated with upstaging. Conclusions: We describe an increase in upstaging, with the overall proportion of upstaged lesions being 25%. Upstaging did not appear to be associated with various clinical, radiological and pathologic parameters. These findings suggest that patients with breast LIN on a core needle biopsy might benefit from surgical excision of the lesion. Conflicts of interest: The authors declare no conflict of interest. No benefits in any form have been or will be received to the subject of this manuscript.

P100 Use of Twitter during the Society of Surgical Oncology and American Society of Breast Surgeons 2014 Annual Meetings M.S. Cowherd, N.J. Gusanli, D.J. Attai.* J. Surgery, David Geffen School of Medicine at UCLA, Burbank, CA; 2. Penn State University, Hershey, PA; 3. Allegheny Health Network, Pittsburgh, PA.

Introduction: Twitter is a social media (SM) platform using 140-character messages. It is increasingly used for communication at medical meetings. By using hashtags (the # symbol with a word/phrase), users can monitor related tweets. We detail the use of twitter during 2 national medical meetings - the Society of Surgical Oncology (SSO) and the American Society of Breast Surgeons (ASBrS). Methods: Both the SSO and ASBrS included specific Twitter content and encouraged Twitter use during their 2014 annual meetings. SSO: For the first time, SSO encouraged all attendees to tweet (#SSO2014). A session entitled “Social Media Update” was offered which included “Twitter for the Surgical Oncologist” and “Hospital/Provider/Patient Apps”. ASBrS: 2014 was the 2nd year that ASBrS encouraged Twitter use, including formal SM content in the pre-meeting and general sessions. Attendees were encouraged to tweet (#ASBrS). Specific SM topics included “Twitter 101,” “Marketing,” and “Social Media For Your Practice”. A live Twitter display was used during the “Benign Breast”, “Hormones/High Risk / Breast Cancer”, and “Survivorship” sessions. The audience was instructed to tweet questions which were reviewed and displayed during the Q&A period. We believe this was the first use of live Twitter Q&A at a medical conference. Results: SSO: There were ~1800 meeting attendees, of which 67% were physicians, generating 36,547 impressions (number of tweets x number of followers). ASBrS: There were 1460 meeting attendees, of which 94% were physicians. 571 Twitter participants authored 3,743 tweets resulting in 14,553,798 impressions. Tweet activity is shown in Figure 1. Compared to 2013, impressions increased by 76%, number of tweets increased by 77%, and participants increased by 83%. Discussion: Twitter has become an important way in which attendees of medical meetings share content and encouraged Twitter use during their 2014 annual meetings. The audience was instructed to tweet questions which were reviewed and displayed during the Q&A period. We believe this was the first use of live Twitter Q&A at a medical conference. Results: SSO: There were ~1800 meeting attendees, of which 67% were physicians, generating 36,547 impressions (number of tweets x number of followers). ASBrS: There were 1460 meeting attendees, of which 94% were physicians. 571 Twitter participants authored 3,743 tweets resulting in 14,553,798 impressions. Tweet activity is shown in Figure 1. Compared to 2013, impressions increased by 76%, number of tweets increased by 77%, and participants increased by 83%. Discussion: Twitter has become an important way in which attendees of medical meetings share information with interested parties. Impressions generated results in increased exposure of the society for non-member physicians, researchers, and the public. Twitter SM will increasingly become a means by which content presented at meetings is disseminated to the health care social media environment.
P102
Clinical Significance of Para-aortic Lymph Node Dissection for Advanced or Metastatic Colorectal Cancer in the Current Era of Modern Chemotherapy
K. Uehara,* A. Arimoto, T. Kato, H. Nakamura, K. Tadahiro, Y. Yokoyama, T. Ebata, M. Nagino. Division of Surgical Oncology, Department of Surgery, Nagoya University Graduated School of Medicine, Nagoya, Japan.

Background: Para-aortic lymph node (PALN) is a common site of metastasis from colorectal cancer. It is considered as systemic disease and surgical resection is not generally indicated, even in the patients with isolated disease. On the other hand, modern chemotherapy accompanied with aggressive surgery not only for marginally resectable liver metastasis but also for initially unresectable disease has improved survival. However, the clinical significance of PALN dissection (PALND) in the current era of modern chemotherapy has not been fully discussed.

Methods: Between November 2006 and February 2013, 14 patients (11 men and 3 women with a median age of 66 years) underwent PALND with curative intent for advanced or metastatic colorectal cancer. Standard resected region was below renal vessels and above aortic bifurcation in the left side colon and rectal primary. Most patients excluding medically unfit patients received aggressive modern chemotherapy. The median follow-up in this study was 33.2 (range, 4.3–50.6) months.

Results: Primary tumors were located on the right in 2 patients, on the left colon in 4 patients, and on the rectum in 8 patients. The timing of metastasis was metachronous in 5 patients and the other 9 patients was stage IV. Eleven patients (79%) received perioperative aggressive modern chemotherapy, although 3 patients did not because of their poor performance status. Neoadjuvant chemotherapy with targeted drugs was introduced in 9 patients (64%) and 6 patients received adjuvant chemotherapy. Recurrence after PALND occurred in 12 patients (86%). The most common site was the lung in 6 patients (43%). Four of 12 relapsed patients could undergo re-resection. The 1 and 3-year disease-free survivals were 39.3% and 7.9%, respectively. The 1 and 3-year overall survival were 92.3% and 41.2%, respectively. Conclusion: Recurrence rate after PALND with curative intent for carefully selected patients was still high even in the current era of modern chemotherapy. However, some patients could be cured or survive for long term, therefore, we should not deny the efficacy of PALND.

P103
Peritoneal Metastases from Small Bowel Cancer: Results of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in the Netherlands
T.R. Van Oudheusden,1,* V.E. Lemmens,2 H.J. Braam,3 B. Van Ramshorst,4 N. Sluiter,2 E.A. Te Velde,5 A.M. Mehta,6 V.J. Verwaal,5 I. De Hingh,1 1. Surgical Oncology, Catharina Hospital, Eindhoven, Netherlands; 2. Netherlands Cancer Registry, Eindhoven, Noord Brabant, Netherlands; 3. St. Antonius Hospital, Nieuwegein, Utrecht, Netherlands; 4. VU Medical Center, Amsterdam, Netherlands; 5. Antonie van Leeuwenhoek Hospital, Amsterdam, Netherlands.

Introduction: Cytoreductive surgery and intraperitoneal chemotherapy (CRS + HIPEC) is currently considered the standard of care for pseudomyxoma peritonei, mesothelioma and peritoneal metastases (PM) from colorectal cancer. CRS + HIPEC has been suggested as a potential treatment option in PM of a rarely occurring entity, small bowel cancer. Therefore, the current study was undertaken to investigate the results of CRS and HIPEC in all HIPEC centres of the Netherlands. Methods: From the four tertiary referral centers for peritoneal surface malignancies in the Netherlands, all patients with peritoneally metastasized small bowel carcinoma intended to undergo cytoreductive surgery and HIPEC were collected between January 2005 and July 2014. Primary tumor characteristics, operative details and survival outcomes were collected. Results: Sixteen (80%) of 20 patients who underwent an explorative laparotomy underwent CRS + HIPEC. The majority of patients were female (14/16), and primary tumors were mainly located in the ileum (8/16). A complete macroscopic resection was achieved in 15 patients. Serious adverse events requiring re-intervention occurred in four patients, although no hospital mortality was observed. Eight patients (50%) had recurrent disease during the follow up period and median survival is 31 months. Conclusion: In a select group of patients in whom a complete macroscopic resection can be achieved, survival rates comparable to those in colorectal PC are attainable with acceptable morbidity. The role of adjuvant chemotherapy needs further research.
**P104**

**Clinical Cancer Staging at Initial Presentation: Are We Improving?**


*Surgi-cal Oncology, Fox Chase Cancer Center, Philadelphia, PA.

**Background:** The efficacy of non-surgical and of neoadjuvant therapy for cancer cannot be determined without appropriate clinical staging. The absence of staging data has been a persistent problem. **Methods:** Using the National Cancer Database from 1998-2011 we reviewed patients diagnosed with cancers of three disease sites, head and neck (HNC), rectal (RC) and bladder (BC). Rates of clinical staging were assessed by institution type, either community (COM) or academic (ACA). Patients treated with surgery alone were excluded from analysis. **Results:** 166,670 patients with HNC, 125,699 patients with RC, and 15,433 patients with BC were identified. Prior to induction therapy, 91% and 92% of HNC patients were clinically staged in COM versus ACA, and 73% and 78% of RC patients, respectively (p<0.0001). BC patients were staged 79% of the time in both institutions (p=0.43). Among HNC patients, clinical staging was assigned to 90% in 1998, which increased to 94% in 2011 (p<0.0001). For RC, clinical staging rates increased from 62% in 1998 to 89% in 2011 (p=0.0001). In BC, 74% were staged in 1998, which declined to 66% in 2007. However, the trend reversed, and 92% received a clinical stage by 2011 (p<0.0001). When comparing trends between COM and ACA, in 1998 stage was reported in 90% and 91% for HNC, respectively. By 2011, the proportions rose to 93% and 94% (p<0.0001). In 1998, 60% of RC were staged in the COM versus 66% in ACA. By 2011, 88% and 91% had staging reported (p<0.0001). For BC in 1998, 75% of patients were assigned a stage in both center types, which fell until 2007, when a steady increase was observed. By 2011, 92% of patients were staged in both center types (p<0.0001). **Conclusions:** Clinical staging improved in all classes of patients with time, although a substantial number still lack staging information. Clinical stage reporting varied by type of institution as well as disease sites. Patients with HNC had the highest rate of clinical staging prior to treatment and RC patients had the lowest. Between 1998 and 2011 RC has seen the most significant upward trend in recording clinical stage. Despite this, thousands of patients have received treatment without documentation of their clinical stage.

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**P105**

**Oligometastatic Micro-RNAs are Regulated by DNA Methylation**

G. Oshima,*1 M.C. Posner,*1 S.C. Wightman,*1 T.E. Darga,*1 M. Stack,*1 S. Lim,*1 X. Huang,*2 T.E. Darga,*2 M.C. Posner,*1 N. Khodarev,*2 R.R. Weischelbaum,*1 1. Department of Surgery, The University of Chicago, Chicago, IL; 2. Department of Radiation and Cellular Oncology, Ludwig Center for Metastasis Research, The University of Chicago, Chicago, IL.

**Introduction:** Oligometastasis is a clinically distinct patient subset characterized by a limited numbers of metastases, low rates of progression and favorable prognosis after resection or ablative therapies. Recently we found that oligometastatic lesions are associated with the expression of several micro-RNAs (miRNAs) encoded in the 14q32 locus that are regulated by DNA methylation. We hypothesized that application of inhibitors of DNA methylation can suppress 14q32 methylation and therefore activate 14q32-encoded miRNAs, leading to the suppression of an aggressive metastatic phenotype. **Method:** To test this hypothesis we stably labeled HCT116 cells by Luciferase and TdTomato, treated them by DNMT1 inhibitor 5'-Aza-C (5uM) followed by splenic injection and then tested growth of liver metastases and whole-genome expression of miRNAs. **Results:** Fifty six of 2578 human miRNAs were significantly up-regulated in HCT116 cell lines treated with 5'-Aza-C in vitro. Out of those 56, 15 miRNAs (27%) reside in 14q32 locus. The volume of liver metastases in the animals injected with 5'-Aza-C-treated tumor cells was more than 10-fold lower as compared with control group, as was assessed by in vivo luminescence (p<0.05). Consistently, fluorescent intensity of harvested livers ex vivo was 18.6-fold lower than control at 2 weeks after injection (p<0.01) (image). **Conclusion:** Our data indicate that the 14q32 locus encodes miRNAs differentially sensitive to DNA demethylation, suggesting that epigenetic regulation of this locus can be implicated in the development of oligometastasis. The data also suggest future therapeutic potential of DNA methylation inhibitors in the treatment of liver oligometastases.

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**P106**

**In vitro Functional Study of RhoA in Colorectal Cancer Cell Line and the Significance of its Expression in Colorectal Cancer Patients**

M. Baek,*1 T. Jeong,*1 T. Kim,*1 C. Kim,*1 T. Ahn,*1 J.A. Ridge,*1 Surgery, Soonchunhyang University Hospital, Cheonan, Korea (the Republic of); 2. Soonchunhyang University, Asan, Chungnam, Korea (the Republic of).

**Objectives:** Ras homolog gene family, member A (RhoA) is a small GTPase protein known to regulate the actin cytoskeleton in the formation of stress fibers. The biological roles of RhoA on the colorectal carcinogenesis and progression have not been fully elucidated. The aim of present study was to evaluate the biological roles of RhoA in the colorectal cancer cell line and to correlate the RhoA expression with the clinicopathological factors of colorectal cancers. **Methods:** The biological roles of RhoA were investigated in HCT116 colorectal cancer cell line that expresses high level of RhoA by knockdown RhoA with shRNA transfection. The functional roles of RhoA were evaluated by invasion assay, wound healing cell migration assay, and cell proliferation assay. Moreover, RhoA expression was investigated by immunohistochemistry on tissue arrays of 260 cases of colorectal cancer and the association of RhoA expression was examined with clinicopathologic features. **Results:** The HCT116 cell line knockdowned RhoA by shRNA revealed significant decreases of viability, invasion, and migration compared to that of control (p<0.05) respectively. The RhoA was expressed in 59.2% of colorectal cancers. The RhoA expression was significantly associated with pT (p=0.038), pN (p=0.042), lymphatic invasions (p=0.047) and TNM stages (p=0.026). The overall survival was significantly decreased in patients of RhoA expression [HR=0.609 (95% CI: 0.394-0.942, p=0.026)]. The cumulative survival was significantly decreased in patients of RhoA expression compared to those of RhoA negative expression by Kaplan-Meier analysis (log rank test, p=0.010). **Conclusions:** The RhoA expression plays some significant roles in carcino-
P107 Association of Nuclear Karyopherin alpha2 with Poor Prognosis in Colorectal Cancer Patients

M. Back,1,2 D. Jeong,1 C. Kim,4 T. Ahn,1 T. Kim,1 J. Surgery, Soonchunhyang University Hospital, Cheonan, Korea (the Republic of); 2. Soonchunhyang University, Asan, Chungnam, Korea (the Republic of).

Objectives: Karyopherin alpha 2 (KPNA2) is a member of the karyopherin family that moves protein molecules into the nucleus by binding to a specific recognition sequence. It has recently been reported to play an important role in carcinogenesis and cancer progression. The aim of the present study was to elucidate the clinicopathological significance of overexpression of nuclear KPNA2 expression in colorectal cancers. Methods: KPNA2 expression was investigated by immunohistochemistry on tissue microarrays of 363 cases of colorectal cancer and the association of KPNA2 expression was examined with clinicopathologic features. Results: Thirty percent (30%) of colorectal cancers demonstrated overexpression of KPNA2. The overexpression of KPNA2 was significantly associated with high pN stages (p=0.005), vascular invasions (p<0.001) and lymphatic invasions (p<0.001). Multivariate Cox regression analysis showed that the overexpression of KPNA2 in pN stage 1, 2 was an independent prognostic factor of decreased survival [HR=2.13 (95% CI: 1.32-3.45, p=0.002)]. The overall survival was significantly decreased in patients of KPNA2 high expression [HR=2.70 (95% CI: 1.74-4.20, p<0.001)]. The cumulative survival was significantly decreased in patients of KPNA2 high expression compared to those of KPNA2 low expression by Kaplan-Meier analysis (log rank test, p<0.001). Conclusion: The overexpression of KPNA2 can be a valuable poor prognostic marker of colorectal cancer and the KPNA2 can be used in therapeutic strategies.

P108 Multivariate analysis of demographics and surgical approach in patients with colorectal cancer

<table>
<thead>
<tr>
<th>Insurance</th>
<th>Robotic vs Open OR (95% CI)</th>
<th>Laparoscopic vs Open OR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uninsured</td>
<td>1.000</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>3.818 (2.136, 6.819)</td>
<td>1.655 (1.475, 1.813)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Medicaid</td>
<td>2.821 (1.484, 5.361)</td>
<td>1.110 (0.978, 1.261)</td>
<td></td>
</tr>
<tr>
<td>Medicare</td>
<td>3.234 (1.790, 5.841)</td>
<td>1.494 (1.166, 1.931)</td>
<td></td>
</tr>
<tr>
<td>Metro</td>
<td>1.000</td>
<td>1.000</td>
<td></td>
</tr>
<tr>
<td>Geographic setting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urban</td>
<td>0.712 (0.573, 0.883)</td>
<td>0.873 (0.820, 0.919)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Rural</td>
<td>0.695 (0.397, 1.218)</td>
<td>0.828 (0.728, 0.943)</td>
<td></td>
</tr>
<tr>
<td>Facility type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Comprehensive CCC</td>
<td>1.347 (1.000, 1.531)</td>
<td>1.407 (1.136, 1.742)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Academic</td>
<td>1.674 (1.584, 2.541)</td>
<td>1.399 (1.311, 1.476)</td>
<td></td>
</tr>
</tbody>
</table>

P109 National Disparities in Minimally Invasive Surgery for Colorectal Cancer


Introduction: Social and racial disparities have been studied as factors contributing to differences in access to care and potentially on outcomes in patients with colorectal cancer (CRC). The aim of this study was to investigate the access to minimally invasive surgery (both laparoscopic and robotic) across different social, racial and geographic populations. Methods: We utilized the National Cancer Database (NCDB) to identify patients with cancer of the colon and rectum from 2004 to 2011 who had undergone definitive surgical procedures through either an open, laparoscopic or robotic approach. Multivariate analysis was performed to investigate differences in age, gender, race, insurance coverage, geographic setting and national location, and hospital type in relation to the surgical approach. Results: A total of 144,774 patients were identified, 115,682 with colon cancer and 29,092 with rectal cancer. The initial surgical approach for all CRC included 58.5% open (84,714), 39.3% laparoscopic (56,957) and 2.1% robotic (3,103). Table 1 shows the multivariate analysis results for patient demographics and surgical approach. In evaluating type of insurance coverage, patients with private insurance were most likely to undergo robotic or laparoscopic surgery for each subset of CRC. Similarly, patients who lived in metropolitan areas and who received treatment at an academic center were more likely to undergo minimally invasive surgery. Patients in the East North Central (IL, IN, MI, OH, WI) and Mountain (AZ, CO, ID, MT, NM, NV, UT, WY) regions of the US had the highest rates of robotic surgery, whereas patients in the New England states (CT, MA, ME, NH, RI, VT) had the highest rates of laparoscopic surgery. Consistent with other studies, race was not a clinically significant characteristic for surgical approach in patients with colon or rectal cancer. Conclusions: Minimally invasive approaches for CRC comprise approximately 40% of surgical procedures. Similar to laparoscopic surgery, robotics is associated with patients who have private insurance, live in metropolitan areas and undergo surgery in academic centers.

P110 Safety and Efficacy of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion in Elderly Patients

P.M. Polanco,1,4 Y. Shuai,1 H. Jones1,2 L. Ramaligam,3 M.E. Hogg,3 A.H. Zureikat,3 M. Holtzman,3 S. Ahrendt,1,2 J. Pingpank,3 H.J. Zeh III,3 D.L. Bartlett,3 H.A. Choudary,1 J. University of Texas Southwestern Medical Center, Dallas, TX; 2. University of Pittsburgh Cancer Institute, Pittsburgh, PA; 3. University of Pittsburgh Medical Center, Pittsburgh, PA.

Background: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) offers meaningful survival to patients with certain peritoneal surface malignancies. However, appropriate patient selection is necessary to optimize perioperative and oncologic outcomes. Our objective was to assess the safety and efficacy of CRS/HIPEC in elderly patients, where its role is poorly defined. Methods: Patients undergoing CRS/HIPEC for mucinous appendiceal carcinomatosis (MAC) and malignant peritoneal mesothelioma (MPM) were identified from a prospectively maintained database between 2000-2012. Perioperative and oncologic outcomes were compared between patients ≥ 70 years of age (elderly group) and those < 70 years of age (young group). Fisher’s exact, Wilcoxon and Log-rank test were used to assess statistical significance. Results: Of the 347 patients undergoing CRS/HIPEC (MAC 282 patients; MPM 65 patients), 42 patients (13.8%) were in the elderly group. There was no significant difference in ASA score, histologic diagnosis, tumor grade, and simplified peritoneal cancer index between the elderly and young groups. Clinically significant postoperative morbidity rates (Clavien-Dindo grades 3-4) were similar between groups (23.8% vs. 29.2%, p=0.585). However, 60-day mortality rate was higher in the elderly group (7.7% vs. 1.3%, p=0.041). Mean hospital-length of stay (LOS) was not significantly different between groups, while the elderly group had longer mean ICU-LOS (5.4 vs. 3.4 days, p=0.008). Median time-to-progression was not significantly different between groups (17 vs. 21 months, p=0.102), however the elderly group had a significantly shorter median overall survival (29 vs. 81 months, p=0.002). Conclusions: Elderly patients undergoing CRS/HIPEC have a higher postoperative 60-day mortality rate, longer ICU-LOS and decreased overall survival compared to younger patients. Further studies are needed to better identify the underlying factors affecting outcomes is elderly patients.
Global Transcriptional Signature of Peripheral Blood Immature Myeloid Cells as a Marker for Abdominal Tumor Progression in Mouse

N. Pencovich,* L. Lupu, S. Langier, I. Nachmany, J.M. Klaussner, Laboratory of Molecular Surgical Oncology, Department of General Surgery, Tel-Aviv Sourasky Medical Center, Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel.

Introduction: Immature myeloid cells (IMC) play significant roles in tumor angiogenesis and progression. We have recently shown that preferential recruitment of CD11b+ GR1+ (Ly6g+/Ly6c−) IMC into aggressive versus dormant tumors is associated with unique global expression patterns along the axis of migration, starting in the bone marrow, through the peripheral blood (PB) and within aggressive and dormant tumors. This data suggest that the transcriptional signature of PB IMC may reflect different stages in tumor growth and vascularization. The aim of this study was to identify changes in PB IMC gene expression in relation to tumor growth. Methods: CT26 colon cancer cells were inoculated into peritoneal cavities of 6 weeks old BALB/c mice. Fast-growing vascular tumors formed in the upper abdominal region, while dormant, non-vascular tumors formed on the bowel mesentery in the lower abdomen. IMC populations in the PB were monitored during tumor growth. CD11b+ Ly6g+ IMC were magnetically separated from the PB, 4, 8 and 11 days following tumor inoculation. Global transcriptional signature was assessed by RNA sequencing. Results: The PB CD11b+ Ly6g+ cell population was demonstrated. This was associated with a substantial increase in tumor vascularization. Global gene expression analysis of CD11b+ Ly6g+ cells at day11 revealed a vast transcriptional response comparing to the same cell populations at days 8, 4 and control. Interestingly, significant changes in global gene expression were also identified at days 4 and 8 following tumor inoculation, despite no significant increase in IMC numbers. The expression pattern of specific genes including Vcan and Pex1 was validated and positively correlated with tumor progression. Conclusions: PB CD11b+ Ly6g+ IMC present unique transcriptional signatures during different stages of intra-abdominal tumor growth. These expression patterns may potentially serve as markers for tumor progression and recurrence.

Long-term Outcome of Rectal Cancer with Clinically Metastatic Mesorectal Lymph Nodes (cN+) Treated by Neoadjuvant Chemoradiation: Implications for Surgical Strategies in Relation to Pathological Response

C. Belluco,* A. De Paoli, V. Canzonieri, M. Tonello, E. Bidoli, M. Forlin, G. Boz, R. Cannizzaro, A. Buonadonna, F. De Marchi, National Cancer Institute, CRO-IRCCS, Aviano, PN, Italy.

Introduction: Organ preserving strategies have been considered in patients with locally advanced rectal cancer (LARC) achieving complete pathological response (pCR) after neoadjuvant chemoradiation (CRT). Our aim was to explore the value of this approach in cases of neoadjuvant chemotherapy (nCRT). Data were retrieved from our Institutional prospective rectal cancer data-base. Tumors with mesorectal lymph nodes >5mm by pelvic MRI and/or endorectal US were staged as cN+. Results: Study population comprised 226 patients (142 men, 84 women; median age 64 yrs, range 25-87) with LARC and no distant metastasis that underwent surgical resection. Patients were staged as cN+. Results: Study population comprised 226 patients (142 men, 84 women; median age 64 yrs, range 25-87) with LARC and no distant metastasis treated by CRT followed by surgery including total mesorectal excision (TME) (n. 179), and by full thickness local excision (LE) (n. 47) between 1996 and 2013. At staging 123 (54.4%) patients were cN+. At pathology, pCR in the primary tumor was observed in 65 (28.7%) cases. Median number of examined lymph nodes was 12 (range, 2-37). Metastatic mesorectal lymph nodes (ypN+) were detected in 45 (42.2%) out of 107 cN+ patients compared to 2 (2.7%) out of 72 cN− patients (p=0.01). In cN+ tumors 4 (16.0%) out of 25 cases with pCR were ypN− compared to 43 (51.8%) out of 83 cases with no-pCR (p=0.01). During a median follow-up of 48 months 30.5% patients had recurrent disease, and 16.3% died of disease. In cN+ patients who underwent TME surgery 5-year DSS and DFS were 100% and 91.6% in pCR patients compared to 71.2% and 58.0% in no-pCR patients (p=0.01). In patients with metastatic lymph nodes at pathology 5-year DSS and DFS were both 100% in pCR cases compared to 59.1% and 43.3% in no-pCR patients (p=0.01). In cN− patients with pCR 5-year DSS and DFS were both 100% and 85.7% in TME patients and 100% and 91.6% in LE patients (p=0.01). At multivariate analysis pCR was the single best independent prognostic factor (Table). Conclusions: Our findings indicate that
in patients with LARC achieving pCR after CRT organ preserving strategies are safe in cN- cases. The favorable long-term outcome of pCR tumors should be balanced with the risk of metastatic mesorectal lymph nodes in cN+ cases.

Multivariate analysis of survival in 226 patients with locally advanced rectal cancer treated by neoadjuvant chemoradiation

<table>
<thead>
<tr>
<th>ct stage</th>
<th>HR</th>
<th>Disease Specific Survival 95% CI</th>
<th>p</th>
<th>Disease Free Survival 95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ct1c2</td>
<td>0.87</td>
<td>0.12-6.51</td>
<td>0.892</td>
<td>1.41</td>
<td>0.55-3.63</td>
</tr>
<tr>
<td>ct1c3</td>
<td>1.29</td>
<td>0.53-3.12</td>
<td>0.570</td>
<td>1.43</td>
<td>0.74-2.76</td>
</tr>
<tr>
<td>ct1c4/ct2</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cT3</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cT4</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cN0</td>
<td>1.44</td>
<td>0.73-2.83</td>
<td>0.292</td>
<td>1.14</td>
<td>0.70-1.87</td>
</tr>
<tr>
<td>cN1</td>
<td>1.70</td>
<td>1.00-3.00</td>
<td>0.007</td>
<td>2.90</td>
<td>1.83-8.33</td>
</tr>
<tr>
<td>pCR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
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<td>No</td>
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<td>Type of surgery</td>
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<td>LE</td>
<td>1</td>
<td></td>
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</tr>
<tr>
<td>TME</td>
<td>1</td>
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</tbody>
</table>
| HR, hazard ratio; pCR, complete pathological response in primary tumor; LE, full thickness local excision; TME, total mesorectal excision

P114
Delay to Colectomy and Survival for Patients Diagnosed with Colon Cancer S.P. Bagaria,* M. Heckman, N. Diehl, A. Parker, N. Wasif, Surgery, Mayo Clinic, Jacksonville, FL.

Background A long wait-time for colectomy for colon cancer should theoretically affect survival but, to date, the association between delay to colectomy and survival remains unresolved. Methods We studied 4,692 patients who underwent colectomy for colon cancer between 1990 and 2012. Wait-time was defined as the number of days between diagnosis and colectomy. Cox regression models were used to estimate all-cause mortality across wait-time categories. Multivariable analyses were controlled for clinicopathologic variables and Charlson comorbidity index. Results The number of patients in the wait-time group of 1-28 days was 3,950 (84.2%), 29-84 days was 681 (22.7%), and >84 days was 61 (1.3%). A wait-time of 29-84 days was not associated with an increased risk of death (HR=1.13; P=0.056) when compared to a wait-time of 1-28 days. Though a wait-time >84 days represented a small group, it was associated with an increased risk of death (HR=1.60; P=0.013). For patients with stage I and II disease, wait-times of 29-84 days (HR =1.44; P=0.0001) and >84 days (adjusted HR=2.24; P=0.0007) were associated with an increased risk of mortality. Conclusions A wait-time for colon cancer surgery of up to 12 weeks is likely safe for most patients. However, those suspected to have early-stage colon cancer may benefit from less of delay. These data provide a framework to address concerns over prolonged wait-times and can direct efforts for timely surgical intervention in patients with colon cancer.

Association between wait-time for colectomy and overall survival.

<table>
<thead>
<tr>
<th>Wait-time for colectomy</th>
<th>Hazard ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-28 days (N=3,950)</td>
<td>1.00 (reference)</td>
<td>N/A</td>
</tr>
<tr>
<td>&gt;28 days (N=681)</td>
<td>1.13 (0.90, 1.40)</td>
<td>0.056</td>
</tr>
<tr>
<td>&gt;84 days (N=61)</td>
<td>1.60 (1.11, 2.32)</td>
<td>0.011</td>
</tr>
<tr>
<td>Stage I and II patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-28 days (N=2,203)</td>
<td>1.00 (reference)</td>
<td>N/A</td>
</tr>
<tr>
<td>&gt;28 days (N=440)</td>
<td>1.44 (1.20, 1.73)</td>
<td>0.0001</td>
</tr>
<tr>
<td>&gt;84 days (N=103)</td>
<td>2.24 (1.41, 3.57)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Stage III and IV patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-28 days (N=1,747)</td>
<td>1.00 (reference)</td>
<td>N/A</td>
</tr>
<tr>
<td>&gt;28 days (N=241)</td>
<td>1.94 (0.76, 1.25)</td>
<td>0.22</td>
</tr>
<tr>
<td>&gt;84 days (N=20)</td>
<td>1.14 (0.61, 2.14)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Multivariable models were adjusted for age, gender, Charlson comorbidity index, surgery site, year of surgery, colon cancer site, grade, number of regional nodes examined, and pathologic stage. CI=confidence interval.

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Predictors of Circumferential Resection Margin Involvement after Curative Surgery for Rectal Cancer E. Al-Sukhni,* K. Attwood, E. Gabriel, S.J. Nurkin, Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.

Introduction The circumferential resection margin (CRM) is a key prognostic factor after curative resection for rectal cancer. We sought to identify factors associated with a positive CRM on a population level. Methods A retrospective review was performed of the National Cancer Data Base (NCDB), 2004-2011. Patients with histologically proven rectal cancer who underwent total mesorectal excision (TME) surgery and had a recorded CRM were included. Multivariate analysis of the association between patient and tumor characteristics and CRM was conducted using ordinal and logistic regression models. Tumor <1mm from the cut margin defined a positive CRM. Results There were 23,464 patients included in the study. Of these, 3,131 patients (13.3%) had a positive CRM. Patients with a positive CRM were more likely to have no health insurance (OR 0.72 and 0.79 for those with private and government insurance, respectively versus uninsured; p<0.013); to have pathological stage II or more advanced disease (OR 3.4, 3.1, and 3.9 for stage II, III, and IV, respectively versus stage I; p<0.001); to have undergone abdominopерineal resection (APR) (OR 1.3 versus low anterior resection; p<0.001); to have other positive margins (OR 18.6; p<0.001); or to receive radiation at any point during their treatment (OR 1.2, 1.2 and 5.8 for neoadjuvant, adjuvant, and intraoperative radiation, respectively versus no radiation; p=0.002). Conclusions Factors associated with positive CRM include lack of health insurance, advanced disease stage, undergoing APR, and requiring radiation therapy. Such factors are potentially modifiable and should be taken into consideration when planning the treatment of patients with resectable rectal cancer.

P116

Introduction: Survival of patients after cytoreduction (CRS) and heated intraperitoneal chemotherapy (HIPEC) for appendiceal neoplasms is traditionally projected by actuarial curves that do not address the issue of survival time that a patient has already accrued. We sought to study the survival of patients contingent on the assumption that they had already survived a fixed duration of time after surgery, otherwise known as conditional survival (CS) and to ascertain if this was a better tool for prognostication. Methods: A retrospective analysis of 513 appendiceal cancer patients from a prospectively maintained database was performed. Overall survival (OS) was calculated for patients who achieved a complete macroscopic CRS. Conditional survival was estimated based on Kaplan-Meier curves to determine what the patient’s long term survival (5, 7, or 10-year) would be if they were already alive at 1, 2 or 3 years from surgery. Results: 312 low grade and 117 high grade primaries underwent CRS/HIPEC for peritoneal surface disease (PSD) between 1992 and 2013. OS at 5 and 10 years for 140 patients with low grade tumors and R0/R1 resections was 83.8% and 74.7% respectively. For the same patients, their survival estimates conditional to their survival for 3 years was 93.7% and 83.5%, respectively. For the 38 patients with high grade tumors and R0/R1 resections who survived to at least 3 years, their estimated survival was 50.9% and 38.2% at 5 and 10 years respectively; using conventional survival analysis, their 5 and 10 year survivals were 30.2% and 20.13% respectively. OS at 5 and 10 years were 30.2% and 22.6%. Conclusions: Conditional survival analysis may underestimate individual OS, due to unpredictable variations in tumor biology. When conditioned for time already elapsed since surgery, improvement in survival estimates are more pronounced with high grade tumors. CS improves survival prognostication in PSD from low and high grade appendiceal primaries treated with CRS/HIPEC.
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MiR-29b is a Novel Potential Prognostic Marker and Regulates Tumor Progression in Colorectal Cancer: A. Inoue,¹,² H. Yamamoto,¹ M. Uemura,¹ J. Nishimura,¹ T. Hata,¹ T. Takemasa,¹ M. Ikeda,² K. Murata,² T. Mizushima,¹ Y. Doki,² M. Mori,² I. Gastroenterological Surgery, Osaka University, Suita City, Osaka, Japan; 2. Department of Surgery, Osaka Rosai Hospital, Sakai, Osaka, Japan.

INTRODUCTION: Recent studies have suggested that microRNA-29 (miR-29) family members in human regulate tumor progression in many types of cancer. In colorectal cancer (CRC), however, few studies have shown the clinical significance and biological function of miR-29. The aim of the present study was to investigate the prognostic impact and the biological significance of miR-29 in CRC.

METHODS: Expression of miR-29 in tissue samples were quantified by quantitative real-time PCR in 245 CRC patients who underwent curative resection. To examine the functional role of miR-29 in vitro, tumor suppressive activity of miR-29 was assessed based on a proliferation assay, PCR, flow cytometry, and Western blot using CRC-derived cell lines. Results: MiR-29b expression was significantly decreased in tumor tissues compared to corresponding normal mucosa (p = 0.012). The disease free survival (DFS) and overall survival (OS) were significantly longer in the high miR-29b expression group compared to those in the low miR-29b expression group (DFS: p = 0.03; OS: p = 0.02). Multivariate analyses indicated that expression of miR-29b was an independent prognostic factor for 5-year DFS (p = 0.026), together with lymph node metastasis (p = 0.004), and tumor invasion (p = 0.002). In a multivariate analysis of 5-year OS, we found a similar association between lymph node metastasis, tumor invasion, venous invasion, and miR-29b expression (p = 0.013). In vitro assays revealed that forced expression of miR-29b was associated with a reduction of proliferative activity. An annexin V apoptosis assay and flow cytometric analysis revealed that miR-29b induced apoptosis and arrested the cell cycle at the G1/S transition. Moreover, miR-29b inhibited the mRNA and protein expression of MCL1 and CDK6. Conclusions: Our findings indicated that miR-29b may be a useful, novel prognostic marker, and it may play important roles in regulating apoptosis and cell cycle in CRC. Restoration of miR-29b expression may represent a potential strategy for miRNA-based therapy against CRC.

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Background Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) has improved survival outcomes with acceptable morbidity. However, cost effectiveness has not been extensively evaluated. This study examines the cost effectiveness of CRS and HIPEC in comparison to palliative chemotherapy. Methods A retrospective review of a prospectively maintained database of 37 patients who underwent 39 CRS and HIPEC procedures from January 2008 to March 2014 and 21 similar patients, who underwent palliative chemotherapy from April 2008 to September 2012, for colorectal peritoneal carcinomatosis, at the National Cancer Centre Singapore (NCCS), was performed. All costs incurred during the admissions for both treatment arms were analysed. The end-points included total cost, cost attributes and cost per year of life attained (CLY). Results The average cost of CRS and HIPEC per patient is $81,725.59 while that of palliative chemotherapy per patient is $44,408.62. The mean overall survivals of patients on CRS and HIPEC and palliative chemotherapy were 21.6 months and 14 months respectively. Correspondingly, the CLY were $45,403.10 and $38,064.53. 33% of patients with CRS and HIPEC required 2 or more readmissions as compared to 57% for those on palliative chemotherapy. 38% of total cost for CRS and HIPEC was used for the management of complications,compared to 48% in the palliative chemotherapy arm. Conclusion The cost per life of year attained for CRS and HIPEC is higher than that for palliative chemotherapy. It may not be the most cost effective than palliative chemotherapy in absolute value but has significantly prolonged survival, lowered readmission rates and reduced cost attribution to managing complications, and continues to be the preferred treatment choice for selected patients with colorectal peritoneal metastasis.

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A Longer Time Interval to Surgery after Preoperative Chemoradiotherapy for Locally Advanced Rectal Cancer Increases the Chance of a Complete Response N. Hugen,¹ A. Rombouts,¹ M. Elferink,² J. De Wilt,¹ I. Department of Surgery, Radboud University Medical Center, Nijmegen, Netherlands; 2. Comprehensive Cancer Centre the Netherlands, Utrecht, Netherlands.

The optimal waiting time to surgery after neoadjuvant chemoradiotherapy for locally advanced rectal cancer (LARC) is debatable. Currently an interval of 6-8 weeks is recommended, but it has been suggested that a longer interval may increase the chance of obtaining a radical resection and thus may improve outcome. This, however, has never been analyzed in large patient groups. For this study prospectively recorded data from the national cancer registry was collected. All patients with a histological proven LARC (stage cT3, cT4 and/or cN2) who received neoadjuvant chemoradiotherapy between 2006 and 2011 were included. A total of 2391 patients was identified, and the interval between neoadjuvant therapy and surgery was known for 1418 patients. The percentage of patients with a pathological complete response (ypT0) was 10.7% after a waiting period of 5-6 weeks, 16.3% for 7-8 weeks, 19.7% for 9-10 weeks and 21.0% for patients with an interval of more than 10 weeks (P = 0.005). The lowest rate of positive circumferential resection margins was seen after an interval of 8 weeks (5.4%). Patients who underwent surgery after 7-8 weeks following neoadjuvant therapy, had a significantly better 5-year overall survival than patients who underwent surgery after 5-6 weeks (74% versus 65%, P = 0.05). There was no significant survival benefit for patients who underwent surgery after 9-10 weeks (5-year overall survival 68%). Based on the low number of irradiated resections and the favorable outcome, the optimal interval to surgery appears to be 7-8 weeks. A longer time interval leads to a higher number of patients with a pathological complete response; therefore, more patients can be treated with organ sparing surgery.

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INTRODUCTION: Recently, patient-derived xenograft (PDX) models that transplanted patient cancer tissue into nude mice subcutaneously, has been gaining ground to be used for drug development. It has been argued that PDX have the advantage since it maintains the tumor heterogeneity and reproduce similar metastatic pattern of human cancer. Sphingosine-1-Phosphate (SIP) is a signaling sphingolipid that is known to promote cancer cell proliferation, invasion, and angiogenesis. Recently our group demonstrated that SIP is associated with worse outcome in cancer patients, making SIP a target for drug development. We sought out to examine if PDX model tumors have similar gene expression patterns with the original tumor making them appropriate for drug development for colon cancer.

METHODS: A dataset from the NCBI’s Gene Expression Omnibus (GEO) Database, including 19 human colon cancers and 27 PDX tumors derived from them, was used. We performed a series of gene expression level with 198 (8%) were overexpressed and 2035 (91%) were underexpressed in the PDX tumor samples. Of the 45 genes with the highest difference in expression (those with 32 fold difference either over- or under-expressed), 53% were cancer related, 24% were immune related and 22% were neither cancer nor immune related. We found there were extreme differences in the mean expression levels between the two groups in many of the key SIP signaling genes, Sphingosine kinase-1 (20-fold); SIP Receptor 2 (21-fold); SIP Receptor 3 (32-fold). This was also the case for genes related to angiogenesis like; CD3 (11-fold); Ang2 (10-fold); Tie1 (8-fold); VEGF-C (23-fold); VEGF-R (18-fold). CONCLUSION: Our findings warn us of the limitation of the PDX model in that gene-expression patterns with the original tumor making them appropriate for drug development for colon cancer.
The Role of Inflammatory Monocytes in Human Metastatic Colorectal Cancer

J.G. Grosman,* T. Nyweening, B. Belt, E. Pittman, W. Hawkins, S. Strasberg, P. Goedegebure, R.C. Fields, D. Linehan. Washington University School of Medicine, Saint Louis, MO.

Intro: Colorectal cancer (CRC) is the most common gastrointestinal malignancy. 60% of CRC patients are diagnosed with metastatic (m) CRC and the 5-year survival is ~20%. Myeloid cells, particularly inflammatory monocytes (IM), are recruited from the bone marrow to the tumor microenvironment where they become tumor associated macrophages and play a crucial role in tumor progression, metastasis, and chemoresistance. While the importance of IM has been shown in other malignancies, little is known about their role in human CRC. Methods: Human tissue was collected under an IRB approved protocol at Washington University. Flow cytometry was performed on PBMCs and single cell suspensions of normal tissue and tumor samples. Qualitative RT-PCR and confocal microscopy were performed for CCL2. T-cell suppression assays were performed using CD14+ IM isolated from patient peripheral blood and tumor samples. Results: Analysis of pre-operative blood revealed that monocyte levels correlate with the extent of disease burden. Monocytes were elevated in CRC patients compared with controls (p=0.0001), additionally patients with liver metastasis had further elevation in monocytes compared with patient’s with primary disease (p=0.01). In metastatic patients, monocyte levels also correlate with survival following resection of hepatic metastasis (p=0.0002). FACTS analysis confirmed these findings and demonstrated that the circulating CD11b+/CD14+/CCR2+ subset of IM was responsible for the increase. Both primary CRC and liver mCRC had increased expression of CCL2 compared to uninvolved tissue (p=0.008 and p=0.03, respectively). Production of CCL2 was localized to CRC cells. FACTS analysis showed CCR2+ tumor infiltrating macrophages were elevated in CRC liver metastasis compared to adjacent normal liver and a paucity of effector T-cells. CD14+ TAMs isolated from mCRC inhibited T-cell proliferation, illustrating the immune suppressive phenotype of these cells. Conclusion: Inflammatory monocytes are critical in the progression of mCRC. Therefore, targeting CCR2+ myeloid cells may improve anti-tumor immunity and patient survival in metastatic disease.

Identification of the Genetic Interaction between the Oncogenic SNP and Environmental Factors in Diabetic Colorectal Cancer Patients

K. Mimori,1 K. Tani,1 K. Hatai,1 N. Kato,1 M. Ueda,2 T. Nakajima,3 D. Linehan,4,* J.G. Grosman,5* D. Linehan.1,2,5 1. Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA; 2. Department of Surgery and Science, Kyushu University, Fukuoka, Japan; 3. Department of Gastroenterological Surgery, Osaka University, Osaka, Japan.

Backgrounds: The oncogenesis of colorectal cancer (CRC) is considered to be determined by interactions among genetic background and environmental factors. We previously determined a significant epidemiologic association between a history of diabetes mellitus and the SNP of rs6983267 at 8q24 in Japanese CRC patients. The aim of this study is to explore the interactions and responsible genes on the interaction between diabetes mellitus (DM) and oncogenic SNPs in CRC. Methods: We collected 109 CRC cases from a multi-institutional collaborative study. Cancer cells were collected by laser microdissection and cDNA expression profiling using microarray and rs6983267 genotyping using the TaqMan method were done. The validation of specific gene expression with clinicopathological parameters was conducted using separate cohort of 132 CRC patients. Meta-analysis of microarray expression data was performed by Meta Gene profiler (MetaGP) to provide possible explanations of apparent interactions. Results: Our study revealed that DM was turned into an insignificant risk factor on CRC oncogenesis when the patients had the minor (risk) allele at the 8q24 rs6983267 SNP. We found Apolipoprotein A4 (ApoA-IV) was a candidate of potential oncogenic genes of CRC in DM patients with 8q24 minor alleles. The ApoA-IV expression was significantly upregulated in CRC cases with an oncogenic allele of the SNP rs6983267. The expression levels of ApoA-IV and msc were significantly correlated. The Apo-AIV high expression group (n=63) had a statistically significantly poorer overall survival rate than that of low expression group (n=49). Univariate and multivariate analysis showed that the Apo-AIV high expression was the independent indicator for poor overall survival. In addition, the MetaGP analysis revealed lower expression of PPAR-γ in CRC cases with DM in comparison to cases without DM. Conclusion: We identified novel genetic pathway related to colorectal carcinogenesis in diabetic patients. Our results indicated that dysregulation of lipid metabolism could be associated with diabetic CRC patients.

Tumor Derived Hypoxia Inducible Factor-1α Modulates Peritoneal Macrophage Activation in a Metastatic Model of Murine Colon Adenocarcinoma

B. Bredebeck,* Y. Yi, K. El-Kasmi, R.D. Schulick, C. Barnett. University of Colorado, Aurora, CO.

INTRODUCTION Macrophages in the tumor microenvironment, known as tumor-associated macrophages (TAMs), are believed to promote tumor progression. Described as classically- (M1) vs. alternatively- (M2) activated, TAMs are also classified by dominant cell-signaling pathways. Tumor-derived Hypoxia Inducible Factor-1α (HIF1α), a transcription factor, is associated with virulent cancer growth. Our lab has shown that HIF1α inhibition decreases tumorigenesis in murine metastatic colon adenocarcinoma. We predict that tumor derived HIF1α modulates peritoneal macrophage activation. METHODS The MC38 murine colon adenocarcinoma cell line was modified for HIF1α knockdown (KD) using short-hairpin RNA (shRNA) via lentiviral transduction targeting the HIF1α gene. Reduction of HIF1α activity by >80% was verified using real-time PCR and Western blot. Control cells had an empty vector. C57/BL6 mice were injected intraspinically with MC38 (n=5) or MC38 HIF1α KD cells (n=5) followed by hemisplenectomy. The control group underwent laparotomy and hemisplenectomy without tumor injection. At 1 week, peritoneal macrophages were harvested. Expression of STAT1 and STAT3 cell signaling pathway genes was evaluated using real-time PCR. RESULTS The relative expression of genes SOCS3, arginase-1 (Arg1), and IL4Rα were significantly higher in mice injected with MC38 HIF1α KD vs. empty vector cells (p=0.0001, p=0.0076, p=0.0002 respectively). Collectively, these markers reflect STAT3 signaling activity and suggest a wound healing phenotype similar to an M2 macrophage. SOCS1 expression, which reflects STAT1 signaling activity, was significantly higher in the HIF1α-intact MC38 cells (p=0.0001) and suggests a predominantly inflammatory or M1 activation phenotype. CONCLUSIONS In our model of metastatic murine colon adenocarcinoma, inhibition of tumor-derived HIF1α results in a distinct phenotype favoring the STAT3 signaling pathway in peritoneal macrophages. In contrast, mice injected with HIF1α-intact tumor cells showed greater STAT1 macrophage polarization. Tumor-derived HIF1α dictates peritoneal macrophage activation, which may influence tumor progression.

Safety and Efficacy of Concurrent Surgical Therapy for Peritoneal Carcinomatosis and Synchronous Hepatic Metastases in Patients with Disseminated Colorectal Cancer


Introduction: Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) improves survival in patients with colorectal carcinomatosis (CRC). The feasibility of hepatic resection and/or radiofrequency ablation (RFA) for colorectal liver metastases (CLM) performed concurrently with CRS/HIPEC is not well studied. Methods: From a prospectively maintained database between 2000-2012, we compared outcomes in 157 patients undergoing CRS/HIPEC alone for CRC (CRC group) and 32 patients undergoing concurrent CRS/HIPEC and hepatic resection and/or RFA for synchronous colorectal liver metastases. Results: The FIT group had a significantly higher mean number of hepatic metastases per patient (16.8 vs. 3.8, p=0.001). Concurrent CRS/HIPEC with liver resection or RFA was feasible in 93% of patients, compared with 76% of patients undergoing CRS/HIPEC alone (p=0.04). Conclusion: Concurrent CRS/HIPEC and liver resection or RFA is a feasible and safe therapeutic approach for patients with disseminated CRC.
chronous CLM with carcinomatosis (CLM group). Results: In the CLM group, median diameter of the largest lesion was 2 cm (range 2mm-5.6cm), 53% of patients had more than one liver metastasis (range 1-9), and 22% had bilobar disease. Four patients (12.5%) had hepatic resection and RFA while 5 patients (16%) underwent RFA only. Of the patients undergoing hepatic resection, 30% had more than one lesion excised (range 1-6). Patients underwent non-anatomic wedge resections (72%) or segmentectomies (28%) and no formal lobectomies were performed. Baseline demographics between the CRC and CLM groups were not different. In the CLM group, median estimated blood loss was higher (800ml vs 500ml, p=0.008). There was no difference in major post-operative morbidity rates (Clavien-Dindo grades 3-5) between groups. None of the patients in the CLM group suffered hepatic failure or in-hospital mortality at 60 days. Hospital length of stay and ICU length of stay were not different between groups. Recurrence-free survival (CLM group 9 months; CRC group 11 months) and overall survival (CLM group 19 months; CRC group 18 months) were similar between groups. Conclusion: Concurrent surgical resection or RFA of liver metastases in patients undergoing CRS/HIPEC for peritoneal carcinomatosis from colorectal cancer may increase intraoperative blood loss. However, concurrent surgical therapy for liver metastases does not adversely impact major morbidity or survival in patients undergoing CRS/HIPEC for disseminated colorectal cancer.

**P125**

**Time to Chemotherapy after Abdominoperineal Resection: Comparison between Primary Closure versus Perineal Flap Reconstruction**

A. Althumairi,* A. Canner, B. Safar, S. Fang, N. Ahuja, J. Sacks, J. Efron, Surgery, Johns Hopkins Hospital, Baltimore, MD.

**Introduction**

Wound complications are frequently encountered in patients who undergo abdominoperineal resection (APR); this can lengthen the time to chemotherapy. Perineal flap reconstruction is being used in an attempt to improve wound healing. We aim to assess the effect of perineal flap reconstruction on time to wound healing and time to administration of adjuvant chemotherapy in patients with rectal adenocarcinoma. **Methods** A retrospective review of patients who underwent APR for the diagnosis of rectal adenocarcinoma between 2002-2012 was performed. Patients were divided into two groups based on type of perineal wound closure (primary vs. flap). Non-delayed wound healing defined as healing within 6 weeks and non-delayed adjuvant chemotherapy received within 8 weeks postoperatively. Major wound complications included necrosis, dehiscence and abscesses. Minor complications included erythema, cellulitis, clear drainage and superficial dehiscence. Patients were compared for time to perineal wound healing, time to adjuvant chemotherapy, major and minor wound complications using student-t test.

**Results**

115 patients underwent APR for rectal adenocarcinoma, 67 patients received adjuvant chemotherapy, mean age was 57 years, 39 (58%) were male. (Table 1 shows the patient characteristics). 56 (84%) patients underwent primary closure while 11 (16%) underwent flap reconstruction. There was no difference in time to perineal wound healing between primary closure and flap group, and no difference in time to receive adjuvant chemotherapy (Table 1). 25 (45%) of the primary closure group had delay in receiving adjuvant chemotherapy vs. 6 (55%) of the flap reconstruction group, p=0.55. Delay in receiving adjuvant chemotherapy because of perineal wound complications occurred in 18 (32%) patients with primary closure vs. 2 (28%) patients with flap reconstruction, p=0.30. **Conclusions** Perineal flap reconstruction did not reduce the length of time to initiating chemotherapy; there was no difference in complication rate or length of healing between the two groups, therefore, flap reconstruction should be selectively used based on the size of the perineal defect.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Primary Closure (n=50)</th>
<th>Perineal Flap (n=65)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>35 (62.5%)</td>
<td>43 (66%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Female</td>
<td>21 (37.5%)</td>
<td>22 (34%)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>38 (60%)</td>
<td>8 (12%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>15 (25%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>3 (5%)</td>
<td>2 (3%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5 (9%)</td>
<td>0 (0%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Stocking</td>
<td>22 (35%)</td>
<td>3 (5%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Received peroperative chemotherapy</td>
<td>45 (80%)</td>
<td>10 (15%)</td>
<td>0.40</td>
</tr>
<tr>
<td>Received peroperative radiotherapy</td>
<td>43 (75%)</td>
<td>10 (15%)</td>
<td>0.29</td>
</tr>
<tr>
<td>Average time to wound healing (SD) (weeks)</td>
<td>6.8 (6.7)</td>
<td>6.3 (4.5)</td>
<td>0.40</td>
</tr>
<tr>
<td>Average time to chemotherapy (SD) (weeks)</td>
<td>9.3 (7.3)</td>
<td>10.7 (5.2)</td>
<td>0.79</td>
</tr>
<tr>
<td>Delay in chemotherapy (days)</td>
<td>36 (51%)</td>
<td>5 (85%)</td>
<td>0.55</td>
</tr>
</tbody>
</table>

**Reason for delay in receiving chemotherapy**

| Perineal wound complication | 18 (32%) | 3 (28%) |
| Abdominal wound complication | 4 (7%) | 0 (0%) |
| Small bowel obstruction     | 2 (4%) | 1 (2%) |
| Pelvic abscess              | 1 (2%) | 1 (2%) |
| Intercostal/spleal         | 0 (0%) | 1 (2%) |
| Major perineal wound complications | 5 (10%) | 0 (0%) |
| Minor perineal wound complications | 16 (30%) | 3 (27%) |
| Major abdominal wound complications | 3 (5%) | 0 (0%) |
| Minor abdominal wound complications | 8 (14%) | 1 (2%) |
| Length of stay (SD) (days) | 9.3 (8.5) | 13.4 (9.9) | 0.98 |
| ICU stay (SD) (days)       | 0.61 (0.82) | 0.72 (0.59) | 0.75 |
| Length of follow up (SD) (months) | 31.3 (25.6) | 19.4 (18.4) | 0.07 |
| Recurrence                  | 15 (27%) | 4 (60%) |
| Mortality                   | 3 (5%) | 1 (2%) |

**Results**

In treatment of rectal adenocarcinoma, an increased time delay of 6-12 weeks from the end of radiation therapy to surgery may increase the rate of complete pathologic response (pCR), but the optimal delay with respect to survival has not been established. This study evaluates the impact of delay on overall mortality. **Methods** The NCDB was queried for patients with adenocarcinoma of the rectum and no evidence of metastasis at diagnosis, who underwent preoperative chemoradiation followed by radical surgical resection. Standard statistical methods were employed for descriptive statistics and Cox model development. **Results** The study included 6805 patients, predominantly Caucasian (87.2%) and males (63.9%) who generally were treated with low anterior resection (57.3%), colonic reanastomosis (8.4%), or abdominoperineal resection (28.4%), and had median survival of 66.6 months. The effects of age, surgical margins (+/−), comorbidity index, time to discharge after surgery, TMN pathologic staging, surgical volume, and patient income significantly impacted survival after radiation and surgery (p<0.05 for all values). There was a significant relationship between time delay and pCR (p=0.0002). At delay <30 days, 4.0% of patients achieved pCR, while 9.3% of patients have achieved pCR by 75 days. In cases with delay of >75 days, the rate of pCR decreased. Overall, 6.8% of patients (n=461) achieved pCR. Using a refined Cox model to examine survival, a delay of more than 60 days was associated with 20% greater risk of mortality (95% CI 1.061 – 1.367). This effect became more pronounced with increasing delay; a delay of >75 days was associated with 28% (95% CI 1.061-1.55) increased risk of mortality, while patients with delay <60 days saw a survival benefit. **Conclusions** Although an interval up to 75 days between radiation and surgery may achieve higher rates of complete pathologic response, delay of more than 60 days from radiation to surgical resection and subsequent systemic chemotherapy decreases overall survival in patients with rectal cancer.
A. Surapaneni, M. Shaik, L.B. Berbiglia, A. Surapaneni, J. Gernand, M. Hicks, S.K. Saha, G. Paez, S. Gre-wald, M. Arora, 1. McLaren Regional Medical Center, Flint, MI; 2. Dana-Farber Cancer Institute, Boston, MA.

Introduction: Tumor size is a prognostic factor in breast, renal, lung and other cancers, but not in colon cancer (CCA), possibly due to lack of prognostic data. Tumor depth(T), nodal status (N), and metastasis (M) are used in the current TNM staging for CCA by American Joint Committee on Cancer (AJCC). Hence, we compared tumor size as an independent risk factor for death in CCA between National cancer database (NCDB) versus Surveillance, Epidemiology, and End Results (SEER) analysis.

Methods: Data included tumor size, age, sex, grade, T-stage, N and M-status for 300,386 and 76,370 CCA patients(pts) from the NCDB and SEER (1998-2010), respectively. We divided pts into 4 “S” groups by tumor size (S1: 0cm; S2: >0-4cm; S3: >4-6cm, and S4:>6cm). Data was analyzed using the Kaplan-Meier method for 5 year overall survival (5yOS).

Results: Adjusted hazard ratios (aHRs) were calculated using a Cox model adjusting for age, sex, grade, T-stage and N status.

Table 1(a): Demographics of NCDB and SEER database patients; (b) SY50 and adjusted Hazard Ratio of NCDB and SEER database patients

<table>
<thead>
<tr>
<th>Table 1(a) Variables</th>
<th>NCDB patients</th>
<th>SEER patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of patients</td>
<td>300,386</td>
<td>76,370</td>
</tr>
<tr>
<td>Median age (yrs)</td>
<td>72</td>
<td>67</td>
</tr>
<tr>
<td>Tumor size (cm)</td>
<td>4</td>
<td>4.5</td>
</tr>
<tr>
<td>Nodal positivity</td>
<td>1.52</td>
<td>17.8</td>
</tr>
</tbody>
</table>

Aim: To evaluate the surgical morbidity and oncological outcome of such aggressive treatment. Patients and methods: Between 2006 and 2012 a consecutive series of 40 patients with locally recurrent rectal cancer underwent abdomin sulfacal resection (ASR) in 18 patients, total pelvic exenteration with sacral resection in 10 patients and extended pelvic exenteration in 12 patients. Patients with sacral resection were 28, with the level of sacral division at S2-3 interface in 10 patients, at S3-4 in 15 patients and S4–5 in 3 patients. Results: Forty patients, male to female ratio 1.7:1, median age 45 years (range 25–65 years) underwent extended pelvic resection in the form of pelvic exenteration and abdominosacral resection. Morbidity, re-admission and mortality rates were 55%, 37.5%, and 5%, respectively. Mortality occurred in 2 patients due to perineal flap sepsis and massive myocardial infarction. A R0 and R1 sacral resection were achieved in 62.5% and 37.5%, respectively. The 5-year overall survival rate was 22.6% and the 4-year recurrence free survival was 31.8%. Conclusion: Extended pelvic resection as pelvic exenteration 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.

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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 morbidity and oncological outcome of such aggressive treatment. Patients and methods: Between 2006 and 2012 a consecutive series of 40 patients with locally recurrent rectal cancer underwent abdominosacral resection (ASR) in 18 patients, total pelvic exenteration with sacral resection in 10 patients and extended pelvic exenteration in 12 patients. Patients with sacral resection were 28, with the level of sacral division at S2-3 interface in 10 patients, at S3-4 in 15 patients and S4–5 in 3 patients. Results: Forty patients, male to female ratio 1.7:1, median age 45 years (range 25–65 years) underwent extended pelvic resection in the form of pelvic exenteration and abdominosacral resection. Morbidity, re-admission and mortality rates were 55%, 37.5%, and 5%, respectively. Mortality occurred in 2 patients due to perineal flap sepsis and massive myocardial infarction. A R0 and R1 sacral resection were achieved in 62.5% and 37.5%, respectively. The 5-year overall survival rate was 22.6% and the 4-year recurrence free survival was 31.8%. Conclusion: Extended pelvic resection as pelvic exenteration 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.

P128

An Investigation of the Role of Irinotecan and Oxaliplatin in Liver Toxicity during First-line Chemotherapy G. Desolenex, M. Desjardin, I. Soubeyran, J. Vara, Y. Becouarn, V. Brouste, S. Evrard, D. Bechade, Surgical Oncology, Digestive Tumors Group, Institut Bergonie, Bordeaux, France.

Background: Neoadjuvant chemotherapy (CT) have been associated with an increased risk of surgery for colorectal liver metastases (CRLM). Irinotecan (IRI) is claimed to induce CT-associated steatohepatitis (CASH) and oxaliplatin (OX) to induce sinusoidal obstruction (SOS). Imputability is sometimes difficult to establish and the impact on postoperative complications is unclear. The objective of this study is to investigate the impact of IRI and OX on induced liver toxicity, and to study the effects on surgical outcomes. Methods: Patients (Pts) who received only one line of CT before resection of CRLM were retrospectively included. CASH and SOS were described according to Kleiner and Rubbia-Brandt classifications respectively. Associations were sought between CASH or SOS and various patient and treatment factors, and between patient and treatment factors and the occurrence of post-operative complications grade 3 or over. Results: Among 379 pts operated on for CRLM from 2003 to 2013, 223 were eligible for inclusion; 57 were excluded as there was no healthy hepatic parenchyma to be analyzed. Median age was 64 [34-88], BMI ≥ 25 kg/m² for 52%, 8% had diabetics, and 28% had hypertension. CRLM were synchronous in 76.5%, 65 (39.2%) received Folfox, 95 (57.2%) Folfox and 6 (3.6%) FOLFIRINOX. Bevacizumab, cetuximab and panitumumab were given in 71 (42.8%), 30 (17.5%), 4 (2.4%) respectively. Extra-hepatic resections were performed in 78 pts (47%). 90-day mortality was 1.8% and 31 pts encountered complications more severe than 3A. Histological hepatotoxicity was established for 82 pts (49%) including 33 (19.9%) with grade 2 or 3 SOS and 22 (13%) with CASH. No significant associations were identified between SOS and OX, nor CASH and IRI. BMI ≥ 25 kg/m² was correlated with an increased risk of CASH. Only septic extra-hepatic surgeries were correlated with the prediction of postoperative complications. Conclusions: In this serie, preoperative CT was not associated to liver toxicity. The presence of histological lesions did not worsen post-operative outcomes. BMI and extra-hepatic surgery were the only co-factors correlated with CASH and post-operative complications.

P130


Introduction: Current risk stratification tools for patients with colorectal cancer (CRC) rely on surgical pathology parameters, but may be improved with the addition of novel serum biomarkers representing the host response to disease. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been shown to have prognostic significance in several disease sites. The purpose of this study was to evaluate the utility of preoperative NLR and PLR in predicting recurrence-free survival (RFS) and overall survival (OS) in patients with operable CRC. Methods: All patients who underwent curative resection for adenocarcinoma of the colon or rectum at a large tertiary academic hospital were identified. NLR and PLR were evaluated preoperatively. RFS and OS were estimated using the Kaplan-Meier method and compared by the log-rank test. Univariate and multivariable Cox proportional hazard regression was used to identify associations. Results: 549 patients were included in the study. High NLR (NLR≥2.6) was associated with worse RFS (HR 2.03, 95% CI: 1.48-2.79, p<0.001) and OS (HR 2.25, 95% CI: 1.54-3.29, p<0.001) on
univariate analysis. High PLR (PLR≥2.95) was also associated with reduced RFS (HR 1.68, 95% CI: 1.06-2.65, p=0.028) and OS (HR 1.81, 95% CI: 1.06-3.06, p=0.028). Patients with high NLR had lower 2- and 5-year RFS and OS relative to the low NLR group (RFS: 76% and 59% vs. 85% and 77%; OS: 87% and 71% vs. 93% and 85%) (Figure 1). Similarly, patients with high PLR had lower 2- and 5-year RFS and OS relative to the low PLR group (RFS: 72% and 54% vs. 82% and 70%; OS: 83% and 66% vs. 90% and 82%). In the multivariable model, high NLR retained significance for lower RFS (HR 1.59, 95% CI: 1.1-2.28, p=0.013) and OS (HR 1.91, 95% CI: 1.26-2.9, p=0.002).

Conclusions: High preoperative NLR in this series was shown to be a negative, independent prognostic factor in patients undergoing surgical resection for non-metastatic CRC. The prognostic ability of this serum biomarker may help to guide use of adjuvant therapies and patient counseling. Further studies are required to validate these results.

Figure 1. Kaplan-Meier survival curves stratified by high and low NLR and PLR. High NLR (NLR≥2.6) and PLR (PLR≥2.95) are associated with worse RFS and OS in patients undergoing curative resection for colorectal cancer.

**P131**
Transanal Local Excision of Rectal Cancer: Social Disparities and Impact on Outcome

Introduction: Indications for transanal local excision of rectal adenocarcinoma have been characterized in highly selected patients. Less is known about the impact of social or racial disparities on access to these techniques. We investigated differences in surgical approach (local excision versus radical resection) across various patient demographics and analyzed their effects on survival. Methods: We queried the National Cancer Database (NCDB) to identify patients from 1998 to 2011 with T1, ≤3 cm, well or moderately differentiated rectal adenocarcinoma without perineural invasion who had undergone local excision or radical resection. We analyzed differences in age, gender, race, insurance coverage, geographic setting, and hospital type in relation to surgical approach. A multivariate Cox regression model was used to evaluate the association between surgical approach and overall survival (OS).

**P132**
Feeding Tube Placement during CRS/HIPEC for Colorectal Cancer does not Improve postoperative Nutrition and is associated with Increased readmission rates
S.P. Dineen,* K. Robinson, K. Beaty, A. Arrington, P. Mansfield, R. Royal, K. Fournier. Surgical Oncology, MD Anderson Cancer Center, Houston, TX.

Introduction: Patients with colorectal cancer and peritoneal carcinomatosis (CRC/PC) may benefit from cytoreductive surgery and heated intraperitoneal chemotherapy (HIPEC). However, the morbidity of HIPEC is substantial. Nutritional support is frequently required in patients during the postoperative period following HIPEC. It remains unclear if placement of feeding access during HIPEC is of benefit. Methods: Patients with CRC/PC who underwent evaluation for potential HIPEC between Jan 2010 and April 2014 were evaluated. Preoperative and postoperative nutritional and outcomes data were retrospectively recorded. The presence of a feeding tube and PCI scores were recorded by review of operative notes. Readmission rates were calculated for patients at 30 days and 60 days post-discharge from hospital. Results: 41 patients underwent HIPEC, 25 of whom had feeding tube placed at the time of HIPEC. PCI and tumor grade were similar between groups. Weight loss was common following HIPEC as 39/41 patients demonstrated some degree of weight loss. The mean weight loss was 7.6%. TPN was required at discharge in 4 patients (7.9%), 3 of these patients had feeding access placed. There was no difference in the degree of weight loss between groups (7.1 ± 3.7% no tube vs 7.9 ± 5.8% patients with tube). The mean preoperative albumin was 4.05 ± 0.99 g/dl compared to 3.58 ± 0.74 g/dl on the first postoperative visit (p < 0.05). The mean decrease in albumin was 12.7%, but was not significantly different in patients with feeding access and those without (10.0% vs 14.7%, p = NS). 60 day readmission rates were higher in patients with feeding tubes (36% compared to 0%, p < 0.01). Conclusions: Significant nutritional loss is common after HIPEC for patients with CRC/PC. Feeding tube placement does not prevent this and appears to be related to higher readmission rates. It is possible that placement of feeding tube access represents a selection of patients with higher burden of disease. Routine placement of feeding access should be avoided and prospective studies are warranted to evaluate which patients benefit from such measures.

**P133**
Selective Loss of MicroRNA 145 in Therapeutic Resistant Colorectal Cancer Cells
V. Findlay, C. Wang, K. Hurst, L. Nogueira, K. Staveley O’Carroll, E.R. Camp,* Medical University of South Carolina, Charleston, SC.

Introduction: Repression of the tumor suppressor microRNA-145 (miR-145) is associated with aggressive neoplastic features across malignancies including colorectal cancer (CRC). Previously, we demonstrated that the
E-cadherin transcriptional repressor SNAI2 enhanced cancer stem cell (CSC) features, led to 5-FU resistance, and directly inhibited miR-145 expression. Furthermore, miR-145 levels inversely correlated with CRC therapeutic response to neoadjuvant chemoradiation. Therefore, we hypothesized that loss of miR-145 expression promotes chemoresistance along with enhanced CSC phenotype. Methods: Colon cancer cell lines were grown in 2D and as tumorspheroids by culturing cells for 7-10 days in ultralow attachment plates. miR-145 and SNAI2 expression were assessed by quantitative real time PCR. Stable knockdown of miR-145 was achieved by lentiviral transduction of antagonim-145 and scramble control in HCT-116 cells (HCT-a145 and HCT-scr respectively). Sensitivity to 5-FU and oxaliplatin was assessed by SRB assay after 72 hours. Results: Tumorspheroids from HCT-116, DLD-1, and SW620 cells displayed chemotherapeutic resistance when compared to standard growth in 2D. HCT-116, DLD-1, and SW620 tumourspheres demonstrated loss of miR-145 expression by ~2, ~41, and ~18-fold respectively (p<0.02). HCT116 cells with stable knockdown of miR-145 (HCT-a145) demonstrated a 3-6-fold increase in SNAI2 expression and increased resistance to both 5-FU and oxaliplatin compared with HCT-scr cells. After 72 hours, HCT-a145 cells demonstrated a ~3.5-fold increased cell viability in response to 0.4uM oxaliplatin (p=0.0001) and ~2 fold increase in response to 2uM 5-FU (p=0.29). Furthermore, viable parental HCT-116 cells following 48 hr exposure to 20uM 5-FU demonstrated a ~70% reduction in miR-145 levels compared with the untreated cells (p=0.0002). Conclusion: These results suggest that miR-145 is selectively repressed in aggressive, chemoresistant CRC cells and promotes chemotherapy resistance. miR-145 replacement may represent a novel gene therapy strategy to enhance CRC conventional therapeutic response.

**P134**

**Intralesional Injection of Rose Bengal Induces an Anti-tumor Immune Response and Potent Tumor Regressions in a Murine Model of Colon Cancer**


**INTRODUCTION:** Early phase studies using intratumoral injection of PV-10 (10% Rose Bengal) have shown regression of in-transit melanoma deposits and non-treated bystander lesions. The effects of PV-10 on colorectal cancer (CRC) cells and established tumors is unknown. METHODS: Murine and human colorectal cancer cells were treated in vitro with varying concentrations of PV-10. Cell viability was determined by the MTS assay, trypan blue, DAF-FM, and SNARF-1 staining. To determine an underlying immune mechanism, a murine CT26 syngeneic CRC model was utilized. Bilateral subcutaneous CRC cell tumors were established in Balb/C mice and one tumor in each mouse was injected with PV-10 at a dose equal to half the calculated tumor volume. Tumors were measured daily. Splenocytes from treated animals were co-cultured with irradiated CT26 cells and supernatants analyzed for INF-γ production by ELISA.

**RESULTS:** PV-10-induced CT26 cell death, corresponding increases in nitric oxide production, and decreased intracellular pH in both CT26 murine and HT29 human CRC cells within hours of exposure compared to controls (p<0.01), and at levels similar to 5FU. Treatment of subcutaneous tumors with a single injection of intralesional PV-10 led to near complete responses in all animals within days of exposure and significant regression of the injected lesions compared to controls (n=6 per group, p=0.027). PV-10 treatment was associated with occasional bystander responses in contralateral untreated tumors and trended towards a decreased rate of growth in these lesions. Splenocytes isolated from tumor bearing mice treated with PV-10 displayed enhanced tumor-specific IFN-γ production compared to splenocytes from PBS-treated mice (p = 0.025). **CONCLUSION:** Rose Bengal induced potent cell death in human and murine colon cancer cells in vitro. Intralesional injection in established tumors induced an anti-tumor immune response and significant tumor regressions in vivo. These studies establish that intralesional PV-10 therapy warrants further study as a potential immunotherapeutic agent in colorectal cancer and metastases.
P136
The Impact of Radiotherapy on Rates of Surgical Site Infection in Patients with Rectal Cancer: Benchmarks for Comparison
N. Yuen,* C. Li, A. Monjazeb, V. Khatri, R. J. Bold, R. J. Canter. General Surgery, UC Davis Medical Center, Sacramento, CA.

Background: Radiation therapy (RT) is a standard component in the multimodality management of rectal cancer. Although prior RT is widely considered a risk factor for poor wound healing and surgical site infection (SSI), limited multi-center data are available, particularly for patients with rectal cancer. We sought to evaluate the effect of RT on the incidence of SSI in a national database of patients with rectal cancer. Methods: Using the NSQIP database (2005-2011) we identified 15,487 adult patients (>18) with a diagnosis of rectal cancer (ICD-09 154.0-154.1) undergoing surgery (LAR, APR, laparoscopic procedures) with or without RT. Endoscopic and transanal procedures were excluded. We evaluated patient demographics, comorbidities, and treatment-related variables on the rates of superficial and deep SSI. Odds ratios (OR) were calculated using multivariable logistic regression analysis.

Results: Mean age was 62.1, 59.5% of patients were male, and 75.0% of patients were white. Diabetes and smoking were present in 15% and 19.2%, respectively. 27.2% of patients received preoperative RT, 9.3% chemotherapy, and 6.8% received both. Overall, the incidence of SSI was 15.1%, with 8.7% superficial, and 7.2% deep/organ/space. On multivariable logistic regression analysis, gender, BMI, diabetes, smoking status, ASA, return to OR within 30 days, and RT predicted higher risk of both superficial and deep SSI. The Odds Ratio (OR) for RT was 1.37 (p=0.01) for all SSI, 1.34 (p=0.01) for superficial SSI, and 1.38 (p=0.01) for deep SSI. Conversely, chemotherapy was associated with an OR 0.80 (p=0.03) for superficial SSI. In contrast to previous studies, we observed a greater risk of all SSI after RT for LAR (OR 1.33, p=0.01) than for APR (OR 1.08, p=0.52).

Conclusions: Preoperative RT is associated with a higher risk of SSI (superficial and deep) in patients undergoing definitive surgery for rectal cancer. These nationwide data serve as current benchmarks for comparison as novel surgical techniques, tailored approaches to patient selection, and quality improvement projects are implemented in the multimodality management of patients with rectal cancer.

P137
Postoperative Morbidity and Mortality after Resection of the Primary Tumor in Patients with Stage IV Rectal Cancer J. 1 Lam-Boer,* J. Rooks,1 K. Verhoeof,1 J. De Witt. 1. Radboud University Medical Center, Nijmegen, Netherlands; 2. Erasmus Medical Center, Rotterdam, Netherlands.

Introduction. There is no consensus about the benefit of a palliative resection of the primary tumor in stage IV colorectal cancer. An increased risk of postoperative mortality compared to stage I-III is often used as an argument against palliative resection in patients with an asymptomatic tumor. The aim of our study was to investigate if patients with stage IV colorectal cancer have an increased risk of postoperative morbidity and mortality after resection of the primary tumor. Methods. All patients who underwent colorectal surgery between 2009 and 2013 were selected from the Dutch Surgical Colorectal Audit, a nation-wide surgical database. Differences in postoperative morbidity and mortality between stage I-III and stage IV were compared with the χ2-test. We used a multivariable logistic regression to identify independent predictors of morbidity and mortality. Results. From a total of 43,827 patients, 37,985 patients (86.7%) had a stage I-III tumor and 5,842 patients (13.3%) had stage IV disease. There were no differences in the occurrence, number or type of postoperative complications between the two groups. Postoperative mortality was higher in stage IV compared to stage I-III (6.4% versus 3.7%, p<0.001). Age (≥70 years versus <70 year; HR 2.20 [95%CI 1.65-2.92]), ASA classification (≥II versus I-II; HR 2.52 [95%CI 1.91-3.31]), Charlson comorbidity index (≥2 versus 0; HR 1.72 [95%CI 1.26-2.36]) or location of the primary tumor (rectum versus colon; HR 0.37 [95%CI 0.23-0.58]) were all strong predictors of postoperative mortality in patients with stage IV colorectal cancer. Conclusion. Patients with stage IV colorectal cancer did not have an increased chance of postoperative complications after resection of the primary tumor. However, mortality within 30 days was higher in stage IV. Important predictors of postoperative mortality were age, ASA score, comorbidity and location of the primary tumor.

P138
The Impact of Nodal Metastasis on Survival in Stage IV Colon Cancer: Analysis of National Cancer Data Base versus Surveillance, Epidemiology and End Results (SEER) data to determine the impact of nodal metastasis on survival in Stage IV CCa patients (pts).

Methods: From 1998-2010 NCDB and SEER pts diagnosed with pathologic Stage IV CCa were divided into groups based on LN status (N0 = LN negative, N1 = 1-3 LN positive, N2 = 4 or greater LN positive). Only Stage IV CCa pts who underwent surgical resection of their primary tumor with available pathologic data were included. Kaplan Meier method and log rank test were used to compare 5 and 3 year overall survival (yrOS) with p-value <0.05 considered as statistically significant. Adjusted hazard ratios (aHRs) were calculated using Cox proportional regression model after adjusting for age, grade and tumor stage. Results: There were 73,567 pts included from NCDB and 12,438 pts included from SEER. Overall LN positivity was 82.4% for NCDB and 82.9% for SEER. The 3yrOS for N0, N1 and N2 was 34%, 25% and 16% for NCDB, and 40%, 30% and 19% for SEER, respectively. The 5yrOS for N0, N1 and N2 was 18.7%, 12.1%, and 7.1% for NCDB, and 22.5%, 15.1% and 9.0% for SEER, respectively (ref. Table 1). The aHRs of pts with vs. without LN mets was 1.8 (95% CI 1.7-1.9) for NCDB, and 1.53 (95% CI 1.41-1.6) for SEER. Conclusion: Stage IV CCa with LN mets was associated with decreased 3 and 5yrOS in both NCDB and SEER. The number of positive nodes also inversely impacted survival. Compared to pts without LN mets, the overall risk of death for LN positive pts in NCDB was 80% higher and for SEER was 53% higher. This suggests separation of Stage IV LN negative versus positive pts may be warranted in staging and treatment, as pts with LN mets have a significantly worse prognosis.

