Annals of Surgical Oncology
An Oncology Journal for Surgeons
The Official Journal of the Society of Surgical Oncology

Abstract Book

Society of Surgical Oncology
67th Annual Cancer Symposium
Phoenix, Arizona
March 12-15, 2014

CONTENTS

Volume 21, Supplement 1, February 2014

S3: Session Titles and Abstracts Contents
S5: Abstracts of Plenary, Parallel and Video Sessions
S43: Abstracts of Poster Presentations
S181: Conflict of Interest Disclosures
S187: Author Index

This supplement was not sponsored by outside commercial interests.
## Session Titles and Abstract Contents

<table>
<thead>
<tr>
<th>Session Title</th>
<th>Abstract Numbers</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oral Presentations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plenary Session I</td>
<td>1, 2, 3</td>
<td>6</td>
</tr>
<tr>
<td>Plenary Session II</td>
<td>4, 5, 6 (7 withdrawn)</td>
<td>6 – 7</td>
</tr>
<tr>
<td>Parallel Sessions: Breast Cancer</td>
<td>8 – 17</td>
<td>8 – 11</td>
</tr>
<tr>
<td>Parallel Sessions: Colorectal Cancer</td>
<td>18 – 28</td>
<td>12 – 15</td>
</tr>
<tr>
<td>Parallel Sessions: Endocrine Cancer</td>
<td>29 – 38</td>
<td>15 – 18</td>
</tr>
<tr>
<td>Parallel Sessions: Hepatobiliary Cancer</td>
<td>39 - 48</td>
<td>19 – 22</td>
</tr>
<tr>
<td>Parallel Sessions: Melanoma</td>
<td>49 - 58</td>
<td>22 – 26</td>
</tr>
<tr>
<td>Parallel Sessions: Quality Improvement/Clinical Outcomes</td>
<td>59 - 68</td>
<td>26 – 29</td>
</tr>
<tr>
<td>Parallel Sessions: Sarcoma</td>
<td>69 – 78</td>
<td>29 – 33</td>
</tr>
<tr>
<td>Parallel Sessions: Thoracic/Esophageal</td>
<td>79 – 88</td>
<td>33 – 36</td>
</tr>
<tr>
<td>Parallel Sessions: Upper Gastrointestinal Cancer</td>
<td>89 – 98</td>
<td>36 – 40</td>
</tr>
<tr>
<td><strong>Top Rated Videos</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Posters: Breast Cancer</td>
<td>P1 – P94</td>
<td>44 – 76</td>
</tr>
<tr>
<td>Posters: Colorectal Cancer</td>
<td>P95 – P135 (P100 withdrawn)</td>
<td>76 – 90</td>
</tr>
<tr>
<td>Posters: Endocrine Cancer</td>
<td>P136 – P157</td>
<td>90 – 97</td>
</tr>
<tr>
<td>Posters: Melanoma</td>
<td>P196 – P242</td>
<td>109 – 125</td>
</tr>
<tr>
<td>Posters: Other (Urology/Head and Neck/Thoracic)</td>
<td>P243 – P254</td>
<td>125 – 128</td>
</tr>
<tr>
<td>Posters: Quality Improvement/Clinical Outcomes</td>
<td>P255 - P296</td>
<td>128 – 142</td>
</tr>
<tr>
<td>Posters: Sarcoma</td>
<td>P297 – P318 (P302 withdrawn)</td>
<td>142 – 150</td>
</tr>
<tr>
<td>Posters: Thoracic/Esophageal</td>
<td>P319 – P332</td>
<td>150 – 155</td>
</tr>
<tr>
<td>Posters: Upper Gastrointestinal Cancer</td>
<td>P333 – P407</td>
<td>155 – 180</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(P339, P352, P369 withdrawn)
ABSTRACTS

Accepted for
PLENARY, PARALLEL and VIDEO SESSIONS

67th Annual Cancer Symposium
Society of Surgical Oncology
March 12–15, 2014
Phoenix, Arizona
**1** Randomized Controlled Trial of Irinotecan Drug Eluting Beads with Simultaneous FOLFOX and Bevacizumab for Patients with Unresectable Colorectal Liver-Limited Metastasis R. Martin,1,4 M. Schreeder,1 J. Kauh,1 W. Rilling,1 C. Laing,1 T. Croczen,1 S. Strasberg1 1. University of Louisville, Louisville, KY; 2. Clearview Cancer Center, Huntsville, AL; 3. Emory University - Winship Cancer Institute, Atlanta, GA; 4. Froedert Medical College, Milwaukee, WI; 5. Radiological Associates of Sacramento, Sacramento, CA; 6. Washington University, St Louis, MO; 7. Providence Medical Center, Portland, OR.

Background: Reports have demonstrated the activity of combining both Irinotecan & Oxaliplatin into a FOLFOXIRI therapy. An option to gain similar benefits & less toxicity to FOLFOXIRI would be to administer the irinotecan eluting bead via a hepatic arterial approach. The aim of this study was to assess the maximal response and adverse event rates of Irinotecan Drug Eluting Beads (DEBIRI) with FOLFOX & Bevacizumab(Bev) as a first line treatment for unresectable colorectal liver metastasis (CLMs). Methods: Metachronous & Synchronous CLMs were randomly assigned to mFOLFOX6/Bev or mFOLFOX6, Bev & DEBIRI (FOLFOXDEBIRI). Primary end point was optimal response rates & adverse events. Secondary endpoints were patients(pts) converted to resection & survival. Results: The intention-to-treat population comprised 70 pts, 40 pts randomly assigned to the FOLFOXDEBIRI arm & 30 pts to FOLFOX/Bev arm. Both were similar with synchronous disease (50%/vs36%), extent liver involvement (35%/vs31%), but greater percentage in the FOLFOXDEBIRI arm of ECOG 1/2 (57%/vs31%), p<0.04) & extrahepatic disease (51%/vs36%,p<0.02). Median number chemotheraphy cycles was similar in both arms of 8, with a similar Grade 3/4 adverse event rate of 54%/vs46% FOLFOXDEBIRI & 46% FOLFOX/Bev arm. The overall response rate was significantly greater in the FOLFOXDEBIRI arm vs FOLFOX/Bev at 2months (78%/vs54%, 4m [95%/vs70%] controlling mon (76%/vs60%, p<0.02). Significantly greater downsizing to resection in the FOLFOXDEBIRI arm vs FOLFOX/Bev (35%/vs16%,p<0.05), with an improved median progression free survival (15.3 mo vs7.6 mon). Overall improvement in hepatic specific progression free survival was seen in the treatment arm (12.8 mo vs 10.5 mon). Conclusions: Simultaneous mFOLFOX6 with bevacizumab and hepatic arterial irinotecan drug eluting beads is safe, without causing chemotherapy delivery delays and without increasing chemotheraphy toxicity. Simultaneous FO LXOXDEBIRI leads to improved overall response rates, improved hepatic progression free survival, and more durable overall progression free survival in patients downsized to resection.


Background – For colorectal cancer (CRC), there is need for an evidence-based follow-up schedule defining frequency of blood tests and imaging to detect recurrent disease as early as possible. The trial CEA Watch assesses the value of frequent CEA measurements and imaging in case of a rise in CEA for detecting recurrent disease in CRC patients and aims to increase the rate of curable resections amongst all detected recurrences from 10% to 25%. Methods – This was a randomized-controlled multicenter prospective study using a stepped wedge cluster design. Eleven Dutch hospitals were timed one after another to change their follow-up “care as usual” into an intensified follow-up schedule for all patients in follow-up after non-metastasized CRC. The intervention protocol consisted of CEA measurements every 2 months, with repetition of the CEA measurement after 1 month in case of a 20% rise and imaging in case of 2 subsequent rises. A sample size calculation was performed and 1,600 patients were needed given a recurrence rate of 25%. Results – 3,223 patients were included; 243 recurrences were detected (7.5%), 104 (43%) recurrences were found while the patient participated in the control follow-up and 139 (57%) recurrences in the intervention follow-up. In total, 90 (37.0%) of the found recurrences could be treated with curative intent. The rate of detected recurrences which could be treated with curative intent was significantly higher for the intervention protocol than for the control protocol (42% vs. 30%, p<0.027). Analyses of these treatments with curative intent will be added. Survival data are to be awaited. Conclusions – The CEA Watch protocol detects recurrent disease after colorectal cancer in a phase that a significantly higher proportion of recurrences can be treated with curative intent.

**3** Long-term Incidence of Lymphedema after Sentinel Lymph Node Dissection for Early Stage Breast Cancer: ACOSOG Z0010 (Alliance) M. Teshome,1 K.V. Ballman,2 L.M. McCall,3 J.N. Cormier,1 A.E. Giuliano,4 K.K. Hunt.1 1. The University of Texas M.D. Anderson Cancer Center, Houston, TX; 2. Alliance Statistics and Data Center, Mayo Clinic, Rochester, MN; 3. Alliance Statistics and Data Center, Duke University, Durham, NC; 4. Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA.

Introduction: Sentinel lymph node (SLN) dissection has an established role as minimally invasive axillary staging with decreased morbidity in early breast cancer. The American College of Surgeons Oncology Group (ACOSOG) Z0010 trial, a prospective multicenter study to evaluate the prognostic significance of micrometastasis in SLNs of women with early stage breast cancer, previously reported a 7% incidence of lymphedema at 6 months. This study examines the long-term incidence of lymphedema in this cohort. Methods: Eligible patients for ACOSOG Z0010 included women with clinical T1-2 N0 M0 breast cancer. In this trial 5,210 women underwent SLN dissection; of those, 885 had completion axillary lymph node dissection (ALND) and were included for comparison. Post-operative symptoms assessment and examination were completed at 30 days, 6 months, and annually for 5 years. Lymphedema was evaluated subjectively as ipsilateral arm swelling and objectively as an increase of ≥ 2 cm from the pre-operative arm measurement. A multivariate Cox regression analysis was conducted to examine associations between clinical factors and lymphedema. Results: The cumulative incidence of lymphedema after SLN dissection was 3.7% at 1 year, 8.9% at 3 years and 11.9% at 5 years by subjective assessment (n=3,993) and 10.5% at 1 year, 17.4% at 3 years and 24.1% at 5 years by objective arm measurements (n=3,918). Following ALND, the incidence of lymphedema was 14.0% at 1 year, 32.9% at 3 years and 41.0% at 5 years by subjective assessment (n=865) and 17.0% at 1 year, 30.6% at 3 years and 40.3% at 5 years by objective arm measurement (n=853). On multivariate analysis, significant predictors of objective lymphedema included increasing age (OR=1.01, [95% CI: 1.01-1.02], p<0.0001), BMI ≥ 30 kg/m2 (OR=1.81 [1.59-2.06], p<0.0001) and ALND (OR=1.74 [1.50-2.02], p<0.0001). After axillary surgery, decreased range of motion and paresthesias occurred more often than lymphedema. Conclusions: Lymphedema after SLN dissection in women with early stage clinically node negative breast cancer occurs more frequently than clinically suspected and with increasing incidence over time.

<table>
<thead>
<tr>
<th>SLN (%)</th>
<th>ALND (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year</td>
<td>3 years</td>
</tr>
<tr>
<td>Objective lymphedema</td>
<td>15.7</td>
</tr>
<tr>
<td>Decreased range of motion</td>
<td>15.9</td>
</tr>
<tr>
<td>Axillary paresthesias</td>
<td>18.8</td>
</tr>
</tbody>
</table>

**4** Efficacy of Adjuvant Radiation Therapy in the Treatment of Soft Tissue Sarcomas of the Extremity: 20-year follow-up of a Randomized Prospective Trial J.D. Beane,* J.C. Yang, D. White, S. Steinberg,* S.A. Rosenberg,3 U. Rudloff. 1. Surgery Branch, National Cancer Institute, Bethesda, MD; 2. Biostatistics and Data Management Sections, National Cancer Institute, Bethesda, MD.

Background Randomized prospective trials have demonstrated the ability of adjuvant radiation therapy (XRT) to enhance local control following limb-sparing surgery for soft tissue sarcoma (STS), but this has not translated into improved overall survival (OS). Patients treated with XRT are at increased risk for secondary cancers and the natural history of these deficits has not been reported. To address the effect of XRT on long term overall survival and limb function, we present a twenty-year follow-up of our randomized
prospective study of the benefit of adjuvant radiation in the treatment of soft tissue sarcomas of the extremity. Methods Patients with extremity STS and a limb-sparing surgical operation were randomized to receive postoperative XRT or surgery alone. Initially, quality of life, functional data, and OS information were collected in a prospective fashion. This report completes long term follow up through medical records and telephone contacts. Results A total of 141 patients with extremity STS of either high or low grade were randomized to receive postoperative XRT (n=70) or surgery alone (n=71). Median follow up was 17.9 years. Ten and 20-year survival was 77% and 64% for patients receiving surgery alone and 82% and 71% for patients receiving adjuvant XRT (p=0.2). There was no difference in overall survival between treatment arms when analyzing patients with high-grade or low-grade tumors separately. Patients treated with postoperative XRT tend to be more debilitated (4% vs 0%, p=0.8), have clinically significant edema (25% vs 12% p=0.2), and suffer from late wound complications (17% vs 12%, p=0.7), but these did not reach statistical significance when compared to patients receiving surgery alone. Late findings included limb loss (n=2, both following XRT), pathological fractures (n=4, three following XRT) and local recurrence (n=1, surgery alone). Conclusion Adjuvant external beam radiation therapy following surgery for soft tissue sarcoma of the extremity improves local control, is associated with some long term limb complications and does not improve overall survival.

Figure 1. Overall survival of all patients with STS randomized to treatment with surgery and adjuvant chemotherapy versus surgery, chemotherapy, and XRT.

5 Phase I/II Trial of Autophagy Inhibition in Combination with Neoadjuvant Gemcitabine in High-risk Pancreatic Adenocarcinoma: Safety, Clinical Response, and Correlative Studies
B.A. Boone,1 2 M.T. Loitze,3 A.H. Zureikat,4 N. Bahary,1 A.D. Singh,1 D.L. Bartlett,2 V. Espina,3 L.A. Liotta,4 H.J. Zeh.1 1. Surgery, University of Pittsburgh, Pittsburgh, PA; 2. George Mason University, Manassas, VA.

Introduction: Autophagy is a cell survival mechanism that is up-regulated in patients with pancreatic ductal adenocarcinoma. Increased autophagy correlatates adversely with response to therapy and prognosis. Use of the autophagy inhibitor hydroxychloroquine (HCQ) represents a novel treatment strategy in pancreatic cancer. Methods: A Phase I/II trial examining pre-operative gemcitabine with HCQ in the treatment of patients with high-risk pancreatic adenocarcinoma. Eligibility was limited to only those predicted to have limited survival advantage following surgical resection. Two doses of fixed dose gemcitabine (1500mg/m2) were administered with oral HCQ (200mg/day-1200mg/day) for 31 consecutive days until day of surgery. Dose escalation followed a Storer phase 1 design. The primary endpoint was safety and tolerability. Secondary endpoints were clinical response as assessed by resectability rate, R0 resection rates and CA 19-9. Measures of autophagy and apoptosis (LC3 and cleaved caspase 3) were assessed in resected tumors and correlated with clinical response. Results: Thirty-five patients were enrolled in the trial. Two patients withdrew consent prior to initiating treatment and two patients were removed from the protocol due to a stroke and allergic rash, resulting in 31 patients (89%) completing treatment. There were no dose limiting toxicities and no treatment delays. 14 patients (45%) had a decrease in CA 19-9 of more than 50% following treatment. 29 patients (94%) underwent surgical resection as scheduled and the R0 resection rate was 81%. Treatment with HCQ led to an increase in pancreatic cancer cell LC3 staining, consistent with suppression of autophagic flux. There was a trend towards increased apoptosis with increasing doses of HCQ. Conclusion: Pre-operative autophagy inhibition with HCQ in combination with gemcitabine is safe and tolerable. When compared with historical controls the regimen appears to have promise as a biologically active strategy. Future trials will examine HCQ in combination with more active neoadjuvant chemotherapy regimens.

6 RCT Comparing Gastrectomy (Gx) plus Chemotherapy (CTX) with CTX Alone in Advanced Gastric Cancer (AGC) with a Single Non-curable Factor: JCOG 0705/KGCA01 Study K. Fujitani,1,2 Y. Han-Kwang,1 J. Mizusawa,1 K. Young-Woo,1 M. Terashima,1 S. Han,1,3 Y. Iwasaki,2 W. Hyung,1 A. Takagane,2 B. Park,2 T. Tsujinaka,2 S. Hahn,1 M. Sasako,5 Y. Bang.1 1. Osaka Prefectural General Medical Center, Osaka, Japan; 2. JCOG Data Center, Tokyo, Japan; 3. Shizuoka Cancer Center, Shizuoka, Japan; 4. Tokyo Metropolitan Komagome Hospital, Tokyo, Japan; 5. Hakodate Goryokaku Hospital, Hakodate, Japan; 6. Kaizuka Municipal Hospital, Osaka, Japan; 7. Hyogo Medical College, Nishinomiya, Japan; 8. Seoul National University College of Medicine, Seoul, Korea, Republic of; 9. National Cancer Center, Seoul, Korea, Republic of; 10. Ajou University College of Medicine, Seoul, Korea, Republic of; 11. Yeouido University College of Medicine, Seoul, Korea, Republic of.

Background: The prognosis of AGC with non-curable factors is poor. Gx is sometimes employed, even in the absence of any serious symptoms, based on the literature showing a survival benefit of Gx (MST 8.0–12.2 M with Gx vs. 2.4–6.7 M without Gx). CTX alone has recently shown MST over 1y in AGC. Based on these situations, we conducted an international RCT among Japan, Korea, and Singapore to investigate the role of Gx for incurable AGC. Methods: Eligibility criteria included histologically proven primary gastric adenocarcinoma, presence of a single non-curable factor confined to either liver (H1), peritoneum (P1), or para-aortic lymph node (16a1/b2) confirmed by both CT scan and laparoscopy/laparotomy, clinical T1-3, no other distant metastasis than H1, P1 or LN 16a1/b2, aged 20-75, PS 0-1. Eligible patients were randomized to Gx followed by CTX or CTX alone. Gx with D1 dissection was performed without resection of metastatic lesions. Patients were placed on a CTX regimen, S-1+CDDP (S-1 80 mg/m2/day for 3 consecutive weeks followed by a 2-week rest, CDDP 60 mg/m2 on Day 8, repeated every 5 weeks). The primary endpoint was OS. The planned sample size was 330, 165 cases per arm, with one-sided alpha of 5%, and an 80% power detecting a 2y-survival difference of 10%, 20% with CTX vs. 30% with Gx. Results: Between Feb 2008 and Apr 2013, 164 patients (82 in Japan, 82 in Korea) were randomized. The first interim analysis was performed in Sep 2013, with 37% (110/294) of the planned events observed. The 2y-survival were 25.7 (95% CI: 15.7 to 36.9) % with Gx plus CTX and 31.4 (95% CI: 20.4 to 42.9) % with CTX alone. Hazard ratio for Gx was 1.08 (95% CI: 0.74 to 1.58) with predictive probability in favor of gastrectomy of 13.2% at the final analysis. Although some interactions favoring Gx plus CTX were suggested on nation and some factors, JCOG DSMC recommended early termination of the trial. Conclusion: RCT Comparing Gastrectomy (Gx) plus Chemotherapy (CTX) with CTX Alone in Advanced Gastric Cancer (AGC) with a Single Non-curable Factor: JCOG 0705/KGCA01 Study

Acknowledgments: This study was supported by JSPS KAKENHI Grant Number 17K08983 and the National Cancer Center Research and Development Fund (28-A-12 and 29-A-04).
Axillary Reverse Mapping: Redefining Axillary Surgery
UAMS, Little Rock, AR.

Introduction: Axillary status in breast cancer patients continues to serve as a major predictor of outcome while also influencing decisions for adjuvant therapy. High morbidity rates in both sentinel lymph node biopsy (SLNB) and axillary lymph node dissection (ALND) are thought to be due to unrecognized variations in arm lymphatic drainage in the axilla. Axillary reverse mapping (ARM) facilitates identification and avoidance of arm lymphatics which has significantly improved our rates of lymphedema. Methods: This IRB-approved study, from June 2007 to April 2013 involved patients undergoing SLNB with or without ALND, or ALND alone. Our technique involves subareolar injection of technetium for localization of the SLN. Lymphazurin (5ml) is injected in the ipsilateral upper arm for localization of non-breast lymphatics. Data were collected on identification and preservation of arm lymphatics, crossovers, metastases, axillary recurrence, and lymphedema as measured by volume displacement. Results: 447 patients underwent SLNB and/or ALND. 433 patients underwent a SLNB. Of those, 303/433 (70%) had a SLNB only and 130/433 (30%) went on to an ALND due to a positive axilla. 14/447 (3.1%) had ALND due to a positive axilla preoperatively. In 294/303 (97%) of patients with SLNB only, breast SLNs were hot but not blue; crossover (hot and blue) was seen in 9/303 (3%) SLNB and 20/144 (14%) ALND patients. Metastases were identified in 0/09 crossover SLNB and 3/20 (15%) of ALND crossover nodes. Blue lymphatics were identified in 101/303 (33.3%) of SLNB and in 111/144 (77%) ALND. Median follow-up was 24 months (range 3 to 54 months). Overall lymphedema rates for SLNB and ALND were 0.33% and 5.5% respectively. During the follow up, 0/303 of the SLNB patients, and 1/144 (0.7%) ALND patients had an axillary recurrence. Conclusions: ARM allows frequent identification of arm lymphatics in the axilla which would have been transected during surgery. Rates of metastases in crossover nodes and axillary recurrence are low. Lymphedema rates are dramatically reduced using ARM when compared to accepted standards. This currently is the largest series to date regarding ARM and its efficacy in minimizing the morbidity of axillary surgery.

The Extent of Extracapsular Extension (ECE) may Influence the Need for Axillary Lymph Node Dissection (ALND) in Patients with T1-T2 Breast Cancer

Introduction: Whether or not the presence of ECE in the sentinel lymph node (SLN) is an indication for ALND in patients managed according to ACOSOG Z0011 criteria is controversial. In this study we examined the correlation between ECE in the SLN and disease burden in the axilla. Methods: From a prospectively maintained database of 11,730 patients treated for invasive breast cancer from 2006-2013, we selected those with clinicopathologic features meeting ACOSOG Z0011 criteria, specifically pT1-T2, clinically N0 patients with metastases in <3 SLN. Records were reviewed to document the presence and extent of ECE. Patients receiving neoadjuvant chemotherapy were excluded. Characteristics of patients with ≤2mm or >2mm ECE were compared with Fisher’s exact test and Wilcoxon rank sum test. Results: Three hundred seventy six (3.2%) patients had pT1-T2, clinically N0 disease with <3 positive SLN and the presence of ECE. Of these, 324 (86%) had ECE size data available. Characteristics of patients with ≤2mm (n=164) and >2mm (n=160) of ECE are compared in Table 1. Median tumor size was 1.8cm for ≤2mm ECE and 2.1 cm for >2mm ECE (p<0.0003) and patients with ≤2mm ECE were more likely to have only 1 positive SLN (p=0.012). ALND was performed in 68% of patients with ≤2mm ECE and 79% of patients with >2mm ECE (p=0.03), yielding a median of 0 (range 0-29) additional positive nodes in the ≤2mm ECE group and a median of 2 (range 0-32) additional positive nodes in the >2mm ECE group (p=0.0001). No additional positive nodes were found in 59% of patients with ≤2mm ECE versus 32% of patients with >2mm ECE, 1-3 additional positive nodes were found in 33% and 31%, and ≥4 additional positive nodes were found in 8% and 36% of patients with ≤2mm and >2mm ECE respectively (p<0.0001). Conclusion: In this large series of consecutively treated patients meeting Z0011 criteria, the extent of ECE was significantly correlated with nodal tumor burden at ALND. Other tumor characteristics were similar between groups. These data suggest that >2mm of ECE may be an indication for ALND when applying Z0011 criteria to patients with metastases in <3 SLNs.

Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>≤2mm (n=164)</th>
<th>&gt;2mm (n=160)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&lt;85)</td>
<td>275 14%</td>
<td>255 25%</td>
<td>0.880</td>
</tr>
<tr>
<td>Pathologic T stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>3/0 6%</td>
<td>70 44%</td>
<td>0.0026</td>
</tr>
<tr>
<td>T2</td>
<td>64 99%</td>
<td>90 56%</td>
<td></td>
</tr>
<tr>
<td>Nuclear Grade (n=293)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>55 29%</td>
<td>55 29%</td>
<td>0.3176</td>
</tr>
<tr>
<td>2</td>
<td>53 34%</td>
<td>53 34%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>21 14%</td>
<td>24 15%</td>
<td></td>
</tr>
<tr>
<td>Hormone Receptor Subtype (n=322)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR+/HER2+</td>
<td>139 85%</td>
<td>138 87%</td>
<td>0.4678</td>
</tr>
<tr>
<td>HR-/HER2+</td>
<td>14 9%</td>
<td>5 3%</td>
<td></td>
</tr>
<tr>
<td>HR-/HER2-</td>
<td>5 3%</td>
<td>5 3%</td>
<td></td>
</tr>
<tr>
<td>Number of positive SLN removed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>126 77%</td>
<td>96 60%</td>
<td>0.912</td>
</tr>
<tr>
<td>2</td>
<td>38 23%</td>
<td>64 40%</td>
<td></td>
</tr>
<tr>
<td>Median number positive SLN (range)</td>
<td>1 (1-2)</td>
<td>1 (1-2)</td>
<td>0.017</td>
</tr>
<tr>
<td>Median number total SLN removed (range)</td>
<td>2 (1-13)</td>
<td>2 (1-10)</td>
<td>0.1814</td>
</tr>
<tr>
<td>Number additional positive axillary nodes (n=239)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1 96%</td>
<td>2 82%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>1-3</td>
<td>37 13%</td>
<td>40 31%</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>9 8%</td>
<td>46 36%</td>
<td></td>
</tr>
<tr>
<td>Medium number additional positive ALN (range)</td>
<td>0 (0-29)</td>
<td>2 (6-32)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Abstracts: Plenary, Parallel and Video Sessions S9

10 The Effect of Margin Status on Local Recurrence and Cost Analysis using a Decision Tree Model S.E. Abe,* J.S. Hill, K. Carpenter, Y. Han, J. Symanowski, R. White. Carolina's Medical Center/Levine Cancer Institute, Charlotte, NC.

Introduction: The definition of an adequate surgical margin for breast conservation therapy (BCT) continues to be controversial. Studies have not consistently demonstrated that reexcision to obtain wider margins, with its attendant increased cost, results in decreased local recurrence (LR). We designed a decision tree model to analyze LR and surgical costs based on margin status.

Methods: A decision tree model was developed for the management of margins after BCT for invasive cancer. Data from 10 published studies (3,930 subjects) was used to determine the proportion of patients who fall into 3 margin status groups: positive, close (≤2mm) and negative (>2mm). Data from 15 studies (6,014 subjects) was used to determine 5 year LR rate for each group. The model assumed 140,000 initial BCT (230,000 new breast cancer patients/year with ~60% BCT), that all patients with a positive margin underwent reexcision, that only one reexcision was required to obtain negative margins, and that mastectomy was performed after LR. Simulation cycles compared a strategy where all patients with close margins underwent reexcision (Strategy 1) versus one where they did not (Strategy 2). Number needed to treat was calculated comparing these strategies. Surgical costs were estimated using 2013 Medicare reimbursement rates. Results: In our model, 19.6% had positive margins, 21.8% had close margins and 58.7% had negative margins. Strategy 1 resulted in overall LR of 5.1%, with total surgical cost of $45,243,228 (reexcision $37,932,875, mastectomy $7,310,353). Strategy 2 resulted in overall LR of 5.5%, with total surgical cost of $25,826,684 (reexcision $17,974,347, mastectomy $7,852,337). Excess surgical cost associated with Strategy 1 was $19,416,544. Number of reexcisions in close margin patients needed to prevent one recurrence was 57. Conclusion: In our model, LR did not markedly differ between the two strategies. However, the strategy to obtain margin widths >2mm resulted in total excess cost of ~$20 million. This does not include hospital costs, the cost of surgical complications after reexcision, nor the reality of multiple reexcisions or mastectomy performed to obtain negative margins.


Objectives: Breast tumors can enact cancer-like gene expression changes in the peri-tumoral stroma, making the stroma genomically similar to the tumor. Genetic alterations in the tumor-free stroma may impact upon disease progression and treatment effectiveness. We characterized alterations of gene expression in the cancer-free peri-tumoral tissue by distance from the primary tumor.

Methods: Tumor samples and stroma every 5mm in two directions from tumor-stroma interface, to 20mm from the tumor margin were analyzed and pathologist verified as devoid of cancer cells from 32 patients undergoing mastectomy for invasive breast cancers from a prospectively collected database at a tertiary care centre. Two cancer tissue arrays, U133A 2+ gene arrays. SVM, ANOVA and PCA were performed. Results: A total of 1503 cases were analyzed, of which 1231 (81.9%) were positive, close (≤2mm) and negative (>2mm). Data from 15 studies (6,014 subjects) was used to determine 5 year LR rate for each group. The model assumed 140,000 initial BCT (230,000 new breast cancer patients/year with ~60% BCT), that all patients with a positive margin underwent reexcision, that only one reexcision was required to obtain negative margins, and that mastectomy was performed after LR. Simulation cycles compared a strategy where all patients with close margins underwent reexcision (Strategy 1) versus one where they did not (Strategy 2). Number needed to treat was calculated comparing these strategies. Surgical costs were estimated using 2013 Medicare reimbursement rates. Results: In our model, 19.6% had positive margins, 21.8% had close margins and 58.7% had negative margins. Strategy 1 resulted in overall LR of 5.1%, with total surgical cost of $45,243,228 (reexcision $37,932,875, mastectomy $7,310,353). Strategy 2 resulted in overall LR of 5.5%, with total surgical cost of $25,826,684 (reexcision $17,974,347, mastectomy $7,852,337). Excess surgical cost associated with Strategy 1 was $19,416,544. Number of reexcisions in close margin patients needed to prevent one recurrence was 57. Conclusion: In our model, LR did not markedly differ between the two strategies. However, the strategy to obtain margin widths >2mm resulted in total excess cost of ~$20 million. This does not include hospital costs, the cost of surgical complications after reexcision, nor the reality of multiple reexcisions or mastectomy performed to obtain negative margins.


Background: Rates of contralateral prophylactic mastectomy (CPM) in women with breast cancer have been steadily increasing. The utility of this procedure has been scrutinized, however, as most studies fail to show a survival benefit. We evaluated the survival differences among CPM patients compared to patients undergoing single mastectomy (SM) alone for treatment of unilateral, non-metastatic breast cancer.

Methods: The Surveillance Epidemiology and End Results database was used to identify newly diagnosed unilateral breast cancer patients who underwent mastectomy with or without CPM from 1998-2010. A 1:1 matched nested case-control analysis was performed with CPM cases matched to SM controls based on age group, race/ethnicity, grade, T stage, N status, AJCC stage, estrogen receptor (ER) status, and propensity score. Survival analyses included Kaplan-Meier estimation and univariate and multivariate Cox proportional hazard models to determine factors associated with overall survival (OS). Results: 28,015 CPM patients were identified. The CPM rate among all mastectomy patients increased from 4% in 1998 to 22% in 2010. On multivariate regression analysis, in addition to increasing T stage and older age, African-American race (OR 1.46, 95% CI 1.32-1.62), poorly differentiated grade (OR 1.80, 95% CI 1.60-2.01), positive nodal status (OR 1.85, 95% CI 1.73-1.97) and ER negative status (OR 1.53, 95% CI 1.39-1.67) were associated with increased risk of death. Patients who underwent CPM had a lower risk of death (OR 0.77, 95% CI 0.73-0.82) relative to patients with SM alone. 10-year OS rates were greater for CPM vs. SM patients, with the greatest effect seen in patients with stage II (79% for CPM vs. 75% for SM) and stage III disease (63% for CPM vs. 60% for SM p=0.0014). Conclusions: CPM rates continue to rise in the US. Along with other known prognostic factors, CPM is associated with a survival benefit. These findings support the indication for CPM in patients seeking treatment for unilateral breast cancer.

13 Characteristics of Multifocal and Multicentric Breast Cancers P. Kanumuri,* B. Hayse, A.B. Chapgar, N.R. Horowitz, B. Killelea, D.R. Lannin. Yale University School of Medicine, New Haven, CT.

Introduction: Multifocal [MF] and multicentric [MC] breast cancers are being increasingly recognized and are known to behave differently compared to unifocal (UF) cancers. However, the significance of focality is ignored in the current staging systems and relatively little is known about the biology of these cancers. Most studies have combined MF and MC disease when comparing it to UF disease. Methods: A retrospective review was performed of invasive breast cancers from a prospectively collected database at a tertiary care academic medical center from 2004 – 2011. MF and MC cancers were defined as two or more lesions in the same or different quadrants, respectively, separated by normal breast tissue. Characteristics of MF and MC cancers were compared to UF cancers using chi-square tests and predictors of lymph node positivity were evaluated using multivariate logistic regression. Results: A total of 1503 cases were analyzed, of which 1231 (81.9%) were...
UF, 178 (11.8%) were MF, and 94 (6.3%) were MC cancers. There were biological differences among the groups when MF and MC cancers were compared to UF cancers (Table). MC but not MF cancers were associated with young age at diagnosis, larger tumor size and node positivity. On the other hand, MF but not MC tumors showed differences by molecular type; they had a greater association with ER/PR+Her2+ tumors and a smaller percent of triple negative cancers in comparison to UF tumors. There were also differences by histology, with MF more likely to be infiltrating ductal carcinomas with an extensive intraductal component and MC more likely to be infiltrating lobular carcinomas. MF and MC cancers had no significant association with tumor grade or lymphovascular invasion (LVI). When adjusted for tumor size, age at diagnosis, grade, and LVI, multicentricity was an independent predictor of node positivity. Conclusion: Our data infer that MF and MC tumors represent biologically different diseases. MC is clinicopathologically more aggressive than MF disease and is significantly associated with younger age and larger tumor size. It was also noted that MC cancers are an independent predictor of node positivity.

Characteristics of Unifocal, Multifocal and Multicentric Breast Cancers

<table>
<thead>
<tr>
<th>Factor</th>
<th>Unifocal</th>
<th>Multifocal</th>
<th>Multicentric</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;50 years</td>
<td>342 (34%)</td>
<td>60 (17%)</td>
</tr>
<tr>
<td>Tumor Size</td>
<td>T1</td>
<td>755 (63%)</td>
<td>110 (63%)</td>
</tr>
<tr>
<td>Lymph Nodes</td>
<td>Positive</td>
<td>352 (31%)</td>
<td>48 (29%)</td>
</tr>
<tr>
<td>Histology</td>
<td>Infiltrating Ductal</td>
<td>720 (59%)</td>
<td>54 (14%)</td>
</tr>
<tr>
<td>Infiltrating Ductal with Examine Intraductal Component</td>
<td>222 (18%)</td>
<td>60 (34%)</td>
<td>0.22</td>
</tr>
<tr>
<td>Infiltrating Lobular</td>
<td>121 (10%)</td>
<td>14 (9%)</td>
<td>0.018</td>
</tr>
<tr>
<td>Molecular Markers</td>
<td>ER/PR+Her2</td>
<td>707 (71%)</td>
<td>106 (76%)</td>
</tr>
<tr>
<td>ER/PR+Her2</td>
<td>ER/PR+Her2</td>
<td>77 (80%)</td>
<td>70 (45%)</td>
</tr>
<tr>
<td>ER/PR+Her2</td>
<td>ER/PR+Her2</td>
<td>61 (60%)</td>
<td>7 (5%)</td>
</tr>
<tr>
<td>ER/PR</td>
<td>ER/PR+Her2</td>
<td>130 (12%)</td>
<td>12 (9%)</td>
</tr>
</tbody>
</table>

77.5% (124/160) were associated with history of adjuvant RT for BC at least 2 years prior to diagnosis of angiosarcoma. The age-adjusted incidence rate of all angiosarcomas increased from 1973 to 2009. Median time from RT to diagnosis of angiosarcoma was 7 years (range: 3-19 years). Among 1,070,769 women diagnosed with BC during this period, receipt of RT increased the odds of developing angiosarcoma (HR=6.595%; CI=[4.5, 9.5]). For women who developed angiosarcoma, the stage distribution at BC diagnosis was 3.1%, 75.5%, 21.4% for in situ, localized, and regional stages respectively. Stage and age at diagnosis affected odds of developing subsequent angiosarcoma. Risk of angiosarcoma was not greater in women undergoing RT after lumpectomy (HR=0.72,95% CI=[0.29,1.81]) compared with RT after mastectomy. The median survival following diagnosis of radiation-associated breast/chest angiosarcoma was 2.3 years. CONCLUSIONS: The incidence of angiosarcoma has increased from 1973 to 2009 with the increasing use of adjuvant RT for BC. Surgery type did not impact incidence of angiosarcoma. This important, rare consequence of adjuvant RT should be considered, particularly in patients with early stage BC with an excellent prognosis.
Abstracts: Plenary, Parallel and Video Sessions S11

**Induced Immunity Correlates with and may Predict Clinical Benefit in the Phase II Clinical Trial of the Anti-HER2 (GP2) Vaccine to Prevent Recurrence in High-risk Breast Cancer Patients**

A. Trappay,1 J.S. Berry,1 E. Schneble,1 J. Aden,1 T.J. Vreeland,1 D.F. Hale,1 A. Sears,1 R. Brown,1 S. Perez,2 G.T. Clifton,2 M. Papamichael,3 S. Ponniah,3 E. Mittendorf,2 G.E. Peoples.1 1. San Antonio Military Medical Center, Fort Sam Houston, TX; 2. MD Anderson Cancer Center, Houston, TX; 3. Cancer Vaccine Development Lab, Bethesda, MD; 4. Cancer Immunology and Immunotherapy Center, St. Savas, Greece; 5. Blanchfield Army Community Hospital, Fort Campbell, KY.

BACKGROUND: A prospective, randomized, multi-center, placebo-controlled, single-blinded, phase II trial was designed to evaluate the safety and clinical efficacy of GP2, an HLA-A2 restricted HER2-derived peptide vaccine, in breast cancer patients (pts). We have previously demonstrated through immunosassay analysis that induced immunity is required for clinical benefit after vaccination with the E75 peptide. Here we report analysis of risk factors for recurrence using logistic regression modeling (LRM) of immunologic factors previously shown to correlate with positive response to E75. METHODS: Data were analyzed using Fisher’s Exact Test, ANOVA, and LRM. RESULTS: Similar to our E75 analysis, lower pre-existing and higher post-vaccination peptide-specific CTL levels correlate with fewer recurrences suggesting that induction of GP2 immunity correlates with clinical outcome in the adjuvant setting. These correlations have been difficult to prove with vaccines in the metastatic setting, but may be predictive in the adjuvant setting.

**Table 1**

<table>
<thead>
<tr>
<th>Variables in the Optimal Model</th>
<th>Odds Ratio (95% CI)</th>
<th>Sensitivity, Specificity</th>
<th>Area Under the Curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0</td>
<td>1.17 (0.60)</td>
<td>100% 94% (R0=0.32 dmi)</td>
<td>0.62</td>
</tr>
<tr>
<td>R6</td>
<td>2.48 (1.11)</td>
<td>100% 65% (R0=0.61 dmi)</td>
<td>0.80</td>
</tr>
</tbody>
</table>

**Tyrosine-kinase Expression Predicts Response to Sunitinib in Breast Cancer**

P.M. Spanheimer,* M.V. Kulak, J.C. Carr, G.W. Woodfield, J.P. De Andrade, S.L. Sugg, R.J. Weigel. Surgery, University of Iowa, Iowa City, IA.

Introduction: Tyrosine kinase inhibitors (TKI) reduce Erk phosphorylation and proliferation. Preliminary data indicate that TKIs function through RET in breast cancer, however, TKIs are not specific and can block several receptor tyrosine kinases (RTK). We used cell lines and primary breast cancer specimens to determine factors associated with TKI response. Methods: Proliferation was assessed after siRNA knockdown with or without sunitinib in breast cancer cell lines by MTT. Breast cancer tissue and matched normal breast was obtained from 30 women with invasive breast carcinoma. Gene expression was assessed by RT-PCR. Fresh tissue was treated in vitro with sunitinib or control media for 30 minutes and response was assessed by phosphorylation specific western blot. Results: Gene knockdown of EGFR, VEGFR1, or VEGFR2 had no effect on proliferation in MCF-7 or BT-474. Sunitinib treatment caused a similar reduction in proliferation independent of gene knockdown in both cell lines. Twenty primary tumors were ER positive, eight triple negative (TN), and four over-expressed HER2. Expression of FGFR1 in highest in ER+ tumors compared to other tumors and normal breast (p=0.03). Expression of EGFR and VEGFR1 were increased in TN tumors compared to normal breast (p=0.05). FGFR4 was expressed highest in HER2+ tumors (p=0.02). The Erk phosphatase DUSP4 was under-expressed in all subtypes compared to normal breast, with the lowest expression in TN tumors (p=0.01). Reduction in Erk activation with in vitro sunitinib was significantly higher in tumors compared to normal tissue (p<0.001). ER positivity and low EGFR expression were associated with reduction in Erk activation after sunitinib treatment (p=0.05). Clinical variables including stage and nodal status were not associated with response to sunitinib. Conclusion: Breast cancer subtypes have characteristic RTK expression patterns. Knockout of EGFR, VEGFR1 or VEGFR2 did not affect growth or TKI responsiveness in luminal breast cancer cell lines and expression in primary breast cancer did not correlate with in vitro sunitinib response. Based on these data, RET remains the most predictive marker of TKI response in breast cancer.
Isolated Tumor Cells are a Negative Prognostic Factor for Disease-free and Overall Survival in Stage I & II Colon Cancer Patients: A Propensity Score Analysis

Background: Lymph node (LN) involvement is the most important prognostic factor in stage I & II colon cancer patients. Despite complete surgical resection up to 20% of these allegedly curatively treated patients will develop disease recurrence within five years. The objective of the present prospective investigation was to assess the prognostic impact of isolated tumor cells (ITC) in sentinel lymph nodes of stage I & II colon cancer patients. Methods: In this prospective single center study 74 stage I & II colon cancer patients were operated between 2005 - 2011. LN at highest risk of harboring ITC were identified via the in vivo sentinel lymph node procedure. LN were analyzed with multi-level sectioning, conventional H&E, and immunohistochemical CK-19 staining. The correlation between ITC and survival was assessed using Cox regression and propensity score analyses. Results: The median follow-up was 4.6 years. ITC were detected in 23 patients (31.1%). ITC in sentinel lymph nodes were associated with an increased risk for disease recurrence in unadjusted (hazard ratio [HR] = 2.82, p=0.043), risk-adjusted (HR = 4.73, p=0.005) and in propensity score-adjusted analyses (HR = 5.24, p=0.022). Similarly, ITC were an independent significant prognostic factor for overall survival after risk-adjusting in multivariable Cox regression analysis (HR = 3.50, p=0.043), in a backward variable selection procedure (HR = 4.48, p=0.010), and in propensity score-adjusted analysis (HR = 4.12, p=0.041). Conclusions: This is the first prospective cohort study applying both multivariable and propensity-score analyses to assess the putative impact of ITC on disease-free and overall survival. The presence of ITC in SLN of stage I & II colon cancer patients should be classified as a high risk factor and therefore may identify patients who benefit from adjuvant chemotherapy.

Single Nucleotide Polymorphisms in XRCC1, XPD, and TGF β Predict the Risk of Proctitis in Patients Receiving Radiation Therapy for Rectal Cancer

Background: Researchers have identified single nucleotide polymorphisms (SNP’s) that are significantly associated with toxicity in patients receiving radiation therapy (RT) for rectal cancer. This study aimed to validate these findings in an independent cohort. Methods: Our study population consisted of patients who received RT for rectal cancer at a single institution from 2006 to 2012. All eligible patients had banked tissue available for analysis and had toxicity information recorded before initiating RT and during the final 2 weeks of RT, at a minimum. Proctitis was defined as severe if patients required opioid therapy. Severe proctitis during RT occurred in 39 patients (23%). The XRCC1 Q399 allele was present in 101 patients (61%), the XPD Q751 allele in 98 (59%), the TP53 P72 allele in 68 (41%), and the TGFβ P25 allele in 26 (16%). Severe proctitis was significantly more likely in patients carrying the XRCC1 Q399 (p = 0.018) and TGFβ P25 (p = 0.003) alleles, and less likely in patients carrying XPD Q751 (p = 0.14). Discussion: In this independent cohort of 166 rectal cancer patients, we have validated the association of SNP’s in XRCC1, XPD, and TGFβ with radiation-induced toxicity. This information may ultimately contribute to treatment recommendations for locally advanced rectal cancer patients.

INTRODUCTION MAC most commonly gives rise to Pseudomyxoma Peritonei. The primary treatment of this disease is cytoreductive surgery (CRS)/HIPEC. Therapy for advanced MAC is poorly effective and often consists of drug regimens validated in colorectal cancer (CRC). We hypothesized that using next generation sequencing, we would identify common mutations in MAC that could suggest novel therapeutic opportunities for PMP patients. METHODS MAC samples were collected at CRS. Laser capture was used to enrich tumor cell content. Matched DNA from 10 MAC’s [9 low grade (LG), 1 high grade (HG)] and peripheral blood was isolated, and whole exomes were sequenced on a HiSeq platform. For replication, ultra-deep-targeted sequencing and digital droplet PCR were performed on 19 additional samples (14 low grade, 5 high grade). IHC was performed on FFPE-samples to confirm activation of altered pathways. RESULTS Mutational analysis revealed an average of 45 nonsilent mutations in MAC. Nearly all MAC harbor oncogenic mutations in KRAS (26/29) and GNAS (21/29). While KRAS mutation was observed in LG (21/23) and HG (5/6) MAC’s, GNAS mutation was predominantly seen in LG MAC’s (20/23) versus HG (1/6), p<0.05. This strongly suggests MAC’s most often arise from a KRAS mutant progenitor, and that HG MAC’s do not arise from LG. IHC revealed that canonical signaling pathways downstream of KRAS (MEK/ERK, PI3K/AKT) and GNAS (Protein kinase A) were activated in nearly all MAC’s. Mutations activating TGF-β signaling were observed in 70% of MAC’s. While MAC’s share some genetic alterations with CRC, mutations in TP53 and APC, common in CRC, are rare in MAC. CONCLUSIONS Genome-wide mutational analysis revealed signature genetic alterations in MAC that are distinct from CRC. Instead, MAC’s share genetic features with pancreatic IPMN, a similarly indolent mucinous lesion. Our findings; 1) suggest MEK and PKA inhibition as new therapeutic opportunities for PMP patients. 2) suggest the use of EGFR monoclonal antibody therapy should be used with caution in MAC patients.
21 Value of Primary Tumor Gene Signature in Colon Cancer when National Quality Standards are Adhered to: Preliminary Results of an International Prospective Multicenter Trial A.J. Bilchik,1*,6 Z.A. Wainberg,7 A. Stojadinovic,6 D.J. Slamon,6 M. Protic,6 D. Halle,4 H. Chen,2, A. Nissen,3 1. John Wayne Cancer Institute, Santa Monica, CA; 2. University of California at Los Angeles, Los Angeles, CA; 3. United States Military Cancer Institute, Washington, DC; 4. Hadassah-Hebrew University, Ein Kerem, Jerusalem, Israel.

Objective: To determine if gene signatures are informative in colon cancer (CC) in a multicenter prospective trial with adherence to National Quality Standards. Several studies have demonstrated the prognostic potential of gene signatures in primary CC. This has never been evaluated prospectively with adherence to National Quality Standards (a12 lymph nodes [LN)s]. Methods: Eligibility criteria included: a) no evidence of metastatic disease; b) ±12 LNs; c) no adjuvant chemotherapy for LN-negative CC; d) focused pathologic analysis of LNs including immunohistochemistry (IHC) for LNs negative by H&E. RNA extraction was done from primary frozen tumor samples and samples were only considered reliable if RIN was >9. Using an Agilent whole human genome array, 44,000 genes were analyzed in primary tumors for differential gene expression. ANOVA was applied at 2-fold expression level in at least 8 experiments to obtain the differentially expressed genes. Results: Of 150 patients enrolled, molecular analysis has been completed in the first 128. At a median follow-up of 27 months, 14% of patients have recurred. There was a significant differential increase in a panel of genes involved in cellular proliferation and a decrease in a pro-differentiating gene panel in those that recurred (p<0.01). The up-regulation of the cysteine protease legumain (LGMN) was found to be significantly associated with recurrence in stage II CC patients following surgery (p<0.01). These genetic signatures did not correlate with T or N stage. Conclusions: This is the first prospective trial to evaluate gene signatures in CC with adherence to the 12-node minimum quality standard. Certain molecular pathways may be prognostically relevant if both surgery and pathology are standardized, regardless of T and N stage. Careful consideration should be made to include surgical quality measures when planning clinical trials to evaluate the true effect of molecular markers in CC.

22 Five-Year Survival after Incorporation of Pre-Treatment CEA Levels into AJCC Staging for Colon Cancer P. Thirunavukarasu,1* C. Talati,2 S. Munjal,3 S. Singla,4 K. Attwood,5 V. Francescutti,6 1. Surgical Oncology, Roxwell Park Cancer Institute, Buffalo, NY; 2. University of Pittsburgh, Pittsburgh, PA.

Background: The American Joint Committee for Cancer (AJCC) has advocated incorporating pre-treatment serum CEA level (C-stage) into the conventional TNM staging system. The latter has been shown to result in significant prognostic stage migration between early and advanced colon cancer. We aimed to study this effect with 5-year overall (OS) and disease-specific (DSS) survival. Methods: We analyzed 16,619 patients diagnosed with colon cancer diagnosed in 2004 and 2005, with a median followup of 71 months. We stratified each AJCC stage as either C0(normal) or C1(elevated) based on the serum CEA prior to first therapy. Results: C1-stage was independently associated with a 51% and 58% increased risk of overall (HR 1.51, 1.43-1.58, p<0.001) and disease-specific mortality (HR 1.58, 1.49-1.69, p<0.001). Significant stage overlap and migration was seen between C1-associated lower and C0-associated higher AJCC stages. For example, the 5-year OS for Stage IC1(68.3%, 63.9-72.2%; HR 2.0) was similar to IIA C0 (63.6%, 61.1-65.9%; HR 2.2) but significantly worse than IIA C0(76.4%, 74.8-77.9%; HR 1.4) and IIA C0(83.7%, 79.5-87.1%; HR 0.8). The 5-year DSS for Stage IC1 (91.7%, 88.7-94.0%; HR 2.6) was similar to II C0 (91.1%, 89.9-92.2%; HR 2.7), and II C0 (91.7%, 88.3-94.2%; HR 2.3), but Stage IIIA C0 was significantly better than IIA C0(84.7%, 82.7-86.6%; HR 4.5), IIB C0(69.5%, 61.1-76.4%; HR 10.3) or II C0(66.6%, 58.0-73.9%; HR 10.5). Multivariate analysis of non-metastatic colon cancers showed that 5-yr OS of N0C1 cancers (62.8%, 60.8-64.7%; HR 1.8) was worse than N1aC0(70.9%, 68.0-73.6%; HR 1.3) but similar to N1bC0 (64.7%, 61.5-67.7%; HR 1.6). Similarly the 5-year DSS of N1aC0(82.2%, 79.6-85.5; HR 2.4) was better than N1bC0 (62.2%, 58.3-66.0; HR 5.8). Conclusion: C1-stage identifies a subset of patients in each AJCC stage who suffer a prognostic effect that is similar to C0-stage patients and of the higher AJCC stages, resulting in significant stage overlap and migration between cancers. This difference in OS and DSS related to C-stage may have bearing on recommendations for those patients who would not routinely be offered systemic therapy, but may potentially benefit from it.

23 NSABP FC-6: Phase II Study to Determine Surgical Conversion Rate in Patients (pts) Receiving Neoadjuvant (NA) mFOLFOX7 plus Dose-escalating Cetuximab (C) for Unresectable K-RAS Wild-type (WT) Colorectal Cancer with Metastases (mCRC) Confined to the Liver L.D. Wagman,1,2 D.A. Geller,3 S.A. Jacobs,1,3 N.J. Petrelli,4 C.J. Allegro,5 M. Buyse,6 N. Wolmark,7 M.J. O’Connell,8 1. National Surgical Adjuvant Breast and Bowl Project (NSABP), and St Joseph Hospital, Orange, CA; 2. NSABP, and the University of Pittsburgh Medical Center, UPMC Liver Cancer Center, Pittsburgh, PA; 3. NSABP, and the University of Pittsburgh Cancer Institute, University of Pittsburgh School of Medicine, Pittsburgh, PA; 4. NSABP, and Christiana Care Health Service / Helen F. Graham Cancer Center, Newark, DE; 5. NSABP, and the University of Florida, Gainesville, FL; 6. International Drug Development Institute, Brussels, Belgium; 7. NSABP, and Allegheny Cancer Center at Allegheny General Hospital, Pittsburgh, PA; 8. NSABP, Pittsburgh, PA.

Based on pre-defined endpoints, the purpose of the FC-6 study is to determine the surgical conversion rate for liver-only metastatic CRC in KRAS WT pts treated with neoadjuvant mFOLFOX7 plus dose-escalating cetuximab. Eligibility: Untreated KRAS WT mCRC confined to liver. Initial unresectability was determined by an experienced surgical oncologist based on liver metastases that cannot be resected/ablated to R0 with >40% and/or 3 uninvolved segments of liver remaining. Prior adjuvant therapy was allowed if chemo-free interval >6 months. Treatment: Oxaliplatin 85 mg/m2 iv, leucovorin 400 mg/m2 iv, 5-FU 3000 mg/m2 iv continuous infusion over 46 hours, C 500 mg/m2 iv (C escalated by 100 mg/m2 q 2 wks to max dose of 800 mg/m2) on d 1, 15, 29, and 43 of each 8-wk cycle. Prophylactic doxycycline 100 mg po bid and application of topical emollient bid was required. A total of 3 cycles were planned, including pre-and post-operative cycles. Pts were evaluated after each cycle for resectability. Results: Of 20 pts enrolled, 2 had prior adjuvant therapy. 17 of 20 had at least one dose of escalated C (median dose intensity 632 mg/m2/2-wk). 18 of 20 underwent attempt at surgical resection; all pts were evaluable for toxicity. Grade 4 adverse events included neutropenia (1) and thrombocytopenia (1), sepsis and pulmonary embolism (1). Grade 3 rash occurred in 4 pts. Six, 8, and 4 pts were deemed resectable after cycles 1, 2, and 3 respectively. Four were found to be unresectable at surgery. Time from end of chemo to OR: 20-217d (median 35d). Best response to neoadjuvant chemotherapy: CR 1, PR 15, SD 3, and PROG 1. 14 of 20 had surgical R0 for conversion rate of 70%. Surgical-specific G3/4 morbidity occurred in 2 pts. Conclusion: mFOLFOX plus escalated C is highly active and resulted in excellent conversion rate with manageable toxicity. It is too early to project long-term survival. In selected KRAS WT pts with mCRC, mFOLFOX7 plus C therapy is worthy of investigation as a first-line option. Support: BMS
24 A Comparison of Rectal Cancer Clinical Practice Guidelines

Z.M. Abdelsattar,* S.L. Wong. Center for Healthcare Outcomes and Policy, University of Michigan, Ann Arbor, MI.

BACKGROUND: Delivery of high quality cancer care involves the explicit and judicious use of the best available evidence. Because the medical literature is so broad, clinicians often rely upon clinical practice guidelines (CPGs) to inform decision making. For rectal cancer, there are several CPGs available, but it is unknown which CPG is most reliable. We qualitatively and quantitatively compare rectal cancer CPGs. METHODS: Five rectal cancer CPGs were selected for qualitative and quantitative analysis. The most up-to-date versions were compared in the following 4 qualitative domains: development process, structure, content, and dissemination strategies. Quantitative comparison was based on the Appraisal of Guidelines Research & Evaluation (AGREE II), a validated CPG appraisal tool which assesses 6 domains: scope & purpose; stakeholder involvement; rigor of development; clarity & presentation; applicability; and editorial independence. Treatment recommendations were further analyzed to determine supporting levels of evidence and scientific agreement. RESULTS: Rectal cancer CPGs from ASCRS, CCO, ESMO, NCCN and NICE showed variation in all domains. The development processes included a systematic review of the literature in only 3 CPGs. Algorithms or clinical pathways were included in the structure of 3 CPGs. Citations ranged from 28 to 348 references, with randomized controlled trials representing a small proportion of citations (median 16%, range 15-39%). AGREE II scores were highly variable (Figure); for example, in the Rigor domain, scores ranged from 18.8 to 88.5%. Importantly, there were major disagreements in recommendations and in the interpretation of evidence. For example, some CPGs strongly recommend adjuvant therapy for Stage II/III patients who were previously treated with neoadjuvant therapy, while other CPGs were unable to make a recommendation in this regard. CONCLUSIONS: There is variation in development processes, evidence interpretation and recommendations between widely used rectal cancer CPGs. These differences mean that there is no comprehensive resource for the management of rectal cancer, which may pose challenges for physicians trying to deliver high quality evidence-based care.