Table 1: NCDB and SEER Stage 4 Colon Cancer Patients: Comparison of Nodal Metastasis and Overall Survival

<table>
<thead>
<tr>
<th># of patients</th>
<th>NCDB 12,438</th>
<th>SEER 23,409</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 4 (N1&gt;1 N mets)</td>
<td>34%</td>
<td>40%</td>
</tr>
<tr>
<td>Stage 4 (N1=N mets)</td>
<td>7%</td>
<td>19%</td>
</tr>
<tr>
<td>Stage 4 (N2&gt;1 N mets)</td>
<td>16%</td>
<td>19%</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.01</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Overall survival of all N groups</td>
<td>23%</td>
<td>26%</td>
</tr>
</tbody>
</table>

P139
Quantifying the Contribution of Stage to Race-related Colorectal Cancer Survival Disparity: A Texas Cancer Registry Analysis
U. Phatak,* C. Green,* G. J. Chang,† T. C. Ko,* L. Kao,† C. J. Vray,* 1. Surgery, University of Texas Houston, Houston, TX; 2. MD Anderson Cancer Center, Houston, TX.

Background Multiple factors contribute to race-related colorectal cancer (CRC) outcomes. However, it is unknown to what degree stage at diagnosis contributes to these survival disparities. The purpose of this study is to quantify the effect of stage at diagnosis on overall CRC survival among African-Americans (AA) and Hispanics compared to Caucasians. METHODS The Texas Cancer Registry was queried for all CRC patients from 1995-2009. Data were collected regarding demographics, stage at diagnosis, and type of treatment. The primary outcome was overall survival. To account for changes in the baseline hazard of death, an accelerated failure time model was used to estimate survival. Results were expressed in time ratios (TR)—the rate at which a subject moves along the survival curve. A TR <1.0 indicates acceleration towards failure (death). To quantify the contribution of stage, the model was tested with and without stage. RESULTS There were a total of 101,200 CRC patients in the registry for whom date of diagnosis was available. AAs had the highest unadjusted mortality rate at 58.9% and the shortest median survival (44 months) (Table 1). Female gender, younger age and higher SES were predictive of improved survival; whereas, AA race and stage (regional or metastatic) were predictive of worse survival. Inclusion of stage in the full AFT model resulted in a TR of 0.83 (95% CI 0.80-0.86) indicating AAs accelerate 17% faster than

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Caucasians towards death. Exclusion of stage resulted in 24% faster progression to death for AAs with a TR of 0.76 (95% CI 0.74-0.79). Given these TRs, 9.2% of the disparity in survival can be attributed to race. CONCLUSION: This study adds an observational angle to the known racial survival disparities, highlighting the potential role of preoperative and perioperative clinical variables as factors contributing to survival disparities.

### Table 1: Cohort characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Caucasian</th>
<th>Neutrophi</th>
<th>Lymphocyte</th>
<th>NLR</th>
<th>PLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years, IQR</td>
<td>69 (68-77)</td>
<td>60 (60-72)</td>
<td>62 (61-65)</td>
<td>62 (60-65)</td>
<td>62 (60-65)</td>
</tr>
<tr>
<td>Sex, % (M/F)</td>
<td>339 (35.2%)</td>
<td>573 (52.6%)</td>
<td>456 (43.6%)</td>
<td>63 (60-65)</td>
<td>12 (9-14)</td>
</tr>
<tr>
<td>Death, %</td>
<td>240 (28.6%)</td>
<td>200 (18.4%)</td>
<td>197 (18.9%)</td>
<td>39 (36.5%)</td>
<td>39 (36.5%)</td>
</tr>
<tr>
<td>Median survival (months, IQR)</td>
<td>30 (25-40)</td>
<td>30 (25-40)</td>
<td>14 (9-21)</td>
<td>14 (9-21)</td>
<td>14 (9-21)</td>
</tr>
<tr>
<td>Socioeconomic Quartile, IQR</td>
<td>&lt;5%</td>
<td>25%</td>
<td>50%</td>
<td>75%</td>
<td>&gt;75%</td>
</tr>
</tbody>
</table>

#### **P141**

**Biologic Factors associated with Survival in Patients with Pseudomyxoma Peritonei**

S.J. Judge, S. Shetty, P. Thomas, V. Govindarajan, P. Sharma, B.W. Loggie.

**Surgery, Creighton University School of Medicine, Omaha, NE.**

**Background**: We have suggested a three-tier classification for Pseudomyxoma Peritonei (PMP) that is a modification of the WHO classification. PMP1 is low-grade (WHO low) and PMP2, 3 split the WHO high-grade category. Having the worst prognosis, PMP3 differs by the presence of any percentage of signet ring cell carcinomas (SRCs). Our aim was to define biologic factors that account for the poor survival in the SRC cohort.

**Materials and Methods**: 211 patients treated for PMP of appendiceal origin by a single surgeon between 2003 and 2011 were included in this retrospective study. Records were reviewed for classification, resection status (R0 vs. R2), chemotherapy agent, and expression of Ki-67, p53, thymidine synthase (TS), and thymidine phosphorylase (TP). **Results**: Median survival for PMP1, 2 and 3 were 120, 88 and 40 months, respectively (p<0.001). Ki-67 was a significant predictor of overall survival (p=0.003) and p53 was a predictor of disease-free survival in PMP1 and PMP2 (p=0.003). No significant difference was seen in SRC patients or between PMP2 and PMP3. Resection status was related to increased overall survival for all PMP patients (p=0.003), and to those receiving chemotherapy in PMP1 (p=0.002), but not in PMP2 and PMP3. TS and TP did not correlate to overall or median survival amongst PMP tiers. **Conclusion**: TS and TP are not useful prognostic factors for survival or response to chemotherapy. As expected PMP1 showed a lower proliferative index (Ki-67) than PMP2 and PMP3. Though similar proliferation rates were seen in PMP2 and PMP3, significantly worse outcomes were seen in PMP3. Increased proliferation is not sufficient to explain the aggressiveness of SRCs.

### P140

**Neutrophil-to-Lymphocyte Ratio Predicts Major perioperative Complications in Patients with Colorectal Cancer**


**Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.**

**Introduction**: The Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) are well-studied serum biomarkers for systemic inflammation. The objective of this study was to evaluate the association of NLR and PLR with the occurrence of major perioperative complications in patients undergoing colorectal surgery. **Methods**: A retrospective cohort study was performed for patients who underwent resection for suspected colorectal cancer at a large tertiary academic center from 2004 to 2011. NLR and PLR scores were calculated from preoperative blood work and high versus low value cohorts were defined via ROC curve generated cut-offs. Regression analysis was performed to determine if patients with an elevated NLR/PLR value cohorts were defined via ROC curve generated cut-offs. Regression analysis was performed to determine if patients with an elevated NLR/PLR value were at increased risk for major complications. Neither NLR nor PLR was associated with minor complications. PLR was not associated with better outcomes. These patients have worse OS and RFS (Table 1). Preoperative CTX was associated with worse outcomes. These patients have worse OS and RFS; therefore CRS/HIPEC can be considered palliative in patients exhibiting ascites, obstruction, need for preoperative CTX, multiple bowel anastomoses, and/or postoperative bowel complications.
P143
Genetic Analysis of Colorectal Cancers in Young Patients
A. Abbott,1 N. Kothari,2 T. Srikrum,3 J. Teer,4 R. Kim,5 D. Reed,5 D. Shibata,1 Surgical Oncology, H. Lee Moffitt Cancer Center, Tampa, FL.

Introduction: The incidence of colorectal cancer (CRC) is increasing in adults <50 years old and these cases may be associated with a worse prognosis. Despite our growing understanding of genetic conditions, a substantial number of CRC in young patients are classified as sporadic but may harbor unique molecular changes. We sought to compare profiles of genetic alterations between young and old patients who lack defects in known hereditary cancer genes. Methods: 283 CRC cases diagnosed between 1998 and 2010 were analyzed by targeted exome sequencing using next-generation targeted cancer genes. Conclusions: The top ten genes mutated with significant differential mutation frequencies are shown in Table 1.

Table 1. Top 10 Differentially Mutated Genes

<table>
<thead>
<tr>
<th>Gene</th>
<th>OR 95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPP1R4</td>
<td>0.90</td>
<td>0.002</td>
</tr>
<tr>
<td>ADAMTS18</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>NRP1</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>INSRR</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>STC2</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>ABIBL</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>DLK1</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>MACF1</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>IFR2</td>
<td>0.012</td>
<td></td>
</tr>
</tbody>
</table>

P144
Oncologic Outcomes following Repeat Cytoreductive Surgery with Hyperthermic Intraoperative Chemoperfusion for Disseminated Peritoneal Carcinomatosis
F. Bednar,1 A. H. Zureikat,2 J. Pingpank,2 M. Holtzman, S. Alhrendt,3 L. Ramalingam,4 H. Jones,5 H. J. Zeh III,6 D. L. Bartlett,6 H. M. Choudry, Surgical Oncology, University of Pittsburgh, Pittsburgh, PA.

Introduction: Locoregional recurrence is common following cytoreductive surgery (CRS) with hyperthermic intraoperative chemoperfusion (HIPEC) for disseminated peritoneal carcinomatosis. The role for repeat CRS/HIPEC remains undefined with limited published data demonstrating meaningful long-term survival. Methods: We reviewed the oncologic outcomes of 55 patients undergoing >2 CRS/HIPEC procedures, who were identified from a prospective database of 1400 CRS/HIPEC patients treated between 2000 and 2012. Results: 45 patients underwent two and 10 patients underwent three procedures. Most patients had mucinous appendiceal carcinomatosis (MAC, n=31) or colorectal carcinomatosis (CRC, n=14). Median follow-up was 54.8 months. For patients with MAC, median survival following the 1st, 2nd and 3rd CRS/HIPEC was 112, 83 and 31 months. Median time was 27 months between the 1st and 2nd CRS/HIPEC and 47 months between the 2nd and 3rd CRS/HIPEC. There was no difference in the time between CRS/HIPEC procedures in patients with MAC when stratified for tumor grade (low-grade: 29 months between 1st and 2nd CRS/HIPEC and 47 months between 2nd and 3rd CRS/HIPEC; intermediate-grade: 19 months between 1st and 2nd CRS/HIPEC and 48 months between 2nd and 3rd CRS/HIPEC; high-grade: 34 months between 1st and 2nd CRS/HIPEC and 9 months between 2nd and 3rd CRS/HIPEC). For patients with CRC, median survival following the 1st, 2nd and 3rd CRS/HIPEC was 55, 32 and 14 months respectively. The median duration between the 1st and 2nd CRS/HIPEC was 24 months and between the 2nd and 3rd CRS/HIPEC it was 12 months. Conclusion: Repeat CRS/HIPEC offers meaningful long-term survival in patients with peritoneal carcinomatosis of appendiceal and colorectal origin. A prolonged surgery-free interval can be achieved following a 2nd CRS/HIPEC procedure in patients with low- and intermediate-grade MAC but not in patients with high-grade MAC or CRC.

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Predictors of postoperative Mortality in Stage IV Colorectal Cancer after Resection of the Primary Tumor
J. Rooks,1 S. Lam-Boer,2 F. Kruit,3 K. Reijnders,4 C. Rosman,5 H. Rutten,6 G. Slooter,7 E. Spillenaar-Bilgen,6 A. Bremers,1 J. De Wilt,1 Surgery: Radboud University Medical Center, Nijmegen, Netherlands; 2. Slingeland Hospital, Doetinchem, Netherlands; 3. Canisius Wilhelmina Hospital, Nijmegen, Netherlands; 4. ziekenhuis Gelderse Vallei, Ede, Netherlands; 5. Catharina Hospital, Eindhoven, Netherlands; 6. Maxima Medical Center, Veldhoven, Netherlands; 7. Rijnstate Hospital, Arnhem, Netherlands.

Introduction: There is increasing evidence that palliative resection of the primary tumor is associated with improved overall survival in patients with stage IV colorectal cancer (CRC). However, postoperative mortality is significantly higher in stage IV CRC compared to stage I-III CRC. The aim of this case-control study was to identify preoperative predictors of 30-day mortality after resection of the primary tumor. Methods: All patients with stage IV CRC who underwent resection of the primary tumor in seven Dutch hospitals between 2008 and 2013 were selected from the Netherlands Cancer Registry. All patients who died within 30 days after surgery were identified, and randomly matched to a control group of patients from the same hospitals who survived beyond 30 days. Differences in preoperative patient characteristics, tumor load and biochemical markers between the two groups were compared using the chi square test. Independent predictors for postoperative mortality were identified performing a multivariable logistic regression analysis. Results: Between 2008 and 2013, 897 stage IV CRC patients underwent primary tumor resection. The 30-day mortality rate was 6.1% (n=55). There were remarkable differences in postoperative mortality between high- and low-risk cases (8.3% versus 1.7%, p<0.001). Multivariable logistic regression analysis included various baseline parameters such as age (OR 1.1 [95%CI 1.0-1.2]), ASA score (OR 1.1 [95%CI 1.0-1.2]), serum albumin (decreased versus normal: OR 4.2 [95%CI 1.3-13.9]) and albumin (decreased versus normal: OR 7.4 [95%CI 1.7-32.2]) were all
We tested the ability of iRGD to potentiate IP chemotherapy and facilitate bicin (DOX), was injected intraperitoneally into peritoneal tumor mice. FAM peptide (FAM-iRGD), quenched FAM-iRGD (Q-iRGD), which detects pro-surgery and IP chemotherapy.

INTRODUCTION: Intraoperative (IP) chemotherapy of peritoneal tumors is limited by poor drug penetration into tumor tissue. iRGD, a tumor-penetrating peptide, facilitates tumor entry of drugs conjugated to iRGD, and even free drugs co-injected with iRGD, through transvascular and local penetration. This approach facilitates intraoperative tumor detection and stratifies patients for iRGD chemotherapeutics and reduces systemic drug toxicity. Q-iRGD may serve as a tumor-penetrating peptide, facilitates tumor entry of drugs conjugated to iRGD, and even free drugs co-injected with iRGD, through transvascular and local penetration. A tumor-penetrating peptide, facilitates tumor entry of drugs conjugated to iRGD, and even free drugs co-injected with iRGD, through transvascular and local penetration. The accumulation was via local penetration as dextran entry into extraperitoneal tumors of colon, gastric and ovarian cancer in mice. IP co-injection of iRGD facilitated tumor-specific dextran accumulation. The accumulation was via local penetration as dextran entry into extraperitoneal tumors of colon, gastric and ovarian cancer in mice.

METHODS: Fluorescein-labeled iRGD peptide (FAM-iRGD), quenched FAM-iRGD (Q-iRGD), which detects proteolytic activation of iRGD, or iRGD combined with free dextran or doxorubicin (DOX), was injected intraperitoneally into peritoneal tumor mice. FAM and DOX accumulation in tissues was evaluated by imaging, microscopy, and spectrophotometry. Effects of iRGD-DOX IP combination therapy were examined in long-term mouse treatment studies.

RESULTS: FAM-iRGD accumulated into peritoneal tumors of colon, gastric and ovarian cancer in mice. IP co-injection of iRGD facilitated tumor-specific dextran accumulation. The accumulation was via local penetration as dextran entry into extraperitoneal tumors of colon, gastric and ovarian cancer in mice.

CONCLUSION: Results suggest clinical relevance of iRGD in both treatment and detection of peritoneal tumors including the potential as a probe to stratify patients for iRGD therapy. Further investigation as a companion to cytoreductive surgery and IP chemotherapy.

PI146 Tumor-penetrating iRGD Peptide Potentiates Intraoperative Chemotherapy and Facilitates Peritoneal Tumor Detection K. Sugahara,1* P. Scodeller,1 G.B. Braun,1 T.H. De Mendoza,1 T. Teesalu,2 E. Ruoslahti,2 A.M. Lowy,1 1. Surgery, Columbia University, New York, NY; 2. Sanford-Burnham Medical Research Institute, La Jolla, CA; 3. University of California San Diego, La Jolla, CA.

INTRODUCTION: Intraoperative (IP) chemotherapy of peritoneal tumors is limited by poor drug penetration into tumor tissue. iRGD, a tumor-penetrating peptide, facilitates tumor entry of drugs conjugated to iRGD, and even free drugs co-injected with iRGD, through transvascular and local penetration. This approach facilitates intraoperative tumor detection and stratifies patients for iRGD chemotherapeutics and reduces systemic drug toxicity. Q-iRGD may serve as a tumor-penetrating peptide, facilitates tumor entry of drugs conjugated to iRGD, and even free drugs co-injected with iRGD, through transvascular and local penetration. A tumor-penetrating peptide, facilitates tumor entry of drugs conjugated to iRGD, and even free drugs co-injected with iRGD, through transvascular and local penetration. The accumulation was via local penetration as dextran entry into extraperitoneal tumors of colon, gastric and ovarian cancer in mice.

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RESULTS: FAM-iRGD accumulated into peritoneal tumors of colon, gastric and ovarian cancer in mice. IP co-injection of iRGD facilitated tumor-specific dextran accumulation. The accumulation was via local penetration as dextran entry into extraperitoneal tumors of colon, gastric and ovarian cancer in mice.

CONCLUSION: Results suggest clinical relevance of iRGD in both treatment and detection of peritoneal tumors including the potential as a probe to stratify patients for iRGD therapy. Further investigation as a companion to cytoreductive surgery and IP chemotherapy.

P147 Usefulness of Carcinoembryonic Antigen (CEA) as Prognosis Factor in Patients with Stage III Rectal Cancer Treated with Neoadjuvant Chemoradiation Therapy (CRT) P. Luna-Perez,1* M. Ramirez, D. Guzman, M. Gutierrez, P. Luna-Merlos. Surgical Oncology, Hospital de Oncologia CMN SXXI, Mexico D.F., Mexico.

Background. Approximately 10–40% of rectal cancer patients undergoing CRT had lymph node metastasis. Most of them developed recurrence. There is little information about the usefulness of prognostic indicators in such patients. The objective was to analyze the usefulness of CEA as a prognostic identifier of recurrence.

Methods. Between 1996 and 2010, 131 patients with rectal adenocarcinoma treated with CRT + surgery were classified as stage III. CEA levels were classified into 3 groups: I (pre and post treatment <5 ng), II (pre treatment >5 ng and post <5 ng) and III (pre and post treatment >5 ng). Factors associated with recurrence were analyzed by Cox regression analysis. Five-year disease-free survival with the Kaplan-Meier method and comparison with log-rank test. Results. There were 72 males and 59 females, mean age was 55.9 years. Mean tumor size, 6 cm; mean pretreatment value of CEA was 15.4 ng. Surgeries were: low anterior resection (63), abdominoperineal resection (35) and pelvic exenteration (33). Mean of harvested lymph nodes and metastatic lymph nodes was 19.5 and 8.8, respectively. Post-radiated surgical stages were: IIA (18), IIB (66) and IIC (47). At median follow-up of 72 months, 59 (45%) patients developed recurrences as follows: locoregional (15.2%), local + distal (2.2%) and systemic (27.4%). Recurrences according to tumor stage were: IIA, 11%, IIB, 51.5% and IIC, 48.9% (p=0.003). Recurrences according to CEA level: 5 ng was: local 15%, distal 17%, conversely with >5 ng was: local 17.8% and distant 37% (p=0.009). Disease-free 5-year survival among the 3 groups of CEA level was: was 59%, 37% and 25%, respectively (p=0.001). Associated factors with recurrence were: group I CEA level, ypN2 stage and tumor size >5 cm. Factors associated with survival were: pre and post-treatment CEA <5 ng and ypN1. Conclusions. Pre- and post treatment CEA level is a powerful tool to identify patients with high risk of recurrences and probably support the administration of induction chemotherapy before CRT in those patients with pretreatment CEA levels >5 ng.

P148 Real-world Treatment Patterns and the Uptake of Biologics in Elderly Medicare Patients with Metastatic Colon Cancer Cancer C. Mullins,1* K. Bikov,2 B. Seal,3 A. Hung,2 N. Hanna,1* 1. University of Maryland School of Medicine, Baltimore, MD; 2. University of Maryland School of Pharmacy, Baltimore, MD; 3. Bayer HealthCare Pharmaceuticals, Whippany, NJ.

Metastatic colon cancer (mCC) patients may receive multiple lines of treatment (Tx1, Tx2, etc.) consisting of one or more cytotoxic (CYT: 5FU/LV, Oxaliplatin [OX], Irinotecan [IRI]) and biologic (BIO: Bevacizumab [BEV], Cetuximab [CET], Panitumumab [PAN]) drugs. The NCCN provides evidence-based Tx recommendations for each line. The objective of this study was to examine real-world clinical practice patterns between 2002 and 2010. In particular, we compared the most common regimens across Tx lines and how Tx patterns changed over time. Methods: We used population-based SEER-Medicare data to determine Tx1, Tx2 and Tx3 regimens of 4,616 mCC patients (the median age at diagnosis was 78) diagnosed in 2003-2009 and followed through 2010. We will use an algorithm previously developed by us to identify regimens. Results: The most common CYT backbone in Tx1 was OX (51% of patients) followed by 5FU/LV (30%). In comparison, IRI was a preferred choice in Tx2 (65%) and Tx3 (31%). In 2003, the most common Tx1 regimens were 5FU/LV (56%) and IRI-based (35%). 5FU/LV and IRI use decreased to 22% and 9% respectively in 2009, while OX use increased from 7% in 2003 to 63% in 2009. In 2004, the FDA approved BEV for Tx1. BEV’s share increased from 9% in 2004 to 53% in 2005. BEV was used in 9% of Tx2 regimens in 2004 and 46% in 2005. CET was approved in 2004. CET use was in less than 5% of Tx1 regimens in any year up to 2010. CET use in Tx2 increased from 19% to 27% between 2005 and 2007, and declined to 23% in 2010. The FDA approved PAN in Sep 2006 for treatment after failure of CYT-based regimens, i.e. primarily in Tx3 and beyond. Only 35 (8%) of patients received Tx3, and of these 59 (17%) received PAN without a CYT backbone. One in three Tx3 regimens consisted of biologics only (54% CET, 43% PAN). Conclusions: This study used SEER-Medicare registry data to examine and document real-world clinical practice patterns in treatment of elderly mCC patients between 2003 and 2010. We observed that as new...
Robotic colectomy is a safe alternative to laparoscopic colectomy, and provides successful completion minimally invasively, those converted to open approach (55 days, P=.64). Conversion rate to open surgery was significantly lower with time from surgery to commencement of adjuvant chemotherapy (55 days vs. 4.2% vs 5.1%, P=.46), 30-day mortality (2.3% vs 2.0%, P=.46) and median survival (13 days vs. 16 days, P=.002).

Median time from surgery to commencement of adjuvant therapy 55 days 55 days 0.63
Conversion rate to open surgery 15.3% 11.7% 40.001

Comparison of Surgical outcomes between Laparoscopic and Robotic Colectomy

### P149

**Intermedin (IMD) Stimulates Cell Growth, Migration and Angiogenesis in Human Colorectal Adenocarcinoma**

**N. X. Guo,** The Ohio State University College of Medicine, Columbus, OH. 1, J.C. Schmitz, 2 E.M. Uchigo, 3 B.C. Kenney, 1 S. Kulkarni, 1 C.H. Cha. 1 Surgery, Yale University, West Hartford, CT. 2 University of California, Irvine, CA.

Introduction Intermedin (IMD) is a calcitonin gene-related peptide (CGRP) that has been shown to act as an angiogenic factor in a rat ischemic hind limb model, human endothelial cells, and in some tumor models via ERK, Akt, and VEGF/VEGFR2 signaling pathways. We hypothesized that IMD was expressed and played a role in colorectal tumor angiogenesis. Methods IMD expression in human colorectal cancer (CRC) tumor tissue was investigated at the mRNA and protein levels via a cDNA panel and CRC tissue microarrays (TMAs). Paraffin-embedded CRC tissue was evaluated by immunohistochemical (IHC) analysis. Eight different CRC cell lines were evaluated for the role of IMD in CRC using WST-1 proliferation assays, tranwell migration assays, invasion assays, and endothelial cell tube formation assays. Results IMD was noted to be expressed in human CRC tumor tissues on IHC with expression was significantly higher in stage I vs. stage 0 disease, with a stage I/0 ratio of 7.7 ± 0.4 (P = 0.05). IMD was also expressed in 7 of the 8 studied CRC cell lines. Analysis of human CRC tumor tissue revealed increased IMD expression in the tumor regions vs. the adjacent benign regions of the specimens. Inhibition of IMD expression by RNA interference in a CRC cell line reduced cell proliferation by 35.0 ± 1.4% (P = 0.018). On the contrary, overexpression of IMD in a CRC cells led to increased cellular growth and significantly increased cellular migration. Treatment of human umbilical vein endothelial cells (HUEVCs) with RKO/IMD conditioned medium increased endothelial cell tube formation by 14.7 ± 0.8% (P = 0.049). Conclusions IMD expression is increased in human CRC, resulting in stimulation of tumor cell growth, migration, invasion, and endothelial cell tube formation. Therefore, IMD likely has an important role in the tumor angiogenesis of CRC and may have a potential role as a tumor marker or therapeutic target.

### P150

**Robotic versus Laparoscopic Colectomy for Colon Adenocarcinoma: A Nationwide Analysis of Surgical Outcomes**


Introduction: Robotic colectomy (RC) is an increasingly adopted approach to minimally invasive colectomy. Our objective was to compare the nationwide surgical outcomes between robotic and laparoscopic colectomies (LC). Methods: We extracted data for all patients who underwent minimally invasive colectomies (RC or LC) for colon adenocarcinoma between 2010 and 2011 from the National Cancer Database (NCDB). Results: Out of the total 31,143 patients who underwent minimally invasive colectomies, 1338 (4.3%) patients underwent RC and the remaining 29,805 (96.7%) underwent LC. The proportion of minimally invasive colectomies performed robotically increased from 3.8% in 2010 to 4.7% in 2011 (P<.001). The patient cohorts for LC and RC were similar in age (P=0.06), sex (P=0.94), race (P=0.49), Charlson-Deyo comorbidity score (P=0.16), primary tumor location (P=0.76), tumor size (P=0.21), histological grade (P=0.23), pathological T-stage and overall clinical AJCC stage (P=0.49). Median time from diagnosis of cancer to surgery was longer with RC compared to LC (16 vs. 13 days, P<0.001). Operative outcomes (Table 1) for RC and LC were similar in terms of positive margin rate (5.1% vs 5.0%, P=0.98), inadequate node retrieval (16.1% vs 14.7%, P=0.14), median postoperative stay (5 days vs. 5 days, P=0.08), unplanned 30-day readmission rate (4.2% vs 5.1%, P=0.46), 30-day mortality (2.3% vs 2.0%, P=0.46) and median time from surgery to commencement of adjuvant chemotherapy (55 days vs. 55 days, P=0.64). Conversion rate to open surgery was significantly lower with RC compared to LC (11.9% vs 15.3%, P<0.001). Compared to colectomies successfully completed minimally invasively, those converted to open approach had significantly higher unplanned 30-day readmission rate (7.0% vs 4.7%, P<0.001) and longer hospital stay (5 days vs 6 days, P<0.001). Conclusion: Robotic colectomy is a safe alternative to laparoscopic colectomy, and provides equivalent surgical outcomes. Compared to laparoscopic colectomy, robotic colectomy has a lower conversion rate to open approach, which in turn, is associated with lower readmission rates and shorter hospital stay.

### P151

**Modified Orthotopic Murine Colon Cancer Cell Implantation Method that Mimics Clinical Cancer Progression**

**K. Terracina,** T. Aoyagi, W. Huang, A. Yamada, M. Nagahashi, K. Takabe. Department of Surgery, Virginia Commonwealth University, Richmond, VA.

Introduction: In breast cancer models, our laboratory has demonstrated using gene expression microarrays that subcutaneous injection models for cancer have very different expression from orthotopic models. In colon cancer, current models are limited in that no model accurately represents human colon cancer progression. Existent models consistently have carcinomatosis prior to lymph node metastasis. We set out to establish a syngeneic orthotopic model for colon cancer that more closely mimics human cancer progression. Methods: CT26 murine colon cancer cells were modified to overexpress the firefly luciferase gene (CT26-luc1), to allow real time in vivo imaging of tumor burden using In Vivo Imaging System (IVIS). CT26-luc1 cells suspended in matrigel basement membrane matrix were implanted submucosally into the cecum wall of syngeneic Balb/c mice under direct visualization. Tumor burden was monitored over time using IVIS. Mesenteric lymph nodes (MLN) were assessed at time of animal euthanasia with ex vivo bioluminescence and MLN weight. Results: The CT26-luc1 submucosal implantation model resulted in consistent tumor formation in the colon (88% n=26). In vivo bioluminescence allowed real time monitoring of total tumor burden with mean bioluminescent fold change of 2,158 at day 17 after implant. Mice maintained body weight throughout the course of the experiment. When MLN metastasis was examined, 33% of the mice (n=15) had MLN metastasis at time of euthanasia at day 28. IVIS performed three days prior showed average total luminescence of 5.4x106 vs 2.5x106 (P=0.02) for animals with and without MLN metastasis, allowing a predictive threshold for MLN metastasis to be formed for this model. Conclusion: The CT26-luc1 submucosal implantation model had a high tumor burden rate and allows for presence of MLN metastasis to be predicted prior to animal euthanasia. This model is expected to provide an invaluable murine metastatic colon cancer model for studies of colon cancer progression.

### P152

**Prenatal Anogenital HPV Tumors are not More Likely to Recur than Benign HPV Tumors**


Introduction: HPV tumors of the anus are an epidemic. Removal of such tumors accounts for the most commonly performed surgical procedure undertaken by a high-volume colorectal surgery practice in an inner-city tertiary care center. Methods: We retrospectively reviewed a database which captured surgical data over a four-year period to find patients who underwent outpatient resection of anal tumors. From these data, we manually reviewed records to note demographics (race, HIV status, use of antivirals) and surgical pathology. Differences were assessed using Fisher’s exact tests. Significance was assessed at p<0.05. Results: 527 surgeries were performed for anal HPV tumors. Many patients had multiple procedures, resulting in 390 individual patients in the study, most of whom were male (n=361, 92.6%). Of these patients, 78 (20%) had a recurrence requiring additional surgery within the study period. The recurrences ranged between one and 9 recurrences (mean 1.8 recurrences). Time to recurrence was on average 6.9 months (SD=8.6, range 11 days to 4 years). Our analyses showed that recurrence was not associated with gender.
and race. 45% of the total patient population was HIV-positive with 70% of these patients on anti-retrovirals. HIV-positive individuals had similar frequency and time to recurrence as HIV-negative patients. Hence, HIV status was not significantly associated with recurrence [Figure]. Neither was the use of anti-retroviral therapy. HIV infection was, however, associated with an increased risk of pre-malignant disease (p=0.003). Based on pathology reports from initial surgery, we found that most of the surgeries were done for benign disease. We did additional analysis on the subset of patients who were diagnosed with anal pre-malignancy on initial surgery (n=61, 15.6%). Interestingly, the risk of recurrence was not related to having a pre-malignant lesion on initial diagnosis (p=0.73). Conclusion: The risk of anal HPV lesion recurrence in D.C. is 20%, which is similar to the general population. Recurrence was not related to gender, race, HIV status, or pre-malignant diagnosis. HIV-positive status was associated with increased risk of pre-malignant disease.

**Time to Anal HPV Tumor Recurrence by HIV-positive (red) versus HIV-negative Status (black)**

\[ p[\text{ChiSq}] = 0.09, \text{Pr}>\text{ChiSq} = 0.77, HR = 1.06 \]

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**P153**

**Disparities in the Treatment and Outcome of Rectal Cancer Patients: A Health Insurance Perspective**

C.M. Kiernan, K. Idrees, N. Merchant, A. Parikh, General Surgery, Vanderbilt University, Nashville, TN.

Introduction: Prior studies have demonstrated that underinsured or uninsured cancer patients often receive substandard treatment and have worse outcomes. The purpose of this study was to evaluate the impact of health insurance on the treatment and outcomes in patients with rectal cancer. Methods: Using the National Cancer Database, we identified 86,848 patients diagnosed with stage 2 or 3 rectal cancer from 2003-2011. Patients were stratified into 5 cohorts: Private, Medicare, Military, Medicaid and Uninsured to test the association of health insurance type with receipt of chemoradiation as well as the extent of surgical resection by multivariable (MV) logistic regression. Overall survival (OS) was estimated using MV cox-proportional hazards. Results: Within the cohorts of Uninsured and Medicaid, a higher proportion of patients were African American (AA) or Hispanic. Patients in these cohorts were less likely to undergo sphincter-preserving resections (p<0.001). By MV analysis, patients who were uninsured (OR 0.57, CI 0.50-0.65) or had Medicaid (OR 0.68, CI 0.60-0.76) or Medicare insurance (OR 0.82, CI 0.76-0.90) and those who received neoadjuvant chemoradiation (OR 0.57, CI 0.53-0.60) were less likely to undergo a sphincter preserving resection. Lack of insurance (OR 1.15, CI 1.01-1.30), Medicaid (1.13, CI 1.00-1.26) and treatment at an academic facility (OR 1.29, CI 1.22-1.37) were associated with higher odds of utilization of neoadjuvant therapy. Lack of insurance (HR 1.51, CI 1.32-1.72), Medicare (HR 1.53, CI 1.36-1.72), Medicaid (HR 1.16, CI 1.08-1.24), AA race (HR 1.15, CI 1.05-1.26), lack of sphincter preservation (HR 1.30, CI 1.24-1.37), and higher stage disease (p=0.027) were independently associated with worse overall survival. Conclusions: In addition to race, insurance disparities contribute to inequality in the treatment and outcome of cancer patients. Although rectal cancer patients who are uninsured or have Medicaid present at similar stage disease and are more likely to receive neoadjuvant chemoradiation compared to those with private insurance, they appear less likely to have a sphincter preserving resection and have worse overall survival.

**P154**

**Changing Pattern of Locally Recurrent Rectal Adenocarcinoma in Post-total Mesorectal Excision (TME) Era**

J.S. Liles, Y. You, J. Skibber, H.S. Tran Cao, M. Rodriguez-Bigas, B.W. Feig, G.J. Chang, UT MD Anderson Cancer Center, Houston, TX.

Local recurrence after resection of rectal adenocarcinoma occurs in 10% of patients. Historically, the predominant pattern of recurrence has been central pelvic (anastomotic and residual mesorectal). We hypothesized that with increasing adherence to TME principles, the patterns of recurrence may change. The purpose of this study was to evaluate this evolving pattern of recurrence and investigate its effect on patient outcomes. We performed a retrospective consecutive cohort study of all patients treated with curative intent salvage surgery at a single referral institution between 1988 and 2012. Patients were categorized into 3 groups based on year of presentation (preTME 1988-98; earlyTME 1999-05; current 2006-12). Patient demographics as well as treatment, pathology, and outcome variables were analyzed. 228 patients underwent resection of locally recurrent rectal adenocarcinoma. 91% of patients underwent pre-referral resection of primary tumor with median time to recurrence for all of 30.6 mos. Recurrences were most commonly central (78.9%) followed by lateral (15.4%) and pre-sacral (5.6%). However, with time, the incidence of lateral recurrences treated with salvage resections significantly increased (7% in 1988-1999 vs 25% in 2006-2012; p<0.05). Among patients treated with surgery for central recurrence and lateral recurrence, there was no significant difference in salvage positive margin status (20.0 vs 25.7%) or rate of subsequent local failure (21.5% vs 22.9%). After a median followup of 36.4 months, there was no difference in disease-free survival (median 21.8 mos vs 24.9 mos; p=0.91) and overall survival (median 54.9 mos vs 56.8 mos; p=0.84) among patients undergoing salvage surgery for lateral recurrence relative to central recurrence. We demonstrate a significant change in the local recurrence pattern of rectal adenocarcinoma with more patients now presenting for salvage resection with lateral pelvic recurrences. With an emphasis on achieving complete resection, outcomes after salvage surgery for lateral recurrence were not different than those achieved after salvage surgery for central recurrence.

**P155**

**A Retrospective Single-center Analysis of Robotic Abdominoperineal Resection**

H.S. Tran Cao, J. Ouellette, R. Shrit, Surgical Oncology, Wright State University, Dayton, OH.

Introduction: Conventional laparoscopy has been applied to colorectal resections for more than two decades. However, laparoscopic rectal resection is technically demanding, especially for low rectal cancers. Robotic surgery is thought to overcome some of these technical limitations. In this single-center study the feasibility of robotics for abdominoperineal resections (APR) was evaluated. Methods: Clinicopathologic data of all patients undergoing robotic APR for low rectal cancers since October 2008 were retrospectively analyzed. All cases were performed by 2 surgeons with a sharp robotic mesorectal excision in lithotomy position. Results: A total of 50 patients (40 male, 10 female) with a median age of 60 years underwent robotic APR. The median BMI was 27 (17.8-43.2) kg/m², and 86% of patients received neo-adjuvant therapy. Median operative time was 300 (199-557) minutes with a robotic console.
time of 83 (51-170) minutes. Median blood loss was 100 (50-1000) ml with 2 patients requiring intra-operative blood transfusions. Intraoperative complications included one urethra injury and one case of acute renal failure. The mesorectum was reported as complete in 70% and near complete in 23.6% of cases. Positive circumferential margins rate was 14% and conversion rate to open was 6%. Postoperative morbidity included the following complications: 25 patients with prolonged perineal wound healing, 5 patients with postoperative small bowel obstruction requiring surgery within 90 days, 5 patients with urinary issues, 2 respiratory and 2 renal failures. Median length of stay was 5.5 (3-25) days. Two patients (4%) had local recurrences with one who had a positive margin resection; 65.3% of patients are alive without evidence of disease. Conclusions: APR is a surgical procedure associated with significant morbidity. Robotic assistance may help improve outcomes. This technique appears to be feasible and can be performed according to oncologic principles with a low conversion rate. We believe that further studies evaluating the use of robotics for abdominoperineal resections should be encouraged.

**P156**

**Lymph Node Ratio is a more Accurate Prognostic Factor in Stage III Colon Cancer compared to Standard Nodal Staging**

A. MacNeill,1* M.C. Cleighorn,2 W. Choi,3 H. Jiang,3 T.D. Jackson,3 A. Okrainec,3 F.A. Quereshy,1 1. University of Toronto, Toronto, ON, Canada; 2. Division of General Surgery, University Health Network, Toronto, ON, Canada; 3. Princess Margaret Cancer Center, Toronto, ON, Canada.

**Introduction:** Lymph node involvement is the most important prognostic factor in non-metastatic colon cancer. Lymph node ratio (LNR) has been suggested to be of greater prognostic significance than absolute lymph node yield, but the optimal cut-off value remains unknown. The purpose of this study was to evaluate the predictive value of LNR with respect to recurrence-free survival (RFS) and overall survival (OS) in stage III colon cancer patients, and to compare it to current TNM nodal staging. **Methods:** A retrospective review was conducted on a prospectively maintained database of all patients who underwent curative resection for colon cancer at a large tertiary academic center from 2004-2012. RFS and OS were calculated using the Kaplan-Meier method and compared by the log-rank test. Univariate and multivariable Cox proportional hazard regression models were used to evaluate clinicopathologic variables. Optimal cut-offs for LNR were identified by maximizing log-rank statistics, and compared with published values. **Results:** 471 patients were included in the study, of whom 156 had nodal metastases. Advanced T stage, lymph node metastases, and LNR were associated with RFS and OS. The optimal LNR cut-off value was found to be 0.32. Patients with LNRS above this threshold were found to have significantly worse RFS (HR 3.02, 95% CI 1.37-6.85, p=0.003) and OS (HR 2.71, 95% CI 1.39-5.29, p=0.003). When a cut-off value of 0.18 was applied, in agreement with existing literature, these results retained significance (RFS: HR 2.31, 95% CI 1.4-3.81, p=0.001; OS: HR 2.01, 95% CI 1.13-3.67, p=0.023). TNM N stage was not found to be a significant predictor of outcome (Figure 1). **Conclusions:** LNR is a valuable predictor of outcome in stage III colon cancer, and may represent a more accurate marker of nodal staging than the standard TNM system. LNR ≥0.32 is highly predictive of reduced RFS and OS. This study builds upon current literature by validating the published cut-off of 0.18 as being a statistically significant threshold. Consideration should be given to incorporation of LNR into future TNM classification.

**P157**

**Total Thyroidectomy versus Lobectomy as Initial Operation for Small Unilateral Papillary Thyroid Carcinoma: A Meta-analysis**

F. Macedo,* V. Mittal. Surgery, Providence Hospital and Medical Centers, Troy, MI.

**Introduction:** Consensus guidelines have recommended total thyroidectomy for papillary thyroid carcinoma (PTC) ≤ 1 cm. However, the optimal surgical approach for low-risk, small and unilateral (<1 cm) PTC remains controversial. Methods: A meta-analysis was performed using MEDLINE and EMBASE databases to identify all studies investigating at thyroid surgery options, total thyroidectomy (TT) versus thyroid lobectomy (TL), for PTC ≤ 1 cm. The primary outcomes were locoregional recurrence and mortality rates. **Results:** The initial literature search identified 309 publications. Six studies met the inclusion criteria comprising 2,939 patients. Among these patients, 2134 (72.6%) underwent TT and 805 (27.4%) underwent TL. Mean follow-up was 10.9 ± 3.4 years (range, 8-12 years). Overall, the recurrence rate was 5.4%; 4.4% in the TT group and 8.3% in the TL group (p=0.001; OR 0.52, 95% CI 0.34-0.66). The mortality rates were 0.3% (8 cases) versus 1.1% (9 cases) in TT and TL groups, respectively (p=0.10; OR 0.42, 95% CI 0.15-1.17). Conclusion: TT was associated with lower recurrence rates, possibly due to a more complete nodal dissection of the central neck compartment at the time of initial surgery. On the basis of these data, it is unclear to establish a definitive correlation between the extent of thyroid resection and long-term mortality rates due to the small number of death events. However, there is a trend toward lower mortality rates in the TT group. Other factors need to be taken into consideration while planning thyroid resection for small PTC, such as multifocality, locoregional involvement, and age at diagnosis. Refinement of current guidelines for the optimal surgical management of PTC <1 cm may be warranted.

![Figure 1](image1.png)

**Figure 1:** A: Forest plot for recurrence rates of papillary thyroid carcinoma after initial operation in six comparative studies (p=0.001). B: Forest plot for long-term mortality rates after total thyroidectomy versus thyroid lobectomy as initial operation for papillary thyroid cancer (p=0.10).
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Rural-urban Disparities in Incidence and Outcomes of Neuroendocrine Tumors: A 15-year Population-based Analysis of 6,271 Cases
J. Hallet,1* C.H. Law,2 P.J. Karanicolas,1 N. Liu,3 R. Saskin,2 S. Singh,1 1. Surgery, Odette Cancer Centre - Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 2. Institute of Clinical Evaluative Sciences (ICES), Toronto, ON, Canada.

Background: Despite rising incidence, Neuroendocrine Tumors (NETs) remain a poorly understood disease. Rural area (RA) living affects incidence and outcomes of other types of cancer. We sought to compare incidence and outcomes of NETs between patients in RAs and in urban areas (UAs).

Methods: We conducted a population-based cohort study of patients with NETs in the province of Ontario, Canada from 1994 to 2011. Census Canada defines an metropolitan area as a population of ≥100,000 with ≥50,000 urban core; we defined an RA as any community with ≤10,000 people and out of metropolitan areas commuting zones, and UA as all other areas. Incidence, advanced stage at presentation (metastases at the time of diagnosis), recurrence-free survival (RFS), and overall survival (OS) were compared between patients who lived in RA and UA using univariate and regression analyses.

Results: The cohort included 6271 patients diagnosed with NETs, of which 13.5% resided in RAs (n=846). Incidence of NETs was higher in RAs with 4.07 compared with 3.77 per 100,000/year in UAs (Relative Rate 1.10; p=0.04). RA living was not associated with advanced stage at presentation (OR 1.15; 95%CI 0.96-1.38). Patients who lived in RAs had a worse 10-year RFS (62.8% Vs. 65.9%; p=0.03) and OS (44.6% Vs. 48.8%; p=0.04). RA was independently associated with decreased OS (HR 1.16; 95%CI 1.06-1.32). Conclusion: Patients are more commonly diagnosed with NETs in RAs, but do not present at more advanced stages compared with patients diagnosed in UAs. Patients living in RAs experience worse cancer recurrence and survival, possibly related to variations in socioeconomic status, rural environmental factors, and access to specialized healthcare.

Factors associated with advanced stage presentation and 10-year mortality for Neuroendocrine Tumors

<table>
<thead>
<tr>
<th>Variable</th>
<th>Advanced stage at presentation</th>
<th>10-year mortality</th>
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<tbody>
<tr>
<td>Rural Area Living</td>
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<tr>
<td>Age *</td>
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<tr>
<td>61-70</td>
<td>1.7 (1.4-2.0)</td>
<td>0.001</td>
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<tr>
<td>&gt;71</td>
<td>2.6 (1.7-3.5)</td>
<td>0.001</td>
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<tr>
<td>Male Gender</td>
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<tr>
<td>Income quintile</td>
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<tr>
<td>1 (lowest)</td>
<td>1.3 (1.1-1.6)</td>
<td>0.001</td>
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<tr>
<td>2</td>
<td>1.2 (1.0-1.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>3</td>
<td>1.0 (0.9-1.1)</td>
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<tr>
<td>4</td>
<td>1.1 (0.9-1.3)</td>
<td>0.001</td>
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<tr>
<td>Primary Tumor Location</td>
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<tr>
<td>Gastro-Esophageal</td>
<td>1.3 (1.1-1.5)</td>
<td>0.003</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>1.6 (1.3-2.1)</td>
<td>0.001</td>
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<tr>
<td>Other</td>
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<tr>
<td>Lack of a regular doctor</td>
<td>2.1 (1.8-2.6)</td>
<td>0.001</td>
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<td>Metastatic status</td>
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<tr>
<td>At presentation</td>
<td>2.1 (1.3-3.3)</td>
<td>0.001</td>
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<tr>
<td>After initial diagnosis</td>
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P159
Sociodemographic Disparities in Treatment of Anaplastic Thyroid Carcinoma
M. Dacey,1* A. Sheppard,2 M. Goldfarb,3 1. Surgery, John Wayne Cancer Institute / Providence St. John’s Medical Center, Santa Monica, CA; 2. University of Southern California Keck SOM, Los Angeles, CA.

Background: Anaplastic thyroid carcinoma (ATC) is an aggressive malignancy with an extremely poor prognosis. Recent studies have shown a mild improvement in survival with aggressive multimodal therapy. This study explores sociodemographic disparities of the timing of and treatment modality used for ATC. Methods: All cases of ATC in the 1998-2011 National Cancer Data Base were evaluated for sociodemographic predictors of different treatment modalities and time from diagnosis to treatment. Forward logistic regression was performed to calculate adjusted odds ratios (OR) for factor affecting the timing of and treatment of ATC. Results: Of 4885 patients with ATC, most were white (86.3%), non-Hispanic (86.2%), female (60.7%) and insured (93%), with a mean age of 69.13 years. Females (OR:1.33, CI:1.08-1.65), aged >65 (OR:2.84, CI:2.21-3.64), with no insurance (OR:2.24, CI:1.35-3.72) and distant metastases (OR:2.31, CI:1.33-2.83) were more likely not to receive any treatment. Of 3991 (82%) patients that received any therapy, 37.2% started treatment >14 days after diagnosis. Whites (OR:1.30, CI:1.05-1.60), and those with distant metastases (OR:1.29, CI:1.11-1.50) had an increased likelihood of starting any treatment >14 days after diagnosis. Patients were more likely to receive multimodal (chemotherapy, radiation, and surgery) therapy if they were male (OR:1.57, CI:1.30-1.89), ≥65 years-old (OR:2.13, CI:1.76-2.57), had ≥2 comorbidities (OR:1.85, CI:1.14-3.01), no distant metastases (OR:2.91, CI:2.30-3.69) and were insured (OR:1.80, CI:1.05-3.09). Conclusion: Age, race, gender and insurance status were important determinants of therapy for patients with ATC whereas race, gender and extent of disease impacted time to initiation of treatment. Recognizing these disparities could affect treatment choice in the future and thus improving survival for some patients with ATC.

P160
Vanishing Tumors of Thyroid: Histological Variations after Fine Needle Aspiration
P. Bhatha,1* A. Deniwar, N. Alsaehe, E. Kandill, Surgery, Tulane University School of Medicine, New Orleans, LA.

Introduction: Fine needle aspiration cytology (FNA) of thyroid nodules can lead to reactive changes that extensively replace cytologically confirmed thyroid lesions. These replaced lesions are called vanishing tumors that are challenging to both endocrinologists and thyroid surgeons to interpret the final pathological diagnosis. We performed a retrospective analysis to identify vanishing tumors that intend to compromise further management plans.Methods: Data of 459 patients referred for surgical intervention in our institution with prior FNA were reviewed. We then compared cytological and pathological results to identify vanishing tumors in patients.FNA-induced reactive changes such as cystic degeneration, hemorrhage, calcification, cholesterol crystals, fibrosis and granulation tissue were looked for in specimen pathology. Results: Thirteen percent (2.8%) were identified with vanishing tumors. Preoperative FNA cytology was indeterminate (atypia of undetermined significance/follicular lesion of undetermined significance) in five (38.4%) and benign in eight patients (61.6%). Surgical pathology revealed widespread replacement in all tumors by reactive changes. Size of vanishing tumors ranged from 0.1-9 cm (median 2.2; mean 2.5±2.8) in greatest dimension. Residual tumor cells with papillary thyroid carcinoma (PTC) in 1 (7.6%), follicular thyroid carcinoma in 1 (7.6%), hemorrhagic cysts in 3 (23%), compressed thyroid parenchyma in 8 (61.5%) assisted with definitive diagnosis. Pathology in 3 (23%) cases had foci suspicious for PTC arising in nodule with extensive fibro-sclerotic changes; however, no malignancy was detected. These lesions had FNA-cytology as benign in 1 and indeterminate in 2. One of the latter two cases had an additional focus suspicious for follicular neoplasm on cytology, however, due to extensive reactive changes no malignancy was detected on surgical pathology. Conclusions: FNA-induced secondary changes can lead to obliteration of nodules leading to surgical pathology diagnosis with no evidence of benign or malignant lesions. Endocrinologists and thyroid surgeons should be aware of this scenario. In the presence of expert opinions, FNA cytology can provide a definitive diagnosis for vanishing tumors.

P161
Comparison of Secondary and Primary Thyroid Cancers: Patient Characteristics and postoperative Outcomes
Z. Al-Qurayshi,1* A. Hauch, E. Kandill, Tulane University School of Medicine, Department of Surgery, New Orleans, LA.

Introduction: Secondary thyroid cancer (SCa) is believed to lead a more aggressive clinical course than primary thyroid cancer (Pca). We aim to examine the differences between Sca and Pca in terms of patient characteristics and post-thyroidectomy outcomes at the national level. Methods: Cross-sectional study utilizing the Nationwide Inpatient Sample (NIS) database for 2003-2010. ICD-9 codes were used to identify adult patients with thyroid cancer. Patients were considered to have SCa if they had previous history of malignancy. Statistical methods included Chi-square test and logistic regression modeling. Results: A total of 21,395 discharge records were included. 16,589 (77.5%) patients had Pca, while the rest (22.4%) had SCa. Younger patients (<45 years) and males were more likely to have SCa than Pca (p<0.05). Blacks
were less likely to develop SCa compared to Whites [OR: 0.64, 95%CI: (0.53, 0.78), p<0.001]; while Hispanics were at a higher risk than Whites [OR: 1.27, 95%CI: (1.11, 1.45), p<0.001]. SCa was most likely to be treated in teaching hospitals (p<0.001). Patients with SCa were at significantly higher risk of postoperative complications compared to patients with PCa [OR: 1.64, 95%CI: (1.44, 1.86), p<0.001]. However the complication risk was higher among low surgeon volume compared to high-volume surgeons [OR: 2.05, 95%CI: (1.10, 3.82), p=0.023]. Additionally, SCa patients were more likely to be hospitalized for more than 2 days (p<0.001); with the risk of longer hospitalization being higher for low surgeon volume compared to high surgeon volume group [OR: 1.86, 95%CI: (1.02, 3.39), p=0.043]. Average cost of SCa management is significantly higher than treating PCa ($10,903.00 vs $6,779.23, p<0.001). SCa was most likely to be treated in teaching hospitals (<0.001). Patients with SCa were at significantly higher risk of a hospital stay of more than 2 days [OR: 2.05, 95%CI: (1.44, 2.86), p<0.001]; with the risk of longer hospitalization being higher for low surgeon volume compared to high-volume surgeons [OR: 2.05, 95%CI: (1.11, 3.82), p<0.001]. SCa is more prevalent in younger male patients. Blacks are at lower risk of SCa than Whites; while Hispanics are at greater risk. Patients with SCa experience disadvantageous postoperative outcomes compared to patients with PCa. However patients treated by surgeons of high volume are more likely to have favorable outcomes. SCa management is linked to higher costs compared to PCa on the healthcare system.

Conclusion: Successful parathyroidectomy (PTx) requires surgeon experience and knowledge of the potential anatomical variations. In this study, we seek to assess the impact of surgeon volume on the outcomes of PTx performed for primary hyperparathyroidism (PHPT). Additionally, we aim to examine the association of patient demographics, socioeconomic status, and hospital factors with accessibility to different SV groups. Methods: Cross-sectional study utilizing the Nationwide Inpatient Sample (NIS) database for 2004-2009. ICD-9 codes were used to identify adult (≥18 year) patients who underwent PTx for PHPT. SV groups were categorized based on quartile classification: low SV: 1-2 PTx/yr, intermediate SV: 3-19 PTx/yr, and high SV: ≥20 PTx/yr. Statistical methods included Chi-square test and logistic regression modeling. Results: A total of 3,503 discharge records were included. Operations by the low SV group were more likely to be associated with postoperative complications compared to the high SV group [OR: 1.81, 95%CI(1.11, 2.97), p=0.018]. Additionally, patients managed by low SV were at a significantly higher risk of a hospital stay of more than 2 days [OR: 7.11, 95%CI: (3.75, 13.45), p<0.001]. The Low SV group cost the health care system more per operation than the intermediate and high SV groups (low SV: $9,224.49, intermediate SV: $5,923.75, high SV: $5,586.84, p<0.001). Male patients, Hispanics, and those with Medicaid or Medicare health coverage were more likely to be managed by low-volume surgeons (p<.05 for all). On the other hand, low-volume surgeons were more likely to operate in rural, non-teaching hospitals, or in hospitals located in the Southern region of the United States (p<0.001 for all). Conclusion: Greater surgeon experience translates into more favorable outcomes following PTx, both clinically and economically. Certain demographic, economic, and administrative factors influence the accessibility and distribution of different surgeon volumes across the United States.

Abstracts: Poster Presentations

P162 Outcome of Surgery for Primary Hyperparathyroidism: Availability and Impact of Surgeon Experience

Z. Al-Qurayshi,* A. Hauch, E. Kandil. Tulane University School of Medicine, Department of Surgery, New Orleans, LA.

Introduction: Successful parathyroidectomy (PTx) requires surgeon experience and knowledge of the potential anatomical variations. In this study, we seek to assess the impact of surgeon volume on the outcomes of PTx performed for primary hyperparathyroidism (PHPT). Additionally, we aim to examine the association of patient demographics, socioeconomic status, and hospital factors with accessibility to different SV groups. Methods: Cross-sectional study utilizing the Nationwide Inpatient Sample (NIS) database for 2004-2009. ICD-9 codes were used to identify adult (≥18 year) patients who underwent PTx for PHPT. SV groups were categorized based on quartile classification: low SV: 1-2 PTx/yr, intermediate SV: 3-19 PTx/yr, and high SV: ≥20 PTx/yr. Statistical methods included Chi-square test and logistic regression modeling. Results: A total of 3,503 discharge records were included. Operations by the low SV group were more likely to be associated with postoperative complications compared to the high SV group [OR: 1.81, 95%CI(1.11, 2.97), p=0.018]. Additionally, patients managed by low SV were at a significantly higher risk of a hospital stay of more than 2 days [OR: 7.11, 95%CI: (3.75, 13.45), p<0.001]. The Low SV group cost the health care system more per operation than the intermediate and high SV groups (low SV: $9,224.49, intermediate SV: $5,923.75, high SV: $5,586.84, p<0.001). Male patients, Hispanics, and those with Medicaid or Medicare health coverage were more likely to be managed by low-volume surgeons (p<.05 for all). On the other hand, low-volume surgeons were more likely to operate in rural, non-teaching hospitals, or in hospitals located in the Southern region of the United States (p<0.001 for all). Conclusion: Greater surgeon experience translates into more favorable outcomes following PTx, both clinically and economically. Certain demographic, economic, and administrative factors influence the accessibility and distribution of different surgeon volumes across the United States.

P163 Long-term Operative Outcomes of Thyroid Cancer: A Comparison of Adults and Children

Z. Al-Qurayshi,* A. Hauch, E. Kandil. Tulane University School of Medicine, Department of Surgery, New Orleans, LA.

Introduction: Surgical interventions in children are associated with different risk and outcome profiles than adults. In this multistate study, we seek to identify differences between children and adult populations with thyroid cancer (TC) undergoing thyroidectomy. Methods: Cross-sectional study utilizing the State Inpatient Databases (SID) 2010-2011 for Florida, New York, and Washington. Patients were classified as children (<18 year) or adults (≥18 year) with TC who underwent thyroidectomy. Subjects were followed for one month postoperatively. Statistical methods included Chi-square test and logistic regression modeling. Results: 10,674 patients were included. 10,557 (98.9%) were adults, while the rest were children (1.1%). Readmission rates were reported in 2.7% of adults and 3.4% of children. Presence of metastasis at the time of thyroidectomy was more than twice as common in children as adults [OR: 2.44, 95%CI: (1.42, 4.19), p<0.001]. Children were more vulnerable than adults for the development of hypocalcemia or admission to the Intensive Care Unit (ICU), specifically when they were managed by low-volume surgeons (1 surgery/year) (p<0.01). Children were significantly more likely to have one-month total health costs greater than the highest quartile ($9,732.26) when compared to adults (p<0.001), regardless of complication status and/or length of stay. Similarly, higher charges (> third quartile: $41,898.00) were billed to the insurance companies for children compared to adults (p<0.001). Conclusion: Children with TC are more likely to present with metastases at the time of thyroidectomy; highlighting the silent nature of TC in children. Children were more susceptible than adults to postoperative complications, and the risk of unfavorable outcomes was higher if they were managed by inexperienced surgeons. In a model controlling for clinical factors, management of children still resulted in higher costs on the healthcare system.
Safety of Outpatient Thyroidectomy

1. Black,1,* J. Yeh,1 T. Cotton,2 1. Surgery, UNC, Chapel Hill, NC; 2. University of Michigan, Ann Arbor, MI.

Background: Historically, total thyroidectomy was an inpatient procedure with patients staying up to 3 days post-operatively to monitor for complications, including hypocalcemia and compressive hematoma. In recent years, total thyroidectomy has transitioned to a 23-hour stay (23HS). National databases such as NSQIP consider <=23 hour stay as outpatient surgery making same day discharge (SDD) challenging to study. We investigated the outcomes of patients undergoing total thyroidectomy with SDD, 23HS and stays that cross 2 midnights (C2M).

Methods: Retrospective review was performed of 414 total thyroidectomies at UNC Hospitals between 2005-2013 after receiving IRB approval. Length of stay data was available on 328 patients. Emergency Department (ED) visits and readmissions within 30 days of surgery were captured but were considered the same for this analysis. The groups were compared based on age, sex, race, and calcium supplementation post-op. IBM SPSS was used to perform Chi-square and t-test analyses as appropriate. Results: Patients were stratified into SDD (n=80), 23HS (n=216), C2M (n=32). Out of 328 total thyroidectomies performed, 21 patients (6.4%) returned to the hospital. 65.9% (216/328) of patients had a 23 stay, 24.4% (80/328) had a SDD, and 9.8% (32/328) had a C2M. Patients discharged same day were more likely to be white (29.1% vs. 19.0%, p=0.02) and male (31.0% vs. 23.0%) although gender was not statistically significant. The average age was similar between groups (46.8 yrs vs. 47.3 yrs). 5.0% (4/80) of SDD were readmitted, compared to 6.9% (15/216) of 23HS and 6.3% (2/32) of C2M. There was no difference in readmission rates based on length of stay (p=0.556), age, sex, race or calcium supplementation.

Conclusion: We found no differences in readmission rates for patients undergoing total thyroidectomies for SDD, 23HS C2M. Although the decision of whether to discharge a patient on the day of surgery is surgeon specific, our data suggests that surgeons currently performing outpatient total thyroidectomies with SDD are successfully selecting patients who are safe to be discharged home on the day of surgery. Further studies are needed to determine which specific patient factors are associated with the best SDD candidates.

Implications of Delayed Normalization of Serum Calcium Levels after Presumed Curative Parathyroidectomy


Background: Following curative parathyroidectomy (PTX) for primary hyperparathyroidism (HPT), serum calcium (Ca) levels typically normalize by postoperative day (POD) 1 and delayed normalization may suggest persistent HPT. The aim of this study was to identify potential factors associated with delayed normalization of Ca levels despite meeting intraoperative parathyroid hormone (IOPTH) criteria for cure, and to compare rates of persistent/recurrent HPT between patients with delayed normalization to those with normal POD Ca levels.

Methods: This is a retrospective review of a prospective database of 554 patients who underwent initial PTX for sporadic HPT from 1/09-7/13. Curative PTX was defined as a decrease of IOPTH levels by ≥50% and into normal range 10 minutes post-excision of the abnormal gland(s). The cohort of patients who had elevated POD Ca levels (≥10.2 mg/dL) were matched 1:2 for age and gender to control patients with normal POD Ca. Demographic and clinical data were collected. Persistent and recurrent HPT were defined as hypercalcemia before or after 6 months of surgery, respectively.

Results: The study includes 156 patients, 52 (9%) with an elevated POD0 Ca and 104 controls. The two groups had significant differences in preoperative calcium, PTH, 25(OH) vitamin D, creatinine, and IOPTH levels (Table). The rate of single gland disease was similar (79% vs 76%; p=0.69). In the cohort group, the median POD Ca was 10.7 (range, 10.3-12.2). Normal Ca levels were reached in 30 (58%) patients by POD1, 38 (73%) patients by POD7, and 50 (96%) patients by POD14. All were normal by POD30. Five (3%) patients had persistent/recurrent HPT, with no difference in cure rates (94% vs 98%, p=0.2) between the groups. Conclusions: After presumed curative PTX, nearly 10% of patients may have transient hypercalcemia; this is more likely in patients with higher preoperative Ca, PTH and creatinine and lower Vitamin D levels. Although most had a normal Ca by POD14, all patients did not normalize until 1 month. Therefore, post-PTX clinical pathways should include a Ca level at the postoperative visit but if elevated, serial measurements prior to 1 month are unnecessary.

The Risk of Thyroid Cancer in Patients with Metabolic Diseases: Demographic Disparities at the National Level

A. Hauch, E. Kandil, Tulane University School of Medicine, Department of Surgery, New Orleans, LA.

Introduction: Demographic disparities affect the incidence and severity of thyroid cancer. In this analysis, we seek to examine the impact of type 2 diabetes mellitus (DM2), obesity, and metabolic syndrome on the risk of thyroid cancer and how age and race affects the risk profile for these factors at the national level in the United States. Methods: Cross-sectional study utilizing the Nationwide Inpatient Sample (NIS) for 2003-2009. ICD-9 codes were used to identify adult (≥18 years) patients with thyroid cancer. Comparative controls were randomly selected from the same database. Statistical methods included Chi-square test, and logistic regression modeling. Results: 27,329 cases and 379,329 controls were included. In the total sample, patients with BMI ≥30 were more likely to have thyroid cancer [OR: 1.22, 95% CI: (1.12, 1.34), p<0.001]. Similarly, a higher prevalence of cancer was in patients with metabolic syndrome [OR: 2.20, 95% CI: (1.34, 3.63), p<0.001]. While no significant risk was observed in patients with DM2. In respect to patient’s age, obesity was a significant risk factor for the younger (<46 years) and older (≥65 years) age groups (p<0.001). Thyroid cancer prevalence was higher in diabetic patients who were <46 years old [OR: 1.54, 95% CI: (1.35, 1.76), p<0.001]. Similarly, metabolic syndrome was a significant risk factor in younger patients only (<46 years) (p<0.001). When considering ethnic groups, obesity was a significant risk factor for thyroid cancer in White and Black populations (p<0.01). While metabolic syndrome posed a risk in the White and Native American groups (p<0.01). Obese patients were more likely to develop postoperative complications following thyroidectomy compared to non-obese patients [OR: 1.37, 95% CI: (1.13, 1.67), p<0.001]. Conclusions: Metabolic diseases demonstrate a significant association with thyroid cancer. Nonetheless, patient’s race and age have a significant effect on the risk profile. This study highlights the racial and age disparities for the risk of thyroid cancer at the national level for previously under-explored risk factors.
Incidental Thyroid Malignancy Found in Thyroidectomy Performed for Benign Diagnoses

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Introduction: Historically, patients undergoing thyroidectomy for benign disease have a 3-5% chance that malignancy will be present on final pathology, however, more recent studies suggest this rate may be as high as 20%. If malignancy is not suspected preoperatively, patients may not undergo the correct oncologic operation and/or work up. The aim of this study is to evaluate the rate of malignancy found on final pathology in patients who had thyroidectomy for presumed benign disease. Method: This is a retrospective review of patients who underwent thyroidectomy for a benign diagnosis identified via Fine Needle Aspiration from January 1, 2000 to October 24, 2013. Data was from pathology reports and electronic medical records. The primary outcome was malignancy on final pathologic report. Secondary outcomes were to identify preoperative risks factors which may predict malignancy in this patient population. Results: We identified 354 patients who had thyroidectomy for a benign diagnosis (Figure 1), of which 86.6% were women. Sixty-five (18.4%) patients had a diagnosis of malignancy on final pathology. Figure 1 shows the comparison between patients with malignant vs benign disease on final pathology. The most common preoperative diagnosis that showed cancer on final pathology was toxic nodular goiter (TNG). When looking at predictors of malignancy, age was statistically significant. Average age of patient with benign vs malignant disease was 52.4 and 48.4 respectively (p=0.04). Sex and preoperative diagnosis were not predictors of malignancy in this study population. Conclusions: Our institutional rate of malignancy for thyroidectomies performed for benign disease is higher than the historical rate of 3-5%, and similar to other institutions’ reports of 15-20%. Younger patients were more likely to harbor malignancy on final pathology. Unlike previous reports, we did not find sex or pre-operative diagnosis to be a predictor for final malignancy.

Figure 1

Does Marital Status Impact Survival in Patients with Carcinoid Tumors?

P169

E. Kenning,* C. Hollenbeck, A. Cooper. Penn State Hershey Medical Center, Hershey, PA.

Introduction. Marital status is a known prognostic factor in overall and disease-specific survival in several types of cancer. However, the impact of marital status on survival in patients with carcinoid tumors remains unknown. We hypothesized that married patients would have higher rates of survival than similar unmarried patients with carcinoid tumors. METHODS. Using the SEER database, we identified 23,126 people with carcinoid tumors. Marital status was categorized as: married, single, separated/divorced, and widowed. Univariate and multivariate analyses were performed to compare characteristics and outcomes between patients as a function of marital status. Overall and cancer-related five-year survival were analyzed using the Kaplan-Meier method. In addition, multivariate survival analyses were performed using Cox proportional hazards models to control for other patient and disease covariates. RESULTS. Marital status was significantly related to both overall and cancer-related five-year survival in patients with carcinoid tumors. Separated/divorced and widowed patients had worse overall survival (HR, 1.35 [95% CI, 1.22-1.52] and 1.40 [95% CI, 1.38-1.53], respectively) and cancer-related survival (HR, 1.15 [95% CI, 1.01-1.31] and 1.20 [95% CI, 1.07-1.35], respectively) than married patients over five years. Single patients had worse overall survival (HR, 1.18 [95% CI, 1.06-1.31]), although not significantly worse cancer-related survival, than married patients over five years. CONCLUSIONS. Even after controlling for other prognostic factors, married patients have a survival advantage after diagnosis of any carcinoid tumor, potentially reflecting better social support than patients without married partners.
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**Surgeon Volume Impact on the Outcomes of Thyroidectomy and Related Hospital Charges: A National Forecast**

Z. Al-Qurayshi,* A. Hauch, E. Kandil. Surgery, Tulane University School of Medicine, Department of Surgery, New Orleans, LA.

**Introduction:** Incidence of thyroidectomy is continuing to increase. Identifying factors associated with favorable outcomes can have major cost-effectiveness at the national level. We aim to assess the impact of surgeon volume (SV) on both clinical outcomes and hospital charges following thyroidectomy.

**Methods:** Cross-sectional analysis and statistical modeling utilizing data from the Nationwide Inpatient Sample (NIS) from 2003-2009. SV included: low SV (≤ 9 surgeries/year), intermediate SV (10-99 surgeries/year), and high SV (≥ 100 surgeries/year). Results: 62,722 patients were included. 18,954 (50.2%) were managed by the low SV group, while intermediate and high SV groups managed 44.8% and 5%, respectively. Low SV was associated with higher risk of postoperative complications compared to high SV [OR: 1.46, 95% CI: (1.03, 2.07)]. Average hospital charges were significantly associated with SV's high SV: $17,204.00 ± 1,765.78, intermediate SV: $16,781.00 ± 604.93, low SV: $19,069.00 ± 409.46, p < 0.001). During the study period, if all operations performed by low-volume surgeons were pushed to high-volume surgeons, a 7.5% savings would be incurred. Savings were even higher (11.4%) if the operations were performed by the intermediate SV group. However, based on the charges growth rate, greater savings are forecasted for high-volume surgeons. With the conservative assumption that there are 150,000 thyroidectomies/year in the United States, the high SV group would produce savings of ($23,726,841,423.00) over the next ten years, while the intermediate and low SV groups would have savings of ($10,532,351,039.00). Conclusions: A surgeon's expertise is associated with favorable outcomes. Our model estimates that considerable cost savings is attainable if experienced surgeons manage thyroidectomies.

**P171**

**Neoadjuvant Chemotherapy in 13 Patients with Locally Advanced Poorly Differentiated Thyroid Carcinoma: A Phase I/II Study**


**Background:** There is a paradigm that chemotherapy is ineffective in thyroid carcinoma. The aim of our study was to find out if neoadjuvant chemotherapy before thyroid surgery had effect on the size of primary tumor in patients with poorly differentiated thyroid carcinoma. Patients/Methods: Altogether 13 patients (8 women, 5 men; median age 61 years) with poorly differentiated thyroid carcinoma were treated with neoadjuvant chemotherapy from 1986-2005. Papillary and follicular poorly differentiated carcinoma was diagnosed in 5 and 8 patients, respectively. Tumor diameter was from 4.3-18 cm (median 9 cm). Regional and distant metastases were detected in 6 and 8 patients, respectively. Eight (61%) patients had pT4 tumor. Chemotherapy consisted of Vinblastine, Vinblastine with Doxorubicin or Vinblastine with Cysplatin in 11, 1 and 1 cases, respectively. Results: Altogether, 29 (range 1-5) cycles of chemotherapy were given. Tumor size decreased for more than 50% in 5 patients (=38%). Chemotherapy was effective in follicular and papillary thyroid carcinoma in 37.5% and 40%, respectively. Total thyroidectomy, lobectomy and neck dissection was performed in 10, 3 and 5 cases, respectively. R0 resection was done in 8 cases and R1 resection in 5 cases. Eight patients had postoperative external beam irradiation of the neck and upper mediastinum. Radioiodine (RAI) therapy was used in patients with initially distant metastatic disease and distant dissemination during follow-up in 7 out of 9 and 3 out of 3 patients, respectively. They received 2-8 (median 3) therapies with RAI in a dose of 3.7-7.4 GBq. Distant metastases were diagnosed in three patients during follow-up of 7-189 (median 118) months. Seven patients died of distant metastases, one of other causes, while five patients are alive. The 5-year and 10-year cause-specific survival rates of the patients were 77% and 46%, respectively. Conclusions: Neoadjuvant chemotherapy may decrease tumor size for more than half in 38% of patients with poorly differentiated thyroid carcinoma.

**Figure:** Cause-specific survival and neoadjuvant ChT (green = effect 50-99%, red = effect <50%).

**P172**

**Long-term Hypercalcemia Recurrence Risk following Successful Minimal Invasive Parathyroidectomy**


Minimal invasive parathyroidectomy (MIP) has replaced conventional neck exploration (CNE) as the standard surgical treatment of primary hyperparathyroidism (pHPT). The surgical success rate of MIP equals CNE. The
high rate of solitary adenomas in pHPT patients since the introduction of MIP raises the question whether multiglandular disease may reveal itself as a recurrence during follow-up. The aim of this study is to investigate the frequency of recurrent HPT after successful MIP for pHPT. Patients with non-familial pHPT who underwent successful MIP between April 2000 and April 2013 were included when normocalcaemia was confirmed at least 6 months postoperatively. Recurrent HPT was defined as a serum calcium value >2.55 mmol/l measured after >6 months of follow up, or a serum ionised calcium value >1.32 mmol/l measured after >6 months follow up. Cumulative 5-year recurrence rates were estimated by Kaplan-Meier statistics. There were 114 patients with sporadic pHPT who underwent successful MIP and had proven normocalcaemia 6 months postoperatively. After a median follow up of 34 months, recurrent HPT was observed in 4 patients, the 5-year cumulative risk of recurrent HPT was 7%. Hypercalcaemia varied between 2.62 and 2.74 mmol/l. Work-up of recurrent hypercalcaemia was done and revealed abnormal parathyroid glands in three patients. These three patients underwent surgery for recurrent HPT, and the localisation of the enlarged glands differed from the primary localisation in two of three patients. In one of the patients with recurrent HPT a MEN1 syndrome was established. Conclusion: following minimally invasive surgery for pHPT the long-term risk of recurrence was modest but not negligible. A long-term follow-up calcium measurement is advised in patients undergoing MIP.

P173
Factors that Contribute to Inadvertent Parathyroidectomy during Thyroid Surgery: Does the Presence of Lymphocytic Thyroiditis, Concomitant Primary Hyperparathyroidism or Hyperthyroidism have an Impact? N. Calcatera,* S. Mahady, M. Shiller, E. Roe, K. Cavaness, S. Celninski, J. Preskitt, C.S. Landry, Surgery, Baylor University Medical Center, Dallas, TX.

Background: Inadvertent parathyroidectomy during thyroid surgery has an incidence ranging between 5-21% across institutions. Many studies have identified malignancy and central neck dissection (CND) as risk factors for losing parathyroid glands, but few studies have evaluated the impact of other factors such as lymphocytic thyroiditis, hyperthyroidism or concomitant primary hyperparathyroidism. The purpose of this study was to investigate which factors contribute to parathyroid loss during thyroid surgery. Methods: A retrospective review of 271 patients undergoing thyroid surgery at a tertiary medical center from 2010-2013 was performed. Patient demographics, operative, and pathologic data were recorded. Statistical analyses were conducted to determine risk factors for parathyroid loss during thyroid surgery. Results: Among the 271 patients evaluated, 220/271(81%) were female, 15/271(5.5%) had hyperthyroidism, 48/269(18%) had lymphocytic thyroiditis on final pathology, 80/269(30%) had malignant disease, 38/271(14%) underwent CND, 142/271(52%) underwent total/subtotal thyroidectomy, 14/271(5%) underwent completion thyroidectomy and 110/271(41%) underwent thyroid lobectomy. 48/271(17.7%) patients had parathyroid tissue on final pathology not accounted for in operative report: 26/48(54%) patients lost entire parathyroid gland (<end>1-4 intra-thyroidal), while the remaining 22/48(46%) patients lost part of a parathyroid gland. The performance of CND(p = 0.001) and malignant pathology(p = 0.001) predicted an increased risk of inadvertent parathyroidectomy. Age, gender, race, operation, surgeon, thyroid size, presence of lymphocytic thyroiditis, hyperthyroidism, and concomitant primary hyperparathyroidism were not significant risk factors for losing parathyroid glands. Conclusions: CND for thyroid malignancy is the strongest risk factor for losing parathyroid tissue during thyroid surgery. The presence of concomitant primary hyperparathyroidism, lymphocytic thyroiditis, or hyperthyroidism does not appear to increase the risk of inadvertent parathyroidectomy.

P174
Implications of Gene Express Classifier Testing in Evaluation of Indeterminate Thyroid Nodules: A Single Institutional Experience A. Deniwar,* T. Mallik, P. Bhattia, A. Sholl, E. Kandil, Department of Surgery, Tulane University School of Medicine, New Orleans, LA.

Background: Afirma gene express classifier (GEC) has been increasingly used as an adjunct to improve the diagnostic accuracy of fine needle aspiration (FNA) in indeterminate nodules. It has been suggested that nodules with indeterminate cytology can be identified as GEC benign to avoid unnecessary diagnostic surgery. Our study aims to examine the accuracy of GEC testing for indeterminate thyroid nodules in surgical practice. Methods: This is a retrospective study of prospectively collected database on patients with indeterminate nodules who had GEC testing done over a year period in an academic institution. Samples for the GEC were collected according to the manufacturer’s protocol. Some patients with benign GEC testing underwent surgery for other indications. Postoperative surgical pathology was used to evaluate the efficacy of Afirma GEC. Results: A total of 60 patients with 64 indeterminate FNA results and Afirma GEC testing were included. Eight (12.5%) samples were not sufficient; five of them decided not to repeat the biopsy and underwent surgery, where 4 (80%) found to be malignant and one benign (20%). 24 nodules (37.5%) had benign GEC; nine of them underwent surgery for various indications, and 6 were confirmed to have benign final pathology giving negative predictive value of 67%. Thirty two nodules (50%) were suspicious by GEC Afirma testing. Fourteen patients out of 24 with suspicious GEC who underwent surgery had confirmed malignancy on final pathology (positive predictive value = 58%). Conclusion: The Afirma GEC showed a significantly lower negative predictive value compared to what is currently reported by the manufacturer. These results doubt the accuracy of Afirma testing in guiding surgical decision-making and further prospective multi-institutional studies are needed.

P175
Can Suspicious Surgeon’s Performed Ultrasound Features Predict BRAFV600E Status in Papillary Thyroid Carcinoma? A. Deniwar,* P. Bhattia, Z. Al-Qurayshi, H. Mohamed, E. Kandil, Department of Surgery, Tulane University School of Medicine, New Orleans, LA.

Background: Papillary thyroid carcinoma (PTC) can be predicted from certain suspicious ultrasound (US) features of thyroid nodules. The aim of this study is to examine if these suspicious features can predict the more aggressive PTC associated with BRAFV600E mutation. Methods: This is a retrospective review of prospectively collected data on patients with PTC and known BRAFV600E status. The patients underwent preoperative ultrasound by the same surgeon who performed all the operations on these patients. We divided patients into BRAFV600E positive and negative groups. All ultrasonographic data were collected including nodule size, echogenicity, solid or cystic nature, presence of calcification, irregular margins, and internal vascularity. Results: Of the patients with PTC, BRAFV600E mutation was detected in 36 (55.7%) patients. There was no significant difference in nodule size (2.1 cm ± 1.39 vs. 2.07 cm ± 1.53, p = 0.8951) between BRAFV600E positive and negative groups. BRAFV600E positivity was associated with higher rate of calcifications (60.6% vs. 23.9%, p = 0.001), and irregular margins (30.3% vs. 9.0%, p = 0.009). There was no significant difference in echogenicity, solid nature or internal vascularity between BRAFV600E positive and negative groups. Presence of three suspicious US features is associated with a PPV of 60.7%. With absence of all suspicious features, NPV was 82.6%. Conclusion: Presence of multiple suspicious US findings of thyroid nodules can predict the BRAFV600E mutation status of papillary thyroid cancer patients. Presence of intra-nodular calcification and irregular margins were the most predictive features. Future multi-institutional studies are warranted to help surgeons in risk stratification and surgery planning for patients with papillary thyroid cancer.

P176
When Would we Advocate a Total Thyroidectomy in Cases of Hypopharyngeal Carcinoma? A. M. Ali,* Surgery, National Cancer Institute, Cairo, Egypt.

Background and aim: The incidence of invasion of the thyroid gland by hypopharyngeal carcinomas is reported to be up to 57%. Our aim was to analyze the frequency of thyroid gland invasion in hypopharyngeal carcinoma treated by thyroidectomy with total laryngopharyngectomy and to identify patients in whom preservation of the thyroid gland is oncologically feasible and hence reduces post-operative hypothyroidism. Patients and methods: This retrospective cohort study included 58 patients with hypopharyngeal squamous cell carcinoma treated by thyroidectomy with total laryngopharyngectomy at the National Cancer Institute, Cairo University between May 1996 and October 2005. Thyroid gland involvement was analyzed through review of charts and pathologic reports. Patients were assessed preoperatively by CT. The correlation between the thyroid gland involvement and the clinical and radiologic CT findings was meticulously examined. Results: Thyroid gland involvement occurred in 37.9% (22/58) of all patients. T4 hypothyroidal tumors were present in 29.3% (n=17/58) of patients, paratracheal LN invasion was present in 37.9% (22/58) of patients, thyroid cartilage invasion was obvious in 19% (11/58) of patients, and previous radiotherapy was present in 5.2% (3/58) of these patients. Lobectomy was performed in 34.4% (20/58) of patients, and thyroidectomy was performed in 7.1% (4/58) of patients. Conclusion: There was no significant difference in patients with thyroid gland invasion to those without thyroid gland invasion. In conclusion, we can recommend a total thyroidectomy in cases of hypopharyngeal carcinoma.
patients. All patients with T4 hypopharyngeal tumors (n= 17/58) and with thyroid cartilage involvement (n=11/58) had thyroid gland invasion as well. T4 hypopharyngeal tumors, paratracheal LN invasion, and thyroid cartilage invasion were statistically significant factors (P < 0.001, P = 0.009 and P < 0.001 respectively) in independent correlation.

P177
Spectrum of Enteral Access Procedures for perioperative Nutritional Management of Oral Cancer Patients S.V. Deco, N.K. Shukla, A. Jakhetiya, P. Kharma, Surgical Oncology, All India Institute of Medical Sciences, New Delhi, India.

INTRODUCTION Perioperative nutritional management of oral cancer patients undergoing major surgery is a vital component of management and various options are available. However there is paucity of literature and lack of clear guidelines regarding these procedures. A Review of the spectrum and outcomes of enteral access procedures performed for peri operative nutritional management of oral cancer patients undergoing surgery in a tertiary care cancer centre was performed. METHODOLOGY A retrospective review of prospectively maintained computerized data-base of Oral cancer patients operated between 1995 - 2010 was performed and the details pertaining to the peri-operative enteral access procedures including the types, frequency of usage and outcome were analyzed. RESULTS A total of 950 major resections were performed for oral cancer patients during this period. 885 (93%) patients could be managed with simple nasogastric tube feeding for short term peri-operative nutritional needs. Only 65 patients (7%) required open feeding Jejunostomy / Gastrostomy and Per Cutaneous Endoscopic Gastrostomy (PEG) for anticipated long term peri-operative nutritional needs. A total of 39 patients had open feeding jejunostomy / Gastrostomy prior to introduction of PEG in 2005. PEG was performed in 26 patients between 2005 and 2010. The clinical profile of patients undergoing these procedures was as follows - mean age 52 years, 54 Male & 11 Female patients, Site distribution - Central Arch mandible (48 % ) Major tongue resections( 20%), Floor of mouth (20%) and alveolo buccal (12 %). Enteral access procedure related morbidities were observed in only two patients. CONCLUSIONS Peri-Operative nutritional support is important and various methods are available for enteral access but no clear cut guidelines are available regarding their usage. Our experience has shown that majority of oral cancer patients requiring short term ( 4 to 6 weeks) enteral access can be managed with simple naso-gastric tube feeding. PEG offers an excellent option in patients undergoing major resections and open jejunostomy/gastrostomy can be recommended if the expertise for PEG is not available.

P178
Changing Treatment Patterns of Early Hepatocellular Carcinoma S. Mohanty, R. Rajaram, K.Y. Bilimoria, T.M. Pawlik, D. Bentrem, Department of Surgery, Henry Ford Hospital, Detroit, MI. 2. Department of Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL. 3. Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD.

Introduction Early hepatocellular carcinoma (HCC) for patients without cirrhosis is typically treated with resection. We hypothesized that the growth of non-surgical therapies such as embolization is not limited to advanced disease. Our objectives were to describe treatment patterns of early HCC over time; identify factors associated with receipt of therapy; and evaluate the association of modality with outcome. Methods Patients with early HCC (solitary tumors without vascular invasion) and without documented cirrhosis were identified from the National Cancer Data Base (2003-2011). Treatment was categorized as one of four groups: ablation, resection, transplant, and non-surgical therapy (chemo- or radioembolization). Trends were summarized using the average annual percent change (AAPC). Regression models were developed to determine factors associated with receipt of treatment and assess the association of modality on survival. Results 14,077 patients were identified with early HCC (median tumor size, 3.7 cm; interquartile range, 2.4-6.0 cm). In the 10,187 (72.4%) patients who received therapy, 62.7% underwent surgery (21.0% ablation; 27.0% resection; 14.7% transplant). As a proportion of all treatment, surgical therapies declined from 61.6% to 44.5% (AAPC, -3.7%; 95%CI -4.9%, -2.6%). The proportion of patients who received ablations was unchanged (AAPC, 0.8%; 95%CI-4.1-2.6%), while resections (AAPC, -2.6%; 95%CI -4.5%, -0.7%) and transplants (AAPC, -9.6%; 95%CI-12.3%, -6.8%) decreased. Non-surgical therapies increased over the study period (17.2% to 39.2%; AAPC 11.4%; 95%CI 8.8%,14.1%) (Figure 1). Younger age, smaller tumor size, female sex, white race, higher income, and private insurance were associated with receipt of surgical treatment. The strongest predictor was treatment in an academic center (OR=1.37; 95%CI 1.13-1.66). Patients selected for non-surgical therapy had worse adjusted five-year survival than patients who had surgery (HR=2.05; 95%CI 1.85-2.26). Conclusion Despite limited evidence of improved long-term outcome, embolization has replaced surgery as the most common treatment modality in early HCC. Randomized studies are needed to compare the effectiveness of treatments for this disease.

Figure 1. Treatment patterns of early stage hepatocellular carcinoma over time

P179

Background: Perioperative Red Blood Cell transfusions (RBCT) are associated with postoperative morbidity and may increase cancer recurrence through immunologic mechanisms following resection of colorectal liver metastases (CRLM). We sought to explore the relationship between RBCTs and long-term survival following resection of CRLM in the contemporary surgical era. Methods: We conducted a retrospective review of a prospectiv database including all patients undergoing partial hepatectomy for CRLM from 2003-2012. Data regarding date of death was abstracted from a validated, population-based cancer registry. Primary outcome was overall survival (OS), compared based on RBCT (defined as time of surgery to 30 days following surgery) and on number of RBC units received using Kaplan-Meier curves. Cox regression analysis was performed to examine the association between RBCT and OS, while adjusting for prognostic factors including Fong score and period of treatment (2003-2007 Vs. 2008-2012). Results: We included 483 patients operated for CRLM, of which 27.5% received RBCT. 90-day post-operative mortality was 4.8% and median follow-up was 33 (IQR: 20.1-54.8) months. Median survival in patients who received RBCT was 44.5 months compared with 93.5 months in patients who did not(p<0.0001). The difference persisted in subgroup analysis excluding patients who died within 90 days of surgery (62.3 vs. 93.5 months, p=0.023). After adjustment for Fong score and period of treatment, RBCT was independently associated with decreased OS (HR 2.15; 95%CI: 1.52-3.04). Conclusion: Perioperative RBCT is independently associated with decreased OS following hepatectomy for CRLM. Interventions to minimize and rationalize the use of RBCT for hepatectomy are warranted in order to mitigate this detrimental effect on long-term outcomes.
**P180**

Non-Invasive Radiofrequency-Induced Hyperthermia Selectively Increases Tumor Vascular Permeability

**Introduction** Radiofrequency (RF) heats tumors more than normal tissue, providing a means of specifically increasing tumor vascular permeability by RF-induced hyperthermia (HT). We investigated a new, non-invasive method to deliver RF-HT to tumor tissue in orthotopic murine models as a novel adjunctive treatment modality for cancer.

**Methods** Two orthotopic tumor mouse models were used: 4T1-luc2-td or PANC-1 tumor cells were grafted in mammary fat pads or pancreas, respectively. Real-time, intravital microscopy (IVM) imaging was used to examine extravasation of fluorescently-tagged albumin within the tumor vasculature. The treatment group received RF-induced HT through an RF transmitter for 10 minutes whereas the control group did not. Relative extravasation between the two groups was quantified by pixel analysis. Albumin uptake was assessed via immunofluorescence (IF) staining for albumin and CD31. Uptake of fluorescein isothiocyanate dextran (FITC-dextran) was measured in a similar fashion.

**Results** RF-HT increased tumor temperature to 37-41°C. In 4T1 mice, treatment with RF-HT led to a 3-fold increase in albumin uptake on IVM imaging and 5-fold increase on IF (p < 0.05). Increased uptake was sustained 30 minutes after RF exposure. In PANC-1 mice, the increase in uptake of albumin and FITC-dextran on IF in RF-HT treated mice was 6-fold (p < 0.05).

**Conclusions** Tumor-selective hyperthermia can be achieved via a non-invasive RF device and results in increased vascular permeability. Future studies will examine whether RF-HT will increase chemotherapeutic uptake into tumor tissue, possibly increasing efficacy with reduced dosages and, thus, negative side effects.

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**P181**

Analysis of Nodal Status and Survival in Early T-Stage Gallbladder Cancers in the Modern Era

**Introduction:** Gallbladder cancer is a rare but aggressive cancer best treated with complete surgical resection. Recent studies suggest guideline recommendations for radical surgery are often not followed. We examined outcomes for early T-stage gallbladder cancer utilizing recent national registry data.

**Methods:** The SEER database was queried from 2004 to 2010 for patients with T1a, T1b, and T2 gallbladder cancer. Lymph node (LN) positivity rates by T-stage were determined and compared with the chi-square test. Overall (OS) and disease-specific survival (DSS) by T-stage were calculated using Kaplan-Meier methods and compared using the log-rank test. Results: We identified 6,713 gallbladder cancer patients with staging data; 262 (4%) T1a tumors, 409 (6.1%) T1b, and 1,477 (22%) T2. Of 71 T1a patients with LN data, 12.7% had positive disease. Of T1b patients, 27.3% had LN-positive disease compared with 49.6% of T2 patients (p<0.001). Median OS was greater than 5 years for T1a and T1b LN-negative patients, compared with 24 months and 15 months, respectively, in LN-positive patients (p<0.05). Of T1b patients, 27.3% had LN-positive disease compared with 49.6% of T2 patients (p<0.001). Median OS was greater than 5 years for T1a and T1b LN-negative patients, compared with 24 months and 15 months, respectively, in LN-negative patients (p<0.05). Of T2 patients, median OS was 59 months with LN-negative disease compared with 19 months in LN-positive disease (p<0.05). Median DSS was greater than 5 years for T1a, T1b, and T2 LN-negative patients, but diminished to 24, 17, and 28 months respectively for T1a, T1b and T2 patients with positive nodes (p<0.05).

**Conclusions:** Nodal positivity predicts significantly decreased survival in T1a, T1b, and T2 gallbladder cancers. Radical cholecystectomy for T1b and T2 gallbladder cancer remains standard treatment, as more than one-fourth of patients with T1b disease and nearly half of those with T2 cancers will have LN-positive disease; however, we found 12.7% of T1a patients had positive lymph nodes, which is higher than historical figures, and radical surgery may be warranted in these patients as well.
Kaplan-Meier curves of T1a, T1b and T2 tumors for overall survival and disease-specific survival.

P182

Introduction: Calculating future liver remnant volume (FLRV) is important in planning treatment of hepatic neoplasm. CE-MRI gadodextrate disodium (Eovist) has been shown to yield more information than 3p-CT, often narrowing the differential of hepatic neoplasms. The purpose of this study is to compare FLRV calculated from CE-MRI to those from 3p-CT. Methods: We performed a retrospective review of 28 patients with liver tumors evaluated with both 3p-CT and CE-MRI prior to treatment. Three-dimensional reconstructions were computed by manual tracing technique. 3p-CT is considered the gold standard. Results: The calculated total hepatic mean volumes for 3p-CT was 1,588 cm^3 and 1,916 cm^3 for CE-MRI, with spearman correlation (p) of 0.91 (p <0.01). The total volume difference was 327 cm^3 (p <0.01). The right hepatic lobe volume was 1,028 cm^3 (3p-CT) and 1,283 cm^3 for (CE-MRI) (p 0.83, p <0.01). The left hepatic volume was 525 cm^3 (3p-CT) and 638 cm^3 for (CE-MRI), (p 0.79, p <0.01). The difference in calculated volume for the right liver is 254 cm^3, p <0.01 (3.23%, p 0.008) and 94 cm^3, p 0.07 (2.09%, p 0.045) for the left liver. Conclusion: Our data demonstrated a strong and positive correlation between 3p-CT and CE-MRI. When the 30% FLRV cut-off used, there is variability in 5 out of 28 patients (17.8%). Our data suggest that patients with FLRV calculated by CE-MRI that are near the resectability cut-off or those with abnormally large calculated FLRV should undergo 3p-CT for verification. Future studies are needed to further validate CE-MRI ability to calculate FLRV.

P183
Addition of Hepatic Arterial Infusional Floxuridine to Adjuvant Chemotherapy after Colorectal Liver Metastasis Resection is associated with Altered Patterns of Disease Progression, Cause of Death and Prolonged Survival M.R. Porembka,¹ T.P. Kingham,² P.J. Allen,² R.P. DeMatteo,² W.R. Jarnagin,² N. Kemeny,² M.I. D’Angelica,¹ 1. Surgery, UT Southwestern Medical Center, Dallas, TX; 2. Memorial Sloan Kettering Cancer Center, New York, NY.

Background: The relationship between recurrence after colorectal liver metastasis (CRLM) resection and cause of death (COD) is unknown. Adjuvant systemic and regional chemotherapy attempt to decrease the risk of recurrence and death, but it is unknown how these therapies might alter the pattern of disease progression and COD. Methods: A prospective database was used to identify patients with CRLM without extrahepatic disease undergoing initial liver resection between 2000 and 2005. Patients who received adjuvant therapy with hepatic artery infusional floxuridine (HAI+Sys) in addition to systemic therapy (FOLFOX or FOLFIRI) were matched and compared to a similar cohort of consecutive patients treated with resection and adjuvant systemic chemotherapy (Sys Only) during the same time period. Relapse-free survival (RFS), disease-specific survival (DSS), recurrence patterns, and COD were compared. COD was categorized by metastatic site (neurologic, hepatic, pulmonary, peritoneal, other). Results: Of the 240 patients included, 120 received HAI+Sys and 120 patients received Sys Only. Clinical risk score and extent of resection were similar. Median follow-up was 79.3 months. HAI+Sys was associated with prolonged RFS (54.5 vs 18.2mo; p<0.001) and DSS (median not reached vs 58.7mo; p=0.00001). Of the 127 patients (53%) who died, 83 had the COD directly related to metastasis (Table). The major COD in the Sys Only group was hepatic (47%). HAI+Sys was associated with fewer liver-related deaths (9%), but more deaths from neurologic and pulmonary compromise (p < 0.001, Table). Hepatic COD was associated with neoadjuvant chemotherapy (p<0.01) and the absence of HAI (p<0.001). Death from peritoneal recurrence was similar in both groups. Conclusion: Treatment with HAI+Sys is associated with reduction in hepatic recurrence, decrease in liver-related death, and prolonged survival after CRLM resection compared to Sys Only. HAI+Sys is an effective method for the long-term control of hepatic metastasis which may account for an associated survival advantage.

Cause of death by responsible metastatic site

<table>
<thead>
<tr>
<th>Metastatic Site</th>
<th>Sys Only</th>
<th>HAI+Sys</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neurologic*</td>
<td>4 (9%)</td>
<td>10 (27%)</td>
</tr>
<tr>
<td>Hepatic*</td>
<td>21 (47%)</td>
<td>4 (9%)</td>
</tr>
<tr>
<td>Peritoneal</td>
<td>9 (20%)</td>
<td>11 (24%)</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>1 (2%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Other</td>
<td>7 (16%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Total</td>
<td>45 (100%)</td>
<td>38 (100%)</td>
</tr>
</tbody>
</table>

*p < 0.05

P184
Effect of Epidural compared to Patient-controlled Intravenous Analgesia on Outcomes for Patients undergoing Hepatectomy S. Allen,* A. DeRoche, L. Adams, K. Slocum, N. Fitzgerald, C.J. Clark, P. Shen, General Surgery, Wake Forest School of Medicine, Winston-Salem, NC.

Introduction: Epidural analgesia is considered to improve postoperative outcomes in major oncologic abdominal surgery. However its role in specific subsets of cancer operations is not well-defined. We examined the effect of epidural versus intravenous patient controlled analgesia (IVPCA) in patients undergoing hepatectomy. Methods: Perioperative records of patients undergoing hepatectomy from 2012 to 2014 were analyzed. Pain-related and clinical data were extracted and correlated with baseline clinicopathologic data and method of analgesia. Chronic pain was defined by specific narcotic requirements preoperatively. Results: Eighty-eight patients underwent hepatectomy with sixty percent having epidurals placed for postoperative pain control. Epidural patients underwent more major hepatectomies and open resections. Thirteen percent of epidurals placed were non-functional. Twenty-five percent of epidural patients experienced hypotensive episodes requiring a median of 2 epidural adjustments (range, 0-5). Excluding patients with chronic pain, twenty percent of epidurals required the addition of an IVPCA for pain control. Also when patients with chronic pain were excluded, comparison of pain scores at specific time points between both groups demonstrated no significant difference at 6, 12, 24, and 48 hours postoperatively (all p>0.05). Use of an epidural was found to significantly correlate with increased total fluid given intraoperatively and in the first 24 hours, 8.2 versus 6.6 liters (p<0.01). There was no major effect of epidural analgesia on time to oral intake, ambulation, or complications (all p>0.05). However epidural use was significantly associated with increased length of stay compared to IVPCA, median 6 versus 4 days (p=0.0386). Conclusions: One in five patients without chronic pain who had an epidural required addition of an IVPCA for analgesia. Though patients with epiduals received significantly more fluids and had a longer length of stay, they underwent larger operations. The use of epidural analgesia for hepatectomy requires further study.
**P185**

**Effect of KRAS Mutation on Long-term Outcomes of Patients undergoing Hepatic Resection for Colorectal Liver Metastases**

G. Margonis,1* G. Spolverato,1 Y. Kim,1 G. Karagkounis,2 M. Choti,3 T.M. Pawlik,1 1. Surgery, Johns Hopkins Hospital, Baltimore, MD; 2. Cleveland Clinic, Cleveland, OH; 3. UT Southwestern, Dallas, TX.

**Background:** The impact of KRAS mutations on overall survival (OS) and recurrence-free survival (RFS) of patients with colorectal liver metastases (CLM) remains poorly defined. We sought to investigate the prognostic value of KRAS in a large cohort of patients undergoing liver resection for CLM.

**Methods:** Between 2003 and 2013, 334 patients underwent hepatic resection for CLM at Johns Hopkins Hospital and met the inclusion criteria. Somatic mutations at codons 12/13 were evaluated through a sequencing analysis of the tumor samples. Clinicopathological characteristics, perioperative details, and outcomes were stratified by KRAS status (mtKRAS vs. wtKRAS) and analyzed.

**Results:** Among 334 patients undergoing liver resection for CLM, mtKRAS was identified in 115 (34.4%) patients. Median CEA was 7.3 ng/dL; 40.4% of patients had a solitary tumor and median tumor size was 2.5 cm. At a median follow-up of 28.2 months, recurrence was observed in 59 (51.3%) patients with mtKRAS and 117 (53.4%) patients with wtKRAS (P=0.71); there was no difference in the pattern of recurrence (liver: mtKRAS, 39.0% vs. wtKRAS, 52.1%; lung: mtKRAS, 55.6% vs. wtKRAS, 64.3%; both P<0.05). While 5-year log-rank OS was comparable among mtKRAS (41.6%) vs. wtKRAS (48.5%), on multivariable Cox survival analysis mtKRAS was associated with worse OS (HR, 1.65; 95% CI, 1.07-2.54). Moreover, among patients who experienced a recurrence, 5-year OS was worse among those patients who had mtKRAS (mtKRAS, 28.1% vs. wtKRAS, 44.5%; P=0.004; Figure). After controlling for tumor factors, as well as receipt of chemotherapy, mtKRAS status remained independently associated with a worse outcome among patients who recurred (HR, 2.07; 95% CI 1.31-3.27; P=0.002). **Conclusion:** mtKRAS was noted in one-third of patients with CLM. While KRAS status did not impact the pattern of recurrence, mtKRAS was an independent predictor of worse OS among patients who experienced a recurrence following resection of CLM.

**P186**

**Neutrophil-lymphocyte and Platelet-lymphocyte Ratio in Patients after Resection for Hepato-Pancreato-Biliary Malignancies**

G. Spolverato, Y. Kim, G. Margonis, R. Gupta, M. Makary, C.L. Wolfgang, M.J. Weiss, K. Hirose, J.L. Cameron, T.M. Pawlik, Surgery, Johns Hopkins Hospital, Baltimore, MD.

**Background:** Neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) may be indicative of the immune response around the time of surgery. We sought to determine whether NLR or PLR were associated with outcomes of patients undergoing surgery for a hepatopancreatobiliary (HPB) malignancy.

**Methods:** Between 2010-2011, 289 patients who underwent an HPB procedure for a malignant indication were identified. Clinicopathological characteristics, NLR and PLR, as well as short- and long-term outcomes were analyzed. High NLR and PLR were classified using a cut-off value of 3 and 150, respectively, based on ROC analysis.

**Results:** Median patient age was 63 years and 52.3% were female. The majority of tumors were pancreatic in origin (67.2%), while a subset were primary (10.3%) or secondary (22.5%) liver tumors. Patients with low vs. high NLR and PLR had similar baseline characteristics with regard to performance status and tumor stage (all P>0.05). Operative interventions included pancreaticoduodenectomy (55.0%), hepatic (29.1%), or extended hepatectomy (2.4%). Within 90-days of surgery, 143 patients experienced a complication for a morbidity of 49.5% (pancreas: 54.9% vs. liver: 40.0%). Patients with either an elevated NLR (OR=1.72) or PLR (OR=2.15) were at higher risk of a postoperative complication (both P<0.05). Among patients with a pancreatic, primary or secondary liver tumor, 3-year survival was 38.6%, 43.0%, and 65.0%, respectively. While elevated NLR was not associated with long-term outcome (HR=1.36) (P=0.14), patients with an elevated PLR had a higher risk of death (HR=2.14) (P=0.01) (Figure).

**Conclusion:** Patients with a high NLR or PLR had an increased risk of a perioperative complication. Elevated PLR was also a predictor of worse survival among patients with HPB malignancy undergoing resection.
Management and Outcomes of Patients with Recurrent Intrahepatic Cholangiocarcinoma following Previous Curative Intent Surgical Resection


Background: Many patients develop recurrence following resection of intrahepatic cholangiocarcinoma (ICC). Management and outcomes of patients with recurrent ICC following previous curative-intent surgery are not well documented. We sought to characterize the treatment of patients with recurrent ICC and define therapy-specific outcomes. Methods: Between 1990-2013, 542 patients who underwent surgery for ICC were identified from an international database. Data on clinicopathological characteristics, operative details, recurrence and recurrence-related management were recorded and analyzed. Results: At initial surgery, treatment was resection only (96.1%) or resection+RFA (3.9%). Overall 5-year survival was 25.9% 376 (69.4%) patients recurred with a median disease-free survival of 11.0 months. Vascular invasion (hazard ratio [HR]=1.43), nodal metastasis (HR=1.40) and poor differentiation (HR=1.30) were predictive of recurrence (all P<0.05). First recurrence site was intrahepatic only (62.0%), extrahepatic only (14.1%), or intra- and extrahepatic (23.9%). Overall 259 (48.9%) patients received treatment for recurrent ICC, while 117 (31.1%) received best supportive care (BSC). Among patients who received treatment for recurrent disease, therapy consisted of systemic chemotherapy only (49.4%), repeat liver-directed therapy (25.9%), or systemic chemotherapy+ liver-directed therapy (24.7%). Repeat liver-directed therapy consisted of repeat hepatic resection+ablation (30.5%), ablation alone (21.4%), and intra-arterial therapy (IAT) (48.1%). Among patients who recurred, median survival from the time of the recurrence was 11.0 months (BSC 7.7 months, systemic chemotherapy 10.0 months, liver-directed therapy 18.0 months). The median survival of patients undergoing resection of recurrent ICC was 26.7 months versus 7.6 months for patients who had IAT (P<0.001). Conclusions: Recurrence following resection of ICC is common, occurring in up to two-thirds of patients. When recurrence occurs, prognosis is poor. In well-selected patients with liver-only recurrence, resection+chemotherapy may offer a modest survival benefit.

Short-term and Long-term Results of Patients with Colorectal Liver Metastases undergoing Surgery with or without RFA


Background By combining surgery and radiofrequency ablation, it is possible to provide alternative treatment for patients with unresectable colorectal liver metastases. Although the results published in literature look promising, uncertainty exists with regard to complication risks and the survival of this specific therapy. The aim of this study was therefore to compare combined hepatic surgery and radiofrequency ablation to conventional hepatic resection. Materials and methods From January 2000 till May 2013, 1007 patients were treated for colorectal liver metastases and included in a prospective multicenter database. Outcome variables such as patient demographics, complications, recurrence rates and survival were retrospectively analyzed from this database. Synchronous surgery for both primary and secondary tumors was one of the exclusion criteria. Results Of these 1007 patients, 632 were included. 98 patients were treated with the combination therapy while 534 patients received only hepatic surgery. There was no difference in age (P=0.42), gender (P=0.99) or BMI (P=0.53). However, patients who received the combination therapy had a higher Fong Clinical Risk Score (CRS) (P=0.001) better ASA classification (P=0.04), more metastases (P=0.001) and more neoadjuvant chemotherapy (P=0.001). There was no significant difference in postoperative morbidity (36.1% and 30.6% respectively; P=0.34) or mortality (respectively 1% and 1.3%; P=1.00). Patients from the combination group had more R1 resections (P=0.001) and more often a local recurrence (P=0.01). After correction for both the CRS and ASA score, there was no difference in 5 year disease-free survival (both 34%; P=0.95), however a lower 5 year overall survival for the combination group (respectively 48.1% and 63%; P=0.02). Conclusion The combination of hepatic surgery and intraoperative radiofrequency ablation, is frequently used for high CRS patients and doesn’t show an increase in complication rate. With this treatment, a high number of patients with colorectal liver metastases can be treated, providing possible curation for patients with those worse clinical risk scores.
P191
HBV and HCC Screening Practices in Immigrant-rich Neighborhoods of New York City

Objective: Worldwide, the majority of hepatocellular carcinoma (HCC) is related to infection with the hepatitis B virus (HBV) and occurs in developing countries, with the highest rates in China and Africa. Immigrants from these regions represent a large and growing ethnic group in New York City (NYC). However, there is a dearth of studies on the practice of HBV and HCC screening in high-risk populations. Methods: A 28 question, multiple-choice, web-based survey was created to assess HBV and HCC knowledge and screening practices. 2010 census data were used to determine the 25 zip codes in NYC with the highest rates of individuals born in China or Africa. The survey was distributed to primary care physicians practicing in these regions. Results: Of the 102 participants, there were 34 and 38 responders with a practice in the zip codes with the highest concentrations of Chinese and African immigrants, respectively. Among all respondents, 73% commonly screen for HBV among immigrant patients, but only 63% recommend HCC screening for those patients who test positive for HBV, with no significant difference between the Chinese and African cohorts. According to respondents, diabetes, hypertension, and heart disease were the top three health concerns of patients in both cohorts; HBV and HCC were not among the top answers. Importantly, physicians in both groups cite lack of clear guidelines on HBV and HCC screening as a main reason for not offering screening for either disease. Practitioners felt the main reason patients failed to get screened was “lack of patient awareness of hepatitis B or liver cancer risk.” Conclusions: HBV and HCC occur at much higher rates in Chinese and African immigrants, however these individuals appear to be unaware of the risks. Furthermore, one-third of primary care physicians practicing in immigrant-rich areas fail to recommend HCC screening for HBV positive patients. Despite the presence of accepted HBV and HCC screening guidelines, knowledge of and adherence to these guidelines is not optimal. There is a need for better distribution of these guidelines to primary care providers, particularly for those serving in neighborhoods with high-risk individuals.

P192
Hepatic Artery Infusion for Recurrent or Chemo-resistant Hepatic Malignancy H.J. Wanebo,1* R. Srinivasa,2 C. Taneja,3 J. Belliveau,4 R. Rathore,5 J. Surgery, Landmark Medical Center, Bristol, Puerto Rico, 2. Hurley Medical Center, Flint, MI, 3. Rhode Island Hospital, Providence, RI, 4. Roger Williams Medical Center, Providence, RI.

Introduction: Previously treated Hepatic Colorectal Metastases (CRC) patients are high-risk for invasive procedures and may be predisposed to poor survival. Early identification of those at risk may prevent complications and allow more informed decision making. The AST/platelet ratio index (APRI) is a measure of cirrhosis that we hypothesize predicts survival and may be used to estimate HCC mortality. Methods: Retrospective study of HCC patients diagnosed in a safety-net hospital system from 1998-2012. Standard demographics as well as lab values (bilirubin, INR, creatinine, AST and platelets) were recorded at the date of diagnosis to calculate APRI (normal< 0.76) and MELD score. Poor survival was defined as death within 30 days from diagnosis. Regression models were created to determine predictors of death within 30 days and overall survival. Results: 654 patients (79% male) were included in the study and <30 day death was observed in 111 patients (17%). Mean age at diagnosis was 55.6 years (SD 9.1) and there was no difference in age between the two groups. Mean APRI and MELD score were higher in the <30 day death group. APRI (OR 1.45, 95%CI: 1.07-1.96) and MELD score (OR 1.21, 95%CI 1.14-1.28) were predictive of <30 Day Death. Stratified by stage, both APRI (HR 1.12, 95%CI: 1.01-1.24) and MELD score (HR 1.07, 95%CI:1.05-1.09) predicted overall survival. Inclusion of both APRI and MELD in the Cox regression resulted in the best fit (c-index = 0.67). Although there was a minor correlation between APRI and MELD (r2=0.14), there was no interaction or collinearity in the logistic or Cox regression models. At fixed values of MELD, the predicted probability of 30 day death increased at higher APRI values (see table). Conclusions: The AST/Platelet ratio index is an innovative marker of cirrhosis and survival for HCC patients. APRI provides additional prognostic information regarding outcome in cirrhotic HCC patients, independent of MELD score. Further study and external validation is needed to determine the clinical utility of using APRI for prognostic and treatment decisions.

P193
AST to Platelet Ratio Index Improves Prediction of Hepatocellular Carcinoma Mortality K.C. Allenson,1* L. Kao,2 N.A. Bhadkamkar,2 T.C. Ko3, C.J. Wray,1 1. Surgery, UTHealth, Houston, TX, 2. MD Anderson Cancer Center, Houston, TX.

Introduction: Hepatocellular carcinoma (HCC) patients with cirrhosis are high-risk for invasive procedures and may be predisposed to poor survival. Early identification of those at risk may prevent complications and allow more informed decision making. The AST/platelet ratio index (APRI) is a measure of cirrhosis that we hypothesize predicts survival and may be used to estimate HCC mortality. Methods: Retrospective study of HCC patients diagnosed in a safety-net hospital system from 1998-2012. Standard demographics as well as lab values (bilirubin, INR, creatinine, AST and platelets) were recorded at the date of diagnosis to calculate APRI (normal< 0.76) and MELD score. Poor survival was defined as death within 30 days from diagnosis. Regression models were created to determine predictors of death within 30 days and overall survival. Results: 654 patients (79% male) were included in the study and <30 day death was observed in 111 patients (17%). Mean age at diagnosis was 55.6 years (SD 9.1) and there was no difference in age between the two groups. Mean APRI and MELD score were higher in the <30 day death group. APRI (OR 1.45, 95%CI: 1.07-1.96) and MELD score (OR 1.21, 95%CI 1.14-1.28) were predictive of <30 Day Death. Stratified by stage, both APRI (HR 1.12, 95%CI: 1.01-1.24) and MELD score (HR 1.07, 95%CI:1.05-1.09) predicted overall survival. Inclusion of both APRI and MELD in the Cox regression resulted in the best fit (c-index = 0.67). Although there was a minor correlation between APRI and MELD (r2=0.14), there was no interaction or collinearity in the logistic or Cox regression models. At fixed values of MELD, the predicted probability of 30 day death increased at higher APRI values (see table). Conclusions: The AST/Platelet ratio index is an innovative marker of cirrhosis and survival for HCC patients. APRI provides additional prognostic information regarding outcome in cirrhotic HCC patients, independent of MELD score. Further study and external validation is needed to determine the clinical utility of using APRI for prognostic and treatment decisions.

Predicted Probability of 30 Day Death

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P194
A Retrospective Review of the University Health Network (UHN)
Multimodal Treatment Experience with Extended Resection of
Pancreatic Ductal Adenocarcinoma (PDAC) in Patients with
Arterial Involvement. A. Tremblay-St-G.,1 A. M. Fox,3 M. Segedi,2
S. Pablo,2 P. Scholtz,2 M. O’Malley,1 A. Borgida,1 B. Teresa,1
A. Dodd,4 M. Krzyzanowska,1 M. Moore,4 J. Kim,4 A. Wei,4 S. Gall-
inger,1 N. Dhami,1 I. McGilvray,1 1. Department of Surgery, Toronto
General Hospital, University of Toronto, Toronto, ON, Canada;
2. Department of Surgery, University of British Columbia, Vancouver,
BC, Canada; 3. Department of Surgery, McMaster University, Hamil-
ton, ON, Canada; 4. Joint Department of Medical Imaging, University
of Toronto, Toronto, ON, Canada; 5. Ontario Pancreas Cancer Study,
Mount Sinai Hospital, Toronto, ON, Canada; 6. McCann Center for
Pancreas Cancer, Princess Margaret Cancer Centre, Toronto, ON, Canada;
7. Department of Medical Oncology, Princess Margaret Cancer Centre;
Toronto, ON, Canada; 8. Department of Radiation Oncology, Princess
Margaret Cancer Centre, Toronto, ON, Canada; 9. St. Vincent Hospital,
University of Melbourne, Melbourne, VIC, Australia.

Involvement of a major artery with PDAC is a criteria of unresectability.
Although major vein resection/reconstruction is now accepted in PDAC resec-
tion, the feasibility of arterial resection requires investigation. The response to
neoadjuvant therapy (NAT) may be a useful tool for identifying appropriate
candidates for extended resection. We retrospectively reviewed the UHN expe-
rience of multimodality therapy in patients (pts) with histologically confirmed
PDAC and single vessel arterial involvement (superior mesenteric, celiac or
hepatic artery) on CT from Jan 2009 to Dec 2013. These pts received NAT
prior to being re-assessed for surgery; pts whose disease was either stable or
improved were considered for surgery. Baseline imaging was reviewed inde-
pendently. Postoperative complications were assessed and oncologic outcomes
were analysed with Kaplan-Meier method. We identified a cohort of 57 pts
of whom 56 received NAT. On reassessment, 26 (46%) had no evidence of
disease progression and were considered operable, while 31 had local or distant
progression and were deemed inoperable. Of 26 pts proceeding to surgery, 21
(81%) underwent resection and 5 had a palliative procedure. In the resection
group, 10 pts required arterial resection/reconstruction to achieve R0. The
median survival for the resection group was 18.7 months (95% CI: 11.2-NA) vs.
13.6 months (95% CI: 11.9- 18.1) for the non-resection group, P=0.0246. Our results suggest that a multimodal approach including
NAT +/- segmental arterial resection/reconstruction, can be considered but
with high post-operative morbidity. The encouraging survival rates of pts after
extended resection must be balanced with the morbidity of this surgery. Given
the poor prognosis of pts with locally advanced PDAC, there is a rationale for
prospective evaluation of this approach to identify pts who are most likely to
benefit from this aggressive strategy.

P195
Survival of Patients with Colorectal Liver Metastases Treated with
Electrochemotherapy. I. Edzunovic,8 E. Breceli1, G. Gasjeljic,1
M. Marolt Music,1 V. Gorjup,2 B. Malj1, T. Jarm,1 B. Kos,3 D. Pav-
liha,1 B. Gercar Kuzmanov,2 D. Miklavcic,2 M. Cemazar,1 M. Snoj,1
E.M. Gadzijev,1 G. Sersa,1 1. Institute of Oncology Ljubljana, Lju-
bljana, Slovenia; 2. University Medical Center Ljubljana, Ljubljana,
Slovenia; 3. University of Ljubljana, Faculty of Electrical Engineering,
Ljubljana, Slovenia.

INTRODUCTION: Electrochemotherapy (ECT) is a new, non-thermal
treatment for patients with colorectal liver metastases. The aim of this study was
to analyze the survival of the specific subgroup of patients from our larger,
recently published study on feasibility, efficacy and safety of ECT on patients
with colorectal liver metastases. PATIENTS AND METHODS: A subgroup
of eight patients with colorectal liver metastases in whom treatment within
standard of care was not possible any more was included. The ECT was offered
to these patients as the only treatment option, alone or in combination with
surgical resection and systemic treatment in case if they had at the same time
also resectable metastases. The ECT was performed during open surgery by
inserting the electrodes into and around the tumor to cover with a sufficiently
intensive electric field the whole tumor and margin of normal tissue, according
to the individualized treatment plan. Electric pulses, synchronized with the
EGC, were delivered after intravenous administration of bleomycin (15,000
HU/m2). RESULTS: Eight patients with total of 14 metastases were treated. 10
out of 14 metastases were in the near vicinity of the major vessels. All patients
in this group died from malignant disease. Survival times were: 8.2, 10.8,
15, 16.8, 17.1, 22.8, 24.3 and 28.6 months. The mean survival time was 17.9
months and the median survival time was 16.9 months. In 5 out of 8 patients
additional resection of resectable metastases was performed. CONCLUSION:
Presented subgroup of patients included only patients who were untreatable
within standard of care. These patients have very poor survival times. ECT of
unresectable metastases or metastases in near vicinity of major vessels, where
radiofrequency ablation is not very efficient, has allowed this patients extended
surgical and/or systemic treatment.

P196
Regional Disparities in the Surgical Treatment of Gallbladder Can-
Surgical Oncology, City of Hope, Arcadia, CA.

Introduction: Surgical resection is the mainstay of treatment for gallbladder
cancer, with radical resection recommended for patients with T1b, T2 and
T3 tumors; however recent studies suggest guidelines are frequently not fol-
lowed. We sought to identify national and regional trends in the use of radical
surgical resection for gallbladder cancer. Methods: The SEER database was
queried for patients with T1b, T2 and T3 gallbladder cancers who underwent
surgical resection. Patients were stratified by region (East, Midwest, South
and West), race (White, Black, Other), and type of surgery performed
within standard of care. These patients have very poor survival times. ECT of
unresectable metastases or metastases in near vicinity of major vessels, where
radiofrequency ablation is not very efficient, has allowed this patients extended
surgical and/or systemic treatment.

Regional Disparities in the Surgical Treatment of Gallbladder Cancer
P198
Biologic Mesh Spacer Placement Facilitates Safe Delivery of
Dose-intense Radiation Therapy: A Novel Treatment Option for
Unresectable Liver Tumors
H.N. Ismuel, C. Cane, P. Das, S. Krishnan, R. Schrott, M. Javle, C. Conrad, J. Vauthery, T. Aloia. University of Texas MD Anderson Cancer Center, Houston, TX.

Introduction Patients with unresectable liver tumors who fail initial treatment modalities have a poor prognosis (<1 yr). Although effective, delivery of high dose radiation therapy to these tumors is limited by proximity of radiosensitive bowel. We have previously reported that placement of a biologic mesh spacer (BMS) can effectively displace the bowel allowing for dose-intense radiation to be delivered with low short-term toxicity. The purpose of this study was to assess and report the long-term safety and oncologic outcomes of this cohort. Methods From 2012 to 2014 seven patients with unresectable hepatic malignancy (6 HICC, 1 CRLM) underwent BMS (acellular human dermis) placement (3 open, 4 MIS) prior to radiation therapy. Prospective registry data were reviewed for tumor and treatment details, progression, metastasis and survival. RTOG guidelines were used to define radiation toxicities. Results Mean patient age was 50.2 years (30-62 years) and 4 patients were male (57.1%). Prior to surgery, all patients had been treated for an average of 12.5 months with surgery, chemotherapy, radiation and/or TACE. After surgery, all patients recovered well and received a mean radiation dose of 67.09 Gy over 4-25 fractions (maximum dose of 100 Gy - Biologic Equivalent Dose of 140 Gy, α/β=10). Mean time to initiation of radiation therapy was 24 days (12-48 days) from surgery. No significant GI toxicity was recorded, and no GI bleeding or ulcers were observed. Mean followup after XRT was 15.9 months (5-28 months). Three patients had no locoregional progression of disease. One patient had local progression of disease and another had progressive lymphadenopathy. 3 patients developed pulmonary metastasis, at a mean time (5-28 months). There are 4 survivors over 2-years from surgery.

Conclusion For patients with unresectable liver tumors, placement of a BMS enhances the safety and efficacy of high-dose radiotherapy, providing a survival benefit via delay in time to progression compared to traditional treatments with no significant short or long term GI toxicity.

P199
Initial Experience with a Surgeon-led Hepatic Arterial Pump Program
N.D. Saunders, J. Hu, G. Davidson, C.R. Schmidt, S. Abdel-Mish, M. Bloomston. Division of Surgical Oncology, The Ohio State University, Wexner Medical Center, Columbus, OH.

Introduction Hepatic arterial infusion pumps (HAIP) have been utilized for metastatic colorectal cancer for the past 30 years. Despite data showing safety and efficacy, use of HAIP has not become widespread. We present our initial experience with HAIP as a delivery system for floxuridine (FUDR).

Methods Our experience with HAIPs began in November 2012. From the outset, a well-trained HAIP team was developed and a prospective database created. Pumps were placed by three fellowship trained surgical oncologists. Pump management and FUDR dose adjustments were likewise directed by these three surgeons with daily oversight by a nurse practitioner. Results Forty-one pumps were placed between November 2012 and August 2014: 34 (83%) for chemotherapy, 1 (2.5%) for VEGF, 4 (10%) for both, 2 (5%) for cholangioglioblastoma, and 1 (2.5%) for palliation. The most common primary was small bowel (n=35, 49%), and the most common histology was carcinoid (n=58, 85%). Forty-four patients were treated with Y-90 (61%) and 28 patients received TACE (39%). KI67 score was available in 28 patients (64%) treated with Y-90 and 16 patients (57%) in the TACE group. In the Y-90 group, there was greater use of Sandostatin (94% vs 75%, p=0.02), longer time between diagnosis and treatment (median, 32 vs 11 months, p=0.001), and fewer number of total treatments completed (89% vs 46%, p=0.001). There was no significant difference in overall survival (OS) between Y-90 and TACE (median, 69 vs 82 months, p=0.47). When adjusted for KI67, patients with KI67 score ≥3% had better OS when treated with Y-90 vs. TACE; for KI67 <3%, OS was better when treated with TACE vs. Y-90 (Table 1). On multivariate analysis there was a significant interaction between KI67 ≥3 and Y90 vs TACE (HR 0.083 CI 0.008-0.85) and KI67 <3 and Y90 vs TACE (HR 13.50 (1.22-148.87) (p=0.008)). Conclusions: Although there was no significant different in OS between Y90 vs TACE there is a significant interaction between KI-67 score and treatment benefit. In patients with metastatic NETs, Ki-67 score ≥3% predicts greater benefit with Y-90 and a Ki-67 score <3% greater benefit with TACE. A prospective validation of these findings is warranted.

P200
Ki67 Score can Predict Benefit for Different Transarterial Liver-directed Therapies in Patients with Metastatic Neuroendocrine Tumors

Introduction: Patients with neuroendocrine tumors (NET) metastatic to the liver are candidates for treatment with yttrium-90 radioembolization (Y-90) or transarterial chemoembolization (TACE), however patient selection criteria are not well defined. We sought to determine if the proliferative index (Ki67 score) could be used to select patients for one therapy over another. Methods: Single institution analysis of NET patients treated with liver-directed Y-90 or TACE between 2001-2014. Pathologists blinded to clinical information performed Ki67 staining. Data were analyzed using multivariate analysis. Results: In 72 patients (M: 39; F: 33; median age, 57 years) included in the study, the most common primary was small bowel (n=35, 49%), and the most common histology was carcinoid (n=58, 85%). Forty-four patients were treated with Y-90 (61%) and 28 patients received TACE (39%). KI67 score was available in 28 patients (64%) treated with Y-90 and 16 patients (57%) in the TACE group. In the Y-90 group, there was greater use of Sandostatin (94% vs 75%, p=0.02), longer time between diagnosis and treatment (median, 32 vs 11 months, p=0.001), and fewer number of total treatments completed (89% vs 46%, p=0.001). There was no significant difference in overall survival (OS) between Y-90 and TACE (median, 69 vs 82 months, p=0.47). When adjusted for KI67, patients with KI67 score ≥3% had better OS when treated with Y-90 vs. TACE; for KI67 <3%, OS was better when treated with TACE vs. Y-90 (Table 1). On multivariate analysis there was a significant interaction between KI67 ≥3 and Y90 vs TACE (HR 0.083 CI 0.008-0.85) and KI67 <3 and Y90 vs TACE (HR 13.50 (1.22-148.87) (p=0.008)). Conclusions: Although there was no significant different in OS between Y90 vs TACE there is a significant interaction between Ki-67 score and treatment benefit. In patients with metastatic NETs, Ki-67 score ≥3% predicts greater benefit with Y-90 and a Ki-67 score <3% greater benefit with TACE. A prospective validation of these findings is warranted.
P201
Multimodality Adjuvant Therapy is associated with Improved Overall Survival following Resection for Extrahepatic Cholangiocarcinoma in Patients with Positive Margins or Lymph Node Metastases
S.M. Sharpe,1* C. Wang,2 D. Caba-Molina,3 M.S. Talampini,2 M.S. Baker,2 1. Surgery, University of Chicago, Chicago, IL; 2. NorthShore University HealthSystems, Evanston, IL.

**Background** The role of adjuvant therapy and the value of a margin negative resection for extrahepatic cholangiocarcinoma have not been definitively determined. Our aim was to determine the effects of chemoradiation (CRT) and margin status on overall survival (OS). **Methods** A retrospective review of the National Cancer Data Base was used to identify patients diagnosed with non-metastatic extrahepatic cholangiocarcinoma who underwent surgical resection. Kaplan-Meier estimates with the logrank test and Cox hazard model analyses were used to evaluate the difference in 5-year OS between patients who did and did not receive (CRT) after surgical resection. **Results** 1,632 patients underwent resection for extrahepatic cholangiocarcinoma between 1998 and 2006. 1,083 (66%) had a margin negative resection (R0); 433 (27%) had a margin positive resection (R1/R2). 478 patients (35%) received CRT. By multivariable logistic regression, patients who were younger, had positive nodes, and had positive margins were more likely to receive CRT. The 5-year OS for the entire cohort was 22% with a median follow-up time of 20 months. 395 (24%) patients had an R0 resection, negative nodes, and did not receive CRT. This subgroup had a 5-year OS of 32%, 125 (8%) had an R0 resection, negative nodes, and did receive CRT. This subgroup had a 5-year OS of 35% (p=0.126). Patients who had positive margins, lymph node metastases, or both demonstrated an improved 5-year OS with CRT when compared to those who had like pathology but did not receive CRT (p=0.005). Factors independently associated with decreased OS on Cox hazard modeling were positive lymph nodes and positive margins; CRT was independently associated with improved OS (HR 0.57, 95% CI [0.478, 0.692], p<0.001). **Conclusions** The addition of multimodal adjuvant therapy for extrahepatic cholangiocarcinoma was associated with an overall survival benefit in patients with a margin positive resection and/or lymph node metastases. There was no overall survival benefit with chemoradiation for patients with margin negative resection and negative lymph nodes.

P202
Colorectal Cancer Liver Metastases: Does TACE, Radioembolization Add a Survival Benefit to Resection?
A. Lewis,* P.H. Ituarte, M. White, J. Kessler, G. Singh. General Surgical Oncology, City of Hope, Duarte, CA.

Introduction: The treatment options for patients with stage IV colorectal cancer have increased over the last decade. Few population studies have examined their combined effects on survival. The purpose of this study is to evaluate the survival benefits of multimodal treatment strategies in colorectal cancer with liver metastases. Methods: The California Cancer Registry (CCR) was queried for patients who presented with stage IV colorectal cancer with metastases to the liver from 2005-2011. Patients were excluded if they had not received chemotherapy. Patients who received chemotherapy only were compared to those who underwent hepatic resection, transarterial chemembolization (TACE), and/or radioembolization with Yttrium-90 (RA). Demographics, CEA level, and extrahepatic disease were evaluated with univariate and multivariate analyses. Survival rates were estimated by the Kaplan-Meier method. Cox proportional hazards model was used to assess demographics and clinical factors predictive of overall survival (OS). Results: A total of 8586 stage IV colorectal cancer patients were evaluated, of which 7.9% underwent liver resection alone, 13.4% liver directed therapy alone, and 1.2% a combination of multimodal treatments. Extrahepatic colorectal metastases were present in 1916 patients (22.3%) and approached significance on multivariate analysis (p = 0.069). Age and intervention performed were independent predictors of OS (p = 0.002, see table). Kaplan-Meier curves demonstrate a stepwise improvement in survival with each additional treatment strategy. Conclusion: A multimodal approach to treatment of liver metastases offers a significant survival benefit in patients with recurrent colorectal cancer and should be integrated more frequently.

P203
Major Liver Resections followed by Radioembolization: Is it Safe?
A. Lewis,* P.H. Ituarte, J. Hamner, G. Singh, J. Kessler. General Surgical Oncology, City of Hope, Duarte, CA.

**Objective:** The purpose of this study was to evaluate the safety of hepatic radioembolization (RE) following major liver resection. **Methods:** A retrospective review was performed of consecutive patients who underwent RE using Yttrium 90 resin microspheres after major liver resection at a single center from 2009-2014. Demographic data, prior surgical history, previous liver-directed therapies, treatment related variables, expected and calculated liver volumes, and toxicities were systematically reviewed. Univariate analysis was performed to determine factors associated with toxicity, and linear regression was used to correlate the measured and calculated liver volumes. **Results:** RE after liver resection was performed in 22 patients. The study group was comprised of 13 men (59.1%) with a median age of 63 (IQR = 8). Underlying malignancies included colorectal (n=8), hepatocellular (n=4), neuroendocrine (n=9), and parathyroid (n=1). Prior resections included sublobar (n=11) and lobar hepatectomy or greater (n=11). Eight patients underwent previous thermal ablation and 6 patients underwent previous transarterial therapy. Median follow up was 323 days (range, 68-1526 days) with stabilization of disease or
response in 12 patients (60%). The median total dose was 1.3 Gbq (IQR=0.55). 13 patients were treated in a single session to the liver remnant and 9 were treated in two sessions. Two patients experienced grade 3/4 toxicities (gastric ulcer n=1, AST n=1). Minor toxicities included pain (n=4), nausea (n=2), fatigue (n=4), and liver function abnormalities (n=9). No procedure related mortality occurred. No demographic or treatment related variables correlated with patient toxicity. Body surface area (BSA) calculated liver volume was not highly correlated with measured liver volumes in this population (r = 0.464). Dose calculations based on BSA did not result in increased toxicity in patients with actual liver volume significantly less than expected. **Conclusions:** Y-90 hepatic radioembolization is a safe adjunct treatment in patients who have undergone both minor and major hepatic resections. BSA based dosing is safe in this population, though patient BSA poorly predicts actual liver remnant volume.

**P205**  
A Comparative Analysis of Transarterial Therapy for Unresectable Hepatocellular Carcinoma with Portal Vein Thrombosis: Radioembolization (90Y) versus Doxorubicin Drug Eluting Beads (DEBDOX)  

**Department of Surgery, University of Louisville, Louisville, KY.**

**BACKGROUND:** Portal vein thrombus (PVT) in HCC is a significant adverse prognostic marker. Conventional transarterial chemoembolization (TACE) was previously considered a contraindicated in PVT but is now being used in selected patients. Embolization with DEBDOX (doxorubicin drug eluting beads) or with 90Y(Radioembolization with Yttrium 90 spheres) has a better safety profile and efficacy than conventional transarterial chemoembolization (TACE) but data comparing the two and for its use in PVT is absent.  

**MATERIALS AND METHODS:** Using our prospectively maintained, multi-center, non-controlled intra-arterial therapy registry, 28 patients with HCC + PVT treated with DEBDOX (65 treatments) were compared to 20 with 90Y (29 treatments). **RESULTS:** There was no difference between groups in HCC cause, age, performance status, baseline AFP, Child Pugh status, Okuda class, proportion of parenchyma involved with tumor, lesion location or extent of portal vein thrombosis. DEBDOX group had a fewer patients with innumerable lesions (21.4% vs. 50%, p=0.04) and larger sum of target lesions (10.9, range 3.6-20.6 vs. 8. range 3.8-16.2 cm, p=0.07) but overall percentage of liver involvement was similar (<50% hepatic involvement: Y90: 85% vs. DEBDOX 92.8%, p=0.15). Adverse effects in the DEBDOX group were lower compared to the 90Y group (11% vs 39%; p=0.03). High-grade adverse effects were similar between groups (5% vs. 7%, p=0.64). There was better disease control per mRECIST in the DEBDOX group compared to the 90Y group (67% vs. 20%; p=0.002). Median survival times were 10 months in DEBDOX and 3 months in the 90Y group respectively (log-rank, p=0.037). **CONCLUSION:** DEBDOX is safe for patients with HCC and PVT and appears to have lower toxicity than 90Y. It may also provide better disease control and survival benefit.

**P206**  
Outcomes of Liver-directed Therapy for Metastatic Carcinoid Tumors  

**J. Hamner, P.H. Ituarte, M. White, G. Singh. Surgery, City of Hope National Medical Center, Duarte, CA.**

**Background:** Patients with liver metastases from carcinoid tumors can have a variable and often indolent disease course. That said, these tumors will often lead to the death of the patient secondary to the effects of tumor burden within the liver and the sequelae of carcinoid syndrome. In this study, we evaluate the effects of liver directed therapy on disease-specific survival in patients with liver metastases from carcinoid tumors.  

**Methods:** The California Cancer Registry was queried for patients with liver metastases from carcinoid tumor. Patients were subdivided into six groups: those who received 1) no liver directed therapy, 2) surgical resection only, 3) trans-arterial chemoembolization (TACE) only, 4) radioembolization (RE) only, 5) surgical resection plus TACE, or 6) surgical resection plus RE. Kaplan-Meier curves were applied to estimate 10 year disease-specific survival. **Results:** 4,566 patients were identified with liver metastases from a primary carcinoid tumor, and 4,277 patients with complete clinical information included in the analysis. A slight majority of cases were male (51.4%), 183 (4%) were less than 40 years of age, 2,066 (44%) were between 40 and 65 years, and 2,363 (52%) were over 65. The 10 year median disease-specific survival was 66 months for those treated with TACE only, 80 months for those who received no liver directed therapy and 111 months for those who received liver resection plus TACE. The 10 year median survival has not yet been reached for the other groups. When compared directly, surgery plus RE had a trend toward better disease specific survival than surgery plus TACE, though statistical significance was not reached. **Conclusions:** While patients with liver metastases from carcinoid tumors often have an indolent disease course, liver directed therapy may help improve disease-specific survival. Surgical treatment, when completely resectable, remains the best treatment, although many patients will not have disease that is amenable to complete resection. In these cases, resection with
the addition of RE appears to be more effective in improving disease-specific survival than other forms of liver directed therapy alone or in combination.

**P207**


**Background:** Transarterial chemoembolization (TACE) has been shown to be an effective treatment strategy for patients with liver-dominant metastases from neuroendocrine tumors. Few studies have investigated the role of doxorubicin loaded beads for the treatment of NET. **Methods:** Patients with neuroendocrine liver metastasis treated with TACE using DEBDOX at a single institution from 2008 to 2014 were identified from a hospital registry. All patients had a pathologic diagnosis of neuroendocrine cancer, and treated with transcatheter LC bead doxorubicin (50-100 mg). **Results:** Twenty-seven pts with liver metastasis from neuroendocrine tumors underwent 103 sessions of TACE with DEBDOX. The median age was 64 (M:F 11:16). Fifty-six percent of pts had a primary tumor in the pancreas, 33% had a primary small bowel tumor, and 11% were unknown. Of these, 17 primary tumors (63%) were resected. Twenty-five pts were found to have synchronous disease, and all but one patient had bilobar liver involvement. Extraperitoneal disease was found in 10 pts, with bone and peritoneum being the most common sites of metastasis. **Results:** The median number of TACE treatments was 3 (range 1-9). After treatment with first TACE, 24 pts had evaluable response. Four (15%) pts had stable disease, 14 (52%) pts had a partial response, and 1 (4%) patient had a complete response. Five (19%) pts were found to have progressive disease. Post-TACE morbidity was 63%, including serotonin release syndrome (n=3), postembolization syndrome (n=2), and hepatic abscesses (n=2). Thirty-day mortality was 3.7% (n=1) secondary to sudden cardiac arrest. Overall survival at 1 year was 77.4%, and at 3 years was 66.4% (median survival 49.5 months). Progression free survival at 1 year was 61.8%; at 3 years was 42.1% (median time to progression 36.1 months). **Conclusion:** Treatment of neuroendocrine liver metastases with transcatheter doxorubicin-eluting beads is a safe and effective procedure. Repeated TACE upon intra-hepatic disease progression results in similar response to initial therapy and should be considered first-line therapy for unresectable hepatic metastases from NET.

**P208**

**Delayed Gastric Emptying following Classic and Pylorus Preserving Pancreaticoduodenectomy: A Meta-analysis and Systematic Review** K. Mahendraraj,*, R. Chamberlain, Surgery, St Barnabas Medical Center, West Orange, NJ.

**Introduction:** Pylorus preserving pancreaticoduodenectomy (PPPD) has replaced the ‘classic’ pancreaticoduodenectomy (CP) as the treatment of choice for the management of pancreatic head and periampullary cancers in many HPB centers based on the belief that PPPD has better postoperative outcomes. However, delayed gastric emptying (DGE) remains a common complication of both procedures. The meta-analysis critically examines the reported incidence of DGE following either PPPD or CP among all published randomized controlled trials (RCTs) involving patients with pancreatic or periampullary malignancies. **Methods:** Cochrane, MEDLINE, and Embase databases were searched systematically for relevant articles using the keywords ‘delayed gastric emptying’, ‘pancreaticoduodenectomy’ and ‘randomized controlled trial (RCT)’. Citations of relevant review articles were examined. Data on patient recruitment, intervention and complications were extracted from the included trials and analyzed. DGE was defined as ‘gastric stasis requiring nasogastric tube (NGT) for ≥ 10 days’ or ‘persistent NGT drainage of more than 500cc for at least 5 postoperative days with or without vomiting’. The risk ratio (RR) was calculated with 95% confidence intervals. **Results:** 6 RCTs involving 434 patients were identified. 218 patients (50.2%) were randomized to PPPD while 216 patients (49.8%) had CP. Overall morbidity was 18%lower in the PPPD group (RR 0.82, 95% CI 0.59-1.18; p=0.68) and overall mortality was 51% lower in the PPPD (RR 0.49, 95% CI 0.17-1.40; p=0.18). Postoperative DGE was 31.3% higher in the PPPD group (RR 1.31, 95% CI 0.62-2.80; p=0.48). **Conclusion:** The incidence of DGE is independent of the pancreaticoduodenectomy operative technique used...Whether the incidence of DGE can be improved upon with modified PPPDor CP using antecolic duodenojejunostomy or antecolic Roux limbs is currently unknown and requires larger, adequately powered randomized trials with low risk of bias to fully assess.
Validation of a Nomogram to Predict Sentinel Lymph Node Metastases in Melanoma in Israeli Population

H. Moshe,* A. Gat, E. Even-Sapir, Y. Skornick, J.M. Klausner, S. Schneebaum, D. Division of Surgery, Tel-Aviv Sourasky Medical Center, Sackler School of Medicine, Tel-Aviv, Israel; 2. Radioguided Surgery Unit Division of Surgery Tel-Aviv Sourasky Medical Center, Sackler School of Medicine, Tel-Aviv, Israel; 3. Department of Pathology Tel-Aviv Sourasky Medical Center Sackler School of Medicine, Tel-Aviv, Israel; 4. Department of Nuclear Medicine Tel-Aviv Sourasky Medical Center Sackler School of Medicine, Tel-Aviv, Israel.

Background: Lymph node involvement in melanoma is an important staging and a crucial prognostic factor. Nevertheless, while indications for sentinel lymph node biopsy remain arbitrary, it is likely that many patients could have avoided this procedure, and its possible complications. A nomogram developed at the Memorial Sloan-Kettering Cancer Center (MSKCC) offers an estimation of metastatic lymph node involvement in melanoma patients, by using clinical and pathologic parameters. Given the nomogram was developed at a single center in North America, applying it as a standard tool for surgeons worldwide is limited until widely validated. The aim of this study is to validate the nomogram in the population of Israeli melanoma patients, and examine its potential in managing these patients.

Methods: Data was collected from a prospective database containing the records of 977 patients with melanoma who underwent radio-guided sentinel lymph node excision between the years 1994-2011, in our medical center. Records of 413 patients (filed between 2003 and 2011) had extended pathological evaluation of their primary lesion, as the nomogram requires. The SLN was positive in 27 of these patients (6.5%). Five parameters were drawn: patients age, location of the primary lesion, Breslow thickness, Clark level and the presence of ulceration. The nomogram score was received using the MSKCC website online nomogram. An ROC curve was then drawn and the area under the curve was measured. Using the ROC curve we established the cut off score for which the specificity and sensitivity was maximal. A nomogram score equal or higher than the cut off score was determined as predictive to SLN involvement.

Results: The area under the ROC curve, representing the nomograms discriminative ability, was found to be 0.78, indicating a good predictive ability. We found the cut off score for which the nomogram is highly predictive to be 0.12, with a sensitivity of 0.77. Conclusions: Despite the differences in the research populations, we find the MSKCC nomogram to be a good predictive tool for SLN involvement and of potential meaningful assistance in determining the treatment plan in melanoma patients.

Multivariate Analysis of Factors Impacting Overall Survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age: &lt;40 years</td>
<td>1.64</td>
<td>(1.38, 1.94)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age: 40-49 years</td>
<td>1.87</td>
<td>(1.59, 2.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age: 50-59 years</td>
<td>1.36</td>
<td>(1.26, 2.60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age: 60-69 years</td>
<td>1.36</td>
<td>(2.31, 4.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age: &gt;70 years</td>
<td>7.65</td>
<td>(6.89, 9.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gender: Female</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Gender: Male</td>
<td>1.39</td>
<td>(1.28, 1.51)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subtype: Superficial spreading</td>
<td>Reference</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Subtype: Nodular</td>
<td>1.15</td>
<td>(1.08, 1.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Subtype: Lentigo maligna</td>
<td>0.96</td>
<td>(0.79, 1.17)</td>
<td>0.7126</td>
</tr>
<tr>
<td>Subtype: Acral lentiginous</td>
<td>0.85</td>
<td>(0.69, 1.04)</td>
<td>0.1190</td>
</tr>
<tr>
<td>Subtype: Desmoplastic</td>
<td>0.86</td>
<td>(0.8, 1.11)</td>
<td>0.6573</td>
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<tr>
<td>Primary Site: Head/Neck</td>
<td>1.42</td>
<td>(1.8, 1.7)</td>
<td>0.0007</td>
</tr>
<tr>
<td>Primary Site: Upper limb</td>
<td>0.82</td>
<td>(0.74, 0.95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Primary Site: Lower limb</td>
<td>0.63</td>
<td>(0.56, 0.71)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depth: 0-2.0mm</td>
<td>1.16</td>
<td>(0.99, 1.22)</td>
<td>0.0864</td>
</tr>
<tr>
<td>Depth: &gt;2.0-4.0mm</td>
<td>1.42</td>
<td>(1.28, 1.59)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ulceration</td>
<td>1.40</td>
<td>(1.57, 1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clark Level 1-2</td>
<td>3.80</td>
<td>(2.65, 3.39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clark Level 3-4</td>
<td>2.33</td>
<td>(4.32, 2.68)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clark Level 3-4</td>
<td>1.17</td>
<td>(1.17, 1.43)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

References:

Background: Nodal status, depth and ulceration are regarded as the most significant prognostic factors in cutaneous melanoma. The role of histologic subtype as a prognostic factor is unclear. This study was conducted to assess outcomes in melanoma based on histologic subtype. Methods: A review of the National Cancer Database was performed for patients diagnosed with cutaneous superficial spreading (SS), nodular (NM), lentigo maligna (LM), desmoplastic (DM), spindle cell (SM) and acral lentiginous (AL) melanoma between 2004-2006. Patients with unknown or unspecified variables were excluded. Univariate analysis (UVA) of demographic and clinicopathologic factors by subtype and multivariate analysis (MVA) of factors associated with overall survival (OS) were performed. Kaplan-Meier (KM) analysis was performed. SS subtype was used as the reference. Results: Of the 13,490 patients with cutaneous melanoma, the distribution of subtypes was as follows: 58% SS, 27.5% NM, 3.9% LM, 3.8% SM, 3.5% AL and 3.3% DM. Fifty-eight percent of patients were male. American Joint Committee on Cancer Stage distribution was 54.8%, 26.4%, 18% and 0.8% for Stages I-IV, respectively. Clark’s level was stage 4 in 68.6% of patients. The most common primary sites were the trunk (33.1%) and upper limb (26.1%). Stage at presentation varied significantly by each subtype (p<0.0001). SS, LM and AL presented most often as Stage 1; DM, NM and SM presented most often as Stage 2. Results of the MVA are shown in Table 1. Primary site of head/neck was worse than other sites. The most significant factors affecting OS were age, nodal status, ulceration and presence of metastases; hazard ratios and p values are in Table 1. Histology affected survival with NM and AL having worse survival compared with SS. Other subtypes, DM, LM and SM, had similar survival to SS. The effect of age was unclear as survival data was not melanoma specific. Conclusion: Although NM and AL subtypes were risk factors for poor survival, their impact was less than ulceration, nodal status and presence of metastases. The data supports treatment based on AJCC stage, regardless of subtype. DM and LM have comparable OS with SS and should be treated similarly.
P212
The Long-term Risk of Upper Extremity Lymphedema is Two-fold Higher in Breast Cancer Compared to Melanoma Patients
R.K. Voss,1,4 K.D. Cromwell,1 Y. Chiang,1 J.J. Armer,2 M.I. Ross,1 J.E. Lee,3 J. Gershenwald,1 R.E. Royal,1 A. Lucci,1 B.R. Stewart,1 J.N. Cormier,1 1. The University of Texas MD Anderson Cancer Center, Houston, TX; 2. University of Missouri, Sinclair School of Nursing, Columbia, MO.

INTRODUCTION: The objective of this analysis was to compare the cumulative incidence of upper extremity lymphedema in breast cancer (BC) and melanoma patients undergoing sentinel lymph node biopsy (SLNB) or axillary lymph node dissection (ALND). Lymphedema, defined as limb volume change (LVC) ≥10%, was compared over time, as were patient-reported symptoms. METHODS: Patients were recruited from two institutions prior to surgical intervention and assessed at 6, 12 and 18 months. Objective limb volume measurements were obtained using a perometer, and symptoms were assessed using a 19-item validated instrument. Longitudinal logistic regression analyses were conducted to identify risk factors associated with LVC≥10%. Symptom scores were correlated with LVC. RESULTS: 205 BC and 144 melanoma patients were included. Except for gender (99.5% vs 42% women in BC vs melanoma), median number of lymph nodes (LN) removed for ALND (14 vs 29 for BC vs melanoma), and radiation therapy (62% vs 15% in BC vs melanoma), demographic and surgical treatment data were similar. At 6 months, 24% of BC and 17% of melanoma patients had LVC≥10% (Table 1). At 12-18 months, the overall cumulative incidence of LVC≥10% remained similar in both groups with the highest incidence observed in melanoma patients undergoing ALND (50%). However in adjusted analyses, breast cancer (OR 2.0, p=0.03), BMI ≥30 kg/m² (OR 1.7, p=0.04), and increasing number of LN removed (OR 1.1, p<0.01) were associated with LVC≥10%. Lymphedema was more likely to occur over time (OR 2.3, p<0.01), and LVC≥10% patients were twice as likely to report an increase in symptoms (OR 1.9, p<0.01). CONCLUSIONS: The incidence of lymphedema increases over time in both BC and melanoma patients. Melanoma patients undergoing ALND were found to have the highest cumulative incidence of lymphedema at 18 months which may be related to more extensive nodal surgery. However, the overall risk of lymphedema is two-fold higher in BC for every LN removed. These results may be attributed to treatment of the primary tumor in the breast and higher use of radiation. Long-term lymphedema surveillance is warranted in both populations.

P214
Increased Visceral to Subcutaneous Fat Ratio is associated with Decreased Overall Survival in Patients with Metastatic Melanoma Receiving Antiangiogenic Therapy
Y. Grignol,1,4 A.D. Smith,2 D. Shlapak,2 X. Zhang,2 S. Martin Del Campo,1 W.E. Carson,1 J.M. Armer,2 A.D. Smith,2 1. Ohio State University, Hilliard, OH; 2. University of Mississippi, Jackson, MS.

Introduction: Body fat distribution is emerging as a prognostic indicator in patients treated with anti-angiogenic (AA) therapy. In patients with metastatic colorectal and renal cell carcinoma treated with AA therapy those with increased visceral fat had decreased overall survival (OS). We sought to evaluate the association of visceral and subcutaneous fat measurements with OS in patients with metastatic melanoma treated with bevacizumab + interferon (IFN). Methods: Patients with stage IV melanoma received bevacizumab ± IFN on a phase II clinical trial. Total abdominal fat, visceral fat area (VFA) and subcutaneous fat area (SFA) were measured at L3-L4 on CT images (cm²). Cox proportional hazards model was used to assess the association of VFA, SFA, VFA/SFA ratio, and baseline clinical variables with OS. The receiver operating characteristic curve with area under the curve (AUC) was used to evaluate accuracy. Results: Forty-two of 44 patients had adequate CT scans for evaluation of VFA and SFA. There were 27 males and 14 females, mean age was 58.5 yr, body mass index (BMI) was 26.7 and LDH was 215.1 (range 71608U/L). The mean VFA at L3-L4 was 188cm²±104cm² and SFA was 206cm²±104cm². The mean ratio of VFA to SFA (VFA/SFA) was 1.01±0.54.

In a univariate analysis VFA/SFA (HR 1.38, 95% CI 1.04-1.82, p=0.023), LDH (HR 1.37, 95% CI 1.07-1.75, p=0.013) and liver metastasis (HR 3.25, 95% CI 1.51-6.98, p=0.003) significantly correlated with OS, BMI did not (p=0.532). These three variables continued to be significant predictors of OS on multivariate analysis [(VFA/SFA HR 1.60 95% CI 1.17-2.18, p=0.003) (LDH HR 1.40 95% CI 1.05-1.85 p=0.022) (liver metastasis HR 3.16, 95% CI 1.42-7.02, p=0.005)]. A prognostic score combining VFA/SFA, LDH, and presence or absence of liver metastasis had a higher accuracy for predicting OS at 24mo (AUC 0.846) than LDH alone (AUC 0.733), however this was not significant (p=0.181). Conclusion: Increased VFA to SFA ratio is associated with decreased OS in patients with metastatic melanoma treated with AA therapy, indicating that body fat distribution is an important prognostic factor.

Table 1: The cumulative lymphedema incidence at 6, 12, and 18 months

<table>
<thead>
<tr>
<th>Cumulative Incidence of Lymphedema</th>
<th>Breast Cohort</th>
<th>Melanoma Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Log Rank</td>
<td>N</td>
<td>No</td>
</tr>
<tr>
<td>at 6 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>45</td>
<td>174 (38.0)</td>
</tr>
<tr>
<td>SLNB</td>
<td>33</td>
<td>193 (22.6)</td>
</tr>
<tr>
<td>ALND</td>
<td>22</td>
<td>181 (24.7)</td>
</tr>
<tr>
<td>at 12 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>50</td>
<td>185 (51.7)</td>
</tr>
<tr>
<td>SLNB</td>
<td>30</td>
<td>168 (51.8)</td>
</tr>
<tr>
<td>ALND</td>
<td>20</td>
<td>117 (24.3)</td>
</tr>
<tr>
<td>at 18 months</td>
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<td></td>
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<tr>
<td>Overall</td>
<td>60</td>
<td>206 (55.5)</td>
</tr>
<tr>
<td>SLNB</td>
<td>30</td>
<td>168 (51.8)</td>
</tr>
<tr>
<td>ALND</td>
<td>30</td>
<td>138 (28.4)</td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
<td>548 (57.7)</td>
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</table>
Management of Melanoma in the Elderly: The Impact of Increasing Age

Division of Surgical Oncology, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia.

Introduction: Evidence suggests elderly patients experience a different spectrum of disease and may have a poorer outcome than younger patients. This study investigated age-related variations in the management and outcome of elderly patients with melanoma. Methods: A retrospective review of all patients aged 65 years and over (481 patients with 525 primary melanomas) presenting with AJCC clinical stage I or II melanoma to an Australian tertiary hospital between 2000-2008. Result: The median age was 74 years (65-94) with a male predominance (313 males, 65.0%) and median tumour thickness of 1.90 mm (T1=32.7%, T2=19.8%, T3=24.2%, T4=23.2%). There was a significant correlation between age and Breslow thickness (BT, p<0.001). With increasing age the proportion of ulcerated melanomas (p=0.001, OR=1.05, 95%CI=1.02-1.08), melanomas affecting the head and neck (p<0.001, OR=1.07, 95%CI=1.04-1.10) and lentigo maligna melanoma (p=0.0013, OR=1.06, 95%CI=1.02-1.10) increased. Optimal surgical margins were less commonly performed in older patients independent of site, BT and ulceration (p=0.037, OR=0.96, 95%CI=0.93-0.99). Sentinel node biopsy (SNB) was less likely to be performed in elderly patients with primary melanomas ≤1.00 mm (p<0.001, OR=0.88, 95%CI=0.84-0.91). Sub-optimal surgical margins were strongly associated with time to local recurrence, independent of site, age, BT, ulceration or the mitotic rate (p=0.00089, OR=3.21, 95%CI=1.59-5.91), but not time to progression (p=0.069) or disease specific survival (DSS, p=0.55). Failure to perform SNB for melanomas ≤1.00 mm was a negative prognostic factor for DSS (p=0.0089, HR=1.65, 95%CI=1.05-2.19) on univariate but not multivariate analysis (p=0.18). Age was not a significant predictor of DSS (p=0.51) or time to progression (p=0.83) on multivariate analysis. Conclusion: With increasing age elderly patients are less likely to undergo optimal margins of excision resulting in higher rates of local recurrence. Failure to achieve optimal excision margins and the lower rates of SNB associated with increasing age are not associated with higher rates of regional recurrence or poorer DSS, possibly as a result of the competing effects of other age related causes of mortality.

Anti-tumor Immunity and Improved Survival with Combination of Immune Checkpoint Blockade and Local Chemotherapy J. Green,* A. Rudensky, C.E. Ariyan. Memorial Sloan Kettering Cancer Center, New York, NY, USA.

Introduction: Immunotherapy has changed the landscape of melanoma treatment; however, response rates are low and advanced melanoma has a poor prognosis. Ipilimumab (α-CTLA-4) was the first drug ever shown to improve survival, with a 10.9% response rate. Keytruda (α-PD-1) has a 34% response rate in early studies. We previously showed improved survival with melphalan + α-CTLA-4, which is the source for a clinical trial combining melphalan limb infusion with α-CTLA-4. Here we look at the addition of α-PD-1 in a model of local chemotherapy with the goal of further enhancing anti-tumor responses. Methods: Mice were injected subcutaneously with 10^6 B16OVA mouse melanoma cells, and treated after tumor development with (1) control: rat Ig + intratumor (IT) PBS, (2) IT melphalan, (3) α-CTLA4, (4) α-PD1, (5) α-CTLA-4 + IT melphalan, (6) α-PD1 + IT melphalan, or (7) α-CTLA-4 + α-PD1 + IT melphalan. Tumors were measured 3x week. Flow cytometry was used to evaluate the immune phenotype after treatment. Results: Treatment with IT melphalan increased median survival from 16 to 21 days (p<0.01). While neither α-CTLA-4 nor α-PD1 treatment alone prolonged survival over IT melphalan, combining α-CTLA-4 + melphalan or α-PD1 + melphalan improved survival over melphalan alone (p<0.02). Triple therapy (α-CTLA-4 + α-PD1 + melphalan) was synergistic and had the greatest survival benefit (median survival not reached) and significantly decreased tumor growth when compared to single therapies (p<0.05). The tumors isolated from mice treated with triple therapy also had significantly higher number of tumor-specific CD8+ T-cells, elevated CD8/Foxp3 ratios, and produced more IFN-γ in response to OVA peptide stimulation than any other treatment (p<0.05). Conclusions: These mouse studies reveal promising results for the potential of improving response rates and survival in malignant melanoma with the combination of local chemotherapy + α-CTLA-4 + α-PD1. This treatment combination induces an increase in cytotoxic T-cells in the tumor and a decrease in inhibitory regulatory T-cells, which are likely responsible for the observed decreased tumor growth and improved survival.