25 The American Society of Peritoneal Surface Malignancies (ASPSM) Multi-institution Evaluation of the Peritoneal Surface Disease Severity Score (PSDSS) in 1,048 Patients with Colorectal Cancer with Peritoneal Carcinomatosis J. Esquivel,1* S. Sanchez-Garcia,2 W. Hicken.1 1. St Agnes Hospital, Baltimore, MD; 2. Hospital Universitario, Ciudad Real, Spain.

Introduction There exists a wide variety of classifications of mucinous appendiceal neoplasms (MAN). Most of them are based on the type of peritoneal dissemination and do not take into consideration the type or primary tumor or the burden of peritoneal disease. The Peritoneal Surface Disease Severity Score (PSDSS) was introduced as a basis to improve patient selection for current therapies in patients with colorectal cancer with peritoneal dissemination. Materials and methods We conducted a retrospective evaluation of 210 patients with MAN. The severity of their disease (PSDSS) was analyzed on a 3-point scale that included: 1) The primary appendiceal tumor, 2) The type of peritoneal dissemination, and 3) The burden of disease. Overall survival was analyzed according to 5 tiers of estimated disease severity based on the above parameters. Results There were 13, 59, 59, 40, and 39 patients with PSDSS 0, I, II, III, and IV respectively. One hundred and sixty five patients underwent cytoreductive surgery (CRS) and HIPEC. Overall survival was 78 months in this group with 5-yr survival of 100%, 82%, 28%, and 5% in patients with PSDSS II, I, III, and IV respectively (p=0.001). On multivariate analysis, female sex (HR 0.4), PSDSS stage (HR 2.4) and type of peritoneal dissemination (HR 5.6), were identified as independent predictors of survival. Conclusions The PSDSS appears to be an important prognostic indicator in patients with mucinous appendiceal neoplasms with or without peritoneal dissemination and may improve selection of patients for appropriate therapy from the time of diagnosis.

26 Evaluation of a New Staging Classification and a Peritoneal Surface Disease Severity Score (PSDSS) in 210 Patients with Mucinous Appendiceal Neoplasms with or without Peritoneal Dissemination J. Esquivel,1* S. Sanchez-Garcia,2 W. Hicken.1 1. St Agnes Hospital, Baltimore, MD; 2. Hospital Universitario, Ciudad Real, Spain.

The American Society of Peritoneal Surface Malignancies (ASPSM) conducted a retrospective review of 1,048 CRCPC patients. The PSDSS was evaluated on 3 specific criteria obtained from the literature in only 3 CPGs. Algorithms or clinical pathways were included in the structure of 3 CPGs. Citations ranged from 28 to 348 references, with randomized controlled trials representing a small proportion of citations (median 16%, range 15-39%). AGREE II scores were highly variable (Figure); for example, in the Rigor domain, scores ranged from 18.8 to 88.5%. Importantly, there were major disagreements in recommendations and in the interpretation of evidence. For example, some CPGs strongly recommend adjuvant therapy for Stage II/III patients who were previously treated with neoadjuvant therapy, while other CPGs were unable to make a recommendation in this regard. CONCLUSIONS: There is variation in development processes, evidence interpretation and recommendations between widely used rectal cancer CPGs. These differences mean that there is no comprehensive resource for the management of rectal cancer, which may pose challenges for physicians trying to deliver high quality evidence-based care.
postoperatively. Pt penetration (LA-ICP-MS) and IHC analysis (MVD, vessel maturation, hypoxia) of tumor are in progress. Results Tumor IPF was significantly lower in the Bevacizumab and Pazopanib pretreatment groups (Fig. 1). Interestingly, the hypoxic fraction (pO2 <5 mmHg) was also significantly increased in the Bevacizumab group. Mouse body weight, tumor size, and blood Pt concentration did not differ between groups. Conclusions Treatment with Bevacizumab and Pazopanib leads to a markedly reduced IPF in colorectal xenograft tumors. This effect may allow for deeper penetration and higher concentration of Oxaliplatin in peritoneal tumors. IHC and Pt analysis are currently ongoing and the results will be presented. Further research will explore therapy effect through a tumor growth delay study and microenvironment mapping with DCE-MRI.

Depletion of MDSC rescues removal of tumor metastases

Fig 1. Graph demonstrating decreased tumor metastases in MDSC-depleted mice following surgery.

28 Surgery-induced Expansion of Myeloid Derived Suppressor Cells Leads to Natural Killer Cell Dysfunction and Postoperative Metastases S.A. Bennett,1* L. Tai,2 A. Alkayyal,2 S. Sahi,2 J. Zhang,2 A.A. Ananth,3 C. Tanese de Souza,2 R.A. Auer.2 1. University of Ottawa, Ottawa, ON, Canada; 2. Ottawa Hospital Research Institute, Ottawa, ON, Canada.

Introduction: Levels of neurokininA (NKA), chromograninA (CgA), serotonin (5HT), and pancreastatin (PT) reflect tumor burden in neuroendocrine tumors (NET). Levels of NKA, CgA, and PT have been reported to correlate with outcomes, but these series included multiple primary NET sites and patients treated with or without surgery. We set out to determine whether preoperative (preop) levels of these markers correlate with survival in surgically-managed small bowel (SBNET) and pancreatic (PNET) neuroendocrine tumors. Methods: Clinical data were collected with IRB approval for patients undergoing surgery at one center. Progression-free (PFS) and overall survival (OS) were calculated from time of surgery. Median event times were estimated by Kaplan-Meier method. Preop laboratory values were log-transformed and tested as continuous and categorical (normal vs. elevated) variables for correlation with outcomes using a multivariate Cox model with adjustment for confounders. Results: Included were 80 SBNET and 73 PNET. Median follow-up was 3.3 years; 60.8% of cases had metastatic disease. SBNET had lower median PFS than PNET (2.6 vs. 5.6 years, p=0.02). Median OS was 10.5 years for PNET and not reached for SBNET. Preop NKA, CgA, PT, and 5HT levels were recorded in 52, 98, 109, and 115 patients. Preop NKA and CgA did not correlate with PFS or OS but PT was significantly correlated with PFS (p=0.03 and 0.09). Higher levels of CgA were associated with worse OS (p=0.001 and 0.04). After multivariate adjustment for primary tumor type and presence of metastases, PT, but not CgA, remained a significant independent predictor of worse PFS (p=0.01) and OS (p=0.03). 5-year PFS was 58% in patients with normal preop PT, vs. 16% in patients with elevated preop PT (Figure). Preop CgA correlated with PFS but not OS (p=0.03 and 0.09). PT most strongly correlated with outcomes, with higher levels predicting worse PFS and OS (p=0.0001 and 0.04). After multivariate adjustment for primary tumor type and presence of metastases, PT, but not CgA, remained a significant independent predictor of worse PFS (p=0.01) and OS (p=0.03). 5-year PFS was 58% in patients with normal preop PT, vs. 16% in patients with elevated preop PT (Figure). Conclusions: Higher preop PT, but not NKA, 5HT, or CgA, is significantly associated with worse PFS and OS in SBNET and PNET. This effect is independent of primary tumor site and presence of metastatic disease. Measurement of preop PT provides valuable prognostic information and identifies surgical patients at high risk of recurrence who could benefit most from novel or more aggressive therapies.
Incidence of Additional Malignancies in Patients with Pancreatic Neuroendocrine and Carcinoid Tumors

R. Kauffmann,1 L. Wang,2 S. Phillips,2 K. Idrees,3 E. Liu,7 N. Merchant,3 A. Parikh.1 1. City of Hope Cancer Center, Duarte, CA; 2. Vanderbilt University, Nashville, TN.

Background: It is known that the incidence of additional malignancies is higher in patients with a prior malignancy. Although the incidence of neuroendocrine tumors (NET), including both pancreatic neuroendocrine tumors (PNET) and carcinoid, is increasing, there have been no large, population-based studies to determine the incidence of and risk factors associated with additional malignancies in these patients. Methods: We determined the incidence of additional non-NET primary cancers that developed before or after a patient’s incident diagnosis of PNET or carcinoid (1978-2008) using the Surveillance, Epidemiology, and End Results (SEER) database and compared these to expected cancer rates among the general U.S. population. Using multivariable regression modeling, factors affecting the risk of an additional malignancy were analyzed. Results: A total of 9727 patients were identified within the SEER database (974 PNET and 8753 carcinoid); 2723 additional primary cancers were identified in 2508 patients. The most common sites of additional malignancies were colorectal (21.1%), prostate (14.5%), breast (13.3%), and lung (11.6%). In patients with PNET, the incidence of nearly all cancers was equal to or less than expected rates, while in patients with carcinoid, the observed incidence of nearly all malignancies, especially colon (4.3x higher) and gastric (4.1x higher) exceeded that of the general population. Age 70 vs. 50 (OR 2.08, 1.09-3.93 for PNET, OR 1.60, 1.32-1.93 for carcinoid), and early vs. late stage NET primary (OR 3.4, 1.61-7.14 for PNET, OR 2.3, 1.82-2.78 for carcinoid) were associated with an increased risk of additional malignancy after PNET or carcinoid. Conclusions: Approximately 25% of patients with NET develop an additional malignancy. Patients with carcinoid are at increased risk of additional malignancies, especially of the colon and stomach, while patients with PNET do not appear to be at increased risk. In patients with a history of carcinoid tumor, particularly older patients or those with localized disease, increased surveillance should be considered. Further studies investigating common etiologic pathways are also warranted.

Octreoscan versus PET for Neuroendocrine Tumor Staging: A Biological Approach

M.H. Squires,1* N. Adsay,2 D.M. Schuster,3 M.C. Russell,1 K. Cardona,1 J.M. Sarmiento,1 B. El-Rayes,1 C.A. Stanley,1 S.K. Maithel,1 D.A. Kooby.1 1. Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Pathology, Emory University, Atlanta, GA; 3. Division of Nuclear Medicine, Department of Radiology and Imaging Sciences, Emory University, Atlanta, GA.

Background: Clinicians may order Octreoscan or positron emission tomography (PET) scan for staging patients with neuroendocrine tumors (NET). Octreoscan identifies tumors by somatostatin receptor targeting, while PET is based on tumor glucose metabolism. We correlated the results of each nuclear imaging modality with pathologic tumor features of NET to clarify which test offers greater sensitivity. Methods: We identified all patients diagnosed with NET of gut or pancreatic origin who underwent nuclear imaging staging by Octreoscan versus PET. Results: Nuclear imaging and pathology results were identified for 153 patients. Of these, 131 patients underwent Octreo-scan, 43 underwent PET, and 21 patients underwent both. Overall sensitivity of Octreoscan versus PET for NET detection was similar (77% vs. 72%; p=NS). For well-differentiated NET, Octreoscan (n=124) demonstrated sensitivity of 82%, versus only 60% (p=0.08) for PET (n=30). For poorly-differentiated NET, Octreoscan (n=7) proved significantly less sensitive than PET (n=13), (57% vs. 100%; p=0.02). The sensitivity of Octreoscan versus PET varied similarly when analyzed by WHO tumor grade: Grade 1 (80% vs. 100%; p=NS), and Grade 2 and 3 (85% vs. 86%; p=NS), and Grade 3 (57% vs. 100%; p=0.02). Conclusion: Tumor differentiation can be used to guide selection of nuclear imaging modalities for staging gastrointestinal and pancreatic neuroendocrine tumors (NET). Octreoscan appears more sensitive than PET for well-differentiated tumors.
33 Risk Factors Associated with Complications following Adrenal Surgery
A. Hauch,* Z. Al-Qarayshi, D. Slakey, E. Kandil. Surgery, Tulane University School of Medicine, New Orleans, LA.

Background: Surgeon experience has been shown to result in better outcomes following a variety of advanced operations. Less information is available regarding adrenal surgery. We sought to compare the outcomes following adrenalectomy for a variety of indications and to determine the effect of surgeon's volume. Methods: Cross-sectional analysis using ICD-9 codes included in the Nationwide Inpatient Sample (NIS) from 1998 to 2013 to identify all adult patients who underwent adrenalectomy. Logistic regression models were used to control for confounders and to test for interaction between surgeon volume and adrenal procedures. Results: 7,829 adrenalectomies were included in this analysis. Rate of complication for low and medium-low volume surgeons was 18.5% and 18.2% respectively, and were significantly higher when compared to high volume surgeons (11.6%, p < 0.001). Bilateral adrenalectomies accounted for only 2.9% of total procedures. Risk of complication was 23.4% while unilateral procedures had a 15.0% risk (OR: 2.15, 95% CI: 1.33, 3.48). Following unilateral surgery, higher rate of complication occurred among low and low-median volume surgeons compared to the high volume group (p = 0.001). Malignancy was associated with higher risk of complication (OR: 1.66, 95% CI: 1.35, 2.05). Low and medium-volume surgeons had significantly higher risk of complications following operations for non-malignant lesions (17.8% and 15.2% of complications respectively) compared to high volume surgeons (10.4%). Low-medium and intermediate volume surgeons had higher risk for malignant lesions (28.5%, and 24.6% respectively) compared to the high volume group (17.0%, p < 0.05 for both groups). LOS was shorter for high volume surgeons compared to other groups (6.6 days vs. 6.10 days for low volume, p = 0.01). Similarly, charges were less for high volume surgeons ($32,337 vs. $45,190 for low volume, p < 0.01). Conclusions: Low-volume surgeons have higher complications and are associated with increased risk of postoperative complications. LOS and charges were significantly less following low-volume surgery.

34 Initial Recurrence Patterns and Survival in Patients Undergoing Curative Resection for Adrenal Cortical Carcinoma: The Prognostic Value of Local Recurrence

Introduction: Adrenal cortical carcinoma (ACC) is a rare tumor with high rates of local and distant recurrence. This study describes initial recurrence patterns and subsequent survival of patients with resected ACC. Methods: Patients were identified from a prospective adrenal resection database. Those undergoing initial curative resection at a single institution were retrospectively reviewed. Imaging studies and/or biopsy identified initial recurrence. Local recurrences were defined as those in the adrenal bed/retroperitoneum. Results: A total of 87 patients were resected with curative intent from 1975-2013. The overall median disease-specific survival was 67 months with a median follow-up of 44 months. There were 49 (56%) recurrences. Initial recurrences were local only in 17 (20%) patients and distant in 32 (37%) patients. Distant metastases were identified in the lung (47%), liver (22%), bone (12%), peritoneum (6%) and other (13%). When compared by initial recurrence patterns (local only vs distant) there was no difference in age, gender, operative approach, tumor size, margin positivity, or Weiss criteria. However, median recurrence-free survival was significantly less in the local recurrence group (8 months) as compared to those with distant metastases (18 months, hazard ratio for local recurrence 1.8, 95% CI: 1.1-4.4, p = 0.029). Additionally, median disease-specific survival was shorter in the local recurrence group (38 months) as compared to the distant metastasis group (100 months, hazard ratio for local recurrence 2.2, 95% CI: 1.3-6, p < 0.01, Figure 1). Conclusions. Patients that have undergone curative resection for ACC are at high risk for local recurrence and distant metastases. Initial local recurrence is a prognostic factor for aggressive disease.

35 The Bethesda System for Reporting Thyroid Cytopathology: A Single Center Experience over Five Years
C.M. Kiernan,* J.T. Broome, C.C. Solorzano. General Surgery, Vanderbilt University, Nashville, TN.

Background: The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) was developed to refine fine needle aspiration (FNA) cytology definitions, improve communication and clinical management. This study evaluates the impact of the BSRTC five years after its adoption at a single institution. Methods: A total of 1625 patients undergoing thyroidectomy for all indications in the pre-BSRTC era of 2000-2004 were compared to post-BSRTC era of 2005-2009. Conclusions: Since the adoption of the BSRTC at our institution, the rate of thyroid cancer at the time of surgery has not changed. The rate of thyroid cancer in suspicious for cancer FNA increased from 44% to 65% (p=0.07) but remained stable for other categories. The AUS/FLUS malignancy rate in patients undergoing thyroidectomy was 15%. The rate of cancer in suspicious for cancer FNA lesions increased significantly (p<0.05). In group-2, there were more indeterminate FNA diagnoses overall (30% vs. 43%, p=0.001). The rate of cancer in suspicious for cancer FNA lesions increased from 44% to 65% (p=0.07) but remained stable for other categories. The AUS/FLUS malignancy rate in patients undergoing thyroidectomy was 15%. The overall rate of thyroid malignancy was 30% and did not change between time periods. Conclusions: Since the adoption of the BSRTC at our institution, the rate of thyroid cancer at the time of surgery has not changed. Although the proportion of indeterminate FNA was increased, the rate of cancer in suspicious for cancer FNA decreased significantly (p<0.05). In group-2, there were more indeterminate FNA diagnoses overall (30% vs. 43%, p=0.001). The rate of cancer in suspicious for cancer FNA lesions increased from 44% to 65% (p=0.07) but remained stable for other categories. The AUS/FLUS malignancy rate in patients undergoing thyroidectomy was 15%. The overall rate of thyroid malignancy was 30% and did not change between time periods. Conclusions: Since the adoption of the BSRTC at our institution, the rate of thyroid cancer at the time of surgery has not changed. Although the proportion of indeterminate FNA was increased, the rate of cancer in suspicious for cancer FNA decreased significantly (p<0.05).
The Use of Fine Needle Aspiration Thyroglobulin Washout for Detecting Metastatic Disease in Patients with Recurrent Papillary Thyroid Cancer


Objective: For many years the standard of care for the workup of cervical lymph nodes suspicious for metastasis has been fine-needle aspiration (FNA). FNA- Thyroglobulin (TG) washout measurement has recently been proven to be useful adjunct in the management of patients with suspicious lymphadenopathy. We hypothesize that surgeon-performed ultrasound using TG washout for suspicious lymphadenopathy would increase the accuracy of diagnosing metastatic disease in patients with recurrent papillary thyroid cancer.

Methods: This is a retrospective study of prospectively collected database for patients with thyroid cancer who underwent preoperative FNA-cytology and FNA-TG washout followed by selective neck dissection by one surgeon at an academic institution. Results of both preoperative FNA cytology and FNA-TG washout were then correlated with the final pathology results of the dissected lymph nodes. Data was then collected to compare the sensitivity and specificity of FNA-cytology alone to that of FNA-cytology in adjunct to FNA-TG.

Results: Fifty-three lymph nodes from 45 patients were included in this study. Twenty-two modified radical neck dissection (MRND), 19 had a central lymph node dissection (CLND), and 4 had a MRND in addition to CLND. The average serum thyroglobulin is 62.28 +/- 13.76ng/ml, however, the average FNA-TG washout levels was 2349.5 +/- 957.73ng/ml. The FNA-cytology alone showed a sensitivity of 80.49%, specificity of 81.82% with a negative predictive value (NPV) of 52.94%. In contrast, FNA-TG had a sensitivity of 100%, specificity of 83.33% with a NPV of 100%. FNA- TG washout led to change in the plan of surgical management in eight patients (15%) with negative FNA-cytology. Combination of the FNA-cytology with FNA-TG revealed a sensitivity of 100%, specificity of 100% with a NPV of 100%. Conclusion: Surgeon Performed FNA-TG washout increases the diagnostic accuracy in detecting metastatic disease in patients with recurrent papillary thyroid cancer. Routine performance of US-guided FNA-TG as an adjunct to FNA-cytology should be considered in patients with suspicious metastatic lymphadenopathy.

Development of an Index to Predict Single Gland Parathyroid Disease and Selectively Eliminate Intraoperative Parathyroid Hormone Testing

M. Kukar,4 E. Cho,1 T. Platz,2 K. Attwood,2 A. Abdelhalmim,3 S. Kumar,3 W.G. Cance.1 1. Roswell Park Cancer Institute, Surgical Oncology, Buffalo, NY; 2. Roswell Park Cancer Institute, Bio-statistics, Buffalo, NY; 3. Roswell Park Cancer Institute, Radiology, Buffalo, NY.

Introduction: Assessing intraoperative parathyroid hormone (iPTH) helps confirm single gland disease during minimally invasive parathyroidectomy. With improved preoperative localization, this study may not be necessary.

Objective: To create a predictive index using clinicopathologic, biochemical and imaging characteristics to accurately predict single gland disease and avoid routine use of iPTH.

Methods: Our study cohort included 150 consecutive patients with primary hyperparathyroidism (pHPT) who underwent surgery at our institution between January 2011 and March 2013. All patients underwent four dimensional computerized tomography (4DCT), reviewed by a single blinded neuroradiologist. Using prospectively collected data, a prognostic model was developed. First, the sample was stratified by single versus multiple gland disease and logistic regression models were used to evaluate discriminatory ability. 4DCT was identified as the most significant predictor of single gland disease. Second, within the 4DCT positive patients, logistic regression models were used to evaluate each variable’s utility. Preoperative calcium added the most prognostic utility. The Youden index criterion was then used to identify the optimal calcium threshold. Results: Stratifying by single gland versus multiple gland disease yielded a slight difference in outcomes for pHPT patients. On univariate analysis, cured patients had higher preoperative calcium levels (10.8 vs. 10.6 mg/dl, p=0.010) than patients who failed operative intervention. Conclusion: Preoperative calcium added the most prognostic utility. The index was applied to the following 30 patients undergoing surgery for primary pHPT and yielded a 100% PPV (87.7-100.0). Conclusions: This predictive index can accurately determine single gland parathyroid disease and avoid the use of routine iPTH testing.

38
What Can We Learn from Failed Parathyroid Operations?


Introduction: Increasing emphasis is placed on the role of imaging in the surgical management of primary hyperparathyroidism (pHPT). We studied our large series of parathyroidectomies to identify factors associated with failed operative intervention with attention to preoperative imaging results.

Methods: We performed a retrospective cohort study of all consecutive patients who underwent initial parathyroidectomy for pHPT with intraoperative parathyroid hormone (PHT) monitoring (2002-2012). Characteristics examined included age, gender, preoperative serum calcium and PHT level, prior thyroid surgery, preoperative localization by sestamibi or ultrasound, histopathology, size and weight of resected gland, and ectopic gland location. The primary outcome was biochemical cure. Univariate analysis was performed using the rank-sum test, Student’s t-test or Fisher’s exact test, as appropriate. A multivariable regression model was developed. Results: 1809 consecutive patients met inclusion criteria; the overall cure rate was 98.5%. On univariate analysis cured patients had higher preoperative calcium levels (10.8 vs. 10.6 mg/dl, p=0.010) than patients who failed operative intervention (Table I). Cured patients also had a higher proportion of single adenomas (82.8 vs. 32.1%, p=0.001), and a lower rate of hyperplasia (8.2 vs. 25.0%, p=0.007). Median gland size and weight were greater in cured patients (1.5 vs. 1.0 cm, p<0.001; 400.5 vs. 136 mg, p=0.001). Analysis of the use of imaging showed that rates of sestamibi (94.3 vs. 96.4%, p=1.000) and ultrasound (70.5 vs. 64.3%, p=0.532) were similar between cohorts. Cured patients were more likely to have gland localization by sestamibi (53.3 vs. 25.0%, p=0.001). Non-localized patients had a high cure rate (97.3 vs. 99.3%). On multivariate analysis, the only preoperative factor associated with a greater likelihood of cure was localization by sestamibi (OR=4.3, p=0.022). Conclusion: Positive sestamibi scan was associated with a slightly higher, yet clinically insignificant difference in cure rate. As only 2.7% of non-localized patients failed surgical intervention, the decision to operate should be based upon clinical indications and not be influenced by localization studies.

<table>
<thead>
<tr>
<th>Table 1: Parathyroid operative failures, univariate analysis of patients by operative outcome</th>
<th>Total (1809)</th>
<th>Cure (1712)</th>
<th>No cure (28)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean (SD))</td>
<td>56.5 (13.1)</td>
<td>58.5 (13.1)</td>
<td>55.1 (13.3)</td>
<td>0.796</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female (%)</td>
<td>1093 (77%)</td>
<td>1370 (73%)</td>
<td>73 (26%)</td>
<td>0.654</td>
</tr>
<tr>
<td>Male (%)</td>
<td>416 (23.7%)</td>
<td>405 (22.7%)</td>
<td>57 (17.3%)</td>
<td>0.654</td>
</tr>
<tr>
<td>Redo neck (%)</td>
<td>26 (1.4%)</td>
<td>25 (1.4%)</td>
<td>1 (0.4%)</td>
<td>0.335</td>
</tr>
<tr>
<td>Imaging</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized (%)</td>
<td>1227 (62.3%)</td>
<td>1110 (60.7%)</td>
<td>117 (40.3%)</td>
<td>0.017</td>
</tr>
<tr>
<td>Lymph node dissection (%)</td>
<td>700 (34.6%)</td>
<td>1070 (50.4%)</td>
<td>27 (9.6%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Localized by sestamibi (%)</td>
<td>957 (52.9%)</td>
<td>950 (43.9%)</td>
<td>7 (25.0%)</td>
<td>0.661</td>
</tr>
<tr>
<td>Ultrasound performed (%)</td>
<td>1224 (67.4%)</td>
<td>1256 (57.5%)</td>
<td>68 (14.3%)</td>
<td>0.532</td>
</tr>
<tr>
<td>Ultrasound localized (%)</td>
<td>483 (27.6%)</td>
<td>476 (26.0%)</td>
<td>7 (17.6%)</td>
<td>0.476</td>
</tr>
<tr>
<td>Ultrasound non-localized (%)</td>
<td>744 (41.3%)</td>
<td>731 (41.6%)</td>
<td>13 (22.0%)</td>
<td>0.648</td>
</tr>
<tr>
<td>Pre-op Calcium, mg/dl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (QR)</td>
<td>10.6 (9.14-11.2)</td>
<td>10.6 (9.14-11.2)</td>
<td>10.6 (9.14-11.2)</td>
<td>0.010</td>
</tr>
<tr>
<td>Pre-op PTH, pg/ml</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (QR)</td>
<td>10 (7.15-13.5)</td>
<td>10 (7.15-13.5)</td>
<td>10 (7.15-13.5)</td>
<td>0.005</td>
</tr>
<tr>
<td>Pathology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parathyroid adenoma (%)</td>
<td>1483 (82.0%)</td>
<td>1474 (68.2%)</td>
<td>9 (25.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Double Adenoma (%)</td>
<td>160 (9.8%)</td>
<td>156 (6.8%)</td>
<td>4 (14.3%)</td>
<td>0.304</td>
</tr>
<tr>
<td>Hyperplasia (%)</td>
<td>156 (8.5%)</td>
<td>146 (6.8%)</td>
<td>10 (25.0%)</td>
<td>0.0027</td>
</tr>
<tr>
<td>Negative exploration (%)</td>
<td>13 (7.0%)</td>
<td>5 (3.0%)</td>
<td>8 (25.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gland size, cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (QR)</td>
<td>1.5 (1.1-2.6)</td>
<td>1.5 (1.1-2.6)</td>
<td>1.6 (1.1-2.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Gland weight, mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (QR)</td>
<td>395 (199-649)</td>
<td>400.5 (205-650)</td>
<td>136 (91-271)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ectopic gland (%)</td>
<td>96 (5.4%)</td>
<td>97 (5.4%)</td>
<td>2 (7.1%)</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Background: The molecular alterations that drive tumorigenesis in intrahepatic cholangiocarcinoma (ICC) remain poorly defined. We sought to define the incidence and prognostic significance of mutations associated with ICC among patients undergoing surgical resection. Methods: 138 patients who underwent resection at 6 centers in the United States and Europe were included. Mutational profiling was performed using nucleic acids that were extracted from resected ICC tumor specimens; mutations were identified using a multiplexed mutational profiling platform. The frequency of mutations was ascertained and the impact on outcome determined. Results: Most patients had a solitary tumor (82%) and median tumor size was 6.0 cm. Most patients had R0 resection (89%); 19% had N1 disease, while 15% had microvascular invasion. A minority received adjuvant therapy (30%). The majority (55%) of patients had no genetic mutation identified. Among the 62 (45%) patients with a genetic mutation, only a small number of gene mutations were identified with a frequency of >5%: IDH1 (17.4%), KRAS (8.7%), BRAF (5.8%), PIK3CA (5.1%). In contrast, other genetic mutations were identified in very low frequency: IDH2 (3.6%), NRAS (3.6%), TP53 (2.2%), MAP2K1 (1.5%), CTNNB1 (0.7%), and Pten (0.7%). Approximately 7% of IDH1-mutant tumors were associated with a concurrent PIK3CA gene mutation, and to a much lower extent, a mutation in MAP2K1 (2%). No concurrent mutations in IDH1 and KRAS were noted. Compared with ICC tumors that had no identified mutation, IDH1-mutant tumors were more often bilateral (OR 3.46), while KRAS-mutant tumors were more likely to be associated with perineural invasion (OR 5.72) (both P<0.05). While clinicopathological features such as tumor number and nodal status were associated with survival, no specific mutation was associated with prognosis. Conclusions: Most patients with resected ICC had no somatic mutation identified on multiplexed mutational profiling. IDH1 and KRAS were the most common mutations noted. While certain mutations were associated with ICC clinicopathological features, mutational status did not seemingly impact long-term prognosis.


INTRODUCTION: We tested the safety of genetically modified "designer" T cell (dTc) hepatic artery infusions (HAI) for patients with CEA+ liver metastases (LM). We hypothesized that dTc HAI would limit systemic toxicity and improve delivery to LM. METHODS: Eight patients with unresectable, progressing LM were enrolled and 6 completed the protocol. The first 3 patients received anti-CEA dTc HAI as an intraportal dose escalation (1e8, 1e9, and 1e10 without IL2). The last 3 patients received 3 dTc doses (1e10) with IL2 by outpatient continuous infusion. Responses were assessed by MRI and PET. Liver biopsies were performed to score necrosis and fibrosis. RESULTS: Five patients presented with colorectal LM and a single patient with ampullary LM. The median age was 54.5 (51-66), 4 were men, and subjects received an average of 2.8 prior chemotherapy regimens. Three patients presented with synchronous LM, the average size of the largest LM was 8.9 cm (1.7-14.4), and 4 had more than 10 LM. HAI of dTc was well tolerated, with 1.7 grade 3 adverse events (AE) per patient. There were no grade 3 or higher hepatobiliary AEs and no grade 4/5 AEs. DTC were not detected in the peripheral blood of any patient and biopsies confirmed dTc within LM. Five patients died of progressive disease and 1 patient is alive with disease at 11 months. The median survival from enrollment was 4.5 months (range, 2-11). Radiographic progression was noted in 4 patients, 1 patient had stable disease, and 1 patient did not obtain follow up imaging. An increase in tumor necrosis or fibrosis was noted in 4 patients. The patients who did not receive IL2 had a mean CEA increase of 63±125% from baseline. In contrast, those who received IL2 + HAI dTc demonstrated a mean decrease in CEA of 37±9% (p=0.10). CONCLUSIONS: HAI of anti-CEA dTc were well tolerated in heavily pre-treated patients with unresectable LM. Clinical activity was demonstrated serologically in patients who received IL2 with dTc, although most patients progressed by mRECIST. Further clinical testing is warranted to determine the efficacy of dTc HAI for LM. Sponsored by the SSO Clinical Investigator Award.


Despite improved outcomes in patients undergoing hepatic colorectal metastasectomy, little is known about the biology of those who are cured or relapse early. We sought to determine the impact of MAPK mutation status on tumor phenotype and survival in patients undergoing curative hepatectomy. K/NRAS, BRAF, PIK3CA and p53 mutation analysis was performed using Sequenom genotyping assay and Sanger sequencing on 165 surgical specimens following R0 hepatic metastasectomy. Clinical characteristics and survival data were retrospectively analyzed from a prospective database and correlated with mutation status. We identified 69 (42%) K/NRAS (55 in exon 2, 8 in exon 3 and 6 in exon 4), 5 (3%) BRAF, 18 (11%) PIK3CA and 100 (61%) p53 mutations in resected specimens. Preoperative characteristics and operative details did not differ significantly between various mutation subsets. There was no impact of p53 or PIK3CA mutation on survival, however, BRAF mutant patients had significantly shorter disease free survival compared to wild-type (median = 3 vs 14 mos, p=0.05). Patients with K/NRAS exon 2 mutations had similar disease free survival to wild-type patients (12 vs 14 mos, p=NS) while exon 3 and exon 4 mutations were associated with significantly shorter (5 mos) and longer (not reached) survivals, respectively (figure 1)(p<0.05). When assessing phenotype, tumors with K/NRAS exon 4 mutations tended to be large (mean = 6.8cm) and few (mean number = 2) while exon 3 mutated tumors were small (mean = 3.3cm) and numerous (mean number = 4.7) (p<0.05). Time from resection of primary to liver metastases (disease free interval) also varied significantly with wild-type, K/NRAS exon 2, 3, and 4 mutations recurring at a median time of 8, 7, 4, and 24 months, respectively (p<0.05). Using gene mutation analysis we identified biologically unique subsets of colorectal liver metastases associated with very good (K/NRAS exon 4) and poor (BRAF and K/NRAS exon 3) oncologic outcomes. The impact of mutation status on survival as well as phenotypic differences such as size, multiplicity and disease free interval warrants further investigation.
role in the progression of LM is poorly defined. Therefore, we attempted to define the features of HBC in the setting of LM. Methods: We used a murine model of CEA+ colorectal LM to study the effects of the tumor microenvironment on HBC. Tumor cells were injected into the portal circulation of C57BL/6 mice to establish LM, and HBC were analyzed after two weeks. Results: HBC comprised 46±10% of lymphocytes in normal livers, and their absolute numbers were similar in mice with LM (see table). A significant increase (2.2-fold, p=0.04) in the frequency of IgMloIgDhi mature B cells was observed in mice with LM, which was associated with an increase in HBC proliferation in response to TLR4, TLR9, or BCR stimulation. HBC exhibited significant down-regulation MHCII and CD80 (2.5-fold, p=0.01, 6-fold, p=0.0006, respectively) following in vivo exposure to tumor. HBC downregulation of CD80 and MHCII was reversible, as these markers recovered to normal levels during ex vivo culture. HBC from tumor-bearing livers that were fixed to maintain their in vivo state significantly less CD4+ T cell proliferation compared to normal HBC. We implicated myeloid derived suppressor cells (MDSC) and liver T cells derived from tumor-bearing livers as mediators of HBC downmodulation of CD80 and MHCII, respectively. MDSC induced CD80 downregulation was dependent on direct contact with HBC. Conclusion: The immune function of HBC may be compromised in the setting of LM as evidenced by the diminished expression of MHCII and CD80. Targeting of MDSC and liver T cells represents a potential strategy for rescuing HBC antitumor function.

Phenotype of HBC in tumor-bearing livers compared to normal HBC

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NORMAL (n=8)</th>
<th>LM (n=9)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall HBC (%)</td>
<td>46±10%</td>
<td>29±5%</td>
<td>0.04</td>
</tr>
<tr>
<td>Absolute HBC number</td>
<td>3.6±1.1x10^5</td>
<td>5.5±1.9x10^5</td>
<td>0.4</td>
</tr>
<tr>
<td>Mature HBC (%)</td>
<td>24.0±1.5</td>
<td>53.3±9.2</td>
<td>0.03</td>
</tr>
<tr>
<td>CD69± (%)</td>
<td>20.0±6.7</td>
<td>3.4±5.0</td>
<td>0.0006</td>
</tr>
<tr>
<td>MHCII± (%)</td>
<td>80.0±21.5</td>
<td>31.3±11.6</td>
<td>0.01</td>
</tr>
<tr>
<td>T cell stimulation (%)</td>
<td>12±2.7</td>
<td>5.3±1.9</td>
<td>0.002</td>
</tr>
</tbody>
</table>

HBC=hepatic B cells; LM=liver metastases.

43 Minnelide as a Novel Therapy for Hepatocellular Cancer


Introduction Sorafenib is the only FDA approved therapy for metastatic hepatocellular carcinoma (HCC) even though it provides minimal survival benefit. In this study, we examined Minnelide (and its metabolite, triptolide) as a novel therapy for HCC, alone and in combination with sorafenib, using in vitro and in vivo models. Methods HuH7 and PLC cells were treated with triptolide (50 nM), sorafenib [1.25 uM (HuH7) or 2.5 uM (PLC)] or combination (C) of both. Cell viability assay (WST-8, Dojindo), caspase 3/7 activation (Promega), and proliferation assay (ECIS, Applied BioPhysics) were performed. For in vivo studies, forty mice were implanted with subcutaneous HuH7 tumors and divided into four treatment groups (n=10): saline control, sorafenib 10 mg/kg PO daily (S), Minnelide (a produg of triptolide) 0.21 mg/kg IP daily (M), and combination of both (C). Treatment began 7 days after implantation. Tumor volumes were assessed weekly. After 2 weeks, 7/10 control mice were crossed over to treatment with combination therapy. Results In HuH7 cells, the combination of triptolide and sorafenib was superior to either drug alone in inducing caspase 3/7 activity (T=670%, S=208%, C=1534% at 48 hours), and decreasing viability (T=45%, S=38%, C=18% at 48 hours) and proliferation (T=90%, S=90%, C=75% at 24 hours). Similarly in the more resistant PLC cells, caspase 3/7 activity was (T=443%, S=254%, C=1263%), and cell viability was (T=52%, S=58%, C=41%) at 48 hours. Figure 1 shows tumor progression in our mouse model. At 2 weeks, efficacy of Minnelide was similar to sorafenib while combination therapy was superior to either drug alone, with tumor growth inhibition rates of S=59%, M=84%, and C=93%. Control tumor volumes were increased 9-fold. Subsequently, 7/10 control mice were crossed over to combination therapy. At 6 weeks, crossover mice had similar tumor control as combination therapy mice. All control mice expired by day 17. But all one crossover mouse survived until day 42 (experiment end). Conclusion Minnelide is a novel therapy for HCC with similar efficacy to sorafenib in vitro and in vivo. Combination therapy is significantly more effective than either drug alone and may be a new option for treatment of HCC.
45 Combination of Bavituximab and Sorafenib Inhibits HCC Growth: Results of Preclinical Data and a Phase I Study A. Yopp,* R. Brecken, X. Cheng, L. Li, P. Thorpe, X. Huang. UT Southwestern Medical Center, Dallas, TX.

HCC, the fastest growing cause of cancer deaths, presents at advanced stage and few therapy options. Bavituximab is a novel antibody targeting phos- phatidylserine (PS), a membrane lipid externalized on cells promoting immune tolerance and immunosuppression. We hypothesize that sorafenib will upreg- ulate PS exposure on HCC tumors providing targets for bavituximab shifting an immunosuppressive to immunoreactive milieu. In addition, we will demon- strate combination bavituximab and sorafenib can be given safely in patients with advanced HCC. Methods: Immunocompromised mice with orthotopic human HCC tumors (Huh7, C3A, or LC/PRF/5), were treated with sorafenib and tumors harvested and analyzed by IHC for vascular endothelium (anti-CD31) and PS exposure (2aG4, murine bavituximab analogue). Efficacy of sorafenib or 2aG4 or combination was evaluated in mice bearing LC/PRF/5 tumors. Tumor volume measured and microvascular density (anti-CD31) and macrophage recruitment and phenotype determined by IHC. In the phase I study, patients with advanced HCC and Child-Pugh A received escalating doses of bavituximab weekly (0.3, 1.0, and 3.0 mg/kg) and sorafenib 400 mg bid for 28 days. Results: Sorafenib treatment of HCC xenografts increased PS exposure in 1.7-2.9 fold compared to control in each model tested (p<0.01). Sorafenib and 2aG4 inhibited tumors more than single agent therapy (p<0.01). MVD was reduced 30% in combination therapy compared to sorafenib alone (p<0.01). Combination therapy increased M1 (pro-inflammatory) macrophages and sorafenib alone increased M2 (anti-inflammatory) macrophages. Phase I trial demonstrated maximum tolerated bavituximab dose of 3.0 mg/kg weekly and 400 mg BID sorafenib with no dose limiting toxicities. Toxicities were related to sorafenib and included hand-foot syndrome (22% grade II), fatigue (33% grade I) and anorexia (22% grade I). Conclusions: Sorafenib increases PS exposure on HCC vascular endothelium and when given in combination with the murine bavituximab analogue inhibits tumor growth greater than sorafenib alone by reactivating innate immunity. Bavituximab and sorafenib can be given safely in patients with advanced HCC.


Introduction: Hepatocellular carcinoma (HCC) is a devastating malignancy in which imperfect imaging plays a primary role in diagnosis. Preoperative assessment for hepatectomy or orthotopic liver transplantation based on sub- optimal imaging negatively impacts patient outcome. Furthermore, small, inde- terminate lesions can lead to incorrect diagnosis, staging or delayed treat- ment. Glypican-3 (GPC3) is an HCC-specific cell surface proteoglycan over-expressed in the majority of HCCs. This study presents the first use of a Zirconium-89 (89Zr) conjugated monoclonal antibody against GPC3 (αGPC3) for intrahepatic tumor localization using micro positron emission tomography (micro-PET). Methods: Radioactive 89Zr was conjugated to homegrown αGPC3 using the chelator p-isothiocyanato-benzyldeferoxamine. In vitro binding, in vivo biodistribution and micro-PET studies using this conjugate were performed in GPC3-expressing HepG2 and GPC3 non-expressing HLF cells and RH7777 orthotopic xenografts established in athymic nude mice. Tumor size was evaluated by histology. Results: 89Zr-αGPC3 demonstrated highly sensitive, antibody-dependent and antigen-specific tumor binding. HepG2 liver tumors exhibited high peak micro-PET signal (83.6± 86.5%ID/g) compared with background liver (27.5± 1.6%ID/g). Tumor-to-liver contrast ratio was high and peaked at 32.5 on day 3. Day 7 radioactivity was still sub- stantial in HepG2 tumors (466.3 ± 87.5%ID/g) compared with control RH7777 tumors (3.8%±1.2%ID/g, p<0.01) indicating antigen-specificity of 89Zr-αGPC3. Animals treated with heat-denatured 89Zr-αGPC3 or co-injected with an excess of unlabeled αGPC3 as a competition assay demonstrated markedly lower tumor uptake (3.9 ± 1.3%ID/g, 29.0 ± 8.6%ID/g, respectively) confirming antibody-dependency. The largest tumor measured 3.8mm on histo- logic examination. Conclusions: This study demonstrates the feasibility of utilizing an 89Zr-αGPC3 PET imaging probe to image minute HCCs in the liver with high specificity. Clarifying the identify of conventionally indeterminate liver lesions would enhance the accuracy of the surgeon’s preoperative eval- uation and therefore warrants further investigation for clinical translation.
FOLFRINOX +/- chemoradiation between 7/10-8/13. Results: After receiving neoadjuvant treatment with FOLFRINOX 24 patients were explored and 20 also received chemoradiation. Pre-operative post-treatment imaging deemed 13/24 patients locally advanced and 4/24 patients borderline by a senior surgeon. Imaging demonstrated persistent arterial involvement in 15/16 patients. A decrease in CA 19-9 occurred in all patients, with normalization in 12 patients. Sixteen patients underwent pancreaticoduodenectomy, 4 underwent distal pancreatectomy, 2 were deemed unresectable due to local invasion and 2 had metastatic disease. Two patients underwent venous resections. Grade 1/2 complications were seen in 20% of patients and grade 3/4 in 5%. No 90-day post-operative deaths occurred. No patients developed pancreatic fistulas or required re-exploration. Median length of stay was 6 days and rate of readmission was 15%. An R0 resection was achieved in 90% of patients (18/20). Moderate to extensive histologic treatment effect was seen in 55% of the patients. Only 45% of patients had positive lymph nodes, despite a median lymph node retrieval of 20. Conclusion: Resection following neoadjuvant FOLFRINOX with or without chemoradiation was not associated with an increase in peri-operative mortality, median length of stay or post-operative complications. Negative margins were accomplished in the majority of patients, despite imaging suggesting an unresectable or borderline tumor.

48
Liver Resection for Metastatic Disease after Y90 Radioembolization: A Case Series with Longterm Follow-up L. Henry, R. Hostetter, B. Ressler, I. Bowser, M. Yan, H. Vaghefi, J. Abad, S. Gines, R.E. Schwwarz, 1. Surgical Oncology, IU Health, Goshen Center for Cancer Care, Goshen, IN; 2. Florida International University, North Miami Beach, FL.

Introduction: There are few reports of liver resections for metastatic disease in patients previously treated with Y-90 radioembolization (RE), and long-term outcome data are sparse. We reviewed our center’s experience in patients undergoing hepatectomy after RE. Methods: A retrospective chart review of patients undergoing RE from 2004 to 2011 was performed. Demographic, clinicopathologic, operative, and long-term outcomes variables were collected. A review of tumor necrosis and normal liver tissue grading of fibrosis and inflammation after resection was performed. Data are expressed as medians and ranges. Results: RE was delivered to 106 patients with primary and metastatic disease in the liver, of whom 9 (6 males, 3 females, median age 54 years (47-76)) with metastatic disease (colorectal: n=4, neuroendocrine: n=3, GIST: n=1, cervical: n=1) underwent resection. RE administration included the right liver in 5, the left liver in 1, and to the whole liver in 3. Six patients had previously received several infusions of cytotoxic therapy. The operations occurred at a median of 115 days (56-245) after RE and included right lobectomy (5), left lobectomy (1), left lateral sectionectomy (1) and bi-lobar wedge resections (2). Median blood loss was 900 ml (250 - 3600). Grade 3 or higher complications occurred in 7 cases (78%). Follow-up was complete in all patients. Three patients (33%) died within 30 days of resection. All remaining had disease recurrence (time to recurrence: 202 days [54 - 315]), and all have died (over-all survival: 584 days [127 - 1230]). Pathologic review demonstrated median tumor necrosis of 70% (20-90). In non-tumor bearing liver, fibrosis grade (0-4) and inflammation score (0-4) was 2 or less in all specimens. Conclusion: In this small cohort of highly selected and heavily treated patients, long term survival after resection following RE appears possible, but the operations may carry substantial risks. Additional reports with long-term outcomes are needed to further clarify the impact of RE on post op complications and death.

49
A Multi-center Phase I Dose Escalation Trial to Evaluate Safety and Tolerability of Intra-arterial Temozolomide for Patients with Advanced Extremity Melanoma using Normothermic Isolated Limb Infusion G. Beasley, P.J. Speicher, C. Augustine, B. Jiang, P.C. Dobler, B.L. Peterson, P.J. Mosca, R.E. Royalt, M.I. Ross, J.S. Zager, D.S. Tyler. 1. Department of Surgery, Duke University, Durham, NC; 2. VA Medical Center; Durham, NC; 3. Cancer Statistical Center, Duke University, Durham, NC; 4. The University of Texas MD Anderson Cancer Center, Houston, TX; 5. Department of Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL.

Background: L-phenylalanine mustard (LPAM) has been the standard for treatment of isolated limb perfusion (ILP) for delivering high dose regional chemotherapy to an extremity. ILI is now progressively performed in tertiary referral centers worldwide to treat patients with locally advanced limb melanoma. We investigated the results of ILI in a national Australian multi-center study. Methods: ILIs in 316 patients in five Australian institutions (1992 - 2008) were collectively analyzed. All 5 institutions used the Melanoma Institute Australia ILI protocol. Melphalan and actinomycin D was circulated in the isolated limb for 20-30 minutes. Cancer response was determined using the WHO criteria and limb toxicity was assessed using the Wieberdink Scale. Results: The median patient age was 74 years (range 28 - 100) and 59% were female. Overall response rate to ILI was 75%, consisting of a complete response of 33% and a partial response of 42%. Stable disease was seen in 18% and progressive disease in 7%. Wieberdink toxicity grade III or higher was seen in 30% of the cases. No toxicity-related amputations occurred. Median follow-up was 22 months and median survival was 48 months. In patients with a CR, median survival was 50 months (p = 0.014). In the univariate analysis a younger age, lower-limb procedures, low Breslow thickness of the primary melanoma and intra-operatively higher achieved intramuscular temperatures were associated with a favorable response. On multivariate analysis Breslow thickness clinical data demonstrated that regional temozolomide (TMZ) may be more effective. Methods: Patients with AJCC Stage IIIb, or IIIc extremity melanoma who failed previous LPAM based RC were treated with TMZ via isolated limb infusion (ILI) according to a modified accelerated titration design. Drug pharmacokinetic (PK) analysis, tumor gene expression, methylation status of the O6-methylguanine methyltransferase (MGMT) promoter, and MGMT expression were evaluated. Primary objectives were: 1) determine dose limiting toxicities (DLT’s) and maximum tolerated dose (MTD) of TMZ via ILI using CTCAE v4.03 and 2) explore biomarker correlates of response. Results: 28 patients completed treatment over 2.5 years at 3 institutions. 19 patients were treated at the MTD defined as 3200 mg/m2 (multiplied by 0.09 (arm), 0.18 (leg)). 2 of 5 patients had DLTs at the 3600 mg/m2 level while only grade 1 (n=15) and grade 2 (n=4) clinical toxicities occurred at the MTD. At 3 months post-ILI, 10.5% (2/19) had a CR, 5.3% (1/19) had PR, 15.8% (3/19) had SD, 68.4% (13/19) had PD. Figure 1 shows the change in tumor sum of longest diameter (SOLD) stratified by dose level. Neither PK parameters of TMZ nor MGMT levels were associated with response or toxicity. Conclusion: In this first ever use of intra arterial TMZ in ILI for melanoma, the MTD was determined. While we could not define a marker for TMZ response, the minimal toxicity of TMZ ILI may allow for repeated treatments to increase the response rate as well as clarify the role of MGMT expression in determining response.
and lower-limb ILI remained significant predictors for response. Conclusion: This Australian national ILI multi-center study is the largest to date. Toxicity and response rates as well as survival are comparable to other studies reporting results following both ILI and conventional ILP. ILI can widely be implemented and safely applied across tertiary referral centers for successful management of advanced extremity melanoma.

### 51 Disease Burden Predicts Response to Melphalan-based Isolated Limb Infusion in Melanoma

**D.J. Muilenburg,1* G.M. Beasley,2 Z.J. Thompson,3 J. Lee,1 D.S. Tyler,7 J.S. Zager.1 1. H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; 2. Duke University, Durham, NC.**

**Background:** Isolated limb infusion (ILI) with melphalan is a minimally invasive, effective treatment for intransit melanoma. However, results are variable: some patients (pts) exhibit dramatic responses while others progress immediately after ILI. While part of this variation is likely due to inherent differences in individual tumor biology, we hypothesized that burden of disease (BOD) may correlate with treatment response. **Methods:** We analyzed a prospectively collected database from two academic centers. BOD was stratified as high or low (less than 10 lesions, none > 2cm). Response rates were measured at 3 months post-ILI, based on modified RECIST criteria for cutaneous lesions. Multivariable analysis (MV) was used to evaluate the association between response rate and BOD, while adjusting for potential confounding factors. Kaplan-Meier methods with log-rank tests and multivariable Cox proportional hazard models were used adjusting for potential confounding factors. **Results:** A total of 160 pts were included, mean age 67, 57% were male. Sixty (38%) pts had low and 100 (62%) high BOD. Median follow up time was 17.5 months. Patients with low BOD had an overall response rate (ORR) of 73%, with 50% CR; compared to an ORR of 47% with 24% CR in patients with high BOD (p=0.002). As seen in Table 1, MV analysis of relevant preop, intraop, and postop parameters showed no significant impact on response at 3 months. Pts with a CR at 3 months demonstrated increased PFS over the remainder of the cohort (PR, SD, PD) (12 vs. 5.9, 5.1, 2.7 months respectively, p<0.001); however this did not translate to a difference in OS. Compared to pts with high BOD, those with low BOD had an increase in median PFS of 6.9 vs 3.8 months (p=0.047), and an increased median OS of 38.4 vs. 30.9 months, although the latter was not statistically significant. **Conclusions:** Low BOD is associated with an increased ORR and CR rate, with significantly improved PFS in patients undergoing ILI for intransit melanoma. BOD provides prognostic information that can be useful in patient counseling and also as a marker to stratify patient risk groups in future research studies.

### 52 Responses of Injected and Uninjected Lesions to Intraleisional Talmogene Laherparepvec (T-VEC) in the OPTiM Study and the Contribution of Surgery to Response

**R.H. Andtbacka,1* M.I. Ross,2 K. Delman,3 D. Noyes,1 J.S. Zager,3 E. Hsueh,2 D.W. Ollila,2 J. Curry,2 T. Amatruda,4 L. Chen,5 A. VanderWalde,6 H. Kaufman.1 1. University of Utah Huntsman Cancer Institute, Salt Lake City, UT; 2. MD Anderson Cancer Center, Houston, TX; 3. Emory University, Atlanta, GA; 4. University of Utah School of Medicine, Salt Lake City, UT; 5. Moffitt Cancer Center, Tampa, FL; 6. Saint Louis University Cancer Center, Saint Louis, MO; 7. University of North Carolina Medical Center, Chapel Hill, NC; 8. Minnesota Oncology-Fridley, Fridley, MN; 9. Amgen Inc., Thousand Oaks, CA; 10. Rush University Medical Center, Chicago, IL.**

Introduction: T-VEC is an oncolytic modified type 1 herpes simplex virus designed to selectively replicate in tumors, produce systemic human GM-CSF, and elicit a response in injected and non-injected tumors. As reported in a melanoma phase 3 trial, T-VEC compared to subcutaneous GM-CSF had a significantly greater durable response rate (primary endpoint). While overall responses were previously reported, individual lesion responses and the utility of surgery as an adjunct to therapy are reported here. **Methods:** Bidimensional measurements were recorded for all measurable lesions every 4-12 weeks and classified as either injected, un.injected non-visceral, or un injected visceral. Injections were identified for regression, tumor infiltrating lymphocytes, growth phase, Clark level, and response rates as well as survival are comparable to other studies reporting results following both ILI and conventional ILP. ILI can widely be implemented and safely applied across tertiary referral centers for successful management of advanced extremity melanoma.

Table 1: Demographic, clinicopathologic variables, and outcomes

<table>
<thead>
<tr>
<th></th>
<th>Low BOD</th>
<th>High BOD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N, % of total N</td>
<td>60, 30%</td>
<td>39, 62%</td>
<td></td>
</tr>
<tr>
<td>Mean Age (range)</td>
<td>67 (29-90)</td>
<td>68 (34-88)</td>
<td>0.619</td>
</tr>
<tr>
<td>Upper Extent (in, %)</td>
<td>9, 15%</td>
<td>23, 23%</td>
<td>0.312</td>
</tr>
<tr>
<td>Lower Extent (in, %)</td>
<td>51, 85%</td>
<td>77, 72%</td>
<td></td>
</tr>
<tr>
<td>Peritumoral Factors</td>
<td>mean (sd)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH ≤ 60 min</td>
<td>7.2 (0.1)</td>
<td>7.2 (0.1)</td>
<td>0.759</td>
</tr>
<tr>
<td>Biopsy ≤ 30 min</td>
<td>0.8 (3.2)</td>
<td>6.4 (4.2)</td>
<td>0.052</td>
</tr>
<tr>
<td>Ischemia time (min)</td>
<td>66.2 (42)</td>
<td>66.6 (47.5)</td>
<td>0.879</td>
</tr>
<tr>
<td>Post-operative C' max peak</td>
<td>218,000 (508)</td>
<td>112,000 (83)</td>
<td>0.008</td>
</tr>
<tr>
<td>ORR @ 3 months (95% Confidence Interval)</td>
<td>23 (73%, 82.9)</td>
<td>31 (66.8, 92.2)</td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>38 (56, 62.5)</td>
<td>24 (16, 36.7)</td>
<td>0.092</td>
</tr>
<tr>
<td>PR</td>
<td>23.3 (13.4, 35)</td>
<td>23 (15.2, 35.2)</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>3.2 (11.5, 11)</td>
<td>14 (7.0, 22.4)</td>
<td></td>
</tr>
<tr>
<td>PD</td>
<td>23.3 (13.4, 30)</td>
<td>30 (29.4, 49.3)</td>
<td></td>
</tr>
<tr>
<td>Median Follow Up Months, (range)</td>
<td>19.9 (2.8-70.1)</td>
<td>14.9 (3.5-68.0)</td>
<td></td>
</tr>
<tr>
<td>Median overall survival Months (95% CI)</td>
<td>38.4 (35.2, NA)</td>
<td>30.9 (25.3, NA)</td>
<td>0.046</td>
</tr>
<tr>
<td>Median Progressive Free survival Months (95% CI)</td>
<td>6.9 (5.7, 9.6)</td>
<td>3.8 (3.0, 4.6)</td>
<td>0.047</td>
</tr>
<tr>
<td>Progression Free Survival by response (95% CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CR</td>
<td>12 (9.2, 27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>5 (4.0, 9.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>5 (4.0, 9.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD</td>
<td>2.7 (2.5, 3.9)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

Introduction: Although SNB is a well established staging practice in pts with primary cutaneous melanoma with tumor thickness ≥1 mm, the role and prognostic significance of SNB in pts with thin melanoma is not well defined. We assessed associations of multiple clinicopathological factors with survival in pts with thin melanoma undergoing SNB in the contemporary SNB era. **Methods:** From a prospective database, we identified 874 pts with clinically node negative melanomas ≤1 mm who had wide excision and SNB during a contemporary time period (1999–2009). We explored associations of known and putative clinicopathological risk factors with respect to melanoma-specific survival (MSS) and recurrence-free survival (RFS). Results: The median age at diagnosis was 56 years, and 60% were female. 39% of melanomas were ulcerated and 45% had 45% had specific survival (MSS) and recurrence-free survival (RFS). Results: The median age at diagnosis was 56 years, and 60% were female. 39% of melanomas were ulcerated and 45% had 45% had
melanoma histologic type, tumor location, or gender. In multivariate analyses, SN status was the dominant independent predictor of MSS. Conclusion: Despite the overall low risk of a positive SN, SN status is the most powerful predictor of MSS in pts with thin melanoma. Since thin melanoma pts represent the most common presentation of invasive melanoma, this small high-risk subset represents a significant proportion of pts who will die of melanoma. Therefore, further studies are warranted to identify factors associated with SN involvement in an effort to develop integrated risk models to personalize clinical care.