In vivo Tracking of Site-directed, Heat-inducible Nanodelivery Vectors: Implications for Cancer Immunotherapy C. Loo,* I.M. Meraz,* M. Wang,³ R. Serda,³ H.Y. Wang,³ M.A. Ferrari,³ R. Wang,³ 1. Surgery, University of Hawaii, Honolulu, HI; 2. Baylor College of Medicine, Houston, TX; 3. The Houston Methodist Research Institute, Houston, TX.

Introduction: Dendritic cells (DC) initiate immune responses by antigen presentation, migration, and T-cell activation. Nanoparticle-based vectors aim to concentrate and deliver antigens/adjuvant to DC. We investigate the feasibility of localized expression of tumor antigens and immunostimulatory molecules using NIR-absorbing gold nanoparticles (AuNP) co-loaded with a plasmid containing a HSP70-GFP promoter into porous silicon (pSi). We then demonstrate a novel nanoparticle/dendritic cell-based approach to cancer immunotherapy in a B16 melanoma pulmonary metastasis model using Tpr2-loaded pSi. Methods: NIR-absorbing AuNP were chosen for this study due to their ability to heat upon NIR absorption and drive downstream expression of GFP. AuNP and HSP70-GFP plasmid were co-loaded into APTES-modified discoidal, 1 µm pSi particles. J774 macrophages were treated with a NIR laser. GFP expression was assessed via live staining, FACS, and fluorescence microscopy. We investigated whether Tpr2-loaded pSi would enhance anti-tumor immunity via similar mechanisms based on Tpr2-cell-penetrating peptides (CPP’s) showing enhanced anti-tumor immunity against B16 pulmonary metastases. C57/B16 mice were inoculated with B16 melanoma cells and received tail vein injections with DC’s loaded with MSV, Tpr2, or Tpr2+MSV. DC/MSV/Tpr2 alone were used a negative controls. Lungs were harvested on Day 20 to assess anti-tumor efficacy. Results: An optimal dose of 60 Jx5-pulses was determined to be optimal for GFP expression with minimal cytotoxicity. No GFP was measured in negative controls. 20 days after B16 inoculation, decreased metastasis was observed in mice treated with DC’s loaded with MSV+Tpr2, an effect not observed in control groups. Discussion: We demonstrate a novel opportunity for site-directed, heat-inducible expression of tumor antigens + immunostimulatory cytokines in DC’s based on the HSP70-GFP plasmid was shown to be effective in a mouse model of local chemotherapy with the goal of further enhancing anti-tumor responses.

The Impact of Sun-avoidance Advice and Vitamin D Levels at a Tertiary Referral Melanoma Service M. Lo, J. Maraka, J. Garioch, G. John, M. Moncrieff,* Department of Plastic & Reconstructive Surgery, Norfolk & Norwich University Hospital, Norwich, United Kingdom.

Introduction & Aims Patients with malignant melanoma are advised to avoid sun exposure to reduce further melanoma risk. This, however, can render patients vitamin D deficient with long-term health consequences, particularly in centres located at higher latitudes, such as ours (52.6 deg north), where the UV index is <3 for 5-6 months of the year. We audited all melanoma patients undergoing vitamin D testing over a 1 year period to determine the effects of sun avoidance advice. Material & Methods A total of 507 melanoma patients who had undergone vitamin D testing from May 2013 to April 2014 at the time of diagnosis or at routine follow-up were reviewed. Patient demographics, histological characteristics and vitamin D levels were analysed. Results A total of 102 patients underwent vitamin D testing a primary diagnosis, 189 at
routine follow-up and 16 at recurrence. Median age was 66 years (21-90 years) and there was equal male to female distribution (153:154). Normal range of vitamin D level was 50-120 nmol/L. Analysis showed the overall incidence of de novo vitamin D deficiency at 46%, compared to 55% of patients being vitamin D deficient at more than 24 months post-primary diagnosis; this is statistically significant (p=0.017). Vitamin D deficiency was associated with higher mitotic index (median 4 per mm² vs median 1 per mm²) and ulcerated primaries (p=0.012 & p=0.06 respectively). Age was also found to be a significantly associated vitamin D deficiency both in the primary and routine follow-up group; patients aged ≥65 years were more likely to be vitamin D deficient (p<0.000, P=0.001). There was no seasonal association with vitamin D deficiency. Conclusion: Vitamin D deficiency has long-term implications not only to bone health but there is also increasing evidence showing association with other diseases. Moreover, sub-optimal vitamin D levels are linked to poorer survival following melanoma. Our study has shown that advising melanoma patients to avoid sunlight attributes to vitamin D deficiency and therefore it is imperative that we continue to monitor vitamin D levels and provide supplementation as required.

P219  
Suppression of CXCL10 Affects Migration, Invasion and Apoptosis in Oligo- and Polymetastatic Tumor Clones  
S.C. Wightman,1,1,1 S. D. Messenger,1 J. Oskvarek,2 S. S. Muller,1 S. S. Posner,1 H. Alabbas,1 S. B. Wightman,1,1  
Introduction: Oligometastasis is a state of limited metastasis with the potential for long-term disease free control by surgery or ablative therapy. We designed syngeneic mouse melanoma models that express oligo- and polymetastatic pulmonary metastasis. We found CXCL10 elevated in polymeta- 
static tumor clones both in vivo and in vitro. Lentiviral knockdowns (KD) of CXCL10 in oligo- (P2M5B) and polymeta- 
static (P2M3C) tumor clones had significantly decreased pulmonary metastases in the KDs. We looked at the 
migration, invasion, and apoptotic properties of CXCL10 in vitro to characterize the mechanisms of the CXCL10/CXCR3 axis.

Methods: Migration and invasion assays were performed on the poly- and oligo- KDs and compared to non-targeting controls (NTCs). The assays were run in transwell inserts with permeable membranes. Apoptosis was induced with Staurosporine and measured by Caspase-Glo 3/7 Assay. Results: Cellular migration of 10.6±4.9 for P2M3C KD #1 and 8.0±4.4 for P2M3C KD #2 were decreased when compared to 45.9±23.9 for the P2M3C-NTC (both p<0.001). The P2M3C KD #1 and #2 decreased to 7.6±4.1 and 7.7± 3.2 respectively, when compared to 15.2±4.2 for P2M3C-NTC (both p<0.01). P2M3C demonstrated no difference between NTC and KDs. At 500nM Staurosporine, luminescence (i.e. apoptosis) increased for P2M3C KD #1 and KD #2 by 65.0±35.4 and 66.0±20.8 respectively when compared to P2M3C-NTC of 4.3±12.3 (both p=0.01). A significant decrease of 1000nM luminescence increased for P2M3C KD #1 and KD #2 by 121.7±73.5 and 97.7±25.6 respectively when compared to P2M3C-NTC of 42.7±22.2 (both p=0.05). Of the P2M3C KDs, only KD #2 had an increase at 500nM and 1000nM (both p=0.03). Conclusions: Our experiments highlight the importance of CXCL10 in migration, invasion, and inhibition of apoptosis for the polymetastatic tumor clone. P2M3C KDs decreased invasive and migratory properties while the P2M5B KDs exhibited no change. CXCL10 in the NTCs protected the cell against apoptosis. P2M3C exhibits a greater dependence on CXCL10 and our experiments stress the vital role of the CXCL10/ 
CXCR3 axis in metastasis invasation into the organ tissue and the resistance of cell death.

P220  
Adverse Events following Lymph Node Dissection for Cutaneous Melanoma  
M.C. Posner,1 H. Alabbas,1,1,1 I. Oskvarek,2 H. Posner,3 C. Wightman,1,1 H. Stoeber,3 J. Oskvarek,2  
Purpose: Despite the survival benefits of lymph node dissection (LND) in cutaneous melanoma (CM), the incidence of adverse events (AE) related to the procedure is not well known. The purpose of this study is to quantify the incidence of AEs associated with LNDs in CM based on the collective experience reported in the literature. Methods: A systematic literature search was performed, identifying all English language studies published until December 2012 to review the incidence of AEs following LND in CM. The methodological quality of the studies was assessed using a modified STROBE checklist.

Results: 86 studies were reviewed, identifying all English language studies published until December 2012. The pooled AE incidence was 10.2% and 33%, respectively. The pooled rates of acute lymphatic complications for cervical, axillary and groin LNDs were 1.9%, 23%, 25.3%, respectively. The incidence of acute lymphedema for axillary and groin LNDs was 10.2% and 33%, respectively. Mild lymphedema was observed in a range of 0-53%, moderate: 0-40% and severe: 0-19%. Intra-operative and systemic complications were uncommon and/or underreported. Conclusions: Morbidity after LND in CM patients remains considerably high, particularly in groin dissections. This study provides the collective knowledge of AEs related to this procedure and proposes a standardized classification system for the use in future publications.

Adverse events following lymph node dissection for cutaneous melanoma

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<th>No. procedures</th>
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<th>Pooled rate (%)</th>
<th>95% CI</th>
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<th>I²</th>
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<th>No. procedures</th>
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<td>3.1-6.6</td>
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CI, confidence intervals
**P224**

**Patient Outcome and Detailed Pathologic Examination of Negative Completion Lymph Node Dissection Specimens in Melanoma Patients with Minimal (<0.1mm) Sentinel Node Metastases**

L.H. Holtkamp,1,* S. Wang,2 J.S. Wilmott,3 J. Madore,2 R. Vilain,2 J.F. Thompson,1 O.E. Nieweg,1 R.A. Scolyer.1 1. Melanoma Institute Australia, Sydney, NSW, Australia; 2. Department of Tissue Pathology and Diagnostic Oncology, Royal Prince Alfred Hospital, Sydney, NSW, Australia.

Background

Based on studies showing that non-sentinel nodes (NSNs) are rarely involved in patients with minimal melanoma metastases in sentinel nodes (SNs), it has been suggested that such cases do not require completion lymph node dissection (CLND). However, pathologic examination of each NSN in the CLND specimens in these studies did not include examination of more than one hematoxylin and eosin (H&E)-stained section or immunohistochemical staining, which may have led to failure to identify additional positive nodes. The present study sought to more reliably determine the tumor status of NSNs in patients with a minimally-involved SN and their clinical outcome.

Methods

All 21 tumor-negative CLND specimens – originally evaluated with a single H&E stained section per bivalved NSN – from 20 patients with a SN metastasis <0.1 mm in diameter treated at our institution between 1991 and 2013 were re-examined with a more detailed pathologic protocol. Five consecutive 4-μm-thick sections were cut from the original paraffin block of each node. The first and last sections were stained with H&E and the second, third and fourth sections were stained immunohistochemically for S-100, HMB45 and MelANa, respectively. Results

A total of 343 NSNs were examined and only one was found to harbor a metastasis. This subcapsular sinus NSN metastasis had a maximum diameter of 0.18 mm. The patient has had no recurrence after 130 months. For the entire patient cohort, the median follow up was 48 months. Six patients (30%) developed a recurrence. Five patients (25%) died of melanoma. Estimated five-year melanoma-specific survival was 64%.

Conclusions Melanoma patients with minimal-volume NSN metastases have a low risk of having additional NSN metastases in CLND specimens and a good prognosis. However, even these patients may occasionally harbor additional NSN metastases not identified utilizing routine pathologic examination protocols. Therefore, until any potential survival benefit from CLND and the associated morbidity have been adequately studied in these patients, nodal clearance appears to remain the safest option.

**P225**

**A High Rate of TP53 Mutation Identified in Patients with Advanced Melanoma using Next Generation Sequencing**


Introduction

Much of the genetic characterization of melanoma has focused on BRAF and NRAS. The incidence of other mutations is less well characterized, and mutations in TP53 in particular have been variably identified. Methods Genomic DNA was isolated from a clinically selected cohort of patients with advanced cutaneous melanoma. Mutations in a panel of 47 prototypic cancer genes were identified via next generation sequencing. Identified mutations were described and compared with clinicopathologic characteristics using chi-square or Wilcoxon rank-sum as appropriate. Results The median age of the 108 analyzed patients was 62 (IQR=54-71), and the majority were male (68%). 5% of patients had stage II disease, 36% had stage III, and 59% had stage IV at the time of DNA sampling. One patient had no identifiable mutations, 47% of patients had a single mutation, and 52% of patients had multiple mutations (maximum of 10). The majority of patients (86%) were found to have mutations in the BRAF, NRAS, or TP53 genes. The distribution of the mutations by BRAF status is shown in Figure 1. Mutations in multiple genes were found with similar frequency in BRAF wildtype (53%) compared to BRAF mutant patients (50%) (p=0.76). Only NRAS mutations were found to be significantly more common among BRAF WT compared to BRAF mutant patients (59% vs. 5%, respectively, p<0.001). There was a trend toward more ERBB4 mutations in BRAF mutants (19% vs. 8%, p=0.07), and toward more TP53 mutations in BRAF WT patients (35% vs 19%, p=0.08). 15% of TP53 mutations were stop mutations, and 88% of other mutations occurred in the DNA binding domain. Increasing age was associated with
an increased incidence of multiple gene mutations (p=0.048). No association was found between specific gene mutation and age, gender, site of biopsy, or sites of metastatic disease spread. Conclusion: Sequencing of a mutation panel in patients with melanoma provides insight into the highly heterogeneous nature of the malignancy. Although BRAF and NRAS mutations are the most common, multiple other mutations, particularly TP53, occur frequently and merit further study.

Figure 1: Mutational Profile by BRAF Mutation Status. ** Indicates statistically significant difference (p<0.05) * Indicates a trend (0.05<p<0.01)

P226 Cutaneous Head and Neck Melanoma (CHNM) in OPTiM: A Randomized Phase 3 Trial of Talimogene Laherparepvec (T-VEC) versus GM-CSF for the Treatment of Unresected Stage IIIIB/C and IV Melanoma


CHNM has worse outcomes and limited treatment options compared to melanomas at other sites. T-VEC is a HSV-1-derived oncolytic immunotherapy designed to selectively replicate in tumors and produce GM-CSF to enhance systemic antitumor immune responses. In OPTiM, intradermal T-VEC compared with subcutaneous GM-CSF improved durable response rate (partial response [PR] or complete response [CR] lasting continuously for ≥6 months) from 2% to 16% (p<0.001) and improved median overall survival (OS) from 18.9 months to 23.3 months (HR = 0.79, 95% CI: 0.62 – 1.00; p = 0.051). Here we report treatment outcomes in patients with CHNM in OPTiM. 20% of patients (87/436) pts; 61 for T-VEC, 26 for GM-CSF) had CHNM. The two groups were balanced by histological characteristics, TNM stage (42% IIIIB/C, 20% IVM1a, 22% IVM1b, 16% IVM1c), age, median time to first recurrence (0.6 years, interquartile range [IQR], 0.3 – 1.3 years) and site of first recurrence (24% local, 32% in-transit, 22% regional nodal, and 22% distant sites), line of treatment (60% first-line), and HSV serostatus (59% positive). The T-VEC group had more patients with liver metastases (5% vs 0% for GM-CSF). Median follow-up (IQR) was 25 months (13 – 39 months) for GM-CSF and 35 months (13 – 43 months) for T-VEC (p = 0.18). Durable response rate as assessed by blinded external review was higher for T-VEC than for GM-CSF (36% vs 4%, p = 0.001). Overall response rate was higher for T-VEC than for GM-CSF (48% vs 8%, p < 0.0001), with 30% CR and 18% PR for T-VEC versus 0% and 8% for GM-CSF, respectively. Median OS (95% CI) for GM-CSF was 25.2 months (12.8 – 37.4 months) and was not reached for T-VEC (29.7 – Not estimable; HR = 0.57, 95% CI: 0.32 – 1.03). In the OPTiM trial, T-VEC treatment resulted in an overall response in approximately half and durable response in more than a third of patients with CHNM. T-VEC has potential as a treatment for patients with regionally and distantly metastatic CHNM.

P227 Outcomes following Lymphoscintigraphy without Sentinel Node Biopsy in Patients who are Elderly or have Medical Comorbidities

N. Ipenburg,1,2, O.E. Nieweg,1, R.F. Uren,2 J.F. Thompson,1 1. Mela-noma Institute Australia, North Sydney, NSW, Australia; 2. Sydney Medical School, The University of Sydney, Sydney, NSW, Australia.

Introduction: Sentinel-node biopsy (SNB) is the most powerful prognostic indicator in melanoma patients and has proven therapeutic benefit in a subset of them. However, it may be considered inappropriate in some patients for various reasons. This study reports the clinical characteristics, management and outcomes for a series of patients managed by wide excision without SNB, but after preoperative lymphoscintigraphy to increase the reliability of clinical and ultrasound (US) follow-up. Methods: Our prospectively-collected database was searched for patients with a clinically localized cutaneous melanoma treated between 2000 and 2009 in whom lymphoscintigraphy was performed but SNB was intentionally not scheduled. Results: Of the 3523 patients who had lymphoscintigraphy, 161 (4.6%) did not undergo SNB because of age and/or comorbidities. On average, these patients were older than the 2945 patients who had SNB (78 vs. 57 years, p<0.001), more often had head-neck melanomas (34% vs. 16%, p<0.001), and had more advanced melanomas (Breslow thickness 2.5 mm vs. 1.8 mm; p<0.001) with a higher mitotic rate (median 5/mm2 vs. 3/mm2; p = 0.002). Of these 161 patients, 148 (91.9%) were followed with high-resolution US of their SNs at each follow-up visit, which identified 31% of the nodal recurrences. After controlling for potential confounders, patients who did not have SNB had worse overall survival (HR=1.40, 95% CI 1.01-1.95) and regional node disease-free survival (HR=1.95, 95% CI 1.19-3.19) than patients who did undergo SNB, but melanoma-specific survival (HR=1.26, 95% CI 0.74-2.13) was not significantly different. Conclusion: Compared to SN-positive patients who underwent immediate completion node dissection, node-negative patients without SNB had more involved nodes when a delayed lymphadenectomy was performed (mean 3.7 vs. 1.7; p = 0.03), but melanoma-specific survival was not significantly different (HR=0.66, 95% CI 0.23-1.86). Conclusions: Lymphoscintigraphy with US follow up of previously identified SNs is a reasonable management option to avoid SNB in patients who are elderly or have comorbidities.

P228 Scalp Melanoma: Role for Enhanced Detection through Professional Training

M. Russell,1,2,1* S. Sharma,3 B. Lovasik,4 K. Delman,5 M. Rizzo,6 1. Surgery, Emory University, Atlanta, GA; 2. University of Miami, Miami, FL.

BACKGROUND: Scalp/neck melanomas have a relatively poor prognosis compared to other sites. The scalp/neck represent an anatomically challenging area for self detection which may delay diagnosis. The aim of this study was to identify the role of the hairdresser in detection of scalp and neck melanoma. METHODS: A single institutional database was retrospectively reviewed for all patients undergoing resection of the hair bearing areas of the scalp, posterior neck, forehead or retroauricular melanoma between 2008 - 2013. Clinicopathologic variables and method of detection were characterized. RESULTS: 137 cases were identified, including: 102 (76%) on the scalp, 26 (19%) in the retroauricular area and 7 (5%) on the forehead. The mean age at diagnosis was 63.3, and 87.6% were male. The median Breslow thickness was 2.64 mm (range 0.16-12) and 25% of primaries were ulcerated. Sentinel lymph nodes were positive in 17.6% of cases; 35% of cases did not undergo sentinel node biopsy. Melanoma arising in a bald area of the scalp were mainly first detected by the patient. All patients with lesions diagnosed by a spouse or family member were male. Overall female patients had thicker melanomas than male (mean 3.58mm vs 2.51mm). Females were 10 times more likely to have their scalp melanoma diagnosed by hairdresser (OR 10.15; 95% CI, 2.75-38.53). CONCLUSION: In this cohort, women had thicker melanomas than men and were more likely to have their lesion diagnosed by a hairdresser. In this region, there is a grass roots movement educating the cosmetology industry that may have increased the detection by hairdressers. Given the significant detection rate in women by hairdresser and the failure of family to detect lesions in women, hairdresser training may result in earlier detection of melanoma, especially for female patients. Consideration should be given for public service training to those individuals working in the cosmetology industry.
Table

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<th></th>
<th>Total</th>
<th>Female</th>
<th>Male</th>
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<td>First discovered</td>
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<td>Patient</td>
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<tr>
<td>Spouse or family member</td>
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<td>6 (35.7%)</td>
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<td>11 (9.1%)</td>
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<td>1 (6.3%)</td>
<td>18 (15.9%)</td>
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<td>31 (27.3%)</td>
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<td>Basal thickness (mean mm)</td>
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<td>5 (43%)</td>
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<td>0</td>
<td>8 (6.7%)</td>
</tr>
<tr>
<td>Previous history of melanoma or scalp skin cancer</td>
<td>49 (36.4%)</td>
<td>7 (41.1%)</td>
<td>42 (33.3%)</td>
</tr>
</tbody>
</table>

* Includes 1 case where the sentinel node was not identified.

P229

Pediatric Melanoma: An Age-based Analysis of the National Cancer Database


Introduction

Pediatric melanoma (PM) is rare, though its incidence is increasing. Single-institution reports suggest that biologic properties of PM may differ from adult melanoma. Current standards for the treatment of pediatric patients, which are based on experience with adults, may not be optimal in children. This study examined a national dataset to identify differences in disease characteristics and patient outcomes among pediatric, adolescent (ADM), and adult melanoma (AM) populations.

Methods

The National Cancer Database was queried for records of primary cutaneous melanoma (1998–2011). 5-year survival data was available for patients prior to 2007. Patients were divided into age-based cohorts: 1–10 (PM), 11–20 (ADM), and ≥21 years old (AM). Demographics, primary tumor characteristics, TNM classifications and survival were compared using bivariate analyses and survival differences were assessed using Cox proportional hazard analyses.

Results

420,353 patients met inclusion criteria (418 PM, 4,364 ADM, and 415,571 AM). PM patients were more likely to present with advanced primaries; 58% of PM patients had T3 or T4 lesions, compared to 26% of ADM and 24% of AM (Cochran-Armitage trend, p<0.001). After adjusting for T-classification, the PM cohort had a higher rate of nodal metastasis compared to the ADM or AM cohort (47% vs. 21%, p<0.001). Pediatric patients showed superior stage-specific survival compared to adolescent counterparts (p<0.001). In the pediatric cohort, nodal positivity had no effect on survival. Unadjusted 5-year OS in node-negative pediatric patients was 95.87% compared to 95.88% in node positive patients. After adjustment for T-classification, the lack of effect persisted (HR 0.52; CI 0.1-3.2). In contrast, OS in adolescents was significantly worse for node positive patients than node negative patients (HR 4.76, CI 3.1-7.4). Discussion

Despite increased rates of nodal metastasis, pediatric patients with cutaneous melanoma have greatly improved survival compared to adult patients. This large series from a national dataset suggests there are important, age-based differences in the biology and pathologic course of melanoma. Further research in pediatric populations is necessary to fully assess the utility of adult-based protocols in the care of pediatric patients with melanoma.

Overall adjusted survival by age in melanoma.

P230

Nodal Positivity does not Affect Survival in Pediatric Patients with Melanoma


Introduction

Survival in adult patients with melanoma is influenced by nodal metastasis. Thus, nodal positivity is an important factor in staging. Evidence suggests that pediatric patients with melanoma have improved stage-specific survival compared to adult cohorts and that nodal positivity may not impact survival in children. This study utilized a national dataset to examine the prognostic effect of regional disease in a large pediatric population. Methods The National Cancer Database was queried for cases of primary cutaneous melanoma (1998–2006). Cohorts of pediatric (1-10) and adolescent (11-20) patients were created. Univariate analyses compared node-negative and node-positive patients with respect to demographics and tumor characteristics. Log-rank and Cox analyses were performed to assess the unadjusted and adjusted effect on overall survival (OS) associated with nodal positivity. Results 1,442 records met inclusion criteria; 121 patients aged 1-10 (57 node-positive, 64 node-negative) and 1,321 aged 11-20 (279 node-positive, 1,042 node-negative). Adjusting for T-classification, the pediatric cohort had a higher incidence of metastatic lymphadenopathy compared to the adolescent cohort (47% vs. 21%, p<0.001). Pediatric patients showed superior stage-specific survival compared to adolescent counterparts (p<0.001). In the pediatric cohort, nodal positivity had no effect on survival. Unadjusted 5-year OS in node-negative pediatric patients was 95.87% compared to 95.88% in node positive patients. After adjustment for T-classification, the lack of effect persisted (HR 0.52; CI 0.1-3.2). In contrast, OS in adolescents was significantly worse for node positive patients than node negative patients (HR 4.76, CI 3.1-7.4). Discussion

The presence of lymph node metastasis has no significant effect on overall survival in patients under 10 years with melanoma. This analysis has demonstrated that pediatric melanoma should not be compared to adolescent melanoma. There is no prognostic value of nodal positivity in this pediatric cohort. Therefore, the role of staging evaluations, such as sentinel node biopsy, is not supported by this data.
Kaplan-Meier curve depicting survival in pediatric and adolescent cohorts with respect to node positivity.

**P231**

**Intraoperative Real-time Visualization of Sentinel Lymph Nodes through a Novel Binocular Goggle-assisted Imaging Navigation in Surgery System**

M.S. Strand,1* S. Mondal,2 J. Margenthaler,2 S. Achillefs,3 R.C. Fields,1 1. Washington University in St. Louis, Department of Surgery, St. Louis, MO; 2. Washington University in St. Louis, Department of Biomedical Engineering, St. Louis, MO; 3. Washington University in St. Louis, Department of Radiology, St. Louis, MO.

Despite high resolution imaging and lymph node mapping techniques, determining oncologic extent of disease remains challenging in multiple diseases including melanoma and breast cancer. Examples include re-excision of breast cancer and completion lymphadenectomy after sentinel node positivity. At our institution, a Goggle-Assisted Imaging and Navigation in Surgery (GAINS) system was developed to detect malignant tissue tagged with a tumor-avid fluorescent dye (LS301, not yet approved for human use) in animal models. Using indocyanine green (ICG), which has an identical spectral profile to LS301, our group demonstrates the intraoperative utilization of GAINS to visualize sentinel lymph nodes (SLNs) in patients undergoing surgery for melanoma or breast cancer. From February to September 2014, ten patients undergoing surgery for melanoma or breast cancer were enrolled under an institutionally-approved IRB. Patients underwent peritumoral injection of 99mTc-sulfur colloid (834 Ci) and methylene blue (MB; 5 mL of 1% solution), followed by indocyanine green (ICG; 5 mL, 645 μM) for visualization with GAINS. Radioactive signal was used to select a site for incision and SLNs were identified by radioactive signal and MB uptake. GAINS was then used to visualize local ICG fluorescence. The sensitivity of GAINS was compared to MB using radioactive signal as the control. GAINS was successfully integrated into surgical procedures without workflow disruption, providing clear visualization of SLNs (see Figure). GAINS identified all 19 SLNs detected by radioactive signal and MB uptake from 5 melanoma and 5 breast cancer patients. MB detected 15 out of 15 SLNs detected by gamma probe in a subset of these patients. All putative SLNs detected were successfully verified histopathologically. GAINS and MB did not identify any non-radioactive tissue. GAINS provides detection of SLNs with 100% sensitivity - equivalent to current standard of care. Given the identical spectral profiles of ICG and LS301, GAINS has the potential to provide intraoperative visualization of malignant tissue, which could reduce reoperation for both margin and sentinel lymph node positivity.

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**P232**

**Oligometastatic Disease in AJCC Stage IV Melanoma: Incidence and Outcomes of Primary Surgical Resection**

S. White,1 J. Maraka,1 M. Lo,1 L. Wingfield,2 K. Almand-Chinn,1 M. Moncrieff,1* 1. Department of Plastic & Reconstructive Surgery, Norfolk & Norwich University Hospital, Norwich, United Kingdom; 2. Norwich Medical School, University of East Anglia, Norwich, United Kingdom.

**Introduction & Aims**

Patients diagnosed with AJCC stage IV melanoma are traditionally considered to have a gloomy prognosis. With the advent of new, targeted chemotherapeutic agents and immunotherapy, it is commonplace to offer these rather then surgical intervention. The aim of this study was to attempt to identify patients who could derive long-term survival benefit from primary surgical intervention.

**Material & Methods**

A total of 198 melanoma patients (125 males, age 22-94 yrs (median 67)), who were treated in a university hospital, tertiary referral melanoma service were identified, presenting with stage IV melanoma between 2004 and 2013. Data regarding location and number of metastases, treatment modalities and outcomes were analysed. Key results with supporting statistical analysis The vast majority of patients were diagnosed using CT scans. Median follow-up was 7 months (0-110 months). The top 3 sites for distant metastasis were lung (53%), liver (28.3%) and brain (27.3%). When brain metastases were excluded (n=54), the median number of sites was 2 (range 1-9). Twenty-four patients (16.7%) with no intracranial disease were offered surgery with curative intent. Thirty-three distant resections were performed: skin/SQ (11), lung (8), lymph nodes (5), bowel (4), adrenal (3), others (2). Seven patients had multiple procedures. Nearly 80% of procedures were performed in the latter five years of this study. Melanoma-specific survival in the oligometastatic surgical cohort was 31% vs. 5.3% in the non-surgical group (P<0.0001). Patients with 2 or less sites treated with surgery had a significantly improved melanoma-specific survival compared to those who were managed medically (18 vs. 8 months, p=0.0021). The addition of a regional lymphadenectomy to the surgery had no bearing on patient outcome. Conclusion Our data would suggest that 1 in 6 patients with extra-cranial stage IV disease, limited to two distant sites, could benefit from primary surgical intervention, with a potential long-term survival benefit of 30%. The use of newer agents in the neoadjuvant setting to increase the number of resectable stage IV patients is an exciting possibility.
T3JAM is a Novel Regulator of Tumor Growth


**1. General Surgery, University of North Carolina, Durham, NC; 2. Department of General Surgery, University of North Carolina, Chapel Hill, NC; 3. McAllister Heart Institute, University of North Carolina, Chapel Hill, NC; 4. Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC.**

**Background:** T3JAM is a transmembrane receptor that acts as a downstream adapter within the JNK pathway in lymphocytes but has never been studied in other cell types. Given its role in the JNK pathway, we hypothesized that T3JAM would regulate tumor growth. **Methods:** The expression of T3JAM in a panel of human tumors was performed on tumor cell lysates by Western blot. A lentiviral vector was then used to silence T3JAM in A-375 melanoma and SVR angiosarcoma cells; and effects on proliferation, apoptosis, and tube formation were evaluated in vitro. Sham-transfected and sh-T3JAM transfected SVR angiosarcoma cells (1 x 10^6) or A-375 melanoma cells (2 x 10^6) were injected s.c. into nude mice and tumor volumes were measured. **Results:** Western blot: T3JAM protein was present in cell lysates from human breast cancer, gastric cancer, osteosarcoma, glioblastoma, melanoma, plasmacytoma, and angiosarcoma, with A-375 melanoma having the highest protein level. 24 hour Proliferation Assay: Sh-T3JAM cells had decreased proliferation rate compared to sham cells: 61% reduction for melanoma (p=0.03) and 66% reduction for angiosarcoma (p=0.006). Angiosarcoma Tube formation: Sham control and sh-T3JAM angiosarcoma cells were plated in a Matrigel tube formation assay. After 4 hours the number of branch points in the sham cells was 262 ± 17 branch points; which was reduced in the sh-T3JAM cells, which was 26 ± 8 branch points (p<0.0001). Apoptosis: 1.0% ± 0.3% of sham melanoma cells subjected to UV light were apoptotic and 55% ± 8.3% of sh-T3JAM transfected cells were apoptotic (p<0.001). Tumor growth in vivo: In sham melanoma xenografts the mean tumor volume at 45 days was 832 mm^3 ± 256, and 56 mm^3 ± 13 in sh-T3JAM tumors, a reduction of 94% (n=10, p = 0.005). In angiosarcoma allografts, the mean tumor volume after 23 days was, 0.3% of sham controls, and 55% in sh-T3JAM tumors. **Conclusion:** T3JAM is a transmembrane protein, T3JAM, is expressed in multiple tumor types. Loss of T3JAM results in reduction in proliferation, apoptosis, and tube formation, and reduces growth of melanoma and angiosarcoma in vivo.
Risk of Second Primary Malignancies Increases with Melanoma Breslow Thickness

A.H. Varey,1* K.C. Young,2 A. Ives,3 J. Verne,3 J.F. Thompson,4 Y. Ben-Shlomo,4 1. Melanoma Institute Australia, North Sydney, NSW, Australia; 2. University of Bristol, Bristol, United Kingdom; 3. Public Health England, Bristol, United Kingdom.

Background Melanoma has been shown to be associated with an increased risk of developing further melanoma and non-melanoma cancers. We hypothesised that this excess risk would be positively associated with Breslow thickness in the primary melanoma. Methods: All primary melanomas diagnosed in England (1996 to 2005) were included from the National Cancer Data Repository. Standardised Incidence Ratios (SIRs) and 95% confidence intervals (CI) were calculated for risk of secondary cancer adjusting for gender, age, follow-up duration, and income-based deprivation quintiles. Poisson regression was used to determine the risk associated with Breslow thickness. We tested for a bi-directional association by creating cancer-specific cohorts based on our initial findings to see if they predicted increased melanoma risk. Results: We had 61,196 primary melanomas (438,447 person-years) with 6,684 secondary malignancies. The SIR for another cancer was 146 (95% CI 143, 150) with another melanoma having the highest relative risk but the risk of kidney, multiple myeloma, non-hodgkin’s lymphoma, prostate cancer, breast cancer and colorectal cancer (men only) were also increased. A dose response effect for Breslow thickness and subsequent melanoma was observed (≤10mm: 736 (631-840) to >40mm: 1249(1043-1455) (p <0.0001) and for other malignancies excluding melanoma (≤10mm: 118(110-125) to >40mm: 144(132-155) (p<0.0001). There was a large and decreasing gradient for a second melanoma with increasing age so that the SIR declined from 46 (95% CI 32.65) for 25 to 29 year olds as compared to 7.5 (95% CI 6.1, 8.9) for those 85 and over (figure 1). A similar but less dramatic pattern was seen for all cancers excluding melanoma. Conclusions: Melanoma patients are more likely to get other cancers and Breslow thickness is a prognostic biomarker of future risk for some cancers. This previously undescribed association may help improve our understanding of the pathophysiology of melanomas.

Outcomes after Lymphadenectomy in Obese and Non-obese Patients with Melanoma: An Analysis of ACS-NSQIP Data

T. Hughes, J. Poirier, J. Kubasiak, S. Bines, General Surgery, Rush University Medical Center, Chicago, IL.

Background: In 2014, there will be an estimated 76,000 new cases of melanoma. When patients have evidence of disease in the lymph nodes, lymphadenectomy is the standard of care. However, this standard is controversial and the focus of an ongoing randomized controlled trial. Obesity is a major health burden, affecting 35% of adults in the United States. We sought to examine the effect of obesity on outcomes after lymphadenectomy. Methods: Patients with cutaneous melanoma undergoing axillary or inguinal lymphadenectomy between 2008-2012 in the ACS-NSQIP database were reviewed. Body mass index (BMI) was calculated based on height and weight. Operative time, length of stay (LOS) and wound complications were compared across groups using Fisher’s exact test. Results: There were 706 total patients, of whom 418 (59%) underwent axillary surgery while 288 (41%) underwent inguinal dissection. 162 patients (23%) had a BMI<25, 229 (33%) had a BMI of 25-29.9, 183 (26%) had a BMI of 30-34.9, and 118 (17%) patients had a BMI>35. 14 patients were excluded for missing data. Among those undergoing axillary dissection, there were no statistically significant relationships between BMI and the outcomes of interest. Among those treated with inguinal dissection, total operative time was 113 minutes for patients with BMI<25 compared to 136, 149 and 183 minutes for those with BMI of 25-29.9, 30-34.9 and >35, respectively (p<0.0058). Patients with an increased BMI also had a higher incidence of wound complications; 6.7% of patients with a BMI>25 experienced a wound complication compared to 9.2%, 9.7% and 30.8% among patients with BMI of 25-29.9, 30-34.9 and >35, respectively (p=0.0036). Conclusions: Obesity has many negative implications in the surgical patient. Increased operative time and wound complications may translate to additional procedures, poor functional or cosmetic outcomes and increased cost associated with surgery. In obese patients undergoing inguinal node dissection, the risks and benefits are clearly different than in non-obese patients. This emphasizes the importance of defining the benefit of surgery for patients with microscopic involvement of the lymph nodes.


Introduction: Several case reports and anecdotal experience have suggested a propensity for melanoma recurrence in skin graft and donor sites. This suggests a possible mechanism of increased growth factor expression that could predispose patients undergoing skin grafting to develop locoregional recurrence. To our knowledge, no studies have looked at this phenomenon across a broader population. Methods: In this post-hoc analysis, patients with melanoma ≥1mm thick enrolled in a multi-center randomized controlled trial were classified by closure type: primary closure, skin grafting, or adjacent tissue rearrangement (ATR). Clinicopathologic features were compared. Local and in-transit recurrence-free survival (LITRFS), disease-free survival (DFS), and overall survival (OS) were evaluated across groups using the Kaplan-Meier method. Skin graft closure was then evaluated along with established risk factors using a Cox proportional hazards model to identify independent predictors of LITRFS, DFS, and OS. Results: A total of 2,472 patients were evaluated. Patients with skin grafts were older, had thicker primary tumors, and an increased rate of positive sentinel lymph nodes (Table 1). Excision margins were larger in the skin graft group compared to primary closure. On Kaplan-Meier analysis, skin graft closure was associated with worse OS, DFS, and LITRFS. Overall, 32 skin grafts had LITR (12.5%), compared to 88 patients with primary closure (5.8%) and 51 with ATR (7.2%) (p=0.0005). After controlling for age, gender, Breslow thickness, ulceration, anatomic location, surgical margins, and nodal status in the multivariate model, skin graft closure emerged as an independent factor predicting worse LITRFS (HR 1.61, 95% CI 1.05-2.42), but not OS (p=0.07) or DFS (p=0.54). Additional independent risk factors for worse LITRFS included Breslow thickness, a positive sentinel node, surgical margins, and nodal status in the multivariate model, skin graft closure represented an independent predictor for local and in-transit recurrence following wide local excision for melanoma. These data should be considered hypothesis-generating, and should stimulate analysis of additional large data sets.

Table 1: Clinical and Pathologic Features by Closure Type

<table>
<thead>
<tr>
<th>All Patients</th>
<th>Skin Graft Closure</th>
<th>Primary Closure</th>
<th>ATR Closure</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=2472)</td>
<td>(N=25%; 10.4%)</td>
<td>(N=1588; 60.9%)</td>
<td>(N=710; 28.7%)</td>
</tr>
<tr>
<td>Mean or Percent (95% CI)</td>
<td>Mean or Percent (95% CI)</td>
<td>Mean or Percent (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Breslow Thickness</td>
<td>2.32 (2.30, 2.34)</td>
<td>2.18 (2.10, 2.36)</td>
<td>2.36 (2.33, 2.49)</td>
</tr>
<tr>
<td>were excluded for primary closure</td>
<td>51.9 (50.0, 53.9)</td>
<td>49.1 (48.8, 50.1)</td>
<td>49.9 (49.0, 50.8)</td>
</tr>
<tr>
<td>Excision Margins</td>
<td>1.98 (1.92, 2.04)</td>
<td>1.87 (1.85, 1.90)</td>
<td>2.01 (1.98, 2.04)</td>
</tr>
<tr>
<td>were excluded for primary closure</td>
<td>40.4 (39.3, 41.5)</td>
<td>41.5 (41.2, 41.7)</td>
<td>41.1 (40.8, 41.4)</td>
</tr>
<tr>
<td>Ulceration</td>
<td>27.7% (22.6%, 33.3%)</td>
<td>30.0% (24.9%, 35.1%)</td>
<td>28.0% (22.3%, 33.7%)</td>
</tr>
<tr>
<td>Positive SN</td>
<td>14.6% (12.4%, 17.0%)</td>
<td>21.3% (18.4%, 24.2%)</td>
<td>18.6% (15.5%, 21.7%)</td>
</tr>
<tr>
<td>overall</td>
<td>7.0% (4.5%, 10.8%)</td>
<td>50.1% (47.9%, 53.0%)</td>
<td>40.1% (36.6%, 43.8%)</td>
</tr>
<tr>
<td>Overall Complications</td>
<td>16.8% (12.7%, 21.9%)</td>
<td>16.3% (14.3%, 18.4%)</td>
<td>19.7% (16.6%, 23.2%)</td>
</tr>
</tbody>
</table>
P238
Topical Diphencyprone for the Treatment of In-transit Melanoma Metastases of the Skin

J. Garioch, M. Moncrieff, Department of Plastic & Reconstructive Surgery, Norfolk & Norwich University Hospital, Norwich, United Kingdom.

Introduction: Various treatments currently exist for treating cutaneous melanoma in transit metastases. Topical diphencyprone (DPCP) has recently been used in Australia to treat cutaneous melanoma metastases. We have used topical DPCP since 2009 and we report our own experience. Methods: All patients had multiple superficial melanoma deposits in the skin. Patients were initially sensitised to 2% DPCP in acetone. DPCP in aqueous cream was then applied to the area to be treated 7 days later. The preparation was applied once weekly. The initial dilution was 0.005% and the concentration was titrated in order to achieve a mild to moderate eczema. DPCP was continued whilst the disease responded but usually discontinued if the disease progressed. Results: Twenty-eight patients, 15 female, were treated. Median follow-up was 9 months (range: 1-56). The majority of lesions (67.8%) were located on the extremities. Seven (25%) of patients had a complete response (CR), 11 patients had a partial or stable response (PR) and 10 (35.7%) patients did not respond (NR). Response rate was independent of disease burden. Median progression free survival (PFS) was 10 months, and none of the patients who had a CR have relapsed to date (p<0.0001). There was no difference in PFS between AJCC IIIB & IIIC patients (p=0.2). Eight (28.6%) patients have since died of their disease. NR was significantly associated with reduced disease-specific survival (p=0.001). Relapse or progression of TMs was also significantly associated with death (p=0.021). 10 (36.7%) patients are currently receiving treatment. The toxicity was minimal with only 2 (7%) patients discontinuing treatment due to side effects. The longest duration of treatment in our group of patients is 36 months. The concentrations used have varied between 0.05% and 0.000001%.

Discussion: DPCP is a simple, effective and well-tolerated treatment for melanoma metastases in the skin. It can be applied over a large surface area so it can also prevent other in transit metastases from developing more proximally. It can be used in conjunction with other treatment modalities. DPCP is a useful addition to our armamentarium in treating this difficult problem.

P239
Gene Expression Profile (GEP) Enhances Prognostic Value of Sentinel Lymph Node Biopsy (SLNB) in a Cohort of Patients with Head and Neck Melanoma


Introduction: We have previously described a GEP signature that predicted metastatic risk in a cohort of cutaneous melanoma cases, providing a binary outcome of Class 1 (low risk of metastasis) or Class 2 (high risk). The current analysis evaluated the prognostic capabilities of the GEP independently, and in combination with SLN status, in a cohort of patients with primary head and neck melanoma. Methods: All samples and clinical data were collected under an IRB approved, multicenter protocol. qPCR analysis was performed to assess expression of the gene signature, and Radial Basis Machine predictive modeling was used to predict risk (Class 1 vs. Class 2). Disease free survival (DFS), includes in transit and regional metastasis) and distant metastasis free survival (DMFS) were assessed. Results: 65 patients were identified with melanomas of the face (n=25), scalp (n=21), ear (n=11), and neck (n=8). Median age was 62 (range 25-87) and median Breslow depth was 2.9 mm. Only 1 SLN (+) patient was GEP class 1 whereas 51% of SLN negative patients were class 2. Median tumor thickness in SLN (+) patients was 4.5 mm; in SLN (-) it was 2.7 mm. Median tumor thickness in Class 1 was 1.7 mm and in class 2 was 4.4 mm. Kaplan-Meier (K-M) analysis of SLN (+) patients demonstrated both a 5-yr DFS and DMFS of 24%. K-M analysis of combined GEP and SLNB predicted risk resulted in 5-yr DFS and DMFS outcomes of 78% and 82%, resp., for class 1(SLNB-) (n=26) cases but 18% and 32% for Class 2(SLNB+) (n=11) cases. 20 of 53 (38%) SLN (+) patients developed distant mets. Median thickness was 3 mm in this subgroup and 12 were ulcerated. Of this subgroup of SLN (+) patients, 27 were GEP class 2 and had DFS and DMFS of 18% and 32% respectively. Conclusion: These results reflect an added prognostic utility for identifying low and high risk cases in this cohort when GEP is used in combination with SLNB.

P240
Incidence of Neuropathic Pain and Quality of Life in Melanoma Patients after Primary Surgery: A Multicenter Study

C. Thomson, O. Cassell, H. Peach, S. Holloway, J. Garioch, M. Moncrieff, J. Wilkinson, M. Moncrieff, 1. Department of Plastic & Reconstructive Surgery, Norfolk & Norwich University Hospital, Norwich, United Kingdom; 2. Oxford University Hospital, Oxford, United Kingdom; 3. Leeds Teaching Hospitals, Leeds, United Kingdom; 4. Cardiff University School of Medicine, Cardiff, United Kingdom.

Introduction: Wide local excision (WLE) and sentinel lymph node biopsy (SLNB) is the mainstay of treatment for patients with melanoma. As survival outcomes improve, longer term quality of life (QOL) questions become more pertinent and this study aims to assess the factors which may play a role in this following surgery. Methods 221 patients who had undergone WLE and a negative SLNB for melanoma (AJCC stage I and II) were recruited from three large cancer centers and completed a patient outcome questionnaire. This included demographic and treatment data as well as QOL and pain questionnaires. Factors included in the analysis were age, gender, Breslow thickness, tumour site, surgical margin, reconstruction, time since surgery and pain. Results: The mean age of the study group was 58.6 (range 20-85), 56% were female and median time from surgery to questionnaire was 19 months (range 0.8 - 96 months). Pain was the only significant factor influencing QOL with a negative correlation seen between pain scores and QOL scores (p<0.001). 35.7% of patients reported pain at their surgical site with 17 patients (7.7%) rating their average pain over the last four weeks as a 5/10. Four patients (1.8%) scored one in the high risk of neuropathic pain category. The patients experiencing pain were significantly younger than those not reporting pain (median 55.0 vs 63.5 years, p=0.001) however other demographic or treatment data did not show any significant relationship with pain or QOL. In particular, length of time since surgery did not appear to correlate with improving pain or QOL. Conclusion: Our results suggest that following wide local excision, a significant proportion of patients experience pain and poorer quality of life which does not improve with time and therefore appears to be chronic in nature. These findings were replicated in each center, indicating a consistent problem with the procedure. The level of pain experienced is clinically significant and merits evaluation and treatment in this group of patients who are increasingly surviving their melanoma diagnosis. Further investigation into potential pre-operative prophylactic measures is suggested.
patients eligibility for BRAF inhibitors. Prior to this study all patients managed in our specialist skin MDT required samples to be sent away for genetic testing at one of the national molecular testing centres using the COBAS technique. Methods: All samples sent for genetic testing for detection of the BRAF mutation over a 26-month period were blindly tested using the VE1 monoclonal antibody immunohistochemistry (IHC) stain. Results: Samples from 129 patients were identified. This included 11 primary melanoma samples, 9 sentinel lymph nodes, 65 metastatic lymph node samples, 11 distant metastatic samples, and 34 skin deposits. All of the patients were stage III or stage IV, except one. There was a 94.6% (122/129) concordance rate, with a sensitivity of 92.2% (47/51) and a specificity of 96.2% (75/78). Conclusion: This study demonstrates that the IHC staining has excellent sensitivity and specificity to detect the BRAF V600E mutation. Discrepancies between the two techniques are likely to result from the inability of the molecular technique to detect a mutation on small tumour deposits in sentinel node biopsies and an inability to distinguish between V600E & V600K mutations. We suggest that the IHC staining technique is an effective first line diagnostic tool in the assessment of BRAF status, with molecular testing necessary for the IHC negative cases only. It also has the major advantage of rapid availability for cancer centres diagnosing melanoma without local access to molecular testing, and being able to detect small amounts of tumour in a sample.

P242
Risk of Sentinel Lymph Node Metastasis in “Truly” Thin Melanoma

Background: Indications for SLN biopsy in patients with thin (<1 mm) melanoma, which represent the majority of newly diagnosed melanomas, remain controversial. Various pathologic and patient factors have been reported as prognostic factors for SLN positivity in this group. While a positive deep margin on initial biopsy has intuitively been considered to elevate the risk for SLN metastasis, its prognostic influence has not been well characterized. Methods: Prospectively maintained databases from two institutions were reviewed to identify patients undergoing SLN biopsy for thin melanoma since 1995. The deep margin (DM) status of the original biopsy was recorded, and SLN positivity rates were compared between patients with positive and negative margins on the original biopsy. The two groups were also compared with regards to pathologic variables using chi-squared statistics. Results: 1413 patients with T1 lesions underwent SLN biopsy, of whom 1159 with known biopsy margin status were included for study. The overall SLN positivity rate was 4.4%. 41% of patients had a positive deep margin on original biopsy (DM+). DM+ patients demonstrated a higher incidence of SLN metastasis compared to DM− patients (5.9% vs. 3.4%, p=0.04). Patients with a positive deep margin had slightly thicker tumors (0.77mm vs. 0.75mm, p=0.02), but there were no significant difference between DM+ and DM− patients with respect to presence of ulceration (6.5% vs. 4.4%, p=0.12), or tumors with mitotic index >=1 (57.4% vs. 54.9%, p=0.39). For T1 lesions >=0.75 mm in depth, SLN metastasis rates were 5.7% and 8.2% respectively for DM+ and DM− patients (p=0.19). SLN metastasis was very uncommon for lesions <0.75 mm in depth (N=479) regardless of deep margin status (0.34% for DM+ vs. 2.1% DM−, p=0.06). Conclusions: Positive deep margin status on melanoma biopsy is associated with an increased risk of SLN positivity in patients with thin melanoma. For lesions <0.75 mm in depth, SLN positivity rates are very low regardless of biopsy margin status, and positive deep margin status should not strongly influence the decision for SLN biopsy in these patients.

P243
Completion Lymph Node Dissection or Observation for Melanoma Sentinel Lymph Node Metastases: A Decision Analysis
E.E. Burke, P.R. Portschy, T.M. Tostle, K.M. Kuntz. Surgery, University of Minnesota, Minneapolis, MN.

Introduction: For patients with melanoma and sentinel lymph node (SLN) metastases, the optimal management of the remaining lymph nodes remains unknown. Randomized clinical trial results comparing completion lymph node dissection (CLND) with observation are not available. Methods: We developed a Markov model to simulate the prognosis of a hypothetical cohort of patients with SLN metastases under two scenarios: 1) immediate CLND and 2) observation with delayed CLND for those who progress to macroscopic disease. Parameters in the model were derived from published studies and included the likelihood and number of non-SLN metastases, the risk of dying from melanoma conditional on lymph node status, CLND complication rates, and health-related quality of life weights for surgical complications. Model outcomes included 5-year overall survival (OS), life expectancy, and quality-adjusted life expectancy. The base case input parameter for risk of non-SLN metastases was estimated at 20%. Results: The projected 5-year OS for a cohort of patients aged 50 with SLN metastases who underwent immediate CLND was 67.2% compared to 63.05% for the observation group. The life expectancy gained by undergoing immediate CLND ranged from 2.19 years in patients aged 30 to 0.64 years for age 70. The quality-adjusted life expectancy gained by undergoing immediate CLND ranged from 3.1% to 5.2% as the probability of non-SLN metastases ranged from 15% to 25%. Immediate CLND was no longer optimal when the incidence of non-SLN metastases was less than 7.4% for age 30 and less than 8.8% for age 70. Conclusion: Immediate CLND was associated with survival and quality-adjusted survival gains, which were dependent upon the risk of non-SLN metastases and patient age. Quality-adjusted survival gains were smaller but still appreciable, especially for younger age.

P244
Breslow Thickness and Ulceration do not Predict Melanoma-specific Survival in Patients with Melanoma >4mm Thick undergoing Sentinel Lymph Node Biopsy

Introduction: The role of sentinel lymph node biopsy (SLNB) for patients with melanoma greater than 4mm in Breslow thickness (BT) is controversial. These patients are at significant risk of distant relapse with a 5 year survival of 45-65%. The prognostic and therapeutic potential of early identification of nodal disease has not been well established in this patient group. We present one of the largest single-centre studies focused on the role of SLNB in these patients. Methods: Patients with primary cutaneous melanoma with BT greater than 4mm without clinical evidence of nodal involvement or metastatic disease undergoing wide local excision (WLE) and SLNB between 2002 and 2012 were included in the analysis. Chart review was performed to collect clinical, pathological and outcome data. Results: During the study period, 211 patients underwent WLE and SLNB with a median follow up of 4.3 years. There was a significant male predominance (68%) and median age was 63 years. The median BT was 6mm and 53% of cases were ulcerated. A positive SLN was identified in 75 patients (36%). The only predictors of a positive SLNB on multivariate analysis were the presence of lymphovascular invasion (OR = 4.915, p=0.001) and melanoma subtype, with superficial spreading melanoma having a higher rate of SLNB involvement than all other subtypes. The predictors of melanoma-specific survival (MSS) on multivariate analysis were a positive SLNB (HR=2.64, p=0.0025), elevated mitotic count (HR = 1.05, p=0.041) and the presence of satellitosis (HR =3.05, p=0.009). BT (HR = 1.03) and ulceration (HR=1.37) were not predictive of outcome. The 5 year MSS for patients without SLN involvement was 75% compared with 56% for those with disease in the sentinel node (p=0.001). Conclusion: Patients with T4 melanoma with a negative SLNB have a significantly better prognosis than those with a positive SLNB. Furthermore, in patients with T4 melanoma who undergo SLNB, known prognostic factors of BT and ulceration do not contribute to risk stratification for MSS. These data lend support to the use of SLNB in thick melanoma for optimal assessment of prognosis.
Surgical Treatment of Melanoma in Elderly: Do We Follow NCCN Guidelines? S. Ajma, D. Comissiong, M. Barsky, M.P. Vezeridis, T.J. Miner, Surgery, Brown University, Providence, RI.

Introduction: Surgical therapy of melanoma requires careful attention to appropriate surgical margins and SLNB. However, surgical resection and lymph node biopsy is sometimes not advocated in the elderly. Goal of this study was to evaluate compliance with NCCN guidelines for the surgical treatment of melanoma in the elderly. Methods: We performed a retrospective analysis of a prospective database of all melanoma patients above 70 years of age receiving an operation from 2005 to 2012. Compliance with NCCN guidelines were reviewed with regards to resection margins and SLNB. Results: 223 patients above 70 years of age underwent wide local excision of melanoma. Patients ranged from 70-109 years (mean 78.8) and included 141 (63.2%) males. Depth of invasion ranged from 0.15mm to 9mm (Mean 0.88mm). 58.7% patients had <1mm invasion, 15.6% had 1-2mm and 26% had >2mm invasion. 85 (38.1%) patients of invasion ranged from 0.15mm to 9mm (Mean 0.88mm). 58.7% patients had ranged from 70-109 years (mean 78.8) and included 141 (63.2%) males. Depth of invasion above 70 years of age underwent wide local excision of melanoma. Patients were compliant with NCCN guidelines for 195 (87.4%) patients. Age groups for patients were 122/138 (88.4%) for 70-80 years, 63/72 (87.5%) for 80-90 years, 5/8 (62.5%) for 90-100 years and 5/5 (100%) in >100 years. Resection margins were deficient in 8 (3.5%) patients. Of SLNB was deficient in 24 (10.7%) patients. 14 (6.27%) patients had loco-regional recurrence and 24 (10.7%) patients had distant metastasis. No significant difference was found in loco-regional recurrence (7.1% vs 6.1%; p=0.69) or distant metastasis (7.1% vs 11.2%; p=0.75) in patients who had deficient margins or SLNB. No age cut-off was identified that triggered variance from NCCN guidelines. Wound complications were found in 5.8% patients. No wound complications occurred in patients who were not managed per NCCN guidelines (p=0.38). There were no perioperative deaths or major complications in these patients. Conclusion NCCN guidelines for resection margins and SLNB were able to be followed in majority of elderly patients. Neither increasing age nor location of tumor was associated with non-compliance from recommendations. In those highly selected patient whose treatment did not comply with NCCN guidelines, recurrence or disease progression was not significantly different.

P246
Association between Durable Response (DR) and Overall Survival (OS) in Patients (pts) with Unresected Stage IIIb-Iv-Melanoma Treated with Talimogene Laherparepvec (T-VEC) in the Phase 3 OPTIM Trial H. Kaufman, R.H. Andtbacka, F.A. Collicchio, M. Wolit, A. Li, M. Shilkrut, I. Puzanov, M. Ross, J. Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; 2. Huntsman Cancer Institute, University of Utah, Salt Lake City; UT; 3. The University of North Carolina at Chapel Hill, School of Medicine, Chapel Hill, NC; 4. Agem Inc., Thousand Oaks, CA; 5. Vanderbilt University Medical Center, Nashville, TN; 6. MD Anderson Cancer Center, Houston, TX.

Background: T-VEC is an HSV-1-derived oncolytic immunotherapy designed to selectively replicate in tumors, produce GM-CSF, and enhance systemic antitumor immune responses. In OPTIM (NCT00769704), a randomized phase 3 trial of intralesional T-VEC vs subcutaneous GM-CSF for unresected stage IIIb-IV melanoma, T-VEC significantly improved DR rate (partial or complete response lasting continuously for ≥6 months; primary endpoint) vs GM-CSF (16% vs 2%, p<0.0001; Andtbacka et al, JCO 2013;31[suppl]:LBA9008). In the primary OS analysis of the intent-to-treat (ITT) population, median OS was 4.4 months longer for T-VEC vs GM-CSF (23.3 vs 18.9 months; HR:0.79, 95% CI:0.62-1.00, p=0.051; Kaufman et al, JCO 2014;32[suppl]:9008a). Here we evaluate an association between DR and OS. Methods: To avoid lead-time bias, OS was compared among pts who were alive and achieved DR vs those who did not at landmark times of 9, 12, and 18 months from randomization. A Cox proportional hazards model with achievement of DR as a time-varying indicator was also evaluated. Potential bias due to confounding was evaluated with sensitivity analyses adjusting for prognostic factors. Results: The analysis included all pts in the T-VEC ITT arm (n=295) who were alive at 9 (n=234), 12 (n=209), and 18 (n=165) months. At 9, 12, and 18 months, 20, 33, and 47 pts had a DR. For pts who had a DR vs those who did not, HRs for improved OS were 0.08 (95% CI: 0.01-0.56), 0.05 (95% CI: 0.01-0.39), and 0.13 (95% CI: 0.02-0.54) at 9, 12, and 18 months, respectively, indicating that achieving a DR was associated with improved OS. When DR was analyzed as a time-dependent covariate, the HR favored pts achieving a DR (HR: 0.09; 95% CI: 0.03-0.29). Conclusion: Achieving a DR was associated with a marked decrease in risk of death (<85% across various analyses). Studio design prevents demonstrating a causal relationship, but we can reasonably assume that achieving a DR would lead to OS improvement; these analyses support that assumption. DR should be further explored as a surrogate for OS in pts with melanoma treated by immunotherapy.

P247
Demographic and Socioeconomic Disparities in the Presentation and Management of Melanoma: A National Perspective Z. Al-Qurayshi, A. Hauch, E. Kandil, Surgery, Tulane University School of Medicine, Department of Surgery, New Orleans, LA.

Introduction: Demographic and economic factors have been recognized as crucial factors in certain diseases outcomes. In this study, we aim to examine the association of selected demographic and socioeconomic factors with the presentation and management of melanoma. Methods: Cross-sectional study utilizing the Nationwide Inpatient Sample (NIS) database for 2003-2009. ICD-9 codes were used to identify adult (≥18 years) patients with melanoma who underwent skin excision. Results: 2,765 discharge records were included. Men were more likely to have melanoma in the head and neck region (p<0.001), while trunk and limbs melanomas were more common in women (p<0.001). However, males had a higher risk of metastasis on presentation [OR: 1.68, 95%CI: (1.34, 2.11), p<0.001] and more likely to undergo radical lymph node dissection (p<0.001). Males and patients older than 50 years were more likely to have a hospital stay of more than 3 days (p<0.05). Similarly for Black patients, Hispanics compared to White (p<0.01). Patients with low annual income ($<48,000) were twice as likely to be treated by a low volume surgeon [OR: 2.24, 95%CI: (1.16, 4.34), p=0.017]. Similarly for patients with Medicaid coverage [OR: 2.34, 95%CI: (1.33, 4.32), p=0.004]. Patients with Medicaid coverage had a longer hospital stay as well [OR: 1.79, 95%CI: (1.09, 2.94), p=0.021]. Moreover, low income patients were more likely to be managed in non-teaching, rural, or low volume hospitals compared to high income patients (p=0.05 for all). The cost of health services was significantly in the highest quartile ($>9,185.30) for Black compared to White (p=0.023). Conclusion: The presentation and outcomes of melanoma have distinguished pattern of distribution based on patients’ demographic and economic backgrounds.

P248
Sentinel Lymph Node Biopsy in Thin Melanoma: A Systematic Review and Meta-analysis E. Cordeiro, M. Gervais, P. Shah, N. Look Hong, F. Wright. 1. General Surgery, The Ottawa Hospital, Ottawa, ON, Canada; 2. The University of Toronto, Toronto, ON, Canada.

Introduction: The majority of patients diagnosed with melanoma have a thin (<1.0mm) lesion and enjoy an excellent outcome. However a small subset, have worse outcomes including lymph node metastases and attenuated survival. We sought to determine the pooled rate of sentinel lymph node (SLN) metastases in patients with thin cutaneous melanoma, and determine the pooled effect of predictors on SLN metastases. Methods: Published literature between 1980 and 2014 was systematically searched and critically appraised. The primary outcome was the rate of SLN metastases in patients with thin (<1.0mm) cutaneous melanoma. Secondary outcomes were the effect of high-risk pathological features of the primary on the rate of SLN metastases. The presentation of SLN metastases was distinguished pattern of distribution based on patients’ demographic and economic backgrounds.
were estimated by the Mantel and Haenszel method, and a random effects model was utilized. Heterogeneity was assessed via the I^2 statistic.

**Results:** A total of 43 studies incorporating 9,644 patients with thin melanoma met criteria for inclusion in the analysis. The pooled proportion of patients with a positive SLN was 5.0% (95%CI: 4.1%, 5.8%). The following pathologic features of the primary melanoma were predictive of having a positive SLN on unadjusted analysis: thickness >0.75mm (OR 2.08 (p=0.0004)), Clark’s level IV/V (OR 1.75 (p=0.008)), presence of mitoses (OR 1.75 (p=0.03)), presence of ulceration (OR 1.64 (p=0.04)) and the presence of microsatellites (OR 6.94 (p=0.001)). The presence of either regression or tumor infiltrating lymphocytes did not significantly impact the rate of SLN metastases. On pooled adjusted analysis, thickness >0.75mm (p=0.02), presence of mitoses (p=0.02) and the presence of ulceration (p=0.003) all significantly increased the odds of SLN metastases; whereas, Clark’s level IV/V did not have a significant impact (p=0.36).

**Conclusions:** This is the most comprehensive, and first meta-analysis to analyze predictors of SLN metastases in the setting of thin melanoma. The overall rate of SLN metastases in thin melanoma is low; however, in the presence of any of the above high-risk features a SLN biopsy procedure should be discussed with the patient.

**Pediatric Melanoma: Staging, Surgery and Mortality in the Surveillance, Epidemiology and End Results (SEER) Database**

**P249**

**Introduction:** Melanoma is the most common skin cancer in children. Current guidelines for management of melanoma in children are not well-defined. Our study aims to identify patient and disease characteristics, outcomes, and current management modalities among children with melanoma using a national population-based database. **Methods:** A retrospective review of the Surveillance, Epidemiology, and End Results (SEER) database from 2004 to 2008 was conducted. Patients ≤21 yo with a diagnosis of melanoma were included. Patient characteristics, body region, histology, staging, treatment modality, and mortality were analyzed. Patients were grouped by age (≤12, 13-18, and 19-21 yo), and descriptive statistics were used to compare stages, surgeries, and mortality within groups. **Results:** 1,255 patients met our inclusion criteria. Of these, most were female (63.27%), White (85.02%), located on the trunk (38.41%), had unspecified histology (64.38%). The mean age was 17 ± 4 yo. Regarding stage, most patients had stage I (47.65%), then in situ melanomas (23.03%); stage III (8.21%); stage II (6.14%); and stage IV (1.35%). The highest proportion of stage I was in 19-21 yo (50.53%) vs. 48.25% in 13-18 yo vs. 31.88% in ≤12 yo (p=0.001). See Table 1 for all stages. Regarding surgeries, 16.81% (n=211) had wide excisions only, 15.4% (n=190) had wide excisions and sentinel node biopsies, 10.68% (n=134) had less than wide excisions and sentinel node biopsies, and 5.90% (n=74) had no surgeries. 19-21 yo had the highest proportion of patients receiving wide excisions only (34.82%) vs. 28.91% 13-18 yo vs. 26.42% ≤12 yo, and 13-18 yo had the highest proportion of wide excision and sentinel node biopsies (30.08%) vs. 27.80% 19-21 yo vs. 24.53% ≤12 yo (p=0.169). Of the 1,255 patients, 26 (2.07%) died of melanoma ≤12 yo had later stage melanomas when compared to the older age groups, less invasive surgery, and higher mortality.

**Conclusion:** Patients ≤12 yo had later stage melanomas when compared to the older age groups, less invasive surgery, and higher mortality.

**Table 1. Pediatric melanoma by stage, surgery, and mortality in SEER from 2004-2008.**

**P250**

**Prognostic Factors Vary after Conditional Survival in a Large Cohort of Stage III Melanoma Patients (n=4586)**


Prognostic factors vary after conditional survival in a large cohort of stage III melanoma patients (n=4586). With the recent success of targeted and immune therapies for stage IV melanoma, the spotlight is now shifting to adjuvant treatment for stage III patients. According to the 7th edition AJCC staging system, five-year survival estimates vary widely (70% to 39%) for this patient population, and are limited to the time-point of primary melanoma presentation. The current study investigates the influence of clinicopathologic factors on stage III conditional survival, defined as the prognosis for patients at time-points of 1 to 5 years after initial diagnosis of loco-regional metastasis. The cohort includes patients who present with stage III disease at initial diagnosis of their primary (primary), as well as those who present with their first loco-regional metastasis as a recurrence (recurrent). After surviving 1 year, primary stage III patients with macroscopic lymph node (LN) presentation were no longer at a significantly higher hazard of death from melanoma compared with patients that presented with microscopically detected LNs. Conversely, for patients surviving up to 5 years from diagnosis of primary stage III melanoma, the presence of ulceration (HR=1.93, 95%CI 1.31-2.82, P=0.008) in the primary tumor and presentation with satellite or in-transit metastasis (HR=2.17, 95%CI=1.34-3.53, P=0.0018) continued to convey significantly worse melanoma-specific survival (MSS). After conditionally surviving 3 years, the prognosis of a recurrent stage III patient was relatively homogeneous with respect to clinicopathologic factors. For the recurrent stage III patient, the only factor that continued to influence MSS up to 5 years after initial diagnosis was age. This study demonstrates that patient prognosis changes in the years following initial diagnosis of loco-regional metastasis with respect to clinicopathologic factors. Careful follow-up and clinical trial stratification is particularly important for patients presenting with primary stage III melanoma with ulceration and/or satellite or in-transit lesions.

**P252**

**Molecular Profiling in Malignant Melanoma: Initial Experience at an NCI-designated Cancer Center**


**INTRODUCTION:** Only a small proportion of mutations in malignant melanoma (MM) have been characterized. Using next generation sequencing to examine mutations in 50 cancer related genes, we sought to investigate our initial experience with molecular profiling of MM to establish prognostic markers and broaden the horizon for directed therapies in the future. **METHODS:** Patients with primary and recurrent MM of all stages were consented to have their tissue samples analyzed for somatic mutations in targeted regions of 50 cancer related genes using next generation sequencing. Clinicopathologic,

**Figure 1:** Summary of Predictors of Sentinel Lymph Node Positivity in Patients with Thin (≤2 mm) Melanoma-Headneck Analysis
### P253

**Is a Wider Margin (2 cm versus 1 cm) for a 1.0-2.0 mm Thick Melanoma Necessary? M.P. Dopeker,1,3 M. Yamamoto,1 K.J. Fisher,1 K.W. Nethery,2 J.N. Harb,1 M.A. Applebaum,3 N.U. Patel,2 W.C. Cruse,1 R.J. Gonzalez,1 A.A. Sarnaik,3 V.K. Sondak,4 J.S. Zager,1 1. Surgical Oncology, Moffitt Cancer Center, Tampa, FL; 2. University of South Florida SOM, Tampa, FL.**

**Background:** The current NCCN recommendation for excision margins in patients (pts) with melanomas between 1-2 mm thick is a 1-2 cm radial margin. We sought to determine if margin width had an impact on wound closure, locoregional recurrence and overall survival (OS) in pts with melanomas between 1-2 mm thick. **Methods:** Pts with melanomas 1.0-2.0 mm were evaluated at a single institution between 2008 and 2013. All pts underwent wide excision with radial margins between 1 and 2 cm at the discretion of the surgeon. Clinicopathologic and treatment parameters were correlated with local and locoregional recurrence rates, graft/flap use and OS. **Results:** 590 pts with melanomas between 1.0-2.0 mm were evaluated. A retrospective review of a prospectively maintained database was conducted on consecutive cases of RPLND done for metastatic melanoma at a single institution. **Conclusion:** Our data show a narrow margin of 1 cm when resecting melanomas between 1-2 mm thick did not increase the risk of local or locoregional recurrence or decrease survival when accounting for location and other factors. Therefore, a 2 cm margin is not clearly necessary for all pts with melanomas 1-2 mm thick. Avoiding a 2 cm margin may decrease the need for graft/flap use on the extremity. Optimal selection criteria remain to be determined for the safe use of a 1 cm margin.

### P254

**Robotic Pelvic Lymphadenectomy for Metastatic Melanoma**

A.M. Abbott,* J.S. Zager, J. Powsang, A.A. Sarnaik. Surgical Oncology, Moffitt Cancer Center, Tampa, FL.

**Background:** Pelvic lymphadenectomy (PLND) for metastatic melanoma to the iliac and obturator nodes is the current standard of care. Robotic PLND (RPLND) offers the potential advantages of 3-D visualization, improved fine motor movement, and less post-operative pain compared to the large muscle splitting incision of open PLND. The purpose of this study was to evaluate the safety and feasibility of RPLND for metastatic melanoma. **Methods:** A retrospective review of a prospectively maintained database was conducted on consecutive cases of RPLND done for metastatic melanoma at a single institution. **Results:** 10 pts (8 women, 2 men) underwent RPLND from 4/2013 to 8/2014. There were no open conversions. The median primary tumor depth was 2.1 mm (range, 0.16 to 9.2). 6 (60%) pts underwent inguinal sentinel lymph node biopsy (SLN) and 5/6 had positive disease. Indications for RPLND included: radiographic findings suspicious for metastasis in the ipsilateral pelvic nodal basin (n=8), direct pelvic drainage via lymphoscintigraphy scan in pts with a positive inguinal SLN (n=1) and positive Cloquet’s node (n=1). 6 pts underwent RPLND with concomitant open inguinal node dissection (ILND), 4 pts underwent RPLND alone. The median operating time for RPLND alone was 156 min (range, 63-173) and estimated blood loss (EBL) 75cc (range, 30-150) compared to 205 min (range, 75-299) and 50cc (range, 25-100) EBL for ILND/ RPLND group. Median pelvic nodal yield was 10 (range, 5-12). The median length of stay (LOS) was 2.5 days for ILND/RPLND and 1 day for RPLND. There were no wound or systemic complications associated with RPLND. Median follow-up from time of RPLND was 312 days (range, 13-479) and there have been no recurrences to date in the pelvic lymph node basin in any pt. **Conclusion:** RPLND for metastatic melanoma appears to be a promising approach with nominal peri-operative morbidity associated with the procedure in this series. We demonstrate an acceptable EBL, LOS, and nodal yield after RPLND. Additional prospective studies are needed to confirm the longer-term oncologic outcome of RPLND.

### Table 1: Types of mutations

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<tr>
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### P255

**Hepatic Progression Free and Overall Survival after Regional Therapy to the Liver for Metastatic Melanoma**


**Background:** Metastatic melanoma to the liver portends a poor prognosis. Control of disease via liver directed therapy is a potential alternative to systemic therapy. The aim of this study was to evaluate outcomes after yttrium-90 (Y90), chemoembolization (CE), or percutaneous hepatic perfusion (PHP) on hepatic progression free survival (HPFS), progression free survival (PFS), and overall survival (OS). **Methods:** A retrospective review of patients (pts) with liver metastases from cutaneous or uveal melanoma treated with Y90, CE, or PHP from 2008-2014 were included. Kaplan-Meier survival estimates, log-rank test, and multivariate time-dependent Cox regression analysis (MVA) were used to relate patient, tumor, and treatment variables to HPFS, PFS, and OS. **Results:** There were 30 pts (16 male, 14 female, 5 unknown primary); 6 Y90, 10 PHP, 12 CE, 1 pt received Y90 after PHP and 1 received PHP after CE. There were no differences in age, adjuvant therapy use, prior hepatic treatment, or post treatment complications between the 3 groups. There was an increased incidence of extrahepatic disease in CE pts (p=0.004) and a trend toward lower ECOG in PHP pts (p=0.051). There was a significant difference in median HPFS; Y90 54 days (d); CE 80d; PHP 310d; p = 0.002. MVA showed improved HPFS for PHP vs Y90 (p < 0.001), PHP vs CE (p=0.008) but not for CE vs Y90 (p = 0.44). Higher ECOG (p=0.014) and greater TB (p=0.03) correlated with worse HPFS. PHP treatment, lower ECOG, and lower TB were also significant predictors of PFS. Median OS from time of treatment was longest for PHP at 736d vs Y90 285d and CE 265d, however it did not reach statistical significance. There was a significant difference on MVA of OS for PHP vs Y90 (p = 0.03) but not for PHP vs CE (p=0.37) or CE vs Y90.
(0.06); ECOG status and TB were also not significant predictors of OS on MVA. **Conclusions:** HPFS and PFS were significantly prolonged in patients treated with PHP vs CE and Y90. Median OS in PHP pts was over double that seen in Y90 or CE pts but was significant on MVA only between PHP and Y90. Larger studies are needed to further evaluate the impact of treatment on OS.

**P256**

**Primary Overall Survival (OS) from OPTiM, a Randomized Phase 3 Trial of Talimogene Laherparepvec (T-VEC) versus Subcutaneous (SC) Granulocyte-macrophage Colony-stimulating Factor (GM-CSF) for the Treatment of Unresected Stage IIIB/C/IV Melanoma**

**Melanoma** H. Kaufman,1,4 R.H. Andtbacka,2 F. Collichio,5 T. Amatruda,6 N. Senzer,6 J. Chesney,6 K. Delman,6 L.E. Spitzer,6 I. Puzanov,9 Y. Ye,6 A. Li,10 J. Gansert,10 R. Coffin,11 M. Ross,12 1. Rutgers Cancer Institute of New Jersey, Rutgers, NJ; 2. Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; 3. The University of North Carolina at Chapel Hill, School of Medicine, Chapel Hill, NC; 4. Hubert H. Humphrey Cancer Center, Robbinsdale, MN; 5. Mary Crowley Cancer Research Center, Dallas, TX; 6. University of Louisville, Louisville, KY; 7. Department of Surgery, Emory University, Atlanta, GA; 8. Northern California Melanoma Center, San Francisco, CA; 9. Vanderbilt University Medical Center, Nashville, TN; 10. Amgen Inc., Thousand Oaks, CA; 11. Amgen Inc., South San Francisco, CA; 12. MD Anderson Cancer Center, Houston, TX; 13. Amgen, Woburn, MA.

**Background:** T-VEC is an HSV type-1-derived oncolytic immunotherapy that selectively replicates in tumors and produces GM-CSF to enhance systemic antitumor immune responses. OPTiM is a randomized, phase 3 trial of T-VEC or GM-CSF in patients (pts) with unresected melanoma with regional or distant metastases (NCT01769704). OPTiM met the primary endpoint of an improvement in durable response rate (partial or complete response continuous for ≥6 months starting within 12 months) with T-VEC vs GM-CSF (16% vs 2%, p < 0.0001) with most common adverse events (AEs) for T-VEC being fatigue, chills, and pyrexia; no ≥ grade 3 AEs occurred in ≥3% of pts in either arm (Andtbacka et al. ASCO 2013). The primary analysis (PA) of OS is reported here. **Methods:** Key entry criteria were age ≥18 years, ECOG PS ≤1, unresectable melanoma stage IIIB/IIIC/IV, injectable cutaneous, SC, or nodal lesions, LDH ≤1.5x ULN, ≤3 visceral lesions (excluding lung), and none ≥3 cm. Pts were randomized 2:1 to intrallesional T-VEC (initially ≤4 mL x 10^6 pfu/mL then after 3 weeks, ≤4 mL x 10^6 pfu/mL q2W) or SC GM-CSF (125 μg/m^2 qd x 14 days q28d). The PA of OS (290 planned events) had 90% power to detect a HR of 0.67 with two sided α = 0.05. **Results:** 436 pts were in the ITT set: 295 (68%) T-VEC, 141 (32%) GM-CSF. 57% were men; median age was 63 years. An increase of 4.4 months in OS with T-VEC vs GM-CSF was observed (p = 0.051): HR (95%CI) = 0.787 (0.621.00); median (95%CI) OS was 23.3 (19.5-29.6) months with T-VEC vs 18.9 (16.0-23.7) months with GM-CSF. In an exploratory subgroup analysis, effects of TVEC on OS were pronounced among pts with stage IIIB/IIIC/V1M1a melanoma (HR [95%CI] = 0.57 [0.40-0.81]) and treatment-naive pts (HR [95%CI] = 0.50 [0.35-0.73]). **Conclusions:** T-VEC provided an improvement in OS approaching statistical significance in the ITT population, with effects pronounced in treatment-naive or stage IIIB/IIIC/V1M1a pts. T-VEC represents a novel potential new treatment option for pts with injectable melanoma and limited visceral disease.

**P257**

**Utility of Sentinel Node Biopsy in Patients with T4 Melanoma**


**Introduction:** Sentinel node (SN) biopsy is the most powerful prognostic factor for patients with intermediate thickness (1-4 mm) melanoma. However, the utility in patients with T4 lesions is less clear. **Methods:** All clinically node-negative T4 melanoma patients undergoing SN between 1996-2013 were identified from a prospectively maintained IRB approved database. Demographics (age/sex) and tumor characteristics (Breslow depth, ulceration, mitotic rate, SN status, nodal recurrence and visceral metastases) were analyzed by Fisher’s exact, Wilcoxon rank sum, and Log rank tests. **Results:** 118 patients were identified (40% T4a/60% T4b). 16 (34%) T4a had a positive SN and 18 (38%) had regional or distant recurrences. 32 (45%) T4b had a positive SN and 37 (52%) had regional or distant recurrences. Median recurrence free survival (RFS) for T4a and T4b was 4.06 and 1.45 years (p = 0.003) and median overall survival (OS) was 7.18 and 3.08 years (p = 0.0004). SN negative patients had better median RFS (3.5 vs 1.3, p = 0.005) and OS (6.5 vs 3.1, p = 0.03) than those with a positive SN. T4a (p = 0.08) and T4b (p = 0.12) subgroups had no significant differences in OS when comparing SN negative to SN positive, although significant differences in RFS were seen in both the T4a (7.18 v 2.3 years, p = 0.03) and T4b (2.5 v 0.78 years, p = 0.05) subgroups. **Conclusions:** Although RFS in SN positive T4 patients is significantly shorter, OS appears to be driven by nodal-independent factors. With the advent of efficacious systemic therapy options, these patients should strongly be considered for inclusion in clinical trials.

**P258**

**NanoString Analysis Prediction of Outcome in a Prospective Trial of Tumor Infiltrating Lymphocytes (TIL) Therapy**


**Background:** TIL therapy is a promising modality for unresectable metastatic melanoma that is associated with >20% durable complete responses reported by our group and others. However, predictive markers of outcome from TIL therapy are lacking. Therefore, we evaluated biomarkers predicting outcome using the NanoString platform using tumors harvested for TIL inclusion in clinical trials.

**Methods:** An IRB-approved pilot trial was conducted on 8 pts with metastatic melanoma. Pts were grouped into two categories based on their response to TIL therapy by RECIST 1.1 criteria. Pts with complete (CR) and partial response (PR) were grouped as “responders”, and pts with stable disease (SD) or progressive disease (PD) were grouped...
as “non-responders”. A custom NanoString panel of 45 genes of potential significance in melanoma and/or tumor immunity was used to assay 12 FFPE tumor samples resected for TIL. **Results:** Of 12 samples analyzed, six were from responders (three CR and three PR), and six were from non-responders (one SD and five PD). Genes trending towards significance, warranting further consideration, included CCL8, 18, 19, 21, FcRL2, STAT3, FOXP3, VEGF and HDAC11. Of these, only histone deacetylase 11 (HDAC11) significantly correlated with response (Figure, p = 0.03). **Conclusions:** NanoString analysis revealed several potential biomarkers of response to TIL therapy. HDAC11 expression correlated significantly with clinical response, warranting further examination of its role in melanoma tumor immunity. HDAC11 has been reported to be important for the proliferation and survival pathways of multiple cancers and also negatively regulates important immunological functions. Our data suggest that targeting HDAC 11 prior to TIL harvest and/or during early *in vitro* TIL generation merits further investigation in order to improve outcome to TIL therapy.

**Figure 1.** HDAC11 expression is decreased in TIL therapy responders. HDAC11 mRNA expression was assessed in six TIL responder and six non-responder melanoma tumors by NanoString assay. Significance was determined by a non-paired, two tailed t-test.

### P259

**Neurotropic Melanomas: Clinical Behavior and Radiotherapy Responsiveness**


oma Institute Australia, North Sydney, NSW, Australia.

Background Neurotropic melanomas is a rare subtype of melanoma that forms nerve-like structures or invade nerves. It has a propensity to recur locally, but a lower risk of distant metastasis, even though the presence of neurotropism is generally thought to be a poor prognostic factor. However, the evidence on their clinical behaviour is limited to a few very underpowered studies and therefore we sought to address this in a large retrospective cohort study.

Methods Using the prospectively maintained institutional Melanoma Research Database, we identified all 671 patients with a neurotropic primary melanoma and a randomly selected control cohort of 718 patients. Multivariate statistical analyses (MVA) were performed with the endpoints of sentinel lymph node biopsy (SLNB) status, recurrence, melanoma-specific overall survival (OS) and response to adjuvant radiotherapy. Results are given as Hazard Ratio (95% Confidence Interval) for MVA unless otherwise specified. Results The univariate tendency for increased local recurrence (HR: 1.93 (1.22-3.05), p = 0.005) was completely abrogated on multivariate analysis (HR: 1.28 (0.73-2.25), p = 0.39). There was no significant effect of neurotropism on OS (HR: 0.79 (0.55-1.15), p = 0.22), however there was a reduced likelihood of SLNB positivity (HR: 0.61 (0.41-0.89), p = 0.01). The overall rate of SLNB positivity was 12% in the neurotropic melanomas, with rates of 21% in the non-desmoplastic and 8% in the desmoplastic sub-groups. The importance of adequate excision margins for all site recurrence was supported (HR: 0.46 (0.31-0.68), p = 0.001). Furthermore, the role of adjuvant radiotherapy halved the risk of recurrence in those with inadequate margins (HR: 0.50 (0.27-0.92), p = 0.03). Conclusions Neurotropism does not alter the risk of melanoma recurrence or survival, but does reduce the likelihood of SLNB positivity. Adequate excision margins are paramount for successfully treating these neurotropic melanomas, but when this is not feasible, adjuvant radiotherapy should be given.

### P260

**Does Serum Vitamin D Level Show a Durable Correlation with Outcome of Locoregional Melanoma?**


Introduction: Although recent studies indicate the prognostic value of vitamin D in melanoma, the relative importance of serum vitamin D level at diagnosis has not been established. Methods: Our database was queried to identify all patients who were seen for stage II/III melanoma between November 1973 – October 2011, whose serum specimens were collected within 4 months after diagnosis, and whose follow-up information was available. Serum 25-hydroxyvitamin D levels were measured by chemiluminescence assay and analyzed as a continuous variable in a multivariable analysis that included age at initial diagnosis, sex, Breslow depth, tumor ulceration, primary tumor site, and stage. Results: The 310 study patients (103 stage II, 207 stage III) had a mean age of 50.5±16.2 years; most (62.3%) were male. Primary tumors had a median Breslow depth of 3.00 mm (interquartile range 1.6-4.6 mm), and 43.9% were ulcerated. Primaries were on the trunk (35.5%), head/neck (22.0%), upper extremity (16.8%), or lower extremity (22.7%). Mean serum 25-hydroxyvitamin D level was 65.7±21.3 Nmol. At a median follow-up time of 90.84 months, the three most significant factors for prolonged disease-specific survival were female sex (p=0.0002), thin Breslow depth (p=0.0179), and higher vitamin D level (p=0.0105). Conclusions: The direct correlation between serum vitamin D level and disease-specific survival of patients with locoregional cutaneous melanoma suggests a benefit for maintaining normal levels of vitamin D in patients with melanoma.

### P261

**Is it Time for a Shift in the Treatment of Advanced Resectable Stage III and Stage IV Oligometastatic Melanoma? Results of a Pilot Trial and Plans for a Randomized Trial of Neoadjuvant Therapy versus Upfront Surgery**


Background: A high rate of significant response is observed with the recently FDA-approved BRAF and combination BRAF/MEK inhibitor regimens in the treatment of disseminated Stage IV and unresectable Stage III melanoma. Given these observations along with the high rate of distant relapse observed following upfront definitive surgery for advanced but resectable Stage III and oligometastatic stage IV melana disease, it is rational to examine the efficacy of a neo-adjuvant treatment strategy in this patients (pt) population. Therefore we propose a pilot trial of upfront BRAF/MEK inhibitor therapy. Methods: Eligible pts include advanced or borderline resectable stage III nodal and or intranodal disease or oligometastatic stage IV disease with proven BRAF 600 VE mutations. Pts are treated with 8 weeks of BRAF-targeted therapy followed by definitive surgery. Tumor tissue samples are obtained prior to treatment, and after surgery to explore mechanisms of response and resistance. Results: To date, 6 pts have been treated. The treatment was well tolerated in all pts. The following observations have been made: all pts had radiographic/clinical responses, pathologic evaluation from surgical specimens showed extensive fibrosis with little, to no, viable tumor cells in 2 pts, and significant necrosis with remaining viable tumor in the other 3, pts, and in 1 pt the radiographic response over-estimated the pathologic response. Genomic and immune profiling studies on these pts are ongoing, and will provide insight into response to therapy. Conclusions: Early results justify the planned randomized phase II trial using neoadjuvant BRAF and MEK inhibition vs the current standard of care in patients with advanced resectable BRAF mutated stage III and oligometastatic stage IV melanic metastases. The primary comparative endpoint is RFS and biologic endpoints in the neo-adjuvant(experimental) treatment arm. Long term survival outcomes may provide the rationale for a shift in treatment.
The Impact of Neoadjuvant Chemotherapy and Extended Lymphadenectomy on Outcomes of Gastrectomy Performed for Malignancy

Introduction - The current NCCN guideline states that gastric resection for malignancy should include perigastric nodes (D1) and the nodes along the named vessels (D2) with the goal of examining at least 15 lymph nodes. Furthermore, while randomized trials have shown that preoperative chemotherapy can improve survival, fear of added morbidity has slowed the adoption of these quality measures. Our aim is to determine the incidence of lymphadenectomy and preoperative chemotherapy and the impact of these quality measures on short-term morbidity and mortality.

Methods - Review of the NSQIP participant user data file was performed from 2005-2011. CPT codes and ICD-9 diagnosis codes were used to examine outcomes of gastrectomies performed for gastric malignancy. Results - Our selection criteria yielded 2,601 cases. Overall, 16.1% of the patients underwent extended lymphadenectomy while 6.2% of the patients underwent preoperative chemotherapy. The rate of extended lymphadenectomy and chemotherapy did not change significantly from 2005 to 2011. Patients receiving neoadjuvant chemotherapy were younger and more likely to have disseminated cancer, however the rate of additional organ resection and medical co-morbidities were similar between the two groups. The mortality in the neoadjuvant group was not significantly different from the group that did not receive chemotherapy (2.5% vs 3.4%, p = 0.506). The major complication rates were similar between the two groups (26.8% vs 23.4%, p = 0.349). Neoadjuvant chemotherapy (OR 1.1, 95% CI: 0.3-3.2, p = ns) and lymphadenectomy (OR 0.5, 95% CI: 0.2-1.2, p = ns) were not associated with an increase in morbidity or mortality. However advanced age, total gastrectomy, additional organ resection, weight loss, dyspnea, and functional dependence were associated with an increase in mortality (table 1).

Conclusion - Extended lymphadenectomy and neoadjuvant chemotherapy did not result in increased morbidity or mortality in the NSQIP cohort. The rate of adoption for both therapies remain low in the United States while the morbidity and mortality of the operation remains high.

Demographics and Outcomes of Patients Receiving Neoadjuvant Chemotherapy Compared to No Chemotherapy Group

<table>
<thead>
<tr>
<th>Characteristics/Outcomes</th>
<th>No Chemotherapy (n=2,359)</th>
<th>Receiving Chemotherapy (n=162)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.9 ± 13.6</td>
<td>61.8 ± 13.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>1,416 (58.1%)</td>
<td>97 (59.9%)</td>
<td>0.875</td>
</tr>
<tr>
<td>Total gastrectomy</td>
<td>927 (39.0%)</td>
<td>99 (61.1%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dismembered Cancer</td>
<td>103 (4.7%)</td>
<td>34 (14.8%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Extended Lymphadenectomy</td>
<td>382 (16.7%)</td>
<td>26 (22.2%)</td>
<td>0.128</td>
</tr>
<tr>
<td>Pancreatic Resection</td>
<td>54 (2.2%)</td>
<td>5 (3.1%)</td>
<td>0.702</td>
</tr>
<tr>
<td>Hepatic Resection</td>
<td>29 (1.2%)</td>
<td>3 (1.9%)</td>
<td>0.359</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>120 (4.9%)</td>
<td>11 (6.8%)</td>
<td>0.292</td>
</tr>
<tr>
<td>Duodenectomy</td>
<td>18 (0.7%)</td>
<td>2 (1.2%)</td>
<td>0.484</td>
</tr>
<tr>
<td>Small bowel Resection</td>
<td>67 (2.7%)</td>
<td>7 (4.8%)</td>
<td>0.243</td>
</tr>
<tr>
<td>Colorectum</td>
<td>68 (2.8%)</td>
<td>8 (4.9%)</td>
<td>0.115</td>
</tr>
<tr>
<td>Death</td>
<td>84 (3.4%)</td>
<td>4 (2.5%)</td>
<td>0.506</td>
</tr>
<tr>
<td>Days to Death</td>
<td>12.6 ± 8.0</td>
<td>12.5 ± 7.9</td>
<td>0.074</td>
</tr>
<tr>
<td>Days to Discharge</td>
<td>11.1 ± 8.8</td>
<td>10.1 ± 6.6</td>
<td>0.074</td>
</tr>
<tr>
<td>Major Complications</td>
<td>654 (26.8%)</td>
<td>38 (23.5%)</td>
<td>0.349</td>
</tr>
<tr>
<td>ASA Classification</td>
<td>1/II</td>
<td>282 (32.1%)</td>
<td>0.184</td>
</tr>
<tr>
<td>III</td>
<td>1,502 (61.6%)</td>
<td>270 (60.6%)</td>
<td>0.689</td>
</tr>
<tr>
<td>IV Multivariate Analysis of Prognostic Factors Associated with Mortality</td>
<td>150 (6.2%)</td>
<td>95% Confidence Interval: &lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Prognostic Factors</td>
<td>Adj. OR</td>
<td>p-Value</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>3.3</td>
<td>(2.0-5.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Colon resection</td>
<td>2.9</td>
<td>(1.7-7.1)</td>
<td>0.017</td>
</tr>
<tr>
<td>Small bowel resection</td>
<td>4.5</td>
<td>(1.9-10.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>3.9</td>
<td>(1.9-7.4)</td>
<td>0.029</td>
</tr>
<tr>
<td>Weight loss</td>
<td>1.7</td>
<td>(0.2-29)</td>
<td>0.036</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>2.0</td>
<td>(1.3-3.5)</td>
<td>0.011</td>
</tr>
<tr>
<td>Cancer stage</td>
<td>3.2</td>
<td>(1.6-6.1)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Major complication was defined as experiencing one of the following adverse events: superficial or deep wound infection, organ space infection, wound disruption, pneumonia, return to operating room, prolonged respiratory failure, pulmonary embolism, deep venous thrombosis, renal failure, stroke, coma, sepsis, septic shock, cardiac arrest, or myocardial infarction.
**P265**

An Outcomes Analysis using Cost-utility Comparing the Sartorius Flap versus VAC Therapy for the Definitive Treatment of the postoperative Infected Groin Wound

A. Chatterjee,1 T. Kosowski,2 B. Pyfer,3 A. Offodile,4 J. Attwood,5 B. Czerniecki.1 1. Surgery, University of Pennsylvania, Drexel Hill, PA; 2. Miami Breast Center, Miami, FL; 3. Dartmouth Medical School, Hanover, NH; 4. Lahey Clinic, Burlington, MA; 5. Maine Medical Center, Portland, ME.

Objective: The oncologic resection of tumor and/or associated lymph nodes in the groin is a relatively common operation. Subsequent post-operative complications include groin infections and regional exposure of vascular structures. The management of such wounds is challenging and can include the use of local flaps or negative pressure wound therapy (also known as VAC therapy). Both approaches incur cost and have variability in clinical success. Given this, our goal was to perform a cost-utility analysis comparing the sartorius flap to negative pressure wound therapy in the treatment of an infected groin wound. Methods: Cost utility methodology involved a literature review compiling outcomes for the flap and VAC interventions, obtaining utility scores for complications to estimate quality adjusted life years (QALYs), accruing costs using DRG and CPT codes for each intervention, and developing a decision tree that could portray the more cost-effective strategy. We also performed sensitivity analysis to check the robustness of our data. As most local flap use and VAC use for groin wounds were related to infected vascular groin structures, we included Szilagy III and Samson III and IV grades of infected groin grafts in our literature review for our study. Results: 32 studies were used pooling 384 patients (234 sartorius flaps, 150 VAC). In general, sicker patients were treated with VAC therapy. Decision tree analysis noted that VAC therapy was the more cost-effective option (Figure 1). It was the dominant treatment option given that it was more clinically effective by an additional 0.54 QALYs when it cost greater than $47,000. Conclusion: For the oncologic surgeon treating an infected, post-operative groin wound, VAC therapy is a cost-effective definitive treatment choice compared to the sartorius flap.

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**P266**

Preoperative Leukopenia is not associated with postoperative Outcomes in Cancer Patients undergoing Abdominal Surgery: A Retrospective Cohort Study

L. L. Davis,* M. Stefan, J. Garb, R. Arenas, J. Kuhn, Baystate Medical Center/Tufts University School of Medicine, Springfield, MA.

Introduction: The purpose of this study is to compare preoperative characteristics and operative outcomes in leukopenic cancer patients undergoing emergent or elective abdominal surgery with similar non-leukopenic patients and determine if preoperative leukopenia is associated with surgical morbidity and mortality. Methods: Retrospective cohort study using the National Surgical Quality Improvement Program Database, containing prospectively collected data from >250 hospitals on 135 variables including preoperative comorbidities, laboratory values, intraoperative details, and 30-day postoperative morbidity and mortality. We included adult patients who received chemotherapy for malignancy within 30 days prior to surgery and underwent emergent or elective abdominal surgery between 2008-2011. Leukopenia was defined as preoperative WBC<4000/ml within 2 days prior to surgery. Primary outcomes included 30-day mortality and 30-day composite morbidity, which combined several major complications. The association of leukopenia and outcomes was examined using multiple logistic regression controlling for confounding factors identified on univariate analysis. Results: A total of 4,369 patients were included, and 20.2% had preoperative leukopenia. Mean age was 60.7 years, 50.2% were male, 83% were white and 18.5% received radiotherapy within prior 90 days. We included adult patients who received chemotherapy for malignancy within 30 days prior to surgery and underwent emergent or elective abdominal surgery between 2008-2011. Leukopenia was defined as preoperative WBC<4000/ml within 2 days prior to surgery. Primary outcomes included 30-day mortality and 30-day composite morbidity, which combined several major complications. The association of leukopenia and outcomes was examined using multiple logistic regression controlling for confounding factors identified on univariate analysis. Results: A total of 4,369 patients were included, and 20.2% had preoperative leukopenia. Mean age was 60.7 years, 50.2% were male, 83% were white and 18.5% received radiotherapy within prior 90 days. Emergency cases comprised 36.2%. Compared with non-leukopenic patients, those with leukopenia were more likely to undergo emergency procedures (43% vs. 34%, p=0.001), to be in a higher ASA class (p=0.001), to have a higher operative wound classification (p<0.001) and were less likely to be functionally independent at baseline (p=0.001).
Multiple Logistic Regression on Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukopenia</td>
<td>1.30</td>
<td>0.94 - 1.53</td>
</tr>
<tr>
<td>Emergency Surgery</td>
<td>1.40</td>
<td>1.15 - 1.74</td>
</tr>
<tr>
<td>Smoker</td>
<td>1.30</td>
<td>1.01 - 1.64</td>
</tr>
<tr>
<td>Functional Status</td>
<td>1.61</td>
<td>1.41 - 1.85</td>
</tr>
<tr>
<td>Wound Classification</td>
<td>1.11</td>
<td>1.00 - 1.24</td>
</tr>
<tr>
<td>ASA Classification</td>
<td>2.20</td>
<td>1.85 - 2.61</td>
</tr>
<tr>
<td>Age</td>
<td>1.01</td>
<td>1.00 - 1.02</td>
</tr>
<tr>
<td>Preoperative BUN</td>
<td>1.02</td>
<td>1.02 - 1.03</td>
</tr>
</tbody>
</table>

P267
Impact of Restricted Fluid Administration during Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion on perioperative Outcomes


Introduction: Excessive fluid administration in the perioperative period is associated with increased morbidity and mortality. Liberal fluid administration is common practice during cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion (CRS/HIPEC) for peritoneal malignancies. We investigated patient outcomes after liberal vs. restrictive fluid management during CRS/HIPEC. Methods: At our institution, a shift from liberal to restrictive fluid administration during CRS/HIPEC commenced in 2008. We compared outcomes of ten patients with appendiceal or colorectal carcinomatosis undergoing CRS/HIPEC between 2006-2008 (liberal cohort) to ten patients undergoing CRS/HIPEC between 2010-2012 (restrictive cohort). Patients receiving cisplatin chemoperfusion were excluded. Patients were matched for peritoneal cancer index (PCI), operative time and intraoperative blood loss. The restrictive cohort received lactated ringers and colloid replacement for blood loss. Pulse-contour analysis was used to determine cardiac output. Results: There was no significant difference between median PCI (28 vs. 26, p=0.32), operative time (558 vs. 693 min, p=0.069) or intraoperative blood loss (2 vs. 1.5 L, p=0.46) between the liberal vs. restrictive cohorts. Total fluid administered to the liberal cohort averaged 27 L, significantly more than the 22 L administered to the restrictive cohort (p=0.015). Mean packed red blood cell (3 U vs. 1 U, p=0.14) plasma (0.8 U vs. 0.7 U, p=0.73) and platelet (0.1 U vs. 0.1 U, p=0.99) administration did not differ significantly between the groups. The liberal cohort had a significantly longer median time to extubation (2 days vs. 0.3 days, p=0.014) and increased median ICU length of stay (6 days vs. 3 days, p=0.016). Median hospital length of stay did not differ significantly between the liberal vs. restrictive groups (18 days, vs. 14 days, p=0.74). Clavien-Dindo grade 3-4 morbidity did not differ significantly between the groups. (30% vs. 30%, p=0.99). Conclusions: Restrictive goal-directed fluid administration during CRS/HIPEC leads to earlier extubation and decreased ICU length of stay.

P268
Volume-outcomes and Resource Utilization in Esophagus and Pancreas Cancers

M.A. Healy,* H. Yin, D.L. Wong, Department of Surgery, University of Michigan, Ann Arbor, MI.

Introduction: Lower cancer mortality at high volume hospitals has been observed, suggesting more effective practice patterns. It is unclear whether these hospitals use more resources, and thus "spend more to get more," or if they simply use the same resources more efficiently. For patients with poor prognosis cancers, relationships between volume, survival and resource utilization have not been specifically studied. Methods: We examined all fee-for-service inpatient claims in the Surveillance, Epidemiology, and End Results (SEER)-Medicare registry for elderly patients (age 65 - 99) diagnosed with esophagus (EC) and pancreas (PC) cancers between 2005-2009 with follow-up to 2011. Patients were attributed to hospitals where they received the majority of care. Very low volume hospitals (<10 patients with each cancer) were excluded. We performed a patient and tumor adjusted hospital-level analysis with clustering: hospitals were stratified by patient volume and significance tested using the Wilcoxon rank-sum test. Results: We identified 4,289 EC and 13,336 PC patients during this time period. Resource utilization was measured by rates of surgical resection, chemotherapy, and ICU services. In the highest vs. lowest volume hospitals, for EC, rates of surgical resection (p<0.001) and chemotherapy (p<0.001) were significantly higher while 2-year survival was also significantly higher (37.6% vs. 23.6%, p=0.05). For PC, in the highest vs. lowest volume hospitals, rates of surgical resection (p<0.001) and chemotherapy (p<0.001) were significantly higher while 2-year survival was also significantly higher (15.9% vs. 5.8%, p=0.001). Rates of ICU use were significantly higher for both EC (p<0.01) and PC (p<0.001) in the highest vs. lowest volume hospitals. Conclusion: In EC and PC, higher volume hospitals are associated with increased utilization of cancer-directed therapy and higher 2-year survival. ICU utilization is also significantly higher in these hospitals. This is informative for surgeons and oncologists, suggesting the benefits of cancer-directed therapy, but also the ability of high volume hospitals to appropriately and not wastefully use ICU services when they can be of benefit to patients.

P269
ACGME Complex General Surgical Oncology Accreditation: Attitudes and Perceptions of Current and Future Fellows


Introduction- With the first qualifying exam administered September 15, 2014, Complex General Surgical Oncology (CGSO) is now a board certified specialty. We aimed to assess the attitudes and perceptions of current and future surgical oncology fellows regarding the recently instituted ACGME accreditation. Methods - A 29 question anonymous survey was distributed to active fellows in accredited fellowship programs and applicants to our fellowship program. Results - There were 109 responses, 78 current fellows representing 71% of all active fellows, and 31 candidate fellows. Almost all (96%) respondents were aware of the recent accreditation process and were also aware (91%) that graduating from ACGME accredited program leads to board eligibility. Significantly more candidates indicated they were likely to apply to an ACGME accredited program than current fellows (84% vs 55%, p=0.05). However, both groups stated that their decision to specialize in surgical oncology was not influenced by the ACGME accreditation (81% candidates vs 79% fellows, p=0.800). Nearly half (47%) of the respondents stated that ACGME accreditation will not impact the education of surgical oncologists. Twenty-eight percent expressed a concern for negative impact while 11% believed that there would be a positive impact. While majority of the respondents were concerned with the cost of the exam (82%) and expressed anxiety in preparing for another board exam (76%), the majority (84%) stated that obtaining a new board certification is important to them and felt that it would be helpful (75%) in obtaining their future career goals. Interestingly, candidate fellows appeared more focused on a career in general complex surgical oncology (p=0.044, highlighting the impact that fellowship training may have on organ-specific subspecialization (Table 1). Conclusion – The majority of the surveyed surgical oncology fellows and candidates believe that obtaining board certification in CGSO is important and will help them pursue their career goals. However, the decision to specialize in surgical oncology does not appear to be motivated by ACGME accreditation or the new board certification.
Table 1- Demographics and Career Goals of the Respondents (N=109)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Candidates (N=31)</th>
<th>Fellows (N=78)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>16 (52%)</td>
<td>44 (56%)</td>
<td>0.601</td>
</tr>
<tr>
<td>Female</td>
<td>15 (48%)</td>
<td>34 (44%)</td>
<td></td>
</tr>
</tbody>
</table>

Type of General Surgery Residency

<table>
<thead>
<tr>
<th>Category</th>
<th>Candidates (N=31)</th>
<th>Fellows (N=78)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community/Military Hospital</td>
<td>3 (19%)</td>
<td>5 (65%)</td>
<td></td>
</tr>
<tr>
<td>University/University Affiliated Hospital</td>
<td>20 (65%)</td>
<td>72 (92%)</td>
<td></td>
</tr>
<tr>
<td>Cancer Center</td>
<td>3 (100%)</td>
<td>75 (99%)</td>
<td></td>
</tr>
<tr>
<td>Academic/University Affiliated Practice</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Private Practice/Research/Additional Training</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
</tbody>
</table>

Multiple answer choices were allowed for board preparation and sub-specialty questions and the percentages will exceed 100%. Not all columns will add up to the total and not all percentages will add up to 100%.

P270

The Management of Small Asymptomatic Pancreatic Neuroendocrine Tumors: A Matched Case-control Study


Background: Overdiagnosis and overtreatment has become an evolving challenge for several cancer sub-types. We hypothesized that a substantial portion of incidentally diagnosed small pancreatic neuroendocrine tumors (PanNET) are overtreated as a result of overdiagnosis and that non-operative management may be reasonable for selected patients.

Methods: Consecutive patients evaluated for incidentally discovered, sporadic, stage I-II PanNET were analyzed retrospectively. Diagnosis was determined either by pathology or unequivocal imaging characteristics. Patients selected for radiographic surveillance (RS) were matched with patients who underwent resection based on tumor size at initial imaging.

Results: During the study period (2000-2013), an increasing number of patients were evaluated and an increasing number were managed by RS (Figure 1). Median tumor diameter was 3.1 cm (2-4.5) during the initial imaging. At the time of last follow-up of the RS group, median tumor size was similar between the RS vs resection groups (1.2 cm (0.8-1.7) vs 1.3 cm (1.9), respectively, p=0.4). The resection group was younger and had a longer median follow-up compared to the RS group (58 vs 65 years, p<0.001; 50 vs 29 months, p=0.006, respectively). At the time of last follow-up of the RS group, median tumor size had not changed (1.2 cm, p=0.4), no patient had developed metastases, and none had experienced radiographic changes in the primary tumor that prompted resection. Within the resection group, low-grade (G1) pathology was recorded in 74 (95%) tumors, one patient had node positive disease, and five developed recurrence (6%). No patient in either group died from disease. Death from other causes occurred in 7 out of 159 (4%) patients.

Conclusion: In this study, no patient who was selected for observation developed metastases or died from disease after a median follow-up of almost 2.5 years. RS for stable, small, incidentally discovered PanNET is reasonable in selected patients.

P271

Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy Perfusion for Carcinomatosis: 100 Cases at a Single Institution

V.V. Simiana, S.R. Bommareddi, L.V. Mann, G. Mann,* Surgery, University of Washington, Seattle, WA.

Introduction: Peritoneal carcinomatosis is seldom curable, with median survival of 6 to 12 months. Maximal cytoreductive surgery (CS) with heated intraperitoneal chemotherapy perfusion (HIPEC) can improve oncologic outcomes, but is associated with high complication rates. Increasing surgeon experience with CS/HIPEC has the potential to reduce complications and improve outcomes.

Methods: A retrospective review of all patients undergoing CS/HIPEC by a single surgeon at the University of Washington. Experience was divided into first versus second 50 cases and patient characteristics, operative details, morbidity and outcomes were compared.

Results: From 2001-2014, 90 patients underwent 100 CS/HIPEC procedures (mean age 57 years, 68% female). Diagnoses included diffuse peritoneal adenosquamous (42%), colorectal cancer (18%), appendiceal cancer (18%), and mesothelioma (13%). Compared to the initial experience, the second 50 cases included more high-grade tumors (68% vs 52%) and greater disease burden. This suggests that increasing experience with CS/HIPEC can meaningfully reduce morbidity and improve outcomes in rigorously selected patients. Survival is improved in selected patients undergoing this aggressive operative treatment, compared to historical controls.

P272

Quality Improvement in Mastectomy Processing: Routine Use of a Standardized Mastectomy Diagram by Surgeons Improves Accuracy and Timeliness of Final Pathology Report

A. Pass, J. Bishop,* R. Babkowski, Z. Cheng, Surgery, Stamford Hospital, Stamford, CT.

Introduction: Identification of non-palpable lesions in the mastectomy specimen can be difficult, sometimes requiring postsurgical image-guided localization and extending the time for a final pathology report (FPR). The completion of a standardized diagram (SD) of lesion(s) by the breast surgeon to aid pathologists in identifying lesion(s) of interest within a mastectomy specimen was instituted as a prospective quality improvement measure.

Objectives: Improve identification of breast cancer(s) and lesion(s) of interest in patients undergoing mastectomy.

Aims: Determine the effectiveness of SD in improving accuracy and timeliness of FPR.

Methods: A review of patients undergoing mastectomies at a Community Breast Care Center from July 2013 through June 2014 was performed. Usual processing (U) of mastectomy specimens was performed during the first six months and SD processing for the second six months. Days from specimen receipt to FDR and number of breast lesions identified were recorded for U versus SD. Statistical comparisons were made.
using the independent t-test with $p=0.05$ considered significant. **Results:** In 27 U specimens with a mean of 1.3±0.2 lesions, FPR was 8.3±0.9 days whereas in the 34 SD specimens with a mean of 2.1±0.3 lesions ($p=0.02$), FPR was significantly decreased to 6.1±0.5 days ($p=0.03$). **Conclusions:** Routine use of SD in the mastectomy patient improves the accuracy and timeliness of FPR.

**P273**

Maastricht Delphi Consensus on Event Definitions for Classification of Recurrence in Breast Cancer Research


**Background:** In breast cancer studies, many different endpoints are used. Definitions are often not provided or vary between studies. For instance, “local recurrence” may include different components in similar studies. This limits transparency and comparability of results. This project aimed to reach consensus on the definitions of local event, second primary breast cancer, regional and distant event for breast cancer studies. **Methods:** The RAND-UCLA Appropriateness method (a modified Delphi method) was used. A Consensus Group of international breast cancer experts was formed, including representatives of all involved clinical disciplines. Consensus was reached in two rounds of online questionnaires and one meeting. **Results:** Twenty-four international breast cancer experts participated. Consensus was reached on 134 items in four categories. Local event is defined as any epithelial breast cancer or ductal carcinoma in situ in the ipsilateral breast, or skin and subcutaneous tissue on the ipsilateral thoracic wall. Second primary breast cancer is defined as epithelial breast cancer in the contralateral breast. Regional events are breast cancer in ipsilateral lymph nodes. A distant event is breast cancer in any other location. Therefore, this includes metastasis in contralateral lymph nodes and breast cancer involving the sternal bone. If feasible, tissue sampling of a first, solitary, lesion suspected for metastasis is highly recommended. **Conclusion:** This project resulted in consensus-based event definitions for classification of recurrence in breast cancer research. Future breast cancer research projects should adopt these definitions to increase transparency. This should facilitate comparison of results and conducting reviews as well as meta-analysis.

**Summary of the consensus on the definition of local event, second primary breast cancer, regional event, and distant event for classification of recurrence in breast cancer research**

**Local event** (after mastectomy or breast conserving therapy)
- Any epithelial breast cancer or DCIS in ipsilateral breast tissue
- Breast cancer in surgical scar
- Breast cancer in biopsy tract

**Second primary breast cancer**
- Any epithelial breast cancer in the contralateral breast (with or without lymph node metastases or that side)

**Regional event**
- Breast cancer in ipsilateral axillary, infraclavicular, supracervical, internal mammary/parietal, or intramammary lymph node

**Distant event**
- Breast cancer in any organ other than breast, excluding the items listed under local event, second primary breast cancer, and regional event.
- Therefore also including any breast cancer event involving the sternal bone
- Therefore also including breast cancer in contralateral lymph nodes (axillary, infraclavicular, supracervical, and internal mammary), as well as synchronous ipsilateral or contralateral breast malignancy or distant metastasis

**Tissue sampling**
- Pathology confirmation (histology or cytology) of a first, solitary lesion suspected for metastasis is highly recommended if feasible. If tissue sampling is impossible, unconfirmed metastasis is acceptable at discretion of the treating physician.
- Multiple lesions consistent with metastases on imaging are acceptable without pathology confirmation.

* Ipsilateral thoracic wall: area between contralateral sternal border medially, posterior axillary line laterally, the clavicle superiorly and the anterior axillary line superiorly. **Abbreviations:** DCIS ductal carcinoma in situ, LCIS lobular carcinoma in situ.

**P274**

Relative Incidence of Uterine Sarcoma and Surgical Treatments for Fibroids

F. Dinan,1* L. Havrilesky,2 E. Myers,2 I. Medical Oncology, Duke Cancer Institute, Durham, NC; 2. Duke University Medical Center, Durham, NC.

**Introduction:** Uterine fibroids are the most common benign neoplasm of the uterus. Whereas fibroids themselves are benign, uterine sarcomas may have similar symptoms and appearance on imaging. Laparoscopic techniques that use electricity to morcellate fibroids into smaller pieces to facilitate minimally invasive removal pose a risk of spreading occult sarcomas. Recent attention to this possibility has led to reassessment of the harm/benefit trade-offs of these techniques by professional societies, the Food and Drug Administration, and device manufacturers. **Methods:** We estimated age- and race-specific incidence of uterine soft tissue sarcomas using data from the Surveillance, Epidemiology, and End Results (SEER) program, and the incidence of inpatient procedures for fibroids from the Nationwide Inpatient Sample (NIS), for 2002-2011. We adjusted the NIS estimates to account for outpatient procedures using weights derived from the North Carolina State Inpatient Database (SID) and State Ambulatory Surgery Database (SASD), and used these estimates to calculate age- and race-specific ratios of fibroid procedures to uterine sarcomas. **Results:** A total of 39,173 discharges within the NC SID, 17,391 discharges within the NC SASD, and a weighted 1,914,584 discharges (395,128 actual discharges) within the NIS met study criteria for inclusion. Both sarcomas
and fibroid procedures were more common in black women and varied by age among all women. The highest ratio of sarcomas to fibroid procedures was observed at ages 35-39 (1 in 2020 for black women and 1 in 765 for white women) decreasing by ages 55-59 to 1 in 42 for black women and 1 in 51 for white women. Estimated ratios were approximately twice as high when outpatient procedures were included (age-adjusted ratio for all women 1 in 716 for all procedures vs 1 in 386 for inpatient procedures only). Conclusions: The probability of an underlying uterine sarcoma in women undergoing surgical management for fibroids varies substantially by age and race. These population-based estimates provide additional information for patients, clinicians, and policy makers considering the relative benefits and harms of different approaches to fibroid treatment.

![Figure 1: Estimated age- and race-specific incidence of inpatient and outpatient procedures for fibroids, US, 2002-2011](image)

**Table 1. Observed Event and Brier Score for All Patients**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>n</th>
<th>%</th>
<th>BS</th>
<th>Null model BS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major Complication</td>
<td>123</td>
<td>30.75</td>
<td>0.725</td>
<td>0.725</td>
</tr>
<tr>
<td>Any Complication</td>
<td>144</td>
<td>36.00</td>
<td>0.2865</td>
<td>0.2865</td>
</tr>
<tr>
<td>Peritonitis</td>
<td>24</td>
<td>6.00</td>
<td>0.0552</td>
<td>0.0564</td>
</tr>
<tr>
<td>Cardiac Complications</td>
<td>3</td>
<td>0.075</td>
<td>0.0079</td>
<td>0.0074</td>
</tr>
<tr>
<td>SSI</td>
<td>84</td>
<td>21.00</td>
<td>0.1658</td>
<td>0.1650</td>
</tr>
<tr>
<td>UTI</td>
<td>18</td>
<td>4.50</td>
<td>0.0427</td>
<td>0.0431</td>
</tr>
<tr>
<td>VTE</td>
<td>12</td>
<td>3.00</td>
<td>0.0192</td>
<td>0.0209</td>
</tr>
<tr>
<td>Renal Complications</td>
<td>6</td>
<td>1.50</td>
<td>0.0209</td>
<td>0.0209</td>
</tr>
<tr>
<td>Return to OR</td>
<td>26</td>
<td>6.50</td>
<td>0.0683</td>
<td>0.0692</td>
</tr>
<tr>
<td>Death</td>
<td>4</td>
<td>1.00</td>
<td>0.0137</td>
<td>0.0117</td>
</tr>
</tbody>
</table>

BS - Brier score, SSI - Surgical site infection, VTE - Venous thromboembolism, UTI - Urinary tract infection, OR - operating room, NH - Nursing home

**P276**

Cancer Care in Low- and Middle-income Countries: Surgical Workforce Limitations


**Introduction**: Each year, approximately 8.0 million people are diagnosed with cancer in low- and middle-income countries (LMIC). Comprehensive cancer control requires surgical services as a fundamental modality for diagnosis and curative or palliative treatment of most cancers. The objective of this study is to assess the availability of trained personnel to perform surgical biopsies, serving as a process metric for access to basic cancer care services in LMIC. Methods: A situation analysis was performed using data from the World Health Organization Emergency and Essential Surgical Care survey. Responses from healthcare managers documented service availability in 1269 health facilities ranging from tertiary hospitals to health centers in 54 countries. Results: There are 608 surveyed facilities (48%) able to perform surgical biopsy, and 454 have trained surgeons on staff (75%). Of the 504 health facilities without surgeons, 157 (31%) offer surgical biopsies, generally performed in district hospitals (35%) and by physicians capable of performing surgical services but without dedicated technical training (77%). Selected reasons that facilities could not perform biopsies are: lack of skills (79%), lack of supplies (47%), and non-functional equipment (45%). Only 70 health facilities surveyed (15%) had the skills but did not have functional equipment or supplies. Patients travel 4 km to reach health facilities where non-surgeon physicians provided surgical biopsy compared to 100 km to access trained surgeons. There are an estimated 1.87 physicians able to perform basic surgical procedures and 0.74 trained surgeons per 100,000 population in the surveyed LMIC facilities. Non-surgeon physicians provide an estimated increase in capacity of 26 basic oncologic procedures per 100,000 per year. Conclusion: It has been projected that at least 60 basic and 110 complex oncology procedures per 100,000 are required to manage the growing cancer disease burden in LMIC. Significant human resource limitations exist to reach this target. Access to cancer care is further compromised by limited resources and transportation barriers. Innovative programs are needed to minimize obstacles to care in LMIC.

**P277**


**Introduction**: Robotic thyroidectomy (RT) utilizes an axillary incision which may improve cosmesis compared to the cervical incision of open thyroidectomy (OT). However, shifting the scar from the neck to the anterior axillary line may affect subsequent screening and lymph node staging for breast cancer. Sentinel lymph node biopsy (SNLB) requires intact dermal lymphatics which may be disrupted by an axillary incision. We hypothesize that RT affects subsequent breast screening and axillary staging. Methods: An endocrine surgery research registry was queried for all women who underwent...
RT or OT by a single surgeon from 2011-3. Demographics, thyroid pathology, visible presence of axillary scar on screening mammogram (MXR), request for additional diagnostic MXR, and success of SNLB after subsequent breast cancer diagnosis were evaluated. Data is reported as means±SD. Associations between factors were analyzed with ANOVA and chi-square; p<0.05 is statistically significant. Results: Of 267 women identified, 150 underwent RT and 117 underwent OT. Women who underwent RT were younger (41±12 vs 54±14 years) and had lower BMI (26±5 vs 32±8 kg/m²) than those who underwent OT (p<0.0001). Total thyroidectomy was performed in 60% and 85% of patients undergoing RT and OT, respectively (p=0.0001). Final thyroid pathology was carcinoma (i.e. papillary, follicular) in 50% after RT and 40% after OT (p=NS). MXRs were available for 28 and 15 women in the RT and OT groups, respectively. After RT, 13/28 (46%) MXRs showed ipsilateral axillary scarring (p=0.0013), and 1/28 required additional imaging due to presence of scar on MXR. However, no additional percutaneous biopsies of the ipsilateral breast or axilla were done and some of the scarring resolved on subsequent MXRs. In the entire cohort, 2 women (1 RT, 1 OT) developed on subsequent MXRs. In the entire cohort, 2 women (1 RT, 1 OT) developed local recurrence. Conclusion: After RT, 46% of screening MXRs demonstrated an axillary scar, but impediment to MXR interpretation was minimal. The study was underpowered to detect the effect of RT on axillary staging, but this warrants further study.

**P278**


Background Anastomotic leakage is one of a critical early complication after esophagectomy. Regardless of the use of precautions such as nasogastric tube, indwelling drains and antibiotic drugs, reported incidence is 0-26%, has a higher frequency than other gastrointestinal tract surgery. Early diagnostics and initiation of treatment are important to minimize complications. We routinely perform thin-slice contrast-CT exam at the 5th postoperative day after esophagectomy for the screening of early surgical complications in principle. Objective To evaluate the effectiveness of contrast-CT exam against anastomotic leakage after esophagectomy. Methods From January 2012 to December 2013, 95 esophagectomy against esophageal cancer were performed. We made a comparative review of the patient’s characteristics, surgical outcome, and findings from the CT images of the 88 cases, which were reconstructed primarily by the gastric tube. Results Eighteen cases (20.5%) suffered Anastomotic leakage (AL+ group), and 70 without (AL- group). There were no significant differences in patient characteristics such as age, sex, tumor location nor surgical outcome such as usage of laparoscope/thoracoscope, field of lymph node dissection, reconstruction route, anastomotic site, operative duration, intraoperative blood loss among the groups (P>0.05). Contrast-CT exam was performed from 3rd to 8th postoperative day (median date=6). Mean number of air-bubble (more than 2 mm in diameter, inconsecutive with artificial material nor subcutaneous emphysema) in the cerebral division and mediastinal space was 5.6 in the AL+ group and 0.7 in the AL- group, significantly higher in the AL+ group (P=0.001). Setting up the cutoff value of the number of air-bubble 3 (Air-bubble Sign), sensitivity and specificity of Air-bubble Sign against anastomotic leakage were 94.4% and 95.7%, respectively. Sensitivity and specificity of the postoperative esophagography against anastomotic leakage were 44.4% and 100%, respectively. Conclusion Air-bubble Sign has a high sensitivity and specificity, suggested to be a valuable screening test to make early diagnosis of anastomotic leakage after esophagectomy.

**P279**

Factors associated with Mortality after Surgical Oncologic Emergencies M.R. Bosscher,* E. Bastiaanmiet,* B.L. Van Leeuwen, H.J. Hoekstra,* 1. Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands; 2. Leiden University Medical Center, Leiden, Netherlands.

Objective: The clinical outcome of patients with oncologic emergencies is often poor and the short term mortality is high, even after surgical treatment. It is important to determine which patients may benefit from invasive treatment, and for which patients conservative treatment, and/or referral to palliative care would be more appropriate. In this study prognostic factors for clinical outcome are identified, in order to facilitate the decision making process for patients with surgical oncologic emergencies. Methods: A prospective registration and follow up was performed patients over 18 years of age, who were consulted for surgical oncologic emergencies between September 2013 and April 2014. Multiple factors and measurements were registered upon emergency consultation including handgrip strength (HGS). The follow up period was 90 days. Multivariate logistic regression analysis was performed to identify factors associated with 30-day and 90-day mortality. Results: During the study period, 207 patients were identified to have surgical oncologic emergencies. There were 101 (48.8%) males and 106 (51.2%) females, and median age was 64 (range 19-92) years. The 30-day mortality was 12.6%, and 90-day mortality was 21.7%. After adjustment for age and sex, the factors that were associated with 30-day mortality were: palliative intention of cancer treatment prior to emergency consultation (p=0.006), ECOCG performance score (ECOG-PS) of greater than 0 (p for trend: p=0.03), raised LDH (p=0.0002), and low albumin levels (p=0.03). Factors associated with 90-day mortality were: palliative intention of treatment prior to emergency consultation (p=0.01), ECOG-PS > 0 (p=0.009), low HGS (p=0.02), raised LDH (p=0.0002), and low albumin (p=0.0005). Conclusions: Defining the intention of previous cancer treatment and the ECOG-PS, and additional measurement of HGS, LDH and albumin levels, are of prognostic value when deciding on the extent of treatment for patients with surgical oncologic emergencies.

**P280**

The Impact of Epidural Analgesia on the Rate of Venous Thromboembolism without Chemical Thromboprophylaxis in Major Oncologic Surgery J.J. Hong,1* M. Kang,1 N. Manguro,2 D. Shouhed,2 S. Popelka,3 F. Amersi,1 E. Hemaya,1 K. Sibert,1 A.W. Silberman.1 1. Surgery, Surgical Oncology, Cedars-Sinai Medical Center, Los Angeles, CA; 2. The Mount Sinai Hospital, New York, NY; 3. UCLA, Los Angeles, CA. Objective: Evaluate the clinical outcomes and the rate of venous thromboembolism (VTE) in patients undergoing major open abdominal oncologic surgery with preoperative epidural analgesia without postoperative chemical VTE prophylaxis Methods: Retrospective analysis of a prospective database between January 2009 and September 2014 was performed. Two-hundred sixty-three patients underwent major abdominal oncologic surgery by a single surgeon at a tertiary referral center. Patients underwent a lower extremity venous duplex preoperatively and prior to discharge. Demographics, procedure types, and VTE outcomes were reviewed. Results: The mean age was 63 years. Procedures included 77 retroperitoneal tumor resections, 41 gastrectomies, 46 colectomies, 23 small bowel resections, 29 hepatobiliary procedures, 10 abdominal wall resections, and 17 combined
Determinants of the Type of Oncologists Providing Breast Cancer Follow-up


**Introduction:** Current guidelines do not provide direction regarding the types of oncologists that should participate in breast cancer follow-up, resulting in significant variation and potential redundancy. Our objective was to evaluate factors associated with receipt of breast cancer follow-up by medical, surgical and radiation oncologists.

**Methods:** Stage I-II breast cancer survivors treated with breast conservation (no chemotherapy) from 2000-2007 were identified in the SEER-Medicare database ($n=18,299$); we hypothesized that patients in this homogenous cohort should have similar follow-up. Oncologist follow-up visits were defined using Medicare specialty provider codes and linked AMA Masterfile. Logistic regression identified factors associated with medical oncologist follow-up, controlling for sociodemographic, cancer, and access factors. Multinomial regression then identified factors associated with medical oncologist only vs. combination follow-up.

**Results:** The majority had follow-up with a medical oncologist (66%). Medical oncologists were less likely to provide follow-up for patients who were older (p=0.0005), ER/PR negative (p=0.0005), node negative (p=0.0005), lived in a rural area (p=0.0005), and lived in an area with many radiation oncologists (p=0.0002). Medical oncologist follow-up was provided alone (39%) or in combination with a radiation oncologist (18%), a surgeon (27%), or both (16%). Age was the only clinical factor associated with combination follow-up. The number of PCP visits/year had the strongest association (table). **Conclusions:** In this homogenous patient cohort, there was substantial variability in the types of oncologists who provide breast cancer follow-up. Clinical factors that reflect appropriateness for systemic therapy (i.e. age, ER/PR status) were associated with medical oncologist follow-up. However, receipt of combination follow-up was influenced by non-cancer factors (i.e. number of PCP visits/year) that may reflect patients’ access to and propensity for health care utilization. Improving guidance regarding the role each oncologist type should play in follow-up could improve coordination and reduce redundancy, with benefits for patients and providers.

**P281**

**Are Clinical Guidelines for the Management of Intraductal Papillary Mucinous Neoplasms followed? A Single Center Analysis**

P. Tabrizian,† Y. Berger,‡ E.S. Pierobon,§ S. Aycart,¶ P. Argiriadi,¶ K. Fei,¶ G. Carrasco,¶ D. Labow,¶ U. Sarpel,¶ 1. Surgery, Mount Sinai Medical Center, New York, NY; 2. Department of Health Evidence and Policy, Mount Sinai Medical Center, New York, NY; 3. Radiology, Mount Sinai Medical Center, New York, NY; 4. Pathology, Mount Sinai Medical Center, New York, NY.

**Introduction:** Guidelines for management of IPMN recommend: 1) Surveillance imaging <2 years of diagnosis, 2) EUS for cyst >3 cm, thickened/enhanced cyst wall, duct size >5 mm, or non-enhancing mural nodule, and 3) Pancreatic resection for solid lesion, duct size >10 mm, or suspicion of malignancy on EUS. We aimed to determine whether guidelines are followed and if failure is associated with socioeconomic variables. We included all patients with radiographic diagnosis of IPMN a1 cm during 1/2003-1/2013, confirmed by a single radiologist at our institution. We defined failure of guideline adherence if at least one of the following occurred: A) failure to undergo at least 1 surveillance image following diagnosis, B) failure of acknowledgment of IPMN by a physician, C) failure to undergo EUS when indicated, or D) failure to undergo resection when indicated in surgical candidates. Results: 445 patients were included in the study with a mean age of 66.8 (±11.8) years and cyst size of 1.8 (±1.3) cm. The majority of patients were white (58%), male (51%), with ASA scores a3 (76%), of mid-high household income (75%), English speaking (92%), with governmental insurance status (84%). 46% had major comorbidities excluding them from surgery. Failure of guideline adherence was high (58%) and evident across all the criteria (A:33%, B:37%, C:25%, D:29%). Age >68 yrs (p=0.0008), ASA score a3 (p=0.0007), governmental insurance status (p =0.0004), and benign findings on imaging (p<0.0001) were factors associated with non-compliance on univariate analysis. Gender, race, income status, or year of diagnosis were not different among the groups. Multivariate logistic regression demonstrated that ASA score a3 and benign findings on imaging were associated with 1.8 times (95%CI:1.26-2.45) and 2.3 times (95%CI:1.53-3.56) higher odds of adherence failure compared to the remaining adjusted group. Conclusions: Poor compliance with IPMN guidelines appears to be related to the presence of serious co-morbidities or competing healthcare priorities. There do not appear to be any disparities in care based on the measured socioeconomic variables.
**P283**

Inconsistent Selection and Definition of Local and Regional Endpoints in Breast Cancer Research


Background: Results in breast cancer research are reported using study endpoints. Most are composite endpoints (such as locoregional recurrence), consisting of several components (for example local recurrence) that are in turn composed of specific events (such as skin recurrence). Inconsistent endpoint selection and definition might lead to unjustified conclusions when comparing study outcomes. This study aimed to determine which locoregional endpoints are used in breast cancer studies, and how these endpoints and their components are defined.

Methods: PubMed was searched for breast cancer studies published in nine leading journals in 2011. Articles using endpoints with a local or regional component were included and definitions were compared.

Results: Twenty-three different endpoints with a local or regional component were extracted from 44 articles. Most frequently used were disease-free survival (25 articles), recurrence-free survival (7), local control (6), and regional recurrence-free survival (3) and event-free survival (3). Different endpoints were used for similar outcomes. Of 23 endpoints, five were not defined and 18 were defined only partially. Of these, 16 contained a local and 13 a regional component. Included events were not specified in 33 of 57 (57%) and 27 of 50 (54%) cases. Definitions of locoregional components inconsistently included specific nodal sites and skin and chest wall recurrences. Regional components inconsistently included specific nodal sites and skin and chest wall recurrences.

Conclusion: Breast cancer studies use many different endpoints with a locoregional component. Definitions of endpoints and events are either not provided or vary between trials. To improve transparency, facilitate trial comparison and avoid unjustified conclusions, authors should report detailed definitions of all endpoints.

**P284**

The ACS-NSQIP Surgical Risk Calculator Lacks Enough Sensitivity to Risk Stratify Patients with Gastric Cancer at Academic Medical Centers


Background The ACS-NSQIP Surgical Risk Calculator is an online tool that estimates probability of postoperative complications, death and other outcomes. An above average risk for each adverse outcome is the proposed threshold for concern; it is not certain if this threshold is appropriate for more select patient populations. Methods Patient characteristics from the U.S. Gastric Cancer Collaborative database were entered into the calculator and risk estimates compared to actual events. Exclusion criteria were palliative or emergent operation, stage IV disease, multi-visceral resection or operation other than total, subtotal or distal gastrectomy. Results Of 965 patients who underwent gastrectomy for cancer between 2000 and 2012 at seven academic medical centers, 653 (68%) met inclusion criteria. There were 266 (40%) patients with at least one complication, and 142 (54%) of these were estimated to be at above average risk by the calculator. Overall, 99 (15%) patients had serious complications and, 17 (17%) had estimated above average risk. When using the calculator thresholds for above average risk, sensitivity ranged between 17-71% for actual events (Table). In order to achieve 80% sensitivity for actual events, a threshold below the calculator’s cutoff for high risk patients was necessary and specificity ranged from 32 to 56%. Calculator estimates underestimated the incidence of adverse outcomes for overall complications (26 vs 40%, p<0.01), death (1 vs 3%, p<0.01), pneumonia (4.3 vs 6.3%, p<0.01), urinary tract infection (3.6 vs 6.1%, p<0.01), discharge to nursing facility (4.6 vs 8.9%, p<0.01) and median length of stay (6.0 vs 8.0 days, p<0.01). Conclusion Due to the potential referral bias of higher risk patients to academic medical centers, the ACS-NSQIP surgical risk calculator may underestimate risk and has low sensitivity for actual events in this population. Surgeons in such settings may need to adjust expectations when counseling patients and modify preoperative optimization of patients. Updates to the NSQIP calculator should be considered, specifically accounting for hospital type and a diagnosis of cancer.

**P285**

Isolated Chemotherapeutic Perfusion as Neoadjuvant Therapy for Advanced/Unresectable Pelvic Malignancy

H.J. Wanebo,* G.J. Begossi,† J. Belliveau,* 1. Surgery, Landmark Medical Center, Bristol, Puerto Rico. 2. Alta Bates Summit Medical Center, Oakland, CA.

Introduction: Previous chemo radiation (CRT) usually precludes neoadjuvant therapy for advanced pelvic cancer. Neoadjuvant isolated pelvic perfusion (IPP) provides higher tissue drug levels with less toxicity than systemic therapy and may enhance resectability. We performed 113 IPP in 75 patients (pts) 59 for pre operative therapy and 16 palliative. Methods: Fifty pts had advanced/irradiated rectal ca (4 pre-op and 16 palliative), 8 pts had advanced anal cancer (SCC), 6 had pelvic sarcoma pts, 4 pts had pelvic/perineal melanoma (MEL), and 7 had other advanced ca (endometrial (2), ovarian cancer (5), and bladder cancer (BC) (6 pts). Hyperthermic IPP for (60 minutes) utilized targeted regimens. 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 resection in 7 pts. The other 8 pts were non-resected because of disease / medical status (5 pts) or patient refusal (3 pts). Median overall survival (OS) post IPP was 24 mos in 15 resectable pts, 20 mos in 7 resected pts (2 survived > 5 yrs) and 8 mos in 11 non-resectable pts. It was 23and 8 mos (resected vs non resected) months in 8 advanced SCC anal pts and 28/24 mo in advanced gyn cancer pts (endometrial/ovarian). 13 mos in 4 advanced melanoma pts and was only 5 mos in 6 sarcoma pts (only 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 reasoning. Conclusion: IPP has promise in augmenting resectability (or palliation) in selected patients with advanced/palindium pelvic malignancy not amenable to conventional chemo RT. IPP responsive tumors included recurrent rectal and anorectal cancers, localized gyn cancers and melanoma, whereas sarcomas were quite resistant. Biologic therapy or stem cell support are viable future options to enhance outcome of IPP.
Inability to Return Home and Hospital Readmission are Frequent among Patients with Disseminated Malignancy undergoing Surgical Intervention


Introduction: Although surgical intervention for patients with disseminated malignancy (DMa) is high risk, few studies have examined the impact of surgery on discharge disposition and readmission rates for these patients. We sought to evaluate the rates of prolonged hospitalization (prLOS), hospital readmission, and discharge to nursing/rehabilitation (N/R) facilities, hypothesizing that these endpoints would be high. Methods: We queried the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) for 2011-2012. Excluding patients undergoing a primary hepatic resection (N=4,552), 94.5% experienced prLOS, 17.6% were discharged to N/R facility had no recorded complication. Among patients undergoing bowel resection (N=2,711), 94.5% experienced prLOS. Overall, 78.8% of patients were discharged to home, 16.3% were transferred to N/R facility, and 3.9% of patients were readmitted within 30 days. 64.7% of those discharged to N/R facility, prLOS, and hospital readmission are high, especially among patients undergoing bowel resection. These results highlight the impact of surgery on quality of life and ability to tolerate additional therapy among patients with incurable cancer.

Should a Resident Participate in My Cancer Operation? Elucidating Trainee Level Effect on Oncologic Surgery Outcomes

M. Simpy, K. Spaniolas, M. Grzybowski, M. Manwaring, W. Pofahl, K.R. Kasten. Surgery, East Carolina University, Greenville, NC.

Introduction: Surgical complications delay adjutant therapy in oncology patients. Current literature remains unclear regarding the effect of resident involvement on oncologic outcomes, with inappropriate resident coverage possibly endangering patients despite surgeon oversight. The aim of this study was to assess resident trainee level effect on 30-day overall morbidity in cancer patients undergoing major surgery. Methods: Cancer patients undergoing non-emergent major intra-abdominal (appendix, bladder, colon, esophageal, gallbladder, gastric, gynecologic, kidney, liver, pancreas, rectal) and major non-abdominal (breast, skin and soft tissue, thyroid) operations from 2005 to 2012 were identified in the ACS-NSQIP database. Demographics, co-morbidities, recent chemistry, resident level and 30-day outcomes were analyzed. Multivariate logistic regression models assessed overall morbidity. Results: 155,620 cancer patients undergoing major intra-abdominal (n=75668) or major non-abdominal (n=79952) procedures were captured. Demographics were clinically similar across attending and PGY levels. Rates of serious, minor and overall morbidity increased significantly with PGY level, along with operative time and length of stay. For major intra-abdominal procedures, all resident levels except PGY2 adversely affected overall morbidity (Table 1). Above PGY4 level, resident involvement had a stronger association with adverse outcome than preoperative co-morbidities and preoperative chemotherapy. In contrast, only PGY2 and PGY5 were independently associated with worsened overall morbidity following major non-abdominal cancer procedures, while PGY1 was associated with improved morbidity. Interestingly, on evaluation of procedure codes, gallbladder, liver, pancreas, and thyroid procedures demonstrated no effect of resident involvement on overall morbidity. Conclusions: Resident level is independently associated with increased overall morbidity in patients undergoing selected major surgical procedures. Understanding which complex oncologic procedures demonstrate effect of resident involvement on overall co-morbidity is necessary to maximize patient outcomes.

Metabolic Complications of mTOR Inhibitors in Solid Tumor Patients: A Meta-analysis and Systematic Review

S. Lew,*, R. Chamberlain. Surgery, Saint Barnabas Medical Center, Millburn, NJ.

Introduction: Mammalian target of rapamycin (mTOR) inhibitors interfere with cell growth, proliferation, metabolism, angiogenesis, and are often used to treat solid tumors. Numerous randomized controlled trials (RCTs) have reported varying degrees of severity for metabolic complications associated with these agents. This meta-analysis critically analyzes the risk of metabolic complications associated with mTOR inhibitors (mTORi) in the treatment of solid tumor patients. Methods: A comprehensive search of all phase 2 or 3 RCTs investigating the use of mTORi for treatment of solid tumors was conducted using PubMed, Cochrane Central Registry of Controlled Trials, and Google Scholar (1966-2014). Keywords searched included “mTOR inhibitor”, “everolimus”, “temsirolimus”, “riboflorolimus”, “hyperglycemia”, “hypertriglyceridemia”, and “hypercholesterolemia”. Outcomes included were hyperglycemia (HGL), hypertriglyceridemia (HTG), and hypercholesterolemia (HC). The incidence and risk ratio (RR) for each metabolic derangement was calculated with 95% confidence intervals. Results: 13 RCTs involving 6,907 patients treated with mTORi were identified; 3,739 in the treatment arm and 3,168 in the control arm. The overall incidence of all-grade (AG) and high-grade (HG) metabolic complications were 39% (27.3-51.5) and 3.4% (1.8-4.9) respectively. mTORi use was associated with an increased risk of AG (RR=2.97 [95% CI 2.25-3.92]; p<0.001) and HG HGL (RR=4.08 [95% CI 2.71-6.14]; p<0.001), AG (RR=2.22 [95% CI 1.70-2.89]; p<0.01) and HG HTG (RR=1.88 [95% CI 1.10-3.20]; p=0.02), and AG (RR=2.48 [95% CI 1.51-4.26] [95% CI 2.50-7.90]; p<0.001). Conclusion: mTORi are associated with significantly increased risk of AG HGL, HTG, and HC. Precise knowledge of the risk associated with these agents will allow physicians to limit or restrict the use of mTORi in specific cancer patients, especially those with pre-existing comorbidities as their use may increase the risk of and/or precipitate cardiovascular events. Clinicians should be aware of these risks, perform regular monitoring, and consider other pharmacologic treatments if necessary and available.
P289
Long-term Patient-reported Symptoms and Quality of Life Outcomes are Favorable following Resection of Pancreatic Neoplasms
H.S. Tran Cao,* M. Petzel, N. Parker, J.S. Liles, M. Kim, J.E. Lee, T. Aloia, C. Conrad, J. Vauthey, J.B. Fleming, M.H. Katz. Surgical Oncology, U.T. MD Anderson Cancer Center, Bellaire, TX.

Background: Patient-reported symptoms and quality of life (QOL) are critically important outcome metrics following cancer operations but are poorly described following pancreatic resection for neoplasms. We sought to evaluate the long-term QOL and surgery-related symptoms associated with pancreatectomy and to identify factors that may influence them. Methods: As part of a broader survivorship project, we conducted a cross-sectional survey of QOL (Functional Assessment of Cancer Therapy-Hepatobiliary Questionnaire) and psychosocial distress (Hospital Anxiety and Depression Scale) among patients with ductal (PDAC) or perianpillary adenocarcinoma (NPAC) or pancreatic neuroendocrine tumors (PNET) who were free of disease at least 6 months following pancreatectomy. Results: Of 348 eligible patients, 232 (66.7%) participated at a median of 50 months (range, 8 - 238 months) following pancreaticoduodenectomy or total pancreatectomy (PD/TP) (n=169), or distal pancreatectomy, central pancreatectomy, or others (DP/Other) (n=63). Overall QOL was influenced by race and pancreatectomy type but not histology; PD/TP survivors reported better QOL and lower symptom severity scores than DP/Other survivors (Figure). Compared to DP/Other survivors, PD/TP patients experienced more frequent problems with abdominal cramping and diarrhea, but less frequent problems with poor appetite, constipation, fatigue, anxiety and depression (p<0.05 for all). Conclusion: In this, the largest study quantifying self-reported, long-term surgery-related symptoms and QOL following pancreatectomy, patients generally reported favorable QOL but clinically significant gastrointestinal and psychosocial symptoms were reported in nearly 20% of patients long after surgery. These critical data are needed to optimize preoperative decision-making, design surveillance strategies, and identify therapeutic targets in the survivorship period.

P290
Palliative Care Training in Surgical Oncology and Hepatobiliary Fellowships: A National Survey of Program Directors

Background Despite literature affirming the importance of palliative care (PC) training, there is scarce literature about the readiness of Surgical Oncology and hepatopancreatobiliary (HPB) fellows to provide such care. Our aim was to capture attitudes of, educational support for and perception of PC within advanced cancer surgical training programs... Study Design A survey used to evaluate residency programs was adapted and sent to Program Directors (PDs) of respective fellowships. The final survey consisted of 22 items. Results Overall 70% (28/40) of programs responded. 40% did not offer any formal teaching in pain management, delivering bad news or discussion of prognosis. Lack of assessment of fellows goals of care and initiation of DNR discussions were reported by 42% and 57% of respondents, respectively. All programs had a PC consultation service with 15% utilizing the service for training of fellows. 42% of programs also had a faculty member with recognized clinical interest/expertise in PC with 35% of programs having a faculty who is board-certified in Palliative Medicine. PDs reported 60%, 70%, 33% and 50% of chairpersons, faculty, fellows and residents were supportive of PC training, respectively. Fellows comfort with dying was the biggest barrier to education (Table 1). Conclusions HPB and Surgical Oncology fellowships do not suffer from shortages of PC resources, or teaching opportunities. Fellows receive poor feedback on communication centered on PC, which may imply a lack comfort for end of life training. Focused efforts by institutions are required to promote competent palliative care utilization following fellowship completion.

Barriers to End of Life Education

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<tr>
<td>Faculty do not provide good end of life clinical care</td>
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<tr>
<td>Faculty are uncomfortable with dying and end of life care</td>
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<tr>
<td>Faculty lack the underlying knowledge to teach about end of life care</td>
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<td>Faculty lack clinical skills to teach about end of life care</td>
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<tr>
<td>Faculty do not think it important to learn how to provide care for the dying patients</td>
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<tr>
<td>Faculty lack teaching skills</td>
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<tr>
<td>Faculty lack skills in follow evaluation and feedback</td>
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<tr>
<td>There is no time for new curricular elements</td>
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<tr>
<td>Our curricular change mechanism is very cumbersome</td>
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</tr>
<tr>
<td>Fellows are uncomfortable with death, dying, and end of life care</td>
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</tr>
</tbody>
</table>

Rating scale 1-5 (1 strongly agree - 5 strongly disagree)

P291
A Novel Prediction Tool for Major Complications after Cytoreductive Surgery and HIPEC
J. Baumgartner,* T.G. Kwong, G. Ma, K. Messer, K. Kelly, A.M. Lowy. Surgery, University of California, San Diego, La Jolla, CA.

Background Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) has an emerging role the treatment of patients
with peritoneal metastases. While the indications and efficacy of CRS/HIPEC are being established, there are known treatment-related toxicities. We sought to determine the predictors of major postoperative complications after CRS/HIPEC in a high-volume center. Methods: From a single-institution database, we investigated preoperative and operative factors for their ability to predict 60 day Clavien Grade (CG) III or greater (major) complications in patients undergoing CRS/HIPEC. A predictive model was created among preoperative factors on univariate logistic regression with p<0.20, using multivariate analysis with various model selection techniques to minimize Akaike’s Information Criterion. Results: We evaluated 247 patients undergoing CRS/HIPEC. Median age was 52 (20-86) and 117 (47.4%) were male. Primary tumor site was appendix in 166 (67.2%), colorectal in 51 (20.6%), mesothelioma in 22 (8.9%), ovarian in five (2.0%) and small bowel in three patients (1.2%). Median peritoneal cancer index was 14 (0-29) and 235 patients (95.1%) had a complete (CC-0/1) cytoreduction. Major complications occurred in 41 patients (16.6%): 33 (13.4%) CG III, five (2.0%) CG IV and three (1.2%) CG V (deaths). Factors predictive of major complications on univariate analysis were Charlson Comorbidity Index (CCI) > 0 (OR 2.335, p=0.044), presence of symptoms (OR 2.186, p=0.024), prior resection status (none or prior CRS/HIPEC vs. prior resection without CRS/HIPEC, p=0.021), number of visceral resections (OR 1.434, p=0.002) and EBL (OR 1.001, p=0.030). CCI > 0 (OR 2.505, p=0.035), presence of symptoms (OR 1.951, p=0.064), and prior resection status (p=0.046) were most predictive of major complications on multivariate analysis and were used to create a predictive model (Fig.). Conclusion: Charlson comorbidity index, presence of symptoms and prior resection status can predict major 60 day complications after CRS/HIPEC. This tool may guide patient selection, informed consent and further investigation into the etiology and prevention of post-CRS/HIPEC complications.

P292
Venous Thromboembolism Prophylaxis: Differences in Practice Patterns in Two Institutions within a Single Health System

N. Kulkarni,1 S. Koller,2 E. Handorf,1 L.O. Sjoholm,2 J. Farma.1,3
1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Temple University Hospital, Philadelphia, PA.

INTRODUCTION: Venous thromboembolism (VTE) is a major cause of preventable death in hospitalized patients. The American College of Chest Physicians (ACCP) and National Comprehensive Cancer Network (NCCN) guidelines for patients with major abdominopelvic surgery, especially with cancer recommend undergoing extended post discharge VTE prophylaxis for four weeks. We sought to look at practice patterns with the use of perioperative VTE prophylaxis in two institutions, an NCI designated cancer center (Hospital 1) and an academic hospital and level one trauma center (Hospital 2). METHODS: An IRB approved electronic survey was sent to surgeons of all specialties at both institutions querying the use of pre and post-operative thrombophrophylaxis, concerns, awareness of the ACCP/NCCN guidelines and adherence to them in the post-operative setting, and results were compared. RESULTS: Surgeon response was 100% (26/26) in Hospital 1 and 41% (47/115) in Hospital 2. All surgeons in Hospital 1 were multispecialty oncologic surgeons, while hospital 2 consisted of surgeons from varied subspecialties. Post-operative DVT chemoprophylaxis was used by 96.1% surgeons at Hospital 1, which was significantly more than 78.2% surgeons at hospital 2 (p=0.04). Only 56% surgeons at Hospital 1 and 39% at Hospital 2 acknowledged using preoperative DVT chemoprophylaxis (p=0.2) with major concerns including intra and postoperative bleeding complications. When queried about their awareness of guidelines 96% surgeons in Hospital 1 expressed awareness, compared to only 60% in Hospital 2 (p=0.012). Nonetheless, only 32% surgeons in Hospital 1 and 40% in Hospital 2 actually follow the guidelines (p=0.6). About 70% surgeons in hospital 1 and 75% in hospital 2 expressed the willingness to follow these guidelines in the future. CONCLUSIONS: Disparities between awareness of current guidelines and practice patterns can be explained in part by the difference in the population of patients and subspecialties in the two institutions. However there needs to be a concerted effort to adhere to national performance initiatives and standardize approaches for perioperative VTE prophylaxis.

Table 1: Survey responses

<table>
<thead>
<tr>
<th>Survey Question</th>
<th>Hospital 1</th>
<th>Hospital 2</th>
<th>p-value</th>
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<td>Intraoperative mechanical DVT prophylaxis</td>
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<td>89.9</td>
<td>0.15</td>
</tr>
<tr>
<td>Post-operative DVT chemoprophylaxis</td>
<td>96.1</td>
<td>78.3</td>
<td>0.04</td>
</tr>
<tr>
<td>Pre-operative DVT chemoprophylaxis</td>
<td>56</td>
<td>39.1</td>
<td>0.2</td>
</tr>
<tr>
<td>Aware of current guidelines</td>
<td>94</td>
<td>60</td>
<td>0.0012</td>
</tr>
<tr>
<td>Follow guidelines</td>
<td>32</td>
<td>60</td>
<td>0.6</td>
</tr>
</tbody>
</table>

P293
Transitional Care Needs Predict Worse Survival after Cancer Surgery

C.J. Balentine,1 A. Artinyan,1 M. Mason,14 A.D. Naik,1 F.A. Richardson,1 D.H. Berger,1 D.A. Anaya,1 1. Surgery- Division of Surgical Oncology, Baylor College of Medicine, Houston, TX; 2. Department of Medicine, University of Wisconsin, Madison, WI; 3. Department of Medicine, Baylor College of Medicine, Houston, TX.

Introduction: Patients having complex cancer surgery are often discharged to long-term care, rehabilitation and skilled nursing facilities to complete recovery before transitioning back home. While this transitional care (TC) is common, its impact on survival has not been examined. The purpose of this study was to assess the impact of TC use on survival following curative cancer surgery using a cohort of colorectal cancer (CRC) patients. We hypothesized that patients discharged to TC would have worse survival than those discharged directly home. Methods: We conducted a cohort study of Veterans Affairs (VA) patients having curative surgery for stage 0-III CRC from 1999-2010. We categorized patients as discharged to TC if they went to any facility other than home. To accurately classify cancer-specific variables, co-morbidities and postoperative complications, we linked VA Cancer Registry to the VA Surgical Quality Improvement Program. We used Cox regression and a 4:1 propensity matching to determine the survival impact of TC use in this cohort. Results: A total of 10,583 patients met inclusion criteria and 805 were discharged to TC. Worse survival for TC patients was seen for all cancer stages (Figure). Additionally, stage I TC patients had similar overall survival (80%) as stage III patients discharged home (78%). Unadjusted mortality for TC compared to home discharge was significantly increased (HR 2.6, 95% CI 2.2-3.1). TC also predicted worse survival after adjusting for age, stage, co-morbidity, postoperative complications, marital status, income, and emergency surgery (HR 2, 95% CI 1.7-2.4). After propensity matching, TC was still associated with a two-fold increase in mortality (HR 2.5, 95% CI 1.7-2.4) compared to home discharge. Conclusions: Patients with TC needs after CRC surgery have significantly worse survival than those discharged home. While the etiology of this disparity is unclear, patients utilizing TC are a vulnerable population with considerable room for improvement in long-term outcomes. Interventions targeting improved postoperative recovery in this group could have a profound impact on survival following cancer surgery.
Preoperative Risk Assessment Tool to Predict Worse Outcomes in Patients with Serious Complications after Major Oncologic Surgery


Introduction: Sparse information is available to predict outcomes after serious complications following oncologic surgery. Our aim was to identify patient-specific factors that are associated with poor outcome following a serious operative complication. Methods: The 2005–2012 NSQIP database was used to identify patients undergoing pneumonectomy, esophagectomy, gastrectomy, pancreatoduodenectomy, and low anterior resection for cancer who experienced a serious complication. Outcomes analyzed were 30-day mortality, discharge disposition, and length of stay (LOS). The sample was split into a testing cohort (TC) and a validation cohort (VC). The TC was used for univariate and multivariate analyses of patient outcomes, and the VC was used to evaluate the multivariate models on an independent sample. Results: 6084 (TC, n=5499; VC, n=585) patients were included. On multivariate analysis, factors associated with worse 30-day mortality after serious complications were advanced age, ASA score (≥3), presence of ascites, dyspnea, longer operative time, lower preoperative albumin, lower preoperative platelets, and preoperative SIRS. Factors associated with non-home discharge status were advanced age, diabetes, poor preoperative functional status, COPD, and longer operative time. A risk model was then constructed to stratify patients into low, intermediate, and high risk groups for each outcome. The model was validated utilizing the VC and performed well to predict 30-day mortality and non-home discharge disposition (Figure 1a and 1b), but not LOS. Age > 70 years and age >50 years were associated with worse 30-day specific mortality and non-home discharge disposition in an incremental fashion, respectively. Conclusions: Based on preoperative variables, our statistical model effectively risk stratifies patients into 3 risk groups with respect to worse 30-day mortality and non-home discharge disposition in patients having a serious complication following major oncologic surgery. Identification of specific patient factors associated with poor outcome will allow for additional risk assessment and more informed discussions with patients in the hospital setting.

Barriers to Cancer Care at a District Hospital in Rural Cameroon

A.M. Ilbawi,1,* E. Einterz,2 D. Nkusu,2 1. Surgical Oncology, MD Anderson Cancer Center, Houston, TX; 2. District Hospital of Kolofata, Kolofata, Extreme North, Cameroon.

Introduction: Approximately 80% of global cancer associated disability-adjusted life-years (DALYs) are lost in low-resource settings where only 5% of global cancer resources are spent. District hospitals function as the primary contact point in the delivery of basic cancer and surgical services. The objective of this study is to assess barriers to care such as cost constraints, human resource limitations, and service availability. Methods: A three-year retrospective review of surgical records at a district hospital in Cameroon was performed. The diagnosis, surgical procedure, pathology findings, complications, and financial costs for all patients were reviewed. DALYs were calculated using disease- and patient-specific outcomes. Results: In the study period, 256 patients (21%) with a presumptive diagnosis of cancer presented for pre-operational evaluation and had a procedure scheduled, representing 899 DALYs (11% of total surgical DALYs). Only 40% of cancer patients returned with payment and underwent the planned operation, representing 587 lost DALYs per 100,000. Factors associated with not returning for care include being female, living outside the district, and undergoing higher cost procedures (USD >300) (p<0.05). The mean age at diagnosis was 45 years old. The most common diagnosed cancers were cervical (53 patients), prostate (51 patients) and breast (22 patients), of which 26%,45%, and 36% of patients returned for surgical management. There were 11 complications (12%) including 1 peri-operative death. The average cost per procedure was USD 250.55 and paid out-of-pocket. Obtaining pathology review added USD 20 to the cost and was purchased by 34% of patients. Only 3 patients were known to have received systemic therapy, and none was treated with radiotherapy. The estimated cost-effective ratio for oncologic surgery is USD/DALY 109.30. Conclusion: Although oncologic surgery is very cost-effective, obstacles to optimal utilization of services exist. Prohibitive out-of-pocket fees limit treatment options, and vulnerable groups face additional barriers. Potential strategies to improve access include restructuring payment schemes, reducing stigma, and subsidizing essential surgical supplies.

Improving Quality Measure Adherence: Non-compliance Timeline Analysis in Adjuvant Therapy Timing in Colorectal and Breast Cancer

O.M. Rashid,* C. Laronga, K.A. Coyne, T.W. Ross, D. Shibata, H. Lee Moffitt Cancer Center, Tampa, FL.