Disease-specific survival stratified according to sentinel lymph node (SLN) status.

54

**Improved Survival in Patients with Thin Melanoma after Positive Sentinel Node versus Clinical Nodal Recurrence**

**M.B. Faries,1* G.C. Karakousis,2 E. Bartlett,3 M. Peters,3 P. Gimotty,3 M. Sim,4 D.L. Fraker,5 B.J. Czerniecki,6 D.L. Morton.1**

1. John Wayne Cancer Institute, Santa Monica, CA; 2. University of Pennsylvania, Philadelphia, PA.

Introduction: The value of sentinel lymph node biopsy (SLNB) in intermediate depth melanoma includes its prognostic value and possible survival benefit for patients who harbor nodal metastases. Randomized clinical trials are not feasible in patients with thin (≤1mm) melanoma due to the low frequency of nodal disease. We compared outcomes of patients with thin melanoma presenting with sentinel node metastases to those who developed subsequent clinical nodal recurrence (NR). Methods: Two independent cohorts with thin melanoma and either SLN metastasis or clinical NR were identified from prospective databases at two centers. In center 1, (1986-2012) patients with a positive SLNB (SLN+) were compared to patients presenting with clinical NR (1971-2010) after an initially negative nodal evaluation (either clinically or by SLNB). In center 2, SLN+ (1996-2011) were compared to a pre-SLN cohort (1973-1989) with NR. Univariate and multivariate Cox regression analyses determined factors associated with melanoma-specific survival (MSS) and Kaplan-Meier curves were developed. Results: In center 1, 427 patients with NR were compared to 91 SLN+ patients. SLN+ patients were older (53 vs. 31% >50 yrs old) and more frequently had ulcerated tumors (9.9 vs. 6.8%) and elevated Clark level (39.6% vs.14.8% level IV-V) (all p<0.0001). The 5- and 10-year survival for the SLN+ group was 88 and 84% respectively, compared to 72 and 49% in the NR group (p=0.0001). By multivariate analysis, age≥50 (HR=1.5, CI=1.2-1.9), present (HR=1.9, CI=1.2-2.9) or unknown (HR=1.6, CI=1.3-2.1) ulceration, truncal site (HR=1.6, CI=1.2-2.2), and NR (HR=3.3, CI=1.8-6.0) were all significantly associated with decreased MSS (each p<0.01). In center 2, 29 SLN+ patients were compared to 39 NR patients. The 5-yr MSS survival was remarkably similar to that of center 1 at 88% in the SLN+ group and 76% in the NR group (p=0.09). Figure 1. Conclusion: Identification of a metastasis in the SLN of patients with thin melanoma is associated with improved MSS compared to the development of clinical NR. This may be a reflection of tumor biology, patient selection, or potential therapeutic efficacy of the SLNB.

55

**Melanoma Patient Quality of Life Outcomes after Sentinel Lymph Node Biopsy, Completion Lymphadenectomy, and Adjuvant Interferon**

**M.E. Egger,1* C. Kimbrough,1 A.J. Stromberg,2 A.R. Quillo,3 R. Martin,4 C.R. Scoggins,1 R.M. McMasters.1**

1. Department of Surgery, University of Louisville, Louisville, KY; 2. University of Kentucky, Lexington, KY.

Patient-centered outcomes for melanoma are important to consider when making recommendations for treatment and adjuvant therapy. Quality of life (QOL) and physical condition (PC) outcomes after sentinel lymph node biopsy (SLNB), completion lymph node dissection (CLND), and adjuvant therapy with interferon alfa-2b (IFN) were evaluated in this study. Self-reported QOL and PC scores were evaluated in patients enrolled in a prospective, multi-center randomized clinical trial evaluating adjuvant IFN in patients with melanoma ≤1.0 mm Breslow thickness. After SLNB biopsy, patients with a positive SLN underwent CLND then were randomized to adjuvant IFN for 12 months or observation. QOL and PC scores were compared between patients who underwent SLNB alone, CLND without IFN, and CLND with IFN. Time to return to baseline QOL and PC scores reported at the time of SLNB was recorded. Absolute, changes, and time to return to baseline in QOL and PC scores were compared between groups. The study evaluated 490 patients with a median follow-up of 36.5 months. At baseline, there were no significant differences in reported QOL and PC scores between the 3 treatment groups. After 3 months, there were no statistically significant differences in changes in QOL and PC scores between SLNB and CLND; IFN was associated with significantly worse QOL and PC at 3, 6, 9, and 12 months. There were statistically significant differences in time to return to baseline QOL and PC scores across the three treatment groups (FIGURE, p=0.0018). Median times to return to baseline QOL were 7, 8, and 15 months for SLNB, CLND, and IFN, respectively. Median times to return to baseline PC were 6, 6, and 14 months for SLNB, CLND, and IFN, respectively. Only after an additional 12 months following conclusion of IFN did the proportion of patients reporting return to baseline QOL and PC approach that of SLNB and CLND. CLND is well-tolerated with a similar effect on self-reported QOL outcomes in both the short and long term compared to SLNB alone. IFN therapy is associated with worse QOL outcomes compared to SLNB and CLND, an effect that may be sustained following cessation of adjuvant IFN.

Figure. Time to return to baseline for (A) Quality of Life (QOL) and (B) Physical Condition (PC) scores by treatment groups: sentinel lymph node biopsy alone (SLNB), completion lymph node dissection (CLND), and adjuvant interferon (IFN).
Cost-effectiveness Analysis of Staging Strategies in Patients with Regionally Metastatic Melanoma

N. Look Hong, T. Petrelli, K. Chan. Surgical Oncology, Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

Background: Considerable variability exists regarding optimal staging for asymptomatic pathologically node-positive melanoma. Options include combinations of physical examination (PE), radiography, computed tomography (CT), and positron emission tomography (PET). Cost-effectiveness of these staging regimens has never been investigated. Methods: A modeled cost-effectiveness analysis was performed to examine the cost per surgery performed and per accurate diagnosis achieved with three staging regimens (PE, PE/radiography, CT, PET/CT) for node-positive melanoma. Costs for approved systemic chemotherapy regimens were considered. Incremental cost effectiveness ratios were used to compare regimens. Deterministic sensitivity analysis was undertaken to estimate the effect of varying key parameters. Costs are direct, from the perspective of the Canadian single-payer system, and 2012 valuations. Results: As seen in Table 1, staging with PE/radiography is the least cost-effective option, resulting in greater costs than CT alone, more surgery, and fewer accurate diagnoses. Compared to CT alone, PET/CT incurs a greater incremental cost ($992.81 CAD), but results in 4% fewer lymphadenectomies and 4% more accurate diagnoses. PET/CT costs $22,570.25 CAD for each additional accurate diagnosis achieved compared to CT alone. Sensitivity analyses demonstrate that the preferred staging strategy is influenced by diagnostic test characteristics and the willingness to pay threshold, but is robust to all other varied parameters. Conclusion: PE/radiography appears to be the least cost effective staging regimen and results in fewer accurate diagnoses. However, the benefit of PET/CT over CT alone depends on a health system’s priorities and willingness to pay.

Table 1: Cost and effectiveness measures for each modeled staging regimen

<table>
<thead>
<tr>
<th>Staging Regimen</th>
<th>Total Cost (CAD)</th>
<th>Probability of surgery</th>
<th>Probability of accurate diagnosis</th>
<th>Incremental change in cost (CAD)</th>
<th>Incremental change in surgeries completed</th>
<th>Incremental change in accurate diagnoses achieved</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE/Radiography</td>
<td>76,623.52</td>
<td>0.94</td>
<td>0.94</td>
<td>-0.16</td>
<td>-0.04</td>
<td>0.04</td>
</tr>
<tr>
<td>CT</td>
<td>69,031.03</td>
<td>0.93</td>
<td>0.93</td>
<td>0.01</td>
<td>-</td>
<td>0.01</td>
</tr>
<tr>
<td>PET/CT</td>
<td>30,834.74</td>
<td>0.94</td>
<td>0.94</td>
<td>-0.16</td>
<td>-0.04</td>
<td>0.04</td>
</tr>
</tbody>
</table>

Inflammatory Adverse Events are Associated with CD8+ T Cell Response and Disease-Free Survival following Multipeptide Melanoma Vaccines


Background: Administration of multipeptide vaccines may produce adverse events with an inflammatory physiology. The purpose of this study is to determine the relationships among inflammatory adverse events (IAE), immune responsiveness (IR), and clinical outcomes in the setting of multipeptide vaccination for high risk melanoma. We hypothesize that IAE’s are associated with a higher rate of IR and improved clinical outcomes. Methods: Adult patients with resected, high-risk (stage III-B IV) melanoma were entered into one of three multipeptide vaccine trials (Mel43, Mel44, Mel48). All patients received a vaccination of 12 melanoma peptides comprised of Class I MHC-restricted epitopes (12MP). IAE’s were recorded, and included pulmonary, dermatologic, and constitutional subtypes. A separate category for immunologic, dermatologic, and constitutional subtypes. A separate category for immune responsive (irritative) events was also assessed. CD8+ T cell immune response was assessed by direct IFN-gamma ELISPOT. Overall survival and disease-free survival were analyzed by Cox proportional hazard modeling for age, stage, gender, and the presence of IAE, IR, and vitiligo. Results: Out of 333 total participants, 56 developed a total of 70 IAE’s, the majority of which were dermatologic. Hypopigmentation developed in 23 patients (7%). 175 patients (53%) developed a CD8+ T cell response. Presence of IAE was significantly associated with development of IR (70% vs 49%, p = 0.005), while vitiligo was not. Development of IAE was associated with increased disease-free survival under multiple regression (HR 0.63, p = 0.037), while hypopigmentation and presence of IAE showed no such association (Figure 1). Conclusions: Inflammatory adverse events are associated with improved disease-free survival under multiple regression (HR 0.63, p = 0.037), while hypopigmentation and presence of IAE showed no such association (Figure 1). Conclusions: Inflammatory adverse events are associated with improved disease-free survival under multiple regression (HR 0.63, p = 0.037), while hypopigmentation and presence of IAE showed no such association (Figure 1).

Gene Expression Profiles of Human Primary and Metastatic Melanoma Reveal UBE2C as a Potential Therapeutic Target Gene for BRAF Resistant Cells


Introduction: Ubiquitin-conjugating enzyme E2C (UBE2C) participates in cell cycle progression and checkpoint control by targeted degradation of short-lived proteins. Gene expression of UBE2C is elevated in various cancers including melanoma. Microarray analysis from primary and metastatic melanoma tissues showed that UBE2C mRNA expression was up-regulated in metastatic as compared to primary melanoma (relative expression: 1.23±0.14 vs. 0.64±0.07 p<0.01) demonstrating the relevance of this gene. Human melanoma cell lines also demonstrate UBE2C gene expression unrelated to BRAF and NRAS mutation status. We hypothesized that UBE2C may be a novel target for treatment of melanoma through a BRAF independent pathway. Methods: We performed western blot analysis of the human melanoma cell lines: M207, M328 and M375; each of them resistant to BRAF inhibitor treatment (PLX4032). All three express UBE2C. When these cell lines are treated with PLX4032 we noted down-regulation of UBE2C gene expression than seen from BRAF inhibitor sensitive cell lines. BRAF resistant cell lines (M207 and M375) were chosen for UBE2C gene silencing based on their high level of UBE2C protein level was reduced by 73.7% and 80.5%, respectively in M207 and M375 cell lines at day 4 after UBE2C siRNA gene silencing and cell proliferation was reduced by 60.4% and 73.8 %. Flow cytometry demonstrated there were higher percentage of apoptotic cells after UBE2C siRNA gene silencing as compared to controls (40.9%±4.4% vs 14.3%±1.5%, p<0.001). M207 was treated with PLX4032 at variable concentrations. There was no down-regulation of UBE2C or ERK phosphorylation from PLX4032. In the BRAF and NRAS mutated M328, PLX4032 inhibited IR, our findings suggest either that antitumor activity of Class I-restricted peptide vaccines depend on immunologic effects beyond simple expansion of CD8+ T-cells or that the intrinsic inflammatory response contributes to clinical outcome in melanoma.
the cell proliferation by 25.1% at day 5. The combination of PLX4032 and UBE2C siRNA gene silencing inhibited cell proliferation by 52.5% (p<0.001) suggesting the synergy of the combination. Conclusions: While BRAF and NRAS signalling pathways have been shown to be important targets for therapy in melanoma, our data suggest UBE2C may be an additional site for design of treatment in resistant melanoma.

59

Coordinated Cancer Care Reduces Costs and Hospital Length of Stay with High Patient Satisfaction


Introduction: Navigating complex cancer care for the average patient and family is difficult. Moreover, there are no billing codes to subsidize this service and therefore the costs are not externally reimbursed. We sought to analyze the potential benefits of pre-hospitalization nurse navigation on hospital costs, length of stay and patient satisfaction. Methods: From 8/2007 thru 9/2012 there were 16,514 patients electively admitted to the hospital either as “in” or “out” patients with a cancer related primary diagnosis. Of this group, 4,258 patients underwent pre-hospitalization navigation by an Integrated Multidisciplinary Cancer Care Program (IMCCP) nurse that coordinated physician visits in surgery, medical and radiation oncology; in addition to identification of social service needs. The Wilcoxon rank-sum test was used to compare hospital cost and length of stay, significance defined as p < 0.05 (two sided). Satisfaction surveys were obtained from only the navigation patients. Results: After adjusting for cancer diagnosis, payer mix and whether surgery was performed as an “in” or outpatient there was a statistically significant decrease in the average hospital cost and length of stay of $200 and 0.05 days, resp.(p < 0.05). If these average savings were applied to all patients that were not coordinated during this time period, the potential cumulative benefit would be $2.45million and 600 inpatient days. Nearly all (99%) of the participants were satisfied and would recommend this program to friends and family. Conclusions: The IMCCP nurse navigation program resulted in decreased costs and fewer hospital days with excellent patient satisfaction. New cancer patients would benefit from this cost effective service.

59

Mean Adjusted 30-Day Costs by Hospital Volume Tercile

<table>
<thead>
<tr>
<th>Procedure and Cost Type</th>
<th>Cost in Dollars</th>
<th>Hospital Volume Tercile</th>
<th>High</th>
<th>Cost Difference Between 1st and 3rd Terciles (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>42,386</td>
<td>41,701</td>
<td>42,983</td>
<td>42,480</td>
</tr>
<tr>
<td>Index Admission</td>
<td>29,140</td>
<td>29,173</td>
<td>29,531</td>
<td>29,718</td>
</tr>
<tr>
<td>Readmissions</td>
<td>3303</td>
<td>2961</td>
<td>3432</td>
<td>3520</td>
</tr>
<tr>
<td>Colorectal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>31,238</td>
<td>30,957</td>
<td>32,560</td>
<td>31,719</td>
</tr>
<tr>
<td>Index Admission</td>
<td>24,412</td>
<td>23,870</td>
<td>25,102</td>
<td>24,281</td>
</tr>
<tr>
<td>Readmissions</td>
<td>1937</td>
<td>1901</td>
<td>1969</td>
<td>1941</td>
</tr>
<tr>
<td>Pulmonary Lobectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>30,412</td>
<td>30,311</td>
<td>30,875</td>
<td>30,658</td>
</tr>
<tr>
<td>Index Admission</td>
<td>25,483</td>
<td>25,041</td>
<td>25,331</td>
<td>25,184</td>
</tr>
<tr>
<td>Readmissions</td>
<td>2005</td>
<td>1942</td>
<td>2065</td>
<td>2050</td>
</tr>
<tr>
<td>Pancreatectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>56,537</td>
<td>56,836</td>
<td>57,079</td>
<td>56,932</td>
</tr>
<tr>
<td>Index Admission</td>
<td>44,506</td>
<td>44,943</td>
<td>45,331</td>
<td>44,433</td>
</tr>
<tr>
<td>Readmissions</td>
<td>3588</td>
<td>3901</td>
<td>3909</td>
<td>3763</td>
</tr>
<tr>
<td>Prostatectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>14,161</td>
<td>14,014</td>
<td>14,265</td>
<td>14,305</td>
</tr>
<tr>
<td>Index Admission</td>
<td>9943</td>
<td>9707</td>
<td>10,014</td>
<td>9990</td>
</tr>
<tr>
<td>Readmissions</td>
<td>926</td>
<td>928</td>
<td>921</td>
<td>925</td>
</tr>
<tr>
<td>Proctectomy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>33,759</td>
<td>32,676</td>
<td>34,224</td>
<td>34,186</td>
</tr>
<tr>
<td>Index Admission</td>
<td>23,643</td>
<td>22,777</td>
<td>23,737</td>
<td>23,519</td>
</tr>
<tr>
<td>Readmissions</td>
<td>2467</td>
<td>2354</td>
<td>2475</td>
<td>2575</td>
</tr>
</tbody>
</table>

61

A Simplified Risk Score for Predicting the Incidence of Major Complications after Complex Abdominal-pelvic Resections

A. Bennett, R. Sharma, G.C. Balch, A. Yopp, J.C. Mansour.* Surgery, UT Southwestern, Dallas, TX.

Background: The POSSUM system is used to predict risk of complications following general surgical procedures. This 17-factor instrument has been challenging to apply to most surgical oncology patient populations. Our aim is to develop a simplified scoring system which is highly correlated with the incidence of major complications. Methods: We queried a single-institution IRB-approved prospective database from a surgical oncology population from January 2008 to December 2012. We identified patients undergoing complex abdominal or pelvic resections and factors associated with the development of major (Clavien >= 3) complications. Factors not included in the POSSUM system were incorporated into a new scoring system based on univariate correlation with complication rates (chi-square). A composite scoring system (POSSUM-SO) was compared to standard POSSUM predictions using ROC analysis. Optimal binning generated an ideal cut-off value associated with major complications. Results: We identified 831 patients undergoing pancreatic (23%), hepatic (23%), colorectal (22%), esophagogastroduodenal (16%), retroperitoneal (4%), combined (3%), or other type (10%) of resection. Major complications occurred in 17% of patients. Two original POSSUM factors were included in the new POSSUM-SO model (cardiac history and EBL). Four factors improved correlation with complication rate: gender (female/male-1/3 points); BMI (underweight or morbidly obese/others-4/1 points); operation type (retroperitoneal/ pancreatic or rectal/others-4/2/1 points); and cancer (no/cancer/cancer-1/2 points). ROC analysis generated a greater AUC for the simplified 6-factor system than standard 17-factor POSSUM (AUC: 0.658 vs 0.631, See Figure 1). A model including the 5 preoperative factors generated a similar AUC compared to the original POSSUM (AUC: 0.622 vs 0.631). Patients with POSSUM-SO >= 12 had a higher risk of major complications (22% vs 9%, p-value < 0.001). Conclusions: A simplified composite scoring system is more closely associated with short term surgical outcomes than the POSSUM evaluation.
Abstracts: Plenary, Parallel and Video Sessions S27

**36**

**Young Age-at-diagnosis Influences Quality of Life Among Long-term Survivors of Colorectal Cancer**


**INTRODUCTION:** The incidence of colorectal cancer (CRC) has decreased overall, but continues to rise among young adults (aged 18-50). Cancer diagnosis can disrupt normal adulthood and impact long-term survivorship. The unique needs of long-term survivors from CRC diagnosed at age 18-50 (young survivors, YS) vs. after age 50 (later survivors, LS) have not been examined.

**METHODS:** CRC survivors >5 years from diagnosis were identified from the institutional tumor registry. YS were matched 1:2 to LS for tumor site (colon vs. rectum) and treatments (surgery, chemotherapy, radiation). A matched cross-sectional survey study was conducted in 1,215 survivors (415 YS and 801 LS) using the self-administered Quality of Life in Adult Cancer Survivors (QLACS), a validated instrument for long-term cancer survivors. Standardized mean scores from 13 domains were compared between YS and LS by two-sample t-test. Bonferroni adjustment for multiple comparisons denoted p-value < 0.004 as statistically significant.

**RESULTS:** 830 survivors (282 YS and 548 LS) responded (response rate: 68% in both YS and LS) at a mean of 10.8 years (10.6 in YS; 10.9 in LS) from diagnosis. The mean age-at-diagnosis was 43.6 ± 7 years in YS vs. LS (p = 0.001). The cohorts were balanced for the matched variables tumor site (p = 0.699) and treatments (surgery, p = 0.121; chemotherapy, p = 0.365; radiation, p = 0.864). Significant differences were found in 7 of the 13 domains with significantly worse scores for YS in Negative feeling, Social avoidance, Financial problems, Appearance concern, Recurrence distress, and Family distress, although YS reported greater sense of Benefit (p < 0.001; Figure). Missing responses were most frequent regarding sexual interest and function (missing 4.9% (YS) vs. 17.7% (LS) and 5.6% (YS) vs. 13.3% (LS), respectively).

**CONCLUSIONS:** Long-term survivors of CRC show good adaptation, but young-onset survivors experience unique QOL deficiencies that persist even 10 years into cancer survivorship. Relative to patients diagnosed at later ages, these young adults may benefit from more attention and support in these specific areas throughout their cancer experience, including late survivorship.
Quality of Colorectal Cancer Care Among Veterans: A 10-year Retrospective Cohort

R.A. Snyder,1* R. Maintinha,1 R.K. Patel,1 R.S. Dittus,2 C.L. Roumie.1 1. Department of Surgery, Vanderbilt University, Nashville, TN; 2. Veterans Health Administration-Tennessee Valley Healthcare System Geriatric Research, Education and Clinical Center, Nashville, TN.

Introduction: Nearly 5,000 patients within the Veterans Health Administration (VHA) are diagnosed with colorectal cancer (CRC) annually. However, the linkage between performance on CRC practice guidelines and subsequent patient outcomes is unclear. The purpose of this study was to evaluate the quality of non-metastatic CRC care in a large VHA system by assessing adherence to National Comprehensive Cancer Network (NCCN) practice guidelines and to determine if receipt of these metrics was associated with improvement in 5-year all-cause mortality. Methods: We performed a retrospective cohort study of all patients who underwent resection for non-metastatic CRC at VHA Tennessee Valley Healthcare System (TVHS) between 2001 and 2010. We defined “excellent” care as receipt of at least 75% of eligible NCCN metrics. We also examined time to treatment and used a Cox proportional hazard model to investigate the relationship between excellent care and all-cause mortality. Results: A total of 331 patients underwent resection for CRC within the study period. Only 47% of CRC patients received excellent care and 9% received 100% of eligible metrics. The median time from diagnosis to definitive treatment was 22 days (IQR 12, 41) and 37 days (IQR 24, 56) among colon and rectal cancer patients, respectively. The likelihood of receiving excellent care increased significantly over the study period (2009 vs. 2002, OR 2.93 [1.51-5.67]). However, there was no association between receipt of excellent care and 5-year all-cause mortality (HR 0.85 [95% CI 0.53-1.36]). Conclusions: Although patients treated at TVHS received timely care overall consistent with those in other health systems, less than half of all CRC patients received “excellent care,” or care consistent with at least 75% of eligible NCCN metrics. The degree of variation in care found in this closed healthcare system suggests that systematic coordination of care is a critical component of quality improvement in CRC. Although receipt of excellent care was not associated with all-cause mortality in this setting, further research will be necessary to identify specific quality metrics likely to influence patient outcomes in CRC.

Distance Traveled is an Unrecognized Bias for Short and Long-term Outcomes following Complex Gastrointestinal Surgery: Results from the National Cancer Database

B.A. Pockaj, R.J. Gray, D.A. Etzioni. Surgery, Mayo Clinic Arizona, Phoenix, AZ.

Introduction: Patients travelling significant distances to participate in phase II oncology trials have better outcomes compared to those enrolling locally. We postulate a similar unrecognized effect exists for patients travelling to undergo complex surgery for gastrointestinal cancers. Methods: Patients undergoing gastrointestinal surgery for cancer between 2003-2006 were extracted from the National Cancer Database. The distance in miles between the patient’s residence and the treating facility was calculated using zip code centroids. The association between distance traveled and overall survival was explored using adjusted Cox regression analyses by controlling for age, race, sex, insurance status, income, education, chemotherapy, radiation therapy, pathological stage, and hospital type. Results: Our population consisted of 28,394 patients with the diagnosis of esophageal (8,853; 32%), liver (7,790; 28%) and pancreatic cancer (11,451; 40%). Patients traveling >50 miles were in the fourth stage, and hospital type. Results of all patients who underwent resection for non-metastatic CRC at VHA Tennesssee Valley Healthcare System (TVHS) between 2001 and 2010. We defined “excellent” care as receipt of at least 75% of eligible NCCN metrics. We also examined time to treatment and used a Cox proportional hazard model to investigate the relationship between excellent care and all-cause mortality. Results: A total of 331 patients underwent resection for CRC within the study period. Only 47% of CRC patients received excellent care and 9% received 100% of eligible metrics. The median time from diagnosis to definitive treatment was 22 days (IQR 12, 41) and 37 days (IQR 24, 56) among colon and rectal cancer patients, respectively. The likelihood of receiving excellent care increased significantly over the study period (2009 vs. 2002, OR 2.93 [1.51-5.67]). However, there was no association between receipt of excellent care and 5-year all-cause mortality (HR 0.85 [95% CI 0.53-1.36]). Conclusions: Although patients treated at TVHS received timely care overall consistent with those in other health systems, less than half of all CRC patients received “excellent care,” or care consistent with at least 75% of eligible NCCN metrics. The degree of variation in care found in this closed healthcare system suggests that systematic coordination of care is a critical component of quality improvement in CRC. Although receipt of excellent care was not associated with all-cause mortality in this setting, further research will be necessary to identify specific quality metrics likely to influence patient outcomes in CRC.

Readmission after Pancreaticoduodenectomy: The Influence of the Volume Effect beyond Mortality


INTRODUCTION: As increased focus is placed on quality of care in surgery, readmission is an increasingly important metric by which hospital quality is measured. For complex pancreatic surgery, we hypothesized that increased pancreaticoduodenectomy (PD) volume may mitigate readmission rates. METHODS: The University HealthSystem Consortium database was queried for all patients undergoing PD (ICD9 code 52.7) from 2009 through 2011. Hospitals were stratified into quintiles based on number of cases performed annually. Univariate and multivariate logistic regression analyses were performed to identify factors associated with readmission. RESULTS: The 30-day readmission rate for the 9805 patients undergoing PD was 18.7%. Stratified by volume, hospitals performing the highest two quintiles of PDs annually (n ≥ 56 cases) had a significantly lower readmission rate than those hospitals performing the lowest quintile (n ≤ 23 cases) (16.7 and 18.0% vs. 20.9%, p<0.05). On univariate analysis, readmitted patients tended to have higher severity of illness (p<0.01), experienced post-operative complications (p<0.01), and longer index admission (10 vs. 9 days, p<0.01). Age and insurance status had no significant association with readmission. Multivariate analysis demonstrated that higher severity of illness (OR 1.36, 95% CI 1.04-1.77, p=0.02), discharge to rehab (OR 1.41, 95% CI 1.19-1.66, p=0.001), and surgery at the lowest volume hospitals (OR 1.28, 95% CI 1.08-1.51, p=0.004) were factors independently associated with readmission. CONCLUSIONS: These data, for the first time, demonstrate that lower hospital volume is a significant risk factor for readmission after pancreaticoduodenectomy. To minimize the excess resource utilization that accompanies readmission, patients undergoing complex oncologic pancreatic surgery should be directed to hospital systems most experienced in caring for this patient population.

Modifications to the AJCC 7th Edition are Essential to Improve Staging Accuracy in Gastric Cancer

G.B. Deutsch,* V. O’Connor, M. Sim, J. Lee, A. Bilchik. Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA.

Introduction: Although D2 lymphadenectomy improves staging accuracy and survival in gastric cancer, lymph node (LN) number is not included in the most recent (sixth and seventh) editions of the American Joint Commission on Cancer (AJCC) staging system. We hypothesized that addition of LN number would improve the accuracy of AJCC-based staging for gastric cancer. Methods: The Surveillance, Epidemiology and End Results (SEER) Program database was queried to identify all patients who underwent gastrectomy for
gastric cancer between 1988 and 2010. Gastric cancer was staged according to both the sixth and seventh editions of the AJCC. We excluded any patient with an unspecified number of resected LNs. Multivariate regression analyses were performed with and without LN number (< versus ≥ 15 nodes), and subsequently compared with the likelihood ratio test. Results A total of 27,464 patients met the inclusion criteria. Five-year DSS and OS were 67.1% and 53.0%, respectively, for 9,515 patients with ≥15 nodes examined, versus 61.4% and 40.3%, respectively, for 17,949 patients with <15 sampled nodes (p<0.0001). The number of patients per stage (IA-IIIc) was significantly different (p<0.0001) when staging was based on sixth versus seventh AJCC editions. The latter demonstrated a superior fit (p=0.0001). The addition of LN number to the seventh AJCC edition improved prediction of DSS and OS (p<0.0001), independent of stage (see table). Conclusions While the newest AJCC staging system is more accurate than the prior version, it does not account for all potential causes of discrepancy in survival. Because the addition of LN number (< versus ≥ 15 nodes) to the AJCC staging system more accurately predicts five-year DSS and OS in patients with gastric cancer, current surgical guidelines (D2 gastrectomy) should be incorporated in the AJCC-based staging of gastric cancer.

### 68 Conditional Survival-based "Abbreviated" Cancer Surveillance for Sentinel Node-negative Stage IB Melanoma

M. Mukar,1 R. May,2 E. Cho,3 M. Lichtenthal,4 A. Groman,5 V. Francescotti,1 J. Skitzki,1 J. Kane,1 1. Roswell Park Cancer Institute, Surgical Oncology, Buffalo, NY; 2. Roswell Park Cancer Institute, Biostatistics, Buffalo, NY.

Introduction: Melanoma cancer surveillance recommendations are vague and often stage independent. Given the high prognostic value of sentinel lymph node biopsy (SLNB), we instituted an "abbreviated" cancer surveillance for SLNB negative stage IB melanoma due to a calculated low risk for recurrence based on the SLNB. Beginning in 2006, cancer surveillance for those patients with negative SLNB underwent routine CXR (5-year recurrence rate of < 15% with an initial median follow-up of 12 months). Results: A total of 87 patients were identified. Median age was 55.4 years (range 31-85 years) and 50.6% were male. Median Breslow thickness was 1.1 mm (range 0.5-2.0mm) and 1.1% ulcerated. 89% were Clark Level IV. Primary tumor site: 49% extremities, 39% trunk, and 12% head/neck. Median follow-up was 55 months (range 1-80 months). The 5 year recurrence-free, disease specific, and overall survival were 87%, 94%, and 85%, respectively. Survival curves for "suspicious" in 2.5% patients; further workup was negative for pulmonary metastases. During follow-up, 10 patients had "concerning" symptoms/physical findings where the subsequent workup was negative for metastases. There were only 3 true melanoma recurrences (at 20, 26, and 44 months); all were widespread hematogenous metastases (including brain). All were symptomatic and presented at an unscheduled visit between follow-ups. Conclusions: SLNB negative stage IB melanoma has a survival similar to clinical stage IA. There were very few recurrences; all were widespread, symptomatic, and would not have been "salvaged" by routine studies. Conditional survival based "abbreviated" cancer surveillance with no routine ancillary studies is an evidence-based, cost effective strategy for this low risk population.

### 69 Open versus Minimally Invasive Management of Gastric Gastrointestinal Stomal Tumors: An International Multi-institutional Analysis of Short- and Long-term Outcomes

Bischof,1 D. G., Blazer III,2 S. K. Maithel,3 T. C. Gamblin,4 T. Bauer,2 P. Karanicolas,1 C. L. Wang,6 F. Quereshy,6 T. Pawlik,5 1. Surgery, Johns Hopkins Hospital, Baltimore, MD; 2. Winship Cancer Institute, Emory University, Atlanta, GA; 3. Medical College of Wisconsin, Milwaukee, WI; 4. University of Virginia, Charlottesville, VA; 5. Odette Cancer Centre, Sunnybrook Health Sciences Centre; University of Toronto, Toronto, ON, Canada; 6. Princess Margaret Hospital, University of Toronto, Toronto, ON, Canada; 7. Duke University Medical Center, Durham, NC.

Background: Overall surgical experience with minimally invasive surgery (MIS) has increased, however, published reports on MIS resection of gastrointestinal stromal tumors (GIST) are currently limited to small, single institution experiences. Methods: 397 patients who underwent resection of a gastric GIST between 1998 and 2012 were identified from an international, multi-center database. The impact of the MIS approach on recurrence and survival was analyzed by the use of propensity-score matching by comparing clinicopathologic factors between patients who underwent open vs MIS resection. Results: Median patient age was 65 years and 50% were female. Median tumor size was 4.3 cm (IQR 3.0-7.6cm). A minority of patients received neoadjuvant therapy (6%). Overall, 186 (47%) patients had a MIS approach: laparoscopic (89%), laparoscopic hand-assist (4%), combined laparoscopic-endoscopic (3%) and robotic (4%). There were 19 (10%) conversions to open; the most common reasons for conversion were tumor more extensive than anticipated (26%) and unclear anatomy (10%). Patients who underwent MIS resections had smaller tumors (MIS: 3.5 cm vs open: 5.8cm; p<0.01). MIS resections were associated with minimal blood loss (MIS: 50cc vs open: 225cc) and shorter operative time (MIS: 160 min vs open: 201 min) (both p<0.01). There was no difference in tumor rupture rates (MIS: 1% vs open: 1%; p=0.81). An R0 resection was achieved in the majority of patients (MIS: 98% vs open: 92%; p=0.07). MIS patients had a lower incidence of grade 3 or 4 complications (MIS: 3% vs open: 10%; p=0.01) and a shorter length of stay (MIS: 3d vs open: 8d; p=0.01). After propensity score matching for age, sex, tumor size, mitotic rate and tumor rupture, there was no difference in risk of recurrence or overall survival for the MIS treated group vs. the open group (HR 0.65 & HR 0.76, respectively; both p<0.05). Conclusions: An MIS approach for gastric GIST is associated with a low incidence of complications and a comparable R0 resection rate. The long-term oncological outcome following MIS is excellent and thus MIS approach should be considered preferable.

### 70 A Decade of Experience with Postoperative Imatinib Mesylate for Gastrointestinal Stromal Tumors: Does the Duration of Treatment Increase Long-term Survival?

O’Connor,1 G. B. Deutsch,1 E. A. Arena,1 J. Albright,1 R. P. O’Connor,2 M. Sim,3 A. Bilchik,3 J. D. Ellenhorn,1 1. John Wayne Cancer Institute, Santa Monica, CA; 2. U.S. Army Reserve, Los Angeles, CA.

Introduction: Few population-based studies have addressed the impact of adjuvant imatinib mesylate (IM), particularly postoperative IM, on the survival of patients with gastrointestinal stromal tumor (GIST). Patient selection, usage patterns, and optimal duration of IM therapy also are not well-defined. Methods: We used Surveillance Epidemiology and End Results (SEER)-Medicare data to identify all patients who underwent surgical resection of GIST from 2001 to 2010. Demographic and tumor characteristics were reviewed to compare patients according to whether or not they received postoperative adjuvant IM. Multivariate analysis evaluated the impact of treatment duration on overall survival (OS) up to 8 years. Results: Of 1,043 GIST patients, 244 received postoperative adjuvant IM (54.5% males, 45.5% females; White 71%, Black 18%, other 11%; T4 4%, T2 14%, T3 32%, T4 40%, unknown-10%; primary site stomach 53%, small intestine 36%, colon/rectum 6%, other 5%). During the decade under study, IM use progressively increased from 18.6% to 70.6% (p<0.0001). The 5-year OS was 70% for the IM group vs. 54% for the non-IM group (p<0.0001). There were no differences in tumor rupture rates (IM: 1% vs non-IM: 1%; p=0.81). An R0 resection was achieved in the majority of patients (IM: 98% vs non-IM: 92%; p=0.07). Patients who received IM resections had larger tumors (IM: 3.5 cm vs non-IM: 5.8cm; p<0.01). IM resections were associated with minimal blood loss (IM: 50cc vs non-IM: 225cc) and shorter operative time (IM: 160min vs non-IM: 201min) (both p<0.01). There was no difference in tumor rupture rates (IM: 1% vs non-IM: 1%; p=0.81). An R0 resection was achieved in the majority of patients (IM: 98% vs non-IM: 92%; p=0.07). IM patients had a lower incidence of grade 3 or 4 complications (IM: 3% vs non-IM: 10%; p=0.01) and a shorter length of stay (IM: 3d vs non-IM: 8d; p<0.01). After propensity score matching for age, sex, tumor size, mitotic rate and tumor rupture, there was no difference in risk of recurrence or overall survival for the MIS treated group vs. the open group (HR 0.65 & HR 0.76, respectively; both p<0.05). Conclusions: An MIS approach for gastric GIST is associated with a low incidence of complications and a comparable R0 resection rate. The long-term oncological outcome following MIS is excellent and thus MIS approach should be considered preferable.
Multivariate regression analysis of incremental increases in imatinib mesylate (IM) therapy duration associated with relative risk of death in terms of the duration of treatment. Duration of treatment significantly influences survival of patients receiving adjuvant IM after surgical resection of GIST.

<table>
<thead>
<tr>
<th>Duration of IM Therapy</th>
<th>P</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 6 months</td>
<td>0.032</td>
<td>0.98</td>
</tr>
<tr>
<td>&gt; 6 - 12 months</td>
<td>0.119</td>
<td>0.84 (0.50 - 0.99)</td>
</tr>
<tr>
<td>&gt; 12 - 18 months</td>
<td>0.358</td>
<td>0.95 (0.69 - 1.30)</td>
</tr>
<tr>
<td>&gt; 18 months</td>
<td>-0.0001</td>
<td>0.99 (0.10 - 0.99)</td>
</tr>
</tbody>
</table>

Abbreviation: HR, hazard ratio.

Comparison of Perioperative Radiation Therapy and Surgery versus Surgery Alone in 204 Patients with Primary Retroperitoneal Sarcoma: A Two-institution Study K.J. Kelly,1* S.S. Yoon,1 D. Kuk,1 L. Qin,1 K. Dudleska,1 K.K. Chang,1 Y. Chen,1 M.F. Brennan,1 T.F. Delaney,1 S. Singer,1 1. Memorial Sloan-Kettering Cancer Center, New York, NY; 2. Massachusetts General Hospital, Boston, MA.

Background: The role of radiation therapy (RT) for retroperitoneal and pelvic sarcomas (RPS) is controversial. We examined the association of perioperative, advanced-modality RT with outcomes in patients (pts) with primary RPS. Methods: Prospective databases were reviewed to compare primary RPS pts treated at two institutions between 2003 and 2011. Clinicopathologic variables were analyzed with endpoints of local recurrence-free survival (LRSF) and disease-specific survival (DSS). Results: At one institution 172 pts were treated with surgery alone, while at the other 32 pts were treated with surgery and perioperative proton beam (PBRT) or intensity-modulated RT (IMRT) ± intra-operative electron-beam RT (IOERT). RT was delivered pre-operatively for 30 pts and post-for 2 pts. External beam RT was delivered by IMRT, PBRT, or both at a median dose of 50 Gy. IOERT was given to 15 pts at a median dose of 10 Gy. The groups were similar in age, gender, tumor grade, tumor size, and margin status (p = NS). The RT group had a lower percentage of retroperitoneal versus pelvic tumors and leiomyo/liposarcoma versus other histologies (p = 0.050). Morbidity was higher in the RT group (41% vs 17%; p = 0.004). After a median follow-up of 39 months, 5-year predicted LRSF was 91% (95% CI, 79-100%) in the RT group and 65% (57-74%) in the surgery only group (p = 0.024). On multivariate analysis, RT was significantly associated with better LRSF (p = 0.026) (Table). Other independent predictors of LRSF were high grade and non-leiomyosarcoma histology. Five-year predicted DSS was 93% (95% CI, 82-100%) in the RT group and 84% (78-91%) in the surgery only group (p = NS). The RT group had a lower percentage of retroperitoneal versus pelvic tumors and leiomyo/liposarcoma versus other histologies (p = 0.050). Morbidity was higher in the RT group (41% vs 17%; p = 0.004). After a median follow-up of 39 months, 5-year predicted LRSF was 91% (95% CI, 79-100%) in the RT group and 65% (57-74%) in the surgery only group (p = 0.024). On multivariate analysis, RT was significantly associated with better LRSF (p = 0.026) (Table). Other independent predictors of LRSF were high grade and non-leiomyosarcoma histology. Five-year predicted DSS was 93% (95% CI, 82-100%) in the RT group and 84% (78-91%) in the surgery only group (p = NS). The RT group had a lower percentage of retroperitoneal versus pelvic tumors and leiomyo/liposarcoma versus other histologies (p = 0.050). Morbidity was higher in the RT group (41% vs 17%; p = 0.004). After a median follow-up of 39 months, 5-year predicted LRSF was 91% (95% CI, 79-100%) in the RT group and 65% (57-74%) in the surgery only group (p = 0.024). On multivariate analysis, RT was significantly associated with better LRSF (p = 0.026) (Table). Other independent predictors of LRSF were high grade and non-leiomyosarcoma histology. Five-year predicted DSS was 93% (95% CI, 82-100%) in the RT group and 84% (78-91%) in the surgery only group (p = NS). The RT group had a lower percentage of retroperitoneal versus pelvic tumors and leiomyo/liposarcoma versus other histologies (p = 0.050). Morbidity was higher in the RT group (41% vs 17%; p = 0.004). After a median follow-up of 39 months, 5-year predicted LRSF was 91% (95% CI, 79-100%) in the RT group and 65% (57-74%) in the surgery only group (p = 0.024). On multivariate analysis, RT was significantly associated with better LRSF (p = 0.026) (Table). Other independent predictors of LRSF were high grade and non-leiomyosarcoma histology. Five-year predicted DSS was 93% (95% CI, 82-100%) in the RT group and 84% (78-91%) in the surgery only group (p = NS).
Abstracts: Plenary, Parallel and Video Sessions S31

74

Fat-induced Retroperitoneal Soft Tissue Sarcoma (STS) Tumorigenesis

N. Lubczynski, S. Lowenstein, J. Klausner, G. Lahat. * Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

Background: Research regarding the association between obesity and different types of cancer is relatively scarce. To date, there is no comprehensive data concerning possible local effects of fat on cancer cells. Since retroperitoneal STS and retroperitoneal fat cells are typically co-localized we sought to evaluate such potential interplay utilizing STS as a model. Methods: A xenograft nude mouse model was used to evaluate the in vivo effects of human retroperitoneal on STS cell line growth. Tissue explants were prepared from retroperitoneal fat. Explants conditioned media (CM) was utilized for various in vitro experiments evaluating STS and endothelial cell lines growth, survival, migration and invasion as well as for mass spectrometry in order to identify secreted pro-tumorigenic factors. Results: Initially, we evaluated the clinical association between retroperitoneal fat (RF) and retroperitoneal STS patients outcomes demonstrating that high RF content is an independent predictor of local recurrence and mortality. Next, we used a xenograft mouse model in vivo experiment to show an increased STS tumor growth rate of SK-LMS1 cells co-localized with human RF as compared to cancer cells only (p<0.05). Utilizing an in vitro model, we found that RF conditioned medium (CM) increased STS cellular growth and reduced apoptosis induced by doxorubicin. In addition, RF enhanced STS cells migration and invasion. Since endothelial cells are of mesenchymal origin we expected similar results; our data depict that RF CM significantly enhanced endothelial cells tube formation, suggesting its role as a pro-angiogenic factor in STS tumor microenvironment. Next, using a robust proteomic approach we identified various potential molecules secreted into the RF CM associated with various pro-tumorigenic biological processes. Conclusion: Our data imply that RF may directly interact with STS cells by secreting specific adipokines into the tumor microenvironment, thus enhancing STS tumor cell proliferation and invasiveness. Fat-induced STS molecular deregulations should be studied to identify new potential prognostic and therapeutic targets.

75

Prognostic Value of CTNNB1-gene Mutation in Primary Extra-abdominal Aggressive Fibromatosis

D. Van Broeckhoven, 1, 6 C. Verhoef, 7 D. Grünhagen, 1 J. Van Gorp, 1 T. Van Dalen. 2 1. Erasmus Medical Centre, Rotterdam, Netherlands; 2. Diakonessenhuis, Utrecht, Netherlands.

Introduction: Aggressive fibromatosis (desmoid) is a tumor with varying biological behavior. Tumor localization appears to influence the risk of recurrence, while the effect of margin width and radiotherapy are disputed. Genetic tumor characteristics may be predictive of recurrence, hence the prognostic value of 3 desmoid-specific mutations on the CTNNB1-gene was evaluated. Methods: A multi-institutional retrospective cohort study was done in patients with extra-abdominal aggressive fibromatosis who underwent surgical treatment. The original pathology specimens were retrieved and analyzed addressing the presence of the T41A-, S45F- and 45P- mutations on the CTNNB1-gene. The risk of recurrence was analyzed using the Kaplan-Meier method and log-rank test. Results: Eighty-seven patients were analyzed. During a median follow-up of 40 months, 10 recurrences were detected (5-year recurrence rate was 15.7%). A localization in the abdominal wall was associated with a low risk of recurrence (0/29; P=0.031). Other clinicopathological variables, the result of surgery (R0 vs R1) and addition of radiotherapy were not associated with recurrence. The pathology specimens of these patients were analyzed. A desmoid-specific CTNNB1-mutation was found in 69 patients, and the majority of these patients had a T41A-mutation (n=45). CTNNB1-mutations were associated with the risk of recurrence. The presence of S45F resulted in a 5-year cumulative risk of recurrence of 41% vs 7.1% when this mutation was absent (P<0.001). No recurrences were observed, when CTNNB1-mutations were absent. Abdominal wall desmoids were associated with a lower frequency of S45F-mutations and a higher frequency of T41A-mutations (P=0.041 Chi-square). Conclusion: CTNNB1-mutation appear to impact the risk of recurrence following surgical treatment for primary extra-abdominal aggressive fibromatosis. In particular S45F-mutation increases the risk of recurrence.

Figure 1. Kaplan–Meier analysis showing the association between the CTNNB1-mutation and local recurrence following surgery for extra-abdominal desmoid-type fibromatosis. P =0.002 (log rank test)

76

Radiation-associated Unclassified Pleomorphic Sarcoma is Associated with Worse Clinical Outcomes compared to Sporadic Lesions

S. Dineen, 1* G. Al Sannaa, 2 C. May, 1 R. Feig, 1 D. Ingram, 2 W. Wang, 2 V. Ravi, 2 K. K. Hunt, 1 J. N. Cormier, 1 B. Feig, 1 A. Lazar, 1 K. Torres. 1. Department of Surgical Oncology, MD Anderson Cancer Center, Houston, TX; 2. Department of Pathology, MD Anderson Cancer Center, Houston, TX; 3. Sarcoma Medical Oncology, MD Anderson Cancer Center, Houston, TX.

Introduction: Radiation therapy is increasingly included in the management of patients with various cancers. However, adverse events can be associated with such treatment, including the development of a radiation-associated soft tissue sarcoma (RA-STS). Unclassified pleomorphic sarcoma (UPS),

INTRODUCTION: Leiomyosarcoma (LMS) is a common form of sarcoma, known to originate from almost any site of smooth muscle in the body, including the retroperitoneum, uterus, extremity, and trunk. It is unclear whether these tumors share a unified behavior or represent discrete biologic entities based on their site of origin. We sought to compare clinicopathologic features, survival, and recurrence patterns following surgical resection of LMS stratified by site of origin. METHODS: Patients with LMS undergoing resection at a single academic institution were retrospectively reviewed. Patients with GIST were excluded. Clinicopathologic variables were compared using Fisher’s exact and ANOVA tests. Survival was calculated using the Kaplan Meier method and compared using the log rank test. Factors associated with survival were evaluated using Cox regression analysis. RESULTS: From 1983 to 2011, 138 patients underwent surgical resection for LMS at our institution, 95 (69%) at initial presentation, 22 (16%) for persistent disease shortly after incomplete resection at an outside institution, and 21 (15%) for recurrent disease following resection at an outside institution (after a median interval of 35 months). Clinical, pathologic, and outcome comparisons are shown (Table). Retroperitoneal and uterine LMS were significantly larger, of higher grade, and associated with synchronous metastases. However, disease-specific survival, recurrence-free survival, and patterns of failure were not significantly different among the 4 anatomic sites. Similarly, in multivariate analysis, synchronous metastases (HR 3.3, P=0.001) were not a significant predictor of worse survival outcomes. DSS was also significantly lower in patients with RA-UPS compared with sporadic UPS (64.9±4.3% sporadic, 39.6%±7.4 RA-UPS; p < 0.01). There was no differential pattern of expression for molecular markers between the RA-UPS and sporadic cohorts. However, high expression levels of pAKT (HR 1.72; CI 1.08 - 2.57; p = 0.02), high levels of p53 (HR 2.02; CI 1.26-3.25; p = 0.015), absence of PTEN (HR 2.17; CI 1.40 - 3.36; p < 0.001) correlated with worse patient outcomes. Conclusions: We found that survival outcomes are significantly worse following a diagnosis of RA-UPS compared with sporadic UPS. Future investigation of molecular markers such as pAKT, PTEN, p53 and pS6RP should be examined prospectively to determine prognostic value.
Abstracts: Plenary, Parallel and Video Sessions S33

Independent Predictors of Overall Survival in 169 Patients Treated for MPM on an Intention to Treat Basis

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>0.54</td>
<td>0.15 - 0.82</td>
<td>0.004</td>
</tr>
<tr>
<td>Age &gt; 70 years</td>
<td>0.32</td>
<td>0.13 - 0.87</td>
<td>0.013</td>
</tr>
<tr>
<td>Epithelioid histology</td>
<td>0.63</td>
<td>0.37 - 1.06</td>
<td>0.081</td>
</tr>
<tr>
<td>Recurrent disease*</td>
<td>0.26</td>
<td>0.13 - 0.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-bulky nodules&gt;0.5 cm</td>
<td>0.32</td>
<td>0.19 - 0.53</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hepatic</td>
<td>0.40</td>
<td>0.23 - 0.71</td>
<td>0.002</td>
</tr>
<tr>
<td>Clinical trial subject</td>
<td>0.56</td>
<td>0.34 - 0.95</td>
<td>0.026</td>
</tr>
</tbody>
</table>

* Initial cytoreduction could be performed (i.e. not an open-close operation)

** Tumor nodules >0.5 cm in depth or plaques >0.5 cm in diameter after initial cytoreduction

Induction Therapy does not Influence Perioperative Outcomes in Patients with Locally Advanced Esophageal Adenocarcinoma: A Propensity Matched Analysis K.S. Naso,1 4 J.D. Luketich,2 H. Zahoor,1 N.A. Christie,3 R.M. Levy,1 D. Winger,1 M.K. Gibson,2 B. Weksler,1 1. Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA; 2. Case Medical Center, Cleveland, OH.

BACKGROUND: Multimodality therapy is commonly used in the treatment of esophageal adenocarcinoma but induction therapy may increase risk for postoperative adverse events. Our study aimed to determine whether induction therapy significantly impacted postoperative outcome in patients undergoing minimally invasive esophagectomy for esophageal adenocarcinoma using propensity-matched analysis. METHOD: From our prospectively maintained database we abstracted demographics, comorbidities, tumor, treatment and outcome variables for patients with stage II or higher esophageal adenocarcinoma (n=375) undergoing IT-MIE (n=197, 53%) or MIE (n=178, 47%) between 1997 and 2009. Using multiple pre-treatment predictor variables 81 propensity-matched pairs (n=162 patients) were identified. Postoperative outcomes were compared overall and within the propensity-matched groups. Significance was defined as p<0.05. RESULTS: Overall, the unmatched groups differed in age (median 65 for IT-MIE and 67 for MIE alone; p=0.001), symptoms at presentation (e.g. dysphagia and gastrointestinal bleeding; 36% versus 16%; p<0.001), clinical disease stage (Stage III 48% versus 43% and Stage IV 16% versus 3%; p<0.001), Comorbid diseases were more common in the MIE alone group with 40% having an age-adjusted Charlson comorbidity index score of >3 compared to 30% of the IT-MIE group (p=0.043). Following propensity matching, there were no significant differences between the 81 match pairs. There were no significant differences in the rate of major postoperative adverse outcome between IT-MIE and MIE (21% and 30%, respectively; p=0.278) or any postoperative adverse event (31% and 40%, respectively; p=0.324) after propensity matching. Pulmonary complications were the most common adverse outcomes. (Table 2) Postoperative length of stay was 8 days for both groups. Combined in-hospital and 30 day mortality was 2% for IT-MIE and 3% for MIE alone (p=0.318). CONCLUSIONS: In a propensity-matched analysis, induction therapy had minimal effects on postoperative outcomes in patients undergoing minimally invasive esophagectomy for esophageal adenocarcinoma.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>IT-MIE</th>
<th>MIE</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major morbidity</td>
<td>17 (21%)</td>
<td>24 (30%)</td>
<td>0.278</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>7 (9%)</td>
<td>12 (15%)</td>
<td>0.329</td>
</tr>
<tr>
<td>Reoperation</td>
<td>10 (13%)</td>
<td>15 (19%)</td>
<td>0.395</td>
</tr>
<tr>
<td>Tracheotomy</td>
<td>7 (9%)</td>
<td>12 (15%)</td>
<td>0.329</td>
</tr>
<tr>
<td>ARDS</td>
<td>2 (2%)</td>
<td>1 (1%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Chylothorax</td>
<td>2 (2%)</td>
<td>0 (0%)</td>
<td>0.407</td>
</tr>
<tr>
<td>Anorexia lute</td>
<td>6 (7%)</td>
<td>5 (5%)</td>
<td>0.746</td>
</tr>
<tr>
<td>Gastric tube occlusion</td>
<td>1 (1%)</td>
<td>2 (2%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Intestine resection</td>
<td>22 (23%)</td>
<td>18 (22%)</td>
<td>0.183</td>
</tr>
<tr>
<td>30 days readmission</td>
<td>13 (16%)</td>
<td>19 (23%)</td>
<td>0.324</td>
</tr>
<tr>
<td>Respiration in hospital/30 days</td>
<td>13 (16%)</td>
<td>11 (14%)</td>
<td>0.825</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>6 (8)</td>
<td>14 (20)</td>
<td>0.825</td>
</tr>
<tr>
<td>30 days post hospital mortality</td>
<td>3 (2%)</td>
<td>6 (3%)</td>
<td>0.318</td>
</tr>
</tbody>
</table>

Relative Delta SUV of Less than 45% on F 18-FDG Positron Emission Tomography (PET) Predicts Residual Disease in Patients with Locally Advanced Esophageal Adenocarcinoma Undergoing Neoadjuvant Chemoradiotherapy M. Kukar,1 R.M. Alnaji,2 J.F. Jafi,1 T.A. Platz,1 K. Attwood,1 K.S. May,1 K. Ben-David,1 K. Kanchira,1 J. Gannon,1 S.N. Hochwald,1 1. Roswell Park Cancer Institute, Department of Surgical Oncology, Buffalo, NY; 2. University at Buffalo, School of Medicine and Biomedical Sciences, Buffalo, NY; 3. Roswell Park Cancer Institute, Department of Nuclear Medicine, Buffalo, NY; 4. University of Florida, Department of Surgery, Gainesville, FL; 5. Roswell Park Cancer Institute, Department of Radiation Oncology, Buffalo, NY; 6. Roswell Park Cancer Institute, Department of Pathology, Buffalo, NY.

Introduction: Neoadjuvant chemoradiotherapy (NCR) is routinely used in the management of locally advanced esophageal adenocarcinoma (EA). Identifying patients with residual disease is critical, since surgery is potentially the only curative option in these patients. There is conflicting data regarding the PET characteristics, being able to predict pathologic response, following NCR in EA as existing studies include squamous histology, have had limited numbers and non-standardized PET imaging. Methods: Patient records were reviewed from a prospective collected database covering 2005-2012. Inclusion criteria included patients undergoing esophagectomy for locally advanced EA post NCR with two standardized PET studies at our institution (pre and post NCR) for review. Data collected included clinical, pathologic, imaging and treatment characteristics. Quantitative and qualitative PET data was collected including SUV measurements and pattern of uptake. PET studies and all pathology slides were re-reviewed by a single nuclear medicine physician (JG) and a single pathologist (KK) respectively, blinded to the clinical data. Results: 77 patients met the inclusion criteria. 22 patients (28.6%) had a pathologic complete response (pCR) versus 55 patients with residual disease (pRD). The two groups were similar in terms of age, gender, race, comorbidity conditions, ECOG status, tumor grade, chemotherapy and radiation regimen and days between the 2 PET CTs. Mean pre SUV was higher in tumors with a pCR (14.45) vs. pRD (11.23, P=0.05). Delta SUV was significantly higher in those with NCR vs pRD (10.25 vs. 6.61, P=0.03) as was relative Delta SUV (p=0.03). Utilizing the Youden’s index, a relative Delta SUV value of less than 45% was significantly associated with residual disease with a positive predictive value of 91.7% (73%-99%, p<0.05). Conclusions: To our knowledge, this is the largest series examining the role of PET characteristics in EA undergoing NCR and demonstrates that relative Delta SUV of less than 45% reliably predicts patients who have residual disease.

The Usefulness of Neoadjuvant Chemoradiation Therapy for Locally Advanced Esophageal Cancer with Multiple Lymph Nodes Metastasis H. Okumura,4 Y. Uchikado,1 I. Onomoto, Y. Kitai, K. Sasaki, M. Matsumoto, T. Owaki, T. Ariigami, Y. Uenosono, S. Ishigami, S. Natsumo. Kagoshima University, Kagoshima, Japan.

Introduction The prognosis of esophageal cancer (EC) patients with multiple lymph nodes metastasis was quite poor. In this study, we examined the neoadjuvant chemoradiation therapy (CRT) effect on the EC patients with more than 4 lymph nodes metastasis and compared the outcome with the patients with less than 3 lymph nodes metastasis without CRT in order to explore the new treatment strategy for the locally advanced EC. Patients and Methods The present study was prospective trial and involved consecutive 50 patients with T3-4 tumor without organ metastasis. Among them, 20 patients had more than 4 lymph nodes metastasis that underwent CRT plus operation (CRT group), and other 30 patients had less than 3 lymph nodes metastasis underwent only operation (Surgery group). Finally, clinical outcome of both groups was compared. 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 seen. The histological complete response (pCR) was defined when no viable tumor cells were seen. The tumor regression grade (TRG) was evaluated according to Japan Esophageal Society classification. Results 77 patients met the inclusion criteria. 22 patients (28.6%) had a patho-logic complete response (pCR) vs. pRD (11.23, P=0.05). Delta SUV was significantly higher in those with NCR vs pRD (10.25 vs. 6.61, P=0.03) as was relative Delta SUV (p=0.03). Utilizing the Youden’s index, a relative Delta SUV value of less than 45% was significantly associated with residual disease with a positive predictive value of 91.7% (73%-99%, p<0.05). Conclusions: To our knowledge, this is the largest series examining the role of PET characteristics in EA undergoing NCR and demonstrates that relative Delta SUV of less than 45% reliably predicts patients who have residual disease.
and 8 patients in Surgery group. The 3-year survival rate was 71% in the CRT group and 72% in the Surgery group (P = 0.97). According to the histological effect in the CRT group, 3-year survival was 50% for Grade 1, 100% for Grade 2 and 80% for Grade 3 (P = 0.05). This prospective trial did not demonstrate a statistically significant survival difference between the CRT group and the Surgery group. Conclusion: The neo-adjuvant CRT was beneficial for the patients of locally advanced EC with more than 4 lymph nodes metastasis.


INTRODUCTION: Esophagectomy is a complex, morbid operation that requires significant devotion of resources. However, factors that influence the extent of cost and care for this high acuity intervention are unclear. We sought to determine which clinical variables contribute to increased resource utilization. METHODS: 6,737 patients undergoing total esophagectomy or esophagegastrectomy from 2009-2012 were identified from the University Health-systems Consortium (UHC). A UHC specific severity of illness (SOI) index was used to examine linear and logistic regression models used to determine patient factors associated with resource utilization, including mortality, length of stay (LOS), readmission rate, cost and discharge disposition. RESULTS: Older age (>70 vs. <70 years old) and higher severity of illness (SOI) were significant predictors of increased use of health care resource. Older patients undergoing esophagectomy cost 7.4% more than younger patients ($25,859 vs $24,084, p<.001) and had a longer median LOS (11 vs 10 days, p<.001). Furthermore, older patients were more likely to be discharged with home health or to a rehabilitation/SNF locale (OR 1.5; 95% CI 1.3-1.7 and OR 4.9; 95% CI 4.1-5.7, respectively). Older patients were readmitted at the same rate as younger patients (17.7% vs. 17.4%, p=0.74) but had a significantly higher rate of perioperative mortality (OR 2.1; 95% CI 1.7-2.7). Similarly, patients with higher SOI cost 51% more ($25,266 vs 17,399, p<.001), had longer median LOS (11 vs 8 days, p<.001) and were discharged with home health or to rehabilitation/SNF at a higher rate (OR 1.8; 95% CI 1.6-2.1 and OR 5.9; 95% CI 4.2-8.3, respectively). Higher SOI patients, however, were more likely to be readmitted (17.9% vs 14.4%, p<.001) and suffer a post-operative death (OR 13.9; 95% CI 4.5-43.6). CONCLUSION: Older patients and those with a higher severity of illness utilize more resources, with higher perioperative mortality and readmission rates. As health care costs are increasingly scrutinized, future efforts should examine patient-center scenarios in which reduction of adverse outcomes can help lower health care utilization.

83 Impact of Inflammation-metaplasia-adenocarcinoma Sequence and Inflammatory Microenvironment in Esophageal Carcinogenesis using Surgical Rat Models T. Miyashita,1 H. Tajima,1 I. Makino,1 H. Nakagawara,1 H. Kitagawa,1 F.A. Shah,2 M.D. Duncan,2 J.W. Harmon,2 T. Ohta,3 J. Gastroenterological Surgery, Kanazawa University Hospital, Kanazawa, Japan; 2. Department of Surgery, Johns Hopkins University, Baltimore, MD.

The incidence of esophageal adenocarcinoma continues to rise in the Western world. Prior studies have suggested that gastroduodenal content reflux from gastro-esophageal reflux disease (GERD) induces the inflammation mediated progression from hyperplasia to metaplasia, and to adenocarcinoma. We proved inflammation-metaplasia-adenocarcinoma sequence with the use of an established surgical rat model without carcinogen. We also found that duodenal contents reflux plays an important role in the inflammation induced transformation of esophageal mucosa to adenocarcinoma than acid reflux in esophageal carcinogenesis. Chronic inflammation has been demonstrated to correlate with tumor onset and progression. An inflammatory microenvironment ensues during tumor growth as a result of the secretion of inflammatory mediators (cytokines, chemokines, growth factors, reactive oxygen and nitrogen species, prostaglandins) by the tumor and/or stromal cells. Recently, we confirmed that macrophages (M1 phenotype macrophage) infiltrate the esophagus and pS6AT3 pathway activated in stromal cells and neighborhood epithelium at the early inflammatory stage of esophageal carcinogenesis. M2 phenotype macrophages infiltrate following infiltration of M1 macrophage and contribute to tumor development. Thus the inflammatory microenvironment is formed. Furthermore, regulatory T cell (Treg) was induced by tumor or M2 phenotype macrophages relating to process of carcinogenesis (Figure). We introduces an esophagus carcinogenic process in clinically relevant surgical rat models.

84 Changing Patterns in Presentation and Therapy of Esophagogastric Junction Cancers in the U.S. E.R. Schwartz,1,2 D.D. Smith,2 R. Nelson,2 1. IUH Goshen Center for Cancer Care, Goshen, IN; 2. City of Hope Cancer Center, Duarte, CA.

Background: Esophagogastric junction cancer (EGJC) has recently been included within the esophageal cancer (EC) AJCC TNM staging criteria. Trends in clinical presentation, therapeutic approach and outcomes are of interest. Methods: We identified EGJCs from the U.S. population SEER database and examined incidence, demographic, therapeutic and outcomes information. Siewert classification-related EGJC subtype-associated findings were also examined. Results: EGJC age-adjusted incidence rates (10.0-5.0) have increased from 3.3 in 1973 to 7.5 in 2009. While the incidence rate for females has remained around 2, rates in males have increased from 6 to 13. Among 30,710 EGJC patients diagnosed between 1992 and 2009, potentially curative resection increased from 31% to 36% and radiation increased from 32% to 41% (p<0.0001). For resected EGJCs, significant trends over time include: increased total LN count (mean: 15.5 vs. 12.3), fewer positive LNs (3.1 vs 4), smaller tumor size (29% vs. 36% >5 cm), lower T category (39% vs. 29% T1/T2), lower N category (42% vs. 35% N0), lower stage group (29% vs. 38% stage 3/4), increased preoperative radiation (26% vs. 3%), decreased 90-day mortality (6.5 vs. 14.1%), longer overall survival (OS, median: 2.9 vs. 1.7 years) and longer disease-specific survival (median: 3.9 vs. 2.0 years) (all at p<0.0001). Multivariate predictors of OS include TNM categories, age, ethnicity, radiation, and total LN count (all at p<0.0001). There were significant differences in stage-for-stage OS between EC subtypes based on histology and primary tumor location, and in DSS between EGJC subtypes (Siewert I, II or III) as well. Conclusions: EGJC incidence rates, diagnosis and treatment have undergone significant changes within the U.S. population. The regional dissection extent remains an area of importance as it is associated with OS. Comparisons of various survival outcomes do not support using the same staging criteria for EGJC as for EC.

85 Surgical Outcomes of Patients with Locally Advanced Non-small Cell Lung Cancer E. Lushaj, W. Abi Jaoude, R. Macke, J. Maloney.* University of Wisconsin, Madison, WI.

Background: Controversy continues regarding the optimal therapy for stage IIIa non-small cell lung cancer (NSCLCa). Survival is improved in patients undergoing multimodality therapy that includes surgery. Surgery in locally advanced stages is presumed to have greater potential morbidity.
The goal of this study was to assess the impact of locally advanced disease on operative outcomes based on STS criteria. Methods: We retrospectively reviewed prospectively collected institutional STS data. 74 consecutive patients with stage IIA NSCLCa were treated surgically between 08/2006 and 11/2012. The cohort was divided into patients having surgery as their initial intervention followed by adjuvant therapy, and patients having neoadjuvant therapy followed by surgery. Demographics, post-treatment survival, complications and survival rates were assessed. Results: Mean age at hospital admission was 64 years. Video-Assisted Thoracoscopic Surgery (VATS) was performed in 17.5% (n=13) of patients (forty-three percent (73%; n=54) of patients had surgery as the initial treatment. 27% (n=20) had neoadjuvant therapy prior to surgery. Length of hospital stay (LOS) of patients having neoadjuvant therapy was significantly higher (p<0.04; mean±3.4 days; median±5 days) compared to LOS of patients having only surgery (mean±7.3±2 days; median±3 days). No difference was found in prolonged (>5 days) air leak (15% of patients having neoadjuvant therapy vs. 9.2% of patients having only surgery; p=0.46), reoperation rate (15% vs. 4% in neoadjuvant and surgery group respectively; p=0.11), pneumonia (0% of patients in each group) or UTI rates (5% vs. 1.8% in neoadjuvant and surgery group respectively; p=0.45). 30-day readmission rate was 9% (n=5) for surgery and 10% (n=2) for neoadjuvant groups (p=0.89). 30 day survival was 100% in both groups. Conclusions: Pulmonary resection as an initial therapy or following neoadjuvant radiation and chemotherapy is a safe for patients with stage IIIa NSCLCa. Though LOS was increased in the neoadjuvant group compared to initial surgical therapy, locally advanced disease does not confer increased risk of morbidity or mortality in our study population.

86 FDG PET/CT versus CT in Predicting Histopathological Response to Epidermal Growth Factor Receptor: Tyrosine-kinase Inhibitor (EGFR-TKI) Treatment in Resectable Non-small Cell Lung Cancer

Introduction: The purpose of this study was to prospectively evaluate diagnostic computed tomography (CT) and 18F-fluorodeoxyglucose positron emission tomography/CT (FDG-PET) for identification of histopathologic response to neoadjuvant erlotinib, epidermal growth factor receptor - tyrosine kinase inhibitor (EGFR-TKI) in patients with resectable non-small cell lung cancer (NSCLC). Patients & Methods: This study was designed as an open-label phase II trial, performed in four hospitals in the Netherlands. Patients received preoperative erlotinib 150 mg once daily for 3 weeks. CT and FDG-PET/CT were performed at baseline and after 3 weeks of treatment. CT was assessed according to the RECIST criteria 1.1 and Hounsfield Units were measured. FDG-PET/CT, tumour FDG uptake and changes were measured by standardized uptake values (SUV). Patients were divided in three groups based on the histopathologic response according to percentage of necrosis (>90% [CrP]; 90%-50% [PrP]; <50%). Radiologic and metabolic responses were compared to the histopathologic response. Results: Relative change in tumour diameter on CT was not significantly associated with histopathologic response. Relative change was similar in the three groups determined by histopathologic evaluation with means close to 0% (p=0.29). Relative change in Hounsfield Units on CT was inconsistent among the three groups (p=0.3715). Relative change in SUVmax on FDG-PET/CT showed significantly more SUVmax decrease in the histopathologic response group versus the no pathologic response group (p=0.0132). The ROC curve for FDG PET/CT was 0.69 (95% CI: 0.51-0.87) with optimal cutoff point at 28%. The ROC curve of CT was 0.53 (95% CI: 0.34-0.71) with optimal threshold of 35%. Conclusion: FDG-PET/CT has an advantage over CT as a predictive tool to identify histopathologic response after 3 weeks of EGFR TKI treatment in patients with resectable NSCLC.

87 Initial Experience of Thoracoscopic Evacuation and Tunneled Pleural Catheters for Palliation of Malignant Pleural Effusion

Introduction: Palliative thoracoscopic evacuation and tunneled pleural catheter installation from January 2012 to June 2013. Palliation was considered successful when the patient required no additional effusion-directed drainage procedures Results We included 29 patients in the final analysis, 14 male (48.3%) and 15 female (51.7%). Mean age 53.9 years (range 20–78). Common primary cancer was lung (9 cases 31%), breast (7 cases 24.1%), ovarian (2 cases 6.9%) and lymphoma (2 cases 6.9%) cancer. Others are described in Table 1. In 24 patients (82.8%) there was a pre-existing procedure for palliation of effusion (median 1.62, range 1–6). A trapped lung was identified preoperatively in 21 patients (72.4%). Average surgical time was 57.52 minutes (range 15–130); median blood loss was 32.76 milliters (range 5–400). There were no peri-operative complications. Mean duration of postoperative chest tube was 2.5 days (range 0–8); mean postoperative stay was 4.55 days (range 1–25). There were no postoperative complications in 23 patients (86.3%), 3 patients developed an atelectasis (10.3%) and 1 patient (3.4%) a wound failure. There were 2 deaths (6.8%) during the first 30 days of postoperative follow-up, none directly related with the catheter (one pulmonary thromboembolic event and one hemorrhagic cerebral vascular event). After a median follow-up of 22 weeks (range 1–67) a total of 21 patients still alive 72.4% with a median duration of tunneled catheter in situ of 29.14 days (range 2–93) Moreover, successful palliation was achieved in 28 patients (96.6%). Conclusions Despite the high variability on practice for palliation of malignant pleural effusion, in our study we found that thoracoscopic evacuation with the use of tunneled pleural catheters is a safe procedure, associated with a short hospital stay, a low rate of catheter-related complications and with a high rate of palliation.

88 Experience with Primary and Metastatic Adenoid Cystic Carci- noma

Introduction: Adenoid cystic carcinoma (ACC) is a rare malignancy. Primary intratho- racic ACC arises in the tracheobronchial tree, whereas pulmonary metastases commonly develop from head and neck (H&N) ACC. The aim of this study was to evaluate outcomes of primary and metastatic ACC encountered on our thoracic surgery service. Departmental database was searched for ACC resections from 1999-2013. Fourteen patients with 1st tracheobronchial ACC and 24 patients with pulmonary metastases from H&N ACC were identified. Studied variables included type and completeness of resection, outcomes included overall survival (OS) and recurrence rate. Kaplan Meier method was used to estimate OS. Surgical resections in 14 patients (6 female, 8 male, median age 47 years with 1st tracheobronchial ACC included: trachea (N=6), carina (N=3), carinal pneumonectomy (N=1), left pneumonectomy (N=3), and sleeve lobectomy (N=1). R0 resection was achieved in 50% (7/14) patients. Adjuvant radiation was used in 93% (N=13) patients. At median follow up 28 months, estimated 5-year survival was 88%, with 14% (2/14) distant recurrence rate. Pulmonary metastases from H&N ACC (N=24, 16 female, 8 male, median age 52 years) developed at median 73 months from primary diagnosis. Total of 73 wedge (median 2) resections was performed. The majority 62% (15/24) of metastases presented bilaterally; R0 resection was achieved in 92% of primary metastases (22/24). Six patients underwent 2nd and two 3rd metastasectomy. Recurrence of metastases occurred in 70% (17/24) of patients; 58% (14/24) was pulmonary at median 16.4 months. The median OS after 1st metastasectomy was 100 months. Estimated OS from the time of 1st metastasectomy was 88% at 5 years, 35% at 10 years, and 17% at 15 years. Despite the high rate of R1 resection, good outcomes with low recurrence rate can be achieved in 1st tracheobronchial ACC. On the contrary, despite the initial R0 resection...
of metastatic ACC many patients experience pulmonary metastases recurrence. Metastasectomy may potentially benefit patients with prolonged initial disease-free interval. Due to the relatively indolent nature of ACC patients experience prolonged survival even with metastatic disease.

89 Utility of the Proximal Margin Frozen Section for Resection of Gastric Adenocarcinoma: A 7-institution Study of the U.S. Gastric Cancer Collaborative M.H. Squires,1,6 D.A. Kooby,1 T. Pawlik,7 S.M. Weber,5 G.A. Poultisides,2 C.R. Schmidt,9 K.I. Votanopoulos,6 R.C. Fields,1 A. Ejaz,4 A.W. Acker,1 D.J. Worhunsky,7 N. Saunders,6 D.S. Swords,2 L.X. Jin,3 C.S. Cho,7 M. Bloomston,5 E. Winslow,8 M.C. Russell,1 C.A. Staley,2 S.K. Matipel,1 1. Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Stanford University Medical Center, Palo Alto, CA; 3. University of Wisconsin School of Medicine and Public Health, Madison, WI; 4. The Ohio State University Comprehensive Cancer Center – The Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH; 5. Washington University in St. Louis, St. Louis, MO; 6. Wake Forest University, Winston Salem, NC; 7. The Johns Hopkins University, School of Medicine, Baltimore, MD.

Background: The proximal gastric margin dictates the extent of resection for gastric adenocarcinoma (GAC). The value of achieving negative margins by additional gastric resection after a positive proximal margin frozen section (FS) is unknown. Methods: The U.S. Gastric Cancer Collaborative includes all patients who underwent resection of GAC at 7 institutions by oncologic surgeons from 2000-2012. Intraoperative proximal margin FS data were classified as R0 or R1 based on final permanent section (PS); positive distal margins were excluded. The primary aim was to evaluate the impact on local recurrence (LR) of converting a positive proximal margin FS to an R0 final margin by additional resection. Secondary endpoints were recurrence-free (RFS) and overall survival (OS). Results: Of 860 patients, 520 had a proximal margin FS; 67 were positive. Of these 67, 48 were converted to R0 on PS by additional resection. R0 proximal margin was achieved in 447 patients (86%), R1 in 25 (5%), and R1 converted to R0 in 48 (9%). Median follow-up was 28 months. Although LR was decreased in the converted R1 to R0 group compared to the R1 group (10% vs 32%, p=0.01), when accounting for other pathologic variables on multivariate (MV) analysis, R1 to R0 conversion was not associated with decreased LR. Median RFS was similar between the R1 to R0 conversion and R1 groups (36 vs 26 months; p=0.14) compared to 50 months for the R0 group. On MV analysis, increasing T-stage and positive lymph nodes were associated with worse OS; R1 to R0 conversion of the proximal margin was not associated with improved OS (p=0.5; Table). Conclusion: Conversion of a positive intraoperative proximal margin frozen section during gastric cancer resection does not decrease local recurrence or improve recurrence-free or overall survival. This may guide decisions regarding the extent of resection.

Multivariate Regression Analysis for Overall Survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal Tumor</td>
<td>0.9</td>
<td>0.6-1.3</td>
<td>0.6</td>
</tr>
<tr>
<td>T-stage</td>
<td>1.4</td>
<td>1.2-1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Signet Ring</td>
<td>1.2</td>
<td>0.8-1.8</td>
<td>0.3</td>
</tr>
<tr>
<td>LN Positive</td>
<td>1.5</td>
<td>1.03-2.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Final Proximal Margin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>Ref</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R1</td>
<td>1.7</td>
<td>0.9-2.9</td>
<td>0.09</td>
</tr>
<tr>
<td>R1-0 Conversion</td>
<td>1.3</td>
<td>0.6-2.9</td>
<td>0.5</td>
</tr>
<tr>
<td>Tumor Size</td>
<td>1.03</td>
<td>0.99-1.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>


Introduction: Circulating angiogenic and growth factors in patients with gastric and gastroesophageal junction (GEJ) cancers may promote tumor progression and metastasis and may also represent targets for therapy. Methods: Serum levels of ligands from four targetable pathways — vascular endothelial growth factor A (VEGF-A), fibroblast growth factor 2 (FGF2), epidermal growth factor (EGF), hepatocyte growth factor (HGF) — were measured before surgery, and levels were correlated to clinicopathologic characteristics and outcomes. Results: For 147 patients who underwent potentially curative resection for gastric and GEJ adenocarcinoma, median age was 67, 59% of patients were male, and 75% were Caucasian. Tumor location was lower in 35%, middle in 24%, upper in 19%, GEJ in 19%, and diffuse in 3%. VEGF-A levels were higher in patients with R1 resection than R0 resection (p=0.037). High EGF level was associated with poorly-differentiated tumors (p=0.02). High FGF2 levels were found in patients with Lauren diffuse type tumors (p=0.017) and tumors with 7 or more metastatic nodes (N3) (p=0.042). High HGF levels were correlated with advanced stage tumors (p=0.012). At a median follow-up of 35 months, 46 patients (31%) had died. High VEGF and HGF levels were associated with decreased overall survival (p=0.009 and 0.005, respectively). As shown in Figure 1, an adjusted total value (ATV) of all factors was better than any single factor in stratifying patients into good and poor prognosis groups (5-year overall survival 84.1% vs. 53.9%, p<0.005). By multivariate analysis, serum VEGF-A and ATV were significant independent prognostic factors (along with T and N status) for overall survival (p=0.028 and p=0.013, respectively). Conclusions: In patients undergoing resection for gastric and GEJ cancer, high levels of angiogenic and growth factors are associated with unfavorable tumor characteristics and poorer overall survival. Thus levels of these factors can help delineate tumor biology, stratify prognosis, and possibly direct targeted therapies.


Introduction Our hypothesis is that circulating tumor cells (CTCs) in patients with gastric cancer are associated with the prognosis and the recurrence. In this study, we evaluated CTCs in gastric cancer and clarified the clinical impact of CTCs. Furthermore, primary tumors and CTCs were confirmed the HER2 expression. Methods A total of 265 consecutive patients with gastric cancer were enrolled. Fourteen patients were excluded in analysis because 12 patients had another cancer and 2 patients refused the treatment. Two hundred fifty-one patients were divided into two groups. One hundred forty-eight patients with gastrectomy were included in Resection Group, and 103 patients without gastrectomy were in Non-resectable Group. Peripheral blood samples were collected before gastrectomy or chemotherapy. The CellSearch system was used for the isolation and enumeration of CTCs. Clinical samples of 36 patients with un-resectable gastric cancer were examined the expression of HER2 in primary tumor and CTCs. Results CTCs were detected in 16 patients (10.8%) of Resection Group and 62 patients (60.2%) of Non-resectable Group. The overall survival rate of all patients was significantly lower in patients with than without CTCs (p=0.0001). In Resection Group, relapse-free and overall survival in patients with CTC was significantly lower than patients without CTC.
It is worth mentioning that expression of CTC was an independent factor for determining overall survival of gastric cancer in multivariate analysis (p=0.0024). In Non-resectable Group, overall survival rate was significantly lower in patients with than without CTCs (p=0.0044). Twenty percent of all patients were pathological HER2 positive. CTCs were found in 25 patients, and HER2 positive expression on CTCs was found in 10 patients. Conclusion: The evaluation of CTCs in peripheral blood may be a useful tool for predicting tumor progression, prognosis, and the effect of chemotherapy in patients with gastric cancer. Her2 expression of CTCs may be extended the adaptation of Trastuzumab for gastric cancer.

CellSearch evaluation of HER2/neu expression in gastric cancer cell lines

<table>
<thead>
<tr>
<th>Comp</th>
<th>CK-PE</th>
<th>DAPI</th>
<th>CD45-APC</th>
<th>HER2/neu</th>
</tr>
</thead>
<tbody>
<tr>
<td>NUGC4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KATO III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

92 Neoadjuvant FOLFIRINOX Combined with Aggressive Surgical Resection Allows Potentially Curative Therapy for Borderline Resectable and Locally Advanced Pancreatic Cancer M. Bloomston,* M. Blazer, J. Onesti, C. Schmidt, P. Muscarella, T. Bekaii-Saab. Surgical Oncology, Ohio State University Wexner Medical Center, Columbus, OH.

Background: Since its first report to improve survival in metastatic pancreatic cancer, we have used neoadjuvant FOLFIRINOX for borderline resectable (BR) and locally advanced (LA) pancreas cancer with planned major vascular resection. Herein we report our early experience with this approach. Methods: Non-metastatic pancreatic cancers not meeting strict NCCN guidelines for resectable disease were treated with 2 months of modified FOLFIRINOX. If tolerance and response were favorable, mFOLFIRINOX was continued until maximum response followed by chemoradiation for those still BR or LA. Surgery was offered if complete resection was feasible +/- arterial or venous resection. Response rates, resection rates, and outcomes were followed. Kaplan-Meier PFS curves were compared by log rank analysis based on resection status. Results: Since January 2011, 43 patients (18 BR and 25 LA) have been treated (Table). BR tumors were more commonly in the head of the pancreas compared to LA (89% vs 36%, p<0.001). Patients received an average of 4.9 cycles of mFOLFIRINOX and 56% received chemoradiation. Ultimately 67% were explored and 49% were resected. Failure to resect was due to metastases in 4, LA in 11, and medical/toxicity in 3. One patient was lost to follow-up and 3 are yet to be restaged. Major vascular resection was required in 19% (venous 1, arterial 3) and negative margins achieved in 90% of those resected. There were no postoperative deaths. Final pathology showed nodal metastases in less than half with complete pathologic responses in 2. Early follow-up shows median PFS 18.4 months in those resected vs 9.2 months for not resected (p<0.05). Median OS has not been reached in either group. Conclusion: Neoadjuvant mFOLFIRINOX is a promising and effective treatment regimen for non-metastatic yet not clearly resectable pancreatic cancer. The modified regimen was associated with acceptable tolerance and led to a high resection rate and downstaging. Even in those with locally advanced unresectable cancer, potentially curative resection was achieved in some with aggressive surgery after neoadjuvant mFOLFIRINOX.

<table>
<thead>
<tr>
<th>Mean age</th>
<th>Total (N=83)</th>
<th>BR (N=18)</th>
<th>LA (N=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location (head)</td>
<td>25 (30%)</td>
<td>62.2</td>
<td>62.6</td>
</tr>
<tr>
<td>FOLFIRINOX cycles Mean (range)</td>
<td>4.9 (1-14)</td>
<td>4.4 (1-8)</td>
<td>5.3 (1-14)</td>
</tr>
<tr>
<td>Chemoradiation</td>
<td>24 (56%)</td>
<td>8 (44%)</td>
<td>16 (64%)</td>
</tr>
<tr>
<td>Explored</td>
<td>20 (60%)</td>
<td>15 (83%)</td>
<td>14 (56%)</td>
</tr>
<tr>
<td>Resected</td>
<td>21 (49%)</td>
<td>11 (61%)</td>
<td>10 (40%)</td>
</tr>
<tr>
<td>Vascular resection</td>
<td>4 (21%)</td>
<td>1 (11%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Node positive</td>
<td>9 (21%)</td>
<td>5 (45%)</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>PD resection</td>
<td>19 (23%)</td>
<td>9 (50%)</td>
<td>1 (40%)</td>
</tr>
</tbody>
</table>


Background: The relationship of post-operative complications and administration of adjuvant chemoradiation therapy following pancreaticoduodenectomy (PD) for adenocarcinoma is poorly defined. Methods: A retrospective review of all patients undergoing PD at our institution between 1995 and 2010 was performed. Clinico-pathological data including Clavien-Dindo complication grade, time to adjuvant therapy (TTA), and survival was analyzed. Results: 1144 patients underwent PD for adenocarcinoma between 1995 and 2010. The overall complication rate was 49.1% and clinically significant complications (≥3b) occurred in 4.2%. 621 patients (54.3%) received adjuvant chemoradiation therapy. The median TTA was 60 days. Neither the presence (p=0.98) nor grade of complication (p=0.430) delayed TTA. On multivariate analysis, only age >68 (p=0.001) and length of stay >9 days (p=0.002) correlated with no adjuvant therapy. Patients with post-operative complications more frequently received single modality adjuvant therapy (31.4%) rather than combined chemoradiation therapy (17.1%, p=0.001). Patients without a complication had a longer median survival compared to patients with complications (19.5 vs 16.1 months, p=0.001). Patients without complications who received adjuvant chemoradiation therapy had longer survival than patients with complications who received no adjuvant (22.4 vs 10.7 months, p=0.001). Multivariate analysis demonstrated that complications (HR 1.19, p=0.013) and adjuvant chemoradiation (HR 0.67, p=0.001) were related to survival. Conclusion: Complications and no chemoradiation therapy are common following PD for adenocarcinoma. Post-operative complications do not delay TTA but reduce the likelihood of multimodality adjuvant therapy. Identifying patients at increased risk for complications and those unlikely to receive adjuvant chemoradiation warrants further investigation, as they may benefit from a neoadjuvant approach.
Defining the Learning Curve for Team-based Laparoscopic Pancreaticoduodenectomy


Introduction: The purpose of this study was to define the learning curve for laparoscopic pancreaticoduodenectomy (LPD) using paired surgical teams consisting of an advanced laparoscopic and advanced oncologic surgeon. Methods: All patients undergoing pancreaticoduodenectomy (PD) using paired surgical teams consisting of an advanced laparoscopic and advanced oncologic surgeon. Methods: All patients undergoing pancreaticoduodenectomy (PD) without vein resection at a single institution were retrospectively analyzed. LPD was first introduced as a hybrid procedure, with the resection performed laparoscopically followed by open reconstruction. After 18 months, a transition was made to total laparoscopic pancreaticoduodenectomy (TLPD). All procedures were performed by a paired team of a surgical oncologist and a fellowship-trained minimally invasive surgeon. Five surgeons participated in this pilot program. Cases were compared with Fisher’s exact test, Kruskal-Wallis ANOVA, and linear regression. Results: Between March 2010 and June 2013, 140 PDs were performed, of which 56 (40%) were attempted laparoscopically. The first 31 cases were undertaken as planned hybrid procedures; however, seven of these cases (23%) required premature conversion to open pancreaticoduodenectomy (OPD) prior to completion of the resection. Following these 23 hybrid procedures, 25 TLPDs were performed. None required conversion to OPD. For the first 10 LPDs, mean operative time was 480 minutes (vs. 417 in pre-LPD era, p=.018). Following these initial procedures, there was a significant reduction in operative time (67 min, p=0.01) (Figure). After 50 LPDs, operative times and EBL were consistently lower than those for OPD. Complication rates were similar across 10-patient cohorts. In addition to improvements in EBL and operative time, LPD was associated with increased node retrieval (14.5 vs. 9, p=.008) and shorter length of stay (8.5 vs. 12 days, p=.04). There were no significant differences in margin status, type C leak, surgical site infection, reoperation, or readmission. Conclusions: Building a LPD program, the initial 10 cases appear to represent the biggest hurdle. For an experienced teaching center using a staged and team-based approach, LPD appears to offer meaningful reductions in operative time, blood loss, and hospital length of stay within 50 cases.

A 13 Gene Expression Signature Predicts Survival of Patients with Pancreatic Cancer and Identifies New Genes of Interest


Objectives: Established pancreatic ductal adenocarcinoma (PDAC) cell lines are used extensively in cancer research. We hypothesized that orthotopic patient-derived xenografts (PDX) tumors would more closely model patient PDAC tumor genetic behavior than established cell lines. We sought to compare the gene expression profiles (GEP), receptor tyrosine kinase activity (RTK), and response to drug therapy of PDAC cell lines and PDX tumors. Methods: Affymetrix GeneChip arrays were used to generate GEPs from normal pancreatic tissue (n=18), human PDAC tissue (n=51), PDX tumors (n=12), established PDAC cell lines (MPanC96, BxPC3, L3.6 fp), and all NCI 60 cell lines, which were compared using hierarchical clustering analysis. RTK profiles from PDX cell line and tumor lysates were generated with R&D systems RTK arrays. Response to drug therapy with anti-EGFR (panitumumab) and anti-HER2 (trastuzumab) agents was assessed using CyQuant proliferation assays and sequential volumetric MRI. Results: Clustering analysis demonstrated differences in genome-wide gene expression patterns. Xenografts clustered most similarly to patient tumor and normal pancreatic tissue, while 3 of 4 established PDAC cell lines were most similar to non-pancreatic NCI 60 cells. PDX tumors and cell lines exhibited differences in baseline activation of surface receptors with Insulin-R, IGF1-R, and c-Met receptors often active.
in culture but not tumor lysates. Combination anti-EGFR/anti-HER2 therapy failed to inhibit cell proliferation in vitro, however, in vivo this combination produced an 85% reduction in PDX tumor growth rate relative to control treatment in our most responsive xenograft. Conclusions: High-passage, established PDX cell lines should be used with caution in preclinical studies as their GEPs are dissimilar to human PDAC tumors. Discordant baseline pRTK profiles reflect microenvironmental differences between PDX tumors and cell lines that impact drug response. Preclinical studies of agents that impact cell-microenvironment interactions should be conducted using orthotopic PDX models.

**97**

**CCR2 Blockade Enhances Anti-tumor Immune Responses in Patients with Pancreatic Cancer**


Introduction: Pancreatic ductal adenocarcinoma (PDAC) is characterized by a uniquely dense stroma where macrophages (MAC) are predominant. These protumor MAC suppress anti-tumor immunity as well as promote angiogenesis, chemoresistance, tumor invasion, and metastasis. Inflammatory monocytes (IM; CCR2+) are produced and stored in the bone marrow (BM), and depend on CCL2 for mobilization from the BM to the primary tumor and premetastatic sites where these cells become protumor MAC. We have previously shown that IM recruitment from the BM depends on CCL2 production by PDAC. Peripheral blood (PB) monocyte count predicts survival in PDAC patients. CCR2 inhibition (CCR2i) decreases tumor growth and metastasis, chemoresistance, tumor invasion, and metastasis. Inflammatory monocytes (IM; CCR2+) are produced and stored in the bone marrow (BM), and depend on CCL2 for mobilization from the BM to the primary tumor and premetastatic sites where these cells become protumor MAC. We have previously shown that IM recruitment from the BM depends on CCL2 production by PDAC. Peripheral blood (PB) monocyte count predicts survival in PDAC patients. CCR2 inhibition (CCR2i) decreases tumor growth and metastasis, chemoresistance, tumor invasion, and metastasis. Inflammatory monocytes (IM; CCR2+) are produced and stored in the bone marrow (BM), and depend on CCL2 for mobilization from the BM to the primary tumor and premetastatic sites where these cells become protumor MAC. We have previously shown that IM recruitment from the BM depends on CCL2 production by PDAC.

Patients are treated with either FX alone (n=6) or FX in combination with CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the CCR2i (FX&CCR2i) (n=6+32 [Phase 2 expansion cohort]). Presented here are the results of the Phase 1b correlative studies on evaluable patients from the
Survival Curves (Overall Survival and Disease free Survival) for PNET based on Final Grade (i.e. worse grade between Ki67 proliferation index and Mitotic rate)
Radio-guided Thoracoscopic Resection for Small Lung Nodules

1. Surgical Oncology Department-Instituto Nacional de Cancerologia (INCan) Mexico, Mexico City, Mexico; 2. Nuclear Medicine Department-Instituto Nacional de Cancerologia (INCan) Mexico, Mexico City, Mexico; 3. Interventional Radiology-Instituto Nacional de Cancerologia (INCan) Mexico, Mexico City, Mexico.

Introduction Thoracoscopic resection of lung nodules is a widespread practice when suspicious of malignancy. Minimally invasive approaches are easy when the nodule is peripherally located and the diameter is < 2 cm. However when they are located deep in the parenchyma or small in size, the lack of palpation becomes a limiting factor for localization and increases the rates of conversion to open thoracotomy. Methods We describe a procedure using tc99m-albumin for preoperative marking of the nodule, via a CT-guided puncture, and intra-operative identification with portable gamma-probe. Results To date we have performed 14 resections with this technique, mean surgical time is 46 min, with a blood loss of 35.6 ml in average. Complications associated with the resection were no reported, however 1 patient developed a pneumothorax during the marking procedure and 1 patient an infra-areola tious bleeding, both asymptomatic and none of these patients required additional procedures after the marking. The success rate of identification was 100%. Conclusions Radio-guided surgery is a safety procedure, associated with a high rate of success, is recommended for lung nodules located > 1.5 cm infra-areolar or when size is < 1 cm.

Minimally Invasive Esophagectomy with Cervical Anastomosis

M. Kukar,∗, S.N. Hochwald. Roswell Park Cancer Institute, Surgical Oncology, Buffalo, NY.

Purpose: This video demonstrates the steps involved in minimally invasive esophagectomy with cervical anastomosis. This technique is routinely employed in patients with esophageal cancer requiring surgical treatment. Methods: The patient is placed in left lateral decubitus position and the dissection is begun in right chest. The esophagus is mobilized past the thoracic inlet carefully preserving the recurrent laryngeal nerve. A penrose drain, looped around the esophagus, is placed at the highest level of dissection and a 24 F Blake drain is placed and chest ports are closed. A 6 cm cervical incision is made along the anterior border of sternocleidomastoid muscle and the penrose drain placed through the chest is identified. The abdominal portion of the procedure involves mobilizing the stomach, carefully preserving the right gastroepiploic vessels and construction of gastric conduit. The gastric conduit is brought into the neck and side to side stapled esophagastrogastrostomy is done. A 16 F T tube is used as a feeding jejunostomy and abdominal ports are closed. Cervical incision is closed with a 7 F Jackson Pratt drain.

Minimally Invasive Surgery (TAMIS) for a Mid-rectal Cancer with Metastatic Melanoma

A.J. Spillane, R.L. Read.1 Melanoma Institute Australia, North Sydney, NSW, Australia.

Metastatic melanoma to the groin is managed by either inguinal (IL) or ilioinguinal (I-IL) dissection. Controversy exists regarding the extent of surgery with some surgeons preferring to offer only IL unless there is clear evidence of pelvic disease. A randomized trial is currently being initiated to try to give evidence based for this decision. Many surgeons lack confidence in the technique of pelvic lymphadenectomy. Both IL and I-IL can have significant morbidity with wound complications occurring in approximately thirty percent of patients. The main focus of this video is to demonstrate a minimally invasive technique for pelvic lymphadenectomy utilizing a retroperitoneal approach through a skin crease and muscle splitting incision in the right iliac fossa. The IL dissection is performed through a second vertical incision over the sartorius muscle below the inguinal ligament. These incisions maintain skin cover over the groin crease as well as the femoral artery and vein and provide excellent exposure. Most of the footage in this video was recorded using a laparoscopic camera to enable the camera to get closer to the operation and to facilitate a unique view. The video was recorded from a single operative case (right I-IL dissection) in a patient who had known inguinal and pelvic metastatic melanoma after nodal observation, including ultrasound surveillance, for a sentinel node positive right leg melanoma. The procedure took ninety minutes to complete.

The Inframammary Approach to Nipple Sparing Mastectomy


As more patients opt for bilateral mastectomy for early stage disease or high risk based on genetic or familial susceptibility, the nipple sparing technique has become more popular. The most common surgical approach is to utilize the peri-areolar skin sparing incision through the mid chest. Although this has been relatively successful, it does compromise a portion of the blood supply to the nipple areolar complex (NAC) with potential skin loss and necrosis. Traction injury is also higher because of retraction of the NAC skin during the procedure. The infra-mammary approach allows for less injury to the NAC and provides the optimum amount of vascular supply to the areolar skin. All anatomic guidelines for a total mastectomy result in the removal of breast tissue to the clavicle, medial sternal border, latissimus muscle and inferior rectus fascia. The NAC is assessed for margins. This approach results in an improved potential survival of the NAC, as well as better cosmetic outcome without compromising the basic requirements of a total mastectomy.

Pushing the Limits of Local Excision for Rectal Cancer: Transanal Minimally Invasive Surgery (TAMIS) for a Mid-rectal Cancer with Post-endoscopic Mucosal Resection Structure

A. Artinyan,∗ 1. Baylor College of Medicine, Houston, TX; 2. Scott and White Hospital - Round Rock, Round Rock, TX.

Background: Transanal Minimally Invasive Surgery (TAMIS) is an evolving technique for the local excision of early rectal cancers1, particularly for...
Modified Surgical Technique for Pancreaticoduodenectomy following Coronary Artery Bypass Grafting using an in situ Right Gastroepiploic Artery S. Fukuhara, M.M. Montgomery, N. Ikoma, R. Miyata. 1. Department of Surgery, Beth Israel Medical Center, New York, NY; 2. University of Texas Health Science Center at Houston, Houston, TX; 3. International Goodwill Hospital, Yokohama, Kanagawa, Japan.

This video demonstrates pylorus preserving pancreaticoduodenectomy (PPPD) in a 66-year-old female with an ampullary tumor who had undergone coronary artery bypass grafting using right gastroepiploic artery (RGEA) 10 years ago. The procedure began with exploration of abdominal cavity through median celiotomy. The RGEA conduit was found at the left of ligamentum teres reaching the pericardial cavity. There was no evidence of peripyloric lymph node enlargement. Clamp test of the RGEA did not cause any remarkable changes on hemodynamics. Dissection of the adhesions surrounding the RGEA followed by division of the duodenum was preceded in order to mobilize and keep it from being in the main resection field. The duodenum was divided 2 cm distal to the pylorus. Pancreatoduodenal arcade was also test-clamped before division to assure that perfusion of RGEA conduit is maintained after ligation of superior mesenteric artery system. Satisfactory mobilization of RGEA conduit was gained after division of the pancreatoduodenal arcade. The RGEA conduit was kept wrapped with papaverine soaked gauze during this procedure. The standard processes of PPPD followed the preservation and mobilization of the RGEA. Pathological examination showed moderately differentiated adenocarcinoma (pT2 N0 stage IB). Postoperative course was uneventful. At present, 5 years after the surgical procedure, the patient remains well. The key to the success of this procedure is to gain curative oncological resection and preserve the conduit. Preoperative assessment of the function of the conduit and its gentle manipulation in its entirety of procedure are crucial. Adequate oncological curability while preserving the RGEA may be achievable considering the negligible incidence of subpyloric nodal metastasis in earlier-stage ampullary adenocarcinoma. By contrast, locally advanced disease may be associated with significantly higher nodal involvement and extensive resection with sacrifice of the RGEA conduit might be needed. Therefore, additional strategies for salvage revascularization of coronary artery should be considered.

Totally Laparoscopic Pancreatoduodenectomy for Pancreatic Head Cancer with Involvement of the SMV-PV Confluence Z. Awad.* Surgery, University of Florida, Jacksonville, FL.

Laparoscopic pancreatoduodenectomy is a technically demanding procedure. In this video we demonstrate the technical aspects of performing the procedure. 50 year old male with ascending cholangitis, ERCP was unsuccessful, PTC was done for biliary decompression. EUS: pancreatic head adenocarcinoma. The procedure was done using 5 trocars. Extensive lymphadenectomy was done. The Uncinate process was skeletonized off the SMA. The SMV portal vein confluence was involved wit the cancer and it was transsected using laparoscopic linear stapler with negative margin. All the anastomosis were done using laparoscopic intracorporeal suturing. Opatative time 8 hours 20 minutes, hospital stay 5 days. Final pathology T3 N1 (one lymph node out of 40 was positive). Conclusion: Laparoscopic pancreatoduodenectomy can be performed safely in selected cases of pancreatic head cancer with vascular involvement. Skilled laparoscopic skills are necessary to execute such procedures safely.
ABSTRACTS

Accepted for
POSTER PRESENTATIONS

67th Annual Cancer Symposium
Society of Surgical Oncology
March 12–15, 2014
Phoenix, Arizona
P1
Survival after Breast Conserving Surgery with Whole Breast or Partial Breast Irradiation in Women with Early Stage Breast Cancer: A SEER Database Analysis

Introduction: An increasing survival rate has resulted in about 3 million women who are breast cancer survivors in the United States and essentially the same trend may also be occurring in Europe. Early stage breast cancer is common, with about 90% of breast cancer cases occurring in women younger than 65 years of age. Breast cancer is now the most common cancer among women worldwide. Mutations in tumor suppressor genes are thought to provide an initial clonal expansion, however, the mechanisms that lead to further growth and metastasis are poorly understood. The pleiotropic bioactive lipid mediator sphingosine-1-phosphate (S1P) has emerged as a key regulatory molecule in cancer progression and inflammation. S1P produced by SphK1 in cancer cells is released into the extracellular environment, where it can bind to S1P receptors. In this study, we examined the role of S1P signaling in obesity-related breast cancer progression and evaluated the effects of the S1P receptor modulator FTY720 on tumor growth.

Methods: In vitro, we used two human epithelial breast cancer cell lines: MCF7 and HCC1806. In vivo, we used two murine breast cancer models: 4T1 and E0771. The mice were fed a high-fat diet and treated with FTY720. We measured tumor size, S1P levels, and S1P receptor expression.

Results: FTY720 treatment decreased S1P levels in both cell lines and in vivo experiments. In addition, FTY720 treatment downregulated S1P receptor expression.

Conclusion: FTY720 treatment inhibits S1P signaling and decreases breast cancer cell proliferation. This suggests that targeting S1P signaling may be a promising therapeutic strategy for breast cancer.

P2
The Effects of TNM Stage on Surveillance after Curative-intent Treatment for Breast Carcinoma
D. Wu,1* E.S. Allam,1 K.S. Virgo,2 J.A. Margenthaler,1 L. Chen,3 F.E. Johnson.1 1. Saint Louis University School of Medicine, Saint Louis, MO; 2. American Cancer Society, Atlanta, GA; 3. Washington University School of Medicine, Saint Louis, MO.

Introduction: The National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO) have published recommendations encouraging low intensity strategies, primarily consisting of office visit and mammogram, unless clinical evaluation suggests otherwise. We aimed to determine whether ASCO experts carry out surveillance differently for patients with breast cancer of different TNM stages.

Methods: We created a web-based survey instrument describing 4 patient vignettes with TNM stages 0 to IIIA. Respondents were asked how often they would recommend 12 specific diagnostic modalities for each vignette during post-treatment years 1-5. A link to the survey was e-mailed to 3,245 members of ASCO who had identified themselves as having breast cancer as a major clinical focus. Statistical analysis utilized repeated measures analysis of variance to generate mean, standard deviation, median, and range.

Results: 1,012 of the 3,245 ASCO members surveyed responded to the survey (31%). There were 915 (90%) evaluable responses. The frequency of recommended surveillance modalities varied with the initial TNM stage of the described patients, but these differences were not significant.

P3
Sphingosine-1-phosphate Signaling Exacerbates Obesity-related Breast Cancer Progression

INTRODUCTION: Although obesity is an established independent prognostic factor for breast cancer patients, the underlying mechanisms are poorly understood. The pleiotropic bioactive lipid mediator sphingosine-1-phosphate (S1P) has emerged as a key regulatory molecule in cancer progression and inflammation. S1P produced by SphK1 in cancer cells is released into the extracellular environment, where it can bind to S1P receptors. In this study, we examined the role of S1P signaling in obesity-related breast cancer progression and evaluated the effects of the S1P receptor modulator FTY720 on tumor growth.

Methods: In vitro, we used two human epithelial breast cancer cell lines: MCF7 and HCC1806. In vivo, we used two murine breast cancer models: 4T1 and E0771. The mice were fed a high-fat diet and treated with FTY720. We measured tumor size, S1P levels, and S1P receptor expression.

Results: FTY720 treatment decreased S1P levels not only in the circulation, but also in the tumor and tumor interstitial fluid. FTY720 treatment also suppressed tumor progression significantly in both mouse models. The number in each cell is the number of times a particular modality is recommended in a particular post-treatment year. These data present all values from all evaluable responses for all vignettes.
 efficacious in the obese mice than the lean mice. CONCLUSIONS: Our data suggest that S1P signaling worsens obesity-related breast cancer progression. Targeting the S1P signaling with FTY720 may be useful for treating breast cancer in individuals with obesity. MN is a Japan Society for the Promotion of Science Postdoctoral Fellow. This work was supported by NIH R37GM043880 and R01CA61774 to SS, and R01CA160688 and Susan G. Komen IIR12222224 to KT.

**P4**

Preoperative Prediction of Cosmetic Results after Breast Conserving Surgery E.L. Vos,1* A.H. Koning,1 I. Obdeijn,1 V.V. Verschuer,1 C. Verhoef,1 P.J. Van der Spek,2 M.B. Menke-Pluijmers,1 L.B. Koppert.1 1. Erasmus MC-Cancer Institute, Rotterdam, Netherlands; 2. Erasmus MC, Rotterdam, Netherlands; 3. Albert Schweitzer Hospital, Dordrecht, Netherlands.

Background: Cosmetic result plays an important role in the choice for mastectomy or breast conserving surgery (BCS) in breast cancer treatment and is associated with quality of life. Preoperative tumor volume as compared to breast volume (TV/BV ratio) was tested as predictor for cosmetic result. Methods: Data was collected prospectively of women treated for invasive breast cancer with (oncoplastic) BCS in our cancer institute and from whom preoperative magnetic resonance imaging (MRI) was available. Using a CAVE-like virtual reality system, the I-Space, tumor and breast volumes were measured in a three-dimensional projection of the preoperative MRI. Cosmetic result was assessed on a linear scale by 9-item patient questionnaire, 11-item panel evaluation of photographs, and breast retraction assessment (BRA). Quality of life was assessed by the EORTC QLQ-C30 and BR23. Results: A total of 67 women with 69 breast cancers were included. Intraobserver and interobserver correlation coefficients for tumor and breast volume as measured in I-Space were all >0.95. Median time between date of BCS and date of inclusion was 33 months (range 6-66). Excellent/good cosmetic result in contrast to moderate/bad cosmetic result was reported in 55 (79.7%) of the patient questionnaire, 49 (71.0%) of the panel evaluation and 43 (62.3%) of the BRA. Increasing TV/BV ratio correlated with a decrease in all three cosmetic result assessments (Figure 1). After linear regression analyses adjusted for excision volume and radiological tumor size, TV/BV ratio was a significant independent predictor for cosmetic result as compared to breast volume and tumor location had good accuracy in predicting panel evaluation of cosmetic result (AUC=0.83). Conclusion: TV/BV ratio can be precisely measured in I-Space with preoperative MRI. TV/BV ratio can be used in a preoperative prediction tool to aid in surgical treatment decision making and informing patients.

**P5**

A Comparison of Complication Rates and Local Recurrence in Early Stage Breast Cancer Patients Treated with Brachytherapy versus Whole Breast Irradiation N. Aikay,1* A.E. Collett,1 E.V. Bloomquist,1 E.J. Gracely,1 T.G. Frazier,1 A.V. Barrio.1 1. Comprehensive Breast Center, The Bryn Mawr Hospital, Bryn Mawr, PA; 2. School of Public Health, Drexel University College of Medicine & Drexel University, Philadelphia, PA.

INTRODUCTION: The adoption of breast brachytherapy into clinical practice for early stage breast cancer has increased over the last several years. Studies evaluating complication rates following treatment with brachytherapy have shown conflicting results. We compared local toxicity and in breast tumor recurrence (IBTR) in patients treated with brachytherapy to those treated with whole breast irradiation (WBI). METHODS: An IRB approved retrospective chart review identified 417 early stage breast cancer patients treated with lumpectomy and radiation between 2004 and 2010. We compared 271 women treated with balloon-based brachytherapy to 146 women treated with WBI. Long-term complications and IBTR rates were assessed using Kaplan-Meier curves with log-rank test. RESULTS: Median follow-up was 4.6 years. The WBI cohort was younger (p<0.001), had larger tumors (p=0.001), had more node positive patients (p=0.001), and was more likely to receive systemic therapy (p=0.01). Five-year incidence of infectious skin complications (9.7% vs 1.1%, p=0.84), abscess (1.1% vs 0%, p=0.4), telangiectasia (8.0% vs 5.3%, p=0.35) and breast pain (14.2% vs 9.4%, p=0.2) were similar between the two groups. The brachytherapy cohort had a higher 5-year rate of seroma (47.8% vs 18.5%, p<0.001), and fat necrosis (39.5% vs 24.4%, p=0.01). Fat necrosis was detected more often as a palpable mass in the brachytherapy group compared to WBI group (54.3% vs 34.4%, p=0.06). Brachytherapy patients trended towards more frequent biopsies as a result of fat necrosis to rule out a recurrence (11.2% vs 6.7%, p=0.13). Five-year IBTR rates were similar between the brachytherapy and WBI cohorts (6.2% vs 4.6%, p=0.41). CONCLUSIONS: Patients treated with brachytherapy had more local toxicity, particularly seroma and fat necrosis, with similar rates of IBTR compared to the WBI cohort. The increased rate of fat necrosis in brachytherapy patients led to more biopsies to rule out recurrence. Patients should be counseled on the possible increased rate of long-term complications associated with brachytherapy treatment.

**P6**

The Clinical Benefit and Safety of Boosting the HER2 Peptide Vaccine (GP2+GM-CSF) in the Adjuvant Setting to Prevent Breast Cancer Recurrence E. Schneble,1* J.S. Berry,1 A.F. Trappey,1 D.F. Hale,1 T.J. Vreeland,1 A. Sears,2 G.T. Clifton,3 S. Ponniah,3 M. Papamichael,1 S. Perez,1 G.E. Peoples,1 E. Mittendorf.1 1. San Antonio Military Medical Center, San Antonio, TX; 2. MD Anderson Cancer Center, Houston, TX; 3. Uniformed Services University of Health Sciences, Bethesda, MD.

Background: GP2 is an HLA-A2+-restricted immunogenic peptide from the HER2 protein that stimulates CD8+ T cells to recognize and kill HER2 expressing tumor cells. Here we present the clinical efficacy and safety of boosters in a prospective, randomized, placebo-controlled phase II trial of GP2+GM-CSF for prevention of breast cancer (BrCa) recurrence. Methods: HLA-A2+, clinically disease-free, high risk BrCa patients (pts) enrolled in our GP2 vaccine trial who completed the primary vaccine series (PVS) more than 6 months prior were offered a series of 4 booster vaccinations every 6 months (500 mcg GP2 peptide + GM-CSF). Boosters were added after trial initiation. The primary endpoint of the trial is disease free survival. Secondary endpoints are local and systemic toxicity including delayed urticarial reactions (DUR).
defined as hypersensitivity reactions generally occurring 9-10 days post-inoculation. Results: A total of 170 pts have enrolled (88 HLA-A2+ controls and 82 vaccinated pts). To assess the benefit of boosters, we have only included pts completing the PVS. Therefore, 13 pts who have not completed the PVS, 1 pt declared ineligible, 4 pts with early recurrence prior to PVS completion, and 1 pt who developed a secondary malignancy were excluded leaving 63 evaluable pts. At 39 mos median follow up, the recurrence rate is 5.0%. Of these 63 pts, 46 have been boosted (B) and 17 were not (NB). There are no differences between B and NB with respect to age, grade, nodal status, tumor size, ER/PR status, and HER2 expression. The safety profile of the booster inoculations was similar to that seen in the PVS. DURs occurred in 6.5% during booster inoculations versus 4.8% during the PVS, p=0.51. The recurrence rate was reduced by 62.7% with booster inoculations (NB, 11.8%, vs. B, 4.4%, p=0.29).