Multiple organizations have developed accountability quality of cancer care measures that have been incorporated into accreditation, managed care contracts and quality monitoring. Among such measures include 90% institutional adherence to: adjuvant chemotherapy (chemo) for Stage III colon cancer (CC) within 120 days of diagnosis (CCT), adjuvant hormonal therapy (BHT), adjuvant radiotherapy (XRT) within 1 year (BXT), and chemo within 120 days of diagnosis (BAT) for stage I-III breast cancer (BC). We previously reported our institutional experience with reasons for non-adherence to these measures. The goal is to estimate non-compliance timelines to identify areas for quality improvement. Methods: A retrospective review of medical records at a large academic cancer center was performed. The 2005-2012 NSQIP database was used to identify patients undergoing surgical resection for cancer who experienced serious complications following oncologic surgery. Our aim was to identify patient-specific factors that are associated with poor outcome following a serious operative complication. Methods: The 2005-2012 NSQIP database was used to identify patients undergoing pneumonectomy, esophagectomy, gastrectomy, pancreatoduodenectomy, and low anterior resection for cancer who experienced a serious complication. Outcomes analyzed were 30-day mortality, discharge disposition, and length of stay (LOS). The sample was split into a testing cohort (TC) and a validation cohort (VC). The TC was used for univariate and multivariate analyses of patient outcomes, and the VC was used to evaluate the multivariate models on an independent sample. Results: 6084 (TC, n=5499; VC, n=585) patients were included. On multivariate analysis, factors associated with worse 30-day mortality after serious complications were advanced age, ASA score (≥3), presence of ascites, dyspnea, longer operative time, lower preoperative albumin, lower preoperative platelets, and preoperative SIRS. Factors associated with non-home discharge status were advanced age, diabetes, poor preoperative functional status, COPD, and longer operative time. A risk model was then constructed to stratify patients into low, intermediate, and high risk groups for each outcome. The model was validated utilizing the VC and performed well to predict 30-day mortality and non-home discharge disposition (Figure 1a and 1b), but not LOS. Age > 70 years and age >50 years were associated with worse 30-day specific mortality and non-home discharge disposition in an incremental fashion, respectively. Conclusions: Based on preoperative variables, our statistical model effectively risk stratifies patients into 3 risk groups with respect to worse 30-day mortality and non-home discharge disposition in patients having a serious complication following major oncologic surgery. Identification of specific patient factors associated with poor outcome will allow for additional risk assessment and more informed discussions with patients in the hospital setting.
measures. We have now undertaken an in-depth comparison of the clinical management timeline in adherent (A) and non-adherent (NA) cases to identify potential areas for process improvement. All CC and BC cases reported at a single tertiary cancer care institution from 2008-2012 were reviewed with ACS Commission on Cancer coding standards. Student t-test was used for statistical comparisons. Of 122 CCT, 897 BXT, 1,433 BHT, and 312 BAT cases, 16 (13.1%), 84 (6.1%), 55 (3.9%), and 40 (12.8%) were deemed NA respectively. For NA and A, the mean total time from diagnosis to adjuvant therapy was 159.5±51 in 68.7±24.5 for CCT (p<0.01); 425.9±99.1 in 198.3±82.6 for BHT (p<0.01); 426.6±166.6 in 112.9±74.5 for BXT (p<0.01); and 147.4±41.3 in 65.1±27.8 (p<0.01) for BAT (p<0.01), respectively. Table 1 reports interval times along the clinical timeline. The most significant differences for CCT were time to initial consultation and subsequent surgical treatment, and for BHT, BXT and BAT time to first visit and time from medical/radiation oncology consultation to adjuvant therapy. Timeline analysis at a single institution highlighted disease-specific delays in NA cases with respect to the timely receipt of adjuvant therapy. All of these areas may be addressed by measure awareness, scheduling streamlining and improved inter-provider communication. With the inevitable implementation of such quality measures, institutions are expected to improve HRQoL can be expected in patients with DPR. This information can be used when counseling high-risk patients preoperatively, to better delineate expectations regarding long-term impact of cancer treatment, and likelihood of regaining baseline HRQoL.

**P298**

**Increasing Incidence Rates and Worse Outcome Measures in Patients with Hepatocellular Carcinoma Initially Diagnosed at Safety Net Hospitals**

**A. El Mokdad,1 A. Singal, M. R. Porembka, G. Balch, M. Chotin, A. Yopp, Surgery, UT Southwestern Medical Center, Dallas, TX.**

**Background:** HCC is the fastest growing cause of cancer related deaths in the US and outcome measures correlate to socioeconomic class. Safety net hospitals (SN) provide disproportionate amount of care to vulnerable populations. The purpose of this study was to examine stage, treatment and outcome measures of patients diagnosed with HCC at SN and non-safety net hospitals (NSN). **Methods:** We conducted a retrospective analysis of patients diagnosed with HCC from 2001-2010 by querying Texas Cancer Registry for ICD-0-3 C220. SN was defined as a facility in the top quartile of the disproportionate share index by annual Medicare data. Demographics, tumor characteristics, treatment, and survival were compared between the two groups. **Results:** 9132 patients with HCC diagnosed during the time period were identified, 4326 in SN and 4806 in NSN. Age-adjusted incidence rates per 100,000 over the study period increased significantly in SN (p<0.0001). SN patients were more likely to be Hispanic (53% vs. 23%, p<0.0001) and living in poverty (56% vs. 31%, p<0.0001) in SN. There was no difference in age or gender between groups. Patients diagnosed at SN were less likely to have local stage tumors (50% vs. 57%, p<0.0001) and to receive treatment of any kind (49% vs. 59%). Of patients receiving surgical treatment SN were less likely to receive transplants (30% vs. 36%, p<0.0001). Median survival was significantly shorter in patients diagnosed at SN compared to NSN (5.6 vs. 7.4 months, p<0.0001). Patients presenting at local and regional stages in SN had worse overall survival than similarly staged patients diagnosed in NSN (10.7 vs. 13.5 months and 3.6 vs. 5.4 months, p<0.0001). There was no difference in survival in distant stage of presentation. On multivariable analysis, diagnosis in SN, regional/distant stage, and lack of treatment was associated with worse overall survival. **Conclusions:** HCC incidence at SN is increasing at a greater rate than NSN. Patients diagnosed at SN had later stage tumors and were less likely to receive treatment of any kind resulting in worse overall survival than patients diagnosed at NSN.

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**Chemotherapy Utilization among Patients with Metastatic Colon Cancer: The Relavance of Insurance Status**

**M. Mason,1 J.T. Li,2 N.N. Massarweh,1 D.J. White,2 J.N. Cormier,1 A.D. Naik,2 A. Artinyan,1 D.H. Berger,1 D.A. Anaya,1 J. Surgery-Division of Surgical Oncology, Baylor College of Medicine, Houston, TX. 2. Department of Medicine, Baylor College of Medicine, Houston, TX. 3. Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.**

**INTRODUCTION:** Transitional care needs (TCN) and unplanned readmissions following cancer surgery are common and represent measures of delayed postoperative recovery (DPR). DPR is associated with worse long-term survival, however its impact on patient-centered outcomes such as health-related quality of life (HRQoL) has not been examined. The goal of our study was to examine long-term changes in HRQoL following cancer surgery and to evaluate the effect of DPR on these outcomes. **METHODS:** A prospective cohort study of patients having elective cancer surgery at a tertiary referral center was performed (2012-2014). HRQoL was prospectively measured using the SF-36 survey preoperatively and 6-months after surgery. The primary outcome of interest was a clinically significant drop in HRQoL, defined using the validated cutoff of a greater than 5 point drop in the Physical Component Summary (PCS) and Mental Component Summary (MCS) scores from baseline to 6 month postoperatively. The association between DPR and clinically significant drop in HRQoL was examined using univariate and multivariate logistic regression analysis, while adjusting for patient, tumor and treatment characteristics, and the occurrence of postoperative complications. **RESULTS:** A total of 252 patients were included, 190 (75.4%) had major surgery, with the majority of procedures performed for GI malignancies (60%). In all, 56 patients (22.2%) had a DPR, and 98 (38.9%) and 67 (26.6%) experienced a significant drop in the PCS and MCS scores, respectively. After multivariate analysis, DPR was not associated with a significant drop in long-term HRQoL for PCS (Odds ratio 1.07, [95% confidence interval, 0.52-2.21], p=0.8) or MCS (1.07, [0.73-1.59], p=0.2) scores. **CONCLUSIONS:** Although delayed postoperative recovery following cancer surgery is common, it does not impact long-term HRQoL for this population. Based on these findings, return to base-
chical modeling, the association between lack of insurance and treatment with chemotherapy persisted (Model 2, 0.62 [0.55-0.69], P=0.0001). CONCLU-
SION: Over one in three mCC patients do not receive chemotherapy. While this finding is not explained by lack of insurance alone, uninsured patients were significantly less likely to receive chemotherapy, even after accounting for geographical variation in healthcare resources. Future studies should focus on establishing the mechanisms through which this association takes place.

P300
Multidisciplinary Tumor Board Evaluation of Hepatocellular Carcinoma Leads to Increased Treatment Delivery and Improved Overall Survival
D.A. Anaya, H. El-Serag, S. Mittal, F. Kanwal, Z. Duan, S. Temple, S. May, Y. Sada, J. Kramer, P.A. Richardson, J.A. Davila, J. Surgery- Division of Surgical Oncology, Baylor College of Medicine, Houston, TX. 2. Department of Medicine, Baylor College of Medicine, Houston, TX.

INTRODUCTION: Prognosis of patients with hepatocellular carcinoma (HCC) is determined by a variety of factors beyond tumor characteristics, including liver function and treatment availability. Guidelines recommend multidisciplinary evaluation (MDE) which is best accomplished through a Tumor Board (TB) forum. However, the impact of TB MDE on the process of care and outcomes for HCC is unknown. We sought to examine the effect of TB MDE on receipt of treatment and overall survival (OS) in a national sample of patients with HCC.

METHODS: A retrospective cohort of HCC patients evaluated in the Veterans Affairs (VA) healthcare system was performed (2004-2012). HCC diagnosis was confirmed by direct chart review and baseline clinical and tumor characteristics were recorded. BCLC staging was used to stratify patients based on disease severity. Patients were categorized and compared based on whether they had TB MDE. Multivariable regression was used to examine the association between TB MDE and receipt of treatment while adjusting for interaction among different BCLC stages. OS was compared on the basis of TB MDE using Kaplan-Meier analysis.

RESULTS: A total of 1500 patients were identified; 336 (22.4%) had TB MDE and 982 (65.5%) received treatment. TB MDE was associated with increased receipt of treatment for the whole cohort (70.2% vs. 64.1%, P<0.03). After multivariable analysis adjusting for interaction between TB MDE and BCLC stages, TB MDE was associated with higher odds of receiving treatment (P=0.05), pre-dominantly impacting patients with advanced stage (BCLC C and D). Subset survival analysis in patients with stage C and D revealed improved 1 and 3-year OS rates in patients having TB MDE (36% and 13%, respectively) as compared to those not having TB MDE (25% and 7%) (P=0.002) (Figure).

CONCLUSIONS: MDE of HCC patients through a TB forum is associated with higher odds of receiving treatment and improved overall survival, primarily in patients with advanced stage for whom the decision-making process is more complex. These results support the use of TB MDE as a critical component in the process of care for patients with HCC.

P301
Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy with and without Early Postoperative Intraperitoneal Chemotherapy (EPIC): Matched Pair Analysis of Survival Outcomes
G. Tan, W. Ong, C. Chia, K. Soo, M. Teo. Surgical Oncology, National Cancer Centre Singapore, Singapore.

Introduction: Peritoneal carcinomatosis (PC) is increasingly being treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) with or without early postoperative intraperitoneal chemotherapy (EPIC). Since January 2000, we have performed 176 CRS + HIPEC procedures. Prior to November 2012, all patients were administered EPIC for 5 days post CRS + HIPEC. Since then, we have ceased EPIC. We hypothesize that HIPEC with EPIC results in more postoperative complications, as compared to HIPEC alone and does not affect overall survival (OS) and disease free survival (DFS). Methods: A prospective database of consecutive patients undergoing CRS + HIPEC in a single institution was maintained. Patients in the study were treated between January 2008 to April 2014, in order to eliminate learning curve bias. A matched case-control analysis of patients was performed and survival outcomes of patients with EPIC were compared with patients without EPIC. Results: In the study period, 42 patients received EPIC after CRS + HIPEC, and 69 patients did not receive EPIC. Match pair analysis of 31 EPIC vs 31 non-EPIC patients were performed. EPIC patients had significantly higher OS than non-EPIC patients (HR 0.36; 95% CI, 0.15 – 0.89; log-rank p = 0.022). The DFS of EPIC patients were superior to that of non-EPIC patients (HR 0.57; 95% CI, 0.30 – 1.09; log-rank p = 0.085). However, the rate of high-grade complications was higher in the EPIC group (58% vs. 43%, P= 0.197). Hospitalization duration was also longer in the EPIC group (16 days vs. 14 days, p= 0.174). Conclusion: The use of EPIC after CRS + HIPEC for PC is associated with an increased rate of high-grade complications, but is associated with improved OS and DFS.
P303
J.H. Wei,1 S.L. Wong, Surgery, University of Michigan, Ann Arbor, MI.

INTRODUCTION: Gastrointestinal stromal tumors (GISTs) are mesenchymal tumors thought to be increasing in frequency, but the exact incidence has been difficult to quantify given their frequent misclassification as smooth muscle tumors. Our objective was to examine temporal shifts in GIST epidemiology over the last 20 years. METHODS: The population-based Surveillance, Epidemiology, and End Results (SEER) 13 registry, was queried for GISTs (histology codes 993X) and GI myomatous lesions (889X; e.g., leiomyomas) from 1992 – 2011. Only microscopically confirmed cases, both benign and malignant, were included. Statistical analysis was performed using SEER*Stat and GraphPad Prism. RESULTS: A total of 3,752 GISTs and 1,782 GI myomatous neoplasms were analyzed. There was a significant increase in the incidence of GISTs, from an age-adjusted rate of 0.034 to 0.82/100,000 (Percent Change [PC] = +2,330%; Annual Percent Change [APC] = +7.7%; p < 0.05). The overall rate of increase slowed after 2000 (APC = 32.2% vs 1.3%; p < 0.05). Conversely, there was a significant decrease in GI myomatous neoplasms, from 0.53 to 0.14 (PC = -74%; APC = -8.5%; p < 0.05). Overall, the combined incidence of GIST and smooth muscle tumors increased (0.6 to 1.0; PC 69.9%; APC = +2.8%, p < 0.05), indicating the rising incidence of GISTs is not due to histologic reclassification alone (see figure). The distribution of organs from which GISTs arose also evolved, with increasing incidence across all anatomic types (p = 0.0078). The overall distribution of cases was 54% from the stomach, 28% small intestine, 3% rectum, 3% colon, 3% peritoneal cavity, 1% retroperitoneum, and <1% from esophagus, liver, pancreas, and anus. CONCLUSIONS: The incidence and anatomic distribution of GISTs has increased since 1992, mainly due to histologic reclassification. Interestingly, the rate of increase has slowed since 2000, despite the introduction of imatinib for the treatment of metastatic and unresectable disease. With the advent of such effective therapies, it is important to recognize the true frequency of this disease. Cancer registries should update their data collection strategies to help plan future analysis and GIST treatment.

P306
Regional Lymph Node Metastasis from Epithelioid Sarcoma is not associated with Disease-specific Survival
M. Dillhoff,1*, M. Hull,1 M.S. Brady,2 E. Athanasian,3 S. Yoon,2 J.T. Mullen,2 J. Ohio State University, Columbus, OH; 2. Massachusetts General, Boston, MA; 3. Memorial Sloan Kettering Cancer Center, New York, NY.

Background: Epithelioid sarcoma is a rare histologic type of sarcoma often located in distal locations (classical form) or the perineum/groin (proximal type) and metastasizes to regional lymph nodes much more commonly than other sarcoma subtypes. METHODS: 116 patients with epithelioid sarcoma were identified from prospective databases from 1978 to 2013 from two institutions. Factors associated with disease-specific survival (DSS) and local/regional recurrence-free survival (LRFS) were analyzed using the Kaplan Meier method, log-rank test and Cox regression. RESULTS: Median age was 40 years (range 4-83), and 58% were male. Twenty-seven percent of patients had tumors located in the perineum/trunk, 42% in non-hand/foot, 31% in the hand/foot. All patients had high-grade tumors. The 5 year DSS for the entire group was 81.2%, and the median DSS for the entire group was not reached. Sentinel lymph node biopsy was performed in 25 patients, and one (4%) was positive. Twelve (10%) patients had positive nodes in the surgical specimen. On univariate analysis, factors associated with decreased LRFS

Standard Retrospective Case Control Study

<table>
<thead>
<tr>
<th>Type of sarcoma - tumor I+2+3</th>
<th>Rosacea</th>
<th>No Rosacea</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>GIST</td>
<td>8</td>
<td>89</td>
<td>97</td>
</tr>
<tr>
<td>Other sarcoma types</td>
<td>3</td>
<td>201</td>
<td>204</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>291</td>
<td>302</td>
</tr>
</tbody>
</table>

| P303 | Primary Retroperitoneal Sarcomas (RPS): Rationale for Organ Resection | M. Fairweather,1* V. Y. Jo,2 J. Wang,1 M. Bertagnolli,1 E. Baldini,1 C. Raut,1 1. Department of Surgery, Brigham and Women’s Hospital/Harvard Medical School, Boston, MA; 2. Department of Pathology, Brigham and Women’s Hospital/Harvard Medical School, Boston, MA; 3. Department of Radiation Oncology, Brigham and Women’s Hospital/Harvard Medical School, Boston, MA.

Objective: Historically, surgery for RPS has included resection of involved contiguous organs. Recently, some have argued for a more aggressive approach involving resection of uninvolved organs, without stipulating rationale for organ resection, personalizing surgery based on histology, or examining microscopically organ invasion (MOI). We reviewed our experience with primary RPS to investigate the rate and rationale for individual organ resection and rate of MOI. METHODS: Operative notes and pathology reports for patients (pts) with primary RPS who underwent resection at our institution were retrospectively reviewed to identify the number of and rationale for organs resected. Perioperative clinical rationale for organ resection was classified into 1 of 6 categories. All resected organs were re-reviewed by a sarcoma pathologist to determine presence of MOI. RESULTS: From 2002 through 2011, 118 pts underwent resection of primary RPS. Ninety-nine pts (84%) had at least one organ resected (median 3 organs, range 0-8). Kidney (n=57), colon (n=51), and adrenal (n=41) were most commonly resected. Of 302 individual organs removed, perioperative clinical rationale for resection was presumed frank invasion/tumor origin (n=52, 17%), involved vasculature (39, 13%), organ encasement (42, 14%), tumor adherence (127, 42%), required for R0/R1 resection (25, 8%), or other (17, 6%) (Figure 1A). MOI was noted in 77/302 (25%) organs resected, including 71% major vessels (12/17), 53% iliopecto (13/25). 50% liver (5/10), 33% small intestine (4/12), 25% colon (13/51), and 16% kidney (9/57) (Figure 1B). Among the 3 most common histologies, MOI was identified in 23/39 (59%) pts with dedifferentiated liposarcoma (DDLPS), 14/27 (52%) pts with leiomyosarcoma (LMS), and 6/23 (26%) pts with well-differentiated liposarcoma. CONCLUSIONS: While >50% of pts with DDLPS or LMS had MOI, among all RPS pts, most resected organs did not have tumor invasion encasement or involvement of vasculature. Since the long-term benefit of radical compartment resection for RPS remains debatable, development of data-driven histology-specific rationale for adjacent uninvolved organ resection is critical.

Image 54x247 to 287x359

Image 54x688 to 287x717

Image 310x303 to 543x508
were non-hand/foot location (p=0.016), positive margins (p=0.035), and positive nodes (p=0.006). On multivariate analysis, non-hand/foot location (HR 6.0, CI 1.3-28.1, p=0.022), and positive nodal status (HR 3.36, CI 1.17-9.64, p=0.024) remained associated with decreased LRFS. Factors associated with improved DSS included size <5cm (p=0.001), hand/foot location (p=0.014), and negative margins (p=0.041). On multivariate analysis, size <5cm (HR 5.9, CI 1.18-29.7, p=0.031) was the only significant variable predicting decreased DSS. Regional lymph node metastasis was not associated with decreased DSS.

**Conclusions:** In patients with epithelioid sarcoma, tumor location and nodal status are the most important predictors of LRFS, and tumor size is the most important predictor of DSS. Lymph node metastasis is not associated with worse DSS. SLNB has a low positivity rate and is of undetermined utility.

![Figure 1: Time to Maximal Downsizing by Mutation Status (A) and Normalized Tumor Size at Time of Maximal Downsizing by Mutational Status (B) for patients who underwent mutational analysis (N=24)](image)

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**P307**

**Neoadjuvant Imatinib for Primary GIST: Mutational Status and Timing of Resection D.A. Bischof,1* J. Swett-Cosentino,2 A.J. Connell,3 K. Kazazian,2 S. Burtenshaw,3 M. Blackstein,3 C.J. Swallow,3 1. Department of Surgery, Mount Sinai Hospital, Toronto, ON, Canada; 2. Department of Surgery, University of Toronto, Toronto, ON, Canada; 3. Department of Surgical Oncology, Mount Sinai Hospital, Toronto, ON, Canada; 4. Department of Medical Oncology, Mount Sinai Hospital, Toronto, ON, Canada.**

**Introduction:** Neoadjuvant imatinib (NI) has been established as safe in primary GIST, however its therapeutic efficacy has not been well-studied. The purpose of this study was to assess the determinants of time to maximal downsizing and time to resection in patients with primary GIST who received NI. **Methods:** Patients diagnosed with primary non-metastatic GIST between 2003-2013 who received NI were identified from a prospective institutional database. Retrospective review of demographic, tumor, treatment and outcome data was conducted. Response to NI was assessed using RECIST criteria by independent serial measurement of the sums of longest tumor diameter in 3 dimensions. **Results:** In the study cohort of 26 patients, 16 were male and median age was 53 yrs (22-78). The site of GIST was stomach in 11(42%), duodenum in 3(12%), small bowel in 8(31%) and rectum in 7(27%) patients. Tumor size decreased in 24 patients (92%) on NI. According to RECIST criteria, 16 patients had a partial response (PR) to NI, 9 had stable disease and 1 had progressive disease. Response varied by mutational status: the majority of patients with Exon 11 mutations had a PR (13/16), while 0/2 patients with Exon 9 mutations had a PR and 2/6 with other mutations had a PR (p=0.02) (in 2 patients, mutation status was not established). Median time to maximal downsizing was 10 mos (2-29 mos). Median time to resection was 12 mos (3-71 mos); 85% of patients underwent surgery within 5 mos of maximal downsizing. For surgery triggered by: stabilization of tumor size (11), desired radiologic response (10), development of a new enhancing nodule within the tumor (2), with intra-tumoral bleeding in 1, lack of response to NI(1) and intolerance of NI(1). Five patients requested delays in surgical intervention, including one patient who continues to defer resection. R0 resection was achieved in 24 patients (96%). **Conclusions:** NI was highly effective in downsizing primary GISTs at all sites, though time to maximal downsizing varied considerably. Mutation status is predictive of response to NI, and should be determined prior to its initiation. Duration of NI should be goal-directed, with serial reassessment by the operating surgeon.

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**P308**

**Early Results of Tissue Ablation with Irreversible Electroporation in Soft Tissue Tumors E.J. Kruse, C. Mentzer,* Surgery, Georgia Regents University, Augusta, GA.**

**Introduction:** Irreversible electroporation (IRE) is a novel ablation modality that does not rely on thermal energy for the resultant cellular death but rather utilizes the inherent electrical potential of the cell membrane coupled with the electric pulse of the generator to disrupt the cell membrane. Over the past several years it has been used in the management of malignant hepatic and pancreatic tumors but limited experiences with soft tissue tumors have been reported. We present our experience with this new treatment modality. **Methods:** A retrospective review was performed of 9 cases in which IRE was utilized for soft tissue ablation of malignant neoplasms. Patients were treated with IRE by a single surgical oncologist at a major tertiary referral center between November 2013 and August 2014. Tumor location, type and size, efficacy of IRE treatment, number of probes, intra and postoperative complications were recorded and analyzed. Results: There were 5 males and 4 females with the average age of patients being 52 years. Mean length of stay was 8.8 days with a median length of stay of 5 days. Tumor types were sarcoma (5), uncertain primary (2), breast (1), and giant cell tumor (1). Ablation locations were retroperitoneum/pelvis (6), extremity (2), and chest wall (1). A greater than 10 Amp increase was observed in the majority of cases corresponding with expectant cellular death. Rationale for IRE was margin enhancement in 5, palliation in 2, and ablation of unresectable disease in 2. There were four post operative complications potentially attributed to IRE which include wound infection, skin blistering, ecchymosis, and failed tendon repair. No intraoperative complications were observed. Follow up at 30 days was remarkable for one death unrelated to the IRE. **Conclusions:** Although IRE is a relatively new a modality with limited widespread use, it has been shown to be safe and offers another tool in the management of soft tissue extremity and retroperitoneal tumors. Further evaluation by prospective randomized trials is needed to determine the long term and disease free survival benefits.

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**P309**

**Validation of a Sarcoma Nomogram using a Cancer Registry N. Wasi,* S.P. Bagaria,1* A. Wagie,2 E.B. Habermann,2 R. Gray,3 Mayo Clinic Florida, Jacksonville, FL.**

**Background:** A Memorial Sloan Kettering Cancer Center (MSKCC) nomogram has been developed to predict disease-specific survival (DSS) following surgery for soft tissue sarcoma (STS). The goal of this study is to compare nomogram-predicted survival with actual survival in a cancer registry and to compare predictive ability with current AJCC staging. **Methods:** A retrospective review of all STS patients from Surveillance, Epidemiology and End Results (SEER) registry data from 1988 to 2011 was conducted. Data for patient age, tumor size, tumor grade, histologic subtype, gender, primary location of tumor, and depth was entered into the nomogram calculator for each patient. Discrimination was quantified using a concordance index. Cali-
Validation of the Memorial Sloan Kettering Cancer Center Sarcoma Nomogram (MSKCCSN) for Sarcoma-specific Mortality in an Asian Population D. Ng, G. Tan, R. Queck, M. Harunul Rashid, M. Teo. Surgical Oncology, National Cancer Centre Singapore, Singapore.

Aim: We aim to evaluate the predictive accuracy of the MSKCCSN in a cohort of patients treated at a single Asian institution. This nomogram has been validated internally and has been validated once by an external patient cohort treated at UCLA. However, it has not been validated in an Asian population and thus its universal applicability remains unproven.

Materials and Methods: Between Jan 1990 and June 2013, 840 adult patients underwent treatment for primary Soft Tissue Sarcoma at the National Cancer Centre Singapore (NCCS). Patients who presented with recurrent or metastatic disease and those whose primary site was skin were excluded from the analysis. 399 patients were included in this analysis. The nomogram was validated by assessing its extent of discrimination (ED) and level of calibration (LC). The ED was quantified using Harrell’s Concordance Index (CI). The LC was assessed by grouping patients into 4 groups according to their nomogram-predicted probabilities and plotting the actual probabilities obtained from Kaplan-Meier estimates against the mean of the predicted probabilities for each group.

Results: The median follow-up time for all patients and surviving patients was 28 and 33 months respectively. The observed 5-year and 10-year Sarcoma Specific Survival (SSS) were 55 and 33 percent respectively. The CI of the NCCS data set was 0.71. For LC, the observed correspondence between predicted and actual outcomes suggest that the MSKCCSN generally predicts well for patients with higher survival probability, but consistently over-predicts survival for the other groups. Conclusion: The MSKCCSN was found to be accurate in terms of ED. In terms of LC, it generally predicts well for patients with higher survival probability but consistently over-predicts survival for the other groups. This could be due to lack of sufficient follow-up time or influence of the learning curve, typical in a chronologically expanded study duration. Longer follow-up or analysis by chronologically determined cohorts will allow determination if modification of the MSKCCSN is required for an Asian population.

P312

Background: soft tissue sarcomas (STS) are a wide group of rare tumors mainly arising from extremities and retroperitoneum. Surgery is the mainstay of treatment and may require complex vascular reconstructions. Aim of the study is to evaluate type of resection/reconstruction and outcome in a large series of patients who had vascular resection as part of STS removal.

Methods:
all consecutive patients affected by localized STS of extremities and retroperitoneum, treated and subjected to vascular resections at Istituto Nazionale dei Tumori of Milan-Italy, between January 2000 and December 2013, were evaluated. Postoperative complications and long-term vascular graft patency were assessed. Overall survival (OS) and crude cumulative incidence (CCI) of local recurrence (LR) and distant metastases (DM) were determined using Kaplan-Meier. Results: 105 patients were identified. Median FU was 28 months. 5-yr OS, CCI of LR and DM for the whole series were 62%, 15% and 57% respectively. In extremities, vascular reconstructions included 45 arterial and 16 venous grafts. In retroperitoneum, 31 venous and 11 arterial grafts were performed [Tab 1]. All patients were treated post-operatively with LMWH. Thrombosis of the vascular reconstruction occurred in 15 patients (7.5% in arterial and 8/49 in venous reconstructions respectively). Arterial occlusions occurred at a median of 36 months after surgery and were treated by Fogarty catheter embolectomy (2 cases), prosthesis replacement (3 cases), percutaneous angioplasty (1 case) and just observation (1 case). No patients had to be eventually amputated. Venous occlusions occurred at a median of 4 months after surgery and all were just monitored. Overall arterial and venous reconstruction patency rate were 88% and 84% respectively. Conclusion: vascular reconstruction is an option that can be safely performed when R0-resection is a goal to optimize local control. However a high risk of metastatic spread was observed. Although the encasement of vascular bundle does not represent a contra-indication for surgery, the association with a high biologic risk should be factored in treatment plan.

Tab. 1: Type of vascular resection/reconstruction in STS surgery

<table>
<thead>
<tr>
<th>Type of Vascular Resection</th>
<th>No. of Patients (%)</th>
<th>Number of Patients</th>
<th>Patency Rate</th>
<th>patency Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>External Iliac Artery</td>
<td>10</td>
<td>1</td>
<td>92%</td>
<td>88%</td>
</tr>
<tr>
<td>Common Femoral Artery</td>
<td>1</td>
<td>1</td>
<td>92%</td>
<td>88%</td>
</tr>
<tr>
<td>Superior Femoral Artery</td>
<td>1</td>
<td>1</td>
<td>92%</td>
<td>88%</td>
</tr>
<tr>
<td>Subclavian Vein</td>
<td>1</td>
<td>1</td>
<td>92%</td>
<td>88%</td>
</tr>
<tr>
<td>Brachial Vein</td>
<td>1</td>
<td>1</td>
<td>92%</td>
<td>88%</td>
</tr>
<tr>
<td>Inferior Vena Cava</td>
<td>12</td>
<td>14</td>
<td>92%</td>
<td>88%</td>
</tr>
<tr>
<td>Portal Vein</td>
<td>1</td>
<td>1</td>
<td>92%</td>
<td>88%</td>
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<td>2</td>
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<td>Superior Femoral Vein</td>
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<tr>
<td>Subclavian Vein</td>
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<td>92%</td>
<td>88%</td>
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<tr>
<td>Brachial Vein</td>
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<td>External Iliac Artery and V</td>
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<td>92%</td>
<td>88%</td>
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<tr>
<td>Superior Femoral Artery and V</td>
<td>6</td>
<td>1</td>
<td>92%</td>
<td>88%</td>
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P313

Soft Tissue Sarcomas in the United States: An Analysis of 56,479 Cases using the Surveillance, Epidemiology and End Results Program (SEER) from 2002-2011

N. Nagarajan,1* S. Khan,1 F. Gani,1 J. Canner,2 C. Morris,1 E. Schneider,1 N. Ahuja,1 1. Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD; 2. Department of Urology, Johns Hopkins University School of Medicine, Baltimore, MD; 3. Department of Orthopaedic Surgery, Johns Hopkins University School of Medicine, Baltimore, MD.

Introduction: Soft tissue sarcomas (STS) represent a heterogeneous group of more than 80 malignant tumors that are challenging and complex to manage. The rare nature of these tumors necessitates long-term data collection to better understand their behavior and outcomes. Our objective was to study the epidemiology of STS over the past 10 years using a nationally representative database. Methods: The Surveillance, Epidemiology and End Results (SEER) database was queried for cases of soft tissue sarcoma from 2002-2011. Patients were included in the study based on ICD-0-3 histology codes. Demographics, primary site, grade, size, metastasis, surgical management, and radiation therapy were analyzed for each major histological group. All-cause and cause-specific mortality along with 5-year survival were calculated. Results: A total of 56,479 cases of STS met inclusion criteria with an incidence of 6.8 cases per 100,000 people. The study population comprised of 50.9% females and 78.8% Whites with a median age of 58 years (IQR=42-72). The most common primary site for STS was soft tissue (42.3%) followed by visceral (38.9%). The majority of tumors were <5 cm (60.9%), of unknown grade (44.9%) and had not metastasized at diagnosis (62.6%). For the management of STS, 79.9% of patients underwent surgery for primary tumor, 16.4% for metastasis and 25.6% patients received radiation therapy. All-cause mortality was 28.9% and case-specific mortality was 22.9%. For cases prior to 2008, 5-year survival was 71.2% and varied according to demographics, tumor-specific factors, and treatment (Table 1). Conclusion: The study summarizes the epidemiology of STS over the past 10 years in the United States. There are marked differences in incidence, and survival by histology, grade, and site. With implications for management, these findings facilitate a better understanding of the natural history of these malignancies.

Table 1: Characteristics of soft tissue sarcoma from SEER 2002-2011

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of patients (%)</th>
<th>5-Year survival (%)</th>
<th>Variable</th>
<th>No. of patients (%)</th>
<th>5-Year survival (%)</th>
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</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>27731 (49.1)</td>
<td>70.7</td>
<td>Soft tissue only</td>
<td>23881 (42.3)</td>
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<tr>
<td></td>
<td>Female</td>
<td>24748 (50.9)</td>
<td>71.7</td>
<td>Visceral</td>
<td>21709 (38.9)</td>
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<tr>
<td></td>
<td>White</td>
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<td>71.8</td>
<td>Renal and Neph</td>
<td>30281 (54.0)</td>
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<tr>
<td></td>
<td>Black</td>
<td>6993 (12.5)</td>
<td>67.2</td>
<td>Bone</td>
<td>6465 (11.5)</td>
</tr>
<tr>
<td>Race</td>
<td>Others(2)</td>
<td>5060 (8.9)</td>
<td>72.0</td>
<td>Others(2)</td>
<td>6081 (11.3)</td>
</tr>
<tr>
<td></td>
<td>&lt;5 cm</td>
<td>3422 (60.9)</td>
<td>72.7</td>
<td>Others(2)</td>
<td>6081 (11.3)</td>
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<td></td>
<td>&gt;5 cm</td>
<td>171 (0.3)</td>
<td>59.9</td>
<td>Others(2)</td>
<td>6081 (11.3)</td>
</tr>
<tr>
<td></td>
<td>&gt;10 cm</td>
<td>50 (0.1)</td>
<td>30.9</td>
<td>Others(2)</td>
<td>6081 (11.3)</td>
</tr>
<tr>
<td>Primary</td>
<td>Muscle sarcoma</td>
<td>5187 (6.3)</td>
<td>56.5</td>
<td>Primary on Primary</td>
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</tr>
<tr>
<td>Site</td>
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<td>56.2</td>
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<tr>
<td></td>
<td>Other(2)</td>
<td>23965 (44.9)</td>
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<tr>
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<td>&lt;5 cm</td>
<td>150</td>
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<td>23965 (44.9)</td>
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<td></td>
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<td>56.0</td>
<td>Other(2)</td>
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<tr>
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<td>250</td>
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<td>Other(2)</td>
<td>23965 (44.9)</td>
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<td>56.0</td>
<td>Other(2)</td>
<td>23965 (44.9)</td>
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P314

Patterns of Systemic Relapse in Curatively Treated Soft Tissue Sarcomas: Long-term Results from a Tertiary Care Cancer Centre

S.V. Deo, N.K. Shukla, J. Sharma,* M. NML, S. Bakhshi, D. Sharma, S. Thulkar, Surgical Oncology, All India Institute of Medical Sciences, New Delhi, New Delhi, Delhi NCR, India.

Introduction: Soft tissue sarcomas (STS) constitute a rare and challenging group of solid tumors. Multidisciplinary care has improved the limb salvage rates and local tumor control. However, despite the curative treatment, a significant number of patients develop systemic disease. We present our experience of systemic relapse patterns in STS. Materials and Methods: A retrospective analysis of prospective database of STS patients treated between 1995 and 2000 was performed. Patients undergoing curative resection and appropriate adjuvant therapy (Radiotherapy for > 5 cm, high grade and recurrent sarcomas (1) Unadjusted; (2) Missing, blank or unknown; (3) Malignant Fibrous Histiocytoma; (4) Fibrosarcoma, Osteosarcoma, Chondrosarcoma, Synovial, Clear cell, Myxosarcoma, Malignant hemangioendothelioma, Malignant giant cell tumor, Malignant granular cell tumor, Alveolar soft part or Desmoplastic small round cell tumor; (5) On distant metastasis or regional lymph nodes
and chemotherapy for high grade sarcomas) were analyzed for incidence of systemic relapse, site distribution and risk factors for systemic relapse including primary site, histopathology subtype, grade and stage. Results: A total of 435 patients with STS were analysed and 375 patients having a curative resection were included for analysis. Seventy six out of 375 (20.26%) had distant relapse, of which 7 (9.21%) also had loco-regional relapse. Median time to relapse was 11.76 months. Overall 26% (66/254) of extremity sarcoma patients and 8% (10/126) of non-extremity sarcoma patients developed distant metastases. Sixty two out of 76 (81.57%) patients had pulmonary metastases and 14 (11.29%) had extrapulmonary metastasis (liver-5, bone-3, brain-1, distant nodes-2, orbit-1, peritoneum-2). Amongst 62 patients with pulmonary metastases 55 (88.70%) had isolated pulmonary only, while 7 (11.29%) had additional sites. Majority of patients with systemic relapse had MSKCC stage III (83%) and high grade tumors (97%). Synovial Sarcoma was predominant histology seen in 42% (32/76), followed by Malignant Peripheral Nerve Sheath Tumor (12/76) and Malignant Fibrous Histiocytoma (9/76). Only 9 patients with pulmonary metastases could be salvaged with metastastectomy and others received palliative treatment only.

P315
Is F-18 fluoro-2-deoxy-D-glucose Positron Emission Tomography (FDG-PET/CT) of Value in Soft Tissue Sarcoma Management?

W.S. Orr,*, 1 K. Watson, 1 R. Feig, 1 N. Ikoma, 2 N. De Rosa, 1 G. Giaccone, 2 V. Ravi, 1 R.S. Benjamin, 3 J.E. Madewell, 4 J.N. Cormier, 1 K.K. Hunt, 1 C.L. Roland, 1 B.W. Feig, 1 K. Torres, 1 Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX; 2. Tumor Registry, UT MD Anderson Cancer Center, Houston, TX; 3. Sarcoma Medical Oncology, UT MD Anderson Cancer Center, Houston, TX; 4. Diagnostic Radiology, UT MD Anderson Cancer Center, Houston, TX.

Background: Positron emission tomography (FDG-PET/CT) is being used with increasing frequency in the staging and treatment response management of soft tissue sarcoma patients. In this study, we evaluate the value of FDG-PET/CT to assess whether initial maximum standardized uptake values (SUVmax) correlate with tumor grade and outcomes. Methods: 323 patients that underwent FDG-PET/CT scans were retrospectively evaluated. The SUVmax of tumors were compared for various histologic subtypes and correlated with histopathologic grade. The SUV change ([SUVmax prior to neoadjuvant therapy] – [SUVmax post neoadjuvant therapy]) was also correlated with histopathologic tumor necrosis and size change based on imaging studies. Results: Primary tumors had a mean SUVmax of 11.2. No significant difference was found in the mean SUVmax for recurrent or metastatic tumors when compared to primary tumors (p=0.4). Tumor SUVmax differed significantly among tumor grades; high grade tumors had a mean SUVmax of 14.8 which was higher than intermediate (mean, 7.9, p=0.001) and low grade tumors (mean, 3.9, p=0.001). ROC analysis indicated a cutoff SUVmax ≥5.45 for intermediate/high grade lesions for a sensitivity = 86% (95%CI, 79-91%) and specificity = 80% (95%CI, 52-96%) and accuracy = 0.92. SUVmax also varied significantly among histologic subtypes. Patients with primary tumors with SUVmax ≥10 were more likely to develop metastatic disease compared to tumors with SUVmax <10 (5-yr MFS: 53.8% vs. 86.2%; HR 4.4, p=0.009). Patients that had SUVmax < 10 had a better disease-specific survival (DSS) when compared to those with SUVmax ≥10 (5-year DSS = 93.7% versus 40.3% respectively, p<0.001). The SUV change correlated with the percent of necrosis on the pathology report (p = 0.05) and change in size (p = 0.001).

Conclusion: SUVmax correlates with tumor grade. Similar to previous studies, FDG-PET/CT can provide important supplemental information regarding tumor biology when used in conjunction with traditional histopathologic findings. The SUVmax of primary soft tissue sarcomas reflects the metastatic potential and correlates with disease-specific survival.

P316
Recurrent Retroperitoneal Liposarcoma: At which Point is Surgery No Longer Useful?

N. Thiruchelvam,*, 1 M. Teo, 1 National Cancer Centre Singapore, Singapore.

Background The management of retro-peritoneal soft-tissue liposarcoma is centred largely on surgical resection but in spite of complete resection, a significant proportion of these tumours still recur locally. Often, with each resection, the disease-free interval becomes progressively shorter. There is currently no consensus as to when surgical re-resection may no longer result in survival benefit. Methodology A retrospective review of patients with retroperitoneal liposarcomas (RPS) who underwent complete surgical resection at our institute between January 1990 and January 2014 was performed, and patients who developed a local recurrence were identified. The end-points of the study included the subsequent disease-free interval and disease-specific survival. The aim was to identify prognostic factors that may influence the clinical dilemma of proceeding with surgical resection for recurrences. Results A total of 76 patients had undergone a first resection for 76 patients, of whom 42 patients had presented to us with recurrent RPS with their primary resections performed elsewhere. 80% (67) of resections required contiguous organ resection to achieve gross surgical margins, with 5% (4) requiring additional major vascular reconstruction or ligation. The presence of multi-centric recurrences was a significant variable influencing the development of a subsequent recurrence but it did not appear to affect disease specific survival. Patients with tumour growth rates of greater than 1.0cm per month had median disease-free intervals of 8 months (4-47) compared to 19.5 months (4-181) in those with slower growth rates. Conclusion A significant proportion of retroperitoneal liposarcomas recur locally and often contiguous organ resection is a necessity to achieve surgical margins. Using a cut-off of 1cm per month for the growth rate of tumour recurrence is likely to be helpful in the decision-making process of proceeding with extensive resection, in particular in the select group of patients with poorer ECOG. Surgeons should then consider the likely shorter disease-specific survival for these patients, and discuss options of palliation with non-operative treatment.

P317
Neoadjuvant Radiation Therapy for Retroperitoneal Sarcoma: A Systematic Review

H. Cheng,*, 1 J.T. Miura, 1 M. Lalehzari, 1 T. Jayakrishnan, 2 A. Donahue, 2 T. Gamblin, 3 K.K. Turaga, 3 F.M. Johnston. Surgery, Medical College of Wisconsin, Milwaukee, WI.

Background: The multi-modal treatment of retroperitoneal sarcoma (RPS) has seen the increased use of neoadjuvant radiation (NART). However, its effect on local recurrence and survival remain controversial. We aimed to evaluate and synthesize the contemporary literature on NART for RPS. Methods: The review was conducted according the recommendation of the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group with pre-specified inclusion and exclusion criteria. DEALE method was used to combine mortality rates. Results: Of 8,701 citations collected, 27 articles reported on 4,585 patients. The median age was 57 years (IQR 54.9-59.1) with 50% (43.85-56.15) male. Of studies that differentiated between primary and recurrent disease, 29.4% (175/596) of patients presented with recurrent disease. The most common subtypes were liposarcoma (51.54%), followed by leiomyosarcoma (23.6%). The average median tumor size was 14.0 cm (9.9-14.9). Most studies used external beam radiation therapy for NART with an average dose of 48 Gy. An average of 89% of patients completed NART regimens. Surgically, 61.68% of patients received an R0 resection, followed by 19.92% for R1 and 18.40% for R2. Using the NC1 Common Toxicity Criteria for Adverse Events, 25.14% of patients developed Grade 1 toxicity, 35.51% Grade 2, 32.07% Grade 3, 2.27% Grade 4, and 5.01% Grade 5. The weighted 5 year overall survival was 55% (IQR 46-61%). Conclusions: NART is safe and provides for improved rates of overall survival as compared to historical controls. Improved quality of reporting is needed to improve the ability to draw conclusion in the absence of randomized trials.

P318
Clinicopathologic Comparison of Retroperitoneal Undifferentiated Pleomorphic Sarcoma and Dedifferentiated Liposarcoma

N. Ikoma,*, 1 S. Landers, 1 K. Watson, 1 G.A. Al Samnaa, 2 D. Ingram, 2 W. Wang, 2 A. Lazar, 2 N. Somaiah, 3 C.L. Roland, 3 J.N. Cormier, 1 K.K. Hunt, 1 B.W. Feig, 1 K. Torres, 1 Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX; 2. Pathology, UT MD Anderson Cancer Center, Houston, TX; 3. Sarcoma Medical Oncology, UT MD Anderson Cancer Center, Houston, TX.

Introduction: The true nature of undifferentiated pleomorphic sarcoma/malignant fibrous histiocytoma (UPS:MFH) of the retroperitoneum and the validity of this diagnostic entity have been questioned. Some propose that virtually all retroperitoneal UPS can be reclassified as highly dedifferentiated liposarcoma (DDLPS). Liposarcomas (LPS) are the most common histologic soft tissue sarcoma subtype in the retroperitoneum. In this study, we compared the clinicopathologic characteristics and treatment outcomes of UPS and DDLPS in the retroperitoneum. Methods: A comprehensive search of...
our institutional tumor registry (2008 to 2013) was used to identify patients with UPS (n=85) and DDLPS (n=124) located in the retroperitoneum. Clinicopathologic variables were assessed for association with local recurrence free survival (RFS), metastasis free survival (MFS), disease-specific survival (DSS) and overall survival (OS). A subgroup (UPS=33 and DDLPS=33) was reanalyzed histologically, and molecularly to determine the presence of a specific line of differentiation or 12q15/MDM2 amplification. Results: UPS patients had significantly longer 5-year RFS than DDLPS patients (55.1% vs 22.0%, p=0.024). Lower MFS was found in UPS when compared to DDLPS (58.6% vs 74.9%, p=0.05). No statistically significant difference in 5-year OS was found among cohorts (DDLPS=51.2% vs UPS=48%, p=0.794; DDLPS=42.4% vs UPS=35.1%, p=0.325). In univariate analysis, surgically resected UPS patients were more likely to receive survival benefit from additional chemo- or radiation therapy than DDLPS (5-year OS 58.5% vs 35.6%, p=0.004) and additional chemotherapy (5-year OS 60.6% vs 47.7%, p=0.086). Conversely, for surgically resectable DDLPS no survival benefit from additional chemo- or radiation therapy was found. MDM2/12q15 gene amplification was positive in 6 of 33 UPS tumors and 33 of 33 DDLPS specimens. Conclusion: This study supports the concept that retroperitoneal UPS classification is clinically important. This histologic entity behaves differently from DDLPS of the retroperitoneum. The clinical differences between retroperitoneal UPS and DDLPS should be considered when treating these patients.


Background: The role of systemic chemotherapy (CT) in the multimodality treatment strategy for retroperitoneal sarcomas (RPS) remains controversial. We hypothesized that CT does not improve survival for patients with surgically resected RPS. Methods: The National Cancer Database was used to identify all patients with RPS that underwent surgical resection from 1998-2011. Log rank tests and multivariable Cox proportional hazards modeling were used to assess overall survival (OS). Results: A total of 8,653 patients with surgically resected RPS were identified; 1,525 (17.6%) received CT. Factors associated with receipt of CT included moderate (OR 2.3) to poorly differentiated (OR 4.3) tumors, liposarcoma (OR 1.8) and undifferentiated pleomorphic sarcoma (OR 2.3) histology, and R2 resection status (OR 2.2) all p < 0.01. Unadjusted median OS for patients receiving CT compared to surgery alone was 40 vs 68.2 months respectively (p=0.01). On multivariable analysis, radiation therapy resulted in improved survival (HR 0.74, 95%CI: 0.67-0.81, p<0.01). However, receipt of chemotherapy was not independently associated with improved long term survival (HR 1.4, 95%CI: 1.26-1.58; p<0.01). Conclusion: Current available chemotherapy regimens for RPS do not confer a survival benefit. Routine use of chemotherapy for RPS should be discouraged until new effective systemic agents become available.


Introduction: Soft tissue sarcomas (STS) are generally considered radio-resistant (RR) tumors; however radiation (RT) may decrease local recurrence (LR). A validated molecular measure of radiosensitivity (RSI) was used to evaluate RR and determine whether RS is predictive of LR in STS. Methods: After IRB approval patients (pts) treated with surgery and RT were identified from a prospective observational protocol. Genomically-profiled patients (Affymetrix Hu-RSTA-2a520709) were obtained from a de-identified metabolomics database and RSI was calculated based upon the gene expression of STAT5, HDAC1, CDK1, androgen receptor, NF-kB, IRF1, SUMO1, c-Jun, PKC, and c-Abl and a linear regression algorithm modeled on SF2 of 48 cancer cell lines, where RSI high = RR. Cox modeling and Kaplan Meier method were used to determine median time to and predictors of local recurrence free survival (LRFS). Results: 32 pts (19 male), median age of 59 years, were included. Site of disease included extremity (72%), trunk (9%) and other (19%). Median follow-up was 60 mos and 15(47%) pts were disease free, 17(53%) recurred [8(47%) LR, 9(53%) distant] and 4(13%) died. Tumors were divided into RR and radiosensitive(RS) by RRI (RR 20(63%) vs. RS 12(38%)) and histologic subtype was classified into 4 categories and further characterized using RSI (RR vs RS) [pleomorphic undifferentiated (4 vs 4), well-differentiated liposarcoma (2 vs 1), dedifferentiated (3 vs 2), leiomyosarcoma (1 vs 2) and other (10 vs 3)]. There were 7 LR in this cohort, 6(86%) RR vs 1(14%) RS, p=0.21. On univariate analysis, RR suggested a worse LRFS compared to RS (HR 3.4, 0.55-65.2, p=0.20). Conclusions: In this cohort utilizing a novel predictive tool for RS the majority of LR occurred in patients with RR tumors. Although a statistically significant difference in LRFS was not due to sample size, our previous work has demonstrated significance using RSI for epithelial tumors [RR(brain, thyroid, soft tissue, pancreas, skin, uterus and rectum) and RS(head/neck, esophagus, cervix and liver)]. There may be a benefit to utilizing RSI score with standard prognostic variables to better define the role of RT in patients with sarcoma.

P321 Predictors of Outcome in Primary and Recurrent Epithelioid Sarcoma O.M. Rashid, * J. Kaplan, O. Binitie, J. Zager, D. Letson, R.J. Gonzalez. H. Lee Moffitt Cancer Center, Tampa, FL.

Epithelioid sarcoma (ES) is rare. We reviewed a high volume sarcoma center experience with ES to evaluate prognostic variables, management and outcomes. ES cases treated at a single institution from 1992-2013 were reviewed for clinicopathological factors, and Kaplan-Meier disease free (DFS) and overall survival (OS) analysis performed. There were 18 patients (pts), median age was 40 years (18-79) and 11(61%) were male. Median follow up was 20 months. 2(11%) lost to follow up and excluded. 12(67%) presented with primary tumors, 6(33%) after recurrence. Primary site included extremity 12(67%) or other 6(33%). Median primary tumor size was 6 cm (range, 1-17 cm). At diagnosis 15 had local disease, 1 nodal disease, and 2 distant metastasis. Of the surgical pts (n=15) 6(40%) underwent amputation and 9(60%) underwent resection. R0 resection was performed in 6(42%), R1 in 8(53%), and R2 in 1(7%). Tumors > 6cm had a higher rate of R1 resection (2/25) vs 6(75%), p=0.03. Neoadjuvant chemo/RT was used for 2(13%) both with final margin being R1. Adjuvant chemo and/or RT were used in 8(53%) pts; 5(30%) received surgery alone. Of 14 pts rendered disease free, 1(7%) remained local disease (65%), distant (54%) with a median DFS of OS of 31 and 33 months, respectively. There was no difference in pattern of recurrence, DFS or OS related to primary treatment rendered or margin (R0 vs R1). Compared to pts not offered surgery for recurrence (n=4), 1 local, 3 distant), pts who underwent surgery (n=7 (5 local, 2 distant)) had a longer median DFS (31 vs 12mos, p=0.005) from primary resection and improved median OS after recurrence (37 vs 5 mos, p=0.02). Primary tumor mitotic activity and microscopic vascular invasion correlated with worse OS. Primary tumor > 6cm correlated with worse DFS. Multivariate analysis was not performed due to sample size. Although ES is rare and results are limited due to sample size, this study provides important prognostic information. Mitotic activity and vascular invasion correlated with OS. Primary tumor size >6cm correlated with R1 resection and worse DFS. Patients with resectable recurrent disease after a long DFS should be considered for surgery.
**P414**

The Contribution of Local Treatment Measures to Control Imatinib-resistant Liver Metastases of Gastrointestinal Stromal Tumors (GIST) P. Hohenberger,2 N. Rathmann,3 M. Sadick,1 F. Menge,2 S. Schönberg,2 S. Diehl.1 1. Dept of Surgery, Mannheim University Medical Center, University of Heidelberg, Germany, Div.of Surgical Oncology and Thoracic Surgery, Mannheim, Germany; 2. Institute of Clinical Radiology and Nuclear Medicine, Mannheim, Ba-Wue, Germany.

**Objectives:** The liver and the peritoneum are the main area of metastatic spread in gastrointestinal stromal tumors (GIST). Liver surgery plays a minor role for hepatic metastases in comparison to f.e. colorectal cancer. However, once the metastases are resistant to 1st line TKI therapy, 2nd line therapy, interventional ablation techniques like RFA or selective internal radiation therapy (SIRT) are treatment options. We were interested to analyze the contribution of the different modalities in controlling hepatic progression. **Methods:** 731 pts with biopsy proven GIST were followed since 2004 (median follow-up 43.6 months); data were prospectively documented. There were 337 males (46.1%) and 101 (13.8%) pts. presenting with M1 disease initially. Of the remaining 630 pts, 358 pts (56.8%) developed tumor recurrence after a median time interval of 22 months. 312/358 pts (87%) developed metastases within the abdomen: liver n=96, peritoneal n=97, liver+peritoneal n=78, locoregional n=10, locoreg. +hep/per n=21. Imatinib was the initial treatment in all patients with M1 disease. **Results:** Out of 205 patients with liver metastases, 118 remained controlled by drug therapy or showed multi-site progression. In the remaining 87 pts., 26 pts each underwent liver resection or 2nd/3rd line drug therapy (sunitinib, regorafenib), 22 pts had RFA and 13 pts were treated by SIRT. Follow-up was done via dynamic MRI and contrast-enhanced (CE)-CT. The median hepatic-progression free survival (H-PFS) was 5.6 (range, 2 – 13) months after 2nd line drug therapy, 7.7 (5-14) months after RFA and 15.9 months (4-29) after SIRT (with 3 CR, 6 PR), p<0.02. **Conclusion:** 90Y radiation loaded particles (SIRT) provides the best hepatic control in metastases that were resistant to TKIs. Liver resection or RFA are options of treatment in imatinib resistant GIST liver metastases. The effect could be mediated by eliminating small (subclinical, micro-) metastases through the intervention. In patients known to have a GIST resistant to TKIs, SIRT could be used in earlier treatment lines.

**P322**

Promoter DNA Hypermethylation of CDO1 Gene Predicts Poor Prognosis in Clinical Stage II/III Esophageal Squamous Cell Carcinoma H. Ushiku,1 K. Yamashita,1 A. Ema,1 H. Moriya,2 K. Hosoda,3 A. Kitasato,3 H. Ushiku,1 K. Yamashita,1 A. Ema,1 H. Moriya,2 K. Hosoda,3 A. Kitasato,3 J. Kim,4 D.J. Raz,1 I.B. Paz,1 J.Y. Kim,1 I. Thoracic Surgery, City of Hope National Medical Center, Duarte, CA; 2. Surgical Oncology, City of Hope National Center, Duarte, CA;

**INTRODUCTION:** Esophageal squamous cell cancers (ES) are rare malignancies reported sporadically in the literature. There have been no population-based studies to determine the incidence, characteristics, and surgical outcomes of ES. METHODS: We identified ES cases using primary site and histology ICD-O-3 codes from SEER registry from 1973-2011. We examined incidence, demographics, tumor characteristics, and therapies and compared these to the results of other esophageal cancers (OEC). Survival data was obtained from Kaplan-Meier estimation. Univariate and multivariate Cox proportional hazards model determined predictors of overall survival (OS). RESULTS: Of 71,577 esophageal cancer patients identified, 182 (0.25%) had ES histology. ES patients were mostly younger than non-white, had localized tumors, and underwent surgery, but less likely to receive radiation than OEC patients. The most common histologies were carcinosarcoma (n=56, 31%), leiomyosarcoma (n=47, 26%) and gastrointestinal stromal tumors (GIST) (n=41, 23%). The most common tumor location was lower esophagus (n=77, 42%). Five-year OS for ES patients was 38% compared to 18% for OES patients. Median survival was 24 and 9 months for ES and OEC surgical patients, respectively. ES patients who received surgery had better OS than those who did not (44% vs. 28% at 5 years). In multivariate analysis, age and advanced disease conferred worse survival (HR 1.03, CI 1.02-1.05 for age, HR 2.28 CI 1.45-3.59 for regional compared to local disease, HR 3.87 CI 2.20-6.81 for distant compared to local disease) while GIST histology was favorable for survival (HR 0.39 CI 0.20-0.74). CONCLUSION: In this study, we found that ES were more likely to be localized and treated with surgery. OS was better in patients with ES than in OEC patients. This was also true for patients who underwent surgical resection. Regional and distant disease and age were predictors of poor survival while favorable histology conferred better survival. ES, although rare, had the advantage of being diagnosed at an earlier stage and having a better prognosis than OEC likely due to underlying tumor characteristics and mechanisms of metastasis.
P325

Treatment of Diaphragmatic Hernia Occurring after Transhiatal Esophagectomy


Introduction: Post-esophagectomy diaphragmatic hernia (DH) is an uncommon problem but important to recognize and treat because of the risk of significant complications such as incarceration and strangulation. Diaphragmatic hernia appears to occur more frequently following transhiatal esophagectomy (THE) than transthoracic procedures, likely because of the enlargement of the diaphragmatic hiatus required to perform THE. Methods: Following 199 consecutive esophagectomies performed at Rutgers Robert Wood Johnson University Hospital between January 2000 and June 2013, ten patients were identified with DH; all underwent diaphragmatic hernia repair (DHR). All patients who underwent THE during this time period were catalogued in a prospectively maintained database which was then retrospectively reviewed. All DH were repaired using a novel biologic plug mesh technique. Results: Ten esophagectomy patients developed DH; nine post THE and one post-McKown esophagectomy. One patient was excluded from analysis because of atypical presentation. Demographic data were similar between esophagectomy patients who developed DH and those who did not. Administration of neoadjuvant chemoradiation correlated with development of DH but did not reach statistical significance. Complications directly related to DHR were few and did not reach statistical significance. Conclusion: Diaphragmatic hernia development post-esophagectomy is an uncommon complication but can have devastating results when there is bowel compromise. Repair by plugging the diaphragmatic hiatus with a biologic mesh is a safe and effective method for closing the defect, resulting in few complications and no hernia recurrences in this series.

P326

Ex Vivo Analysis of Human Esophageal Adenocarcinoma Demonstrated the Selective Infectivity of a Conditionally Replicative Oncolytic Adenovirus C.J. LaRocca,* A.R. Oliveira, R.S. Andrade, J. Davydova, M. Yamamoto. University of Minnesota, Minneapolis, MN.

Introduction: Esophageal adenocarcinoma (EAC), whose incidence is rising in Western countries, continues to present treatment challenges for clini-
cians. Our group has designed conditionally replicative adenoviruses (CRAd) controlled by the cyclooxygenase 2 (Cox2) promoter. Given the high expression of Cox2 on human EAC, our vectors selectively infect and replicate in cancer cells while minimizing toxicities to normal tissues. In this study, we tested the function of Cox2-CRAds in multiple models including human tissue slices created from resected surgical specimens. Methods: Using multiple esophageal cancer cell lines, oncolytic adenoviruses were tested in vitro to determine their cytotoxic effect. Additionally, an interferon (IFN) expressing Cox2-CRAd was tested in vivo using nude mice. Then, samples of normal human esophagus and biopsy-proven EAC were obtained following surgical resection. Using a KrumDieck tissue slicer, samples were prepared and then infected with viruses. Results: In vitro, an IFN-expressing Cox2-CRAd showed a robust cytocidal effect across all tested cell lines. Additionally, when this vector was used in combination with cisplatin and radiation, there was a more pronounced in vitro cytotoxic effect. Furthermore, that same virus demonstrated a strong anti-tumor effect against subcutaneous EAC tumors established in nude mice. For the patient-derived tissue slices, a luciferase assay was used to analyze the degree of viral replication in a Cox2 promoter-controlled adenovirus and in an otherwise identical virus lacking promoter control. For EAC, both vectors showed strong infections of the samples as expected, and there was no significant difference in the degree of viral replication. Importantly, in the samples of normal esophageal tissue, there was minimal replication of the Cox2 promoter-controlled adenovirus when compared to the virus without the promoter (p<0.05). Conclusion: Our oncolytic adenovirus controlled by the Cox2 promoter clearly demonstrated selective infection of a patient-derived EAC sample, while only minimally affecting normal esophageal tissue.

**P327**

Effectiveness of Neoadjuvant Concurrent Chemoradiotherapy versus Upfront Esophagectomy for Locally Advanced Esophageal Squamous Cell Carcinoma Patients: A Propensity Score Matched Analysis

H. Fang,1 C. Lin,2 C. Chien,*1 1. Department of Chest Surgery, China Medical University Hospital, Taichung, Taiwan; 2. Department of Hematology & Medical Oncology, China Medical University Hospital, Taichung, Taiwan.

Introduction: Neoadjuvant concurrent chemoradiotherapy (NCCRT) is often considered for locally-advanced esophageal squamous cell carcinoma (LA-ESqCC) patients. There were few data regarding the population-level effectiveness. Our study aimed to evaluate the effectiveness of NCCRT vs Upfront Esophagectomy (UE) for LA-ESqCC in the population level. Methods: We identified LA-ESqCC (AJCC 6th cT2-3N0M0 or cT1-3N0-1M0) patients and treated with either NCCRT or UE through a population-based retrospective cohort analysis. We included potential confounding covariables (age, gender, residency region, stage) and used propensity score (PS) to construct a 1:1 population. The Effectiveness was measured as overall survival (censored on Jan 1st, 2013). Moreover, we performed the sensitivity analysis to evaluate the potential impact of unmeasured confounders on survival. Results: 1511 LA-ESqCC patients treated with either NCCRT or UE were identified as the initial study population. After exclusion of those with missing data and matching by PS, the final study population included 272 patients. Well balance in covariables was seen for all covariables. The median RT dose in NCCRT was 45Gy (inter-quartile range: 40-50.4). The hazard ratio of death when NCCRT was compared to UE was 0.62 (95% confidence interval 0.47-0.817, p=0.0007). The Kaplan-Meier survival curve was depicted as figure 1. All patients in NCCRT received UE except two. Among the remaining 134 pairs where all patients received UE, 36 patients had pathological complete remission after NCCRT. NCCRT was also associated with higher R0 resection (123 vs 108). In sensitivity analysis, the effect of NCCRT (vs. UE) on survival for LA-ESqCC remained statistical significant (p-value<0.05) even if there is an unmeasured confounder increased the odds of receiving NCCRT (vs. UE) no greater than 10%. Conclusions: When compared to UE, NCCRT is likely to improve survival in the population level. The results should be interpreted with caution given that our result is sensitive to potential omitted variable bias in sensitivity analysis.

**P329**

A Study of Relationship between Neutrophil Lymphocyte Ratio and postoperative Complications and Prognosis for Esophageal Cancer Patients


Background: The neutrophil lymphocyte ratio (NLR) has been reported to predict prognosis of the patient in some malignant tumors. In this study, we evaluated relationship between NLR before treatment and prognosis and postoperative complications in esophageal cancer patients.

Methods: We aimed at 143 patients with esophageal cancer (squamous cell carcinoma) who had measured NLR before treatment and underwent esophagectomy from January, 2008 to December, 2013 in our hospital. A total of 126 men and 17 women, with a mean age of 63.4 were included. The stage before treatment was 0-15+/ A+B=A/B+46/53/40/4 (UICC TNM 6th Edition). All the cases except Stage 0+ were received neoadjuvant chemotherapy. Chemoradiation therapy cases were excepted from this study. More than NLR 2.0 cases were classified high NLR group, and under 2.0 cases were classified low NLR group. Results: High NLR group was 96 cases and low NLR group was 47 cases, and there was no statistically significant difference of the stage before treatment between two groups. The overall survival of high NLR group were significantly worse than low NLR group (61.8 months vs 48.7 months, p=0.03). And in low NLR group, incidence of postoperative pneumonia was significantly less than those in high NLR group (15% vs 32%, p=0.03). Conclusions: High NLR may be a biomarker of postoperative complications and poor prognosis for esophageal cancer patients.

**P330**

Ferredoxin Reductase is Useful for Predicting the Effect of Chemoradiation Therapy on Esophageal Squamous Cell Carcinoma


Background: Ferredoxin reductase (Fdxr) is the 54 kDa mammalian mitochondrial cytochrome P-450 NADPH reductase and transfers electrons from NADPH to substrates. Under substrate-limiting conditions, electrons can leak from this system and generate ROS. Over-expression of Fdxr increases sensitivity of tumor cells to apoptosis on anti-cancer agents' treatment, through ROS production. The aims of this retrospective study were to examine the expression of Fdxr in biopsy specimens of esophageal squamous cell carcinoma (ESCC) and to evaluate whether such expression is useful for predicting the response to chemoradiation therapy (CRT). Methods: A total of 50 patients with ESCC who received curative surgery after CRT were enrolled in the current study. Fdxr expression in the biopsy specimens before CRT was examined immunohistochemically using anti-Fdxr antibody. The correlation Fdxr expression and clinical factors, histological and clinical response to CRT were analyzed. CRT consisted of 5-fluorouracil plus cisplatin and 40 Gy of radiation. The histological criteria for the response of CRT were as follows; Grade 1: tumor is present...
in more than 1/3 of the whole lesion. Grade 2: tumor is present in less than 1/3 of the whole lesion. Grade 3: No viable tumor cells are observed. Results: The rate of Fdxr-positive expression was 42%. The number of patient with Grades 1, 2 and 3 was 23, 15 and 12, respectively. In the Fdxr- positive and Fdxr-negative groups, there were 1 and 22 Grade 1 cases, 13 and 2 Grade2 cases and 7 and 5 Grade 3 cases, respectively. There was a significant difference in the histological effect of CRT between the Fdxr-positive and -negative groups (p = 0.001). Furthermore, the 5-year survival rates were 76.6% in the Fdxr-positive group and 38.4% in the Fdxr-negative group (p = 0.006). Multivariate analysis showed that Fdxr expression status was an independent prognostic factor. Conclusions: Fdxr expression was found to be closely related to the effect of CRT and could predict the CRT outcome in patients with ESCC.

**P331**

**Impact of Surgical Care on Survival in Esophageal Cancer**

J. Plukker,1* J. Hill,1 D. Boselli,1 J. Salo,1 1. Surgical Oncology, Levine Cancer Institute, Charlotte, NC; 2. Carolinas Medical Center, Charlotte, NC.

Background: Survival after multimodality treatment of localized esophageal cancer depends upon complex interactions between the patient, tumor biology, and treatment factors. The National Cancer Database (NCDB) was used to analyze prognostic factors to identify areas for treatment optimization.

Methods: 8,072 patients with localized esophageal cancer treated with neoadjuvant therapy undergoing surgical resection between 2004 and 2006 were identified from the NCDB. Covariates were analyzed for association with survival using univariate and multivariate Cox models. Results: A multivariate Cox proportional hazards model was constructed; significant factors predictive of survival are presented in Table 1. Survival varied markedly based upon the annual surgical volume of esophageal resection performed at the hospital. For hospitals performing 5 or fewer esophageal resections per year (15% of cases), 5-year survival was 40.0%, compared with 48.6% for patients treated at hospitals performing 20 or greater (26% of cases). Hospital length of stay after surgery also profoundly affected survival. For patients with a post-operative length of stay of less than 14 days, 5-year survival was 40% and median survival 39.1 months. Median survival was 28 months, 19 months, and 15 months in patients with a hospital length of stay of 14-21 days, 21-28 days, and greater than 28 days, respectively. Conclusions: Data from the NCDB confirms the association between perioperative events and long-term survival after resection for esophageal cancer. Given the wide variance in outcomes confirms the association between perioperative events and long-term survival in patients treated with neoadjuvant CRT was compared to surgery alone patients (S). Results: Previously, we identified a putative CSC-like population (CD24-/CD44+) in EC cell lines and in esophageal adenocarcinoma (EAC). From a panel of 84 CSC related genes, Pth1r was found to be up-regulated in the OE21 CD24-/CD44+ putative CSC-like population when compared to CD24+/CD44+ population and the solid tumor (2.5 and 3.7 fold, respectively). Furthermore, in OE33 this up-regulation was 1.4 and 1.7 fold. From 6 preselected candidate CRT response markers, CD44 and Sonic Hedgehog (SHH) expression was 55% (p<0.05) and 64% (p<0.005) enhanced in mRD compared to the S group in IHC material. Moreover, SHH expression showed a positive correlation coefficient of 0.531 (P<0.005) with CD44 and 0.512 (P<0.05) with Excision Repair Cross-Complementation group I (ERCC1) in mRD tissue. Conclusion: These findings indicate that the Hedgehog pathway might be involved in regulating EC CSC-like properties. Although requiring further research, an exciting prospect would be the modulation of the Hedgehog pathway in combating CSC-like populations and the potential predictive value of SHH expression on treatment outcome.

**P332**

**Hedgehog Pathway Regulates a Putative Cancer Stem Cell-like Population in Esophageal Cancer**

D. Wang,1* J. Smit,1 R. Chiu,1 J. Plukker,1 R. Coppe,1 1. Dept. of Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands; 2. Dept. of Surgery, VU Medical Center, Amsterdam, Netherlands; 3. Dept. of Radiation Oncology, University Medical Center Groningen, Groningen, Netherlands.

Introduction: Despite advances in the treatment of esophageal cancer (EC), most patients face poor outcome. Mounting evidence indicates that cancer stem cells (CSCs) might contribute to the poor prospects. Whereas most cancer cells are sensitive to chemo- and/or radiotherapy (CRT), CSCs are resistant and ultimately have the potential to generate a new tumor. Mechanisms regulating EC CSCs are poorly understood and need to be elucidated. Methods: To identify up-regulated CSC related genes, qPCR arrays were performed on CD24-/CD44+ CSC-like population in OE21 esophageal squamous cell carcinoma (ESCC) and OE33 (EAC). CD24-/CD44+ was compared to CD24+/CD44+ and solid tumors generated from the same cell lines obtained from xenografts. Immunohistochemical (IHC) staining from tumor material of microscopical residual disease (mRD) in patients treated with neoadjuvant CRT was compared to surgery alone patients (S). Results: Previously, we identified a putative CSC-like population (CD24-/CD44+) in EC cell lines and in esophageal adenocarcinoma (EAC). From a panel of 84 CSC related genes, Pth1r was found to be up-regulated in the OE21 CD24-/CD44+ putative CSC-like population when compared to CD24+/CD44+ population and the solid tumor (2.5 and 3.7 fold, respectively). Furthermore, in OE33 this up-regulation was 1.4 and 1.7 fold. From 6 preselected candidate CRT response markers, CD44 and Sonic Hedgehog (SHH) expression was 55% (p<0.05) and 64% (p<0.005)

**P333**

**Impact of Surgeon Volume on Outcomes with Esophagectomy**

R. Shridhar,1 S. Hoffe,2 K. Alhmann,3 K. Meredith,1* 1. Surgery, University of Wisconsin, Madison, WI; 2. Moffitt Cancer Center, Tampa, FL.

Surgery is pivotal in the management of patients with esophageal cancer. It has been suggested that annual overall hospital volume predicts outcomes rather than individual surgeon volume. Recent data however, demonstrates that high volume surgeons have better outcomes irrespective of hospital volume. We sought to examine the impact of volume on outcomes with esophagectomy at a single institution with varying individual surgeon volume. We queried a prospectively maintained esophageal database to identify patients who underwent esophagectomy from 2010-2013. Surgical approaches included open, laparoscopic, thoracoscopic, and robotic assisted. Operative variables including length of operation, estimated blood loss, anastomotic leak, and mortality were compared and considered significant at p<0.05. A total of 245 (82 yr) esophagectomies was performed by 3 surgeons during the study period: Surgeon A (n=22, 7.3 yr), Surgeon B (n=62, 20.6 yr) and Surgeon C (n=161, 53.6 yr). Surgeon A had the highest length of operation compared to other surgeons, (Surgeon A=415 min, Surgeon B=229 min, and Surgeon C=399 min, p=0.0001). Surgeon A performed 8 (36%), Surgeon B, n=31 (51%) and Surgeon C, n=137 (85.1%) minimally invasive esophagectomies. The lowest volume surgeon, A, had elevated EBL compared to both high volume surgeons (402 ml vs 142 ml vs 157 ml) for surgeons A, B and C respectively, p<0.001. There were 15 (6.1%) anastomatic dehiscences (AD) among all surgeons. Surgeon A had higher AD n=5 (22.7%) compared to Surgeon B, n=5 (8.1%) and Surgeon C, n=5 (3.1%) p=0.003. There were 12 (4.9%) deaths amongst all surgeons. Mortality was substantially higher with the lowest volume surgeon. Surgeon A, n=2 (9.1%), Surgeon B, n=3 (4.8%), and Surgeon C, n=7 (4.3%), but this did not reach significance, p=0.3. Our data comparing outcomes from a high volume esophageal center reveals that surgeon volume not hospital volume is the major determinant of outcomes after esophagectomy.

**P334**

**Pulmonary Metastasectomy for Soft Tissue Sarcoma at the National Cancer Institute of Mexico: The Value of Repeated Metastasectomy and Other Factors associated with Prolonged Survival**


Introduction: Patients with Soft Tissue Sarcomas develop pulmonary metastases in up to 20% of cases and in most of them the lung will be the only...
P335
The Prognostic Value of Residual Nodal Disease following Neoadjuvant Chemoradiation for Esophageal Cancer in Patients with Complete Primary Tumor Response
A. Blackham,* K. Almhanna, N. Saeed, J. Fontaine, S. Hoffe, R. Shridhar, J.M. Pimiento. Surgical Oncology, Moffitt Cancer Center, Tampa, FL.

Introduction: Complete pathological response after neoadjuvant therapy for esophageal cancer is associated with improved survival; however, the prognostic value of complete response in the primary tumor (ypT0) with residual disease in the lymph node basin (ypN+) is unknown. Methods: Complete responders to neoadjuvant chemoradiation were identified from a single institution, prospectively maintained database of esophageal cancer patients undergoing esophagectomy. Clinico-pathologic and survival data in patients with an ypT0N+ response were compared to patients with no residual tumor (ypT0N0) and to non-complete responders. Results: Of the 522 patients who were treated with neoadjuvant chemoradiation prior to esophagectomy, 205 had an ypT0 response (39%). Fifteen patients had no residual invasive primary tumor (ypT0 or ypTis) but had residual nodal disease (ypN+). Pre-treatment stage was similar in both ypT0NO and ypT0N+ groups: 63.4 vs. 75.0% had cT3 disease (p=0.45) and 77.2 vs. 58.3% had cN+ disease (p=0.16), respectively. Mean overall survival (OS) was significantly worse in ypT0N+ patients compared to ypT0NO patients (28.9 vs. 85.6 months, p=0.01). ypT0NO patients trended toward improved mean OS compared to patients with post-neoadjuvant stage I disease (85.6 vs. 67.5 months, p=0.20). Mean OS in ypT0N1 patients (28.9 months) was similar to post neoadjuvant stage II (35.8 months, n=120, p=0.98) and post-neoadjuvant stage III disease (20.1 months, n=36, p=0.43). Among all patients with ypN+ disease (n=165), there was no difference in mean OS in patients with complete primary tumor response (ypT0N0) compared to patients with residual primary tumor (ypT1/2/3/4N+) (p=0.765).

Conclusions: Residual nodal disease in patients with complete primary tumor response (ypT0N0) following neoadjuvant chemoradiation for esophageal cancer portends a worse prognosis than ypT0NO responders and behaves similar to more advanced pathologic stage (II/III) disease.

P336
Outcomes associated with Varying Approaches to Minimally Invasive Esophageal Resection

Surgery is pivotal in the management of patients with esophageal cancer. Varying surgical techniques preclude the recommendation of a standard approach. We sought to examine our outcomes with differing approaches to minimally invasive esophagectomy (MIE) from 1994 and 2014. Surgical approaches included trans-hiatal (TH), Ivor Lewis (IVL), and robotic assisted Ivor Lewis (RAIL). Demographics, operative variables and post-operative complications were all compared. We identified 280 patients who underwent MIE with a mean age of 65.65 ± 10.5 and a median follow-up of 48 months. Fifty-seven patients underwent IVL, 78 underwent TH, and 145 underwent RAIL. The length of operation was significantly longer in IVL and RAIL approaches compared to TH (TH=242, IVL=320, RAIL=415, p=0.001). Estimated blood loss did not differ between cohorts (TH=150, IVL=125, RAIL=158, p=0.8). Anastomotic leakage, stricture, pneumonia, and wound infections were all higher in the TH compared to the trans-thoracic approaches p=0.04, p=0.02, p=0.01, and p<0.001 respectively. Operative mortality was low for each cohort and did not differ between approaches (TH=2.6%, IVL=0%, RAIL=2%, p=0.2). The median length of hospitalization also did not differ between groups (TH=10 days, IVL=8.5 days, and RAIL=9 days, p=0.15). Oncologic outcomes were measured by completeness of resection and nodal harvest. There was decreased R1 resections in both the IVL and RAIL compared to TH (TH=8%, IVL=0%, RAIL=0%, p=0.04). Additionally, the mean number of lymph nodes harvested was lower in patients undergoing TH compared to IVL and RAIL groups (TH=9.2, IVL=12.8, and RAIL=20.6, p=0.05). In series comparing techniques of MIE we have demonstrated improved operative outcomes in trans-thoracic approaches compared to trans-hiatal approaches. Additionally, improved nodal harvest and increased R0 resections rates were noted with the trans-thoracic approaches. We recommend that patients undergoing MIE be strongly considered for a trans-thoracic approach.
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Long-term Survival in Patients with Gastroesophageal Junction Cancer Treated with Neoadjuvant Therapy: Do Thoracic and Abdominal Approaches Differ? P.J. Kneuertz,1* W.L. Hofstetter,2 Y. Chiang,1 P. Das,3 A.M. Blum,3 K.F. Fournier,4 P.F. Mansfield,3 J.A. Ajanji,1 B. Badgwell,1 1. Department of Surgery, University of Texas Medical School at Houston, Houston, TX; 2. Department of Thoracic and Cardiovascular Surgery, University of Texas M.D. Anderson Cancer Center, Houston, TX; 3. Institute for Cancer Care Excellence, University of Texas M.D. Anderson Cancer Center, Houston, TX; 4. Department of Radiation Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX; 5. Department of Gastrointestinal Medical Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX; 6. Department of Surgical Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX.