Conclusions: The GP2 vaccine is safe overall, and the current 5% recurrence rate is half that expected in this population. The boosters have not added toxicity but have been associated with a trend towards decreased disease recurrence. This data suggests that boosting CD8+-eclatting, peptide vaccines will optimize their clinical benefit.

P7

Introduction Determining which lymph nodes are considered sentinel lymph nodes (SLNs) in breast cancer staging involves some subjective interpretation by the operating surgeon. We hypothesized that patient and tumor characteristics considered “higher risk” may influence the number of SLNs harvested. Methods A single institution prospectively collected database was queried for all clinically node-negative breast cancer patients undergoing SLN surgery from January 2002 to June 2013. Mean SLN counts were compared by clinical factors known to influence risk of metastases or false-negative SLN biopsy. Results 2,394 SLN biopsy procedures were performed. The mean and median number of SLNs per patient for the entire cohort was 2.6 and 2 respectively. The mean number of SLNs removed per patient was significantly greater for younger patients with mean SLN count for those ≤ 50 years being 2.88 compared to 2.56 for those ≥ 50 years (p<0.0001). This difference persisted when the age threshold was set at 60 years or at 70 years (p<0.0001 for each). Fewer SLNs were removed in smaller tumors with the mean SLN count for those ≤ 1 cm being 2.51 compared to 2.63 for those with tumors >1 cm (p=0.002). Patients with tumor grades 2 or 3 had more SLNs removed than those with a grade 1 tumor: 2.64 vs. 2.52 (p=0.03). Patient receipt of neoadjuvant therapy was associated with more SLNs being removed (2.96 vs. 2.61 for no neoadjuvant therapy, p=0.005). Estrogen receptor status (2.60 vs. 2.64, p=0.63) and ductal carcinoma in situ vs. invasive cancer (2.46 vs. 2.58, p=0.17) did not influence number of SLNs removed. Conclusion The number of SLNs removed in breast cancer staging varies significantly based on risk factors for SLN metastases or false-negative SLN biopsy. With the exception of patient age, these factors would not be expected to influence SLN mapping itself. Thus the pre-test probability of SLN metastases and risk of false negative SLN biopsy appears to influence surgeons to retrieve a greater number of SLNs. Across broad populations this has the potential to bias the staging of breast cancer patients.

P8
Deviation from the Standard of Care for Early Breast Cancer in the Elderly: What are the Consequences? S. Sun, C. Hollenbeck, A.M. Leung,* Surgery, Penn State Hershey Medical Center, Hershey, PA.

Introduction: Operative lymph node sampling and adjuvant radiation are standards of care in the treatment of early breast cancer. In the elderly populations, however, these standards are often not strictly adhered to due to either clinician biases of patient health and longevity or patient refusal of treatment. We hypothesized forgoing the standard of care for elderly patients would have a negative impact on survival. Methods: Using the SEER database we identified 53,619 women over the age of 55 with Stage I breast cancer undergoing partial mastectomy. These groups were then examined for adjuvant radiation and lymph node sampling. Patients were further stratified by age, race, hormone receptor status, and other demographics. Univariate and multivariate analyses were performed and survival was analyzed using the Kaplan-Meier method. Results: As patients aged they were significantly less likely to receive the standards of care of radiation and lymph node sampling both on univariate and multivariate analysis. When we examined survival for those who had adjuvant radiation versus no adjuvant radiation we found those with adjuvant radiation had a 15.8 percentage point increase in survival (p=0.005). Survival for those who had lymph node sampling versus no lymph node sampling was 27.1% increased (p=0.05). However, when propensity score was done to address selection bias and covariate imbalance we found the survival improvement for the radiation group decreased to 0.9% and was no longer statistically significant (p=0.617). The same held true for lymph node sampling when matched by propensity score as the survival advantage for those with sampling was only 0.2% after matching (p=0.522) (Figure 1). Conclusions: Although as patients age they are less likely to receive the standard of care in early breast cancer, results from this large population study show that when matched for other factors survival is not affected.

P9
SFRP2 Regulates Angiogenesis via the FZD5 Receptor J. Samples,* C. Patterson, D. Glatt, R. J. Mumper, S. Snyder, E. Hilliard, S. Siamakpour-Reihani, D. Ketelsen, N. Klauber-DeMore. 1. University of North Carolina at Chapel Hill, Chapel Hill, NC; 2. UNC McAllister Heart Institute, Chapel Hill, NC; 3. Division of Molecular Pharmaceutics, UNC Eshelman School of Pharmacy, Chapel Hill, NC.

Introduction: Secreted frizzled related protein-2 (SFRP2) is a secreted protein highly expressed in breast cancer endothelium. We previously reported that antagonism of SFRP2 inhibits triple negative breast cancer growth. We have shown that that SFRP2 stimulates angiogenesis via activation of calcineurin, which results in nuclear translocation of NFATc3, a transcription factor involved in angiogenesis. We hypothesized that frizzled 5 (FZD5) is the receptor that the ligand SFRP2 binds to stimulate angiogenesis. Methods: FZD5 was silenced in endothelial cells with shRNA and compared to sham-transfected endothelial cells. Matrigel tube assay was used to quantify angiogenic branches after treatment with or without recombinant SFRP2 (10nM) in sh-FZD5 transfected cells or sham-transfected cells. NFATc3 activation: Sham transfected or sh-FZD5 transfected cells were treated with control media or SFRP2 7nM for 1 hour, nuclear lysates were extracted and subjected to Western blot. SFRP2/ FZD5 binding affinity: The dissociation constant (Kd) between FZD5 and SFRP2 was determined using a microplate solid phase binding assay. Results: Western blot showed successful silencing of FZD5 in sh-FZD5 transfected cells. Matrigel tube assay. Sham-transfected cells had 476 ± 6 branch points; and sham cells treated with SFRP2 had 665 branch points ± 23 (p=0.001). sh-FZD5 transfected cells had 101 ±14 branch points, which did not increase with the addition of SFRP2 (98 branchpoints ± 6, p=NS). NFATc3 activation: Western blot showed that nuclear NFATc3 was increased in SFRP2 treated sham-transfected cells compared to untreated sham-transfected cells. However, nuclear localization of NFATc3 did not increase in the...
sh-FZD5-transfected cells with or without SFRP2 treatment (Fig. 1). SFRP2/FZD5 binding affinity: SFRP2 and FZD5 bound with high affinity, with a KD value of 0.084 nM. Conclusion: We report that FZD5 is a high affinity receptor of SFRP2, and interference with FZD5 expression abolishes SFRP2-stimulated NFATc3 activation and angiogenesis. We propose a previously unknown function of this molecule: the ability to mediate SFRP2-stimulated calcineurin/NFAT activation to induce angiogenesis via binding to the FZD5 receptor.

Fig. 1. FZD5 is required for SFRP2-stimulated NFATc3 activation. Sham transfected or sh-FZD5 transfected cells were treated with control media or SFRP2 7nM for 1 hour, nuclear lysates were extracted and subjected to Western blot. Western blot showed that nuclear NFATc3 was increased in the SFRP2 treated sham-transfected endothelial cells compared to untreated sham-transfected cells. However, nuclear localization of NFATc3 did not increase in the sh-FZD5-transfected cells with or without SFRP2 treatment.

P10

The Impact of Routine Sentinel Lymph Node Biopsy of Internal Mammary (IM) Lymph Nodes on the Risk of Recurrence in the IM Chain


Introduction: Preoperative lymphoscintigraphy frequently identifies internal mammary sentinel lymph nodes (IM SLNs) in addition to axillary SLNs in breast cancer patients. Following peritumoral tracer injection IM SLNs are observed in up to 25% of the patients, whereas uptake is seen in less than 5% following periareolar injections. We studied the impact of identifying and retrieving IM SLNs and adjusting treatment accordingly impacts the risk of recurrence in the IM chain. The absolute incidence of regional recurrence in the IM lymph nodes remains very low and should be reason to question the pursuit of IM SLNs.

Retrieving IM SLNs and adjusting treatment accordingly impacts the risk of recurrence in the IM lymph nodes. The cumulative 5-year regional IM recurrence rate was 0.1% in cohort A and 1.4% in cohort B (P<0.001). Overall, the cumulative 5 year ipsilateral locoregional recurrence rate was 2.0% and 3.9% respectively (P=0.011). Conclusions: Retrieving IM SLNs and adjusting treatment accordingly impacts the risk of recurrence in the IM chain. The absolute incidence of regional recurrence in the IM lymph nodes remains very low and should be reason to question the pursuit of IM SLNs.

Breast Cancer Characteristics with and without Chemoprevention in Patients with Atypical Breast Lesions


1. Massachusetts General Hospital, Boston, MA; 2. Dana Farber Cancer Institute, Boston, MA; 3. Newton Wellesley Hospital, Newton, MA.

Background: Chemoprevention significantly reduces breast cancer risk in patients with atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH), and lobular carcinoma in situ (LCIS). The objective of our study was to determine if there is a difference in cancers which develop in patients taking and not taking chemoprevention for atypical breast lesions. Methods: Natural language processing was used to review and parse 76,333 breast pathology reports from a single healthcare system from 1987-2010. This identified 2938 women with atypical breast lesions. Subsequent pathology reports were reviewed to identify those who developed invasive cancer and ductal carcinoma in situ (DCIS). Cancer details were obtained. Cancers that developed with and without chemoprevention were compared. Use of chemoprevention (tamoxifen, raloxifene, or exemestane) was determined by chart review; follow-up documentation that medication was taken was required. Estrogen receptor (ER) was considered positive if ≥ 1% of tumor nuclei stained. Results: We identified 2938 women with atypical breast lesions (1198 ADH, 827 ALH, 568 LCIS, 345 severe ADH). 263/2938 (9.0%) patients developed cancer at a mean follow-up of 67 months. 164/263 (62.4%) cancers were invasive and 99/263 (37.6%) were DCIS. 184/1472 (12.5%) patients not treated with chemoprevention and 24/466 (5.2%) patients treated with chemoprevention developed cancer (p<0.001). There was no significant difference in the proportions of cancer subtypes which developed in those taking and not taking chemoprevention (p=0.21) and no difference in invasive tumor sizes between groups (p=0.081) [Table 1]. We found no significant difference in the proportions of ER positive cancers in the chemoprevention and no chemoprevention groups (p=0.92). Cancers that developed in patients taking chemoprevention had a higher rate of lymph node positivity (p=0.0012), although this represented few patients (n=15). Conclusion: The vast majority of breast cancers which developed in patients previously diagnosed with atypical breast lesions were estrogen receptor positive, regardless of whether or not they took chemoprevention.

Comparison of breast cancers that developed with and without chemoprevention

<table>
<thead>
<tr>
<th>Type of Cancer</th>
<th>No Chemoprevention (n=184)</th>
<th>Chemoprevention (n=24)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCIS</td>
<td>67 (36.4%)</td>
<td>9 (37.5%)</td>
<td>0.21</td>
</tr>
<tr>
<td>IDC</td>
<td>79 (42.9%)</td>
<td>8 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>LCIS, other</td>
<td>35 (19.0%)</td>
<td>5 (20.8%)</td>
<td></td>
</tr>
<tr>
<td>Other invasive</td>
<td>3 (1.6%)</td>
<td>2 (8.3%)</td>
<td></td>
</tr>
</tbody>
</table>


eEnucleation Receptor

<table>
<thead>
<tr>
<th>Value</th>
<th>1.5 (range: 0.5-9.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turner Syndrome</td>
<td>1.3 (range: 0.1-1.0)</td>
</tr>
</tbody>
</table>

Chemoprevention status known for 208/263 (79.1%) patients who developed cancer. ER status known for 181/263 (68.8%) cancers.

Incidence of Chronic Pain after Continuous Local Anesthetic in Comparison to Standard Systemic Pain Treatment after Axillary Lymphadenectomy or Primary Reconstruction with a Tissue Expander in Breast Carcinoma Patients: A Prospective Randomized Study

N. Besic, B. Strazisar. Institute of Oncology, Ljubljana, Slovenia.

Background and Objectives: Continuous wound infusion of local anesthetic reduces acute postoperative pain and consumption of opioids com-
pared to the standard intravenous piritramide analgesia after breast cancer surgery. Our aim was to evaluate if continuous wound infusion of a local anesthetic into the surgical wound reduces incidence of chronic pain compared to standard analgesia after axillary lymphadenectomy or primary breast reconstruction. Methods: Altogether 120 patients were enrolled: 60 (mean age 60 y.) after axillary lymphadenectomy and 60 (mean age 48 y.) after primary breast reconstruction with a tissue expander. Half of the patients from each group had for two days postoperative wound infusion of local anesthetic. The other half had standard analgesia: a continuous intravenous infusion with piritramide (30 mg), metoclopramide (20 mg) and metamizole (2.5 g) until the next morning. The nursing staff was instructed to maintain the lowest rate of drip infusion, which relieved the patient of her pain. From the first post-operative day, all patients received analgesics in the form of tablets. All patients completed a questionnaire on pain three months after surgical procedure and were seen by a pain management team six months after surgical procedure. Results: Chronic pain was reported three months after axillary lymphadenectomy by 17% and 50% of patients from local anesthetic and standard analgesia group (p≤0.01), respectively. A neuropathic chronic pain was diagnosed six months after lymphadenectomy in 20% and 40% of patients from local anesthetic and standard analgesia group (p=0.09), respectively. Three months after primary breast reconstruction with a tissue expander, chronic pain was reported by 17% and 50% of patients from local anesthetic and standard analgesia group (p=0.01). Conclusions: Wound infusion of a local anesthetic reduces chronic pain in comparison to standard analgesia after axillary lymphadenectomy or primary breast reconstruction with a tissue expander in breast carcinoma patients.

P13
Measuring the Impact of ACOSOG Z0011 on Breast Cancer Surgery in a Community Health System: When, Where, and How Practice has Changed

Introduction: The ACOSOG Z0011 trial has been lauded as a practice-changing trial by demonstrating lack of a survival benefit in performing axillary lymph node dissection (ALND) in patients with sub-clinical sentinel lymph node (SLN) metastases. To date, no studies have measured the direct impact of the results on patient care in the post-Z0011 era. Methods: A retrospective chart review was performed for patients with invasive breast cancer who underwent lumpectomy and SLN biopsy. The time period was November 1, 2008 to June 30, 2013, 28 months before and after the publication of the Z0011 trial. Data from seven hospitals were obtained and analyzed in 14 month time periods. The primary outcome measures were the rate of completion ALND and performance of intraoperative SLN analysis in patients meeting the Z0011 criteria. Significance was assessed for p<0.05. Results: A total of 1125 lumpectomies with SLN biopsies were performed. There were 180 subjects meeting the inclusion criteria, 70 of which were in the post-Z0011 era. Performance of ALND (p<0.0001) and intraoperative SLN analysis (p<0.0001) steadily declined during each time period (Fig. 1). Despite these reductions, the rates of ALND and intraoperative SLN analysis were still 29% and 45%, respectively, in the latest time period. On multivariate analysis, patients more likely to undergo ALND on multivariate analysis included those with extracapsular metastases who may benefit from avoiding the morbidity of unnecessary ALND.

Fig 1. Practice Changes Over Study Period

P14
The Value of Screening Breast MRI in an At Risk Population
E. Bloomquist,* N. Ajkay, T.G. Frazier, A.V. Barrio. The Bryn Mawr Hospital, Bryn Mawr, PA.

Background: In 2007, the American Cancer Society published guidelines for screening breast magnetic resonance imaging (MRI) in patients at high risk for breast cancer. However, the low specificity of MRI may result in unnecessary biopsies and elevated healthcare costs. The aim of our study was to assess the value of screening MRI in a high risk population. Methods: Following IRB approval, a retrospective chart review identified 152 high risk patients who underwent one or more screening MRIs (mean 2.4, range 1-8) between January 2006 and December 2012. MRIs were ordered in asymptomatic women with a personal history or family history (Tyrer-Cuzick lifetime risk ≥ 15%) of breast cancer, atypical hyperplasia (AH), lobular carcinoma in situ (LCIS), or dense breasts. Patients with a BRCA mutation were excluded. Results: In total, 372 screening MRIs and 745 screening mammograms were performed in 152 high risk women. Personal history (45%) and family history (30%) were the most common reasons for screening with MRI. Of 372 MRIs, 39 (10.5%) biopsies were recommended in 28 patients. Cancer was detected in 4/39 (10.3%) MRI biopsies and in 4/152 (2.6%) MRI screened patients. Three cancers were detected by MRI alone (2 breast, 1 axillary) for a cancer detection rate of 0.8% (3/372). All 3 cancers were detected in women with a personal history of breast cancer as their only risk factor. Of 745 screening mammograms performed in the same cohort, 31 (4.1%) biopsies were recommended in 25 patients. Cancer was detected in 12/31 (38.7%) mammogram-generated biopsies and in 12/152 (7.9%) patients, for a cancer detection rate of 1.6%. Over the 6 year study period, the cost to detect one cancer with MRI screening was $98,020.79. Conclusions: Screening with breast MRI led to a substantial number of biopsies and resulted in detection of occult malignancy in a limited number of patients with a personal history of breast cancer. The cost to detect one cancer with screening MRI was significant in this population. Further refinement of the ACS guidelines for screening with MRI in high risk patients may be needed to avoid unnecessary healthcare expenditures.

Table 1. Medicare reimbursement rates and cost to detect one cancer with screening MRI in a high risk population

<table>
<thead>
<tr>
<th>Imaging</th>
<th>Medicare Reimbursement</th>
<th>N</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast MRI</td>
<td>$626.02</td>
<td>372</td>
<td>$217,079.44</td>
</tr>
<tr>
<td>MRI biopsy</td>
<td>$1,257.05</td>
<td>78</td>
<td>$33,782.00</td>
</tr>
<tr>
<td>Ultrasound guided biopsy</td>
<td>$1,024.35</td>
<td>10</td>
<td>$10,243.30</td>
</tr>
<tr>
<td>Serologic biopsy</td>
<td>$594.76</td>
<td>1</td>
<td>$594.76</td>
</tr>
<tr>
<td>6 month FU MRI</td>
<td>$56,824.12</td>
<td>12</td>
<td>$78,131.24</td>
</tr>
<tr>
<td>Pathologic analysis of core biopsy</td>
<td>$223.60</td>
<td>39</td>
<td>$8,883.40</td>
</tr>
<tr>
<td>Total cost for screening MRI</td>
<td>$242,062.56</td>
<td></td>
<td>$98,020.79</td>
</tr>
</tbody>
</table>

MRI magnetic resonance imaging
**P15**

The Clinical Value of the 21-gene Recurrence Score (RS) Assay for High-grade Tumors is Questionable

M. Gage,1,7 M. Rosman,1 C. Mylander,1 E.M. Giblin,1 L. Tafra,1 J. Breast Surgery, Anne Arundel, Annapolis, MD; 2. Walter Reed National Military Medical Center, Bethesda, MD.

Introduction: Controversy exists over the ability of Oncotype Dx (ODX) to add benefit over routine pathological analysis. Although published results show high grade and RS have equal hazard ratios, high tumor grade is not routinely considered an exclusion criterion for ODX testing. Our purpose was to determine if ODX testing on high grade tumors has significant clinical utility. Methods: Three pathologists using the same staining and computer-aided slide reading methodology from 4/08 to 7/13 evaluated 226 samples that underwent ODX testing; the retrospectively analyzed data included RS, tumor type, tubular formation, nuclear pleomorphism, mitotic count, and ER, PR, HER2 and Ki67 status. Results: Of the 226 samples, 37 (16.4%) have a Nottingham Grade (NG) of 8 or 9 (high grade). When evaluated separately, the high grade group and the rest of the cohort showed no statistical difference in mean age and tumor size. However, mean Ki67 is significantly higher (59% ± 9% vs. 19% ± 4%). The vast majority of patients with high grade tumors (n=31, 83.8%) have a RS of 26 or above (the threshold for the chemo-sensitive group in the TAILORx trial). The distribution of RS is shown in the Table. Of the 27 with a NG of 9, only one has a RS below 26, it is 25. Additionally, 5% (n=11) have low ER (<20%); a group previously shown to have high RS (30 and above in this sample). To determine the potential impact of excluding from ODX testing the group of high-grade-or-low-ER patients we examined our breast center’s population of invasive, sentinel lymph node negative, hormone positive cancer patients. It contains 20.4% high-grade-or-low-ER patients, while 16.8% in this study are in that group. Conclusion: ODX testing has limited clinical utility in patients with high grade tumors, because of their strong concordance with a high RS. In view of equal hazard ratios of RS and high grade, as evaluated by a multivariate Cox model (using age, several pathologic variables, and RS) (P<0.01), the decision to give or withhold chemotherapy based solely on ODX testing is not supported. Further studies may confirm the limited clinical value of ODX testing in these patients.

**P16**


Introduction: Axillary node status predicts survival in breast cancer. The current classification system (pN) is determined in part by an absolute number of positive lymph nodes (LN). Some authors have reported LNR to more accurately predict recurrence and survival versus pN, but this has not been evaluated in the NAC setting. It has also been reported that fewer lymph nodes are retrieved after axillary lymph node dissection (ALND) following NAC. A decrease in the number of lymph nodes identified by ALND in this cohort of patients is presumably the effect of chemotherapy on their “normal” lymph nodes, making them unidentifiable during pathologic exam. As such, NAC may falsely elevate the LNR while having no effect on the number of positive nodes. Therefore, pN may not be the best predictor of disease-free or overall survival (OS). We sought to compare the utility of LNR versus pN in predicting recurrence and OS after NAC. Methods: A retrospective review was completed through the Cancer Registry. Patients (pts) who underwent NAC with documented node-positive breast cancer were evaluated from 2005-10. LNR was calculated by dividing all positive nodes by total LN retrieved. Pts were then divided into 3 groups according to their LNR (1-20%, 21-60%, >61%), in keeping with previous reports. Overall recurrence (OR), loco regional recurrence (LRR), distant recurrence (DR) and OS were analyzed. Results: A total of 252 pts with clinically node positive disease received NAC. Pts who had a complete axillary response or only sentinel lymph node biopsy were excluded from analysis. Two hundred seven pts who had ALND of >6 nodes were then analyzed. Average LN retrieved was 16 ± 4. Average pN was 5 ± 5. On univariate analysis, LNR was predictive of LRR and DR, but not OR or OS. In contrast, pN was predictive of OR, LRR, DR and OS. Conclusions: In our cohort of pts who received NAC and had persistently positive LN, pN was superior to LNR in predicting OR and OS. This calls into question the utility of calculating LNR in pts who have undergone NAC.

### Comparison of LNR to pN

<table>
<thead>
<tr>
<th>LNR</th>
<th>1-20%</th>
<th>21-60%</th>
<th>&gt;61%</th>
<th>N1</th>
<th>N2</th>
<th>N3</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>25 (24%)</td>
<td>22 (30%)</td>
<td>14 (47%)</td>
<td>0.006</td>
<td>25 (22%)</td>
<td>19 (31%)</td>
</tr>
<tr>
<td>DR</td>
<td>8 (6%)</td>
<td>2 (3%)</td>
<td>1 (3%)</td>
<td>0.002</td>
<td>8 (7%)</td>
<td>7 (12%)</td>
</tr>
<tr>
<td>OS</td>
<td>17 (17%)</td>
<td>19 (26%)</td>
<td>13 (43%)</td>
<td>0.002</td>
<td>17 (15%)</td>
<td>17 (27%)</td>
</tr>
</tbody>
</table>

*NR= no recurrence

### Distribution of Oncotype Dx Recurrence Score in Study

<table>
<thead>
<tr>
<th>Score</th>
<th>≤10</th>
<th>11-17</th>
<th>18-25</th>
<th>&gt;25</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NG 3.7</td>
<td>47</td>
<td>75</td>
<td>48</td>
<td>9</td>
<td>189</td>
</tr>
<tr>
<td>NG 8</td>
<td>0</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>NG 9</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>Total</td>
<td>47</td>
<td>77</td>
<td>52</td>
<td>11</td>
<td>226</td>
</tr>
</tbody>
</table>

**NG: Nottingham Grade Score. A NG of 8 or 9 defines high grade tumor.**

---

**P17**

Time to Fixation Significantly Impacts Prognostic Factor Testing


Background: Accurate prognostic factor testing is essential for the appropriate use of targeted therapies in breast cancer. Based on bench studies showing that estrogen receptor (ER) staining diminishes with increasing specimen ischemic time, guidelines for specimen processing currently recommend a time to fixation of 10 min, from specimen extraction to specimen fixation) of < 60 minutes (min). This study sought to evaluate whether TTF impacts prognostic factor testing in the clinical setting. Methods: All breast cancer biopsies and resections from a single institution between 2008-2013 were reviewed. ER, progesterone receptor (PR), Human Epidermal Growth Factor Receptor 2 (Her2) status and TTF were recorded. Core biopsies were assigned a TTF of 10 min. Critical Time Analysis was performed to identify the earliest time at which the fraction of + cases significantly changes. The fraction of positive (+) specimens (ER,PR; Alrred>2, Her2: IHC 3+ or FISH ratio >2.2) was then compared between TTF above and below the critical time value using Chi-Square test. The effect of increasing TTF on the fraction of + cases was determined by linear correlation. Results: Out of 736 breast cancer specimens, the mean TTF was 53.8 min (SD=37.8 min). 453 (61.5%) cases had a TTF <60min and 283 (38.5%) had TTF >60min. The critical time points for ER, PR and Her2 were 55, 45, and 25 min, respectively. 83.5% of specimens with TTF less than 55 min were ER+ compared to 73.2% of those with longer TTF (p=0.001). 74.7% of specimens with TTF less than 45 min were PR+ compared to 66.5% of those with longer TTF (p=0.016). 20.0% of specimens with TTF less than 25min were Her2+ compared to 8.9% of those with longer TTF (p=0.004). All 3 prognostic factors had a negative correlation with TTF (ER: Pearson’s Correlation Coefficient (r) = -0.945, p=0.004, Figure 1; PR: r = -0.846, p=0.016; Her2: r = -0.720, p=0.068). Conclusion: This is the first clinical study to demonstrate that ER, PR, and Her2 staining decreases with increasing TTF, with significant changes seen as early as 25 minutes. Minimizing TTF is critical for accurate prognostic factor testing and appropriate therapeutic decisions in breast cancer.
P18
Risk of Breast Cancer in Women Observed after Core Biopsy Diagnosis of Atypical Ductal Hyperplasia
N. Ganesan, T.B. Bevers, J. Ying, R. Coyne, D. Lane, C. Albarracin, I. Bedrosian.* University of Texas, MD Anderson Cancer Center, Houston, TX.

Background: Surgical excision remains standard practice to rule out occult carcinoma after a diagnosis of atypical ductal hyperplasia (ADH) on core biopsy. We hypothesized that multidisciplinary team review could identify women with ADH at low risk for occult carcinoma who could be observed and whose outcomes would be similar to those undergoing excision. Methods: Our prospective departmental registry was reviewed to capture the management and outcomes of patients with ADH. Breast cancer (BrCa) events were classified as index site (site of ADH biopsy), ipsilateral breast unrelated to index site or contralateral breast. Patients were excluded from analysis if they had no follow-up, had ADH based on excisional biopsy or had been upstaged to carcinoma following diagnostic excision. Results: We identified 125 women who had been observed and 50 who had undergone excision with benign findings. Thirteen percent had a prior BrCa history and 24% took chemoprevention. There were no significant differences in age, race, prior BrCa history, use of chemoprevention and median follow-up between the 2 groups. With a median follow-up of 3 years, 14 BrCa events were noted in 13 patients. 5-year probability of any BrCa event for the cohort was 20%. Six BrCa events, including 1 bilateral, (12%) were reported in the surgery group and 7 (5.6%) in the observed group (p=0.14). Index site events were the same in both groups (2% vs 0.8%, p=0.49) as were ipsilateral cancers outside of the index site (4% vs 4.8%, p=1.00). All the contralateral cancers were in the surgical group (8 vs 0%, p<0.01). Prior BrCa history was the only variable significantly associated with any subsequent BrCa event. When follow-up time was taken into account, Cox proportional hazards regression analysis showed that this association remained significant even after adjusting for all significant variables (HR 12.5 [95%CI 0.95-160.6]). Conclusion: Observation is appropriate in select women with core biopsy diagnosis of ADH. Breast index site failures are rare and are superseded by contralateral risk of cancer elsewhere in the breast. Outcomes are similar among women managed with observation or with excision of ADH.
with chemotherapy. It can also be omitted for patients with pT1N1M0 disease with single node involvement if treated with hormonal therapy alone.

P21
Neutrophil Elastase Uptake by Breast Cancer Increases Anti-tumor Adaptive Immune Response by Upregulation of HLA Class I Molecules
A. Chawla,* A. Philips, N. Qiao, P. Sukhumalchandra, C. Kerros, J. Molldrem, G. Alatrab, E. Mittendorf. Surgical Oncology, MD Anderson Cancer Center, Houston, TX.

Introduction: Neutrophil elastase (NE) is an inflammatory mediator that is taken up by breast cancer cells. We have previously shown that NE uptake increases susceptibility to lysis by cytotoxic T lymphocytes (CTL) targeting the tumor antigens PR1 and cyclin E. This study was undertaken to determine if NE uptake has a more ubiquitous effect on adaptive immunity through regulation of HLA class I expression. Methods: Healthy donor HLA-A2+ peripheral blood mononuclear cells (PBMC) were used to generate antigen specific CTL by stimulation with I7, I2, and dendritic cells pulsed with E75, a HER2-derived epitope we are currently investigating as a vaccine in clinical trials. Calcine-AM cytotoxicity assays were performed to evaluate E75-specific lysis of MDA-MB-231 breast cancer cells maintained in standard media ± NE (10ug/mL). NE uptake was confirmed using flow cytometry. HLA-A2 expression was determined by staining with anti-HLA-A2 antibody (bb7.2) and assessed using flow cytometry. Cells were maintained with NE ± protease inhibitors elafin or phenylmethanesulfonyl fluoride (PMSF) to determine if the effects of NE on HLA expression required enzymatic activity. Results: NE uptake resulted in increased lysis by E75-specific CTLs (Fig 1, *p<0.05). NE uptake also led to a concentration- and time-dependent increase in HLA-A2 surface expression. At a 12-hour time point, the MFI for cells in NE-supplemented media ± NE was 7341 ± 867 vs. 5144 ± 272 for cells in standard media, p<0.05. NE co-elution with elafin or PMSF resulted in a 3-fold decrease in protease activity (p<0.05) and abrogated the effect of NE on surface HLA-A2 expression (MFI: 8687 ± 419 vs. 5490 ± 330 for NE vs. NE+elafin; 8569 ± 395 vs. 4644 ± 564 for NE vs. NE+PMSF; p<0.05). MCF-7 cells, which took up NE poorly, exhibited no change in HLA-A2 expression ± NE (MFI: 722 ± 69 vs. 693 ± 75, p=0.69). Conclusions: NE uptake leads to increased lysis by antigen-specific CTL in part by increasing HLA class I expression. These results show an important link between innate and adaptive immune responses that could be exploited to improve anti-tumor immunotherapy.

Figure 1: E75-Specific CTL Lysis of MDA-MB-231 Cells

E75-specific CTL were used in calcine-AM cytotoxicity assays at various effector to target ratios (E:T) versus MDA-MB-231 cells maintained in low serum media ± NE supplementation (10ug/mL). Uptake of NE by MDA-MB-231 cells resulted in increased E75-specific lysis. E75-specific lysis was confirmed using T2 cells pulsed with E75 peptide or irrelevant PR1 peptide (data not shown). Assays were performed in triplicate; results are compiled from 3 separate experiments, (p<0.05).

P22
Invasive Breast Cancer with and without Ductal Carcinoma in situ: Do Outcomes Differ? M. Ruszczynski,* A. C. Hong, H. Hwang, S.E. McCann, F. Schedin, P. Starostik, P. Masso-Welch, C. Ambrosone, S. Kumar. 1. Roswell Park Cancer Institute, Department of Cancer Prevention, Buffalo, NY; 2. University of Texas, Southwestern Medical Center, Dallas, TX; 3. University of Colorado, Department of Medicine, Denver, CO; 4. Roswell Park Cancer Institute, Department of Clinical Diagnostics, Buffalo, NY; 5. University at Buffalo, School of Medicine and Biomedical Sciences, Buffalo, NY; 6. Roswell Park Cancer Institute, Department of Surgical Oncology, Buffalo, NY.

Invasive carcinoma in the absence of concomitant ductal carcinoma in situ (DCIS) may reflect a biologically more aggressive breast tumor than invasive carcinoma with DCIS. The objective of this study was to compare clinical characteristics and survival endpoints for invasive cancer with and without a DCIS component. From 1522 consecutive patients treated surgically for invasive ductal carcinoma between July 1997 and December 2005, we identified 1386 women who met study criteria and had pathology available. We compared clinical characteristics and survival outcomes between patients with a DCIS component (mixed IDC/DCIS) and without concomitant DCIS (pure IDC). Local recurrence, distant metastasis, breast cancer specific survival and overall survival were examined using clinical characteristics and treatment information. Survival analyses were performed by creating Kaplan-Meier curves and constructing proportional hazards models for hazard ratios (HRs). Models were adjusted for age at diagnosis, tumor size, grade, lymph node status, lymphovascular invasion, estrogen receptor (ER) status, and surgical margin status. IDC from 238 (19%) patients were considered pure IDC. Pure IDC was associated with older age, larger tumor size, higher grade and negative ER status. Mean follow-up time for recurrence and death was 80.2 (SD, 37.2) and 103.0 (SD, 38.1) months respectively. Patients with pure IDC were less likely to experience a local recurrence, even after adjustment for clinical variables (HR 0.32; 95% confidence interval (CI) 0.11-0.90). Distant metastasis and death from breast cancer were less likely to occur among patients with pure IDC; however, estimates were not statistically significant (HR 0.79; 95% CI 0.48-1.30 and HR 0.78; 95% CI 0.47-1.29, respectively). There was no difference observed between patients with mixed IDC/DCIS and pure IDC in overall survival (HR 0.99; 95% CI 0.70-1.38). Recurrence was higher among patients with mixed IDC/DCIS, even after adjustment for surgical margin status. Patients with pure IDC may represent a unique group who are less likely to recur. Although patients with pure IDC have poorer pathologic features, survival is unchanged.
P23
Predicting Occult Malignancy or High-risk Lesion in Contralateral Prophylactic Mastectomy

INTRODUCTION The increase in rates of contralateral prophylactic mastectomy (CPM) for patients with unilateral breast cancer has prompted criticism that surgeons fail to adequately counsel patients. Identifying risk factors for contralateral high risk lesion (HRL) or occult malignancy (OM) can aid individual risk assessment. Our aim was to evaluate the frequency and predictors of HRL or OM identified in CPM specimens. METHODS We identified breast cancer patients undergoing CPM from 10/2008 to 06/2013 from a prospectively collected breast surgery database. Logistic regression was used to assess potential risk factors for the outcome of occult finding in CPM. RESULTS We identified 740 women with unilateral cancer undergoing concurrent therapeutic mastectomy and CPM with no prior history of cancer in the CPM breast. Clinically occult HRL or OM was identified in 108 (14.6%) CPM specimens: HRL in 78 specimens (10.5%) and OM in 30 specimens (4.1%), invasive in 17 (2.3%) and in situ only in 13 (1.8%). In univariate analysis, age, estrogen receptor (ER) positivity, progesterone receptor (PR) positivity, and invasive lobular carcinoma (ILC) in the index breast were significantly associated with an occult CPM finding. Patients treated with neoadjuvant chemotherapy (NAC) were less likely to have occult findings (7% vs 17%, \(p=0.0006\)). Age, ILC, and PR positivity remained significant on multivariate analysis. The adjusted effects for these variables were: age, \(OR = 1.35\) (95% CI: 1.10-1.66) per 10-year increase; ILC vs other histology, \(OR = 2.71\) (95% CI: 1.50-4.81); and PR positive, \(OR = 1.81\) (95% CI: 1.01-3.40). There remained a trend for NAC with \(OR = 0.49\) (95% CI: 0.22-1.04). There was no significant association of contralateral presentation, HER2-neu status, or clinical stage with occult finding on CPM. CONCLUSION Although invasive cancer is infrequently identified in CPM specimens, the rate of either HRL or OM was 14.6%. We identified older age and index breast cancer characteristics of ILC and PR positivity as predictive factors for HRL or OM in the CPM. These findings can assist with counseling patients regarding the risk of contralateral cancer and improve selection of patients for CPM.

Univariate Analysis: Factors Associated with Occult Finding in Contralateral Prophylactic Mastectomy

<table>
<thead>
<tr>
<th>Factor</th>
<th>N</th>
<th>Occult Finding (in CPM N%)</th>
<th>(p)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td></td>
<td>36 (11.1%)</td>
<td>0.02</td>
</tr>
<tr>
<td>(&lt;50)</td>
<td>325</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(\geq50)</td>
<td>415</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Contralateral preoperative diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DCIS</td>
<td>158</td>
<td>23 (14.6%)</td>
<td></td>
</tr>
<tr>
<td>IDC</td>
<td>428</td>
<td>47 (11.0%)</td>
<td></td>
</tr>
<tr>
<td>ILC</td>
<td>71</td>
<td>33 (47.2%)</td>
<td></td>
</tr>
<tr>
<td>IMC</td>
<td>78</td>
<td>7 (9.2%)</td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td>32</td>
<td>8 (25.0%)</td>
<td></td>
</tr>
<tr>
<td>Other malignancy</td>
<td>13</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Neoadjuvant therapy</td>
<td></td>
<td></td>
<td>0.0006</td>
</tr>
<tr>
<td>No</td>
<td>351</td>
<td>94 (17.3%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>189</td>
<td>14 (7.4%)</td>
<td></td>
</tr>
<tr>
<td>Contralateral presentation</td>
<td></td>
<td></td>
<td>0.41</td>
</tr>
<tr>
<td>Symptomatic*</td>
<td>374</td>
<td>59 (15.9%)</td>
<td></td>
</tr>
<tr>
<td>Symptomatic</td>
<td>340</td>
<td>40 (13.3%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>15</td>
<td>1 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Contralateral ER status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>177</td>
<td>15 (8.5%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>530</td>
<td>80 (16.2%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>33</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Contralateral PR status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>302</td>
<td>28 (9.2%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>404</td>
<td>73 (18.6%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>33</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Contralateral Her2 status</td>
<td></td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>Negative</td>
<td>427</td>
<td>66 (15.5%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>89</td>
<td>8 (9.0%)</td>
<td></td>
</tr>
<tr>
<td>DCIS</td>
<td>158</td>
<td>23 (15.1%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>66</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Contralateral Clinical T stage</td>
<td></td>
<td></td>
<td>0.94</td>
</tr>
<tr>
<td>T0</td>
<td>3</td>
<td>1 (33.3%)</td>
<td></td>
</tr>
<tr>
<td>Ts</td>
<td>162</td>
<td>26 (16.0%)</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>240</td>
<td>36 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>200</td>
<td>28 (13.6%)</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>81</td>
<td>12 (14.9%)</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>17</td>
<td>2 (11.8%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>21</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Contralateral Clinical N stage</td>
<td></td>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td>N0NX</td>
<td>574</td>
<td>90 (15.7%)</td>
<td></td>
</tr>
<tr>
<td>N1-SX</td>
<td>105</td>
<td>16 (15.0%)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

*Symptomatic presentation combined the categories palpable abnormality, palpable axillary mass, nipple discharge, focal breast pain, skin abnormality, and Paget’s disease.

P24
Impact of Axillary Ultrasound (AUS) on Axillary Dissection in Breast Conserving Surgery (BCS)

Introduction: The American College of Surgeons Oncology Group (ACoSOG) Z0011 trial has revolutionized management of the clinically negative axilla. Increasing use of preoperative AUS for clinically node-negative disease and subsequent FNA may drive axillary lymph node dissection (ALND) in patients (pts) undergoing BCS who fit the ACoSOG Z0011 criteria. We hypothesize that incorporation of preoperative AUS does not lead to excessive ALND in this select population. METHODS: After IRB approval, a single-institution retrospective review of female breast cancer pts receiving AUS from 2004-2012 was performed; pts with clinical T1 and T2 tumors undergoing BCS were included. Preoperative chemotherapy and recurrent breast cancer cases were excluded. Four pts refused axillary staging after AUS and were excluded. Clinical, radiologic, and pathologic data were collected and analyzed. Results: Of 903 preoperative AUS pts, 121 of the 141 pts (86%) with BCS had no palpable axillary nodes at presentation; 48/121 pts (40%) had an abnormal AUS and 15/48 (31%) had a positive FNA. Fourteen of 15 pts had ALND with 10/14 (71%) having \(\geq3\) positive nodes. In contrast, 6/33 pts (18%) with abnormal AUS and FNA negative had a positive sentinel lymph node (SLN); only 1 pt (17%) had ALND (\(\geq2\) positive nodes). Of the 73 normal AUS, 16 pts (22%) had a positive SLN; 9/16 (56%) had ALND, of which 1 pt (11%) had \(\geq3\) positive nodes. In all, 24 pts had ALND; 13 SLN positive did not. In the overall population, AUS plus FNA had sensitivity of 56%, specificity of 100%, and negative predictive value (NPV) of 84%. When evaluating for total nodal disease \(\geq3\), AUS plus FNA had a sensitivity of 94%, NPV of 99%, and PPV of 71%. Conclusions: Since the publication of ACoSOG Z0011,
preoperative AUS/FNA in clinically node-negative BCS pts has raised concerns about unnecessary ALND. Our data demonstrates a high NPV of AUS/FNA for axillary metastasis and remarkable sensitivity of AUS/FNA for operative axillary disease. This supports the practice of considering abnormal AUS/FNA as clinically node-positive despite a normal physical exam, and it should be considered even in patients planning BCS.

Figure 1. Consort Diagram of the Impact of Axillary Ultrasound (AUS) on Axillary Dissection in Breast Conserving Surgery (BCS)

P25


Background. Despite recent advances, up to 30% of breast cancer (BC) patients will relapse. Preclinical assays based on breast cancer xenografts (BCx) are the most convincing model for conducting drug development. The objective of the study was to assess the rate of success establishing BCx and to analyze the effectiveness of anti-IL-6 therapy on the growth of BCx from surgical specimens. Methods. Patients with a diagnosis of invasive BC who underwent surgery signed an informed consent. After surgery, isolation of breast cancer cells was performed from some samples. Purified BC cells or tumor specimens. The Ethics Committee approved the study. Results. One hundred NOD-SCID mice. Posteriorly, mice were treated with anti-IL6 neutralizing antibodies. The Ethics Committee approved the study. Results. One hundred NOD-SCID mice. Posteriorly, mice were treated with anti-IL6 neutralizing antibodies. The Ethics Committee approved the study.

P26


Introduction: Technical innovations to improve mammography’s sensitivity and specificity have included digital breast tomosynthesis (DBT). DBT has been shown to decrease findings related to tissue overlap, thereby reducing false positives and improving detection of cancer. Optimal screening regimens for patients at increased risk for breast cancer remain to be defined. We investigated the utility of DBT in patients at increased risk for breast cancer. Methods: DBT was performed in combination with Full Field Digital Mammography (FFDM) on 2005 patients presenting over one year. 324 patients at increased risk of breast cancer (BRCA mutation, 1st degree relative with breast cancer, or previous biopsy showing LCIS or atypia) were identified. 30/324 (9.9%) had more than one risk factor. FFDM was performed and management recommendations were prospectively recorded blinded to DBT results. Change in recommendation based on DBT was then determined and recorded. Results: For 324 high risk patients mean age was 52 (range 25-88). 191 (59%) had dense breasts. Tomosynthesis affected interpretation and changed management in 39/324 (12%). The most common change was elimination of recommendation for further imaging in 28/324 (87%) patients. In 9/324 (29%) DBT detected findings not seen on FFDM that led to additional mammographic views or ultrasound, and in 2/324 (5%) DBT resulted in decreased imaging for one breast, but increased for the other. Findings on DBT led to image guided biopsy in 4 cases yielding 2 with fibrocystic changes, 1 papilloma, and 1 radial scar. Of the 324 patients, 8 (2%) were diagnosed with breast cancer. All cancers were seen on both FFDM and DBT with the exception of one case diagnosed by ultrasound only. There was no individual risk group where change in management based on DBT was significantly higher; age and breast density also did not affect change in management. Conclusion: In a population of patients at increased risk for breast cancer, DBT decreased the need for additional imaging. Further evaluation of DBT relative to other imaging modalities may define the role of this technology in the screening regimens for high risk patients.

P27


Background: Surgical practice variation may lead to adverse outcomes. It is unclear whether post-graduate training in breast surgery affects practice patterns. Methods: National, web-based survey. Participants were board-certified US surgeons. The survey consisted of 25 clinical case-scenarios which were ambiguous with regards to the appropriateness of surgical intervention. Surgeons rated their likelihood to recommend surgery on a five-point Likert scale. We defined tendency to operate (TTO) as the mean of the responses. There were 3 breast-relevant scenarios. Fellowship training status was by self-report. Results: Of 907 total respondents, 64 (7.1%) reported receiving fellowship training in breast surgery or surgical oncology. There were 102 practicing breast surgeons, of whom 26 (25%) were fellowship trained. There were no differences between fellowship-trained and non-fellowship-trained breast surgeons in terms of gender (p=0.23), race (p=0.56) or ethnicity (p=0.27), but fellowship-trained breast surgeons were significantly younger, mean (SD) age 45.8 (1.8) vs. 53.4 (1.1) years, p=0.0004. Regarding the breast scenarios, breast surgeons had significantly lower TTO scores versus non-breast surgeons, mean (SD) TTO 2.10 (0.08) vs. 2.95 (0.03), p<0.0001. Fellowship-trained breast surgeons had a similar TTO to non-fellowship trained breast surgeons,
mean TTO 2.27 (0.17) vs. 2.04 (0.09), p=0.24. TTO in non-breast cases did not differ between breast surgeons and non-breast surgeons, mean TTO 3.11 (0.05) vs. 3.14 (0.02), p=0.50. In multivariable analysis, working with residents, working in small private practice, and higher TTO in non-breast cases were associated with higher TTO in breast cases. Malpractice concerns, surgical volume, and fellowship training were not associated with TTO. Conclusions: Breast surgeons are significantly less likely to operate on ambiguous breast cases than surgeons who don’t perform as much breast surgery, despite having similar operative tendencies for non-breast cases. This effect does not appear to be mediated by fellowship training. Our research suggests that greater specialization, even after surgical training is completed, may act to decrease practice variation.

P28 Identification of BRCA Gene Mutation Carriers through Systematic Family History Screening in Mammography Populations

Introduction: Historically, BRCA gene mutation carriers are identified when physicians recognize high-risk family histories and refer patients for genetic counseling. Even with special training and software tools, this approach is inefficient. An alternative approach is to automate genetic screening and referral processes at just a few points of service rather than across the entire primary care system. Methods: A validated family history screening tool was incorporated into the mammography intake processes at three sites: two County Hospitals primarily serving uninsured/underinsured women and one University Hospital primarily serving affluent insured women. Results: Between October 1, 2011 and June 30, 2013, 57,996 women underwent family history screen in the County Hospitals and 34,131 in the University Hospital. 2,650 (4.6%) of the screened County hospital population met criteria for referral to Cancer Genetics as compared to 1,557 (4.6%) in the screened University hospital population. Only 15% of the County hospital patients whose screening forms met criteria for genetic counseling referral were found to be ineligible when viewed by a patient navigator. Ultimately, 446 patients were tested for BRCA gene mutations in the county hospital with a 4.9% positivity rate, and 115 patients in the University hospital with 15.6% positivity rate. Barriers to mutation carrier identification included refusal to schedule a Genetic counseling appointment (22% for County patients and 17% for the University patients) and failure to attend a counseling appointment (50% for the County patients and 15% for the University patients). Conclusion: Systematic family history screening is feasible and reasonably accurate in uninsured/underinsured mammography populations, but unresolved barriers to accessing genetic counseling services significantly hampers identification of mutation carriers.

P29 Breast Reconstruction is not Associated with Reduced Overall or Breast Cancer Specific Survival: Long-term Follow-up of a Retrospective Population-based Cohort
J. Platt,* N.N. Baxter, J. McLoughlin, J. Semple, 1 University of Toronto, Toronto, ON, Canada; 2. Women’s College Hospital, Toronto, ON, Canada; 3. St. Michael’s Hospital, Toronto, ON, Canada.

Introduction: Many women with breast cancer require mastectomy and may consider breast reconstruction (BR) as an option to restore the breast mound. Concern that BR has a negative impact on survival has not been thoroughly evaluated using long-term follow-up data. Randomized study design may not be feasible or ethical. Methods: A retrospective cohort study using population-based data from Ontario Cancer Registry (OCR). We selected records of women who underwent BR within 5 years after mastectomy for invasive breast cancer from OCR (1980 to 1990). We analyzed the records of an age, cancer histology matched cohort from OCR who did not undergo BR to form the control group. We obtained patient demographic and oncologic information including pathology. To account for our time-varying exposure, an extended Cox proportional hazards model was used to compare overall and breast cancer specific survival (OS, BCS) after adjusting for age, tumor size, lymph node status and hospital. Secondary analysis examined differences in OS across 3 periods (< 10, 10 – 19, 20 – 30 yrs from diagnosis) using Kaplan-Meier curves. Results: 758 matched pairs formed our cohort, with a median age of 44 years (interquartile range, IQR 39 to 51). Median time to BR was 1.5 years (IQR 0.9 – 2.4) and follow-up was 23.4 years (IQR 11.1 – 33.0). BR participants had lower nodal disease status compared to controls (44% vs. 36% with N0, p = 0.004), but did not differ on tumor size (p = 0.067). Fewer BR patients died overall or from breast cancer compared to controls (OS: 44.5% vs. 56.7%, p < 0.0001; BCS: 31.8% vs. 42.6%, p = 0.0002; respectively). BR was associated with a 15% reduced risk of death and 18% reduced risk of breast cancer death, after adjustment (OS: hazard ratio 0.85, 95% CI 0.73 to 0.97; BCS: hazard ratio 0.82, 0.69 to 0.97). Among 879 (58%) women surviving > 20 years, there was no difference in OS (Log Rank p = 0.45). Conclusion: In a large cohort of women with breast cancer followed over 20 years, there is no evidence that BR is associated with reduced overall or breast cancer specific survival compared to mastectomy alone.

Events overall, 10 & 20 years from breast cancer diagnosis, breast reconstruction and mastectomy alone

<table>
<thead>
<tr>
<th></th>
<th>Death from any cause</th>
<th>Death due to breast cancer</th>
<th>Metastasis n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 year</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>BR</td>
<td>178 (23.5)</td>
<td>163 (21.5)</td>
<td>94 (12.4)</td>
</tr>
<tr>
<td>Control</td>
<td>229 (29.0)</td>
<td>198 (26.1)</td>
<td>133 (17.2)</td>
</tr>
<tr>
<td>20 year</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>BR</td>
<td>277 (16.5)</td>
<td>226 (29.8)</td>
<td>96 (12.7)</td>
</tr>
<tr>
<td>Control</td>
<td>354 (16.7)</td>
<td>206 (30.1)</td>
<td>135 (17.8)</td>
</tr>
<tr>
<td>Overall</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>BR</td>
<td>345 (45.5)</td>
<td>241 (31.8)</td>
<td>96 (12.7)</td>
</tr>
<tr>
<td>Control</td>
<td>430 (26.7)</td>
<td>324 (42.6)</td>
<td>135 (17.8)</td>
</tr>
</tbody>
</table>

BR, Breast reconstruction; control, mastectomy alone

P30 The Association of Health Literacy with Screening Mammography

Background: Patient compliance with screening mammography, starting at either 40 or 50 years, is suboptimal. The current study was performed to determine factors which affect use of screening mammography in an underinsured population. Methods: From January 2010 to April 2013, every female patient at least 40 years of age seen at a Breast Clinic was included. Use of screening mammography was determined from the medical records. Health literacy was assessed using the Newest Vital Sign (NVS) validated screening instrument. Multivariate analysis was performed to determine factors associated with use of screening mammography. Results: A total of 1664 patients were included. The population was racially and ethnically diverse (NHW 23%, AA 11%, Hispanic 61%). Ninety percent of patients were insured by Medicaid or uninsured. Health literacy assessment found that 80% of patients had low health literacy and 20% had adequate health literacy. Only 22% of those with a high school education had adequate health literacy. Of the 1664 patients, only 31% had undergone screening mammography. The rate of mammography screening among women 40 – 49 years of age was 35% and the rate among women 50 years of age and older was 27%. Univariate analysis found that Hispanic ethnicity and being uninsured were associated with not undergoing screening, while younger age, NHW race, English as primary language, family history of breast cancer, more years of education, adequate health literacy, current employment, non-smokers, and higher income were associated with greater use of screening mammography. After adjustment for all of the aforementioned variables in multivariate logistic regression analysis, only three factors were associated with poor compliance with screening mammography: low health literacy (OR=0.27; 95% CI 0.19 – 0.37; p < 0.001), smoking (OR=0.64; 95% CI 0.47 – 0.85; p=0.0019) and being uninsured (OR=0.66; 95% CI 0.51 – 0.85; p=0.0011). Conclusions: Health literacy was the strongest predictor of use of screening mammography. Tailored interventions not only to increase awareness of screening, but also of the availability and coverage of screening may have the potential to improve mammography screening rates.
**P31**

**Correlated Intrinsic Breast Cancer Subtypes and Expression of CD47 in BM and PB Predicts Poor Prognosis**  
M. Nagahara, K. Sugihara, M. Mori. 1. Department of Surgical Oncology, Tokyo Medical and Dental University, Tokyo, Japan; 2. Osaka University, Osaka, Japan.

Introduction: The intrinsic breast cancer subtypes have shown the prognostic features. Focused on CD47 expression in bone marrow (BM) and peripheral blood (PB), we found the correlation between breast cancer subtypes and CD47 expression in BM and PB, which may indicate important implications for prognostic factor. Experimental Design: Quantitative real-time PCR was used to evaluate CD47 mRNA expression in BM and in PB from 452 cases of breast cancer. ER, PR, and HER2 scores were obtained from immunohistochemistry (IHC) staining and Her2 FISH analysis conducted for Her2 score ≥ 2+. Results: According to ER, PR, and HER2 statuses, the groups of HER2 enriched (ER- and PR- and HER2 3+) and triple negative (ER- and PR- and HER2-) were divided (n=38 and 72). In HER2 enriched patients with high CD47 expression in BM and PB, survival was significantly poorer compared to patients with low CD47 expression (DFS in BM: P=0.003, DFS in PB: P=0.001). 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=0.001) and 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 (DFS in BM: P=0.002). 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 high expression might represent a dormant state in BM initiation of CD47’s signal transduction cascade, resulting in inhibition of phagocytosis. CD47 high expression may represent a dormant state in BM. CD47 is a useful prognostic biomarker for predicting survival of HER2 enriched and triple negative subtype in breast cancer and could be used as an index of therapeutic effect marker.

Kaplan-Meier curves of disease free survival (DFS) and overall survival (OS) in BM.

**P32**

**Lobular Carcinoma in situ (LCIS): What Happens after Chemoprevention (CP)?**  

Background: LCIS is both a risk factor and non-obligate precursor of estrogen receptor positive (ER+) breast cancer (BC). Current CP options reduce the risk of BC in women with LCIS, yet these strategies fail in some women. We sought to identify factors associated with failure of CP in LCIS pts and to describe the features of BC that develop after CP use. Methods: From a prospective database of 1317 pts in surveillance for a diagnosis of LCIS (11/1980-7/13), we identified pts who took CP (tamoxifen or raloxifene) for ≥ 6 months. Comparisons were made between CP pts who did and did not develop BC. Tumor characteristics were compared between CP pts and those in surveillance only. Results: Among 1317 pts with LCIS, 70(5%) chose risk reducing surgery and were excluded. Of 1247 pts in surveillance, 1190(95%) had ≥ 6 mos of follow-up and 192 pts(16%) took CP. Among CP pts, median age at LCIS diagnosis was 51yrs, 46% were postmenopausal, 41% had a family history (FH) of BC, 85/192(44%) pts completed 5yrs of CP, 64/33% pts remain on CP, 30(16%) pts stopped CP, and 13(7%) pts were lost to follow-up. At a median followup of 67 mos(range 6-380 mos), 11/192(6%) CP pts developed BC; compared to 147/1190(12%) pts not taking CP. Among CP pts, median time from LCIS to BC was 82 mos(range 9-194 mos). 3/11(27%) CP pts developed BC after 5yrs of CP, 4 were still on CP and 4 stopped prior to 5yrs of CP. Among pts that completed or stopped CP, BC diagnosis occurred at a median of 46 mos(range 3-104 mos) after CP. There was no significant difference in age at LCIS, menopausal status, FH of BC, number of biopsies, BIRADS breast density, or length of CP use between CP patients who did and did not develop BC. Conclusions: Despite the efficacy of CP in reducing the risk of ER+ breast cancer, the uptake of CP in women with LCIS remains low. We were unable to identify factors associated with failure of CP, however we do demonstrate that failure of CP in LCIS pts is not associated with the development of more aggressive ER negative BC. These data should be considered when counseling LCIS pts on the risks and benefits of CP.

**P33**

**Measuring Effects of System Changes on Breast Cancer Outcome Variability**  
W.C. Dooley,* C. Wilson, D. Luu, D. Zhao. University of Oklahoma, Oklahoma City, OK.

Introduction: Previous reports have shown breast cancer outcome differences based on whether the surgical provider was a surgical oncologist or a general surgeon. Our breast program instituted a series of measures to achieve identical rates of NCCN guideline compliance and research protocol enrollment to address these discrepancies in outcomes. Methods: We have performed an IRB approved retrospective analysis of prospectively collected data on all breast cancer cases at our institution from 2000-2013. Using all electronically available diagnostic, treatment and outcome data we have looked at the effects of system changes to address differential outcomes between surgical providers. Results: Standardized work-up and treatment indices (SWI and STI) were compared for two over-lapping intervals: 2000-2008 and 2004-2013. Each interval had long enough average follow-up to have statistically relevant and comparable data. As can be seen in the table the system changes, which nearly equalized NCCN guideline compliance and enrollment rates in clinical trials, had their most dramatic effect on STI or the stage specific survival outcomes using a standardized index. Effects on SWI (or work up index) showed much smaller changes between the two time periods between surgical oncologist and general surgeon. Surgical oncology was less likely to employ pre-operative MRI and more likely to use systemic staging radiographic exams on the basis of clinical exam findings and in patients with poorer prognostic markers. Surgical oncology had lower rates of up-staging within a year of diagnosis. Conclusions: More accurate staging prior to treatment remains as a major distinguishing characteristic between surgical oncologic care and general surgeon care for breast cancer patients. Developing methods to decrease this difference could substantially address disparities in breast cancer treatment outcomes.

<table>
<thead>
<tr>
<th>Pathologic Characteristics</th>
<th>Surveillance only/ Surveillance+CP (n=67 tumors)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Histology</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DCIS</td>
<td>51 (72%)</td>
<td>6 (46%)</td>
</tr>
<tr>
<td>Invasive (I BC, IL, special types)</td>
<td>106 (60%)</td>
<td>7 (54%)</td>
</tr>
<tr>
<td><strong>Cancer isolated to breast with LCIS</strong></td>
<td>90 (29%)</td>
<td>6 (60%)</td>
</tr>
<tr>
<td><strong>Mean tumor size (cm)</strong></td>
<td>L1.1+(1.42)</td>
<td>0.65(2.11)</td>
</tr>
<tr>
<td><strong>Nodal Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>79(25%)</td>
<td>6 (86%)</td>
</tr>
<tr>
<td>T1</td>
<td>21 (29%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Hormone-receptor Status</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ER+</td>
<td>92 (76%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>ER-/PR+</td>
<td>6 (60%)</td>
<td>0</td>
</tr>
<tr>
<td>ER/PR-</td>
<td>8 (8%)</td>
<td>1 (14%)</td>
</tr>
</tbody>
</table>

*Based on invasive cancer only
Effects of Eribulin on Cell Growth and Phosphoinositide-3-kinase (PI3K) Pathway Activity with and without Everolimus in Triple-negative and Human Epidermal Growth Factor Receptor 2 (HER2) Expressing Breast Cancer

D. Luyimbazi,* T. Luu, X. Qing, Y. Yan, T. Tully, E. Han, R. Yip, J. Yim. City of Hope National Medical Center, Duarte, CA.

INTRODUCTION: Patients with triple-negative breast cancer have high levels of Akt expression and activation of the PI3K pathway. Eribulin is a microtubule-targeting agent with benefits in treating refractory triple negative disease. Our objective was to evaluate its efficacy in inhibiting PI3K pathway activity and cell growth both alone and in combination with mammalian target of rapamycin (mTOR) inhibitor Everolimus. METHODS: Multiple breast cancer cell lines were used to assess the effect Eribulin has on growth. IC50 values for each cell line were calculated using MTT assay. Western blots were used to evaluate the expression of phosphorylated Akt-Ser473 (pAkt) and S6K1 after MDA468 and SKBR3 cell lines were treated with both agents for 24 hours. MDA468 and BT549 breast cancer cell lines were used to assess growth inhibition after 72 hour treatment with Eribulin alone and in combination with Everolimus. Combination indices (CI) generated by Chou-Talalay plots were used to quantify synergy. RESULTS: Both MDA468 and SKBR3 cells treated with Eribulin in varying concentrations showed inhibition of pAkt expression. Standard dilutions of Eribulin in combination with log dilutions of Everolimus resulted in marked synergistic growth inhibition (CI<1) in both MDA468 and BT549 cells. Western blot analysis for MDA468 cells treated with the combination of Eribulin and Everolimus showed a dose related suppression of pAkt along with complete inhibition of S6K1, while Everolimus alone increased pAkt. CONCLUSION: Our study shows dose related inhibition of Akt activation as well as inhibition of cell growth in triple negative breast cancer and HER2 cell lines treated with Eribulin alone or combined with Everolimus. We also show reversal of the pAkt feedback response seen with mTOR inactivation, and a significant synergistic growth inhibition with combination treatment. These findings point to a potential role for Eribulin and Everolimus in the treatment of refractory triple-negative breast cancer.

BT549 cells treated with a combination of Eribulin and Everolbin

<table>
<thead>
<tr>
<th>Concentration (nM)</th>
<th>0 nM</th>
<th>0.1 nM</th>
<th>0.2 nM</th>
<th>0.4 nM</th>
<th>0.8 nM</th>
<th>1.6 nM</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0 nM</td>
<td>0.83% 0.041</td>
<td>0.49% 0.077</td>
<td>0.39% 0.022</td>
<td>0.34% 0.005</td>
<td>0.26% 0.000</td>
<td>0.23% 0.000</td>
</tr>
<tr>
<td>0.1 nM</td>
<td>0.79% 0.034</td>
<td>0.27% 0.023</td>
<td>0.25% 0.001</td>
<td>0.24% 0.001</td>
<td>0.22% 0.001</td>
<td>0.18% 0.001</td>
</tr>
<tr>
<td>0.2 nM</td>
<td>0.77% 0.016</td>
<td>0.28% 0.001</td>
<td>0.26% 0.001</td>
<td>0.25% 0.001</td>
<td>0.25% 0.001</td>
<td>0.25% 0.001</td>
</tr>
<tr>
<td>0.4 nM</td>
<td>0.77% 0.035</td>
<td>0.22% 0.012</td>
<td>0.22% 0.010</td>
<td>0.22% 0.010</td>
<td>0.22% 0.010</td>
<td>0.22% 0.010</td>
</tr>
<tr>
<td>0.8 nM</td>
<td>0.94% 0.037</td>
<td>0.16% 0.003</td>
<td>0.16% 0.003</td>
<td>0.16% 0.003</td>
<td>0.16% 0.003</td>
<td>0.16% 0.003</td>
</tr>
<tr>
<td>1.6 nM</td>
<td>0.24% 0.018</td>
<td>0.06% 0.001</td>
<td>0.06% 0.001</td>
<td>0.06% 0.001</td>
<td>0.06% 0.001</td>
<td>0.06% 0.001</td>
</tr>
</tbody>
</table>

CI: Combination Indices
Top Concentrations: Eribulin in log dilutions
Side Concentrations: Everolimus in standard serial dilutions

P35 Outcomes with and without Axillary Node Dissection (ALND) for Node-positive Mastectomy Patients C. Laronga,* R. Snow, C. Johns,2 W. Sun,1 W. Fulp,1 J. V. Kiluk,1 M. Lee,2 M. Moffitt Cancer Center, Tampa, FL; 2. USF Morsani College of Medicine, Tampa, FL.

Background: The ACoSOG-Z0011 trial identified women with sentinel lymph node biopsy (SLN) positive breast cancer having breast conservation and demonstrated no difference in survival or local-regional recurrence between SLN+ALND vs. SLN alone. We hypothesize that the outcome is the same in SLN only and SLN+ALND for SLN-positive women treated with mastectomy. Methods: An IRB-approved retrospective review of women with SLN (N1) disease at mastectomy from January 1, 1995 to November 1, 2012 was performed. Noadjuvant therapy and noninvasive breast cancer cases were excluded. Demographic, co-morbidity, tumor type/size, receptor status, surgery type, adjuvant treatment, recurrence, and survival data were collected. Statistical analyses via Exact Chi square Test with Monte Carlo estimation, Kaplan-Meier curves, and log-rank tests were used to compare SLN alone vs. SLN+ALND cohorts. Results: Of 528 pts reviewed, 192 with positive SLN (N1) disease and mastectomy were identified. 32 (16.6%) received SLN alone; 160 (83.4%) received SLN+ALND. Median age was 53.6yrs (range: 21-86), (SLN: 55.8yrs, ALND: 53.2yrs; p=0.11). There were no differences between the SLN and SLN+ALND cohorts in co-morbid conditions, histology, receptor status, or mean number of nodes retrieved in SLN (SLN and SLN+ALND: 2.91; p=0.81). The mean number of positive nodes retrieved was significantly different (SLN: 1.09, SLN+ALND: 1.64; p=0.001). Of pts undergoing ALND, the median number of nodes retrieved was 15 (range 4-42) and the median number with metastases was 0 (range 0-20). Rates of chest wall radiation and chemotherapy were not significantly different between the cohorts (p=0.93, p=0.15). At median follow-up of 44 months (range: 0-150), there were no statistically significant differences in local, regional, or distant recurrence (p=0.24), or in overall survival (p=0.16) between SLN alone and SLN+ALND. Conclusions: In patients with clinically node-negative invasive breast cancer undergoing mastectomy, the extent of axillary surgery had no impact on survival or recurrence. These data suggest that the findings of the ACoSOG-Z0011 trial can be extended into the mastectomy population.

P36 Surgical Site Infections after Mastectomy and Breast Reconstruc- tive Surgery A. Kirane,* P. Sreeramoju, D. Euhus, J. Huth, A. Leitch, R. Wooldridge, R. Rao. UT Southwestern, Dallas, TX.

Surgical site infectionsSSI are a significant source of postoperative morbidity and cost; data regarding the incidence of SSI following mastectomy and breast reconstruction is highly variable and series dependent. In response to a cluster SSI after breast reconstructive surgery in our population, an epidemiologic investigation was performed to identify risk factors for SSI. All female patients who underwent mastectomy with or without reconstruction, from 2010 to 2013, were identified. Patients who underwent primary procedure without reconstruction, or reconstruction surgery without implantation of prosthesis were followed for 30 days from date of surgery for development of SSI. Patients who underwent any breast reconstruction involving implantation of prosthesis were followed for 1 year (or until January 31, 2013) for development of SSI. Definitions from CDC-NHSN were used. A total of 1,311 eligible procedures were performed during the study period. The incidence of SSI was 5.1% (49/963) in patients undergoing mastectomy alone, 13.3% (2/15) in patients undergoing mastectomy with delayed reconstruction and 35.6% (32/90) in patients undergoing mastectomy with immediate reconstruction. Of 108 patients undergoing reconstructive surgery, 40 (37%) had muscle flap; 31 (29%) had biologic matrix implanted. A third of these patients (36, 33.3%) developed SSI. Use of muscle flap was significantly associated with development of SSI (18/40 vs. 18/68; Unadjusted OR 1.7, 95% CI 1.07, 2.87, P=0.05). Use of any implant was not associated with development of SSI. History of diabetes, smoking, hypertension or prior admission to the hospital was not significantly associated. Preliminary data show a trend for association of higher BMI (P=0.08). Our population demonstrated an unusually high rate of SSI during this time period. In this series, the greatest incidence of SSI was encountered in patients undergoing immediate breast reconstruction or reconstruction with muscle flap. Further investigation of operative factors specific to this finding may elucidate opportunities to reduce SSI events.

P37 Incidence Patterns of Breast Cancer among Women 35 and Younger at Diagnosis R.A. Greerup,* K. Arbee, I. Akushevich, A. Mackey, L. Tlnitch, E.S. Hwang. Duke University Medical Center, Durham, NC.

INTRODUCTION: Recent attention to young women with breast cancer has called into question an increasing incidence of breast cancer in this population. We sought to determine whether an observable increase in the incidence of breast cancer exists among women ≤35 when compared to women in older age groups. METHODS: The SEER database was queried to determine whether age-adjusted breast cancer incidence rates changed among women ≤35 years old when compared to women ages 36-50 and 51-60. The SEER registry consists of 18 cancer registrars covering distinct geographic U.S. regions. Initiation of data collection varied among sites: nine registries began in 1973-1975, four in 1992, and five in 2000. Patient demographics, clinicopathologic fea-
Abstracts: Poster Presentations S57

Variable Analysis, there was no difference in LN positivity among subtypes 108/278 (39%) in TNBC, and 65/144 (45%) in HER-2 (p=0.0007). On multi-subtypes with 734/2,201 (33%) in Luminal A, 143/344 (42%) in Luminal B, tases were detected in 1050 (35%) patients. The LN positivity rate varied across (37%), ALND in 756 (25%), and 1,117 (38%) patients had both. LN metas-

Multivariable Analysis of Predictors of Lymph Node Positivity

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &lt; 50 vs 50-79</td>
<td>1.53</td>
<td>1.20 - 1.83</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age ≥ 80 vs 50-79</td>
<td>1.05</td>
<td>0.94 - 1.18</td>
<td>0.79</td>
</tr>
<tr>
<td>Grade 2 vs Grade 1</td>
<td>1.71</td>
<td>1.33 - 2.19</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Grade 3 vs Grade 1</td>
<td>1.87</td>
<td>1.43 - 2.43</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVI</td>
<td>3.88</td>
<td>2.41 - 6.27</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>T2 vs T1</td>
<td>3.24</td>
<td>2.71 - 3.86</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>T3 vs T1</td>
<td>11.15</td>
<td>7.90 - 16.57</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TNBC vs Luminal A</td>
<td>0.79</td>
<td>0.58 - 1.06</td>
<td>0.12</td>
</tr>
<tr>
<td>TNBC vs Luminal B</td>
<td>0.72</td>
<td>0.50 - 1.03</td>
<td>0.07</td>
</tr>
<tr>
<td>TNBC vs Her2</td>
<td>0.68</td>
<td>0.44 - 1.06</td>
<td>0.09</td>
</tr>
</tbody>
</table>

P39

Background. Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer related death in females in Mexico as in other Western Countries. The most widely used model for breast cancer risk assessment is the Gail Model (GM), which is currently the most validated tool, however considering it was mainly done for western populations, its validation in an international context is required. The validation of the GM has never been done for a Latin American country. Methods: In 2002 a cohort of 1000 female patients were recruited in a tertiary referral center in Mexico City. An assessment of individual breast cancer risk was performed for these patients. At that moment, the mean calculated absolute risk utilizing the GM at 5 years was 1.18%. These patients were followed for 10 years and those who developed breast cancer were identified retrospectively from the medical charts at the institute. Results: Thirty-three patients were lost to follow up. Twenty-four out of nine hundred sixty seven individuals developed invasive breast cancer (2.48%). The mean age of these individuals at the time of cancer diagnosis was 63. By the five-year mark, twelve of these patients had developed invasive breast cancer, exactly to the predicted GM risk calculated in 2002. Conclusions: Despite the limitation of a small sample, our results suggest that the GM is a well-fitting model for breast cancer risk assessment for a Mexican population.

P40
Dose-dependent Effects of Autophagy on Ductal Carcinoma in situ (DCIS) D.D. Brown, P. McAuliffe.* Surgery, University of Pittsburgh, Pittsburgh, PA.

INTRODUCTION: If left untreated, most DCIS will not progress to invasive cancer. However, current clinic-pathologic features cannot reliably predict aggressive versus indolent course. Therefore, many patients with DCIS are over-treated. Refining our understanding of DCIS will allow better selection of risk-appropriate therapy for patients. Autophagy is a central growth regulator in the breast, both physiologically, as in post-weaning involution, and pathologically, in invasive breast cancer, but its role in in situ lesions has not been extensively evaluated. Autophagy is a cytoprotective process whereby cells utilize their own non-essential proteins, organelles and subcellular membranes to conserve nutrients. We hypothesize that autophagy plays a crucial role in DCIS proliferation and survival. METHODS: Human DCIS cell lines SUM225 and MCF10DCIS.COM were treated for 24 or 72 hours with escalating doses of rapamycin, an autophagy promoter, or chloroquine, an autophagy inhibitor. Proliferation was detected with automated cell imaging, MTT and sulforhodamine B (SRB) assay. Cell death was determined using CellTox green. All were done in triplicate. Activation of autophagy and mTOR pathways was identified on Western blot. SQSTM1 immunochemistry was used to visualize autophagosome accumulation. RESULTS: In both cell lines, proliferation decreased with induction of autophagy by rapamycin. Cell death did not increase with increasing dose. In contrast, cellular proliferation was 1.4-2.5), size >2cm (HR 3.2, CI 2.7-3.9), and LVI (HR 3.9, CI 2.4-6.3) were significant predictors of LN positivity. Four or more involved nodes were seen most commonly in the HER2 (28/144; 19%) and Luminal B (47/344; 14%) subtypes, but not TNBC (26/278; 9%) or Luminal A (199/2201; 9%) (p<0.0001). Conclusions: Predictors of LN metastases include younger age, higher grade, larger size, and presence of LVI. Patients with TNBC are not more likely to have lymph node metastases than those with non-TNBC.

P38
Triple-negative Breast Cancer is not Associated with Increased Nodal Metastases A. Gangi,* J. Mirocha, T. Leong, A.E. Giuliano. Surgery, Cedars Sinai Medical Center, Los Angeles, CA.

Introduction: Axillary lymph node metastases are a prognostic indicator for breast cancer. Studies suggest that breast cancer subtypes are associated with the presence of lymph node (LN) metastases. The purpose of this study was to determine if patients with triple negative breast cancer (TNBC) have a higher risk of LN metastases than those with non-TNBC. Methods: Prospective database review identified 3,289 female patients with invasive breast cancer treated with mastectomy or breast conserving surgery (BCS) between January 2000 and May 2012. Patients who received neoadjuvant therapy were excluded. Patients who underwent sentinel node biopsy (SNB) and/or axillary lymph node dissection (ALND) and those with complete information regarding age at diagnosis, tumor size, grade, stage, histologic subtype, presence of lymphovascular invasion (LVI), estrogen (ER), progesterone (PR), and human epidermal growth factor receptor 2 (HER2) status were included in the final analysis. Results: A total of 2,967 patients met inclusion criteria. BCS was performed in 1,889 and mastectomy in 1,078 patients. Breakdown by subtype included 2,201 (74%) patients with Luminal A, 344 (12%) with Luminal B, 144 (5%) with HER2, and 278 (9%) with TNBC. SNB was performed in 1,094 (37%), ALND in 756 (25%), and 1,117 (38%) patients had both. LN metastases were detected in 1050 (35%) patients. The LN positivity rate varied across subtypes with 734/2,201 (33%) in Luminal A, 143/344 (42%) in Luminal B, 108/278 (39%) in TNBC, and 65/144 (45%) in HER-2 (p<0.0001). On multivariate analysis, there was no difference in LN positivity among subtypes (p=0.24). Only age ≤50 (HR 1.5, CI 1.3-1.8), grade 2 or 3 tumors (HR 1.8, CI
promoted at low doses and inhibited at high doses of the autophagy inhibitor, chloroquine (see Figure), with an associated dose-dependent increase in cell death (p<0.05, ANOVA). In addition, autophagy induction resulted in a decrease in phosphorylated P70 S6 kinase, indicating inhibition of the mTOR kinase signaling pathway in conjunction with autophagy inhibition. SQSTM1 immuno-cytochemistry demonstrated marked inhibition of autophagosome-lysosome fusion in response to chloroquine. CONCLUSION: Modulating autophagy affects DCIS cellular proliferation and survival. Future mechanistic studies in DCIS cell cultures derived directly from fresh patient specimens may reveal a new therapeutic target in the treatment of DCIS.

Figure: Rapamycin (top) or chloroquine (bottom) sensitivity of DCIS cell lines, SUM225 (left) and MCF10DCIS.COM (right), treated at 10-fold dilutions. Cell proliferation measured at 72 hours using SRB assay is displayed as mean ± standard deviation of three independent experiments.

P41 Which Patients Benefit from Post-mastectomy Radiation Therapy in the Setting of T3 Node-negative Breast Cancer? L. Elmore, A. Deshpande, J.A. Margenthaler.* Surgery, Washington University School of Medicine, St. Louis, MO.

Background: We investigated the predictors of adjuvant radiation therapy for patients undergoing mastectomy for a T3 node-negative invasive breast cancer. Further analyses were conducted to determine whether survival outcomes varied according to receipt of adjuvant radiation. Methods: Characteristics associated with post-mastectomy radiation therapy among women with T3 breast cancers but negative axillary lymph nodes were identified from the 1988-2009 Surveillance, Epidemiology, and End Results (SEER) database. The primary outcome was breast cancer-specific mortality. Predictors associated with receipt of adjuvant radiation were ascertained through bivariate analyses. Cox models were used to calculate adjusted hazard ratios (aHR) and 95% confidence intervals (CI). Results: Of those identified, 3125 (60.3%) did not receive adjuvant radiation therapy, and 2053 (39.6%) received adjuvant radiation therapy, and 3 (0.06%) had adjuvant radiation status unknown. Factors that were predictive of receipt of adjuvant radiation therapy included younger age at diagnosis, positive marital status, grade 3 tumors, and increasing tumor size (p<0.001 for each). Receipt of post-mastectomy adjuvant radiation therapy resulted in lower breast cancer-specific mortality (22.6% versus 43.5%, p<0.0001) and patients were less likely to die during the follow-up period (aHR=0.696, 95% CI: 0.624-0.776) compared to patients who did not receive post-mastectomy adjuvant radiation therapy. Conclusion: Analysis of the SEER database indicated that several patient and tumor characteristics predict a higher likelihood of receiving post-mastectomy adjuvant radiation therapy in the setting of T3, node-negative disease. Further, receipt of radiation resulted in over 30% reduction in breast cancer-specific mortality for this sub-group of patients.


INTRO: Psychosocial (PsySoc) distress in caregivers is a well-described entity, but most studies are in patients with chronic conditions or terminal illnesses. PsySoc needs of caregivers of patients with early-stage operable breast cancer has not previously been studied. However, some caregivers experience more distress than patients themselves, and emotional support is a predictor of PsySoc well-being in both patients and caregivers. METHODS: We developed a program for newly-diagnosed breast cancer patients and their primary caregiver (partner). Both were screened for common stressors. The couple was then paired with two social workers trained in communication and gender differences, who educated them in communication-based problem solving. Program satisfaction surveys were administered at the conclusion of the visit, along with appropriately triaged referrals to supportive service teams to address identified stressors. RESULTS: Eighty-six patients and eighty-two partners returned surveys. Compared to partners, patients were more likely to report feeling anxious or fearful (59% vs. 38%, p=0.014), report difficulty in managing their emotions (46% vs. 11%, p=0.003), experience distress over being unable to take care of themselves (37% vs. 6% p=0.000), and report substance use by themselves or in their environment (9% vs. 2%, p=0.049). Interestingly, there was no difference between patients and partners in feeling unsupported by their partner (6% vs. 5%, p=0.85), or in feeling down or depressed (29% vs. 30%, p=0.96). CONCLUSIONS: Both patients and partners experience significant distress after a breast cancer diagnosis. We found that partners are equally likely to feel unsupported by their partner (patient) and feel down or depressed. The magnitude of this distress was similar between groups. Further study is needed to learn about both patients’ and partners’ significant distress over lack of support and depression. Partner-focused PsySoc interventions should be initiated in all cancer centers in order to address the emotional needs of both breast cancer patients and their partners.


Background: Accurate identification of ductal carcinoma in situ (DCIS) that will recur, either as invasive breast cancer (IBC) or in situ disease is highly desirable but currently not possible. Most reports of local recurrence (LR) after treatment for DCIS have not examined the pathological features of the recurrences. We used a large cohort of patients treated for DCIS in a single program to investigate the characteristics of LR to compare and correlate features of the original DCIS and those of recurrences. Methods: A retrospective review of prospectively collected data of women diagnosed with DCIS through screening mammography between the years 1994-2008. Follow-up on all patients was obtained, including invasive tumor on local and distant recurrence. Results: 431 women were diagnosed with DCIS, underwent wide local excision and had >6 months follow-up. 88 of 431 (20.4%) developed a LR. Of these recurrences, 41 of 88 (46.5%) were IBC and 47 of 88 (53.4%) were DCIS. Significant predictors of LR were high nuclear grade (p=0.006), comedonecrosis (p=0.021), calcification (p=0.045) and positive surgical margins (p=0.046). High-grade DCIS recurred significantly more often as invasive disease than low or intermediate-grade DCIS (27/215, 12.6% vs. 14/216, 6.5%, p=0.03).
invasive cancers from patients with originally low and intermediate-grade DCIS were node-negative, whereas 6 of 21 (28.6%) high-grade index DCIS cases developed node-positive disease. All low-grade DCIS developed Luminal A IBC. Recurrences after intermediate-grade DCIS were Luminal A, Luminal B and HER2-like IBC, while those after high-grade DCIS were Luminal A, Luminal B, HER2-like and Basal-like IBC. Initial ER status was a significant predictor of ER status in invasive recurrence (p=0.01). Conclusion: While some histological characteristics are associated with LR rate, no standard features can identify a large group of patients at minimal risk of recurrence. Type and features of recurrence is influenced by initial nuclear grade and ER status. Bio-markers or gene expression analysis is needed to more accurately identify lesions that may recur and present as potentially more lethal disease.

**P44**

Modified Core Wash Cytology: A Reliable Same Day Biopsy Result in the One-Stop-Shop Breast Clinic J. Buite,1* C.A. Wauters,2 L.E. Duijnm,3 J.H. De Witm,2 L. Strobbe,4 1. Surgical Oncology, UMC St Radboud, Nijmegen, Netherlands; 2. Canisius Wilhelmina hospital, Nijmegen, Gelderland, Netherlands.

Background: International breast cancer guidelines require women with suspicious breast lesions be diagnosed expediently. For a definitive diagnosis a biopsy is often required. Besides Fine Needle Aspiration (FNA) and Core Needle biopsy (CNB), hybrid techniques including Core Wash Cytology (CWC) are available to establish a same-day diagnosis in these cases. CWC combines the speed of cytology with the superior diagnostic power of CNB. A washing of the otherwise regular CNB specimen is evaluated as a cytological specimen, yielding a provisional diagnosis. The CNB specimen is subsequently processed and analyzed. Literature reports of test characteristics for CWC vary substantially. Materials & methods: All CWC procedures performed on Ultrasound guided CNB specimens in our clinic between May 2009 and May 2012 were reviewed, correlating CWC results with the result of the CNB specimen, the post-operative pathology report and/or follow-up through the automated Dutch national pathology database ‘PALGA’. Results: 1,253 CWC procedures were performed during the study period. Of the evaluated lesions 849 (68%) were malignant and 404 (32%) lesions were benign. 80% of CWC procedures yielded a provisional diagnosis. The CNB specimen is subsequently processed and analyzed. The sensitivity of a conclusive CWC result was 98.3%, specificity 90.4%. Conclusion: In the largest series currently available we demonstrate CWC can be used as an adjunct to regular CNB provide a reliable provisional diagnosis of a breast lesion within the hour. Increasing numbers of inconclusive results in benign lesions means the technique is especially well suited for high risk populations.

**P45**


Introduction: Despite their common use in determining residual in-breast disease after neoadjuvant chemotherapy (NAC), neither MRI nor ultrasound (US) has been recommended to radiographically assess nodal response following treatment. Recent studies have demonstrated accuracy of sentinel lymph node biopsy (SLNB) after NAC for patients (pts) who present with a clinically positive axilla. As a result, preoperative imaging that could predict residual axillary disease would be helpful for operative planning. Methods: A retrospective review was completed using our institutional Cancer Registry. Clinicopathologic data was collected from pts who presented with clinically node positive disease and underwent NAC from 2005 - 2010. Those who had a post-NAC breast MRI and/or axillary US were evaluated. Axillary imaging response was determined by the official radiology dictation. A positive result was defined as a node >1 cm and/or a cortex >2 mm. Nodal involvement was confirmed pathologically after surgery. Results: Of 252 pts with clinically node positive disease treated with NAC, 151 had breast MRI, 99 had axillary US, and 45 had both. No significant difference in sensitivity or specificity between MRI and US is identified (Table 1). The positive (PPV) and negative (NPV) predictive values of MRI for axillary evaluation following NAC is 90% and 23%, respectively. The PPV and NPV of US is 95% and 21%, respectively. In pts with concordant results on both MRI and US, comparable predictive values are obtained. Within the MRI group, a subset analysis by phenotype demonstrates that triple negative (TN) breast cancer has the highest sensitivity (83%) and luminal cancers have the highest PPV (100%). Conclusions: This study demonstrates that imaging of the node positive axilla after NAC cannot reliably predict pathologic nodal status. The predictive value of MRI and axillary US for residual axillary disease following NAC is equivalent. Because of high false negative rates (low NPV), preoperative imaging is not a good protector of complete axillary response to NAC. However, the high PPV suggests it may be helpful for determining the utility of SLNB following NAC, especially in luminal tumors.

**Imaging modality**

<table>
<thead>
<tr>
<th>MRI</th>
<th>US</th>
</tr>
</thead>
<tbody>
<tr>
<td>True positive</td>
<td>55 (50%)</td>
</tr>
<tr>
<td>True negative</td>
<td>21 (14%)</td>
</tr>
<tr>
<td>False positive</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>False negative</td>
<td>69 (60%)</td>
</tr>
</tbody>
</table>

| Sensitivity | 44% | 29% |
| Specificity | 78% | 100% |
| PPV | 90% | 100% |
| NPV | 23% | 13% |

*Ten patients with an unknown receptor status were excluded from the subtype analysis.

**P46**

Combined Efficacy Analyses from Three Phase 3 Trials of (99mTc) Tilmanocept for Sentinel Lymph Node Biopsy cN0 Breast Cancer, Melanoma, and Head and Neck Cancer Patients A. Wallace,* J. Kim,* A. Agrawal,† J. UC San Diego Moores Cancer Center, La Jolla, CA; 2. University Hospitals Seidman Medical Center, Cleveland, OH; 3. The Ohio State University Wexner Medical Center, Columbus, OH.

INTRODUCTION: CD206 receptor-targeted [99mTc]tilmanocept has been evaluated in three Phase 3, prospective, multi-institutional, open-label, single arm trials for the identification of sentinel lymph nodes (SLNs) in clinically N0 breast cancer, melanoma, and head and neck cancer patients (ClinicalTrials.gov identifiers NCT00671918, NCT01106040, and NCT00911326). In the two breast cancer and melanoma trials in which [99mTc]tilmanocept was used in comparison to blue dye, lymph nodes were removed if they were hot, blue, palpable, or discretarily “suspicious.” In the single head and neck cancer trial, patients with intraoral or cutaneous squamous cell carcinoma (SCC) underwent SLN biopsy with [99mTc]tilmanocept alone, and elective neck dissection to remove regional non-SLNs. All excised lymph nodes from the studies, regardless of identification method, were subjected to histopathology analyses. METHODS: Patient data were integrated for the three [99mTc]tilmanocept Phase 3 trials. The primary endpoint was Per Patient Sensitivity of [99mTc]tilmanocept (identification of pathology-positive SLNs). Secondary endpoints included other pathology analyses of negative predictive value (NPV) and overall accuracy. SLN localization rate (% of patients with a SLN identified by [99mTc]tilmanocept), and degree of localization (DL, # of SLNs per patient). RESULTS: 384 out of 390 patients injected with [99mTc]tilmanocept in the Phase 3 trials had complete data for the integrated analyses, and 100 of these (34 melanoma, 27 breast cancer, 39 intraoral SCC) had pathology-positive lymph nodes identified. Table 1 summarizes the per patient integrated results. No differences were observed between tumor types, except for DL.

CONCLUSIONS: High sensitivity, NPV, and accuracy indicate that...
Per Patient Analyses of Integrated Phase 3 $^{[99mTc]}$Tilmanocept Trial Results

<table>
<thead>
<tr>
<th>Sensitivity (combined)</th>
<th>Pooled Analysis</th>
<th>Weighted Least Squares Meta-Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>99.8% (95% CI: 99.3% - 99.8%)</td>
<td>99.8% (95% CI: 99.3% - 99.8%, 100%)</td>
<td></td>
</tr>
<tr>
<td>Malignoma (n=34 pN+): 27 / 27</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Breast Cancer (n=27 pN4): 96.4%</td>
<td>99.9%</td>
<td></td>
</tr>
<tr>
<td>Head and Neck SCC (n=39 pN1): 97.4%</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Negative Predictive Value (combined):</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>Overall Accuracy (combined):</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>Localization Rate (combined):</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td>Malignoma (n=153): 98.8%</td>
<td>99.5%</td>
<td></td>
</tr>
<tr>
<td>Breast Cancer (n=448): 99.7%</td>
<td>99.5%</td>
<td></td>
</tr>
<tr>
<td>Head and Neck SCC (n=83): 97.6%</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Degree of Localization (combined): 2.9</td>
<td>2.2</td>
<td></td>
</tr>
<tr>
<td>Malignoma (n=153): 2.4</td>
<td>2.3</td>
<td></td>
</tr>
<tr>
<td>Breast Cancer (n=448): 2.1</td>
<td>2.4</td>
<td></td>
</tr>
<tr>
<td>Head and Neck SCC (n=83): 3.9</td>
<td>n/a</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CI = confidence interval, SCC = squamous cell carcinoma, n/a = not applicable.

*Intraoral and cutaneous SCC were only tested in 1 trial, so a meta-analysis between trials is not applicable.

Table 1: Summary of our patient cohort

<table>
<thead>
<tr>
<th>BI-RADS</th>
<th>No of patients (%)</th>
<th>No of patients biopsied (%)</th>
<th>No of cancers (%)</th>
<th>False Negative (%)</th>
<th>False Positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>954</td>
<td>284 (30.0%)</td>
<td>98 (15%)</td>
<td>2 (0.3%)</td>
<td>5 (0.5%)</td>
</tr>
<tr>
<td>1-2</td>
<td>686 (72%)</td>
<td>206 (30%)</td>
<td>56 (15%)</td>
<td>2 (0.3%)</td>
<td>5 (0.5%)</td>
</tr>
<tr>
<td>3</td>
<td>294 (27%)</td>
<td>28 (10%)</td>
<td>8 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>4</td>
<td>24 (27%)</td>
<td>11 (37%)</td>
<td>1 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>5</td>
<td>3 (12%)</td>
<td>1 (07%)</td>
<td>1 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

* Percent of total number of patients in cohort (N=954)
** Percent of number of patients in each BI-RADS category
*** Percent of number of patients biopsied

§ 40% of patients without tissue diagnosis had follow-up imaging; none developed cancers

P47
False Negative Rate of Combined Mammography and Ultrasound for Women with Palpable Breast Masses C.H. Chan,* S.B. Coopey, P.E. Freer, K.S. Hughes. Massachusetts General Hospital, Boston, MA.

Introduction: Mammography and ultrasound are often used concurrently for patients with breast masses. While mammography by itself has a false negative rate of approximately 15%, the addition of breast ultrasound may decrease this rate among patients with palpable breast masses. There are currently no outcome data regarding the use of Combined Reporting of Ultrasound and Mammography (CRUM) for breast masses. Methods: We retrospectively reviewed female patients presenting with a breast mass in a prospectively entered database at a single institution by a single surgeon from June 2010 to July 2013. We identified a patient cohort with CRUM and tissue diagnosis. False negative and false positive rates were calculated.

Results: We identified 1240 female breast mass patients in our database; 954 (77%) patients had CRUM (Table 1). 98 patients were found to have cancer. While 96% of patients with combined Breast Imaging-Reporting and Data System (BIRADS) score of 4-5 had tissue diagnosis, 33% and 33% of patients with BIRADS 1-2 and 3, respectively, also underwent biopsy due to patients’ insistence or worrisome clinical features. 40% of patients without tissue diagnosis had follow-up imaging; none developed cancers. 2/686 (0.3%) patients with BIRADS 1-2 and 2/54 (3.7%) patients with BIRADS 3 had either ductal carcinoma in-situ or invasive cancers. 112/176 (64%) patients with BIRADS 1-2 and 3, respectively, also underwent biopsy due to patients’ insistence or worrisome clinical features. 40% of patients with breast masses. While mammography by itself has a false negative rate of approximately 15%, the addition of breast ultrasound may decrease this rate among patients with palpable breast masses.

Table 1: Summary of our patient cohort

<table>
<thead>
<tr>
<th>BI-RADS</th>
<th>No of patients (%)</th>
<th>No of patients biopsied (%)</th>
<th>No of cancers (%)</th>
<th>False Negative (%)</th>
<th>False Positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>954</td>
<td>284 (30.0%)</td>
<td>98 (15%)</td>
<td>2 (0.0%)</td>
<td>5 (0.5%)</td>
</tr>
<tr>
<td>1-2</td>
<td>686 (72%)</td>
<td>206 (30%)</td>
<td>56 (15%)</td>
<td>2 (0.0%)</td>
<td>5 (0.5%)</td>
</tr>
<tr>
<td>3</td>
<td>294 (27%)</td>
<td>28 (10%)</td>
<td>8 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>4</td>
<td>24 (27%)</td>
<td>11 (37%)</td>
<td>1 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>5</td>
<td>3 (12%)</td>
<td>1 (07%)</td>
<td>1 (0.0%)</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

* Percent of total number of patients in cohort (N=954)
** Percent of number of patients in each BI-RADS category
*** Percent of number of patients biopsied

§ 40% of patients without tissue diagnosis had follow-up imaging; none developed cancers

P48
Predictors of Use of Adjuvant Chemotherapy and Overall Survival Outcomes in Elderly Breast Cancer Patients P. Kanumuri,* D.R. Lannin, M. DiGiovanna, B. Killelea, N.R. Horowitz, M. Abu-Khalaf, A.B. Chapgar. Yale University School of Medicine, New Haven, CT.

Introduction: The average age of breast cancer incidence is steadily on the rise. There are limited data on the utilization and benefits of adjuvant chemotherapy (CT) in breast cancer patients older than 70 years of age. We sought to determine factors influencing the decision to administer CT in this population, along with outcomes in terms of overall survival (OS) using data from the National Cancer Database (NCDB). Methods: Patients ≥ 70 years of age with Stage I – III breast cancer, who underwent surgical treatment for their breast cancer were identified from the NCDB [1985 – 2010]. Univariate and multivariate analyses of predictors of CT use and survival were performed using SPSS. Results: Of the 434,660 patients ≥ 70 years of age with surgically resected stage I-III breast cancer for whom data was available regarding receipt of chemotherapy, 56,574 (13%) received treatment. Clinicopathologic variables associated with the receipt of chemotherapy on multivariate analysis are shown in the table below. On univariate analysis, overall survival was significantly lower in patients who did not receive CT [67.3 (Mean) months (M); 95% CI, 66.9-67.7 vs 69.6 M; 95%CI, 69.4-69.8; p<0.001]. On multivariate analysis controlling for age, sex, race, Charlson-Deyo Score, region, urban-rural location, insurance, facility type, tumor size, tumor grade, node positivity, and surgery type, chemotherapy remained a predictor of worse overall survival [OR: 1.091; 95%CI, 1.08 -1.10; p<0.001]. Conclusions: Use of adjuvant chemotherapy appears to be associated with worse overall survival in the elderly with surgically treated, non-metastatic breast cancer, independent of tumor size, tumor grade, lymph node status and comorbidities. While these data do not control for the type of chemotherapy offered, nor compliance with the prescribed regimen, they offer a note of caution for use of chemotherapy in the elderly.

Factors Associated with Adjuvant Chemotherapy Use in Elderly Breast Cancer Patients - Multivariate Logistic Regression

<table>
<thead>
<tr>
<th>Factors</th>
<th>Odds Ratio (95%CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age **</td>
<td>0.82 (0.81-0.818)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Race</td>
<td>Caucasian</td>
<td>1.11 (1.06-1.16)</td>
</tr>
</tbody>
</table>
| | African American | 1 |<referral> 
| Facility Type | Community Cancer Program | Referral |<referral> |
| | Comprehensive Cancer Program | Referral |<referral> |
| Tumor Grade | Low | Referral |<referral> |
| | Intermediate | Referral |<referral> |
| | High | Referral |<referral> |
| | Negative | Referral |<referral> |
| Surgery Type | Partial Mastectomy | Referral |<referral> |
| | Total Mastectomy | 1.30 (1.27-1.34) |<referral> |

* Continuous variable

P49
Breast Cancer Outcomes according to Mammographic Screening Status J. Fong,1 H. Farrugia,2 A. Noon,3 G.B. Mann,* 1. The Royal Women's Hospital, Parkville, VIC, Australia; 2. The University of Melbourne, Melbourne, VIC, Australia; 3. The Victorian Cancer Registry, Melbourne, VIC, Australia.

Background: The value of population-based mammographic screening has been the subject of debate over recent years. We aimed to investigate the impact of mammographic screening by examining all cases of breast cancer diagnosed over a 13 year period in a defined area of Melbourne, Australia, and comparing those women who had undergone screening with those who had not. Methods: All women diagnosed with breast cancer between 1994 and 2006 were identified. Demographic and pathology details were recorded. Vital status was determined from the National Death Registry. BreastScreen Victoria records were cross-referenced to identify patients known to the screening program, and to identify cancers were screen-detected or interval cancer. Cancers in Non-
screened and Screened women were compared, and Screen-detected and Interval cancers were also analysed. Results: 5579 women residing in the catchment area of NorthWestern BreastScreen were diagnosed with invasive cancer between 1994 and 2006. 3408 were diagnosed in non-screened women and 2171 in women undergoing screening. 404 of these were interval cancers. Cancers in Non-screened women were larger - 24.7% were >30mm compared with 9.8% in the Screened population. Non-screened cancers were more likely to be high grade (42.7% vs 28%) and node positive. 5-year overall survival after diagnosis was 91% vs 81% for Non-screened. Size, grade and nodal status was significantly better for Screen-detected, but not significantly different between Interval and Non-screened groups. Breast Cancer Specific Survival was similar for Interval and Non-screened cancers. Conclusion: Breast cancer outcomes after diagnosis are better for patients within a screening program. Those diagnosed outside a program are similar to interval cancers diagnosed within a program. Figure 1: Breast cancer specific survival for Screened and Non-Screened population (1a), and according to screen-detected vs interval (1b).

P50
Lymph Node Ratio is a Prognostic Indicator of Overall Survival for Non-metastatic Breast Cancer Patients after Neoadjuvant Chemotherapy M. Miller,* R. Ottesen, J. Niland, L. Kruper, S. Chen, C. Vito. City of Hope National Medical Center, Duarte, CA

Background Neoadjuvant chemotherapy (NAC) is utilized for more advanced breast cancers to decrease tumor burden. Other than "y" notation, current AJCC staging does not take into account NAC downstaging in the pathologic stage. NAC decreases the total number of lymph nodes (LNs) harvested limiting the value of current staging which is based only on total positive LNs. Lymph node ratio (LNR) may provide more useful predictive information of overall survival (OS) in a NAC setting. Methods A retrospective review of institutional data collected for the National Comprehensive Cancer Network database was performed, identifying women diagnosed between 1997-2009 with primary, unilateral, LN positive breast cancer, excluding those with Stage IV disease. Patient demographics, tumor characteristics, and survival data were analyzed. The LNR was calculated from pathologic reports at definitive resection (total positive/total harvested). Patients were divided into 3 strata (>0-0.1, 0.1-0.5, and >0.5). Kaplan-Meier curves were constructed to compare OS and evaluated using the log-rank test. A Cox proportional hazard model was constructed for multivariable analysis to control for potential confounders. Results The cohort had 168 women with primary, unilateral, LN positive breast cancer. OS was significantly improved in the lower LNR groups (p=0.014). In multivariable analysis, after adjusting for age at and year of diagnosis, T stage, her2/Neu and hormone receptor status, patients with LNR of >0 to 0.1, patients with a LNR of >0.10 to 0.50 (HR=4.04 95% CI: 1.33-12.23) and >0.50 (HR=3.95 95% CI: 1.20-12.99) had significantly higher hazard of death with increasing LNR. AJCC staging N1-3, in same model, was not predictive of OS (p=0.48). Conclusions In the post NAC setting, LNR is a statistically significant prognostic indicator of OS in operable breast cancer patients and provides better prognosis prediction than standard N-stage criteria. Further study is merited.

P51

Background and Objectives Current surgical approaches for in situ and early stage invasive breast cancer include partial mastectomy or total mastectomy. Previous studies have suggested that total mastectomy rates are rising while SEER data analysis has not confirmed this. We therefore sought to determine the trend of total mastectomy rates in the state of Tennessee and explore patient and tumor factors that may influence the surgical choice. Methods: Registry analysis was carried out for women diagnosed with in situ or invasive breast cancer between 2000 and 2009 using the Tennessee Cancer Registry. Type and rate of surgical treatment was examined over time. Factors influencing the probability of total mastectomy were analyzed using univariate and multivariate logistic regression. Results: A total of 39,640 women with breast cancer were analyzed. There were 6,969 (18%) in situ and 32,671 (82%) invasive carcinomas. Overall, 51% and 49% of women underwent partial or total mastectomy, respectively. The rate of total mastectomy decreased from 2000 to 2006 (52% to 45%, p<0.001) however from 2006 to 2009 the rate increased significantly to 50%. (p<0.001) On multivariate analysis, age at diagnosis (p=0.0001), race when compared to white (black OR 0.64, CI 0.59-0.71, Asian OR 1.03 CI 0.72-1.50 p<0.0001), year of surgery (p<0.0001), tumor size (p=0.0001), invasiveness (in situ vs. invasive, OR 1.56, CI 1.35-1.80, p<0.0001), ER positive (OR 0.76 CI 0.68-0.85, p=0.0001), PR positive (OR 1.35 CI 1.22-1.49 p<0.0001) grade (1.06 CI 1.01-1.11 p=0.01), and stage (1.73, CI 1.64-1.82, p<0.0001), were found to be significant predictors of total mastectomy. Conclusion: The rate of total mastectomy in Tennessee declined until 2006 however since that time it has been increasing. Multiple patient and tumor factors are associated with the preferential use of total mastectomy. Further studies are needed to determine the etiology of these trends.

P52

Introduction: Androgen Receptor (AR) is the most commonly expressed nuclear hormone receptor in breast cancer and may be a marker of response to targeted anti-androgen therapy, a particularly attractive option in the setting of triple negative breast cancer (TNBC). Gene expression studies suggest that AR-positivity may distinguish a luminal/AR TNBC subtype from mesenchymal, stem cell-like, and basal-like subtypes. Furthermore, frequency of TNBC is 2-3 times higher in African American and African compared to White American and European breast cancer patients, yet little is known regarding the distribution of TNBC subtypes in the high-risk African-ancestry populations. We sought to characterize AR expression and TNBC patterns among a series of breast cancers from Ghana, Africa. Methods: Invasive breast cancer specimens from 147 pts treated at a single teaching hospital in Ghana were studied at a comprehensive cancer center in the United States and analyzed for estrogen receptor (ER), progesterone receptor (PR), HER2/neu, ALDH1 and AR expression via immunohistochemistry. Results: Median patient age was 45 (range, 28-76yrs). Only 51 cases (31%) were ER-positive, and 14 (10%) were HER2-positive; 89 tumors (61%) were TNBC. For the entire group, 44% were AR-positive and 45% were ALDH1-positive. ER/PR-positive tumors were more likely to be AR-positive compared to ER/PR-negative tumors (87% versus 26%; p<0.0001) but there was no association between ALDH1 and AR expression. Among the TNBC cases, 45% were ALDH1-positive and 24% were AR-positive. Within the subset of TNBC tumors, ALDH1-positive lesions were more likely to be AR-positive compared to ALDH1-negative lesions (36% versus 14%; p=0.019). Conclusions: We confirmed the results of others showing...
that the majority of African breast cancers are triple-negative. We also found that AR expression is lower than that reported in other populations. Surprisingly, a marker of mammary stem cell expression was found to correlate with AR expression among triple negative tumors in this series, suggesting that patterns of TNBC subtypes may differ in populations with substantial African ancestry.

P53
Cannula-assisted Flap Elevation (CAFE): A Novel Technique for Developing Flaps during Skin-Sparing Mastectomies (SSMs)
M.D. Grant.* Baylor Charles A. Sammons Cancer Center and Baylor University Medical Center, Dallas, TX.

One of the most challenging procedures in breast surgery is the SSM. Various techniques and incisions have evolved that characterize this procedure; however, what is common in all of them is the smaller the incision, the more difficult it is to develop skin flaps. Here we report a procedure which incorporates the use of liposuction cannulas (without suction) to create skin flaps. Briefly, the plan for mastectomy incision would be the same as for any procedure, but small “access incisions” are made along incision lines, with enough room for the cannula. The skin incision is made with a scalpel and hemostasis is done with cautery. A plane is started with a hemostat and blunt-spreading technique is used to find the plane in fascia. The cannula is inserted in this opening and passed radially towards the periphery of the breast parallel to skin surface in a back and forth motion. Multiple small channels are created in the plane, but no fat removed. At least 2 quadrants of breast can be accessed through each incision. This same technique is repeated from different angles until the entire superficial plane has been perforated with multiple intersecting channels. After this first step, the rest of the planned surgery is done as normal. In over a year, 100+ mastectomies have been performed using this procedure. Postoperatively, no problems were experienced with flap viability. The main side effect of the CAFE technique was more bruising than normal, but this resolved rapidly. The results for use of this technique were consistently impressive. The learning curve for this procedure is very short, especially for those who perform SSMs using scissors. Residents and fellows became proficient with the CAFE technique in a relatively short amount of time. Plastic surgeons were pleased with the cosmetic outcomes of their reconstructions that follow this type of mastectomy. Patients were extremely satisfied with their reconstructions as well. Incorporating the use of liposuction cannulas makes the creation of flaps for SSM a relatively simple and rapid method. It is especially useful to assist in developing skin flaps with even the smallest of skin incisions.

Figure 1. CAFE technique for flap development. A. “Access incisions” are made along incision lines, which are large enough to accommodate the cannula (arrow). B. A hemostat is used to get the appropriate plane started in the superficial fascia. C. A cannula is inserted in the opening and passed radially towards the periphery of the breast parallel to skin surface in a back and forth motion (arrow). D. At least 2 quadrants of the breast can be accessed through each incision using the back and forth motion (arrows). E. This technique is repeated circumferentially from different angles until the entire superficial plane has been perforated with multiple intersecting channels. Ovals represent completed areas of the breast skin flaps that have been subcutaneously perforated with cannulas before flap elevation (M= medial, S= superior, L= lateral, and I= inferior). F. A pair of Cooley scissors is used to finish this part of the procedure. G. A skin hook can be used to assist in counter tension if necessary.

P54
Predictive Factors of Response to Neoadjuvant Chemotherapy in Hormone Receptor Positive Breast Cancer

Background: Previously reported low response rates of hormone receptor positive (HR+) breast cancer to neoadjuvant chemotherapy have limited the use of this treatment algorithm. Our objective was to identify clinical and treatment factors that may predict for response to neoadjuvant chemotherapy in HR+ breast cancer patients. Methods: An institutionally approved prospective breast cancer database incorporating the NCCN Breast Cancer Outcomes Project data dictionary was used to identify patients with cancers that expressed estrogen receptor (ER) and/or progesterone receptor (PgR) who received neoadjuvant chemotherapy from 1997 – 2012. Only patients who underwent surgical resection were included. Response to neoadjuvant chemotherapy was confirmed by pathological findings. Logistic regression analyses were performed to identify demographic, clinical and treatment factors predictive of response to neoadjuvant chemotherapy. Results: Of the 2,473 patients in the database, 153 with HR+ breast cancer patients were treated with neoadjuvant chemother-
apy followed by definitive surgical resection. The mean age of the patients was 49 years. 54 (35%) patients demonstrated response with downstaging of disease. Complete pathological response was identified in 12 (7.8%) patients. Using a multivariable logistic regression model, ER (p=0.0456), clinical stage (p=0.0018) and LV1 (p=0.0220) were associated with response to neoadjuvant chemotherapy. Patients with disease that did not express ER (OR=4.86 95%CI 1.03 – 22.91), with Stage II disease (OR=2.37 95%CI 1.09-5.18), with cancers that lacked lymphovascular invasion (OR=2.95 95%CI 1.17-7.45) were more likely to respond. Age, menopausal status, race/ethnicity, HER2 receptor status, and grade were not predictive of response. Conclusions: The use of neoadjuvant chemotherapy in HR+ breast cancer is associated with encouraging response rates. In patients with ER-PgR+ cancers, node negative disease, and no lymphovascular invasion, neoadjuvant chemotherapy is more likely to result in disease downstaging and complete pathological response.

**P55**

**Cytotoxic T Lymphocyte Infiltration of Normal and Benign Breast Lobules Diminishes with Age and Epithelial Abnormality**


Introduction: CD8+ tumor infiltrating lymphocytes have a predominantly cytotytic phenotype and a hypothesized role in tumor immunosurveillance. Here we investigate whether cytotoxic T lymphocyte (CTL) density varies in non-malignant breast lobules according to confirmed breast cancer risk factors: age and histologic features of fibrocystic change/epithelial proliferation and involution. Methods: Archived breast tissue samples were obtained from 81 women: 54 with benign breast disease (BBD) and 27 normal women without clinical breast disease from the Komen Tissue Bank at Indiana University (KTB). Up to 10 representative lobules in each sample were characterized by HE for fibrocystic changes/degree of epithelial proliferation (normal, non-proliferative, proliferative) and involution (none, partial, complete). Consecutive sections were immunostained for CD8+ CTLs. Using digital image analysis, quantitative CTL density (cells/mm2) was obtained on a per lobule basis and analyzed by linear mixed effects regression. Results: Among 81 women (age 37-70), 756 lobules were evaluated. 236 KTB and 520 BBD. The majority of lobules were normal (419, 55%); 190 (25%) had nonproliferative fibrocystic changes, and 141 (19%) had epithelial proliferation. Among normal lobules, 52 (8%) had no involution, 131 (21%) had partial involution, and 256 (61%) had complete involution. CTL density was higher in younger women than those over 55 years (152 cells/mm2 compared to women 55 years and older (108 cells/mm2; p=0.04). Mean CTL density decreased with increasing abnormal epithelial proliferation: 143 cells/mm2 in normal lobules, 120 cells/mm2 in nonproliferative fibrocystic lobules, and 88 cells/mm2 in lobules with epithelial proliferation (Figure, p=0.0001, significant after adjusting for age). CTL density did not vary with involution status, even when adjusted for age. Conclusions: CTL infiltration of breast lobules decreases with age and with increasing degrees of epithelial abnormality, features associated with breast cancer risk. These findings raise questions about a possible role of CTLs in tumor immunosurveillance and in early steps of carcinogenesis.

**P56**

**Phosphatidylinositol 3-kinase (PI3-kinase) Pathway Aberrations Are Frequently Seen in Triple-negative Breast Cancer**


Background: Triple negative breast cancer (TNBC) has limited therapeutic options. Activating mutation or focal amplification of the PIK3CA gene is the most common oncogenic event found in breast cancer including TNBC. The emergence of PI3-kinase pathway inhibitors has led to their potential use in the treatment of breast cancer, including in the context of Androgen Receptor (AR) positive status. Methods: Paraffin samples from 18 patients with TNBC were obtained from an IRB approved, annotated biorepository. Pure tumor populations were flow sorted from each block using DNA content-based flow cytometry. Array-based comparative genomic hybridization (aCGH) was performed to evaluate genomic amplifications and deletions. Multiple genes in the PI3-kinase pathway (PIK3A, PTEN, AKT1, AKT2) were analyzed and compared with clinical data. AR status was determined by IHC. Results: Average age of the 18 TNBC cases was 51 years (range 34-77 years). Mean tumor size was 3.0 cm (range 0.7-6.5 cm) and 8 patients were lymph node positive. 7 patients were AR+. A total of 7 patients developed systemic recurrence. 15/18 patients (83%) had an aberration in a PI3-kinase pathway gene by aCGH. There was no difference in patients who were AR+ (6/7) compared to those who were AR- (9/11). More than one aberration was seen in 8 patients (53%) and no difference between those who were AR+ or AR-. There were also no differences between patients based upon systemic recurrence. Heterozygous PTEN deletion was the most common abnormality found occurring in 9 patients (50%) and 4 patients were homozygous for the PTEN deletion. Abnormalities in PIK3CA, AKT1, and AKT2 were less common. Conclusions: Aberrations in the PI3-kinase pathway were very common in our TNBC cohort. The presence of alterations in the PI3-kinase pathway in the presence of AR positivity suggests that dual therapy with an AR inhibitor and PI3-kinase pathway inhibitor could potentially be a biomarker-driven therapeutic approach in TNBC. Evaluation of larger datasets including DNA sequence analysis of PIK3 pathway genes and functional assays will be performed to verify these results.