BACKGROUND: The optimal surgical approach for gastroesophageal junction (GEJ) cancer treated with neoadjuvant therapy remains controversial. The purpose of this study was to determine the outcomes of patients who underwent an abdominal or thoracic surgical approach and identify variables associated with overall survival (OS). METHODS: Medical records of patients with Siewert type II/III GEJ adenocarcinoma who underwent a negative staging laparoscopy and were treated with neoadjuvant therapy and resection from 1995 to 2013 were reviewed. OS was assessed using Kaplan Meier and Cox proportion regression analysis. RESULTS: Of 143 patients, 110 (77%) had type II and 33 (23%) had type III tumors. Most patients had stage T3 (83%) and N+ (62%) disease as per endoscopic ultrasound. The majority (93%) received neoadjuvant chemoradiation; 7% received chemoradiation alone. Patients with type II tumors underwent thoracic (75%) or abdominal (25%) resection. Those with type III tumors primarily underwent abdominal surgery (89%). Eighty-six patients (60%) underwent extended (D2) abdominal lymphadenectomy. We saw no differences in R0 resection rate (94% vs. 95%; p=0.9), number of nodes removed (18 vs. 19; p=0.6), or 90-day perioperative mortality rate (4.6% vs. 5.4%; p=0.9), between thoracic and abdominal surgery, respectively. Thirty-one patients (22%) had complete pathologic responses. The median follow-up period for survivors was 65 months. The 5-year OS rate (51%) was similar for the thoracic and abdominal approaches (Figure). In multivariate analysis, the surgical approach was not associated with OS. The strongest predictors of OS were node positivity (hazard ratio, 2.1 [95% confidence interval, 1.9–2.3]) and ypT1 (hazard ratio, 3.6 [95% confidence interval, 1.3–9.7]). CONCLUSIONS: R0 resection and OS rates were similar in patients undergoing neoadjuvant therapy and thoracic or abdominal resection. Independent of the surgical approach, D2 lymphadenectomy may improve OS rates after neoadjuvant therapy.

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Laparoscopic Transhiatal Esophagectomy Improves Hospital Outcomes and Reduces Cost: A Single-institution Cohort Analysis of Laparoscopic and Open Techniques B. Ecker,1* G. Savulionyte,2 J. Datta,1 K. Dumon,1 N. Williams,1 J. Kucharczuk,1 D. Dempsey,1 University of Pennsylvania Health System, Philadelphia, PA.

While several case series have demonstrated that laparoscopic transhiatal esophagectomy (LTHE) is associated with reduced operative times, shorter length of stay and reduced morbidity compared to historical data for open transhiatal esophagectomy (OTHE), concurrent evaluation of open and laparoscopic techniques at a single institution is rare. The purpose of this study was to test the hypothesis that LTHE is associated with improved hospital outcomes and reduced hospital costs compared to OTHE. Following IRB approval, all patients who underwent OTHE (n=37) and LTHE (n=36) at our institution from 1/2012–4/2014 were identified and patient charts were retrospectively reviewed. Data are reported according to operation received; 4 patients were converted from LTHE to OTHE (conversion rate 10%). Indications for operation in the 73 patients were primary esophageal malignancy (adenocarcinoma 68; squamous cell carcinoma 4), melanoma (1), and achalasia (2). There were no significant differences between OTHE and LTHE groups in distribution of histology, clinical stage, use of neoadjuvant chemoradiation, mean age, sex, ASA score, or BMI. There were no hospital or 30 day mortalities. There was no significant difference in median operative time, yet LTHE was associated with reduced EBL (p<0.01) and a lower incidence of intraoperative blood transfusion (p<0.01), which remained significant on an intention-to-treat analysis. There were no significant differences in the frequencies of R0 resection or number of lymph nodes harvested. The laparoscopic technique was associated with a reduced time to reach 24-hour tube feeding goals (p<0.02), shorter length of stay (p<0.01), and 10% reduced median direct cost (p=0.04). Patients were followed for a median 10 months during which there were no significant differences between cohorts in disease-free survival, time to recurrence, disease-specific mortality or overall survival. When compared to OTHE, LTHE improves surgical outcomes and decreases hospital costs; short term oncologic outcomes are similar. LTHE is preferable to OTHE in patients requiring transhiatal esophagectomy.

<table>
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<th><strong>Patient Demographics</strong></th>
<th>OTHE (n=37)</th>
<th>LTHE (n=36)</th>
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<td>65±9</td>
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<tr>
<td>Sex (male) (%)</td>
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<td>77%</td>
<td>.66</td>
</tr>
<tr>
<td>BMI (mean±SD) (kg/m²)</td>
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<td>28±6</td>
<td>.76</td>
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<td>Clinical Stage</td>
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<tr>
<td>0 (0 %)</td>
<td>2 (6%)</td>
<td>1 (3%)</td>
<td>.84</td>
</tr>
<tr>
<td>I (0%)</td>
<td>1 (3%)</td>
<td>1 (2%)</td>
<td>.82</td>
</tr>
<tr>
<td>II (5%)</td>
<td>11 (32%)</td>
<td>8 (25%)</td>
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<tr>
<td>Overall Mortality (%)</td>
<td>6%</td>
<td>0%</td>
<td>.56</td>
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*Independent samples t-test; *p<.05; †p<.01.
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Tumor Differentiation and Lymph Node Ratio: Impact on Survival in Esophageal Cancer E. Paulus,1,2 G. Tiess,1 T. Kuru-Sengul,2 D. Franceschi,1 A. Livingstone,1 D. Yakoub,1 1. University of Miami Miller School of Medicine, Miami, FL; 2. University of Miami, Miami, FL.

Background: No clear evidence connects tumor differentiation with the ratio of positive lymph nodes. Studies suggest that a decreased positive lymph node harvest is associated with better survival in some cancers. The aim of this investigation is to determine the relationship between tumor differentiation and the ratio of positive lymph nodes in esophageal cancer patients following transthoracic esophagectomy (THE) and the correlation with survival rates. Methods: Data from a prospectively maintained database of esophagectomies performed for cancer (1999 – 2012) in a single high volume institution was reviewed. Tumor differentiation (well, moderate and poor) was used to subclass patients. Univariate logistic regression was employed to test the correlation between the degree of differentiation and the ratio of positive lymph nodes to total nodes harvested. The well-differentiated group was used as a reference. Ratio cutoff of 0.2 was used. Survival at 1, 3, and 5 years was projected according to lymph node ratios. Results: THE plus standard lymphadenectomy with or without neoadjuvant therapy was performed in 376 patients. Degree of differentiation was well, moderate or poor in 31, 175 and 170 patients, respectively. Ninety-three percent of patients with well-differentiated cancer had a positive lymph node ratio of < 0.2, as opposed to 78.2% in moderate and 67% in poorly differentiated. Poorly differentiated cancers were directly correlated with a positive lymph node ratio of > 0.2 (OR 0.96, CI 1.6-3.0, p=0.009). There was a significant survival advantage at 1, 3 and 5 years in patients with a positive lymph node ratio of < 0.2 regardless of whether neoadjuvant therapy was given. Conclusions: In this investigation there was a significant relationship between tumor differentiation and positive lymph node harvest. Specifically, poorly differentiated tumors were correlated with a higher rate of lymph node metastasis (> 0.2) and thus portended a survival disadvantage in a large volume single institutional experience. Stratifying patients based on differentiation as well as positive lymph node ratio may assist in patient prognostication.

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Tumor Size Correlates with Mediastinal Lymph Node Metastasis after Robotic-assisted Pulmonary Lobectomy for Non-small Cell Lung Cancer: Retrospective Analysis of 159 Consecutive Cases F.O. Velez-Cubian,1 E. Ng,2 K.L. Rodriguez,2 C.C. Moodie,3 J.R. Garrett,1 J.P. Fontaine,4 L.A. Robinson,5 E.M. Toloza,6 1. Thoracic Oncology, Moffitt Cancer Center, Tampa, FL; 2. University of South Florida Morsani College of Medicine, Tampa, FL.

INTRODUCTION: Tumor size is important in deciding treatment for non-small cell lung cancer (NSCLC). We have shown that robotic-assisted lobectomy for NSCLC improves mediastinal lymph node (LN) dissection efficacy. We investigated whether rates of LN involvement correlates with increasing tumor size after robotic-assisted lobectomy for NSCLC. METHODS: We retrospectively studied prospectively collected data from all patients who underwent robotic-assisted lobectomy for NSCLC by one surgeon over 34 months. Clinical stage was based on clinical history, physical examination, computerized tomography, positron-emission tomography, brain imaging, and endobronchial ultrasound. Pathologic stage was based on intraoperative findings and final pathology. Tumor size, extent of resection, histology, and N1 and N2 LN involvement were noted. Changes from clinical stage to pathologic stage were also noted. RESULTS: Of 159 consecutive patients (mean age 67.6±9.8 yr; range 39-86 yr) who underwent robotic-assisted pulmonary lobectomy for NSCLC, mean tumor size was 3.3±2.0 cm (range 0.8-11.0 cm). Nine patients had tumors ≤10 mm in size, 40 had tumors 11-20 mm, 43 had tumors 21-30 mm, and 67 patients had tumors ≥31 mm. Tumors <20 mm were mostly detected by lobectomy, with the occasional additional wedge resection, while more extended lobectomies, with en bloc segmental lob (i.e., bilobec- tomy), or chest wall resection, were performed for tumors ≥21 mm. All tumors ≤10 mm were adenocarcinomas, while various histologies comprised larger tumors. Robotic-assisted lobectomy is adequate for tumors ≤10 mm, but tumors >20 mm often require extended lobectomies, with en bloc segmental lob (i.e., bilobectomy), or chest wall resections, which are feasible via robotic-assisted approach. More N1 disease were identified as tumor size increased >10 mm, and more N2 disease were identified with tumors >20 mm. CONCLUSION: Tumor size not only dictates extent of lung resection but also correlates with LN metastases and predicts need for adjuvant treatment after robotic-assisted lobectomy for NSCLC.

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Laparoscopic Gastrectomy with D2 Lymphadenectomy as a Standard Approach to Gastric Adenocarcinoma in a Community Setting V. Palter,1* D.A. Bischoff2 P.K. Stotland3 J.A. Hagen,4 L.V. Klein,2 C.J. Swallow,2 1. Surgical Oncology, University of Toronto, Toronto, ON, Canada; 2. Department of Surgery, North York General Hospital, Toronto, ON, Canada; 3. Department of Surgery, Humber River Regional Hospital, Toronto, ON, Canada; 4. Department of Surgery, Mount Sinai Hospital, Toronto, ON, Canada.

INTRODUCTION: The role of laparoscopy for resection of locally advanced gastric adenocarcinoma remains controversial. Some experts have questioned the adequacy of lymphadenectomy and local clearance of T3/T4 tumors that can be achieved laparoscopically. The purpose of this study was to assess perioperative and oncologic outcomes after implementing a program for laparoscopic gastrectomy with D2 lymphadenectomy in a North American community setting. METHODS: All patients who underwent curative-intent laparoscopic gastrectomy at two university-affiliated community sites from 2008 to 2014 were identified from a prospective database. Retrospective review of demographic, tumor, treatment and outcome data was conducted. Survival curves were constructed using the Kaplan-Meier method. RESULTS: In the study cohort of 58 patients, median age was 70 (28-84), and 35 (60%) were male. 11 (19%) received neoadjuvant chemotherapy. Extent of gastrectomy was Type I in 38 (65%) and total in 20 (35%) patients. Pathologic T stage was T1a in 3, T1b in 12, T2 in 10, T3 in 16, and T4 in 17 patients. 34 (59%) had node positive disease. The median number of nodes retrieved was 29 (range 12-75), and 91% of patients had ≥16 nodes assessed. R0 resection was achieved in 57 patients (98%). In the postoperative period, there were 3 deaths (5%) and 18 patients (31%) had Grade 3 or 4 complications. 28 (48%) patients received postoperative chemotherapy (combined with radiotherapy in 17), with only 19 completing the planned course of therapy. Median follow-up was 21 mos (days 6-65 mos), and 17 patients (29%) developed recurrent disease. The overall survival (OS) at 3y was 73% (95% CI=62% - 88%). The 3y OS was 92% in node negative and 61% in node positive patients (p<0.016). Conclusions: Laparoscopic gastrectomy with D2 lymphadenectomy for adenocarcinoma can be performed at a community site with high rates of adequate lymph node assessment and R0 status, and acceptable morbidity and mortality. Barriers to receipt of adjuvant therapy in the community setting must be explored.

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Overexpression of Lysophosphatidylcholine Acyltransferase 1 and Concomitant Lipid Alterations in Gastric Cancer H. Kikuchi,1* T. Uehara,2 S. Miyazaki,3 Y. Hiramatsu,1 M. Ohta,1 K. Kamiya,4 Y. Morita,2 S. Baba,5 M. Setou,2 T. Sakaguchi,1 H. Konno1 1. Second Department of Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan; 2. Oncology Center, Hamamatsu University School of Medicine, Hamamatsu, Japan; 3. Department of Pathology, Hamamatsu University School of Medicine, Hamamatsu, Japan; 4. Department of Cell Biology and Anatomy, Hamamatsu University School of Medicine, Hamamatsu, Japan.

INTRODUCTION: Gastric cancer is of major importance worldwide and the second most common cause of cancer-related death in Japan. Recently, the involvement of lipids in the tumorigenesis and development of some malignancies such as colorectal cancer has been reported. However, the roles of lipids or their alterations in gastric cancers are not well understood. In this study, we compared the lipid content of gastric cancer tissue and adjacent non-neoplastic mucosa using imaging mass spectrometry to address the roles of lipid alterations. METHODS: Mass spectra were acquired from 12 sections of human gastric cancer tissue and adjacent non-neoplastic mucosa using a MALDI-TOF/TOF type mass spectrometer equipped with a 355-nm Nd:YAG laser. Protein expression of lysophosphatidylcholine acyltransferase 1 (LPCAT1), which converts lysophosphatidylcholine (LPC) to phosphatidylcholine (PC) in the presence of acyl-CoA in Lands’ cycle, was immunohistochemically analyzed in 82 gastric cancer specimens. RESULTS: The average mass spectra from the cancer tissue and non-neoplastic mucosa were identical. Most of the signals that differed between cancer tissue and non-neoplastic mucosa corresponded to phospholipids, the majority of which were PC and LPC. Two
signals, m/z 798.5 and 496.3, were higher and lower, respectively, in cancer tissues, predominantly in differentiated adenocarcinoma. A database search enabled identification of the ions at m/z 798.5 and 496.3 as potassium-adducted LPC (16:0) and proton-adducted LPC (16:0), respectively. Immunohistochemical analysis revealed that LPCAT1 was highly expressed in cancer lesions compared with non-neoplastic mucosa, predominantly in differentiated adenocarcinoma. LPCAT1 expression levels correlated positively with tumor differentiation and negatively with tumor depth, lymph node metastasis, and tumor stage. However, there was no correlation between LPCAT1 expression levels and disease-free survival or overall survival. **Conclusions:** Over-expressed LPCAT1 protein in gastric mucosa appears to play important roles in the tumorigenic process rather than in the progression of gastric cancer by converting LPC to PC.

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Introduction: Total gastrectomy for gastric carcinoma is a complex surgical procedure with incompletely described post-operative resource utilization and hospital costs. **Methods:** Detailed post-operative outcomes on 238 patients who underwent curative intent total gastrectomy at a single institution over ten years were reviewed. Clinical resource utilization and hospital reimbursement associated with post-operative complications and their sequelae were analyzed.

To generate the normalized costs we report, hospital costs were adjusted to Medicare reimbursement levels using the ratio of our costs to diagnosis related group (DRG) reimbursement. Differences between costs can be interpreted as the amount that would be reimbursed to an average hospital by Medicare if it paid differentially based on types of post-operative complications. **Results:** Of the 238 patients who underwent a curative intent total gastrectomy, the median age was 66; 68% were male. At least one post-operative adverse event was experienced by 62% of patients; 28% experienced a major adverse event, defined by Grade 3 on our modification of the Clavien-Dindo classification. Median normalized cost was $11,082 (IQR: 8,859 - 17,653) for the entire group. Patients without adverse events (38%) had a median normalized cost of $9,043 (IQR: 7,725 - 10,631), compared to $17,618 (IQR: 12,172 - 28,689) for patients with at least one major adverse event. Major esophageal anastomotic leak, our most frequent major adverse event (10%), had a median cost of $9,043 (IQR: 7,725 - 10,631), compared to $17,618 (IQR: 12,172 - 28,689) for the DRG group. Patients without adverse events (38%) had a median normalized cost of $9,043 (IQR: 7,725 - 10,631), compared to $17,618 (IQR: 12,172 - 28,689) for patients with at least one major adverse event. Major esophageal anastomotic leak, the most common major adverse event, results in more than a three-fold increase in normalized costs as compared to an uncomplicated total gastrectomy.

Medicare Normalized Charges and Length of Stay following Curative Intent Total Gastrectomy

<table>
<thead>
<tr>
<th>No Adverse Events</th>
<th>Major Adverse Events</th>
<th>Major Esophageal Leaks</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N=90; 38%)</td>
<td>(N=68; 28%)</td>
<td>(N=32; 13%)</td>
</tr>
<tr>
<td><strong>Number Occurring During Initial Hospitalization</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>37 (96%)</td>
<td>17 (68%)</td>
</tr>
<tr>
<td><strong>Normalized Costs for Initial Hospitalization (2012 Dollars)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>59,043</td>
<td>57,168</td>
<td>52,845</td>
</tr>
<tr>
<td>(7,725 - 10,631)</td>
<td>(12,172 - 28,689)</td>
<td>(15,860 - 50,580)</td>
</tr>
<tr>
<td><strong>90-Day Normalized Costs (2012 Dollars)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>59,233</td>
<td>52,808</td>
<td>53,039</td>
</tr>
<tr>
<td>(7,725 - 10,639)</td>
<td>(18,098 - 39,299)</td>
<td>(25,179 - 50,580)</td>
</tr>
<tr>
<td><strong>Initial Length of Stay</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.0 (5.0, 9.0)</td>
<td>10.0 (7.0, 15.0)</td>
<td>12.0 (8.0, 16.0)</td>
</tr>
<tr>
<td><strong>Any ICU admission</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>12 (29%)</td>
<td>8 (25%)</td>
</tr>
<tr>
<td><strong>Any reoperation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (1.1%)**</td>
<td>19 (29%)</td>
<td>8 (28%)</td>
</tr>
<tr>
<td><strong>Any Interventional Radiology Procedure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 (9.7%)**</td>
<td>7 (11%)</td>
<td>23 (92%)</td>
</tr>
<tr>
<td><strong>Any Endoscopic Procedure</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>20 (50%)</td>
<td>12 (48%)</td>
</tr>
<tr>
<td><strong>Readmission Rate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (1.1%)**</td>
<td>17 (24%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td><strong>Readmission Length of Stay (N= 78)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>9.0 (5.0, 17.0)</td>
<td>10.0 (6.0, 25.0)</td>
</tr>
</tbody>
</table>

Continuous variables are expressed as median (IQR) and categorical variables as N (%).

* Normalized Costs are in 2012 US Dollars
** One patient with a positive duodenal margin who required readmission and re-operation.

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The Impact of Adjuvant Therapy on Survival in Clinically Relevant Subsets of Patients with Pancreatic Head Cancer R.A. Snyder,* A. Parikh, K. Idrees, N. Merchant, Surgical Oncology, Vanderbilt University, Nashville, TN.

Introduction: In patients (pts) with resected pancreas adenocarcinoma, level 1 data supports the use of adjuvant chemotherapy (CX) while the role of adjuvant chemoradiation therapy (CXRRT) remains controversial. The purpose of this study was to evaluate the association of adjuvant therapy and 5-year overall survival (OS) in pts with pancreatic head cancer, specifically examining the impact of lymph node (LN) and margin status. **Methods:** A review of resected pancreatic head adenocarcinoma pts between 2003-2006 from the National Cancer Database (NCDB) was performed. **Results:** Of 5,226 pts, 47.5% were treated with CXRT, 16.7% with CX, and 35.9% with surgery alone (SX). For the entire cohort, both CXRT and CX were associated with improved OS compared to SX [HR 0.71 (0.67-0.76) and HR 0.81 (0.74-0.88)], by Cox Proportional-Hazard regression controlling for demographics, comorbidities, stage, margin status, and LN positivity. Analysis of pts stratified by LN and margin status showed that neither CXRT nor CX was associated with improved OS in pts with LN and margin negative disease while both CXRT and CX resulted in improved OS in patients with LN+ disease (See table). Other factors associated with improved OS included younger age, female sex, earlier stage, and fewer comorbidities. **Conclusions:** This large population based study suggests that the use of adjuvant CXRT or CX is beneficial only for patients with LN+ disease. However the use of adjuvant therapy in pts with LN- disease may not be warranted.

Cox Proportional-Hazard model, stratified for LN and margin status

<table>
<thead>
<tr>
<th>LN negative, margin negative</th>
<th>LN negative, margin positive*</th>
<th>LN positive, margin negative</th>
<th>LN positive, margin positive*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adjuvant Chemotherapy</td>
<td>0.97 (0.79-1.20)</td>
<td>1.10 (0.85-1.50)</td>
<td>-</td>
</tr>
<tr>
<td>Adjuvant Chemotherapy</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

**Underpowered for regression model due to small sample size.

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Introduction: Sarcopenia, a loss of muscle mass and strength, is linked to poor outcomes after abdominal surgery. We previously found geriatric assessments of frailty to predict negative outcomes after pancreatoduodenectomy (PD). We hypothesized that adding sarcopenia data would enhance prediction of post-PD complications. **Methods:** Pre-operative frailty data (Fried’s exhaustion and Short Physical Performance Battery (SPPB)) and CT scans of patients in a prospective study undergoing PD were reviewed. Sarcopenia was assessed at the L3 level by psoas muscle volume using the total psoas area index (TPAI) and HU density on non-contrast scans. Outcomes included 30-day serious complications defined as the American College of Surgeons National Surgical Quality Improvement Program, highest grade of Clavien-Dindo complications, unplanned ICU admission, and discharge to skilled nursing facility (SNF). Regression analyses were performed. **Results:** Among 104 patients, rates of 30-day mortality and serious complications were 4.8% and 51%, respectively. TPAL and HU were not highly inter-correlated but both correlated with age (TPAI: r=–0.41, p<0.0001; HU: r=–0.51, p<0.0001) and SPPB (TPAI: r=0.39, p=0.0184; HU: r=0.30, p=0.0184). Low HU predicted serious complications (r=–0.31, p=0.0098), highest grade of Clavien-Dindo complications (r=–0.29, p=0.0183), unplanned ICU admission (r=–0.26, p=0.0374), and discharge to SNF (r=–0.25, p=0.0426). After controlling for age, BMI, ASA, and co-morbidities, Fried’s exhaustion (OR=4.72 [1.23 - 17.71], p=0.021) and HU (OR=0.88 [0.79-0.98], p=0.024) predicted serious complications. Based on area under the receiver-operator characteristic curves (AUC), combining clinical, frailty, and sarcopenia factors (AUC=0.81) trended towards increasing the accuracy of predicting serious complications above only clinical (AUC=0.70) or clinical and frailty factors (AUC=0.74) (p=0.09). **Conclusion:** Psoas muscle...
The Prognostic Value of Signet Ring Cell Histology in Resected Gastric Cancer

T.M. Pawlik,6 G.A. Poultsides, A.W. Acher

dictate treatment strategy. Signet ring histology during preoperative evaluation should not, in isolation, be considered a significant independent adverse pathologic feature. Identification of adverse pathologic features including higher grade and higher TNM stage but not SRC was associated with decreased recurrence-free survival (RFS). Multivariate analysis revealed a negative association of SRC with decreased RFS persisted in multivariate analysis in Stage 1 patients (HR 3.11; p = 0.015). Survival analysis showed no association between SRC and RFS or OS in Stage 1 or 3. In Stage 2, SRC was associated with more advanced clinical stage (TNM Stage; HR 2.10; p < 0.001), greater size (HR 1.05; p = 0.014), and adjuvant therapy (HR 0.50; p < 0.001) were associated with OS. SRC was not an independent predictor of OS. Stage-specific analysis showed no association between SRC and OS or RFS in Stage 1 or 3. In Stage 2, SRC was associated with earlier recurrence (38.1 mo vs MNR; p = 0.005; Figure) but not OS. The negative association of SRC and RFS or OS in Stage 2 patients (HR 2.10; p = 0.001) was not independent of other adverse pathologic features including higher grade and higher TNM stage but is not independently associated with reduced RFS or OS. Identification of signet ring histology during preoperative evaluation should not, in isolation, dictate treatment strategy.

Correlations Between Sarcopenia and Outcome Measures

<table>
<thead>
<tr>
<th>Outcome Measures</th>
<th>Sarcopenia Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total Fascia Area</td>
</tr>
<tr>
<td></td>
<td>Average Weighted</td>
</tr>
<tr>
<td></td>
<td>Index</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>r  p-value</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>r  p-value</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>-0.02  0.8677</td>
</tr>
<tr>
<td></td>
<td>-0.17  0.1776</td>
</tr>
<tr>
<td>30-day serious complications</td>
<td>0.02  0.8234</td>
</tr>
<tr>
<td></td>
<td>-0.31  0.0098</td>
</tr>
<tr>
<td>Highest grade of Clavien-Dindo complications</td>
<td>-0.03  0.7942</td>
</tr>
<tr>
<td></td>
<td>-0.29  0.0183</td>
</tr>
<tr>
<td>Unplanned ICU admission</td>
<td>-0.15  0.1547</td>
</tr>
<tr>
<td></td>
<td>-0.26  0.0374</td>
</tr>
<tr>
<td>30-day return to OR</td>
<td>-0.05  0.6485</td>
</tr>
<tr>
<td></td>
<td>-0.21  0.0874</td>
</tr>
<tr>
<td>Length of stay</td>
<td>0.01  0.9147</td>
</tr>
<tr>
<td></td>
<td>-0.23  0.0565</td>
</tr>
<tr>
<td>Discharge to skilled nursing facility</td>
<td>-0.16  0.1262</td>
</tr>
<tr>
<td></td>
<td>-0.25  0.0426</td>
</tr>
<tr>
<td>30-day readmission</td>
<td>-0.08  0.4163</td>
</tr>
<tr>
<td></td>
<td>-0.12  0.3149</td>
</tr>
</tbody>
</table>

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IDH1 Mutation in Small Bowel Adenocarcinoma

C.H. Chan,* R.T. Williams, D. Dias-Santagata, A. Iraflate, J.E. Murphy, D.P. Ryan, J.C. Cusack, Massachusetts General Hospital, Boston, MA.

Background: Small bowel adenocarcinoma (SBA) is a rare malignancy. Management of this disease is often based on clinical data extrapolated from the colorectal cancer literature. However, gene mutation profile differs between the two entities; for example, frequency of APC mutation has been shown to be much lower in SBA. In this study, we aim to identify new genetic mutations in SBA through tumor genotyping. Methods: Tumor samples of patients who presented with SBA were analyzed using the “SNApshot Genotyping Assay” (a multiplexed PCR-based assay testing up to 90 known mutational hotspots in 23 genes – AKT1, APC, BRAF, CTNNB1, EGFR, EML4-ALK, ERBB2, FGFR3, GNA11, GNAQ, GNAS, HRAS, IDH1, IDH2, KIT, KRAS, MAP2K1, NOTCH1, NRAS, PIK3CA, PTEN, RET, TP53) at our institution between 2009 and 2013. Mutations detected were analyzed and compared to the published data on colorectal cancers using the same tumor genotyping platform. Results: In the SNApshot database, 18 SBA were identified during this 5-year period; 6 in the duodenum, 5 in the jejunum, 4 in the ileum, and 3 of unspecified small bowel location. Fourteen RAS/RAF mutations (12 KRAS, 1 BRAF and 1 NRAS) were found in 15 of 18 samples (72%), which was higher than the one in colorectal cancer (133/222, 51%, P = 0.09). Interestingly, a case of poorly differentiated adenocarcinoma with neuroendocrine features carried both KRAS-Q61H and BRAF-G469V mutations. Mutations were also detected in IDH1 (1/16, 6%) and TP53 (2/18, 11%) genes. The IDH1 mutation was found in an adenocarcinoma with signet-ring cell features in a patient with Crohn’s disease. Conclusion: Genetic mutations in the RAS/RAF pathway are very common in SBA. Mutation in the metabolic gene IDH1, which has not been previously reported, may also be found. Whole genome sequencing may facilitate the identification of new mutations and therapeutic targets for treating this rare malignancy.

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Table 1: Frequency of mutations detected

<table>
<thead>
<tr>
<th>Gene*</th>
<th>KRAS</th>
<th>BRAF</th>
<th>NRAS</th>
<th>HRAS</th>
<th>RAF</th>
<th>Pathway</th>
<th>TP53</th>
<th>IDH1**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small Intestine</td>
<td>12/18 (67%)</td>
<td>1/18 (6%)</td>
<td>1/18 (6%)</td>
<td>1/18 (6%)</td>
<td>1/18 (6%)</td>
<td>1/18 (6%)</td>
<td>1/2 (100%)</td>
<td>1/18 (6%)</td>
</tr>
<tr>
<td>Duodenum</td>
<td>6/9 (66%)</td>
<td>2/9 (22%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/1 (100%)</td>
<td>1/9 (11%)</td>
</tr>
<tr>
<td>Jejunum</td>
<td>5/9 (55%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/1 (100%)</td>
<td>1/9 (11%)</td>
</tr>
<tr>
<td>Ileum</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/9 (11%)</td>
<td>1/1 (100%)</td>
<td>1/9 (11%)</td>
</tr>
</tbody>
</table>

* SNApshot covered > 95% of known KRAS, BRAF, NRAS, and IDH1 mutations, but only 50% of TP53 mutations.
** Two samples were tested on the original SNApshot platform that did not include IDH1 gene.
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Preoperative Helicobacter pylori Infection is associated with Increased Survival after Resection of Gastric Adenocarcinoma
L.M. Postlewati,¹ M.H. Squires,¹ D.A. Kooby,¹ G.A. Poultsides,² S.M. Weber,¹ M. Bloomston,² R.C. Fields,³ T.M. Pawlik,⁴ K.I. Votanopoulos,⁵ C.R. Schmidt,⁶ A. Ejaz,⁶ A.W. Acher,⁶ D.J. Worhunsky,⁷ N. Saunders,⁷ D. Swords,⁷ L.X. Jin,⁷ C.S. Cho,⁷ E.R. Winslow,⁷ K. Cardona,¹ C.A. Staley,¹ S.K. Maithel,¹ 1. Division of Surgical Oncology, Emory University, Atlanta, GA; 2. Department of Surgery, Stanford University Medical Center, Stanford, CA; 3. Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 4. Division of Surgical Oncology, The Ohio State University Comprehensive Cancer Center, Columbus, OH; 5. Department of Surgery, Washington University School of Medicine, Saint Louis, MO; 6. Department of Surgery, The Johns Hopkins Hospital, Baltimore, MD; 7. Department of Surgery, Wake Forest University, Winston-Salem, NC.

Background: Limited data exist on the prognostic implication of pre-operative Helicobacter pylori (H. pylori) infection in gastric adenocarcinoma (GAC). Our aim was to assess the association of H. pylori with recurrence and survival in patients undergoing resection of GAC. Methods: All patients who underwent curative intent resection for GAC from 2000 to 2012 at seven academic institutions comprising the US Gastric Cancer Collaborative were included. 30-day mortalities were excluded. Survival analyses were conducted with Kaplan Meier log rank and multivariate Cox regression. Primary endpoints were recurrence-free survival (RFS) and overall survival (OS).

Results: Of 965 patients, 559 met inclusion criteria and had documented pre-operative H. pylori testing. 18.6% (n=104) of patients tested positive for H. pylori. Data regarding treatment of H. pylori was not available. H. pylori infection was associated with younger age (62.1 vs 65.1 yrs; p=0.041), distal tumor location (82.7% vs 71.9%; p=0.033), and receipt of adjuvant radiation therapy (47.0% vs 34.9%; p=0.032). There were no significant differences in ASA class, margin status, Grade, PNI, LVI, or nodal metastases. The distribution of TNM stage I-II was similar between the two groups. H. pylori status was not associated with tumor recurrence. However, pre-operative H. pylori infection was associated with longer OS (84.3 mo vs 44.2 mo; p=0.008; Figure). When accounting for differences in age, tumor location, and delivery of radiation therapy, H. pylori infection persisted as a positive prognostic factor for OS (HR 0.60; CI 0.40-0.91; p = 0.016). Conclusion: Patients with and without preoperative H. pylori infection had no significant differences in adverse pathologic factors including positive margin, high grade, lymph node metastases, or advanced TNM stage. Despite similar disease presentation, pre-operative H. pylori infection was independently associated with improved overall survival. Further studies examining the interaction between H. pylori and tumor immunology and genetics are needed to better understand the relationship between H. pylori and survival in gastric cancer.

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An Assessment of Feeding Jejunostomy Tube Placement at the Time of Resection for Gastric Adenocarcinoma: A 7-institution Analysis of 837 Patients from the U.S. Gastric Cancer Collaborative
G.C. Damm,¹ M.H. Squires,¹ L.M. Postlewati,¹ D.A. Kooby,¹ G.A. Poultsides,² S.M. Weber,¹ M. Bloomston,² R.C. Fields,³ T.M. Pawlik,⁴ K.I. Votanopoulos,⁵ C.R. Schmidt,⁶ A. Ejaz,⁶ A.W. Acher,⁶ D.J. Worhunsky,⁷ N. Saunders,⁷ D. Swords,⁷ L.X. Jin,⁷ C.S. Cho,⁷ E.R. Winslow,¹ M.C. Russell,¹ K. Cardona,¹ C.A. Staley,¹ S.K. Maithel,¹ 1. Division of Surgical Oncology, Emory University, Atlanta, GA; 2. Department of Surgery, Stanford University Medical Center, Stanford, CA; 3. Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 4. Division of Surgical Oncology, The Ohio State University Comprehensive Cancer Center, Columbus, OH; 5. Department of Surgery, Washington University School of Medicine, Saint Louis, MO; 6. Department of Surgery, The Johns Hopkins Hospital, Baltimore, MD; 7. Department of Surgery, Wake Forest University, Winston-Salem, NC.

Background: A recent single institutional study demonstrated that jejunostomy feeding tubes (J-tubes) placed during resection of gastric adenocarcinoma (GAC) are associated with increased complications and no change in receipt of adjuvant therapy. Our aim was to validate these findings in a large multi-institutional cohort. Methods: All patients who underwent resection for GAC at 7 institutions participating in the U.S. Gastric Cancer Collaborative from 2000-2012 were identified. Patients with metastatic disease were excluded. Univariate and multivariate logistic regression were performed to assess the association of J-tubes with postoperative complications and receipt of adjuvant therapy. Subset analysis of patients who underwent total vs subtotal gastrectomy was also performed. Results: Of 965 patients, 837 were included for analysis, of whom 265 (32%) received a J-tube. Patients receiving J-tubes demonstrated greater incidence of preoperative weight loss, lower BMI, greater extent of resection, and more advanced TNM stage. J-tube placement was associated with increased infectious complications (36% vs 19%; p<0.001), including surgical site infections (14% vs 6%; p<0.001) and deep intra-abdominal infections (11% vs 4%; p<0.001). On multivariate analysis, J-tubes remained independently associated with increased risk of infectious complications (HR=1.93; p=0.001), surgical site infections (HR=2.85; p=0.001), and deep intra-abdominal infections (HR=2.13; p=0.04). J-tubes were not associated with increased receipt of adjuvant therapy (HR=0.82; p=0.34). Subset analysis of patients undergoing total and subtotal gastrectomy similarly demonstrated an association of J-tubes with increased risk of infectious outcomes and no associ-
cification with increased receipt of adjuvant therapy. **Conclusion:** J-tubes placed during resection of gastric adenocarcinoma are independently associated with increased postoperative infections and are not associated with increased receipt of adjuvant therapy, despite being placed in patients with advanced TNM stage tumors. Selective use of J-tubes is recommended.

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**Exploration of Rural Disparities in Pancreas Cancer Staging and Mortality to Incidence Ratio in Illinois**


**Background:** Despite recent impetus towards regionalization of pancreatectomy to high-volume centers, rural disparities have not been explored for pancreas cancer outcomes. Analysis of the National Cancer Database showed less than one third of patients with resectable disease actually undergo surgery, suggesting opportunities for improvement in global systems related to pancreas cancer care including appropriate referral for surgical resection. We intended to explore the impact of rurality and gastroenterologist (GI) density on staging and mortality for pancreas cancer.

**Methods:** Age-adjusted pancreas cancer incidence and staging proportion were calculated for each county using 1991-2010 data from the Illinois State Cancer Registry. Age-adjusted mortality rates were calculated using SEER*STAT. Choropleth maps were created to illustrate Mortality-Incidence Ratios (MIRs) by Illinois county using ArcGIS. Mean GI density for each county was calculated from the US Area Health Resource File: USDA Economic Research Service rural-urban continuum codes (RUCC) and US census percent rurality data were used to designate county rurality and adjacency to metro counties. Chi-square, ANOVA, and Spearman’s rho calculations were performed.

**Results:** A greater proportion of counties with high MIR were in Southern, more rural, Illinois. No GIs were located in 65 out of 102 Illinois counties (64%) during the time interval analyzed, with a mean density of 1.0 per 100,000. Counties without GIs were significantly more rural, poorer, and less educated than counties with GIs. Unstaged pancreas cancers were inversely correlated with GI density (Spearman’s rho=-0.20; p=0.04). MIR was also predicted by RUCC category, and was significantly greater in rural regions not adjacent to metro counties (p=0.02).

**Conclusions:** Higher rates of unstaged pancreas cancer and higher MIR were noted in rural regions, which may be influenced by the availability of gastroenterologists or other specialty services. Further exploration of the impact of distance from high volume cancer centers on rural cancer outcomes is warranted.

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**Value of Peritoneal Drain Placement after Total Gastrectomy for Gastric Adenocarcinoma: A Multi-institutional Analysis from the U.S. Gastric Cancer Collaborative**

G.C. Dann,1 M.H. Squires,1 L.M. Postlewait,1* D.A. Kooby,1 G.A. Poultsides,2 S.M. Weber,1 M. Bloomston,1 R.C. Fields,1 T.M. Pawlik,1 K.I. Votanopoulos,1 C.R. Schmidt,1 A. Ejaz,1 A.W. Acher,1 D.J. Worhunsky,1 N. Saunders,1 D. Swords,1 L.X. Jin,1 C.S. Cho,1 E.R. Winslow,1 M.C. Russell,1 C.A. Staley,1 S.K. Maithel,1 K. Cardona,1 1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Surgery, Stanford University Medical Center, Stanford, CA; 3. Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 4. Division of Surgical Oncology, The Ohio State University Comprehensive Cancer Center, Columbus, OH; 5. Department of Surgery, Washington University School of Medicine, Saint Louis, MO; 6. Department of Surgery, The Johns Hopkins Hospital, Baltimore, MD; 7. Department of Surgery, Wake Forest University, Winston-Salem, NC.

**Introduction:** A recent randomized trial of peritoneal drain (PD) placement after pancreaticoduodenectomy concluded that placement of PDs decreased the frequency and severity of complications. The role of PD placement after total gastrectomy for gastric adenocarcinoma (GAC) is not well-established.

**Methods:** Patients who underwent total gastrectomy for GAC at 7 institutions from the U.S. Gastric Cancer Collaborative from 2000-2012 were identified. Univariate and multivariate analyses were performed to evaluate the association of PD placement with postoperative outcomes.

**Results:** 344 patients were identified and anastomotic leak rate was 9%. 253 (74%) patients received a PD. Those with PD placed had similar ASA class, tumor size, TNM stage, and need for additional organ resection when compared to their counterparts with no PD. No difference was observed in the rate of any complication (54% vs. 48%; p=0.45), major complication (25% vs. 24%; p=0.90), or 30-day mortality.
(7% vs. 4%; p=0.51) between the two groups. In addition, no difference in anastomotic leak (9% vs. 10%; p=0.90), need for secondary drainage (10% vs. 9%; p=0.92), or reoperation (13% vs. 8%; p=0.28) was identified. On multivariate analysis, PD placement was not associated with a decrease in frequency or severity of postoperative complications. Subset analysis of patients stratified by whether they underwent concomitant pancreatoduodenectomy similarly demonstrated no association of PD placement with reduced complications or mortality. In patients who experienced an anastomotic leak (n=31), placement of PD was similarly not associated with a decrease in complications, need for secondary drainage, or mortality. Conclusion: Peritoneal drain placement after total gastrectomy for adenocarcinoma, regardless of concomitant pancreatoduodenectomy, is not associated with a decrease in the frequency and severity of adverse postoperative outcomes, including anastomotic leak and mortality, or decrease in the need for secondary drainage procedures or reoperation. Routine use of peritoneal drains is not warranted.

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An Alarming Trend in the Incidence of Advanced Gastric Adenocarcinoma in Young Hispanic Males


Background: Although the incidence of gastric adenocarcinoma in the US has been decreasing, our recent experience suggested an increased rate of younger patients with this disease. We sought to further investigate our observations by evaluating temporal trends in gastric cancer incidence. Methods: The Surveillance, Epidemiology and End Results (SEER) database, which captures incidence data for a large proportion of the US population, was queried for patients with gastric adenocarcinoma during the period 1992–2011. We evaluated tumor characteristics and trends in gastric cancer incidence by calculating the annual percent change (APC), which is the percent change in rate of gastric cancer over each year of the study period, with 95% confidence intervals (CI) in patients of three age groups (20–49, 50–64, 65+) and four racial/ethnic groups (Hispanics, non-Hispanic Whites, Blacks, and Asian/Pacific Islanders). Results: We identified 38,031 patients with gastric adenocarcinoma (males=21,369 and females=16,662). For this entire cohort, we observed that the APC in gastric cancer incidence decreased over the study period. When patients were grouped according to sex, the APC was flat or decreased in women of all age and racial/ethnic groups. The APC was also flat or decreased for men of all age and racial/ethnic groups except for young Hispanic males. For Hispanic males aged 20–49 there was an increase in the APC of nearly 2% per year (1.57%, 95% CI: 0.23-2.94%). Furthermore, these young Hispanic males were the only group to have increased incidence of Stage 4 disease (APC 4.06%, 95% CI: 2.57-5.58%) and Grade 3 tumors (APC 2.18%, 95% CI: 0.53-3.86%) compared to older Hispanics and other racial/ethnic groups. Conclusions: In young Hispanic males, the APC of gastric cancer placebo was increasing along with the rising incidence of advanced disease in the US. This alarming rate of increase is concomitant with increased incidence of advanced disease presentation. Our data suggests that this major public health concern warrants additional research to determine the etiology of the increasing incidence and methods of early disease detection in this group.

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A Novel Orthotopic Murine Model of Pancreatic Cancer: Recapitulation of Stromal and Immune Microenvironment

K. Majumder, R. Chugh, N. Arora, S. Modi, S. Banerjee, R. Dawra, A. Saluja, V. Dudeja,* University Of Minnesota, Minneapolis, MN.

**BACKGROUND:** Development of new therapies for pancreatic cancer has been hindered by a lack of relevant preclinical models. Besides recapitulating tumorigenic properties, a relevant tumor model has to recapitulate the immune and stromal microenvironment which is absent in subcutaneous or orthotopic models in immunodeficient mice. SCID, Alynmic nude). While these components are present in the KPC (Pdx-Cre KrasG12D/+P53−/−) model, this genetic model has an immense variability in time to invasive disease (47-355 days of life) which makes it unsuitable for the study of novel therapies. Moreover the entire pancreas in this model has Kras-p53 mutation as opposed to the sporadic mutations generally seen in human pancreatic cancer. We therefore propose a novel orthotopic model with tumors from KPC mice implanted in C57Black6 mice to address the shortcomings of previous models. **MATERIALS AND METHODS:** Pancreatic tumors were extracted from 6 month KPC and were cut into ~3mm³ pieces. Laparotomy was performed on female C57BL/6 mice and the tumor piece was sewn into a pocket of pancreas using 7-0 prolene to incorporate the superior and inferior border of the pancreas. Mice were sacrificed at two time points: 4 and 8 weeks. Stromal component and immune infiltration were studied by immunohistochemistry. **RESULTS:** Tumor take rate was ~90%. Similar growth rate among tumors was observed at both time points (4 weeks: 331 ± 122 mm³, 8 weeks: 433 ± 77 mm³). Mortality at 8 weeks was ~30%. H&E staining confirmed presence of pancreatic adenocarcinoma. Staining for stromal components (collagen and HABP), activated stellate cells (αSMA) and immune markers (CD45) showed intense desmoplastic stromal reaction, activated stellate cells and intense infiltration of tumor and surrounding pancreas with leukocytes respectively. **CONCLUSIONS:** Our model of pancreatic cancer has a consistent growth rate, mimics the stromal and immune microenvironment observed in human pancreatic ductal adenocarcinoma as well as circumvents the issue of variability seen in previous mouse models. This clinically relevant model can be a valuable tool to evaluate novel therapeutics in pancreatic cancer.

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Routine Feeding Jejunostomy Placement is Unnecessary following Curative Resection for Gastric Cancer

A.M. Blakely,‡ M.F. Winkler, J. McPhillips, W.G. Cioffi, T.J. Miner. Brown University / Rhode Island Hospital, Providence, RI.

**Introduction** The appropriate role of advanced nutritional support, namely enteral or total parenteral nutrition (TPN), following curative resection for gastric cancer is controversial. Feeding jejunostomy (FJ) tubes are often placed routinely in total gastrectomy (TG) and selectively in subtotal gastrectomy (SG). Despite recent reports suggesting high FJ tube-associated complication rates, appropriate literature on this practice is lacking. Methods All curative resections performed for gastric adenocarcinoma were evaluated from Jan 2004 to Dec 2013. Intraoperative FJ tube placement, usage, tube-associated complications, and postoperative TPN requirements were analyzed. Results Of 105 patients undergoing gastrectomy, 47 (45%) had an FJ tube placed (39 of 42 TG (93%) vs 8 of 63 SG (13%), p<0.0001). FJ tube-associated complications occurred within 30 days in 6 of 47 patients (12.8%), all after TG, and 5 of 6 required reoperation; complications were closed-loop obstruction around the FJ tube (2), tube leak (2), small bowel perforation (1), and multi-organ failure upon tube feed initiation (1). Despite placement, FJ tubes were not utilized at discharge in 22 of 47 patients (47%)(19 of 39 TG (49%) vs 3 of 8 SG (38%), p=0.71); these patients either did not need or tolerate enteral feeding. FJ tubes were associated with longer length of stay (median 15 days vs 10 days, p=0.0022). Temporary TPN was needed in 21% overall, in patients with FJ tubes (11 of 47, 23%) or without (11 of 58, 19%; p=0.58). Median time of inpatient TPN administration was 11 days. Only 3 of 22 patients (13.6%)...
required TPN after discharge, all for over 90 days, 2 of whom had FJ tube-related complications. **Conclusions** Routine feeding jejunostomy tube placement is not indicated in patients undergoing curative resection for gastric cancer. FJ tubes were used in only half of patients, were associated with major complications, and did not obviate temporary TPN administration. Since advanced nutritional support may be required for adequate calorie intake in the immediate postoperative period, a short term nasojejunal feeding tube placed at initial operation may be a well-tolerated, low-risk alternative.

Flow chart of patients by extent of surgery, feeding jejunostomy tube placement, dependence on tube feeds, and total parenteral nutrition administration.

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**Inhibition of Hypoxia Inducible Factor-1α in Pancreatic Adenocarcinoma Attenuates Phenotypic Polarization of Tumor-associated Macrophages**

**Introduction:** Tumor-associated macrophages (TAMs) are thought to promote tumor progression, particularly the alternative/M2 phenotype as compared to the classic/M1 phenotype. Similarly, pathologic studies have demonstrated that hypoxia inducible factor-1α (HIF1α) is a marker of advanced malignancy in pancreatic cancer. HIF1α is a transcription factor that regulates multiple cellular processes with potential pro-tumorigenic effects. We hypothesize that tumor-specific HIF1α activity is critical for paracrine-mediated activation of TAMs. **Methods:** Pan02 murine pancreas adenocarcinoma cells were modified using short-hairpin RNA targeting HIF1α via lentiviral transduction to create Pan02 SH- cells lacking HIF1α activity. Cells were grown to 80% confluence and cell culture conditioned media (CCM) was collected. RAW 264.7 murine macrophage cells were exposed to CCM for 24 hours followed by real-time PCR to determine polarization. **Results:** Decreased expression of SOCS3, an M2 marker, was found in macrophages exposed to Pan02 SH+ CCM (p=0.0067). There was no significant difference in SOCS1 expression, an M1 marker (p=0.0848). However, expression of additional M2 markers IL4Rα and arginase-1 (Arg-1) were not different between treatment groups. Pan02 SH+ CCM-exposed macrophages did have reduced expression of the pro-inflammatory cytokine IL6 (p=0.0192) and transcription factor C/EBP-β (p=0.0033). **Conclusion:** Overall, decreased induction of TAMs from CCM was seen with HIF1α suppression. These macrophages had a distinct phenotype outside of canonical M1/M2 polarization, with increased expression of both pro-inflammatory (IL6, C/EBP-β) and alternative macrophage genes (SOCS3) while lacking expression of other pro-inflammatory (SOCS1) and alternative macrophage genes (IL4Rα, Arg-1). Thus, HIF1α activity in pancreatic adenocarcinoma cells is a critical determinant of macrophage polarization and may be an important target for immunomodulatory therapies. Furthermore, the mixed phenotype observed in these macrophages suggests that tumor-associated macrophage biology is more complex than previously known.

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**Early Surgical Bypass versus Endoscopic Stent Placement in Pancreatic Cancer**

**Methods:** We performed a retrospective analysis of unselected pancreatic cancer patients in the Healthcare Cost and Utilization Project (HCUP) Florida State Inpatient Database and Florida State Ambulatory Surgery Database (2007-2011) using revisit variables. Patients with early surgical biliary bypass or endoscopic stent placement were analyzed. The early surgical bypass group included patients undergoing bypass within 30 days of initial stent placement. Subsequent admissions and surgical, endoscopic or percutaneous interventions were identified. Propensity score matching by intervention was performed with univariate analysis of patient characteristics and outcomes before and after matching. Multivariate analyses of readmission and reintervention were performed by logistic regression. **Results:** 1,823 and 342 underwent endoscopic treatment versus early surgical bypass, respectively. After propensity score matching, 684 patients were analyzed (table). 64.0% (219) of endoscopic and 70.5% (241) of surgical patients were readmitted (p=0.07) and 15.2% (57) and 9.1% (31) underwent reintervention (p=0.01). Endoscopic patients had lower index median length of stay (6 vs 11 days, p<0.01) and admission cost ($11,549 vs $23,215, p=0.01). In multivariable analysis, surgical biliary bypass was predictive of readmission (OR 1.50; 95% CI 1.03-2.20) and initial procedure was not predictive of reintervention (p=0.20). **Conclusions:** Surgical biliary bypass is less commonly performed than endoscopic stenting. Among propensity score-matched patients, readmission rates are similar, though endoscopic patients require more subsequent interventions, including stent exchanges. Candidates for both techniques may experience fewer subsequent invasive procedures if offered early surgical biliary bypass.

**Propensity Score Matched Outcomes following Early Surgical Bypass versus Endoscopic Stent Placement**

**Abbreviation:** LOS, length of stay
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What is the Accuracy of preoperative Abdominal CT Staging for Gastric Cancer? A Population-based Analysis
D.J. Kagedan,1* F. Frankul,2 A. El-Seedly,3 M. Elmii,2 B. Zagorski,3 C. McGregor,2 M. Dixon,4 A. Mahal,4 J. Vasilevska-Ristovska,2 L. Helyer,4 C. H. Law,2 N.G. Coburn.1 1. General Surgery, University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 3. Saint Barnabas Medical Center, Livingston, NJ; 4. Maimonides Medical Center, Brooklyn, NY; 5. Queen’s University, Kingston, ON, Canada; 6. Dalhousie University, Halifax, NS, Canada.

Introduction: Accurate preoperative staging of gastric adenocarcinoma (GA) is essential for selecting patients for curative-intent resection. Most patients undergo abdominal computed tomography (CT) scan to determine contraindications to resection (local invasion, metastases), however the reported accuracy of CT is variable, and the literature is mostly limited to single-institution studies. Methods: Using a provincial cancer registry, 2414 patients with GA diagnosed 2005-08 at 116 institutions were identified, with a primary chart review of radiologic, operative, and pathologic reports performed for all patients. 570 patients underwent operative intervention with no neoadjuvant therapy, and had a preoperative CT report available. Preoperative abdominal CT and intraoperative findings were compared to final pathology reports (the gold standard) to determine the accuracy of assessing local invasion, nodal metastasis, and intra-abdominal distant metastases (American Joint Committee on Cancer, AJCC M1). Results: Based on final pathology reports, 77 patients (13.7%, n = 561) had evidence of local invasion (AJCC T4) and 350 patients (62.2%, n = 563) had nodal metastasis. The mean time between CT scan and operative intervention was 29 days. For local invasion, the accuracy of CT scan alone was 84.3% (n = 561); when combined with intraoperative findings, the accuracy was 74.2% (n = 233). For nodal metastasis, the accuracy of CT alone was 51.5% (n = 563) and 61.9% when combined with intraoperative findings (n = 312). The accuracy of CT scan for detecting M1 was 65.1% (n = 361). Understaging occurred in 12.5% for local invasion, 45.3% for nodal disease, and 31.6% for M1. Overstaging occurred in 3.2% for local invasion, 3.2% for nodal disease, and 3.3% for M1. Conclusions: Preoperative abdominal CT is most accurate in determining local invasion, and least accurate in nodal assessment, with infrequent overstaging. The poor accuracy of CT in detecting nodal disease should be taken into account when selecting patients for neoadjuvant therapy. As CT missed M1 disease in 31.6% of patients, diagnostic laparoscopy should be considered as part of the preoperative evaluation.

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Effect of Complications after Pancreatoduodenectomy on Adjuvant Therapy Utilization and Survival in Pancreatic Cancer

Background: While adjuvant therapy (AT) completion is a necessary component of multimodality therapy for pancreatic adenocarcinoma (PDAC), its timing and utilization can be hindered by complications after pancreatoduodenectomy (PD). The primary aim of this study was to evaluate the impact of post-PD complications on AT utilization and overall survival (OS). Methods: Patients treated with PD for PDAC at a single institution (2000-2012) were evaluated. Data on 90-day complications were extracted from the electronic medical record with postoperative major complications (PMC) defined as Grade ≥3. Patient records were linked to the Surveillance Epidemiology End Results (SEER)-Kentucky Cancer Registry (KCR) from 2004-2012, those undergoing pancreatectomy were stratified by postoperative chemotherapy/radiotherapy delivery and timing. Patients with preoperative therapy, no AT, or postoperative therapy beyond 16 weeks were excluded. Remaining patients were stratified into 2 groups defined as “early” (<8 weeks) and “late” (8-16 weeks). A Cox regression model was created to analyze the impact of AT timing, adjusting for clinicopathologic variables. Results: Of the 4,882 total patients with PDAC, 1,193 (24%) underwent pancreatectomy. Of these, only 364 (30%) received AT within 16 weeks. With median age 65 years (range 20-101), 86% patients were stage II and 76% were node-positive. Median time to AT initiation was 22 days (range 5-111). Timing of AT did not affect OS (median OS: early AT, 19.5 vs. 19.7 mo, late AT, p=0.63). Median OS for stages I, II, and III were 46.1, 19.3, and 8.6 mo, respectively (p=<0.001). Poorly/undifferentiated tumors were associated with worse median OS 17.6 vs. 21.3 mo for well/moderately differentiated tumors (p=<0.001). Lymph node positivity was associated with worse median OS 18.1 vs. 25.8 mo for node negativity (p=0.001). On multivariate analysis, factors that affected OS included stage (II, HR 2.54, p=0.022; III, HR 5.16, p=0.001), node positivity (HR 1.57, p=0.008), poorly/undifferentiated grade (HR 1.50, p=0.002), but not AT timing. Conclusions: In this SEER-KCR analysis, there was no difference in OS between early and late AT initiation. Despite its proven value, the ideal window for AT initiation remains unknown as tumor biology continues to trump current treatment regimens.
P361 Warfarin Blocks Gas6-mediated Axl Activation Required for Pancreatic Cancer Epithelial Plasticity and Metastasis

A. Kirane,* K. Ludwig,1 N. Sorelle,1 G. Haaland,1 T. Sandal,1 S.P. Dineen,1 J. Lorenz,2 R. Brekken,1 1. UT Southwestern, Dallas, TX; 2. University of Bergen, Bergen, Norway.

Background: Activation of the receptor tyrosine kinase Axl is induced by its ligand Gas6, a vitamin K-dependent protein, and is associated with poor outcome in pancreatic cancer (PDAC). Therefore, we hypothesized that the vitamin K antagonist warfarin may be effective in PDAC due to Axl inhibition.

Methods: Gas6-dependent Axl activation was inhibited with low dose warfarin or other tumor-specific Axl targeting agents in vitro and in orthotopic and transgenic models of PDAC (10 animals/group), comparing both Axl+ and Axl- cell lines. Outcomes measured were primary tumor growth, metastatic progression, and changes in tumor microenvironment. Results: In an orthotopic splenic injection model of metastasis, warfarin pretreatment abrogated tumor formation, while warfarin initiation 48 hours later inhibited growth (p<0.005). Warfarin reduced growth of tumors established by pancreatic injection and profoundly reduced metastatic events. Warfarin had no effect on Axl- cell lines (p=0.05). Inhibition of Axl using shRNA in Mia PaCa2 prevented tumor growth in vivo. Warfarin effect on orthotopically grown tumors was recapitulated by administration of mAb specific to Axl (p<0.005) and warfarin treatment augmented response to gemcitabine (p<0.005). Tumors from warfarin treated animals demonstrated increased E-Cadherin and decreased Vimentin expression (p<0.0001). In vitro, Warfarin significantly inhibited tumor cell migration, invasiveness, proliferation and EMT (p<0.0001) while increasing apoptosis (p<0.05) and sensitivity to chemotherapy. Treatment of Axl- lines with TGF-β and collagen resulted in 4 fold induction of Axl and resultant warfarin sensitivity. Conclusion: Axl inhibition reduced the plasticity and metastatic capacity of pancreatic carcinomas and is necessary for the maintenance of EMT. Axl signaling is a critical driver of pancreatic cancer progression and its inhibition with low dose warfarin or Axl-selective targeting agents may improve outcomes in patients with Axl-expressing tumors.

P360 Vitamin E δ-Tocotrienol (VEDT) Transiently Activates PI3K/AKT Signaling in Pancreatic Cancer Cells: Rationale for Inhibiting AKT Pathway with VEDT Therapy

E.S. Glazer,1* A. Cheng,1 R.A. Francois,2 H. Kazem,1 C. Xu,1 J.O. Cheng,3 S.M. Sebti,1 M.P. Malafa,1 1. Moffitt Cancer Center, Tampa, FL; 2. University of Florida, Gainesville, FL.

Introduction: Vitamin E, δ-Tocotrienol (VEDT) is under early clinical investigation in the treatment of pancreatic carcinoma (PC) based on preclinical studies demonstrating compelling chemoprevention and therapeutic activity. We observed transient activation of AKT by VEDT, and therefore, we hypothesized that AKT inhibition might enhance VEDT bioactivity in human PC cells. Methods: PANC-1 & MiaPaCa-2 cells were utilized in vitro and in vivo to investigate the effects of VEDT in combination with the AKT inhibitor MK-2206 on AKT phosphorylation, cellular viability (MTT assay), apoptosis (PARP cleavage & Caspase-3 expression), and tumor weight. Mice with PANC-1 flank tumors were treated for 21 days with VEDT orally, MK-2206 orally, both, or neither. Results: The activation of AKT by VEDT alone was important for VEDT bioactivity because the inhibition of AKT by MK 2206 significantly enhanced VEDT induction of PC cell apoptosis (see figure). The combination index of MK 2206 with VEDT was <1, indicating synergistic activity between MK-2206 and VEDT in inducing apoptosis. Moreover, VEDT combined with MK 2206 significantly inhibited the growth of PANC-1 human PC cells in nude mice compared to either agent alone (P = 0.003), increased activity of caspase-3 over 10-fold (P = 0.004), decreased p-AKT expression (see figure), and increased PARP cleavage (see figure). In contrast, the expression of constitutively active AKT significantly attenuated VEDT-induced apoptosis and tumor growth in human PC cells. Conclusion: Taken together, our studies indicate that VEDT transiently activates the PI3K-AKT pathway, which protects PC cells from VEDT-induced apoptosis. These results provide novel insights into VEDT signaling in PC cells and provide the rationale for targeting the AKT pathway to enhance VEDT chemoprevention and therapy of PC.
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Nodal Involvement in Gastric Adenocarcinoma Decreases with Age: A Population-based Analysis
A. Ahmad,1,2 H. Khan,1 A.J. Olszewski,1 P. Somasundar,1 1. Surgical Oncology, Roger Williams Medical Center, Warwick, RI; 2. Memorial Hospital of Rhode Island, Pawtucket, RI.

BACKGROUND: In gastric adenocarcinoma, the disparity in lymph node involvement between different age groups has not been thoroughly investigated. It may impact prognosis and define strategies for multimodality management in elderly patients. The objective of our study was to compare adequate lymph node harvest and nodal involvement in gastric adenocarcinoma patients, with a focus on appropriate surgical staging in the elderly.

METHODS: We analyzed data extracted from the Surveillance, Epidemiology and End Results (SEER) database on 16,213 patients diagnosed with stage I-III gastric adenocarcinoma between 2004 and 2011. All patients underwent surgical resection. Comparison between age groups was made on adequate surgical staging with >15 lymph nodes examined (LNE) and nodal involvement using the chi-square test. Relative risk (RR) of adequate lymph node harvest and node-positive cancer between age groups was compared in a multivariate log-linear model.

RESULTS: Among 16,213 gastrectomy patients, proportion of patients that had >15 LNE decreases significantly with increasing age (p <0.0001). When adequately staged, older patients had a significantly lower proportion of node-positive tumors (P <0.0001). Additionally, older patients had a significantly higher proportion of well differentiated and moderately differentiated tumors (P <0.0001).

CONCLUSIONS: In gastric adenocarcinoma, older patients are less likely to be adequately staged. However, when adequately staged, they are less likely to have node positive tumors. The guidelines for extent of surgical resection and pathological examination should be diligently adhered to in all patients regardless of age, since appropriate staging may significantly alter multimodality management in the elderly.

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Optimal Extent of Lymphadenectomy in Gastric Adenocarcinoma: A 7-Institution Study of the U.S. Gastric Cancer Collaborative
R.W. Randle,1,2 D. Swords,1 E.A. Levine,1 N.F. Fino,2 M.H. Squires,2 G.A. Poultsides,2 R.C. Fields,4 M. Bloomston,2 S.M. Weber,1 T.M. Pawlik,1 L.X. Jin,1 G. Spolverato,1 E.R. Winslow,1 C.R. Schmidt,1 D.A. Kooby,2 D.J. Worhunsky,1 N.D. Saunders,1 C.S. Cho,1 S.K. Mai-thel,1 R.I. Votanopoulos,1 1. Wake Forest University, Winston-Salem, NC; 2. Emory, Atlanta, GA; 3. Stanford, Stanford, CA; 4. Washington University, St. Louis, MO; 5. Ohio State University, Columbus, OH; 6. University of Wisconsin, Madison, WI; 7. Johns Hopkins University, Baltimore, MD.

Introduction: The optimal extent of lymphadenectomy in the treatment of gastric adenocarcinoma continues to be a subject of intense debate. We aimed to compare gastrectomy outcomes following limited (D1) or extended (D2) lymphadenectomy.

Methods: Using the multi-institutional US Gastric Cancer Collaborative database, we reviewed the morbidity, mortality, recurrence, and overall survival (OS) of 727 patients receiving D1 or D2 lymphadenectomies. Patients with stage IV disease, prior gastrectomy, and age 85 or greater were excluded. The study was approved by the Institutional Review Board of each institution.

Results: Overall survival was significantly better for D2 compared to D1 lymphadenectomy (p = 0.001). The risk of death was 1.33 times higher for patients receiving D1 compared to D2 lymphadenectomy (HR 1.33, 95% CI 1.16-1.43, p <0.0001). Pathologic Stage III (HR 2.23), node involvement (HR 1.31, 95% CI 1.29-1.33) were strong predictors of risk-adjusted mortality (all p <0.001).

Discussion: The optimal extent of lymphadenectomy in gastric adenocarcinoma continues to be a subject of intense debate. We aimed to compare gastrectomy outcomes following limited (D1) or extended (D2) lymphadenectomy. Patients with stage IV disease, prior gastrectomy, and age 85 or greater were excluded. The study was approved by the Institutional Review Board of each institution.
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Tumor Regression Grade in Gastric Cancer: Predictors and Impact on Outcome J. Wong,* A. Blackham, M. Yamamoto, E. Kenning, C. Hollenbeck, N. Gusani, J. M. Pimiento, Penn State Hershey Medical Center, Hershey, PA; 2. Moffitt Cancer Center, Tampa, FL.

Introduction: Advanced gastric adenocarcinoma is predominantly treated with neoadjuvant chemotherapy prior to resection in the U.S. Tumor regression grade (TRG), coded from 0 (complete response) to 3 (no treatment effect) has an unclear impact on long term outcomes. This study aims to determine if pre-chemotherapy factors may predict TRG and its impact on survival. Methods: Two institutional databases were reviewed for patients who underwent neoadjuvant chemotherapy and underwent resection for gastric and gastroesophageal adenocarcinoma, with TRG recorded. TRG of 0 and 1 were grouped and compared to TRG 2 and 3. Results: 58 patients were evaluated. 30 (52%) were female, and the median age was 65 years. The majority (71%) were Caucasian. 24 (41%) were overweight and 15 (25%) obese; only 16 (27%) were normal weight. Eight (14%) were active smokers, while 23 (40%) were former smokers. The majority had tumors of the gastric body or antrum (N=40, 69%); 14 (24%) had cardia or proximal tumors, and 4 (7%) had limited. Chemotherapy regimens were predominantly epirubicin, cisplatin and fluorouracil (N=42, 72%) or a similar regimen, followed by FOLFOX or similar regimen (N=9, 16%). 39 (67%) had PET scans prior to and following neoadjuvant chemotherapy. Response was denoted as unchanged, decreased or increased in SUV activity. Only 11 (19%) demonstrated a TRG 0 or 1; the majority (N=36, 62%) had TRG 3. Demographic variables such as age, gender, body mass index, smoking status, and race were not associated with treatment response. Comorbidities such as HTN, DM and cardiovascular disease also did not correlate. Change in PET scan did not predict TRG. Tumor size, however, predicted TRG, with larger tumors less likely to respond, OR 0.35, p<0.003. Neither signet ring pathology or tumor location predicted response. Median follow-up was 13.8 months; TRG 0/1 vs. 2/3 did not predict overall survival or time to recurrence. However, positive lymph nodes predicted both overall and disease-free survival. Conclusions: In this small series, demographic factors did not predict TRG. However, TRG did not predict survival, although positive lymph nodes did. Larger studies are needed to evaluate predictors and utility of TRG in gastric adenocarcinoma.

Methods: We identified 308 patients undergoing a surgery-first approach and 145 patients undergoing neoadjuvant therapy (CTX, n = 73 and CTX-RT, n = 72) followed by curative-intent surgery for adenocarcinomas of the stomach and GEJ from 1995-2014. We compared the baseline characteristics and the postoperative outcomes between the two groups using univariate and multivariate analyses. Results: Patients receiving neoadjuvant therapy were more likely to be of younger median age (63 vs 71 years, P < 0.0001), have tumors of the GEJ (37% vs 17%, P < 0.0001), to undergo esophagogastrectomy (51% vs 26%, P < 0.0001) and D2 lymphadenectomy (39% vs 27%, P = 0.015), and to have more advanced stage disease (P < 0.0001) than patients undergoing surgery first. There were no differences in overall 30-day morbidity (42% vs 40%, P = 0.72) or mortality (6% vs 2.3%, P = 0.07) rates between the neoadjuvant therapy and surgery-first groups, respectively (see Table). However, patients undergoing surgery first were significantly more likely to have higher-grade complications than those undergoing neoadjuvant therapy. The median length of hospital stay and the 30-day readmission rates were similar between the two groups. Conclusions: Despite having more advanced disease and undergoing higher-risk surgical procedures, patients with adenocarcinomas of the stomach or GEJ who receive neoadjuvant therapy prior to surgery are less likely to have major post-operative complications, including death, than patients treated with a surgery-first approach. Concerns about higher rates of post-operative complications should not deter the use of neoadjuvant therapy for gastroesophageal cancer.

Postoperative Morbidity and Mortality

<table>
<thead>
<tr>
<th>Complication Grade</th>
<th>Surgery First</th>
<th>Neoadjuvant Therapy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>18 (5.3%)</td>
<td>11 (1.7%)</td>
<td>0.030</td>
</tr>
<tr>
<td>II</td>
<td>26 (8.2%)</td>
<td>24 (4.5%)</td>
<td></td>
</tr>
<tr>
<td>IIIa</td>
<td>14 (4.5%)</td>
<td>12 (2.3%)</td>
<td></td>
</tr>
<tr>
<td>IIIb</td>
<td>23 (7.5%)</td>
<td>4 (2.8%)</td>
<td></td>
</tr>
<tr>
<td>IIIa</td>
<td>3 (1.5%)</td>
<td>2 (0.6%)</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>7 (2.3%)</td>
<td>1 (0.7%)</td>
<td></td>
</tr>
<tr>
<td>Any Complication</td>
<td>121 (35.3%)</td>
<td>61 (21.9%)</td>
<td>0.07</td>
</tr>
<tr>
<td>Median Hospital Stay</td>
<td>9 days</td>
<td>9 days</td>
<td>NS</td>
</tr>
<tr>
<td>30-Day Readmission Rate</td>
<td>44 (14%)</td>
<td>24 (16%)</td>
<td>0.53</td>
</tr>
</tbody>
</table>

*According to the Clavien-Dindo Classification

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Chemotherapy is not Indicated for Early Stage Pancreatic Adenocarcinoma K. O斯塔fop, Ph. Thirunuvakarasu, B. Kuvshinoff, S. J. Nurkin, S. Hochwald, Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.

Introduction: The CONKO trial and current NCCN guidelines recommend chemotherapy for all patients with resected pancreatic adenocarcinoma (PDAC). However, prior studies have addressed the impact of chemotherapy on survival benefit for early stage patients as they comprise <10% of the study population. Methods: Using the NCDB from 1998-2006, patients with PDAC who underwent a pancreatectomy were included and those with pT3 and or pN1 were excluded. Median survival was estimated using Kaplan-Meier with log-rank comparison and Cox regression. Results: Over this 8 year period, 4227 patients were identified with resected Stage 1A or 1B PDAC, of which 41% received chemotherapy (CTX) and median follow up was 23.8 months. For all patients, univariate analysis, female gender, CTX, radiation (RT), lymph node (LN) yield of ≥ 11 were associated with an improved overall survival (OS). Positive LNs (>11) (p<0.001), tumor grade (p<0.001), age >70 (p<0.001) were associated with worse OS. CTX (33.9 vs 32.5 months), RT, race, sex, and facility type were not associated with OS (Figure 1). For Stage 1B patients (n=2812, 67%), CTX (27.3 vs 20.7 months, p<0.0001), LN ≥ 11 (p<0.001), female sex (p<0.02), tumor grade (p<0.0001), facility type (p<0.0001), insurance (p<0.0001), negative margin (p<0.001) and age >70 (p<0.001) were all associated with an improved OS. For Stage 1A patients, on multivariate analysis only age >70 (p<0.001) and LN yield of ≥ 11p (p<0.001) were associated with a significant improvement in survival. Conclusions: Inpatients with Stage 1A PDAC, survival is predicted by quality of operation (as suggested by LN yield) and age >70. 

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Background: The effects of neoadjuvant chemotherapy (CTX) or chemoradiotherapy (CTX-RT) on postoperative complications following surgical resection of adenocarcinomas of the stomach and gastroesophageal junction (GEJ) have not been well studied. We sought to compare the postoperative outcomes of patients with gastroesophageal cancer treated with neoadjuvant therapy followed by surgery to those undergoing a surgery-first approach.

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patient age. Importantly, patients with Stage 1A do not have a survival benefit with the addition of chemotherapy and its omission should be considered.

P369 Integrin-linked Kinase Over-expression in the Pancreatic Stellate Cells of Pancreatic Cancer Stroma Portends a Poor Prognosis

L.A. Shirley, M. Yang, B. Swanson, W. Fraker, T. Bekaii-Saab, M. Bloomston, C. Chen. 1. Surgical Oncology, The Ohio State University Wexner Medical Center, Columbus, OH; 2. The Ohio State University College of Pharmacy, Columbus, OH.

Introduction: Integrin-linked kinase (ILK), a serine/threonine protein kinase that normally plays a role in cell-extracellular matrix interactions, has been shown to promote invasion in pancreatic cancer. Due to these functions, we examined ILK expression in the stroma and malignant epithelium from pancreatic cancers, to determine if a relationship exists between ILK expression and survival. Methods: A tissue microarray of 150 pancreatic cancers was stained for ILK by immunohistochemistry and scored from zero (no expression) to three (high expression) in both epithelium and stroma. A clinical database was queried to identify specific PDA phenotypes. Results: ILK expression was significantly higher in the stroma and malignant epithelium from pancreatic cancers, to determine if a relationship exists between ILK expression and survival. With low to no stromal ILK expression (Grades 0 and 1) had a median survival of 21.2 months vs. 13.2 months in Grades 2 and 3 (P = 0.016). PSCs had increased ILK expression when compared to all pancreatic cancer cell lines (AXPC-1, MiaPaCa-2, PANC1, SW 1990) as well as normal pancreatic cells. Transfection of PSCs with shILK led to morphologic changes, decreased expression of fibroblast proteins, and altered cytokine release. Conclusions: In patients with pancreatic cancer, increased ILK expression in the stroma was associated with worse survival, revealing a possible role of ILK in the crosstalk between tumor and stroma and progression of disease. Within the stroma, activated PSCs appear to be the source of increased ILK levels. Silencing ILK expression produces altered functions of PSCs. ILK inhibition may specifically target the dysregulated tumor microenvironment while sparing normal stroma.

P370 Effect of Neoadjuvant Chemotherapy on 30-day Morbidity and Mortality following Resection of Gastric Malignancy


Background: The Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial led to the advent of neoadjuvant chemotherapy in the treatment of patients with gastric adenocarcinoma. The MacDonald regimen, in contrast, employs adjuvant chemotherapy and radiation therapy and has likewise been shown to have a survival benefit. While the former trial demonstrated improved overall survival, the effects of this regimen on 30-day post-operative morbidity and mortality are not well characterized. Methods: The 2005-2012 American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) database was used to identify patients who underwent gastrectomy for a primary diagnosis of gastric malignancy. Receipt of neoadjuvant chemotherapy up to 30 days prior to surgery was used to predict 30-day post-operative morbidity and mortality, using logistic regression. Results: 3,614 patients underwent gastrectomy for gastric malignancy. 317 (8.8%) received neoadjuvant chemotherapy in the 30 days prior to resection. Patients who received neoadjuvant chemotherapy had similar 30-day mortality to those who did not (OR 0.67, P = 0.29). Patients who received neoadjuvant chemotherapy also had similar rates of 30-day complications, including wound infection, venous thromboembolism, pneumonia, progressive renal insufficiency, stroke, myocardial infarction, and sepsis, compared to those who did not receive neoadjuvant chemotherapy. Patients who received neoadjuvant chemotherapy were less likely to develop post-operative urinary tract infections (OR 0.41, p = 0.03). Conclusion: Patients who were treated with neoadjuvant chemotherapy had similar rates of 30-day post-operative morbidity and mortality following resection of gastric malignancy compared to those who did not receive neoadjuvant chemotherapy.

P371 Hypoxia in Pancreatic Cancer Microenvironment Interacts with Metabolic and EMT Features to Define Prognostic Subtypes


Introduction: Pancreatic ductal adenocarcinoma (PDA) is notable for its desmoplastic stroma creating a hypoxic tumor environment, which may, in turn, contribute to cancer cell invasiveness and metabolic reprogramming. Carbonic anhydrase IX (CAIX) is a well-established marker of hypoxia. Here we investigated CAIX expression in tumor cells and the stromal environment, its impact on overall survival, and its relationship to other aggressive features of PDA. Methods: Tumor tissue-microarrays containing 203 PDA cases annotated with clinicopathologic data were stained for CAIX, p53, Vimentin, and MCT4. Stromal volume was evaluated by whole tissue section and mean vessel density was measured using automated analysis. Survival curves were plotted and correlations between biomarkers were determined. Random forest clustering was performed to identify specific PDA phenotypes. Results: CAIX expression in stromal compartment, indicative of a hypoxic microenvironment, was associated with decreased survival (HR 1.76, p = 0.03). Stromal CAIX expression positively correlated with Vimentin (EMT marker) and MCT4 (glycolytic metabolism marker) in the epithelial tumor compartment. These markers were also independently associated with decreased survival, and demonstrated an additive effect when combined. Stromal volume and mean vessel density did not correlate with the aforementioned biomarkers, nor were they associated with patient survival. Random forest clustering yielded four discrete PDA subtypes with the best prognosis cluster having low CAIX and high Vimentin and MCT4, and a mean survival of 21 months. In contrast, the cluster with elevated stromal CAIX, p53, Vimentin and MCT4 had a particularly poor prognosis, with a mean survival of 10.5
months. **Conclusion:** Our data demonstrates an important interplay between the hypoxic tumor environment and features of aggressive tumor biology, such as EMT and glycolytic metabolism, which stratifies PDA into subtypes with distinct prognosis.

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**Delayed Gastric Emptying (DGE) after Pylorus Preserving Pancreateoduodenectomy (PPPD): Does Gastrointestinal Reconstruction Technique Matter?**

M. Hanna,* L. Tamariz, R. Gadde, D. Sleeman, C. Allen, A. Livingstone, D. Yakoub. University of Miami-Miller School of Medicine, Miami, FL.