**P57**

**Papilloma on Core Biopsy: Excision versus Observation**

F. Nakhlis, M. Ahmadiyeh, S. Lester, S. Raza, P. Lotfi, J. Brock, M. Golshan. 1. Dana Farber/Brigham and Women’s Cancer Center, Boston, MA; 2. UCSF School of Medicine, San Francisco, CA.

INTRODUCTION: Intraductal papillomas (IP) are commonly seen breast lesions with variable clinical presentation. For a palpable lesion and/or evidence of cellular atypia or pathologic nipple discharge (PND), an excision is warranted to rule out adjacent carcinoma, while for asymptomatic IPs lacking atypia current data for excision vs. observation are controversial. We reviewed outcomes of IPs diagnosed at our institution. METHODS: With IRB approval a retrospective review was done of consecutive patients with IPs seen on core biopsy (CBx) between 2005 and 2013. Those with PND were excluded. All patients had an excision, with sub-specialty breast pathology review of CBx and excision specimens. The rate of upgrade to invasive cancer or DCIS on excision was recorded. Differences between atypia and no-atypia groups (Table 1) were determined by two tailed t test and by Fisher’s exact test. RESULTS: We identified 97 patients (age range 31-83 years) with IP’s on CBx. Among 52 patients with atypical IPs, DCIS was seen in 11 (upgrade 21%). In 45 patients with IPs without atypia 3 cancers were seen (upgrade 6.7%): 2 had palpable lesions and were found to have DCIS; 1 invasive cancer (grade 2, 1.9 cm) was found in a non-palpable mammographically detected BIRADS 4C lesion, whose CBx result was discordant. If the 2 palpable lesions are excluded the upgrade rate for IPs without atypia was 2.2%. Since all 3 upgraded patients had undergone IP excision it is warranted to rule out adjacent carcinoma, while for asymptomatic IPs lacking atypia current data for excision vs. observation are controversial. We reviewed outcomes of IPs diagnosed at our institution. CONCLUSIONS: This series shows a low upgrade rate for IP without atypia seen on CBx in the absence of a palpable mass and radiographic/pathologic discordance, suggesting that close mammographic surveillance for such patients may be appropriate and that a surgical biopsy may not be necessary. Further prospective studies to better estimate the upgrade rate for IPs without atypia may be helpful to better counsel such patients.
Table 1

<table>
<thead>
<tr>
<th>Alycia</th>
<th>Yes</th>
<th>No</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ps, N</td>
<td>52</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Mean age</td>
<td>56</td>
<td>51</td>
<td>0.02</td>
</tr>
<tr>
<td>Percentable mass</td>
<td>46 (98%)</td>
<td>35 (100%)</td>
<td>NS</td>
</tr>
<tr>
<td>BRADY 4</td>
<td>51 (98%)</td>
<td>43 (96%)</td>
<td>NS</td>
</tr>
<tr>
<td>Concordant (agreement between radiographic appearance and pathology)</td>
<td>40 (77%)</td>
<td>24 (53%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean number of cores</td>
<td>5.2</td>
<td>5.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

PS8

Wait Times for Breast Cancer Surgery, 2003-2010: A Report from the National Cancer Database
E. Liederbach,1* C. Pesce,1 S. Sharpe,2 M. Sisco,1 D.J. Winchester,1 K. Yao.1 1. Surgery, Northshore University Healthsystem, Evanston, IL; 2. University of Chicago, Chicago, IL.

Background: There are few multicenter studies that have examined wait times for breast surgery and no benchmarks exist. We hypothesized that wait times have increased and these increases are related to certain patient and facility factors.

Methods: Using the NCDB, we analyzed time from diagnosis to surgery for 666,803 non-neoadjuvant AJCC stage 0-III breast cancer patients treated in 2003-2010. Chi-square and logistic regression models were used to examine factors associated with longer wait times.

Results: Sixty-seven percent of patients underwent a lumpectomy (LP), 23% a mastectomy (MA), and 10% a mastectomy with reconstruction (MR).

The median time from diagnosis to surgery was 25 days for LP, 27 days for MA, and 35 days for MR. The median time from diagnosis to operation increased from 2003 to 2010 (Figure 1, p<.001). In a multivariate analysis the following variables were independent predictors of a longer wait time across all procedures: increasing age, African American race, Medicaid insurance, low educational status, greater Charlson-Deyo co-morbidity score, academic/research facilities, and facilities located in the Northeast and Atlantic regions. Academic/research facilities had longer relative wait times than community centers for LP (OR=1.75 95% CI: 1.7-1.8), MA (OR=2.0 95% CI: 1.9-2.1) and MR (OR=1.50 95% CI: 1.3-1.6) and wait times for facilities in the Northeast were over two times longer (OR=2.16-2.58, 95%CI: 1.9-2.8) for all mastectomies. The largest discrepancies were noted for MR; median wait time was 42 days for African Americans compared to 35 days for Caucasians, 44 days for Medicaid patients compared to 33 days for private insurance, 39 days for facilities located in the Northeast compared to 28 days for facilities in the Midwest, and 38 days for academic/research facilities compared to 32 days for community facilities.

Conclusions: Wait times have increased for all surgical procedures. Facility and socioeconomic factors are associated with longer wait times across all breast operation types. These findings can be used as benchmarks to determine timely delivery of care.

PS9

Increase in Contralateral Prophylactic Mastectomy Rates is Associated with Increased Use of Immediate Reconstruction
Mayo Clinic, Rochester, MN.

Background: Contralateral prophylactic mastectomy (CPM) rates have been increasing nationally. Reasons for this are not fully elucidated and immediate breast reconstruction (IBR) has been proposed as a factor. This study’s goal was to evaluate 5 year trends in CPM rates and IBR at a tertiary referral center.

Methods: With IRB approval we evaluated the selected surgical procedures for women with newly diagnosed unilateral Stage 0-III breast cancer (without a prior breast cancer history) from 10/08 to 6/13. Proportions were compared across years using chi-square tests for linear trend.

Results: We identified 2886 patients. Median age was 60 yrs (range 24-93). The stage distribution was 0 (25%), I (45%), II (23%), and III (7%). Surgical procedure was lumpectomy in 49% and mastectomy in 51%. Of the 1473 patients undergoing therapeutic mastectomy, 706 (48%) additionally underwent CPM and 615 (42%) underwent IBR. Therapeutic mastectomy rates did not change significantly over the study period (p=0.46), but use of IBR increased from 30% in 2008 to 58% in 2013 (p<0.0001). CPM rates increased significantly from 38% in 2008 to 52% in 2013 (p=0.01). The choice of IBR was significantly associated with the choice of CPM; 57% of patients who elected CPM opted for IBR compared to 27% choosing IBR in the unilateral mastectomy (UM) group (p<0.0001). Within the therapeutic mastectomy subset, rates of therapeutic unilateral mastectomy (UM) decreased from 2008 to 2013 (62.5% to 48%) with the major decrease in UM without IBR, from 52% in 2008 to 27% in 2013 (p<0.0001). Despite the overall decrease in UM, rates of UM with IBR increased from 11% in 2008 to 21% in 2013 (p<0.001). The increase in CPM was entirely due to an increase in CPM with IBR from 19% to 38%, p<0.0001, while CPM without IBR rates decreased from 19% to 15%, p=0.16. Conclusion: CPM rates increased significantly over the past 5 years, driven by an increase in the choice of CPM with IBR. Use of IBR may influence patients’ decisions to pursue CPM. Further work to evaluate these trends nationally and to better understand the patient decision-making process regarding CPM is warranted.

Introduction Postoperative ischemic complications after total skin-sparing mastectomy (TSSM) and expander-implant reconstruction can negatively impact outcomes, particularly in the setting of post-mastectomy radiation therapy (PMRT). The goal of this study is to determine if rates of ischemic complications after PMRT are impacted by TSSM incision. Methods We queried a prospectively-collected database of patients undergoing TSSM and immediate 2-stage expander-implant reconstruction. Our hypothesis was that, in the setting of PMRT, patients with inflammatory (IMF) incisions would be more likely to develop ischemic complications than those without incisions on the dependent portion of the breast. We divided our patient cohort into two groups, those with IMF incisions and those with other TSSM incisions and then analyzed the proportion that received PMRT. Results Of 756 cases of TSSM and immediate expander-implant reconstruction during the six-year period included in the analysis, 469 (62%) had IMF incisions and 287 (38%) had other incisions. Overall, rates of TSSM incision breakdown (2.6% vs. 4%, p = 0.4) and mastectomy skin flap necrosis (6.4% vs. 8.7%, p = 0.3) were equivalent amongst incision types. A subgroup of 91 patients (12%) received PMRT, 62 (68.1%) with IMF incisions and 29 (31.9%) with other TSSM incisions. Mean follow-up was 3.1 years (range 0.8 – 6.6 years). Rates of mastectomy skin flap necrosis (3.2% vs. 6.9%, p = 0.4) following PMRT were not significantly higher in the IMF group. However, breakdown of the TSSM incision after PMRT was twice as likely in the IMF group vs. others (21% vs. 10.3%, p = 0.2) and was more likely to lead to subsequent implant removal when incisional breakdown occurred (77% vs 0%, p = 0.03), despite attempts at implant salvage. Conclusions In the setting of PMRT, TSSM incision type may impact the development of incisional breakdown and implant loss, with higher rates of complications seen with IMF incisions. Multiple factors, including preoperative breast size, degree of breast ptosis, and likelihood of PMRT, should be considered in determining optimal TSSM incision and reconstructive choice.


Background: Concomitant with widespread adoption of axillary ultrasound (AUS) with ultrasound-guided needle biopsy (USNB) of suspicious lymph nodes (LN) for preoperative nodal staging of breast cancer patients, utilization of breast MRI, which includes axillary imaging, has increased. Little is known about the added value of MRI imaging of the axilla in this context. We undertook this study to assess the role of breast MRI in preoperative axillary nodal staging. Methods: We studied 988 consecutive invasive breast cancers in patients undergoing primary operation including axillary surgery, without neoadjuvant therapy, from 2010-2011 from our prospective institutional breast surgery database. Results: 505 patients (51%) underwent MRI of which 168 (33%) demonstrated suspicious findings in the axilla. Abnormal axillary MRI findings included cortical thickening, edema, enhancement, hilar effacement, and/or altered nodal shape and size. 114 patients (68%) with abnormal axillary imaging on MRI had findings concurrent with a prior abnormal AUS. 54 patients (32%) had suspicious LNs on MRI either without a preceding AUS (31 cases) or after an initially negative AUS (23 cases). Second-look AUS was performed in 35 of these cases and was abnormal in 3 (9%). The 35 second-look AUSs included 27 performed in patients with no prior AUS (of which 1 AUS was abnormal) and 8 repeat AUSs after a pre-MRI negative AUS (of which 2 were abnormal). All 3 patients with abnormal second-look AUSs were confirmed LN+ on preoperative USNB. Of the 54 cases with MRI-detected suspicious LNs, 20 (37%) were node positive at operation with a pN stage of N0 (63%), N0i (5%), N1mic (4%), N1 (10%), N2 (6%), and N3 (2%). Extramodal extension was seen in 7 of 20 LN+ patients (35%). Conclusions: Second-look AUS, when performed subsequent to suspicious axillary MRI findings, identified LN metastasis preoperatively in 9% of patients. When MRI is done to evaluate the breast in newly diagnosed breast cancer patients, axillary findings can enhance the accuracy of preoperative nodal staging. We recommend second-look AUS when MRI demonstrates suspicious axillary LN findings.

P62 Validation of Intraoperative Radiation Therapy Dose for Breast Cancer using Radiochromic Film V.V. Villescas,1* R. Rudolph,1 A. Pederson,2 C.I. Price,3 P.C. DeNitto,1 C. Frazier,2 J. Duttenhaver.2 1. Department of Surgery, Memorial Health University Medical Center, Savannah, GA; 2. Memorial Health University Medical Center - Department of Radiation Oncology, Savannah, GA.

BACKROUND: Intraoperative Radiation Therapy (IORT) is a novel single session procedure that applies partial breast irradiation at the low photon energy of 50 kv, reducing regional tissue damage and increasing convenience of treatment. The purpose of this study was to quantify dose absorbed within the partial mastectomy cavity and surrounding tissue. STUDY DESIGN: This prospectively collected data was retrospectively reviewed to evaluate actual dose absorbed versus the intent of 20 Gy per treatment. Skin exposure to radiation was also evaluated above and below the applicator site using radiochromic film. RESULTS: A total of 78 patients have been treated with IORT since inception of the program in October of 2012. The first 11 patients were treated before the use of radiochromic film for in vitro measurement of dose absorbed in the breast cavity. Another was excluded due to mechanical malfunction, resulting in less than one minute of radiation therapy. The measured dose of radiation absorbed by the breast cavity in the remaining 65 patients was 19.08 ± 3.08 Gy, and the superior and inferior skin exposure was measured to be 2.36 ± 1.29 Gy and 2.22 ± 0.93 Gy, respectively. A final patient was excluded after being administered a radiation dose 4 standard deviations below the mean. Recalculating the data with this final patient excluded, the measured radiation mean within the breast cavity was 19.54 ± 1.58 Gy, with skin measurements of 2.29 ± 1.28 Gy and 2.23 ± 0.89 Gy superiorly and inferiorly respectively. CONCLUSIONS: In our cohort, it appears that IORT delivers the prescribed 20 Gy to the partial mastectomy cavity, while virtually eliminating tissue toxicity to surrounding skin with levels of radiation less than those currently accepted in conventional whole breast irradiation. The use of radiochromic film has been shown to be a practical, reproducible, and cost effective method of ensuring minimal tissue damage and establishing a permanent record of intracavity and skin dose delivery.
P63

Introduction: APBI is offered as an alternative to whole breast radiation for selected patients with early breast cancer who choose breast conservation. While initially adopted with enthusiasm, we have recently observed decreased utilization of APBI. Possible influencing factors include decreasing rates of breast conservation and/or physician reaction to the publication of practice guidelines in 2009. Our goal in this study was to evaluate our clinical experience with APBI over the past 9 years and identify possible causes for the current loss in case volume. Methods: Analysis of prospective database of patients with Stage 0, I or II breast cancer treated with APBI via brachytherapy between 2004 and 2012. APBI cases were classified as suitable, cautionary or unsuitable based on the 2009 ASTRO consensus guidelines. Tumor Registry data for the study period was also reviewed. Results: 259 patients received APBI, most having stage I (74%) or stage 0 (22%) breast cancer. Distribution by guidelines was 40% suitable, 51% cautionary, 9% unsuitable. Since 2004 the number of APBI cases per year rose to a peak of 57 in 2009 (19% of stage I cancers that year), declining thereafter to a nadir of 22 in 2012 (5% of stage I cancers that year, P<0.001 compared to 2009). Loss of case volume over the past 3 years was not correlated to changes in breast conservation cases (270±17 cases/year), loss of breast surgeons (6±1 surgeons/year), or poor clinical results (cancer recurrence rate 3.1%). The initial drop in APBI cases occurred in 2010 following the appearance of ASTRO guidelines in 2009. After publication of the guidelines less unsuitable cases received APBI (12% vs. 4%, P=0.036), but there was no difference in the proportion of suitable and cautionary cases before and after 2009. Conclusions: Decreased utilization of APBI followed the publication of the ASTRO guidelines, although a cause-and-effect relationship was not demonstrated. A reduction in unsuitable cases treated after 2009 does not explain the global loss of referrals. Other factors for future analysis include decreasing surgeon remuneration and negative effects of terminology such as cautionary or unsuitable within the guidelines.

APBI cases per year.

P64

Introduction: We are performing an ongoing study of gene expression profiling of circulating tumor cells (CTCs) in Stage II-III breast cancer patients. We have developed a method for isolating CTCs that uses immunomagnetic separation followed by fluorescence activated cell sorting (IE/FACS) and a rapid processing algorithm. We hypothesized that pre-analytical variables such as time to CTC testing may influence CTC enumeration results. Methods: IE/FACS was performed with magnetic beads coated with monoclonal antibody (mAb) to the epithelial cell adhesion marker (EpCAM) followed by FACS with positive selection by EpCAM and thioflavin and negative selection for CD45. Our protocol requires a 20 mL peripheral blood draw to be processed for CTC testing in less than 20 minutes. CTC positive status was defined as 1 or more detectable CTC. We assayed healthy control subjects during initial assay set-up and serially as cross-sectional validation that the assay shows no CTCs in healthy subjects. Results: To date we have enrolled 14 patients and 10 healthy controls. All negative control subjects had no detectable CTCs. The median patient age was 57.8 years. 12/14 (85.7%) patients had CTCs. The median number of CTCs isolated was 6 (range 0-65) with a mean of 0.85 CTCs per mL of blood. CTCs were identified in 8/10 (80%) ER positive, 8 of 9 (89%) PR positive, 2/2 (100%) HER2 positive, and 3/3 (100%) triple negative patients. 8/14 (57.1%) patients were node positive; no association between CTC and nodal status was present. Similarly, no association between tumor size and CTC status was found. Historical controls using a commercially available CTC enumeration strategy found 30-40% of Stage II-III patients to be CTC positive with processing generally performed within 72 hours. Conclusions: The time interval between blood draw and CTC processing assays involving cell surface markers may impact the rate of CTC detection. Using a rapid processing algorithm we were able to double the number of CTCs isolated for future RNA profiling. This strategy may increase the probability of isolating non-degraded nucleic acids for Next Generation Sequencing to study the biomarker CTCs in breast cancer.

P65

Introduction: Our purpose was to study the impact of type of surgery on survival of women with T3/T4 breast cancer treated with neoadjuvant therapy. Methods: Population-based Florida Cancer Data Registry was screened for women diagnosed with T3/T4 breast cancer and received neoadjuvant therapy followed by either breast conserving surgery (BCS) or mastectomy. A multivariable Cox regression was used to identify significant predictors of overall survival. Variables including sociodemographics characteristics, clinicopathological characteristics, type of surgery and type of neoadjuvant therapy were all entered in the model. Adjusted hazard ratios (HR) and 95% confidence intervals (95%CI) were calculated. Type-I error rate was set to 5%. Statistical analyses were done in SAS v9.3. Results: Out of 712 patients, 72 (10%) had BCS and 640 (90%) had mastectomy post neoadjuvant therapy. After adjusting for aforementioned characteristics, neoadjuvant chemotherapy+ hormonal therapy was associated with a better prognosis than chemotherapy alone (HR=1.94; 95%CI:1.25,3.01; p=0.003) or hormonal therapy alone (HR=2.34; 95%CI:1.02,5.36; p=0.044). Hispanics (HR=0.48; 95%CI:0.27,0.88; p=0.018), middle-high SES (HR=0.66; 95%CI:0.45,0.97; p=0.034) compared to lowest, medicare (HR=1.69; 95%CI:1.08,2.65; p=0.023) and uninsured (HR=1.70; 95%CI:1.11,2.60; p=0.016) compared to private insurance, poorly-differentiated (HR=2.59; 95%CI:1.22,5.54; p=0.014) and undifferentiated (HR=3.55; 95%CI:1.42,8.87; p=0.007) compared to well-differentiated grade, and distant SEER stage (HR=3.92; 95%CI:1.65,9.30; p=0.002) were significant predictors of overall survival. Survival between patients with BCS vs. mastectomy did not differ significantly (HR=0.74; 95%CI:0.45,1.21; p=0.229). Conclusions: The type of breast surgery after neoadjuvant therapy for T3/T4 breast cancer does not impact survival. Predictors of survival include tumor grade and stage, type of neoadjuvant therapy, ethnicity, SES and health insurance. In-depth studies are needed to help understand the mechanism by which these factors impact the overall survival.

P66

Background: Cox2 is a key enzyme responsible for prostaglandin production and is frequently overexpressed in breast cancer. Experimental studies showed that COX2-expression stimulates angiogenesis, cell proliferation, inhibits apoptosis, and promotes development of cancer metastases. Almost all clinical studies found predominance of Cox-2 expression in high grade breast cancer compared to grade 1-II. The aim of our study was to evaluate the significance of Cox-2 expression in group of patients with high grade breast cancer. Materials and methods: Three hundred and three patients (median age 55; range 25-95 years) were included in the study. The mean follow-up period was 65.2 months. Cox2 expression was evaluated immunohistochemically using score system, based on the sum of staining intensity and percentage of positive cells. Results 129 out of 303 patients (42.6%) were Cox-2 negative.
and 174 (57.4%) Cox-2 positive. There was no correlation between any clinicopathological pattern and Cox expression. There was no difference in Cox-2 expression according to ER/PR status and Her2 overexpression. In group of patients with triple-negative breast cancer the 5-year disease-free survival rate was 58.3% for the group of patients with Cox-2 expression as compared to 83.9% for patients without Cox-2 expression (p=0.042). In other intrinsic subtypes of high grade breast cancers Cox-2 expression did not provide prognostic significance. 5-year DFS in patients with Cox-2 positive and Cox-2 negative tumors were: Luminal A type 86.9% versus 83.3% (p=0.587), Her2-negative type 52.6% versus 50.0% (p=0.894) and Luminal type B 83.3% versus 60.9% (p=0.116), correspondently. Conclusion: We found no correlation between Cox-2 expression in high grade breast cancer and primary tumor characteristics, hormonal receptor status and Her2 expression. Cox-2 expression is associated with poor disease free survival in triple-negative breast cancer. Efficacy of Cox-2 inhibitors combination with standard regimens of chemotherapy needs further evaluation.

P67

Limits of Real-time 2D and 3D Ultrasound (US) for Volumetric Analysis: A Prospective Study S.J. Gonzalez, B. Mooney, B. Robert, J.V. Kiluk, N. Khakpour, C. Laronga, M. Lee. Surgical Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; 2. Virginia Baptist Hospital, Lynchburg, VA.

Introduction: US allows real-time imaging and has great potential for intraoperative soft tissue assessment in breast and abdominal surgeries. We evaluated the volumetric limits of 2-dimensional (2D) and 3-dimensional (3D) US compared to MRI. Methods: This is an IRB-approved, prospective clinical trial evaluating US-to-MRI volumetric correlation. 2D and 3D US images of pre- and post-neoadjuvant breast cancer tumors were obtained. Cases with skin involvement, incomplete or poor images were excluded. The US-to-MRI volumetric discrepancies were calculated by non-parametric Wilcoxon Signed-Rank test. Expected inter-observer variability (IOV) of ≤14% was evaluated as Relative Paired Difference (RPD) and the clinical relevance of this variability was analyzed using the volumetric Standard Error of the Mean (SEM); values ≤3cm³ were considered clinically usable. Subgroup analyses of size, age and treatment status were performed. Results: Forty-two patients enrolled; 133/170 US were evaluable with 65 2D and 68 3D US images paired to MRI. In tumors ≤20cm³, both probes showed high correlation to MRI with RPD within IOV, SEM <0.6cm³ and p>0.09. Lesions 20-40cm³ had significantly different US-to-MRI volumes (p=0.05 for both US); the discrepancy was within IOV for 2D (RPD:11%) but not 3D US (RPD:27%); however, this was small and reproducible in both probes (SEM:1.47cm³ for 2D and SEM:2.28cm³ for 3D), suggesting some clinical utility. Tumors >40cm³ had significantly different US-to-MRI volumes (p=0.02 for 2D and p<0.001 for 3D); RPD values were within IOV (RPD:<13%) but SEM exceeded clinical utility limits (8.3cm³ for 2D and 9.9cm³ for 3D US). Age <40 had no effect on US-to-MRI correlation but post-treatment status showed a high US-to-MRI volume correlation (p=0.17 for 2D and p=0.21 for 3D US) with measurements within IOV and acceptable variability for clinical use (SEM:<4.4cm³ for 2D and 4.2cm³ for 3D US). Conclusion: Post-neoadjuvant tumors and those ≥20cm³ showed high US-to-MRI correlation even after IOV correction. Tumors 20-40cm³ may also be amenable to US volumetrics. Future studies of clinical and intraoperative volumetric applications of 2D and 3D US are needed.

P69

Perceptions of Contralateral Breast Cancer Risk: A Prospective Longitudinal Survey P. Portschy, A. Abbott, E.E. Burke, R. Nzara, K.M. Kuntz, T.M. Tuttle. Department of Surgery, University of Minnesota, Minneapolis, MN; 2. Division of Health Policy and Management, School of Public Health, University of Minnesota, Minneapolis, MN.

Introduction: An increasing proportion of breast cancer patients undergo contralateral prophylactic mastectomy (CPM) to reduce their risk of contralateral breast cancer (CBC). Our aim was to evaluate the perceived risk of CBC among breast cancer patients and determine if this perceived risk changes over time. Methods: We conducted a prospective longitudinal study of women with newly diagnosed unilateral breast cancer. Patients completed a standardized survey before and approximately 2 years after treatment. Survey questions used open-ended responses or 5-point Likert scale scoring (5 = very likely, 1 = not at all likely). Results: A total of 74 women completed the pre-treatment survey, and 43 completed the post-treatment survey. Baseline characteristics were not significantly different between responders and non-responders of the follow-up survey. The mean time between surveys was 2.4 years. The mean estimated 10-year risk of CBC on the pre-treatment survey was 35.7% and 13.8% on the post-treatment survey. (p = 0.0005). On the Likert scale, the perceived risk of CBC significantly decreased from 2.8 to 2.0 (p = 0.0001). Moreover, the perceived risks of developing cancer in the same breast and elsewhere in the body significantly decreased between surveys. Overall, 26% of women underwent CPM. For both CPM and non-CPM patients, the perceived risk of CBC significantly decreased from pre- to post-treatment surveys. As compared with non-CPM patients, CPM patients had a significantly lower perceived 10-year risk of CBC (5.8% vs. 17.3%, p=0.046) on post-treatment surveys. Conclusion: Although women substantially overestimated their risk of
CBC before treatment, the perceived risk significantly attenuated over time for both CPM and non-CPM patients. These data emphasize the importance of early physician counseling to provide women with accurate information before treatment.

**P70**


INTRODUCTION Although breast conserving therapy (BCT) has been established as an appropriate alternative to mastectomy, uncertainty remains about the direction of recent trends in BCT versus mastectomy. We hypothesized that the discrepancies in mastectomy trends noted across the literature reflect differences in cohort characteristics and practice patterns. MATERIALS AND METHODS Using information in the National Cancer Database (NCDB) from 1998 through 2010, we evaluated women who either underwent a mastectomy or BCT for stage 0-4 breast cancer. The mastectomy rate decreased from 53% in 1998 to 44% in 2006 (p<0.001). Thereafter, the mastectomy rate stabilized at approximately 46% through 2010. Mastectomy rates increased with increasing stage of disease and with hormone receptor negative tumors (p<0.001). After adjusting for disease characteristics, other factors associated with the use of mastectomy include lower income, less education, no health insurance and rural residence (all p<0.001). Mastectomy rates also varied depending on the type of institution delivering care; Community Cancer Programs had a higher rate of mastectomy (50%) than Comprehensive Community Cancer Programs (47%) and Academic/Research Programs (46%) (p<0.0001). Facility location affected rates of mastectomy, with the highest rates seen in the West (60%) and South (59%) and lowest rates in the Northeast (34%) (p<0.001). Institutional and geographic variations in mastectomy rates persisted even after adjusting for socio-economic variables. CONCLUSION Data from this comprehensive population based registry shows declining rates of mastectomy over the last decade. However, differences in mastectomy rates remain across socio-economic demographics, hospital practice type and geographic location.

**P71**

A Novel Animal Model for Locally Advanced Breast Cancer J. De Andrade,* M. Bogacheck, J. Park, M.V. Kulak, P.M. Spanheimer, G. Babiera, I. Bedrosian. UT MD Anderson Cancer Center. Houston, TX.

INTRODUCTION Although breast conserving therapy (BCT) has been established as an alternative to mastectomy, uncertainty remains about the direction of recent trends in BCT versus mastectomy. We hypothesized that the discrepancies in mastectomy trends noted across the literature reflect differences in cohort characteristics and practice patterns. MATERIALS AND METHODS Using information in the National Cancer Database (NCDB) from 1998 through 2010, we evaluated women who either underwent a mastectomy or BCT for stage 0-4 breast cancer. The mastectomy rate decreased from 53% in 1998 to 44% in 2006 (p<0.001). Thereafter, the mastectomy rate stabilized at approximately 46% through 2010. Mastectomy rates increased with increasing stage of disease and with hormone receptor negative tumors (p<0.001). After adjusting for disease characteristics, other factors associated with the use of mastectomy include lower income, less education, no health insurance and rural residence (all p<0.001). Mastectomy rates also varied depending on the type of institution delivering care; Community Cancer Programs had a higher rate of mastectomy (50%) than Comprehensive Community Cancer Programs (47%) and Academic/Research Programs (46%) (p<0.0001). Facility location affected rates of mastectomy, with the highest rates seen in the West (60%) and South (59%) and lowest rates in the Northeast (34%) (p<0.001). Institutional and geographic variations in mastectomy rates persisted even after adjusting for socio-economic variables. CONCLUSION Data from this comprehensive population based registry shows declining rates of mastectomy over the last decade. However, differences in mastectomy rates remain across socio-economic demographics, hospital practice type and geographic location.

**P72**


Department of Surgery, Division of Breast Surgery 1, and Radiation Oncology 2, Beaumont Cancer Institute, Oakland University William Beaumont School of Medicine, Royal Oak, Michigan Purpose: To evaluate clinical outcomes following breast conservation therapy (BCT) with whole breast irradiation (WBI) or partial breast irradiation (PBI) in women ≥ 80 yrs old. MATERIALS AND METHODS: 157 women ≥ age 80 were treated with BCT from 9/91–5/12 at a single institution. BCT included surgery and adjuvant radiation therapy. WBI (n=81) was delivered via standard fractionation (50–61Gy, 25-33 fx) or hypofractionation (42.56Gy, 16 fx). 39 patients had a lumpectomy cavity boost with median dose 16 Gy (8-16). APBI (n=76) was delivered via low dose rate (n=23) or high dose rate (n=25) brachytherapy or 3D-conformal RT (n=28). Clinical outcomes were retrospectively analyzed, including ipsilateral breast tumor recurrence (IBTR), regional recurrence (RR), contralateral breast tumor recurrence (CBTR), distant metastases (DM), cause-specific survival (CSS), and overall survival (OS). Results: Median follow-up was 4.4yrs (0.1-16.7), with slightly longer in the APBI group (5.6 v 3.7yrs, p=0.001). Patient characteristics are in Table 1. WBI patients were more likely to have larger tumors (median 13 v 10mm, p=0.042), T2 disease (29 v 8%, p=0.007), LN+ disease (N1/2 15 v 1%, p=0.004), positive final margins (13 v 0%, p=0.012), and receive chemo (9 v 0%, p=0.02). There were no differences in histology, tumor grade, lymph nodes removed, or ER/PR/Her2 status. 59% of ER+ patients received hormone therapy. Clinical outcomes were similar between the two groups. Few events were noted at 5 years, with no RR or other failures. 5% of patients in the WBI group had CBTR at 5 years, compared to 0% in the APBI group (p=0.07). OS and CSS at 5 years were 81% and 95% overall, and not significantly different between APBI and WBI (OS 78 v 86%, p=0.52; CSS 95 v 97%, p=0.64). Conclusion: Breast cancer outcomes for women ≥80 yrs. were excellent, with a 5-year CSS of 95%. Both APBI and WBI appear to be reasonable treatment options. Further analysis with comparison to a matched cohort treated with surgery alone is underway.
**P73**

Detrimental Association of Blood-product Transfusions on Survival of Breast Cancer Patients

D. Franceschi,1,2 D. Yakoub1, L. Kourias2, A.S. Livingstone,1 T. Koru-Sengul1, D.J. Lee1, F. Miao1, S.L. Tannenbaum1, M. Byrne1, J. University of Miami, Miami, FL; 2. Indiana University, Bloomington, IN.

Background: Transfusion of blood products is associated with worse survival for certain cancer patients. This effect has not been clearly defined in patients with breast cancer. Methods: Florida cancer registry data linked to the Florida Agency for Health Care Administration (AHCA) database were examined for breast cancer patients (1996-2009). Data were corrected for potential confounders related to blood transfusions, including age, gender, race, treatment, and comorbidity conditions. Results: Overall 208,461 breast cancer patients were identified; 26,392 (12%) had transfusion of at least 1 unit of blood products. Patients receiving blood transfusion were older (66 versus 62 years, p<0.0001), with more advanced stage disease. Transfused patients had reduced overall median survival of 94 months versus 162 months for non-transfused patients (p=0.0001). Of 184,635 patients who received breast surgery with therapeutic intent, 1,271 (0.06%) received blood peri-operatively, while 21,521 (11%) received blood at some other point during breast surgery with therapeutic intent, 1,271 (0.06%) received blood peri-operatively, while 21,521 (11%) received blood at some other point during breast surgery with therapeutic intent. Patients with breast cancer were identified; 26,392 (12%) had transfusion of at least 1 unit of blood products. Patients receiving blood transfusion were older (66 versus 62 years, p<0.0001), with more advanced stage disease. Transfused patients had reduced overall median survival of 94 months versus 162 months for non-transfused patients (p=0.0001). Of 184,635 patients who received breast surgery with therapeutic intent, 1,271 (0.06%) received blood peri-operatively, while 21,521 (11%) received blood at some other point during breast surgery with therapeutic intent.

**P74**

**Thickness of Lumpectomy Shaved Cavity Margins Impacts Rec-Excision Rates**

B. Wexelman,* R. Tang, M. Gadd, K.S. Hughes, M. Specht, B.L. Smith, S.B. Coopey. Surgical Oncology, Massachusetts General Hospital, Boston, MA.

Introduction: Shaved cavity margins (SCM) are often taken at the time of breast cancer lumpectomy to decrease rates of positive margins and minimize volume of resection. The optimal thickness of these “shaved” margins is not well established, and there is considerable variability in surgical practice. We sought to determine the optimal thickness of SCMs and the impact of SCM thickness on rates of re-excision, mastectomy, and local recurrence. Methods: We performed a retrospective review of all newly diagnosed breast cancer patients who underwent lumpectomy with complete SCM (4-6 individual shaved margins, or 2 hemispheric shaved margins) at our institution from 2004-2006. We excluded patients who had an excisional biopsy for diagnosis. Pathology reports were reviewed to determine the thickness of each shaved margin, and mean thickness of all SCM was calculated for each patient. Local recurrence, defined as in-breast recurrence, was recorded. Mean SCM thickness was correlated with re-excision, completion mastectomy, and local recurrence rates. Statistical significance was evaluated using chi-square tests between thickness groups. Results: 437 patients underwent lumpectomy with complete SCM, with median follow-up of 77.8 months. The mean shaved margin thickness was 6.4mm, range 2-25mm. Patients were grouped by mean SCM thickness into four groups: 1.0-3.9mm, 4.0-6.9mm, 7.0-9.9mm, and greater than 10.0mm. Thicker shaves were associated with significantly decreased re-excision rates (p=0.046) [Table 1]. Mean SCM ≥10mm achieved the lowest re-excision rate of 19.2%, while SCM <7mm and <4mm had re-excision rates that were twice as high (38.6%, 39.3%). We found no correlation between SCM thickness and ultimate success of breast conserving surgery. While there was a trend toward lower local recurrence rates with SCM ≥7mm, this did not reach statistical significance. Conclusions: Shaved margin thickness has an inverse relationship with re-excision rates. Optimal shave thickness to avoid re-excision was 10mm in our cohort of patients.

**P75**

**Pleomorphic Invasive Lobular Carcinoma: Characterizing a Lobular Carcinoma Variant**


INTRODUCTION: Pleomorphic invasive lobular carcinoma (PILC) is a subtype characterized by nuclear atypia and irregularity in contrast to the cytologic uniformity of classic invasive lobular carcinoma (ILC). It is considered a more aggressive based on limited reports in the literature with small series. We aim to further characterize this variant from a larger series at a single institution.

METHOD: Following exclusion of PILC on core biopsy only, presence of ductal carcinoma on final pathology, and stage 4 disease not undergoing surgery. Excisional biopsy for diagnosis. Pathology reports were reviewed to determine the thickness of each shaved margin, and mean thickness of all SCM was calculated for each patient. Local recurrence, defined as in-breast recurrence, was recorded. Mean SCM thickness was correlated with re-excision, completion mastectomy, and local recurrence rates. Statistical significance was evaluated using chi-square tests between thickness groups. Results: 437 patients underwent lumpectomy with complete SCM, with median follow-up of 77.8 months. The mean shaved margin thickness was 6.4mm, range 2-25mm. Patients were grouped by mean SCM thickness into four groups: 1.0-3.9mm, 4.0-6.9mm, 7.0-9.9mm, and greater than 10.0mm. Thicker shaves were associated with significantly decreased re-excision rates (p=0.046) [Table 1]. Mean SCM ≥10mm achieved the lowest re-excision rate of 19.2%, while SCM <7mm and <4mm had re-excision rates that were twice as high (38.6%, 39.3%). We found no correlation between SCM thickness and ultimate success of breast conserving surgery. While there was a trend toward lower local recurrence rates with SCM ≥7mm, this did not reach statistical significance. Conclusions: Shaved margin thickness has an inverse relationship with re-excision rates. Optimal shave thickness to avoid re-excision was 10mm in our cohort of patients.

**Table 1. Patient Outcomes**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Race</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Situ</td>
<td>Local</td>
<td>Regional</td>
</tr>
<tr>
<td>In Situ</td>
<td>NR</td>
<td>164</td>
</tr>
<tr>
<td>Yes</td>
<td>142</td>
<td>118</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Note: NR = Not Reached; Mets = metastatic
Impact of Tumor Histology on the Performance of Preoperative Axillary Imaging for Staging of Breast Cancer Patients


Introduction: Preoperative staging of the axilla with ultrasound (AUS) and US-guided needle biopsy (USNB) of suspicious lymph nodes (LN) can identify patients with significant nodal disease, triage patients to axillary LN dissection (ALND) and guide the use of neoadjuvant systemic therapy. While overall performance characteristics have been described, little is known of the influence of tumor histology on the utility of preoperative axillary imaging. We examined whether preoperative AUS was equally useful across breast cancer histologic subtypes. Methods: With IRB approval we identified 1510 consecutive new invasive breast cancers in 1455 patients undergoing operation including axillary surgery at our institution from 1/2010 to 7/2013 using our prospective institutional database. DCIS and neoadjuvant therapy patients were excluded. We reviewed preoperative imaging and surgical pathology. Results: 1375 patients (91%) had a preoperative AUS of which 401 (29%) had abnormal findings. USNB was performed in 374 of which 124 were USNB+ and the remainder negative. AUS findings were modified in 26 (21%) of USNB+. 386 patients (28%) were node positive. The sensitivity and specificity of AUS for infiltrating ductal (IDC), infiltrating lobular (ILC) and mixed mammary (MMC) carcinoma were 55% and 79%, 45% and 85%, and 50% and 77%, respectively and 17% and 85%, respectively and 17% and 85% for special (ILC) and mixed mammary (MMC) carcinoma. The majority of IDC, ILC and MMC cases (p=0.83). Conclusions: Despite their differing histologies and growth patterns, AUS with USNB performed comparably for IDC, ILC and MMC. The majority of IDC, ILC and MMC patients with significant nodal disease were proven LN+ preoperatively, helping tailor operative management and patient expectations appropriately and efficiently. Given the low yield of USNB in special tumor types, routine USNB may not be warranted in this patient population.
P78
Impact of Z0011 on the Surgical Management of the Axilla in Patients with Breast Cancer

Background: The American College of Surgeons Oncology Group Z0011 trial redefined the standard of care for breast cancer patients with positive sentinel lymph nodes (SLN). Z0011 illustrated that axillary lymph node dissection (ALND) is not necessary for all breast conservation patients. This study aimed to evaluate changes in the surgical management of the axilla in breast cancer patients at a tertiary care center before and after Z0011. Methods: Patients who met Z0011 criteria were identified and sorted into pre- and post-Z0011 cohorts. Similar patients who underwent mastectomy were analyzed for comparison. Results: This analysis included 494 patients that had breast cancer surgery from July 2008 to February 2013. Of these, 255 were pre-Z0011 and 239 were post. Pre-Z0011, 152 (60%) had breast conservation surgery (BCS). Fourteen patients had T1/2 tumors and 1-2 positive sentinel lymph nodes (SLN) without extracapsular extension. ALND was performed in 10 of these patients (71%). Post-Z0011, 147 patients (61.5%) underwent BCS. Sixteen patients had T1/2 tumors with 1-2 positive SLN, two had extracapsular extension. In the 14 patients without extracapsular extension, only 1 received ALND (7%). The decrease in the rate of axillary dissection from 71% to 7% was statistically significant (p<0.001). In the mastectomy subgroup, 103 patients were in the pre-Z0011 era and if Z0011 criteria were extrapolated to this population 28 met criteria. Of these, 23 patients underwent ALND compared with 5 that did not. Post-Z0011, 92 patients had mastectomy and 14 of these met the extrapolated criteria. Five of these patients underwent ALND compared with 9 who did not. Comparing the pre and post Z0011 groups there was a statistically significant reduction of ALND from 82% to 36% (p<0.005). Conclusion: This study demonstrates that the results of the Z0011 trial significantly altered the management of the axilla in breast cancer patients with positive sentinel lymph nodes. Even though these treatment recommendations were to apply only to patients with breast conservation surgery, they have clearly affected the management of the axilla in all breast cancer patients.

P79
Long-term Results of Excision of Ductal Carcinoma in situ followed by Radiofrequency Ablation to Extend Intraoperative Margins

Excision followed by radiofrequency ablation (eRFA) is an intraoperative method which utilizes heat to create an additional tumor-free zone around the lumpectomy cavity in breast cancer patients similar to partial breast irradiation. We hypothesize that eRFA after lumpectomy for ductal carcinoma in-situ (DCIS) could reduce the need for re-excision for close margins while maintaining local control. Methods: This prospective phase II institutional review board (IRB)-approved study was conducted from February 2004 to April 2013. A standard lumpectomy was performed and the RFA probe was deployed 1 cm circumferentially into the lumpectomy cavity. The cavity was heated to 100 °C for 15 minutes. Validated doppler sonography was used intraoperatively to monitor the ablation zone and assess the adequacy of ablation. Results: 46 patients were accrued to the trial. Age: 65 ± 9 years. Stage: Tis. Tumor size: 9 ± 9 mm. Grade 2 ± 0.8. Number with negative margins: 37. Number with close margins: 4. Number with focally positive margins: 4. Number with gross positive margins: 0. Number with close or positive margins spared surgery: 6/8 spared. Mean follow-up: 46 ± 32. Median follow-up: 48 ± 32 months. Number of in site recurrences: 1. Number of elsewhere recurrences: 1. Conclusion: Long-term follow up suggests that eRFA may reduce the need for re-excision for close or focally positive margins in patients with DCIS. eRFA may be beneficial for patients that desire a single operation for DCIS.

P80
Impact of Obesity on Breast Cancer Surgical Decision Making
G. Porter,* L. Helyer,* T. Topp, V. Calverley, A. Hilkie-Pye. 1. Canadian Partnership Against Cancer and Dalhousie University/QEI Health Sciences Centre, Halifax, NS, Canada; 2. Dalhousie University/QEI II Health Sciences Centre, Halifax, NS, Canada.

BACKGROUND: The association between obesity and both breast cancer risk and prognosis has been well-investigated. However, little is known about the impact of obesity on surgical decision-making, specifically related to the use of breast conservation surgery (BCS) vs. mastectomy. We hypothesized that obesity may be associated with an increased use of BCS. METHODS: This cohort study involved patients with invasive breast cancer or ductal carcinoma in situ diagnosed on core needle biopsy who preoperatively were considered candidates for BCS. Body mass index (BMI), identified at the time of hospital admission for surgery, was categorized according to National Institutes of Health criteria: normal/underweight (NW; BMI < 25 kg/m2), overweight (OW; BMI = 25-29.9 kg/m2), obese (OB; BMI = 30-34.9 kg/m2), and severely obese (SOB; BMI ≥ 35 kg/m2). The use of BCS, controlling for age, tumor size, bra cup size, and detection method (screening vs. clinical), was compared among the BMI groups. RESULTS: The study cohort consisted of 315 patients; 149 (47.3%) NW, 83 (26.3%) were OW, 48 (15.2%) were OB, and 35 (11.1%) were SOB. A significant association with increasing BMI was observed with both larger bra cup size (p<0.001), and larger tumors (p<0.002), although no differences in age or detection method were identified between the BMI groups. Overall, 257 (81.6%) underwent BCS while 58 (18.4%) underwent mastectomy. On univariate analysis, no significant differences in use of BCS was identified among NW, OW, OB, and SOB groups (80.5%, 83.1%, 84.4%, 77.1%; respectively, p<0.01). Controlling for age, tumor size, bra cup size, and detection method (screening vs. clinical), no significant association between use of BCS and any of the weight groups was identified (p>0.50). CONCLUSIONS: Although eligibility for BCS among overweight and obese patients involves larger tumors, the decision to perform or undergo BCS among eligible women does not appear to be associated with presence or extent of obesity.

P81
A Cosmosis Outcome Sub-study in a Prospective, Randomized Trial Comparing Radioguided Seed Localization to Wire Localization for Nonpalpable, Invasive and in situ Breast Cancers
E. Parvez,* S.D. Cornacchi, N. Hodgson,* A. Thoma, I. Kong,* G. Foster,* J. Cheng, C.H. Goldsmith, D. Doo, P.J. Lovrics.* 1. Department of Surgery, McMaster University, Hamilton, ON, Canada; 2. Department of Surgery, St. Joseph’s Healthcare, Hamilton, ON, Canada; 3. Department of Surgical Oncology and Oncology, Juravinski Hospital and Cancer Centre, Hamilton Health Sciences, Hamilton, ON, Canada; 4. Department of Clinical Epidemiology and Biostatistics and Biostatistics Unit, McMaster University and St. Joseph’s Healthcare, Hamilton, ON, Canada.

INTRODUCTION: The goal of breast conserving surgery is to obtain negative margins while achieving an acceptable cosmetic result. Radioguided seed localization (RSL) is purported to have benefits over wire local-
ization (WL) for intraoperative identification of nonpalpable tumours including more precise localization, smaller specimen volumes and improved incision placement. The primary study objective was to compare the cosmetic result of WL to RSL. METHODS: Patients enrolled in a multicentered, randomized trial comparing WL to RSL were invited to participate in the cosmesis study. Frontal photographs were taken 1 and 3 years post-surgery. The European Organization for Research and Treatment of Cancer (EORTC) Cosmetic Rating System was used to evaluate cosmesis. Breast size and shape, areola location and shape, scar appearance and overall cosmesis were assessed by the patient and a panel of 5 raters. Panel members were blinded to group allocation. RESULTS: Seventy-three patients (n=38 WL, n=35 RSL) enrolled into the sub-study between June 2007 and January 2010. Assessment was completed by 57 (73%) and 64 (82%) patients at 1 and 3 years, respectively. There was no difference between groups in patient or tumor characteristics, rate of positive margins, rate of reoperation or specimen volume. Panel inter-observer agreement was moderate for overall cosmesis (kappa statistic=0.55). The majority of patients rated their overall cosmetic outcome as “excellent” or “good” (76% WL, 80% RSL). Patient and panel ratings on all cosmetic outcomes were similar between RSL and WL. Multivariable regression analysis for overall cosmesis found larger specimen volume (p=0.044) and reoperation (p=0.015) to be predictors of worse panel rating. Reoperation was also predictive of worse patient rating (p=0.011). CONCLUSION: This is the first study to compare the aesthetic result of WL to RSL. Within the limitations of a cosmetic evaluation in a relatively small sample, outcomes were similar after WL and RSL. The comparable outcomes may reflect similar reoperation rates and volumes of excision between groups.

### P82
**The Significance of Core Needle Biopsies with Ductal Carcinoma in situ Suspicious for Microinvasive Carcinoma**

J. Mueller,1 M. Kocherginsky,2 S. Kulkarni.1 1. Department of Surgery, University of Chicago, Chicago, IL; 2. Department of Pathology, University of Chicago, Chicago, IL; 3. Department of Health Studies, University of Chicago, Chicago, IL.

Background: Sentinel lymph node biopsy (SLNB) is a staging procedure used to guide adjuvant treatment planning in patients with invasive breast cancer, however, in a patient with ductal carcinoma in situ (DCIS), invasion cannot always be ruled out in core needle biopsy (CNB) specimens. Although some have advocated SLNB in this setting, the incidence of upstaging to invasive cancer and presence of axillary nodal metastasis is unknown. With 2% or less of T1mi cases associated with macrometastatic nodal involvement, the clinical utility of SLNB in DCIS without definite microinvasion is unclear.

Methods: From 2000 to 2012, the institutional pathology database was queried to identify women with Smic (n=203) and Mi (n=316) diagnosed on CNB. The incidence of macrometastatic nodal disease was compared between Smic and Mi. Core needle biopsy sizes were correlated with the incidence of metastatic disease found on SLNB. We also included a cohort of patients with Smic on CNB who underwent complete axillary dissection. RESULTS: Of the 203 Smic patients, 96% (n=195) underwent SLNB with 1% (n=2) of those cases negative for micrometastatic disease. The incidence of metastatic disease was not different between the Smic and Mi groups (p=0.92). In the cohort of patients with Smic on CNB who underwent complete axillary dissection, the incidence of metastatic disease was 5% (n=8). CONCLUSION: Although the incidence of metastatic disease found on SLNB is low, there is still debate regarding the clinical value of SLNB in these patients. Further multicenter studies are needed to compare the clinical utility of SLNB in these patients with Smic.}

### P83
**Is Sentinel Lymph Node biopsy Justified In Patients Undergoing Mastectomy for DCIS?**

S. Mohammed,1* R. Fernandez,2 J. Salmons Lacross,1 B. Lassinger,1 E. Bonefas,1 K. Liscum,1 E.J. Silberfein.1 1. Department of Surgery, Baylor College of Medicine, Houston, TX; 2. Feinberg School of Medicine, Northwestern University, Chicago, IL.

Introduction: The rate of sentinel lymph node biopsy (SLNB) positivity in ductal carcinoma in situ (DCIS) is low and debate regarding the clinical value of SLNB in these patients continues. The purpose of this study is to assess the rate of positive SLNB in patients undergoing mastectomy for DCIS and correlate this with preoperative factors. Methods: A retrospective consecutive cohort study of 109 patients treated with mastectomy and SLNB for DCIS from 2003 to 2011 was performed. Demographic, clinical, operative and pathologic data were analyzed utilizing descriptive statistics and chi-square analysis for comparison of proportions. Results: The mean age at diagnosis was 54.9 years. In 65.7% of the biopsy specimens comedo necrosis was present in greater than 50% of the sample and 40.7% had histologic grade 3 disease. Intraoperatively, the sentinel lymph node contained metastatic disease in 8 patients (7.3%), all of whom underwent concomitant complete axillary dissection. Two of these patients had evidence of further disease in the axilla on final pathology. Five additional patients had either micrometastatic disease (n=3, 2.8%) or isolated tumor cells (n=2, 1.8%) in the sentinel node on final pathology, one of whom subsequently underwent complete axillary dissection without additional axillary disease. Of the 13 patients with axillary disease, comedo necrosis and grade 3 histology were present 46% (n=6) and 23% of the time (n=3) respectively but did not predict positivity (p=0.33 and 0.84). Patients with positive sentinel node were significantly more likely to have invasive disease on final breast pathology (64.3% vs 11.5%, p=0.001) than their DCIS counterparts with negative sentinel nodes. Conclusions: Despite the relatively high incidence of invasive disease after mastectomy for DCIS, the incidence of metastatic disease found on SLNB remains low. With recent trials failing to show survival advantage of axillary dissection for invasive disease, the need for SLNB in DCIS must weigh the potential benefit against the added morbidity of this procedure. Further multicenter study is warranted to evaluate the value of SLNB for DCIS.

### Risk Factors for ID in Smic Patients

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Upstaged ID (%)</th>
<th>p value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCIS grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>15/45 (53)</td>
<td>1.000</td>
</tr>
<tr>
<td>Low or Intermediate</td>
<td>5/14 (36)</td>
<td>0.307</td>
</tr>
<tr>
<td>Necrosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>18/49 (37)</td>
<td>0.000</td>
</tr>
<tr>
<td>N</td>
<td>2/11 (18)</td>
<td></td>
</tr>
<tr>
<td>Calcifications</td>
<td></td>
<td>1.000</td>
</tr>
<tr>
<td>Y</td>
<td>18/54 (33)</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>2/6 (33)</td>
<td></td>
</tr>
<tr>
<td>Mass on US</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>9/19 (47)</td>
<td>0.146</td>
</tr>
<tr>
<td>N</td>
<td>11/41 (27)</td>
<td></td>
</tr>
<tr>
<td>Biopsy guidance</td>
<td></td>
<td>0.164</td>
</tr>
<tr>
<td>Stereotactic</td>
<td>12/39 (31)</td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>7/16 (44)</td>
<td></td>
</tr>
<tr>
<td>MR</td>
<td>0/4 (0)</td>
<td></td>
</tr>
<tr>
<td>Manual</td>
<td>1/1 (100)</td>
<td></td>
</tr>
<tr>
<td>Size</td>
<td></td>
<td>0.018</td>
</tr>
<tr>
<td>≥ 14 mm</td>
<td>6/8 (75)</td>
<td></td>
</tr>
<tr>
<td>&lt; 14 mm</td>
<td>2/13 (15)</td>
<td></td>
</tr>
<tr>
<td>Biopsy needle</td>
<td></td>
<td>0.006</td>
</tr>
<tr>
<td>9 gauge</td>
<td>0/14 (0)</td>
<td></td>
</tr>
<tr>
<td>11, 12, or 14 gauge</td>
<td>9/22 (41)</td>
<td></td>
</tr>
<tr>
<td>Myoepithelial IHC</td>
<td>11/19 (58)</td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>11/19 (58)</td>
<td>0.009</td>
</tr>
<tr>
<td>N</td>
<td>9/41 (22)</td>
<td></td>
</tr>
</tbody>
</table>

† Fisher’s exact test
Abstracts: Poster Presentations

### P84

**Complex Sclerosing Lesions: Excision or Observation after Core Biopsy**

A. Mongiu, S. Lester, M. Golshan, F. Nakhlis.

**Brigham and Women’s Hospital, Boston, MA.**

Background: Complex sclerosing lesion (CSL) of the breast is an uncommon histopathologic entity of unclear biologic potential. When seen on core biopsy with other high risk lesions, such as atypical ductal hyperplasia (ADH), CSL is routinely excised. However, the management of isolated CSLs is controversial. An upgrade rate of up to 10% on excision of CSL has been reported. We sought to determine the rate of upgrade to DCIS and/or invasive cancer on excision of CSL and to learn about the risk of future breast cancer development when CSL is not excised, seen at our institution. Methods: With IRB approval, our core biopsy database was queried for CSL. Between 2005 and 2013 65 CSL lesions were identified, 47 of them were pure CSL. Of these 23 had an excision, while 24 have been followed (Table 1). Results: In the excision group, 2 DCIS lesions (both found in pts with cellular atypia on core biopsy) and 1 invasive cancer (a 0.4 cm tubular carcinoma, not associated with CSL) representing a 13% upgrade rate. Of note, both patients with CSL and atypia in whom DCIS was found would have been referred for excision due to the presence of atypia, while the patient with invasive cancer had a BIRADS 5 discordant lesion warranting an excision on radiographic basis. In the group followed with imaging (mean follow up of 2.3 years) 1 pt developed ipsilateral invasive cancer 4.5 cm from the CSL site 5 years later. Conclusion: In our series of excisions for pure CSL on core biopsy, we realized an upgrade rate of 13%. However, all 3 of these pts would have been referred for excision due to histologic (atypia) or radiographic (BIRADS 5 and discordant) indications and therefore would not have been missed. Based on this we recommend considering observation for CSL found on core biopsy of BIRADS 4 concordant lesions. We also found a very low risk of future breast cancer development for CSL managed by observation. Further studies to address the upgrade rate for pure CSL would be helpful.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Excised (n=23)</th>
<th>Not excised (n=58)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at diagnosis</td>
<td>46.5</td>
<td>49</td>
<td>0.74</td>
</tr>
<tr>
<td>Mean core biopsy grade</td>
<td>13</td>
<td>12</td>
<td>0.75</td>
</tr>
<tr>
<td>Mean number of cores</td>
<td>6.7</td>
<td>5.4</td>
<td>0.04</td>
</tr>
<tr>
<td>Concurrent (pathology report explains imaging findings) (%)</td>
<td>10 (43.5%)</td>
<td>17</td>
<td>0.06</td>
</tr>
</tbody>
</table>

### P85

**Comparing Seed versus Needle Localization: Is there a Difference?**


Introduction: Seed Localization (SL) is a novel technique for localizing non-palpable breast lesions, and offers an alternative to needle localization (NL). SL de-couples the localization process from surgery, and therefore is associated with shorter patient experience on the day of surgery and can optimize surgical scheduling. We compared outcomes of single site SL vs NL. We also sought to determine whether there was a significant learning curve for performing the procedure by comparing endpoints from SL cases earlier in our experience with later cases. Methods: A retrospective review of a prospective database identified all patients undergoing SL or NL for single, nonpalpable breast lesions between May 2012 and August 2013. Operative, pathology, and radiology reports were reviewed. Lesions requiring more than one seed or needle (ie bracketing) were excluded. Excisions for both benign and malignant lesions were included. Results: 113 patients were identified who underwent SL and 99 patients were identified who underwent NL. As expected mean volumes of excision was greater for malignant lesions compared to benign (35 vs 23 cm³, p=0.001), however there was no difference comparing SL and NL volumes excised for either benign or malignant lesions (23.4 vs 23.4 cm³, p=0.99; 35.4 vs 30.6 cm³, p=0.14). There was no significant difference in the operative time comparing SL with NL (26.6 vs. 27.6 minutes, p=0.51). Recurrence rate for positive margins in patients with malignant lesions excised using SL was (12/58, 21%), and was the same as that for patients who underwent NL (10/48, 21%). When comparing operative time and specimen volume of our first 25 SL cases to our last 25 cases to see if performance improved, there were no significant differences noted for either volume (28.3 vs 28.6 cm³, p=0.95) or operative time (23.0 vs 25.8 minutes, p=0.19). No complications related to SL or NL occurred, and target retrieval was 100% for both SL and NL. Conclusions: SL is as effective and accurate as NL when excising non-palpable breast lesions. SL should be an integral part of the armamentarium for surgical excisions, and can be advantageous for optimizing surgical scheduling and patient satisfaction.