**BACKGROUND:** DGE continues to be a common complication after PPPD. Literature review and meta-analysis was used to evaluate whether antecolic gastrointestinal reconstruction can decrease the rate of this complication.

**METHODS:** A search for studies comparing antecolic to retrocolic reconstruction after PPPPD was done in PubMed, MEDLINE, EMBASE, SCOPUS, and COCHRANE databases (2003 to present). Primary outcome was DGE. Secondary outcomes included other postoperative complications. Quality of included studies was evaluated by CONSORT and STROBE criteria. Relative Risk (RR) and 95% Confidence Intervals (CI) were calculated from pooled data in RCTs and retrospective studies separately and heterogeneity was assessed.

**RESULTS:** The search strategy yielded 153 studies, of which 10 met our selection criteria. The included studies comprised 1067 patients who had PPPD, where 504 patients underwent antecolic and 563 patients underwent retrocolic reconstruction. Median age was 65 (R: 57 – 70). Average Male / Female ratio was 54.5% vs. 45.5%. Meta-analysis showed decreased DGE with antecolic reconstruction in both RCTs (RR 0.44, CI 0.24-0.77, p=0.005) and retrospective studies (RR 0.21, CI 0.14-0.30, p=0.001). Operative time was less with antecolic reconstruction in RCTs (RR -0.007, CI -0.256-0.242, p=0.957). Nonetheless, pancreatic fistula was increased with antecolic reconstruction in both RCTs (RR 1.25, CI 0.788-1.998, p=0.339) and retrospective studies (RR 1.319, CI 0.538-3.234, p=0.546). Also, incidence of abdominal abscesses was increased with antecolic reconstruction in both RCTs (RR 1.019, CI 1.064-1.664, p=0.939) and retrospective studies (RR 1.394, CI 1.045-2.496, p=0.563). There was no significant heterogeneity between studies for these results. Reporting on overall morbidity, length of stay and operative blood loss showed significant heterogeneity between studies. **CONCLUSIONS:** Antecolic reconstruction seems to be associated with less DGE, more pancreatic fistula and abscess formation postoperatively. More standardized randomized studies are needed to investigate other postoperative complications in more depth.

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**Adherence to Expected Treatment for Pancreatic Cancer Improves Outcomes**


**Purpose:** National Cancer Database (NCDB) analysis from 1995-2004 showed 70% of patients with stage I pancreatic adenocarcinoma (PDA) did not have surgery. We sought to analyze adherence to expected treatment (ET) by stage for PDA and identify factors that led to no treatment (NT) or unexpected treatment (UT) in a recent cohort.

**Methods:** Using our Cancer Registry (CR) that populates the NCDB, we identified patients with PDA from 2004-2013. ET was defined as surgery (chemotherapy (CTX), radiation (XRT) or combination (CTX+XRT) (stage I&II), XRT (stage III), and CTX (stage IV). UT was defined as no surgery (I&II), surgery (III), or surgery+XRT (IV).

**Results:** 2341 patients were identified (I=4%, II=47%, III=11%, & IV=38%): NT=24%; ET=58%; UT=18%.

Stage at diagnosis predicted survival. 1191 patients had resectable PDA (I&II): NT=15%; ET=58%; UT=27%. ET demonstrated the best overall survival, but UT had better survival than NT (p<.0001). Of the 183 I&II patients in the NT group, 57 (31%) refused surgery and 37 (20%) were deemed poor surgical candidates. Abstracted charts were concordant with 94% of CR for non-surgical I&II. 261 patients had unresectable PDA (III): NT=18%; ET=70%; UT=12%. Unexpectedly, survival was best in UT, but ET had a survival advantage over NT (p<.0001). 896 patients had metastatic PDA (IV): NT=36%; ET=55%; UT=9%. NT had worse survival than ET and UT (p<.0001). Compared to ET, patients receiving NT were older (p<.05). Males and Caucasians were more likely to receive treatment in select groups. IV was associated with a higher rate of NT, and I&II were associated with a higher rate of UT (p<.0003). ET was not affected by tumor location, but head lesions had higher rates of UT (p<.004).

**Conclusions:** Unlike previous reports, the majority of patients with early stage disease had surgery. ET and NT were associated with better survival than NT in all stages. Older age was associated with NT. The higher proportion of UT in the resectable group may reflect neoadjuvant intent to treat, and better survival in stage III UT may reflect downstaging after neoadjuvant therapy, allowing for resection. Similar analysis using NCDB would offer interesting comparisons to tertiary high volume centers.
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Clonal Composition and Selection during PanIN Progression

K.J. Lajaro,1,4 A. Hendley,1 J. Bailey,1 S. Sinha,1 C.A. Iacobuzio-Donahue,1 S. Leach,1 1. Center for Pancreatic Research, Memorial Sloan Kettering Cancer Center, New York, NY; 2. Johns Hopkins University, Baltimore, MD; 3. University of Texas, Houston Health Science Center, Houston, TX.

By 2020, pancreatic cancer will become the 2nd most common cause of cancer death in the US. Given the genetic complexity of invasive pancreatic cancer, we have focused on early events underlying pancreatic intraepithelial neoplasia (PanIN). We hypothesized that stage-specific bottlenecks may lead to clonal selection during PanIN progression. To test this, we examined evolving clonal complexity during PanIN progression in the Mist1CreER, LSL-KrasG12D mouse model. Following Kras activation in adult acinar cells, these mice develop acinar-to-ductal metaplasia (ADM) and PanIN lesions in a manner that faithfully recapitulates human disease. Our strategy involves crossing MistCreER, LSL-KrasG12D to Brainbow2.1Tg/Tg “Confetti” mice, in which individual cells undergo stochastic recombination of the Confetti reporter to active expression of either GFP, CFP, RFP or YFP. Following tamoxifen induction of CreER, mice were sacrificed at 4, 9 and 16 weeks post-tamoxifen, and confocal imaging was performed. Lesions were characterized by grade (ADM, early PanIN and late PanIN), and the number of participating clones (defined as adjacent cells sharing an identical fluorescent protein signature) was determined. For ADMs, early PanIN and late PanIN, we observe both monocolonal and polyclonal lesions. Preliminary analysis suggests a time-dependent decrease in clonal complexity. The average number of clones per 100 labeled PanIN cells decreased in mice sacrificed at 9 weeks and 16 weeks compared to those sacrificed 4 weeks (36.14 +/- 8.96 at 4 weeks; 18.8 +/- 3.91 at 9 weeks; 15.45 +/- 6.85 at 16 weeks). In addition, a significant increase in clonal size was observed over time (3.67 +/- 0.29 cells/clone at 4 weeks; 4.57 +/- 0.31 cells/clones at 9 weeks; 8.37 +/- 1.36 cells/clones at 16 weeks). This increase in clone size was also observed as a function of PanIN severity (3.28 +/- 0.37 cells/clone in ADM vs. 4.3 +/- 0.25 cells/clone in early PanIN vs. 5.75 +/- 0.90 cells/clone in late PanIN). These data suggest an overall trend towards decreased clonal complexity of PanIN lesions and an increase in clone size over time, suggesting significant selective pressure at even the earliest stages of pancreatic cancer.

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Prognostic Value of the Circumferential Resection Margin after Neoadjuvant Treatment in Esophageal Cancer Patients

J. Hulsloth,1,2 Z. Faiz,1 J.K. Smit,1 G. Kats-Ugurlu,1 J.G. Burgerhof,1 J.A. Pijlman,1 1. University of Groningen, University Medical Center Groningen, Dept of Surgical Oncology, Groningen, Netherlands; 2. University of Groningen, University Medical Center Groningen, Dept of Pathology, Groningen, Netherlands; 3. University of Groningen, University Medical Center Groningen, Dept of Epidemiology, Groningen, Netherlands.

Background: Involvement of the circumferential margin (CRM) is an important factor in esophageal cancer (EC) patients. CRM definitions are commonly based on the College of American Pathologists (CAP) at 0 mm and the Royal College of Pathologists (RCP) at >1 mm. We evaluated which CRM definition is useful in current practice with neoadjuvant chemoradiotherapy (CRT) and whether the CRM cut-off value differs after CRT.

Methods: We prospectively included 209 patients (104 with CRT) with locally advanced EC who underwent radical transthoracic esophagectomy. Patients were followed for at least 2 years after surgery or until death. Patients with <1 mm longitudinal resection margins were excluded. Cancer related death was scored as event and death of other causes as end of follow-up (median 27: IQR 14.0 - 42.8 months). CRMs were measured in tenths of millimetres by experienced pathologists. Pathologic proven tumor regrowth, unequivocal radiologic suspicion or obvious clinical manifestations were marked as recurrence. Prognostic factors with P<0.1 in univariate analyses were incorporated in multivariate Cox-regression analyses in which both CRM definitions were assessed separately. In an explorative analyses the CRM cut-off values in the surgery-only and CRT group for 2-year disease free survival (DFS) was assessed using CRM between 0-1.5 mm in the Cox-regression model. Results: Independent prognostic factors on 2-year DFS (P<0.05) in the surgery-only group were: patient age <70 yrs, N1/N2, T1/T2, pT4, pN1, and 0.2 L/N ratio, angioinvasion and CAP R0. In the surgery group, tumor length >4 cm, >0.2 L/N+ ratio, angioinvasion and CAP R0 were independent prognostic factors (P<0.001). In the CRT group only pN stage (P<0.01) was independent prognostic for 2-year DFS. The CRM cut-off value was significant at 0.2-0.3 mm for the surgery and CRT group, respectively.

Conclusion: The CAP value was the only independent prognostic for 2-year DFS in the surgery alone group. The CRM cut-off value was significant at 0.2 and 0.3 mm in the surgery and CRT group, respectively.

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Targeting Pancreatic Cancer with Sigma-2/Erastin Conjugate SW V-49s

Y. Hashim,1* D. Spitzer,1 S. Vangveravong,2 P. Goedegebuure,2 R. Mach,2 W. Hawkins,1 1. Department of Surgery Washington University in St Louis, Saint Louis, MO; 2. Department of Radiology University of Pennsylvania, Philadelphia, PA.

Introduction: Pancreatic cancer is a devastating disease that needs new therapy. Here we delivered a novel drug selectively to pancreatic cancer cells using sigma-2 ligands to induce apoptosis and generate reactive oxygen species (ROS). Erastin was chemically conjugated with sigma-2 ligand to create the drug (SW V-49s). Sigma-2 receptors are found in different organs, but they are upregulated in proliferating tumor cells. We have previously shown that Sigma-2 receptors are highly expressed in pancreatic cancer cells. We have also demonstrated that sigma-2 ligands are rapidly internalized in cancer cells and induce apoptosis. Erastin mediates cytotoxicity through generation of (ROS).

Methods: We synthesized a novel compound SW V-49s which is a conjugate of Sigma-2 ligand (SV119) with Erastin. We tested the compound on pancreatic cell lines by applying escalating concentrations of SV119, Erastin, SW V-49s, and SV119 plus Erastin. Viability, caspase, and ROS assays were performed after treatment. In vivo testing was performed on nude mice with subcutaneously implanted patient derived pancreatic adenocarcinoma xenograft. Mice were treated with the SW V-49s and vehicle as a control, daily for 2 weeks.

Results: There was a significant increase in cell death, caspases activity, and ROS production with SW V-49s treatment as compared to controls. Tumor volumes were significantly smaller and the survival rate was higher in the mice treated with the conjugate as compared to the control group (P value < 0.001).

Conclusion: We developed a novel molecular therapeutic based on the concept of cancer selective delivery and dual functionality. This strategy for drug delivery has the potential to expand the therapeutic window for conventional agents and may have a great clinical implication for pancreatic cancer and other malignant tumors.

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Age Bias and Under-treatment in Octogenarians with Pancreatic Cancer


Introduction: Morbidity and mortality following pancreatic resection is at an all-time low and chemotherapeutic options for pancreatic cancer (PC) are growing, yet there is still reluctance to treat elderly patients. We aimed to examine the reason for failure to treat and analyze outcome in octogenarians with PC.

Methods: We performed retrospective chart review for patients ≥80 years-old from 2005-2013. Demographics, tumor characteristics, treatment, reason for lack of treatment, Charleston Comorbidity Index (CCI), treatment, and outcome were analyzed. Results: 446 octogenarians were analyzed comprising 18% of
all patients. Mean age was 83.9±3.3, 58.8% female. Overall 44% received no treatment. Octogenarians with operable tumors (stage I=35 [7.8%], 2a=100 [22.4%], 2b=120 [26.9%]) had surgery 39% of the time (compare to 58% of all-comers) with the smallest proportion undergoing surgery for stage I (17.1% vs stage 2b 54.2%; p=0.001). Higher stage patients were more likely to undergo surgery (OR 2.02 95%CI 1.34-3.03; p=0.001). Increasing age was a predictor of not receiving surgery (OR 0.83 95%CI 0.74-0.91; p=0.001) whereas CCI was not. The most common reason for no surgery was ‘contraindicated by comorbidity’ (29.8%) despite similar CCI for stage and treatment. Only 19.6% of patients with resectable disease refused surgery of which 66% were female (p<0.01), in 11.4% the reason for not undergoing surgery was unknown. Median overall survival was better in the surgical group 15.9 vs 5.6 mo in the nonsurgical group (p=0.001). Advanced stage patients (stage 3=55 [12.3%], 4=136 [30.5%]) had similarly low treatment rates: chemo stage 3=36.4%, stage 4=34.6% with better survival seen in treated patients (7.0±5.3 vs 2.3±2.7 mo; p=0.01). Younger patients were more likely to undergo chemotherapy (OR 0.81 95%CI 0.72-0.92) but CCI was not related (OR 0.99 95%CI 0.67-1.47).

Conclusion: There is significant deviation from expected treatment for octogenarians with PC. While no correlation existed between CCI and treatment, age correlated with therapy for nearly all stages and few patients refused therapy. Chronological age, not comorbidity, may drive recommendations for treatment in elderly patients.

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Background: Pancreatic neuroendocrine tumors (PNET) constitute about 3% of pancreatic neoplasms. In borderline resectable disease, there is a lack of data to support an optimal neoadjuvant approach for curative outcomes. We describe our institutional experience with a multimodality approach. Methods: We identified all patients with borderline resectable PNET, using NCCN criteria for adenoacarcinoma of the pancreas, who received neoadjuvant therapy at our institution between 2000 and 2013. The reason for borderline status was noted. Neoadjuvant regimen, radiographic response, pathologic response, surgical margins, nodal harvest, number of positive nodes, and recurrence were all documented. Results: A total of 112 patients had undergone pancreatic resections for neuroendocrine tumors during the study period. Six patients had borderline resectable disease. The mean age was 55 years (24-70). They all received at least 1 cycle of Temodar and Xeloda. Three of the six patients also received concurrent 5-FU and radiation. There was radiographic evidence of treatment response in all patients. Five of six patients (83 %) had negative margin (R0) resection. Low volume miliary metastatic disease in the liver was detected in 1 patient at the time of surgery. The median number of lymph nodes harvested was 12. Half of the patients had node positive disease. On pathologic review, 4 patients had histologic evidence of a moderate response. All patients are alive and 5/6 are free of disease. Range of follow up is 3.0-4.32 years. The patient with metastatic disease has had no progression and is the only one who is currently receiving any form of treatment. Conclusion: Neoadjuvant Temodar and Xeloda ± radiation with 5-FU sensitization can lead to R0 resection with durable response in patients with borderline resectable PNET. To our knowledge, this is the first report of the use of multimodality therapy (neoadjuvant chemotherapy ± chemoradiation and surgery) in the treatment of borderline resectable PNET.

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Single Cell Mutational Analysis of Isolated Circulating Tumor Cells in Pancreatic Cancer
C.M. Court,1,* J.S. Ankeny,1 S. Hou,2 M. Lin,2 M. Song,2 M.M. Rochefort,2 H. Tseng,2 J.S. Tomlinson,1 J. UCLA Department of Surgical Oncology, Los Angeles, CA; 2. UCLA Department of Molecular and Medical Pharmacology, Los Angeles, CA.

Introduction: First generation circulating tumor cell (CTC) platforms are plagued by false positives, due to the lack of specificity of immunocytochemistry (ICC) in distinguishing CTCs from other mononuclear cells. Our group employs a NanoVelcro microfluidic CTC chip platform with laser micro-dissection (LMD) to capture and isolate single CTCs. We used genetic analysis to validate our ICC definition of CTCs in pancreatic cancer (PDAC) and highlight the limits of current single cell genetic analysis. Methods: NanoVelcro uses streptavidin bound polymer fibers to capture CTCs using biotinylated anti-EpCAM antibodies. CTCs were identified using ICC (DAPI+/CD45-/CK+, and size ≥6 μm). Human PDAC cells lines were spiked in donor blood to validate the platform. CTCs and WBCs were obtained from 5 PC patients, and LMD was used to isolate single cells. Whole genome amplification (WGA) was then performed. WGA products underwent quality control with 8 band PCR followed by PCR amplification of KRAS exon 1. Sanger sequencing was then used to detect KRAS mutations relative to patient-matched normal WBCs. Results: KRAS mutations were identified in 9/18 (50%) CFPAC-1 (heterozygous G12V) cells versus 8/8 (100%) AsPC-1 (homozygous G12V) and 100% of cell line genomic DNA (gDNA). Forty-nine CTCs and 38 WBCs were then dissected and isolated from 5 PDAC patients. WGA and subsequent KRAS amplification was successful in 28/49 (57%) CTCs and 16/38 (42%) WBCs. KRAS mutations (G12V in 3 patients, G12D in 2 patients) were confirmed in 13/28 (46%) CTCs. All 16 WBCs from matched patients had wild-type KRAS sequences. Conclusions: Using the NanoVelcro platform, we both captured CTCs and confirmed tumor origin using single cell mutational analysis. We show the necessity of validating the ICC definition of a CTC for second generation CTC capture platforms given the nonspecific cytokeratin staining of WBCs. Allele dropout and preferential allele amplification is demonstrated strongly in the heterozygous cell line data and helps clarify why approximately 50% of single cell WGA products failed to show typical KRAS mutations seen in PDAC.
Myofibroblast Expression of Smooth Muscle Actin in Pancreatic Cancer Correlates with Changes in the Immune Infiltrate following Neoadjuvant Therapy

Y. Jiang, F. Jalikis, V.G. Pillarisetty, Surgery, University of Washington, Seattle, WA.

Introduction: Stromal elements of pancreatic cancer (PC) including myofibroblasts and immune cells are thought to play a role in the progression of this devastating disease. As the ability to modulate various components of the stroma is entering the armamentarium of treating physicians, we sought to determine if myofibroblast density correlates with the hematopoietic cell infiltrate in PC.

Methods: We performed immunohistochemistry for smooth muscle actin (SMA) and hypoxia-inducible factor 1alpha (HIF-1α) on a set of primary PC tumors upon which we have previously performed an extensive characterization of their immune infiltrate.

Results: Stromal SMA expression in PC was moderate (n=13) to high (n=14) in the majority of the 38 cases, while minimal (n=3) or low (n=8) expression was rare. Quantification of SMA expression using image capture and analysis software strongly correlated with pathologist SMA scoring (r=0.83, p<0.0001). There was concordance between SMA expression and the numbers of CD3+ T cells (r=0.36, p=0.03), FOXP3+ regulatory T cells (Treg; r=0.39, p=0.02), and CD11b+ myeloid cells (r=0.37, p=0.02) within the tumors. As hypoxia is a defining feature of PC and is known to affect immune response polarization, we measured carcinoma cell nuclear HIF-1α expression in a subset (n=14) of the tumors and noted a direct relationship with SMA expression (r=0.54, p=0.05). Since our tumors included both untreated (n=18) ones and those from patients who underwent multimodal neoadjuvant therapy (n=20), we examined the relationship between SMA expression and the immune markers in both subgroups. While we were unable to detect significant correlations in untreated tumors, there were tight correlations between SMA and CD3 (r=0.64, p=0.003), FOXP3 (r=0.62, p=0.004), and CD11b (r=0.55, p=0.01) in neoadjuvant treated tumors (Figure). Conclusion: Stromal myofibroblast expression of SMA in PC following neoadjuvant therapy correlates with hypoxia and induction of a broad immune infiltrate including large numbers of potentially immunosuppressive Treg and myeloid cells.

Objective: Obesity is an important risk factor and negative prognostic indicator for patients with pancreatic ductal adenocarcinoma (PDAC). We hypothesized that obesity results in pancreatic carcinogenesis and tumor progression due to specific patterns in gene expression and metabolic pathway alteration. Methods: Affymetrix GeneChip Arrays were used to generate gene expression profiles from resected PDAC tumors from 15 patients. The corrected body mass index (BMIc) was calculated for each patient as the quotient of weight (kg) prior to PDAC-associated weight loss and height (m2). Gene set enrichment analysis (GSEA) was performed to identify pathways that differed between tumors from normal weight (BMIc<25), overweight (25≤30) patients. Human metabolic network reconstruction was performed to identify differentially expressed metabolic pathways between overweight/obese vs. normal weight patients. Results: GSEA and human metabolic network reconstruction revealed that metabolic gene expression is significantly altered in overweight/obese patients relative to normal weight patients with PDAC (Fig. 1). Several metabolic pathways were enriched for increased expression in tumors from overweight/obese vs. normal weight patients, including glutathione metabolism (p = 0.003), the citrate and TCA cycle (p = 0.013), glycolysis and gluconeogenesis (p = 0.030), the pentose phosphate pathway (p = 0.038), and fatty acid metabolism (p = 0.056). Examples of available inhibitors targeting each of these upregulated metabolic pathways are shown in Fig. 1. Conclusions: Deregulated metabolism is an important mechanism of tumor growth and progression. Here we demonstrate upregulation in the gene expression of key metabolic pathways in PDAC tumors from overweight/obese patients vs. normal weight patients. Future preclinical experiments targeting these pathways with metabolic inhibitors will explore the efficacy of tumor prevention and treatment of PDAC in obese patients.

The Prognostic Added-value of FDG-PET in the Staging of Gastric Adenocarcinoma. O.K. Serrano,* C. Love, I. Goldman, N. Ng, T. Abraham, R. Da Silva, P. Friedmann, S.K. Libutti, T.J. Kennedy, 1. Department of Surgery, Montefiore-Einstein Center for Cancer Care, Montefiore Medical Center, New York, NY; 2. Department of Nuclear Medicine, Montefiore-Einstein Center for Cancer Care, Montefiore Medical Center, New York, NY; 3. Department of Radiology, Montefiore-Einstein Center for Cancer Care, Montefiore Medical Center, New York, NY; 4. Albert Einstein College of Medicine, New York, NY.

INTRODUCTION: The value of 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography (FDG-PET) in the staging work-up of gastric adenocarcinoma has been subject to debate. The aim of this study was to demonstrate the added-value of FDG-PET to contrast-enhanced computed tomography (CT) in the staging of a newly-diagnosed gastric adenocarcinoma. METHODS: We performed a retrospective review of all patients treated at our institution for gastric adenocarcinoma between 2006 and 2013. We identified patients who had undergone a contrast-enhanced CT and FDG-PET before initiating treatment. The CT and FDG-PET images were prospectively analyzed by an experienced blinded body radiologist and an experienced blinded nuclear physician, respectively. Disease stage was assessed, looking at primary tumor (PT), locoregional (LLN) and distant lymph node disease (DLN), and metastasis (M). RESULTS: At our institution we identified 608 patients who had biopsy-proven gastric adenocarcinoma and 207 (34.0%) had a contrast-enhanced CT and an FDG-PET as part of their staging work-up. Of these, imaging from 165 patients was available for independent prospective review. CT identified PT, LLN, DLN, and M in 120 (72.7%), 84 (50.9%), 25 (15.2%), and 32 (19.4%) patients, respectively; while FDG-PET identified PT, LLN, DLN, and M in 125 (75.8%), 78 (47.3%), 41 (24.8%), and 27 (16.4%) of patients, respectively. FDG-PET up-staged 31 (18.9%) patients while it down-staged 4 (2.4%) patients.
17 (10.3%) patients. Of patients who were up-staged, 20 (64.5%) developed progressive disease, 5 (16.1%) were lost to follow-up, and 6 (19.4%) did not meet the follow-up period criteria. Of patients who were down-staged, 11 (64.7%) developed progressive disease, 3 (17.6%) were lost to follow-up, 1 (5.9%) had stable disease, and 2 (11.8%) did not meet the follow-up period criteria. CONCLUSIONS: Our findings support the use of FDG-PET as a valuable adjunct to contrast-enhanced CT in the staging of gastric adenocarcinoma.

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Underreporting of Gastrointestinal Stromal Tumors to the National Cancer Registry: Is the True Incidence being Captured? I. Hammer,1,* A.H. Choi,2 S.J. Merchant,1 V. Trisal,1 C. Warren,1 C. Garberoglio,2 J. Kim,1 J. Surgery, City of Hope National Medical Center, Duarte, CA, 2. Loma Linda University, Loma Linda, CA.

Background: Based on cases reported to the National Cancer Registry (NCR), there are an estimated 5000-6000 new cases of GIST annually in the United States. These tumors underwent reclassification in 2002 and tumor registries in California are only required to report to the NCR GISTs that are labeled malignant or metastatic on pathology reports. We hypothesized that a significant proportion of GISTs are not captured by NCR and our objective was to determine the rate of underreporting GISTs. Methods: Review of pathology cases with final diagnosis of GIST was performed at two academic medical centers from 2010-2013. Patients with recurrent GIST were excluded. Risk for metastasis or tumor-related death based on National Comprehensive Cancer Network (NCCN) guidelines was assigned to each patient. Pathology cases were cross-referenced to NCR-reported cases from each institution’s cancer registry. Results: Forty-nine cases of non-recurrent GIST were identified. Overall, only 19 (38.8%) cases were reported to NCR. Five of 20 (25.0%) cases were reported from Loma Linda University Medical Center (LLUMC), and 14 of 29 (48.3%) cases were reported from City of Hope (COH). None of the 30 non-reported cases had been labeled malignant or metastatic on the final pathology reports. The 30 non-reported cases were risk stratified for metastatic disease or tumor-related death by NCCN criteria. Of 15 non-reported LLUMC cases, 26.7% were high risk, 13.3% intermediate risk, and 60.0% low risk. Of 15 non-reported COH cases, 1 was high risk, intermediate risk, and 9 (60.0%) low risk. There were 4 (26.6%) patients with unknown risk. In the 30 non-reported cases, 20.0% were treated with a receptor tyrosine kinase, further highlighting clinical concern for malignant GIST. Conclusions: GIST remains a relatively rare malignancy. These data, however, show that the true incidence may be severely underreported, with nearly two-thirds of patients diagnosed with GIST unreported at our two academic medical centers. This study suggests that a nationwide review of reporting practices and standardization of these methods may more accurately reflect the true incidence of this disease.

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Number of Evaluated Lymph Nodes, Number of Positive Lymph Nodes, Lymph Node Ratio and Log Odds: Numerology or Valid Indicators of Pancreatic Ductal Adenocarcinoma (PDAC) Patient Outcome? G. Lahat,* N. Lubezky, I. Wolf, F. Gerstenhaber, E. Nizri, I. Nachmany, J. Goichman, R. Nakache, J.M. Klauser, Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

Introduction: Several classifications of nodal involvement have been developed in order to better predict outcome in patients undergoing curative surgery for PDAC. Yet, their validity and relevance are a matter of debate. We aimed to evaluate the prognostic significance and universal validity of total number of evaluated lymph nodes (ELN), number of positive lymph nodes (PLN), lymph node ratio (LNR) and log odds of positive lymph nodes (LODDS) in a relatively large and homogeneous cohort of surgically treated PDAC patients. Methods: Prospectively accrued data were analyzed for 282 PDAC patients who had pancreaticoduodenectomy (PD) with negative resection margins (R0) at our institution. Long term survival was analyzed according to the ELN, PLN, LNR and LODDS. Results: Of these patients, 168 patients (59.5%) had LN metastasis (N1). Mean ELN and PLN were 13.5 and 1.6, respectively. LNR positivity correlated with a higher number of evaluated lymph nodes; positive lymph nodes were identified in 61.4% of the patients with ELN≥13 compared with 44.9% of the patients with ELN<13 (p=0.014). Median overall survival (OS) and 5-year OS rate were higher in N0 than in N1 patients; 22.4 vs. 18.7 months, and 35% vs. 11%, respectively (p=0.008). Mean LNR was 0.12; 91 patients (54.1%) had LNR<0.3. Among the N1 patients, median OS was comparable in those with LNR≥0.3 vs. LNR<0.3 (16.7 vs. 14.1 months, p=0.950). Neither LODSS nor various ELN and PLN cutoff values provided a more discriminative information within the group of N1 patients. Conclusion: Our data confirms that lymph node positivity strongly reflects PDAC biology, thus patient outcome. While a higher number of evaluated lymph nodes may provide a more accurate nodal staging, it does not have any prognostic value among N1 patients. Similarly, PLN, LNR, and LODDS had a limited prognostic relevance.

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MicroRNA Profiling of Pancreatic Ductal Adenocarcinoma (PDAC) Reveals Signature Expression Related to Lymph Node Metastasis M. Lemberger,1 S. Loewenstein,1 N. Lubezky1, M. Pasmanik-Chor,2 J.M. Klauser,2 G. Lahat,* 1. Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; 2. Sackler School of Medicine Tel Aviv University, Tel Aviv, Israel.

Introduction: miRNAs have been shown to have an important role in cancer initiation, progression, and metastasis. However, lymphatic metastasis-related miRNAs in PDAC have not been well documented. Our aim was to identify miRNAs associated with PDAC lymph node (LN) metastasis and to explore related molecular pathways regulated by these miRNAs. Methods: miRNA expression profiling was performed on 24 PDAC and matched normal pancreatic tissue samples; signature expression related to LN metastasis was identified and validated on 54 PDAC specimens using quantitative real-time polymerase chain reaction. Pan-1 cells were utilized for in-vitro studies. Results: Two differently expressed miRNAs were differently expressed in patients with N1 (compared to LN negative (N0) PDAC samples (p<0.05). Of them, six miRNAs have previously been reported to play a role in cancer invasion and metastasis. miR-141 and miR-720 were down regulated (1.65 fold and 2.2 fold, respectively) in N1 compared to N0 PDAC specimens. miR-141 and miR-720 significantly inhibited in vitro proliferation, migration and invasion of pancreatic cancer cells as proved by gain- and loss-of-function studies. Loss of miR-141 was associated with high nuclear expression of ZEB-1, a key regulator of cancer invasiveness. miR-720 and TWIST1 were highly expressed by Pan-1 cells. Transfection of pancreatic cancer cells with miR-720 inhibited TWIST1 expression resulting in decreased migration, invasion and resistance to chemotherapy. Conclusion: miRNA profiling revealed distinct alternations in lymph node positive PDAC specimens. This signature expression could be a useful tool to identify lymphatic metastasis and predict patient survival. Further investigation of the pathways identified in our study may enhance our knowledge regarding PDAC progression and metastasis hopefully leading to novel therapeutic strategies.

P389
Omental Spread of GI Malignancies: New Insights and Potential Therapeutic Strategies S. Loewenstein, V. Feygenzon, O. Kersy, E. Nizri, N. Lubezky, J.M. Klauser, G. Lahat,* Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

Introduction: GI malignancies have a clear predilection for omental metastasis, reflecting end-stage disease and short survival. Our aim was to evaluate whether the omental microenvironment has an active role in epithelial cancers omental spread. Methods: A xenograft mouse model was used to evaluate the potential in-vivo effect of human omentum on pancreatic ductal adenocarcinoma (PDAC), and gastric cancer tumor growth. Condition medium (CM) of non-cancerous human omental cells, incubated for 24h, was used to investigate its in-vitro effects on PANC-1 PDAC, and AGS (gastric cancer) cellular growth, migration, invasion and resistance to chemotherapy. A non-targeted proteomic approach was used to study the omental proteome. Results: An in-vivo experiment showed an increased PDAC and gastric cancer tumor growth when cancer cells were co-localized with human omentum as compared to subcutaneous human fat (p<0.05). H&E stain of paraffin-embedded omental tissues (n=10) mostly identified visceral fat cells (95%), fibroblasts, endothelial cells, and seldom lymphocytes. Utilizing an in vitro model, we found that omental CM increased PDAC and AGS cellular growth and decreased chemotherapy-induced apoptosis. Omental CM enhanced epithelial cancer cell migration and invasion capacities and significantly enhanced endothelial cells tube formation, suggesting its role as a proangiogenic factor in the microenvironment of epithelial omental metastases. Using a robust pro...
teomic approach we compared non-cancerous omental samples (n=15) to same patients subcutaneous samples (n=15). We identified numerous distinctive omental proteins related to high metabolic activity and increased cellular stress, potentially involved in the formation and progression of epithelial cancers omental metastasis. Conclusion: Our findings suggest that the omentum has an active role in epithelial cancers omental metastasis. Investigation of potential cellular interactions between the omentum and cancer cells could enhance our understanding of the localization and growth of cancer cells in the omentum. Such data could provide alternative strategies aimed at preventing and treating omental metastasis.

P390
Role of Multivisceral Resection in the Management of Gastrointestinal Stromal Tumor J. Wong,1,2 G. Tan,1 R. Quek,1 B. Goh,1 K. Soo,1 L. Koh,1 M. Teo.1 National Cancer Centre, Singapore; 2. Singapore General Hospital, Singapore.

Introduction: Management of gastrointestinal stromal tumors (GIST) has been revolutionized since the introduction of Imatinib mesylate. While the efficacy of targeted therapy cannot be over-emphasized, surgery remains the only curative treatment for patients with localized disease. Median size of GIST at diagnosis is approximately 5-7 cm, however it is not uncommon for tumors to be as large as 30-40 cm and involving multiple viscera. En-bloc resection with gross negative margins is favoured in the absence of distant metastasis.

Methodology: Data was collected retrospectively from GIST patients treated at Singapore General Hospital over 14 years. Standard resection of GIST without additional organ removal was termed as a single organ resection. If the tumor was adjacent to another organ necessitating the removal of multiple organs, it was defined as a multivisceral resection (MVR). Comparison was made between the patients who underwent single organ vs. MVR. Patient, tumor characteristics, disease-free (DFS) and overall survival (OS) were analyzed.

Results: 188 patients underwent curative surgery for GIST between Jan 2000 and Jan 2014. 57 (30%) underwent MVR while 131 (70%) had single organ resection. Patients undergoing MVR had a median age of 63 years and 63% were male. 31 had tumour size greater than 10 cm. There was a significant difference (p < 0.03) in tumour size when comparing MVR vs non-MVR patients. Of the 57 patients who underwent MVR, 22 (38.6%) suffered recurrence, of which only 7 (12%) were local recurrences. Amongst the 131 non-MVR patients, 34 (26%) recurred. At median follow up time of 4.6 years, median DFS was 6.3 years in the MVR group; 3- and 5-year DFS was 67.4% and 59.2% respectively. In the single organ resection group, median DFS was not reached; 3- and 5-year survival was 75.8% and 66.9% respectively. OS was not reached in patients who underwent MVR; 3- and 5-year OS was 87.9% and 79.6% respectively. OS was 11.9 years for patients who underwent single organ resection; 3- and 5-year OS was 91.3% and 84.7%. There was no significant difference in OS between MVR vs Non-MVR patients (p = 0.341).

Conclusion: MVR is required in 30% of GIST patients in order to attain negative margins and prolonged DFS and OS.
randomized to 2 groups: bright light surgery (BLS)-only and BLS + PIT. Each treatment arm consisted of 7 tumor-bearing mice. BLS was performed under standard bright-field using an MVX10 microscope on all mice. For BLS + PIT, anti-CEA antibody conjugated with IR700 (anti-CEA-IR700) (50 mcg) was injected intravenously in all mice 24 hours before surgery. The resection bed was then irradiated with a red-light-emitting diode at 690 ± 5 nm with a power density of 150 mW/cm². Results: The pancreatic cancer PDOX was diagnosed as moderately-differentiated adenocarcinoma. The PDOX tumor was strongly stained with anti-CEA antibody using immunohistochemistry. Anti-CEA-IR700 labelled and illuminated the pancreatic cancer PDOX. Minimal residual cancer of the PDOX after was detected by fluorescence after BLS. The local recurrence rate was 85.7% for BLS-only and 28.6% for BLS + PIT-treated mice (p = 0.05). The average recurrent tumor weight was 1149.0 ± 794.6 mg for BLS-only and 210.8 ± 336.9 mg for BLS + PIT-treated mice (p = 0.015). Conclusion: Anti-CEA-IR700 is able to label and illuminate a pancreatic cancer PDOX nude mouse model sufficiently for PIT. PIT reduced recurrence by eliminating remaining residual cancer cells after BLS.

**Figure Legend.** Recurrence in each treatment group. (A) Representative whole body images in each treatment group. A recurrent tumor indicated by the yellow broken line was detected in BLS only group. Scale bars: 10 mm. (B) Gross images of recurrent tumors in 6 mice in the BLS-only group (85.7 %) and 2 mice in BLS + PIT group (28.6 %). Scale bars: 10 mm. (C) Recurrent tumor weight of each treatment group. The average recurrent tumor weight was 1149.0 ± 794.6 mg for BLS-only and 210.8 ± 336.9 mg for BLS + PIT-treated mice (p = 0.015).

**P394** Predicting Delayed Gastric Emptying after Pancreatoduodenectomy for Enhanced Recovery after Surgery A. Saunders,* C. Chavez de Paz, C. Fancher, N. Solomon, N. Gomez, General Surgery, Loma Linda University Medical Center, Loma Linda, CA.

**Background:** Delayed gastric emptying (DGE) is a common complication of pancreatoduodenectomy (PD), contributing to delay in postoperative recovery and increase in costs of care. Patients with DGE often require alternative enteral access for nutrition, but predicting which patients will experience DGE can be difficult. **Methods:** A retrospective review was performed of 58 consecutive PD cases completed for periampullary neoplasms. Hypothesized predictors of DGE were reviewed, including both preoperative patient characteristics and perioperative management strategies. Univariate analysis was performed to identify factors correlating with DGE, and multivariate regression analysis was performed using the correlating factors. **Results:** DGE was defined as intolerance of oral diet or requirement for gastric decompression beyond postoperative day 7. Among the patient characteristics evaluated, including preoperative diabetes, BMI, biliary stenting, neoadjuvant chemotherapy or radiation, narcotic use and a history of pancreatitis, only node positivity correlated with increased incidence of DGE (p = 0.0472). In evaluating perioperative management decisions, use of epidural analgesia (p = 0.0457) and provision of oral diet by postoperative day 2 (p = 0.0486) correlated with decreased incidence of DGE. Mobilization on postoperative day 1 (p = 0.0567) and minimizing use of postoperative nasogastric tube decompression (p = 0.0695) trended toward decreased incidence, without significance. **Conclusion** Multivariate analysis demonstrated a significant decrease in DGE with epidural analgesia (OR 0.199, 95% CI 0.041-0.959, p = 0.0441) and a tendency toward decreased DGE in node-negative patients (OR 0.224, 95% CI 0.046-1.082, p = 0.0626). **Conclusions:** These findings reinforce the difficulty in predicting DGE based upon the preoperative history and physical, and appear to highlight the importance of perioperative management strategies, many of which have been supported in the growing body of literature on enhanced recovery after surgery (ERAS) for pancreas. These findings will be incorporated into our own ERAS protocol and further, prospective analysis will be undertaken.

**P395**

7th AJCC Staging Classification Correlates with Biological Behavior of Pseudomyxoma Peritonei (PMP) Tumors Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC) A. Sardi, V. Milovanov,* C. Nieroda, M. Sittig, V. Gushchin, Surgical Oncology, Mercy Medical Center, Baltimore, MD.

**Background:** It is important to assess biological behavior of PMP of appendiceal origin by using a proper classification. There are debates about classification of these malignancies. We evaluated the 7th AJCC staging classification (SC) in terms of overall survival (OS) in patients with PSP treated with CRS/HIPEC. **Methods:** 208 patients with PSP treated with CRS/HIPEC were identified from a prospective database. PMCA patients were retrospectively staged at the time of diagnosis according to the AJCC SC. Patients with disseminated peritoneal adenomucinous (HPAM) were evaluated in a separate group. OS and progression-free survival (PFS) were estimated by plotting Kaplan-Meier survival curves. The impact of AJCC SC on OS was estimated by Hazard Ratio (HR). **Results:** 77 men and 131 women, mean age 54 years (range 26–81) had a median follow-up of 5.2 years. Of 208 patients, 124 had PMCA and 84 patients had HPAM. According to the AJCC SC 47 lymph node (LN) negative patients with well differentiated (G1) PMCA, were classified as stage IVA. Seventy-seven patients with either moderately (G2) or poorly (G3) differentiated PMCA irrespective of LN status, and well differentiated PMCA with positive LN were classified as stage IVB. Eighty-four patients with no cellular atypia, otherwise known as DPAM, constituted a separate group to determine if DPAM had different survival from stage IVA PMCA patients. Table 1 reflects OS of stage IVA, IVB PMCA and DPAM from time of diagnosis. PFS was only estimated for IVA and IVB PMCA patients who were considered disease free after CRS/HIPEC and was 78%, 52%, 43% in the IVA patients and 65, 15, 0% in the IVB group at 1, 3, and 5 years, respectively (p=0.004). The adjusted HR for AJCC stages (IVA/IVB) was 3.7 (95% CI: 2.0-6.7) (p<0.001). **Conclusion:** The 7th edition AJCC SC is simple, reproducible and valid classification for staging patients with PMCA undergoing CRS/HIPEC. DPAM patients have different OS compared to that of PMCA stage IVA. We recommend using AJCC SC in reporting treatment outcomes from peritoneal surface malignancy centers.

<table>
<thead>
<tr>
<th>Stage</th>
<th>OS (%)</th>
<th>PFS (%)</th>
</tr>
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<tbody>
<tr>
<td>IVA</td>
<td>88</td>
<td>67</td>
</tr>
<tr>
<td>IVB</td>
<td>74</td>
<td>57</td>
</tr>
<tr>
<td>DPAM</td>
<td>52</td>
<td>27</td>
</tr>
</tbody>
</table>

**P397**

Preoperative Inflammatory and Tumor Markers associated with Outcomes in Patients with Appendiceal Neoplasms undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC) M.F. Nunez,* A. Sardi, C. Nieroda, V. Milovanov, M. Sittig, V. Gushchin, Surgical Oncology, Mercy Medical Center, Baltimore, MD.

**Background** Outcomes of patients with appendiceal neoplasms undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC) depend on several clinicopathological factors. We evaluated the association of preoperative inflammatory and tumor markers in this group of patients. **Methods** A retrospective review of patients with neoplasms of appendiceal origin undergoing initial CRS/HIPEC was conducted. Associations between preoperative inflammatory markers [neutrophil:lymphocyte ratio (NLR), platelet:lymphocyte ratio (PLR), albumin and C-reactive protein (CRP)] and tumor markers [CEA, CA-125, & CA19-9] were related to...
baseline variables of interest and surgical outcomes. Results A total of 175 patients with appendiceal neoplasms, 105 peritoneal mucinous carcinomatosis (PMCA) and 70 disseminated peritoneal adenocarcinomatosis (DPAM), underwent CRS/HIPEC between February 1998 and August 2013. PClas20 was related to elevated PLR, CRP, CEA and CA-125; incomplete cytoreduction was related to elevated NLR, PLR, CRP, CEA, CA-125 and low albumin. Complications were associated to elevated CEA and CA-125 (Table 1). OS at 1, 3, and 5 years was 90%, 68% and 59%, respectively. Median OS was 6.9 years. PFS at 1, 3, and 5 years was 89%, 73% and 66%, respectively. The median PFS was not reached. The 5 year OS in patients with NLR>2.4 and NLR<2.4 was 53% and 67% (p=0.012). PLR>172 and PLR<172 was 54% and 66% (p=0.016). CRP<1 and CRP>1 was 55% and 73% (p=0.005), albumin<3.5 g/dl and albumin>3.5 g/dl was 28% and 61% (p=0.001), respectively. The 5 years PFS in patients with CRP<1 and CRP>1 was 52% and 77% (p=0.002), CA19-9>35U/ml and CA19-9<35U/ml was 46% and 71% (p=0.04), respectively. The worst outcome was observed in patients with PLR>172 and albumin<3.5 g/dl in PMCA patients (p=0.031 and 0.009, respectively) and NLR<2.4 and CA125>35U/ml in DM patients (p=0.016 and 0.050, respectively). Conclusion Preoperative inflammatory and tumor markers are associated with outcomes and may predict high tumor burden, incomplete cytoreduction, and morbidity in patients with appendiceal neoplasms undergoing CRS/HIPEC.

Table 1: Correlation of preoperative inflammatory and tumor Markers with surgical variables

<table>
<thead>
<tr>
<th>Tumor Extension (CRS/HIPEC)</th>
<th>Incomplete Cytoreduction (CA-23)</th>
<th>Morbidity (Grade III IV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNI II R&gt;4</td>
<td>0.06</td>
<td>0.001</td>
</tr>
<tr>
<td>PLR&gt;172</td>
<td>1.53</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP&gt;1</td>
<td>3.89</td>
<td>0.001</td>
</tr>
<tr>
<td>Albumin&lt;3.5 g/dl</td>
<td>0.66</td>
<td>0.001</td>
</tr>
<tr>
<td>CA19-9&gt;35U/ml</td>
<td>0.003</td>
<td>0.005</td>
</tr>
<tr>
<td>CA125&gt;35U/ml</td>
<td>0.025</td>
<td>0.007</td>
</tr>
<tr>
<td>CA19-9&lt;35U/ml</td>
<td>0.038</td>
<td>0.003</td>
</tr>
</tbody>
</table>

*Peritoneal Cancer Index

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Over 90% of pancreatic ductal adenocarcinomas (PDAC) have KRAS mutations. Given the lack of anti-RAS therapies, recent approaches have been aimed at inhibiting key RAS effectors, such as PI3K and MEK. However, results have been disappointing. There is growing evidence that single agent kinase inhibitor therapy fails because tumor cells rapidly develop resistance. One method in which tumors can adapt is by the activation of alternate kinases. To measure this adaptive response, we used a novel multiplex inhibitor head- mass spectrometry (MIB/MS) assay which measures the activation state of the kinome in order to investigate possible mechanisms of resistance to single kinase inhibition. MIB/MS has been used to identify mechanisms of resistance to MEK inhibition in breast cancer. We used MIB/MS to identify possible mechanisms of resistance to single agent kinase inhibition in PDAC. Single agent treatment using either a MEK (trametinib) or PI3K (BKM120) inhibitor in patient-derived xenograft and genetically engineered mouse models of PDAC resulted in slowed tumor growth but not tumor shrinkage, suggesting that neither inhibitor will be dramatically effective in patients. MIB/MS showed an adaptive response to single agent kinase inhibition early as three days after treatment with activation of multiple kinases, including ephrins, Src, and PDGFR. We therefore hypothesized that tailored pan-kinase inhibition using dasatinib, a pan-kinase inhibitor with anti-ephrin, anti-Src, and anti-PDGFR activities, may be more effective than single agent therapy. The combination of dasatinib with BKM120 inhibited the growth of 6/7 PDAC cell line and showed synergy with a mean combination index (CI) of 0.32 (0.18 – 0.61). The combination of dasatinib with trametinib inhibited the growth of 7/7 PDAC cell line and showed impressive synergy with a mean CI of 0.13 (0.0007 – 0.77). MIB/MS is a powerful unbiased approach to identify second targets for combination therapy. Our results suggest that multi-targeted kinase inhibition will be necessary in PDAC due to its ability to rapidly adapt to single agent kinase inhibition and should be taken into consideration when designing clinical trials.

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Importance of Anastomotic Site (AS) Resection during Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC) in Patients with Peritoneal Carcinomatosis (PC) of Appendiceal Origin N. Aydin,* V. Milovanov, M. Sittig, V. Gushchin, A. Sardi. Surgical Oncology, Mercy Medical Center, Baltimore, MD.

Background: It is common for patients with PC of appendiceal origin to undergo surgical procedures of various extents before definitive CRS/HIPEC. We evaluated the role of resection of previous anastomoses during CRS/HIPEC with regards to recurrence at AS. Methods: Patients with PC of appendiceal origin who underwent CRS/HIPEC involving resection of anastomoses performed during previous surgeries were identified from a prospective database. Intraoperative macroscopic findings at the AS were compared to pathological evidence of recurrence at the resected AS. Chi square test was used for determining correlations between recurrence at AS and tumor grade, peritoneal carcinomatosis index (PCI). Results: Thirty eight patients (10 men and 28 women) with AS resection were identified from a prospective database. Mean age was 57 years (range 33–77). All patients had right hemicolectomy as the initial surgical procedure. Two patients had segmental resection of small bowel and 1 had sigmoid colectomy additional to the right hemicolectomy procedure. Twenty-two patients had high grade PC, 6 patients had low grade PC and 10 patients had disseminated peritoneal adenocarcinomatosis (DPAM). Percentage of patients with PCI> 20, complete cytoreduction and positive LN status were 68%, 84% and 37%, respectively. Thirty-eight ileocolonic, 2 small bowel and 1 colorectal AS were resected at the time of CRS/HIPEC. At 16 of 41 resected AS (39%) recurrence had been detected. Five of 38 patients (13%) had positive LN associated with the resected AS. Table 1 reflects the comparison of intraoperative findings at the AS to pathology reports. Correlation between recurrence at AS and PCI>20 was found (χ2=6.2, p=0.004). No correlation between AS recurrence and tumor grade was found (χ2=1.3, p=0.248). Conclusion: Recurrence at the AS is common (39%) in patients with PC who had previous bowel resections. Macroscopic findings are not always reliable in decision making for AS resection. We recommend resection of previous AS during CRS/HIPEC even if there is no evidence of macroscopic disease at the AS.

Table 1: Intraoperative Findings vs. Recurrence at AS

<table>
<thead>
<tr>
<th>Intraoperative Findings</th>
<th>Nodules (n=17)</th>
<th>Nodules and Fitzitis (n=13)</th>
<th>Presence of tumor (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodules</td>
<td>10/17 (59%)</td>
<td>9/13 (69%)</td>
<td>2/6 (33%)</td>
</tr>
<tr>
<td>Nodules and Fitzitis</td>
<td></td>
<td></td>
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<td>Presence of tumor</td>
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Introduction CA 19-9 is a biomarker for pancreatic ductal adenocarcinoma (PDAC) whose levels are thought to correlate with overall tumor cell burden. False elevations occur with biliary obstruction. We hypothesize that CA19-9 elevation is a marker of and secondary to distant metastasis, and is unrelated to locoregional tumor-cell burden. Methods Anatomically resectable cases of PDAC (2009-2013) from our center were reviewed. Pre-operative CA 19-9 was analyzed with linear regression for correlation with primary tumor characteristics (size and grade), nodal status, operatively identified occult metastases, and recurrence and overall survival in resected patients. Both raw and bilirubin-corrected CA19-9 levels were evaluated. Neoadjuvant cases and CA 19-9 non-secretors were excluded. Results We identified 303 patients with evaluable pre-op biomarker that underwent exploration for seemingly localized tumors. Median tumor size was 3cm (range 0.2 – 7 cm). There was no correlation between pre-operative CA 19-9 and primary tumor size (R2=0.001), even after bilirubin-correction (R2=0.013). Correction for tumor grade and nodal status did not improve correlation. There were 42 patients that were found to harbor occult metastases at operation. Median CA19-9 for the patients with (214 U/mL) and without (122 U/mL) metastatic disease identified at operation.
was significantly different. (p=0.04). Patients with elevated pre-op CA19-9 were 2-fold more likely to harbor occult metatases at operation compared to those with normal levels (p=0.03). Elevated pre-op CA19-9 levels predicted early recurrence and decreased overall survival. Conclusions There is no correlation of preoperative CA19-9 with tumor size, grade, and nodal status, even after bilirubin correction. Elevated CA19-9 levels should not be assumed to be secondary to locoregional tumor cell burden (primary tumor characteristics), but rather a marker of and secondary to occult distant metastases. Alternative treatment sequencing should be considered in these otherwise anatomically resectable patients with elevated preop CA19-9.

CA 19-9 Vs. Tumor Size with grouping by secretors, with bilirubin correction, compared with pathologic imaging, and grouping by nodal status.

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Background. Anaplastic pancreatic carcinoma (APC) is a rare and poorly characterized disease that encompasses different histologic variants. We sought to compare the clinical characteristics and outcome of APC to pancreatic adenocarcinoma (PAC). Method. The American National Cancer Database (NCDB) was queried for patients diagnosed with resected APC and PAC using histology codes and surgical codes. APC cases were matched 1:5 with PAC’s based on age, gender, pathologic tumor stage, surgical margin status, lymph node positivity ratio (number of metastatic positive over total harvested nodes), and use of adjuvant therapy. Result. Following 1:5 matching, 192 APC and 960 PAC were analyzed. Mean age at diagnosis was 65 years for both groups. The median tumor size was 45 mm (IQR 33–60) vs. 30 mm (IQR 23–40; p<0.001) and metastatic nodal disease was present in 43% of the cases in both groups (p=0.72). APC cases were equally distributed between the head and the body/tail region of the pancreas (75% vs. 50% respectively; p<0.001). Adjuvant chemotherapy was administered in 39% of the cases in both groups. Although the resected APC group had a higher mortality rate during the first year following the diagnosis (49% vs. 31%), the overall survival was similar in the two groups with 21.6% vs. 17.4% alive a 5-year, respectively for APC and PAC (p=0.32; Figure 1). Furthermore, a subgroup analysis of patients diagnosed with osteoclast-like giant cells (OCCGs, n=32) variant showed a 5-year survival of 50% vs. 15% in the subgroup of anaplastic pancreatic carcinoma without OCCGs (n=159). Conclusion. Patients with resected APC present commonly with large tumors that are equally distributed between the head and body/tail of the pancreas. While APC is thought to have a more aggressive biology, our matched analysis showed similar overall survival compared to PAC. Furthermore the osteoclast-like giant cell variant portends a better prognosis compared to other histologic variants of anaplastic pancreatic carcinoma.

Figure 1. Overall survival of Anaplastic Pancreatic Cancer (APC) compared to Pancreatic Adenocarcinoma (PAC) with 95% Hall-Wellner bands.

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Background: High throughput chemosensitivity testing of patient derived cell lines can be used to assess the efficacy of novel therapeutics. However, the generation of cell lines from xenografts is complicated by the growth of contaminating murine stromal cells. Methods: Human pancreatic cancer (PC) cell lines were generated from heterotopic murine xenografts established from primary and metastatic tumors. Cell lines were established from xenografts by enzymatic digestion. Mouse CD326: MHC Class I (H-2Kd) cells were eliminated by flow cytometric FACS sorting using human-specific CD326 (EpCAM) and murine-specific MHC Class I (H-2Kd) antibodies. Cell lines were characterized by immunohistochemistry (IHC), doubling time, colony sorting with high purity. Results: Tissues were obtained from 192 APC and 960 PAC's. APC cases were matched 1:5 with PAC's based on age, gender, pathologic tumor stage, surgical margin status, lymph node positivity ratio, number of metastatic positive over total harvested nodes, and use of adjuvant therapy. Result. Following 1:5 matching, 192 APC and 960 PAC were analyzed. Mean age at diagnosis was 65 years for both groups. The median tumor size was 45 mm (IQR 33–60) vs. 30 mm (IQR 23–40; p<0.001) and metastatic nodal disease was present in 43% of the cases in both groups (p=0.72). APC cases were equally distributed between the head and the body/tail region of the pancreas (75% vs. 50% respectively; p<0.001). Adjuvant chemotherapy was administered in 39% of the cases in both groups. Although the resected APC group had a higher mortality rate during the first year following the diagnosis (49% vs. 31%), the overall survival was similar in the two groups with 21.6% vs. 17.4% alive a 5-year, respectively for APC and PAC (p=0.32; Figure 1). Furthermore, a subgroup analysis of patients diagnosed with osteoclast-like giant cells (OCCGs, n=32) variant showed a 5-year survival of 50% vs. 15% in the subgroup of anaplastic pancreatic carcinoma without OCCGs (n=159). Conclusion. Patients with resected APC present commonly with large tumors that are equally distributed between the head and body/tail of the pancreas. While APC is thought to have a more aggressive biology, our matched analysis showed similar overall survival compared to PAC. Furthermore the osteoclast-like giant cell variant portends a better prognosis compared to other histologic variants of anaplastic pancreatic carcinoma.

Figure 1. Overall survival of Anaplastic Pancreatic Cancer (APC) compared to Pancreatic Adenocarcinoma (PAC) with 95% Hall-Wellner bands.
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Novel Genotype-phenotype Correlations in Patients with Hereditary Diffuse Gastric Cancer
2. National Cancer Institute, Center for Cancer Research, Biostatistics and Data Management Section, Bethesda, MD; 3. Indiana University School of Medicine, Dept of Surgery, Indianapolis, IN.

Hereditary diffuse gastric cancer (HDGC) is a rare autosomal dominant cancer syndrome associated with germline mutations in the gene encoding E-cadherin (CDH1). To date, no genotype-phenotype relationship between the type of mutation and the clinical presentation of the HDGC phenotype has been identified. Methods: Four families with confirmed CDH1 germ line mutations were prospectively followed at NIH from 2010 to 2013. In addition, PubMed was queried from inception to December 2013 for original reports that describe HDGC families with associated CDH1 germline mutations. The type of germline mutation was compared with respect to age at diagnosis, presence of other HDGC-associated cancers, country of origin, association overall risk of gastric cancer, and clinical penetrance. Results: We identified 43 articles that, together with the NIH families, describe 926 individuals from 57 families with complete family history, clinical, and CDH1 variant data. Compared to patients with truncating mutations, family members with missense mutations were more likely to be affected by gastric cancer (increased clinical penetrance (>50%) (p=0.012)) and were more likely to come from countries with a high overall risk of gastric cancer (p=0.0037 for early vs late truncation, p=0.0057 for extracellular vs intracellular truncation). Families in which the youngest affected family member was younger than 30 years of age were found to have a higher incidence of other HDGC cancers including lobular breast and colon cancer (p=0.002). Conclusion: Families with HDGC due to missense mutations have increased clinical penetrance of gastric cancer and are more likely to come from a country with a high overall risk of gastric cancer compared to those with truncating CDH1 mutations. The association of a greater number of family members affected by gastric cancer in families harboring CDH1 germline missense mutations, and a higher incidence of the HDGC-associated lobular breast and colon cancers in families diagnosed with gastric cancer before the age of 30, suggests these families might benefit from increased surveillance.

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Factors associated with Failure to Reach Surgical Resection in Patients undergoing Neoadjuvant Chemotherapy for Resectable and Borderline Resectable Pancreatic Head Adenocarcinoma

Introduction: Neoadjuvant chemotherapy (NAC) is being increasingly administered to patients with resectable and borderline resectable pancreatic head adenocarcinoma (PDAC). A significant portion of these patients do not undergo resection despite a lack of disease progression. We sought to determine the factors associated with the inability to resect PDAC in patients receiving neoadjuvant therapy in the absence of disease progression. Methods: Patients with resectable or borderline resectable (SSO/NCCN criteria) PDAC who received NAC at a tertiary referral center were identified. Univariate (UVA) and multivariate (MVA) analysis were performed to identify factors associated with failure to undergo surgical resection in the absence of tumor progression. Results: Between 2005-2013, 188 patients underwent NAC for resectable or borderline resectable PDAC. 69.7% proceeded to surgery, 18.1% had disease progression and 12.2% were not resected due to clinical deterioration or death despite lack of progression on imaging. On UVA, age >70 years (RR 3.88; 95% CI 1.82-8.32), ECOG performance status >2 (RR 7.27; 95% CI 3.38-15.62), vessel involvement at baseline (RR 9.64; 95% CI 3.14-69.38), s1 episode of cholangitis (RR 2.74; 95% CI 1.82-6.14) and hospitalization for any cause during chemotherapy (RR 4.39; 95% CI 1.86-9.94) were associated with a higher risk of derailment from surgery in the absence of disease progression. Other factors such as diabetes, BMI, baseline CA19-9, type of chemotherapy (including modern regimens) as well as presence and type of biliary stent were not associated with inoperability. On MVA, age >70 years old (OR 4.38; 95% CI 1.52-12.63), any hospitalization (OR 3.77; 95% CI 1.29-10.69) and vessel involvement (OR 15.10; 95% CI 1.84-124.05) remained independently associated with failure to undergo surgical resection. Conclusion: In the absence of disease progression, age >70 years, borderline resectable disease and those requiring any hospitalization during neoadjuvant treatment are at higher risk of not undergoing surgical resection after neoadjuvant chemotherapy for PDAC.

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Adjuvant Chemotherapy for Adenocarcinoma of the Small Intestine in a Veteran Population: Minimal Impact on Survival
S. Suleiman, I. Tawdav, S. Ali, S. Courville, R. Chahal, D.H. Berger, A. Artykin. Department of Surgery, Baylor College of Medicine, Houston, TX.

Background: Surgical resection is the primary treatment for adenocarcinoma of the small intestine. While the benefit of radical resection is clear, the role of adjuvant chemotherapy is uncertain. We hypothesized that adjuvant chemotherapy confers a survival benefit in patients treated with radical resection. Methods: Patients with non-metastatic primary small intestinal adenocarcinoma who underwent radical resection were identified from the Veterans Affairs Central Cancer Registry (VACCR) (1995-2010). Clinical and pathologic factors were described. The impact of adjuvant chemotherapy on overall survival was evaluated with univariate Kaplan-Meier and multivariate Cox-regression analyses. Results: 269 patients met inclusion criteria. Mean age was 65±10.1 years. Tumors originated in the duodenum in 120 patients (69.9%). Median overall survival for the entire cohort was 21.7 months. A total of 68 patients (25.3%) underwent adjuvant chemotherapy. Patients treated with chemotherapy were younger (62±9.9 vs 67±9.9 years, p=0.001), had smaller tumors (4±2.6 vs 5±6.8 cm, p=0.04), and were more likely to have nodal disease (60.3% vs 22.6%, p<0.001). On stratified Kaplan-Meier analysis, receipt of adjuvant chemotherapy was associated with improved overall survival only for patients with stage III disease (median survival 21.8 vs 8.6 months, p=0.001) but did not impact survival for other stages. On subset analysis of stage III patients (n=76), those who received adjuvant therapy (n=38) were significantly younger than untreated patients (n=38) (60±9.2 vs 68±9.8 years, p=0.001). On multivariate Cox regression analysis controlling for age and stage, adjuvant chemotherapy did not improve overall survival (HR 0.80, 95% CI 0.51-1.26, p=0.32). Conclusions: Patients receiving adjuvant chemotherapy for small intestinal adenocarcinoma tend to be younger and are more likely to have nodal disease. The benefit of adjuvant therapy remains unclear and may be mediated primarily by age. Further studies are needed to support the selective use of adjuvant chemotherapy for patients with advanced stage disease.

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Nationwide Trends and Outcomes associated with Neoadjuvant Therapy in Pancreatic Cancer: An Analysis of 18,243 Patients
L.M. Youngworth, M.A. Adam, D.P. Nussbaum, P. Goffredo, T.J. Robinson, D.G. Blazer, S.A. Roman, J.A. Sosa. Duke University Hospital, Durham, NC.

INTRODUCTION: Neoadjuvant therapy has several theoretical benefits for patients with pancreatic cancer; however, its effect on perioperative outcomes and survival remains highly controversial. The purpose of this study was to evaluate variation in the use of neoadjuvant therapy and outcomes following resection. METHODS: The NCDB (1998-2011) was queried for all patients with stage I or II pancreatic adenocarcinoma who underwent pancreaticoduodenectomy (PD). Subjects were classified by the use of neoadjuvant chemotherapy and/or radiation therapy. Factors associated with the use of neoadjuvant therapy were evaluated, and outcomes were compared between groups. RESULTS: In total, 18,243 patients were identified, among whom 1,375 (7.5%) received neoadjuvant therapy. From 1998 to 2011, the rate of neoadjuvant therapy increased from 4.3% to 14.5%. Patients receiving neoadjuvant therapy were younger (63.1 vs 66.1 years, p=0.001), and more likely to have private insurance (51.6% vs 38.6%, p=0.001) and be treated at an academic facility (64.1% vs 50.8%, p=0.001). In centers that performed <10 PD/year, 8.0% of patients received neoadjuvant therapy, compared to 8.6% in centers that performed >10 PD/year (p=0.034). Of these higher-volume centers, 81.2% were academic facilities. At surgery, patients who received neoadjuvant therapy were more likely to have negative margins (85.5% vs 77.8%, p=0.001), negative lymph nodes (40.7% vs 57.1%, p<0.001), and tumors locally confined to the pancreas (65.8% vs 70.6%, p<0.001). These patients also had lower 30-day mortality (2.0% vs 4.6%, p=0.001) and readmission rates (7.4% vs 9.5%, p=0.006). The median overall survival was 24.3 months in the neoadjuvant group and 18.7 months in the group that did not receive neoadjuvant therapy (p=0.001). CONCLUSIONS: While neoadjuvant therapy...
therapy is only utilized in a minority of cases, and concerns remain regarding its effect on perioperative morbidity, its use is increasing. In this analysis, neoadjuvant therapy did not demonstrate inferior short term outcomes. Prospective studies are needed to better define the oncologic benefits associated with neoadjuvant therapy.

**P407**

An Immunomodulating Peptide that Enhances Gemcitabine Inhibition of Pancreatic Cancer in the KRAS / p16 Mouse Model of Pancreatic Cancer

N. Schaub,1* R. Sorber,2 J. Janes,3 H. Lopez,4 G. Martin,5 A. El-Sedfy,1 U. Rudloff,1 I. Thoracic and GI Oncology Branch, Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD; 2. Indiana University, Department of Surgery, Indiana University, Indianapolis, IN; 3. Tuskegee University, Tuskegee, AL; 4. Murigenics, Inc., Bethesda, MD; 5. Dalhousie University, Halifax, CA; 6. National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, MD.

**Introduction:** Inflammation and desmosplasia are hallmark characteristics of pancreatic cancer. We tested whether 10N, a synthetic 10mer peptide designed after the interleukin-10 active moiety, could synergize with gemcitabine to treat transgenic mouse pancreatic tumors. **Methods:** We established a colony of Pdx1-CRE; LSL-KRAS-G12D, INK4A-ARF-Lox/Lox transgenic mice. Mice with 4-mm pancreatic tumors were treated with vehicle, gemcitabine (20 mg/kg q4 days), 10N (2 mg/kg SC daily) or a combination of gemcitabine and 10N. Tumor volumes, survival, intratumoral fluorescent dextran, intratumoral fibrosis, collagen I and IV, cytokerine, and tumor immunocyte fluorescence-activated cell sorting (FACS) analysis were recorded for each group. **Results:** The tumors in mice treated with gemcitabine plus 10N showed no volume growth (83%) at 14 days compared to animals treated with gemcitabine, 10N, or vehicle (274%, 382%, 443%, respectively, p = 0.002). The median overall survival was significantly increased in animals receiving gemcitabine plus 10N compared to gemcitabine alone (26d vs. 20d, respectively, p = 0.034). 10N did not increase tumor tissue perfusion of dextran or gemcitabine. Serum TNFα remained significantly increased during the 14 day treatment course, with no difference between the treatment arms. FACS analysis of tumor lysates performed after 4 days of treatment with 10N demonstrated increased intratumoral B-cell (24.6 vs 2.7, p = 0.023) count (35.2 vs 69.2, p = 0.031). **Conclusion:** Combining the immunomodulatory peptide 10N with the standard anti-tumor chemotherapeutic agent gemcitabine effectively impacts tumor growth and improves survival in a transgenic animal model of pancreatic cancer. 10N does not improve gemcitabine uptake, but appears to alter immune subpopulations within tumors.

**P408**

Level of Adherence to Processes of Care in the Treatment of Gastric Cancer: A Population Level Assessment

M. Dixon,1* A. El-Sedfy,2 A. Mahan,3 B. Zagorski,4 J. Vasilevska-Rishtova,3 L. Heyler,1 C. H. Law,4 N. G. Coburn,4 J. Surgery, Maimonides Medical Center, Brooklyn, NY; 2. Queens University, Kingston, ON, Canada; 3. Saint Barnabas Medical Center, Livingston, NJ; 4. Sunnybrook Research Institute, Toronto, ON, Canada; 5. Dalhousie University, Halifax, NS, Canada; 6. University of Toronto, Toronto, ON, Canada.

**Background:** An international multidisciplinary expert panel, using a RAND/UCLA Appropriateness Method, defined processes of care that are RAND/UCLA Appropriateness Method, defined processes of care that are consistent with evidence of best practices. Consensus on the appropriateness of care received by patients, and we found wide variations in the management of GC over a large population. Uptake of best practices may improve survival in this uncommon cancer.

**Conclusion:** of the cases, and intra-operative frozen section was performed in 26%. Stage IV patients with no major symptoms were managed non-operatively in 64% of cases. Conclusions: Appropriate and necessary indicators for the treatment of GC have been identified to provide guidance to clinicians and improve quality of care received by patients, and we found wide variations in the management of GC over a large population. Uptake of best practices may improve survival in this uncommon cancer.

**P409**

Role of Inflammatory Monocyte Mobilization in Growth of Liver Metastasis in a Murine Model of Metastatic Pancreatic Cancer

R. Patnaik,1* T. Nywening,1 B. De,1 D. E. Sanford,2 R. Sorber,2 D. Linehan, Surgery, Washington University in St. Louis, St. Louis, MO.

**Background:** Metastasis is the leading cause of death in Pancreatic Cancer (PC). Our group and others have shown that PC induces cellular changes in the liver long before metastatic spread. Our preliminary data supports that changes in murine liver occur at cellular level long before development of metastasis. Based on the results, we developed a murine model of metastatic PC to study the role of chemotherapy in addition to novel inflammatory monocyte (10N) blocking agents in established PC metastasis. **Methods:** We implanted spontaneously derived murine PC cell line (KCKO) orthotopically in the tail of pancreas of WT mice. 10 days later, we resected tumor from pancreas. There was no evidence of tumor metastasis at this stage in the liver. We injected plucKCKO mice with the inferior pole of the spleen which was removed. Liver metastases were detectable by bioluminescence (BLI) in 100% mice after 15 days of splenic injection. The burden of liver metastasis was quantified by ex-vivo BLI imaging after four weeks of treatment. Mice with established liver metastasis were randomized to treatment with FOLFIRINOX, CCR2i, CCR2i+FOLFIRINOX or vehicle. Mice were imaged biweekly in order to quantify tumor burden in the liver. After 4 weeks of treatment, flow-cytometry studies were performed on peripheral blood, bone marrow and liver and survival was compared. **Results:** The peripheral blood IM were significantly increased in mice bearing liver metastasis. However, CCR2i efficiently blocked the recruitment of IM and macrophage population in liver (p<0.01). The CD14+ T cell infiltrate was increased in the liver with CCR2i(p<0.05). Interestingly, the lowest tumor burden was found in livers of mice treated with CCR2i & FOLFIRINOX. Of significance, the two treatment groups which received CCR2i alone or in combination with chemotherapy had significantly prolonged survival compared to chemotherapy alone (p<0.01). This suggests that targeting CCR2+ IM decreases the growth of liver metastasis in PC and prolongs survival. **Conclusion:** We demonstrate that CCR2i in combination with FOLFIRINOX impairs growth of liver metastasis and prolongs survival in murine model of PC.

**P411**

Gemcitabine Cooperates with TGFβ Inhibition to Effectively Suppress Tumor Growth in Genetically Engineered Mouse Models of Pancreatic Cancer

N. Schaub,1* T. Bapiro,2 H. Pfilicke,1 I. Chen,1 A. Avital,1 D. Schrump,2 J. Dordeti,2 U. Rudloff,1 I. Thoracic and GI Oncology Branch, Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD; 2. Cancer Research UK, Cambridge Research Institute, Cambridge, England, United Kingdom; 3. Bon Secours Cancer Institute, Richmond, VA.

**Introduction:** The desmoplastic microenvironment in pancreatic cancer contains abundant pro-survival cues mediated by cytokines such as transforming growth factor-β (TGFβ). We tested whether TGFβ antagonism could break the stromal barrier, increase intratumoral drug delivery, and synergize with gemcitabine to treat pancreatic cancers in two distinct transgenic mouse models. **Methods:** We established colonies of Pdx-CRE; LSL-KRAS; INK4A-ARF-Lox/Lox (KP16) and Pdx-CRE; LSL-KRAS; TGFβ2-Lox/Lox (TGFβ-KO) mice. With 6 mm pancreatic tumors were treated with LY364947 (1mg/kg) plus gemcitabine (50mg/kg), LY364947 alone, gemcitabine alone, or control. Histology, intratumoral fluorescent dextran, dynamic contrast-enhanced MRI (DCE-MRI), intratumoral gemcitabine, immune subpopulations determined by flow cytometry and tumor volumes were recorded for each group. **Results:** Tumors from both models demonstrated abundant collagen and smooth muscle actin staining, but poor staining for vascular endothelial (CD31). Upon treatment with LY37497, tumor perfusion measured by dextran increased in the KP16 (0.11 vs 0.23, P = 0.041) and TGFβ-KO (0.21 vs 0.37, P = 0.047) models, and perfusion increased on DCE-MRI (1.21 vs 1.377, P = 0.045). In contrast, only KP16 animals demonstrated increased intratumoral...
Reduction of Transfusion Rates in Major Oncologic Surgery: Preliminary Results of a Randomized, Double-blind, Placebo-controlled Trial using Preoperative Tranexamic Acid

G. Wright,* T.L. Waldherr,† D. Ritz-Holland,‡ B.R. Lane,§ M.H. Chung,∥ T. GEEMEP/Michigan State University, Grand Rapids, MI; 2. Spectrum Health, Grand Rapids, MI.

Introduction: Allogeneic blood transfusions have been associated with poorer postoperative outcomes in patients undergoing major oncologic surgery. Currently available medications may aid in reducing the need for perioperative transfusion. Methods: Adult patients undergoing major oncologic surgery in six categories were recruited for enrollment. Exclusion criteria included: history of hypercoagulopathy or thromboembolic event, creatinine >2.83 mg/dL, hypersensitivity to TXA, or vulnerable populations. Enrollees received a single preoperative dose of placebo or tranexamic acid (TXA) 1000 mg. Transfusion is performed intraoperatively by provider discretion and postoperatively for patients with a hemoglobin <7.0 g/dL or symptomatic anemia. The primary outcome measures are perioperative transfusion rate and operative blood loss. A sample size estimate of 200 patients (100 in each arm) was calculated to achieve an adequate endpoint. Per study protocol, interim review was performed following increments of 40 patients enrolled. Significance was determined by \( p < 0.05 \). Results: Ninety-five patients were eligible for enrollment. Forty patients consented during the enrollment period, 36 of which received the planned surgical treatment and were included for analysis. There were 17 patients in the TXA group and 19 in the placebo group. Presentation variables were similar between groups though more hepatectomies occurred in the placebo group compared with more pancreatectomies and cytoreductive surgeries in the TXA group (\( p = 0.18 \)). There were no significant differences between groups for any of the outcome measures. Overall transfusion rates were 4/17 (24%) in the TXA and 3/19 (16%) in the placebo arm, respectively. One thromboembolic event occurred in the placebo group. Multivariate analysis demonstrated no significant independent predictors of perioperative transfusion. Conclusion: TXA has demonstrated an adequate safety profile with no clear signs of benefit in reducing perioperative transfusion rates. A larger sample size is needed to reach appropriate conclusions regarding the primary outcome measure.

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Reducing Transfusion Rates in Major Oncologic Surgery: Preliminary Results of a Randomized, Double-blind, Placebo-controlled Trial using Preoperative Tranexamic Acid

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Clinical Characteristics of Familial Pancreatic Cancer Kindreds: Comparable Staging at Presentation to Sporadic Pancreatic Cancer


Background: Five to 10% of pancreatic adenocarcinomas (PC) have a hereditary basis. Familial Pancreatic Cancer (FPC) is defined as a family that

has at least one pair of first-degree relatives with PC without an identifiable PC syndrome associated with risk for PC. The objective is to report the presentation and management of our institutional series of PC patients that meet the definition of FPC. Methods: Patients that met the definition of FPC were identified from our pancreatic tumor registry (2004-2013). Descriptive analysis of demographics, family history, staging and management of patients with FPC was performed. Age, demographic variables and stage at presentation were compared between FPC and sporadic PC. Results: 962 PC were seen and consented for the pancreatic tumor registry: 58 patients (6%) met criteria for FPC while 903 were sporadic. Median age of diagnosis was 69.5 years in the FPC group and 67.8 in the sporadic group (\( p = 0.36 \)). Male patients represent 60.3% and 51.8% of the FPC and the sporadic group, respectively (\( p = 0.22 \)). There were no racial differences between groups. 97% were symptomatic: pain, weight loss, and jaundice were the most common at the time of diagnosis. Of the 18 pts with FPC underwent genetic testing, 9 (50%) pts were negative and 9 pts revealed a genetic mutation related to FPC. 2 had established ATM mutations, 3 had more than one mutation, and many had variants of uncertain significance (Table). No significant difference was found across all stages (\( p = 0.37 \)) at time of diagnosis. 28 (48.2%) patients were found to be unresectable at time of diagnosis. Only 23 (39.6%) patients with FPC underwent resection: 17 whipples, 4 distals, and 2 total pancreatectomies. 5 others were explored but not resected, and two others did not have evaluable surgical records. Conclusions: FPC patients were not found to have more advanced disease on presentation. When FPC and sporadic PC cases were compared, no significant differences were found in age, gender, race, and overall staging at the time of diagnosis. Half of patients with FPC who underwent genetic testing presented with a mutation related to FPC.

Comparison of demographics and staging among patients with Familial versus Sporadic Pancreatic Cancer

<table>
<thead>
<tr>
<th>Age (mean ± SD)</th>
<th>Familial Pancreatic Cancer</th>
<th>Sporadic Pancreatic Cancer</th>
<th>( p ) value</th>
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<td>n=903</td>
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<td>Gender:</td>
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<tr>
<td>Male</td>
<td>35 (60.3%)</td>
<td>468 (41.8%)</td>
<td>( p = 0.22 )</td>
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<tr>
<td>Female</td>
<td>23 (39.7%)</td>
<td>435 (38.2%)</td>
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<td>Race:</td>
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<tr>
<td>Caucasian</td>
<td>56 (96.5%)</td>
<td>854 (94.8%)</td>
<td>( p = 0.78 )</td>
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<tr>
<td>African American</td>
<td>2 (3.5%)</td>
<td>45 (4.2%)</td>
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<tr>
<td>Asian</td>
<td>0 (0%)</td>
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<td>IA</td>
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<td>ATM mutation (c.1564_1565delG) APC VUS (c.5877_5878delCTOCCoins TA) PALB2 VUS (c.250G&gt;A)</td>
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Kulkarni, Nandini P252, P292
Employee: CSL Behring

Rakovitch, Eileen 1
Grant: Genomic Health, Inc

Roessner, Eric 20
Research: Deutsches Institut fur Zell-und Gewebeersatz, Berlin, Germany

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