### P86

**Factors Associated with Surgical Treatment of Second Primary Breast Cancers**

A. E. Voel,* L. Reparez, W. Fry, A. Arrington.

University of South Carolina School of Medicine Palmetto Health Richland, Columbia, SC.

**INTRODUCTION:** Given improvements in treatments, more survivors are faced with the challenge of a second primary breast cancer (2BC). Though many may wish for lumpectomy, 2BC treatment remains a dilemma due to prior therapies. We hypothesize that mastectomy rates are high and reconstruction rates will be low even in contralateral disease; there will also be a number of demographic differences between the treatment groups. **METHODS:** SEER was queried to identify patients age ≥18 with a 2BC from 1998-2010 without metastatic disease. Ipsilateral 2BC (IL-2BC) and contralateral 2BC (CL-2BC) were analyzed separately; treatment groups were divided into lumpectomy, mastectomy, and mastectomy/reconstruction. **RESULTS:** 4375 patients had CL-2BC while 765 had IL-2BC. Lumpectomy rates were 33% (n=1443) in CL-2BC and 31% (n=234) in IL-2BC, mastectomy rates were 67% (n=2932) in CL-2BC and 69% (n=527) in IL-2BC. Mastectomy/reconstruction rates were 20% CL-2BC and 22% IL-2BC. Younger patients (age<50) were more likely to undergo mastectomy (73.3% CL-2BC, 77.6% IL-2BC) compared to older patients (58.6% CL-2BC, 55.4% IL-2BC; p<0.001). Older patients (age≥80) were statistically more likely to undergo lumpectomy (41.3% CL-2BC, 44.6% IL-2BC; p<0.001). Mastectomy/reconstruction patients were significantly younger than mastectomy alone (53yrs vs 63yrs, p<0.001). White race and marital status were significant factors on univariate and multivariate analysis for mastectomy/reconstruction in CL-2BC (11.7%, p=0.025 and 14.3%, p<0.001) and IL-2BC (15.2% p<0.001 and 19.2% p<0.001) respectively. Of lumpectomies, 66.1% CL-2BC and 61.7% IL-2BC underwent radiation. In all 2BC, mastectomy patients had a better overall survival than lumpectomy (log-rank p=0.028). **CONCLUSIONS:** With advancements in treatments, women will be faced with the dilemma of a 2BC. Therapies for the initial cancer must be taken into account when determining treatment recommendations for a 2BC. We found that older age, single marital status, and non-Caucasian women elected for lumpectomies more often in both CL-2BC and IL-2BC. Nonetheless, 2BC must be treated aggressively given that opting for less treatment results in measurably higher mortality.
Management of Premenopausal Women with Neoadjuvant Endocrine Therapy: A Single Institution Experience T. Barbie, C.X. Ma, J.A. Margenthaler. Surgery, Washington University School of Medicine, St. Louis, MO.

Background: In premenopausal women with hormone receptor positive (HR+) breast cancer, neoadjuvant endocrine therapy (ET) provides effective down-staging of tumor for improved surgical outcome and offers the advantage of assessing tumor endocrine responsiveness for individualized adjuvant treatment planning. While approximately 60% of breast cancer in premenopausal women is HR+, the role of neoadjuvant ET in this population is not defined. Methods: Retrospective review of our prospectively maintained database from 2003 to 2012 identified 18 premenopausal women with 20 different tumors treated with neoadjuvant ET. All patients were required to have estrogen receptor Allred scores of 6 or greater for eligibility. Data collected included patient and tumor characteristics, surgical, systemic, and radiation treatment received, and outcomes. Descriptive statistics were utilized for data summary. Results: The average age of the 18 patients was 46 years. Patients were treated with a combination of gonadotropin releasing hormone agonist with either an aromatase inhibitor (n=16) or tamoxifen (n=2); 5 patients underwent oophorectomy during the systemic therapy course. The average duration of ET was 4.25 months. Of the 20 tumors, 16 (80%) were grade 1 and 4 (20%) were grade 2. At 4-6 weeks post-initiation of ET, 15 (75%) tumors demonstrated a partial clinical response by examination and/or Ki-67 suppression, while 5 (25%) did not; the 5 non-responders were switched to neoadjuvant chemotherapy. Of the 15 tumors completing neoadjuvant ET, all were noted to have some partial clinical response (4 had non-palpable tumors at the time of surgical resection; 11 had >30% reduction in size by pre-surgical imaging measurements). Negative surgical margins were obtained in 14 of 15 (93%) patients; breast-conserving therapy was performed on 5 and mastectomy was performed on 10. Conclusions: As with all neoadjuvant systemic interventions, we identified responders and non-responders to ET, emphasizing the heterogeneity of HR+ breast cancers. In addition to improving surgical outcomes overall, this approach helps identify the highly-endocrine sensitive tumors.

P89

Management of Premenopausal Women with Neoadjuvant Endocrine Therapy: A Single Institution Experience T. Barbie, C.X. Ma, J.A. Margenthaler,* Surgery, Washington University School of Medicine, St. Louis, MO.

Background: In premenopausal women with hormone receptor positive (HR+) breast cancer, neoadjuvant endocrine therapy (ET) provides effective down-staging of tumor for improved surgical outcome and offers the advantage of assessing tumor endocrine responsiveness for individualized adjuvant treatment planning. While approximately 60% of breast cancer in premenopausal women is HR+, the role of neoadjuvant ET in this population is not defined. Methods: Retrospective review of our prospectively maintained database from 2003 to 2012 identified 18 premenopausal women with 20 differ
Table 1: Demographics and Clinical Profile of 714,503 patients with Invasive Breast Cancer from the Surveillance Epidemiology and End Results (SEER) Database (1973-2010).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Overall</th>
<th>Infiltrating Ductal</th>
<th>Infiltrating ductal carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean ± 1 SD)</td>
<td>60.9 ± 14.2</td>
<td>61.4 ± 14.2</td>
<td>60.4 ± 14.2</td>
</tr>
<tr>
<td>Gender (%)</td>
<td>55.5 (P = 0.08)</td>
<td>56.7 (P = 0.08)</td>
<td>54.3 (P = 0.08)</td>
</tr>
<tr>
<td>Race (%)</td>
<td>60.7 (P = 0.04)</td>
<td>59.8 (P = 0.04)</td>
<td>61.6 (P = 0.04)</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td>71,077 (99.2)</td>
<td>71,238 (99.2)</td>
<td>70,959 (99.2)</td>
</tr>
<tr>
<td>Tumor Response Rate (%)</td>
<td>81.6%</td>
<td>81.6%</td>
<td>81.6%</td>
</tr>
<tr>
<td>pT (%)</td>
<td>33.0 (P = 0.04)</td>
<td>34.0 (P = 0.04)</td>
<td>32.0 (P = 0.04)</td>
</tr>
<tr>
<td>cN (%)</td>
<td>45.4 (P = 0.04)</td>
<td>46.4 (P = 0.04)</td>
<td>44.4 (P = 0.04)</td>
</tr>
<tr>
<td>Grade (%)</td>
<td>89.7 (P = 0.04)</td>
<td>90.7 (P = 0.04)</td>
<td>88.7 (P = 0.04)</td>
</tr>
<tr>
<td>Stage (%)</td>
<td>89.7 (P = 0.04)</td>
<td>90.7 (P = 0.04)</td>
<td>88.7 (P = 0.04)</td>
</tr>
<tr>
<td>Prognostic Index (%)</td>
<td>71,077 (99.2)</td>
<td>71,238 (99.2)</td>
<td>70,959 (99.2)</td>
</tr>
<tr>
<td>Treatment (%)</td>
<td>71,077 (99.2)</td>
<td>71,238 (99.2)</td>
<td>70,959 (99.2)</td>
</tr>
</tbody>
</table>

The number of lymph nodes removed was higher in the IRCI group: 3.39 nodes versus 2.46 nodes (P = 0.0192). The number of lymph nodes removed did not differ when analyzed by cN or pN. The incidence of positive SNB was higher for the IRCI group: 58.1% versus 30.6%, (P = 0.0095). When analyzed by pT, the positive SNB rate was higher for T1 cancer in the IRCI group: 61.5% versus 27.3%, (P = 0.0441). Conclusion: The timing of SNB for patients requiring NAC remained controversial. The SNIDR appear similar whether the injection of radiocolloid was preoperative or intraoperative. IRCI would reduce the pain experienced by breast cancer patients undergoing axillary SNB.

P91 Sentinel Node Biopsy after Neoadjuvant Chemotherapy for Breast Cancer: Intraoperative Injection of Radiocolloid

Introduction. Preoperative radio-colloid injection is painful for breast cancer patients undergoing sentinel node biopsy (SNB). This study sought to determine the sentinel node identification rate (SNIDR) with radiocolloid injection pre- or intra-operative in patients who have received neoadjuvant chemotherapy (NAC). Methods. A retrospective comparison of sentinel node identification rate of patients who received neoadjuvant chemotherapy (NAC) and preoperative radiocolloid injection (PRCI) after NAC was performed. All injections used ImCi 0.5 ml of filtered (0.22 micron) Tc-99m sulfur colloid. All surgeons included injections into the retroareolar tissue. The SNIDR was tested for non-inferiority test by a two-proportion z-test. The difference between demographics, SNIDR, tumor response rate, pathologic T stage (pT), clinical N stage (cN), and incidence of positive sentinel nodes was evaluated by Fisher’s exact test. The number of sentinel node removed was analyzed by two-sample t-test. Results. 134 SNBs were performed after NAC in the six-year study period: 96 received PRCI of radiocolloid and 38 received IRCI. There were more African-Americans (P = 0.0159) and more pT3 cancers (P = 0.0286) in the IRCI group. The SNIDR was similar for the two groups: 88.5% for the PRCI group and 81.6% for the IRCI group. By two-proportion z-test and by Fisher’s exact test the SNIDR of the two methods did not differ and remained equivalent for both groups when analyzed by tumor response rate, pT, and cN. The mean

P92 Preoperative MRI: Much Ado about Nothing?

Introduction. Preoperative MRI has been used to identify mammographically occult lesions and to determine extent of disease. However, the role of preoperative MRI in breast cancer remains controversial. We previously found that preoperative MRI does not increase total mastectomy (TM) rate. In this study we sought to identify a specific subgroup of patients in which preoperative MRI may be useful. Methods: In this IRB approved study, we conducted a retrospective review of 257 breast cancer patients who underwent preoperative MRI from 2010-2012. We evaluated whether additional imaging and pathologic examination was recommended after MRI and whether it influenced the final surgical plan and decreased re-excision rate after partial mastectomy (PM). We collected data on several clinical factors and tested these for significant associations with both upgrading to TM and with the need for post-MRI imaging and biopsy using crosstab analysis and Fisher’s Exact test. Age as a continuous variable was also evaluated using binary logistic regression. Results: In our study cohort, additional imaging and biopsies were performed in 62% (n=158) and 32% (n=83) of patients respectively. Of those biopsies prompted by MRI, 39% revealed cancer. However, only 3% of patients upgraded to TM. Preoperative MRI did not decrease re-excision rates. We did not find any statistically significant differences in patients who were upgraded to TM by clinical factors such as age, menopausal status, mammographic breast density, ER/PR, HER2/neu status, or pathologic T stage; though there was a trend towards upgrade to TM in those who required additional imaging (P=0.16). We found no clinical factors associated with the need for additional biopsies. Conclusion: We did not find a specific subgroup of patients in which preoperative MRI influenced management. Although preoperative MRI slightly increased the rate of TM, it does lead to numerous additional imaging studies and biopsies. These biopsies may be helpful in guiding PM, but we did not see a decreased re-excision rate after PM. Given these results, we are no longer using preoperative MRI routinely at our institution. Additional studies will be needed to determine strict indications for the use of MRI in the preoperative setting.

P93 The Impact of Calcium Ionophore on Dendritic Cell Cytokine Production and Induction of Th1 and Th17 Responses

Introduction. Calcium ionophore (CI) is known to rapidly mature human monocytes into mature dendritic cells (DCs) with typical expression of co-stimulatory cell surface markers and enhanced T cell sensitization efficiency. We sought to investigate the role CI has on the production of cytokines from DCs in type-17 polarizing conditions and the subsequent impact on induction of Th17 versus Th1 immune responses. Human monocytes were cultured with pharmacologic agents to investigate the role CI has on the production of cytokines from DCs in type-17 polarizing conditions and the subsequent impact on induction of Th17 versus Th1 immune responses. Human monocytes were cultured with pharmacologic agents to...
for quantitative measurement of cytokine production and the DCs were analyzed for cell surface markers of maturity. The mature DCs were used to stimulate purified human CD4+ T cells; T cell cytokine production was measured and T cells were analyzed by flow cytometry for the presence of the same cytokines intracellularly. Dendritic cells with receiving no maturation agents are referred to as immature DCs (iDCs) and upon co-culture with T cells did not induce any significant cytokine production. Interferon-γ (IFN-γ) & lipopolysaccharide (LPS)-matured DCs produce high levels of the cytokines IL-12, IL-23, and IL-6 with modest IL-1β and polarize CD4+ T cells into both Th1 and Th17 phenotypes. The combinations ATP & lipoteichoic acid (LTA) or prostaglandin E2(PGE2) & LPS resulted in less IL-12 and IL-23 production, similar levels of IL-6, high levels of IL-1β and polarize Th17 responses. The addition of calcium ionophore to Th17 maturation conditions led to decreased levels of IL-1β and IL-6 and enhanced levels of IL-23. CI-matured DCs induced CD4+ T cells into predominantly Th1 responses with high levels of IFN-γ and minimal IL-17 production even when DCs were matured in type-17 polarizing conditions. Th1 responses occurred despite minimal or undetectable IL-12 production by CI-matured DCs. The addition of calcium ionophore to DC maturation protocols that induce Th17 immune responses resulted in less IL-17 production by the CD4+ T cells and instead resulted in immune responses characteristic of Th1 cells. We believe these results suggest that calcium signaling in DCs limits these cells’ ability to induce type-17 T cell responses.

Introduction. Sentinel lymph node biopsy (SLNBx) is used to assess the axillary status in breast cancer patients. The role of SLNBx in microinvasive (Tmic) and T1a breast cancer has not been well studied. It has been suggested that smaller breast cancers yield fewer positive SLNBx results. This study examines the rate of SLN positivity in patients with Tmic or T1a breast cancer that underwent axillary evaluation. Methods. An IRB approved retrospective chart review of patients diagnosed with Tmic (n=19) or T1a tumors (n=114) that underwent SLNBx or ALND. At this time SLNBx biopsy is still beneficial for patients with T1a breast cancer. Larger studies need to be performed to determine if there is a subset of T1a patients for which SLNBx may be omitted.

**Sentinel Lymph Node Biopsy Results for T1a and Tmic patients**

<table>
<thead>
<tr>
<th></th>
<th>T1a</th>
<th>Tmic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients</td>
<td>19</td>
<td>123</td>
</tr>
<tr>
<td>T1a</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Tmic</td>
<td>106</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>114</td>
<td>29</td>
</tr>
</tbody>
</table>

**P95 Boost Radiation Treatment for Anal Cancer Decreases the Risk for Lifetime Colostomy: Analysis from the National Cancer Data Base (NCDB)** C. N. Bu delve, K. M. Hirshfield, I. Adelaja, T. J. Kearney, L. Kirstein, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ; 2. Rutgers Cancer Institute of New Jersey, New Brunswick, NJ.

Introduction. Sentinel lymph node biopsy (SLNBx) is used to assess the axillary status in breast cancer patients. The role of SLNBx in microinvasive (Tmic) and T1a breast cancer has not been well studied. It has been suggested that smaller breast cancers yield fewer positive SLNBx results. This study examines the rate of SLN positivity in patients with Tmic or T1a breast cancer that underwent axillary evaluation. Methods. An IRB approved retrospective chart review of patients diagnosed with Tmic or T1a breast cancer from 1987-2013 was performed. Patient and tumor characteristics were observed, including age at diagnosis, tumor size, hormone receptor status and tumor histology. Only patients with Tmic or T1a tumors who underwent axillary evaluation were considered. Axillary nodal status was examined. Results. Of 133 patients with Tmic (n=19) or T1a tumors (n=114) that underwent SLNBx or ALND, 8 patients (6%) had positive results. All 8 patients with a positive node had a T1a breast cancer. None of the patients with Tmic breast cancer had a positive node. For axillary evaluation, 10 of 133 patients underwent ALND; none had positive nodes. 123 patients had a SLNBx. Two of the 8 node positive patients (25%) had 2 positive nodes and 6 patients (75%) had 1 positive node. There was no statistically significant correlation of positive nodal status with any tumor or patient characteristics. Conclusions. This study found that SLNBx positivity is very low in patients with Tmic and T1a breast cancer. No tumor or patient characteristic correlated with SLN positivity. None of the patients with Tmic breast cancer had positive nodes, although fewer Tmic patients were studied. These data suggest that for Tmic breast cancer, consideration can be made to omit SLNBx. At this time SLNBx biopsy is still beneficial for patients with T1a breast cancer. Larger studies need to be performed to determine if there is a subset of T1a patients for which SLNBx may be omitted.


Introduction. Sentinel lymph node biopsy (SLNBx) is used to assess the axillary status in breast cancer patients. The role of SLNBx in microinvasive (Tmic) and T1a breast cancer has not been well studied. It has been suggested that smaller breast cancers yield fewer positive SLNBx results. This study examines the rate of SLN positivity in patients with Tmic or T1a breast cancer that underwent axillary evaluation. Methods. An IRB approved retrospective chart review of patients diagnosed with Tmic or T1a breast cancer from 1987-2013 was performed. Patient and tumor characteristics were observed, including age at diagnosis, tumor size, hormone receptor status and tumor histology. Only patients with Tmic or T1a tumors who underwent axillary evaluation were considered. Axillary nodal status was examined. Results. Of 133 patients with Tmic (n=19) or T1a tumors (n=114) that underwent SLNBx or ALND, 8 patients (6%) had positive results. All 8 patients with a positive node had a T1a breast cancer. None of the patients with Tmic breast cancer had a positive node. For axillary evaluation, 10 of 133 patients underwent ALND; none had positive nodes. 123 patients had a SLNBx. Two of the 8 node positive patients (25%) had 2 positive nodes and 6 patients (75%) had 1 positive node. There was no statistically significant correlation of positive nodal status with any tumor or patient characteristics. Conclusions. This study found that SLNBx positivity is very low in patients with Tmic and T1a breast cancer. No tumor or patient characteristic correlated with SLN positivity. None of the patients with Tmic breast cancer had positive nodes, although fewer Tmic patients were studied. These data suggest that for Tmic breast cancer, consideration can be made to omit SLNBx. At this time SLNBx biopsy is still beneficial for patients with T1a breast cancer. Larger studies need to be performed to determine if there is a subset of T1a patients for which SLNBx may be omitted.

**P96 Diagnostic Performance of Multi-detector Row CT for Assessment of Lymph Node Metastasis in Patients with Distal Rectal Cancer** H. Kobayashi, K. Sugihara, Center for Minimally Invasive Surgery, Tokyo Medical and Dental University, Tokyo, Japan.

INTRODUCTION: The accurate preoperative diagnosis of depth of tumor invasion and nodal status in distal rectal cancer is important, because neoadjuvant chemotherapy or pelvic lymph node dissection is indicated in patients with T3-T4 tumor or nodal involvement. The aim of this study was to determine the optimal cut-off value for predicting lymph node metastasis in patients with distal rectal cancer using multi-detector row computed tomography (MDCT). METHODS: 77 patients who had undergone surgery for distal rectal cancer at a single institution between 2008 and 2011 were investigated. Diagnostic performance for the maximum diameter of tumor invasion and mesorectal fat invasion were evaluated. The optimal cut-off value was determined by receiver operating characteristic curve analysis. RESULTS: The sensitivity and specificity of MDCT for depth of tumor invasion, mesorectal-
Optimization of Regional Adoptive Cell Therapy for Liver Metastases through Prevention of Myeloid Derived Suppressor Cell Expansion and Blockade of PDL-1 Mediated T Cell Suppression

R.A. Burga,1,4 M. Thorn,1 E. Santos,1 G.R. Point,1 A. Ayala,2 R. DeMatteo,3 N. Espat,1 R.P. Junghans,1 S.C. Katz.1 1. Surgical Immunotherapy, Roger Williams Medical Center, Providence, RI; 2. Brown University School of Medicine, Providence, RI; 3. Memorial Sloan-Kettering Cancer Center, New York, NY.

Introduction: Myeloid-derived suppressor cells (MDSC) possess the ability to suppress genetically-modified “designer” T cells (dTc), which presents an obstacle for this form of adoptive cell therapy. It has been demonstrated that granulocyte-macrophage colony-stimulating factor (GM-CSF) drives MDSC expansion while PDL-1 on the surface of MDSC engages PD-1 on dTc to mediate suppression. We hypothesized that combined neutralization of GM-CSF and PDL-1 would enhance dTc anti-tumor efficacy in a murine model of liver metastases (LM). Methods: CEA+ MC38 colorectal tumor cells were transduced to express luciferase and injected into the spleens of C57BL/6 mice to establish LM. Mice were treated with anti-CEA dTc 7 days after tumor injection, and in vivo blockade was performed with PDL-1 and GM-CSF-neutralizing antibodies. Luciferin was administered prior to bioimaging. Results: DC cultured with Flt3 ligand displayed a baseline level of B7-2 expression (42.9%). At increasing concentrations of soluble LIGHT (100 ng/mL, 500 ng/mL, and 1000 ng/mL), B7-2 expression increased to 60% (p=0.0001), 84% (p=0.0001), and 92% (p=0.012), respectively. B7-H2 expression on DC similarly increased from a baseline expression of 18% to 26% (p=0.034), 45% (p=0.005), and 54% (p=0.022). LIGHT alone at 1000 ng/mL concentration increased the expression of co-stimulatory molecules to a level comparable to DC stimulated with the known DC stimulant, LPS. Conclusions: Soluble LIGHT substantially increased the expression of the T-cell co-stimulatory molecules B7-2 and B7-H2 on bone marrow derived DC. Techniques to increase co-stimulatory signals on dendritic cells are a promising strategy in cancer immunotherapy. These results introduce LIGHT administration as a potential cancer treatment modality that warrants further investigation.

DC B7-2 and B7-H2 Expression

Did Modern Treatment of Rectal Cancer Make the Change for the Mucinous Subtype? N. Hugen,1,4 C.J. Van de Velde,1 M.A. Elferink,2 J.H. De Wilt,1 J.D. Nagtegaal.1 1. Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands; 2. Leiden University Medical Center, Leiden, Netherlands; 3. Comprehensive Cancer Centre the Netherlands, Utrecht, Netherlands.

BACKGROUND Introduction of preoperative radiotherapy has improved outcome in rectal cancer (RC) patients, but it is unclear whether benefits are applicable to all histological subtypes. Rectal mucinous adenocarcinoma (MC) has been associated with impaired prognosis compared with nonmucinous adenocarcinoma (AC). This study analyzes overall survival (OS) of MC in RC patients over time and evaluates efficacy of preoperative radiotherapy in MC.

METHODS Two patient populations were selected. From the nationwide population-based cancer registry data on 51,200 RC patients diagnosed between 1989 and 2010 and was retrieved and 5-year OS rates were calculated. In addition, 1530 patients were selected from the prospective randomized multicentre TME-trial, that investigated the value of short-term preoperative radiotherapy compared with TME-surgery alone. RESULTS Results from the population-based study showed that 5-year OS in AC patients improved from 41.9% in 1989-1994 to 55.3% in 2006-2010 (p=0.0001), compared with 34.2% and 53.5% in MC patients (p=0.0001). In the TME-trial in the surgery alone group we found a higher rate of positive circumferential resection margin (CRM) in MC versus AC (35.3% versus 18.6%; P=0.004) with a higher rate of local recurrence.
Abstracts: Poster Presentations

P101
Surveillance for Local Recurrence of Rectal Cancer is Futile
M.E. Gross,1 M.C. Mone,1 C.K. Whiting,1 E.M. Mechem,1 H.J. Hansen,1 W. Peche,1 C.L. Scaife.1
1. I. Surgery, University of Utah, Salt Lake City, UT; 2. University of Texas Medical Branch, Galveston, TX

National Comprehensive Cancer Network (NCCN) guidelines recommend routine proctoscopy every 6 months for 5 years after low anterior resection for rectal adenocarcinoma. There are no studies to support this recommendation, which was based on high local recurrence rates prior to total mesorectal excision (TME). The purpose of this study was to determine the value of rectal surveillance after TME. This is a single-center, retrospective review of stages I-III rectal adenocarcinoma patients who underwent TME (2004-2011). The primary endpoint was cancer recurrence. The methods of identifying each recurrence as well as the number of procedures for rectal surveillance were collected. The study included 108 patients who underwent TME with at least one year of postoperative follow-up. Of these, 53 (49%) had stage III rectal cancer, 38 (35%) had stage II, and 17 (16%) had stage I disease. The average age was 57.8±12.2, with the majority being male (67%). The mean length of follow-up was 4.1 years (1–9.4 years). There were 16 recurrences, 15% (1 local, 15 distant). The majority of recurrences were stage III patients (75%), and occurred between 0.7-4.2 years. The local recurrence, at 1.3 years, was found by CEA, followed by a mass biopsy. A total of 20 anoscopies, 43 rigid proctoscopies, and 489 flexible sigmoidoscopies were performed. The majority of patients (56%) had 4 or more procedures. The total charges for these procedures were estimated to be $150,000, or $600 dollars per patient per year. Local rectal surveillance was unnecessary, as it added no information relative to recurrence in 108 patients. The only local recurrence was identified with CEA screening. As TME is now the standard surgical approach, with continued neoadjuvant chemoradiation for advanced disease, the rates of local recurrence have dropped significantly. Routine rectal surveillance did not add accuracy to CEA, imaging studies, and standard colonscopic screening of rectal cancer. This retrospective study challenges the NCCN guidelines to reconsider the use of an invasive, expensive, and uncomfortable procedure in the clinic for rectal surveillance, and we feel that the NCCN guideline should be reconsidered.

P102
Increasing Trends in Positron Emission Tomography (PET) Utilization after Colon Cancer Diagnosis
C. Bailey,* C. Hu, Y. You, H. Kaur, R. Ernst, G.J. Chang. University of Texas, MD Anderson Cancer Center, Houston, TX.

Background: Current colon cancer surveillance guidelines do not routinely include PET imaging however, the utilization of PET scans has been increasing. The primary aim of this study is to evaluate the trends in PET utilization during the first 2 years after colon cancer diagnosis or surgical resection among elderly patients. Methods: A retrospective cohort study of patients ≥65 years old with colon cancer who underwent surgical resection or received chemotherapy in the Surveillance, Epidemiology, and End Results-Linked Medicare database (July 2001 to December 2009, Medicare Part A/B only) was performed. All patients had at least 2 years of follow-up. PET utilization was assessed using the test for trends and multivariate logistic regression for patient, tumor and treatment characteristics. Results: Of 43,924 patients diagnosed with colon cancer, 8,160 (18.6%) underwent PET scan within 2 years after colon cancer diagnosis or resection. The utilization rate steadily increased from 9.1% in 2001 to 23.6% in 2009 (P<0.001). A total of 15,555 PET scans were performed and 4,661 patients (57.1%) had 1 PET scan, 1,750 (21.5%) had 2 PET scans and 1,749 (21.4%) had >2 PET scans. The majority of PET scans (n=3,005) were performed within 2 months after colon cancer diagnosis or resection (Table). Among patients who underwent resection, 51% (n=19,993) underwent imaging (PET/CT, CT, or MRI) ≤3 months prior to surgical resection and 18.0% (n=1,977) of these patients were reimaged with PET scan within 2 months after resection. In multivariate analysis, year of diagnosis, stage and chemotherapy were significantly associated with increased PET utilization. Conclusion: The utilization of PET scans after colon cancer diagnosis among patients with either localized or metastatic disease has steadily increased since 2001. The majority of PET scans are being performed within 2 months after diagnosis or resection. As clinicians are obtaining PET imaging despite lack of support for their use in guidelines, further study is needed to understand the clinical value and effectiveness of PET scans and the reasons for this departure from guideline based care.

P103
Identifying Predictors of One-year All-cause Mortality after Colon Cancer Surgery in Patients 65-years of Age and Older: The Potential of Billing Claims
M. E. Gross,1* S. Kroteva,1 H. Alabtas,2 A. Ramjaun,3 T. Eguale,1* A. Meguedichian,1 1. Surgical Oncology, McGill University, Montreal, QC, Canada; 2. Clinical Health and Informatics Group, McGill University, Montreal, QC, Canada; 3. Brigham and Women’s Hospital and Harvard Medical School, Boston, MA.

Background: Although elderly patients are at increased risk of short-term postoperative morbidity and mortality, many elderly patients are physiologically fit for operation. This study aims to quantify one-year all-cause postoperative mortality and identify patients at risk based on health service utilization in the year before surgery as a surrogate for physiologic condition. Methods: A historical prospective cohort of colon cancer patients aged ≥65 years was assembled from hospitalization data provided by a single universal healthcare insurance provider between 2000 to 2006. Kaplan-Meier and Cox multivariable survival were employed to determine independent predictors and hazard ratios (HR) of postoperative one-year all-cause mortality. Results: 3789 patients underwent colonic resection for cancer (2000-2006). 1731 (45.7%) were male while 2058 (54.3%) were female. Overall 30 day, 90 day and one year all-cause mortality were 5.0%, 8.6% and 19.2% respectively. Multivariable analysis demonstrated that patient age at surgery, receipt of health care for cardiovascular disease (HR = 1.4) or dementia (HR = 1.9) and type of admission (emergency vs. elective) (HR = 2.1) independently predicted one-year postoperative mortality (all P < .05). Relative risk of mortality was decreased in those who underwent a physical exam by a general practitioner in the year prior to operation (HR = 0.7). Higher mean income as defined by residential area income, reduced mortality at a relative rate of 0.94 per $10,000 increase in the first postoperative year (all P < .05). Conclusion: Mortality after colon resection in the postoperative year is high in the elderly population (19%). Age, use of medical resources for geriatric comorbidities, and lack of continuity of care were strong predictors of mortality. Although the
ability to identify such risk factors through billing claims remains to be refined,
a potential to prospectively identify patients at highest risk of decreased sur-
vival exists.

P104
A Phase II Multicenter Single-arm Trial of Adjuvant Chemother-
apy with S-1 after Curative Resection of Colorectal Liver Metaesta-
sis (N-SOG 01 Trial) K. Uehara,1* A. Maeda,2 E. Sakamoto,3 K. Hira-
matsu,4 E. Takeuchi,5 K. Sakaguchi,1 Y. Tojima,1 T. Ebata,5 M. Nagino.1
1. Nagoya University Graduate School of Medicine, Nagoya, Aichi,
Japan; 2. Ogaki Municipal Hospital, Ogaki, Gifu, Japan; 3. Nagoya
Daini Red Cross Hospital, Nagoya, Aichi, Japan; 4. Toyohashi Munici-
pal Hospital, Toyohashi, Aichi, Japan; 5. Japanese Red Cross Nagoya
Daini Red Cross Hospital, Nagoya, Aichi, Japan; 6. Chubu Rosai Hospital,
Nagoya, Aichi, Japan; 7. Chukyo Hospital, Nagoya, Aichi, Japan.

Background: This phase II trial was designed to evaluate the safety and
efficacy of adjuvant chemotherapy with S-1 in patients with curatively resected liver metastasis from colorectal cancer. The primary endpoint was 3-year disease-free survival (DFS). Methods: We enrolled 62 patients from 19 Japanese hospitals between October 2008 and August 2010. Patients who underwent curative resection of liver metastasis from colorectal cancer received S-1 monotherapy (on days 1 to 28, followed by a 14-day rest, 8 cycles) as adjuvant chemotherapy. We report the safety and survival at 3-year. The mean duration of follow-up was 40.5 (5.4-57.2) months. Results: Among 62 patients, 60 patients were eligible for analysis. The most frequent grade >3 hematologic toxicity involved neutropenia in 3 patients (5.0%), Non-hematologic toxicities of grade >3 were fatigue in 6.7% of patients. Grade 4 enteritis occurred in one patient, but resolved promptly after withdrawal of S-1 therapy. The completion rate of the 8 scheduled cycles of chemotherapy was 58.3%. The most common reason for withdrawal of treatment was the detection of early relapse in 16 patients (64%). When the 16 patients who had recurrence during adjuvant treatment were excluded from analysis, 79.5% of the remaining 44 patients completed the scheduled treatment. Early recurrence within 1 year after curative liver resection occurred in 21 patients (35%). The most common site was the remnant liver in 14 patients. The 3-year DFS and overall survival were 43.6% and 78.1%, respectively. Univariate analysis showed that time from primary resection to liver resection (p=0.008), location of primary tumor (p=0.009), and lymph node metastasis at primary site (p=0.002) were significant prognostic indicators of DFS. Conclusion: Orally administered S-1 after curative liver resection had an acceptable toxicity profile and a high rate of completion of the therapy. Additionally, 3-year DFS was comparable to previous reports. A randomized trial comparing adjuvant S-1 to FOLFOX in colorectal liver metastases is anticipated. (UMIN number, 000001498.)

Table. Univariate risk analysis for disease-free survival (n=60)

<table>
<thead>
<tr>
<th>Variables</th>
<th>0 (%)</th>
<th>3y-DFS (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synchronous</td>
<td>26 (43.3)</td>
<td>34.1</td>
<td>0.061</td>
</tr>
<tr>
<td>Metachronous</td>
<td>34 (56.7)</td>
<td>57.2</td>
<td></td>
</tr>
<tr>
<td>Time from primary resection to liver resection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;24 month</td>
<td>39 (65.0)</td>
<td>85.7</td>
<td>0.001</td>
</tr>
<tr>
<td>&gt;24 month</td>
<td>21 (33.0)</td>
<td>69.6</td>
<td></td>
</tr>
<tr>
<td>Location of primary tumor</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td>40 (66.7)</td>
<td>59.1</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>7 (33.3)</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>Lymph node metastasis at primary site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present</td>
<td>37 (61.2)</td>
<td>31.1</td>
<td>0.002</td>
</tr>
<tr>
<td>Absent</td>
<td>23 (38.8)</td>
<td>73.4</td>
<td></td>
</tr>
</tbody>
</table>

P105
Effects of Hyperthermia versus Drug Dose on Toxicity and Pharn-
macodynamics of Oxaliplatin-based Intraoperative Chemoperfu-
sion: Results of a Phase II Trial L. De Smet,1* A. Izmer,2 F. Van-
haecke,3 J. Remon,2 C. Vervaet,2 W. Ceelen.1* 1. GI Surgery, UZ Gent,
Ghent, Belgium; 2. Laboratory of Pharmaceutical Technology, Ghent
University, Ghent, Belgium; 3. Departement of Analytical Chemistry,
Ghent University, Ghent, Belgium.

Background: Intraoperative regional chemotherapy (IC) is used to treat patients with colorectal metastasis. There are to date no clinical studies that have compared hyperthermic with normothermic IC using oxaliplatin (OX). Methods: patients underwent CRS and were treated with OX at 37°C, 90 min, 200 mg/m2 (group 1), 37°C, 30 min, 460 mg/m2 (group 2), or 41°C, 30 min, 460 mg/m2 (group 3). The amount of platinum (Pt) in the perfusate and blood was determined by induc-
tively coupled plasma-mass spectrometry (ICP-MS), and platinum tissue pen-
etration in healthy abdominal wall was analysed by laser ablation ICP-MS (LA-
ICP-MS). Postoperatively, morbidity and mortality were also evaluated. This trial was registered with ClinicalTrials.gov, NCT01575730. Results: no sig-
ificant differences in pharmacokinetic parameters (Cmax, AUC) were observed between groups 2 and 3. Also, no effects of hyperthermia were observed on Pt tissue penetration. Increased postoperative and systemic toxic-
ity was, however, observed in the group treated under hyperthermic condi-
tions. Among patients treated under normothermic conditions, short high dose treatment (group 2) resulted in a significantly higher Cmax while the AUC(t=7days) was similar for both groups resulting in a similar systemic toxicity. Also, tissue Pt penetration was much higher in the short high dose group. Conclusions: addition of hyperthermia does not enhance tissue pene-
tration of OX used as IC, but increases postoperative and systemic complica-
tions. Short, high dose OX IC results in a similar AUC over 7 days, but enhanced tissue Pt penetration compared to a long, lower dose IC.

P106
Rectal Cancer Treatment and Complications in Patients with IBD

Background IBD patients have an increased risk of developing colorectal cancer (CRC). For sporadic rectal cancer (RC), neoadjuvant therapy followed by total mesorectal excision (TME), is standard of care. Data on the effects of this treatment for IBD related CRC are rare, since IBD patients are usually excluded from neo-adjuvant trials. Methods All IBD-RC patients between 1990 and 2010 were selected using a Dutch nationwide search in the Dutch Pathology Database (PALGA). Surgical complications were scored according the Clavien-Dindo scale. Results from patients with IBD were compared with data from the Dutch surgical colorectal audit containing all colorectal cancer patients treated in the Netherlands. Results 180 patients from 36 hospitals were identified. All IBD-RC patients between 1990 and 2010 were selected using a Dutch nationwide search in the Dutch Pathology Database (PALGA). Surgical complications were scored according the Clavien-Dindo scale. Results from patients with IBD were compared with data from the Dutch surgical colorectal audit containing all colorectal cancer patients treated in the Netherlands. Results 180 patients from 36 hospitals were identified (84 Ulcerative Colitis (UC), 72 Crohn’s Disease (CD), 7 indeterminate colitis). 112(61.9%) were males and 67(37%) females with mean age of RC diagnosis of 59.9 years (± 12.4). Neoadjuvant therapy was used in 66(36.5%) patients, 29(16.1%) received short course radiotherapy(RT), 10(5.6%) long course RT, 23(12.8%) chemoradiation therapy (CRT). 158(87.8%) patients underwent intracavitary resection of the tumor. Diagnosis of RC was known preoperatively in 137(86.2%) patients (CD 80% and UC 92.7%; p< 0.001). Stage distribution was: 1 patient stage0(0.9%), 27 stage2(13.2%), 41 stageIII(36.3%), 30
Abstracts: Poster Presentations

P107
Patients with Complete Pathological Response to Preoperative Chemoradiation Surgically Treated with Local Excision have a Low Systemic Relapse Risk


Introduction: Our phase I human clinical trials utilizing a GM-CSF secreting allogeneic colon tumor vaccine (GVAX) have been shown to be safe in inducing anti-tumor immune response in colorectal cancer patients. The study of patients treated with GM-CSF secreting CRC tumor vaccine (mice GVAX) in combination with dendritic cell (DAC). GVAX was given subcutaneously to mice on day 11 following tumor transplantation, together with a single low dose of 5-azacytidine (DAC). DAC was administered intraperitoneally for five consecutive days at a dose of 0.14 mg/kg at varying time periods in relation to vaccine therapy (Figure 1A). Results: DAC pretreatment plus GVAX demonstrates a reduction in percentage of mice disease free at 25 days compared to DAC alone, GVAX followed by DAC and no treatment controls. In mice that rejected tumor, infiltrating lymphocytes from DAC+GVAX treated mice have increased IFNγ production compared to single modality treatment (P=0.001) (Figure 1B). DAC pretreatment or concurrent treatment with GVAX increases IFNγ production from splenocytes following ex vivo co-culture with tumor targets (P=0.03). DAC pretreatment also increases a CT26 MHC Class I-restricted epitope (AH-1) specific immune response compared to vaccine alone (P=0.003). Conclusions: Combinatorial treatment with DAC followed by GVAX results in increased antigen specific responses in a preclinical model of CRC. Our study provides strong rationale that combining epigenetic and GVAX will improve vaccine induced CRC responses.

Figure 1. Decline of tumor size in mice administered with a single cell CT26/GVAX colon tumor vaccine (GVAX) and/or 5-aza2-deoxycytidine (DAC) 5-aza2-deoxycytidine (DAC) produces a synergistic effect. A: Effect of DAC treatment alone or in combination with GVAX on tumor volume in mice administered with a single cell CT26/GVAX colon tumor vaccine. B: Effect of DAC treatment alone or in combination with GVAX on tumor volume in mice administered with a single cell CT26/GVAX colon tumor vaccine.
P110
30-year Review of Surgical Resection and Intraoperative Radiation Therapy for Locally Advanced Rectosigmoid and Rectal Carcinoma


It has been proposed that surgical resection with intraoperative radiation therapy (IORT) may improve local control rates for locally advanced rectosigmoid or rectal adenocarcinoma (LARSA). We retrospectively evaluated patients with LARSA treated with surgical resection and IORT. We evaluated the impact of combined treatment on overall survival (OS), disease-free survival (DFS) and local control (LC). The prognostic impact of resection margins was assessed. Between 1979 and 2010, 438 patients with LARSA were referred for consideration of IORT. Of those, 110 patients received IORT for primary LA disease. The average age was 60 ± 14 years old; 49 (45%) were female and 61 (55%) were male. Preoperative radiation therapy was delivered to 94.5% of patients, and 19.1% received post-operative radiation. Neoadjuvant chemotherapy was given to 72.7% of patients, and 41.8% received adjuvant chemotherapy. The median cone size, radiation dose and beam energy delivered were 6 cm, 12.5 Gy and 9 MeV respectively. The resection margins achieved, measured as R0, R0.5 (margins within 1 mm), R1 and R2 were 60%, 10%, 21.8%, and 0.3%, respectively. The overall 5-year DFS, LC, and OS were 45.2%, 79.6%, and 57.0%, respectively. Patients with R0 margins had an improved OS (HR 0.48, 95% CI 0.28-0.82, p=0.008), and DFS (HR 0.48, 95% CI 0.28-0.81, p=0.006) when compared to R0.5, R1 and R2 margins. Patients with R0.5 margins showed worse OS when compared to R0 resections (HR 3.66, 95% CI 1.46-9.18, p=0.006), and were in fact no different when compared to R1 resections (HR 1.74, 95% CI 0.66-4.05, p=0.261). The overall radiation-associated morbidity was 17.3%. Improved OS (HR 0.73, 95% CI 0.54-0.99, p=0.040) was observed in the most recently treated cohort when compared to the earlier treatment cohorts. Optimal DFS, LC and OS were achieved when IORT was performed in conjunction with a margin negative surgical resection of LARSA. The outcome of patients who were found to have surgical resection margins ±1 mm was prognostically similar to that of patients with positive resection margins, and was not significantly improved by IORT.

P111
Transduction of a KRAS V12 Oncogene into a Caco-2 Cell Line Establishes a Gene Expression Profile known to be Associated with KRAS Mutation in Colorectal Cancers

O.S. Chow,1 R. Pelosof,1 C. Chen,1 Z. Chen,2 J. Garcia-Aguilar,1 1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. City of Hope, Duarte, CA.

Background: KRAS mutation in rectal cancer is associated with response to neoadjuvant therapy as well as overall prognosis. We previously identified a profile of 61 differentially expressed genes when comparing KRAS wild-type to KRAS mutant rectal cancer tissue. This signature was validated in colorectal samples of The Cancer Genome Atlas, as well as in an independent cohort of colon cancer resection samples. Many genes in our differential expression profile are known to be involved with cell proliferation and regulation of the extra-cellular matrix. We hypothesized that transduction of a KRAS V12 mutant oncogene into a KRAS wild-type colon cancer cell line would recapitulate our expression profile. Methods: A retroviral KRAS V12 vector was created by subcloning GFP and KRAS V12 into pQCXIP. This vector was co-transduced into Caco-2, a colon cancer derived cell line that is normally KRAS wild-type. Cells with the mutant oncogene were isolated using fluorescence-activated cell sorting. Total RNA was extracted from the two cell lines at four time points with the same directionality as predicted by our profile. Results: Comparing KRAS wild-type with KRAS V12 Caco-2 cells, qRT-PCR revealed DUSP6, HOXB6, HOXB8, LOX, COL1A1, and SPARC. Conclusions: KRAS mutant CRCs have a unique profile of differential expression compared with KRAS wild-type, which we have previously validated. Transduction of a KRAS V12 oncogene establishes a subset of this profile in a KRAS wild-type colon cancer cell line. This in vitro finding shows that KRAS mutation drives a distinct gene expression profile involving genes known to modulate cell proliferation and regulation of extra-cellular matrix. This expression profile may help elucidate the mechanisms by which KRAS mutation affects response to neoadjuvant therapies and prognosis.

P112
The Impact of Fondaparinux on the Prophylaxis of Venous Thromboembolism: The Efficacy, Safety and Prognosis after Resection for Colorectal Cancer

Y. Yamaoka,1 M. Ikeda,1 M. Ikenaga,2 N. Haraguchi,1 M. Miyake,1 K. Yamamoto,1 T. Asaoka,1 K. Nishikawa,1 A. Miyamot,1 M. Miyazaki,1 M. Hira,1 S. Nakamori,1 M. Sekimoto,1 1. Surgery, Osaka National Hospital, Osaka, Japan; 2. Osaka Rosai Hospital, Sakai, Japan.

Background: Colorectal cancer (CRC) surgery is a risk factor for venous thromboembolism (VTE). The aim of this study is to examine the efficacy, safety and impact on survival of fondaparinux (FPX) combined with intermittent pneumatic compression (IPC) after resection for CRC. Patients and Methods: We reviewed 953 patients with CRC who underwent colorectal resection between April 2006 and March 2013. Patients were divided into two groups, the IPC group (n=591) and the FPX group (n=362). The FPX group was treated with IPC alone as a control. The FPX group was treated with IPC and received subcutaneous injections of FPX (2.5mg) once daily for 4 days. The incidence of VTE, postoperative bleeding, postoperative complications, and prognosis were compared. Results: No statistical difference was found in age, sex, prevalence of arteriosclerotic disease, ASA-PS, operating time, tumor location, and disease stage between the two groups. Body mass index (FPX:23.0 kg/m2, IPC:22.4 kg/m2) and the rate of laparoscopic surgery (FPX:59.4%, IPC:34.7%) were higher in the FPX group. Blood loss was less in the FPX group (FPX:67.4ml, IPC:109.5ml). Significant VTE was found only one patient (0.1%) in the IPC group, who died on post-operative day 14. The incidence of major bleeding was 0.55% in the FPX group and 0.51% in the IPC group (p=0.93), and the incidence of minor bleeding was 9.4% and 3.4%, respectively (p=0.001). The incidence of postoperative complications (Clavien-Dindo classification≥3a) (FPX:9.4%, IPC:9.0%) was similar. There was no significant difference in overall survival rate in stage 0, I, II, and IV. However, in stage III 3-year overall survival rate was significantly better in the FPX group than IPC group (FPX:93.3%, IPC:81.1%, p=0.0061). Conclusions: The use of FPX increases the incidence of minor bleeding, but not major bleeding. Postoperative anticoagulation with FPX may inhibit cancer cell metastasis in high risk patients. VTE prophylaxis with FPX was safe, and effective, randomized prospective study investigating the efficacy of FPX on prognosis in curatively resected CRC patients needs to be warranted.

P113
Analysis of Cancer-related Genes in Mucinous Appendiceal Neoplasms using High Resolution, Targeted Amplicon Sequencing


Introduction: We sequenced 7405 exon domains of 409 cancer genes in mucinous appendiceal neoplasms (MAN) to identify diagnostic and prognostic biomarker candidates and prospective therapeutic targets. Methods: Genomic DNA from primary tumors (MAN), corresponding metastases (pseudomyxoma peritonei, PMP), and matched blood samples (PBMCs) from four patients with MAN/PMP underwent amplicon sequencing of 409 tumor suppressors and oncogenes. Tumors were macro-dissected to minimize cellular heterogeneity (>70% tumor cells) and amplicon sequencing was performed at high
depth (average base depth >150X) and coverage (99% of targets). Results: We identified shared, non-synonymous, single base variants (SNVs) present in every tumor and/or every metastatic specimen that were not found in the normal reference genome. Fourteen SNVs were present in all MAN, 13 SNVs were common to all PMP, and 9 SNVs were present in both MAN and PMP specimens. We identified 5 germline SNVs that were common to all MAN, PMP and PBMC samples. Copy number variation (CNV) analysis using exonspecific base depth comparison (p=0.002; 1.5<CNV<1.5) revealed 94 genes with significant gains or losses (losses=86) in MAN and 98 genes with significant CNV in PMP (losses=89). MAN and PMP samples were remarkable for highly similar CNV profiles (94 in common). The aberrant genes containing SNV and/or CNV were widely classified into five functional protein categories including chromatin remodeling; extracellular matrix; cellular transport/scaffolding; stem cell signaling, cellular oncogenic signaling; and transcription factors. There was a cluster of gene deletions in both MAN and PMP samples specific to DNA damage-response enzymes. (Table) Top canonical pathways associated with these genomic changes were NF-kappaB and PTEN-p signaling (p<0.0001). Conclusions: We identified several candidate cancer genes potentially associated with malignant transformation in MAN/PMP that may comprise diagnostic, prognostic and/or predictive disease biomarkers. The finding that these genes cluster in essential oncogenic signaling pathways suggests that they may represent efficacious targets for therapy.

**Candidate Cancer Genes**

### Categories
- **Chromatin Remodeling Proteins**
  - SNVs: ARID1A, NSD1, SPDEF, CCNE1, KDM5C, SMARCA4, WSC1 (NSD2), EZH2, KAT6A, BRD3, ASXL1, BAP1
- **Extracellular Matrix Proteins**
  - SNVs: FN1, ITGA9, ADAM17, PTGS2, TGFBR2, FGF7, EFO4, KAT6A, BRD3, ASXL1, BAP1

### Cellular Transport, Structural and Scaffold/Proteins
- SNVs: TPR, UBE2I, AKAP9, PDE4D, LAMC1

### Stem Cell Signaling Proteins
- SNVs: NOTCH1, TGFBR3, NEU1,2, SFRP1, S24, S6K1,1, SIK1,1, PTEN,1,2

### Cellular Oncogenic Receptors and Signaling Proteins
- SNVs: EGFR, PLCG1, CARD11, LFR1, CD274

### Transcription Factors
- SNVs: FOXO1, GATA3, ARNT, PML, AR

### DNA Damage Response Enzymes
- SNVs: PDK1, CDK6, SMUG1, MUTYH, RECP, ERCC2, PARP1, MSH2, MSH6

**P114**

**Body Mass Index x Visceral Fat Area/Subcutaneous Fat Area Ratio: A New Fat Parameter Associated with Severe Postoperative Complications after Colorectal Surgery**

M.M. Buijs,1,2 J.W. Splieothoff,2 R. Bezooyen,2,1 I. Grossmann,1 M. Brusse-Keizer,2 C.H. Slump,2 J.M. Klaase,1 1. Medisch Spectrum Twente, Enschede, Netherlands; 2. University of Twente, Enschede, Netherlands.

Introduction: Obesity is considered an important risk factor for postoperative complications after colorectal surgery but evidence in literature is still weak. Visceral fat is strongly related to the metabolic syndrome as opposed to BMI. This study investigates whether BMI multiplied by VFA/SFA ratio is a valueable new fat parameter related to postoperative complications after colorectal cancer surgery. Methods: A retrospective chart review was conducted in 100 randomly selected patients who were surgically treated for colorectal cancer. VFA/SFA was determined using 20 consecutive CT-slices cranial to the diastum. BMI, VFA/SFA and BMI x VFA/SFA were used as obesity measures and tested in relation to severe complications. Results: Eighty-five patients fulfilled the inclusion criteria, 43 males (50.6%), 42 females (49.4%) with mean age of 69 years. Post-operative complications occurred in 33 patients (38.8%) of which 14 (16.5%) were severe according to the Clavien-Dindo classification (IIIA or higher). Eleven patients needed reintervention, in 7 because of anastomotic leakage, in 2 because of fascial dehiscence, in one case because of iatrogenic ureter injury and in one case because of abdominal abscess. Three patients died of surgery related complications. According to BMI 33 (38.8%) patients were overweight (BMI>25) and 22 (25.9%) other patients were obese (BMI>30). Only BMI x VFA/SFA and hypertension were found to have a significant relation to the development of complications. All variables significantly associated with severe complications and a raised BMI, VFA/SFA or BMI x VFA/SFA in univariate analysis were entered into multivariate analysis using logistic regression. Three explanatory models were developed of which BMI x VFA/SFA was best correlated to severe complications (OR 1.06; 95% CI: 1.01-1.12). Conclusion: BMI x VFA/SFA is a fat parameter associated with severe postoperative complications in colorectal cancer patients. prognostic significance of BMI x VFA/SFA should be further determined in a prospective study with a larger population.

**P115**

**The iRGD Peptide Potentiates Tumor Penetration of Intraperitoneal Chemotherapy**

R. Bezooijen,1 I. Grossmann,1 M. Brusse-Keizer,1 C.H. Slump,2 V. Kotamraju,1,3 A.M. Lowy,2 E. Ruoslant,1 1. Sanford-Burnham Medical Research Institute, La Jolla, CA; 2. University of California, San Diego, La Jolla, CA.

Introduction: Intraperitoneal (IP) chemotherapy for peritoneal metastasis is limited by poor drug penetration into tumor tissue. iRGD, a tumor-specific, tissue-penetrating peptide, facilitates intratumoral distribution of attached drugs, and even free drugs co-injected with iRGD, through transvascular and local penetration (Cancer Cell 16:510-520, 2009; Science 328:1031-1035, 2010). Here, we examined the ability of iRGD to potentiate IP chemotherapy in murine models of peritoneal carcinomatosis. Methods: Fluorescent dextran or doxorubicin (DOX) was co-injected with iRGD into the abdominal cavity in mice with peritoneal carcinomatosis. Intratumoral accumulation of dextran and DOX was evaluated with imaging, microscopy, and/or spectroscopy. The anti-tumor effects of iRGD/DOX IP combination therapy were examined in long-term treatment studies. Results: Fluorescein-labeled iRGD efficiently accumulated into disseminated peritoneal tumors of colon, gastric and ovarian cancer in mice. Co-injection of iRGD and fluorescent dextran into the peritoneum resulted in tumor-specific accumulation of dextran. The accumulation occurred via local penetration as dextran entry into subcutaneous tumors that were only accessible through the circulation was minimal. Intraperitoneally injected CRGDC, a tumor-targeting peptide with no tissue-penetrating properties, only labeled the surface of peritoneal tumors, and failed to enhance the entry of co-injected dextran into the tumors. iRGD enhanced the accumulation of free DOX into peritoneal tumors by 5 fold, and significantly potentiated the anti-tumor activities of DOX in a long-term treatment study. No enhanced systemic toxicity was observed in the iRGD/DOX treated mice. iRGD also facilitated penetration of biological nanoparticles into freshly excised human peritoneal tumor explants suggesting clinical relevance of the iRGD drug delivery system. Conclusion: iRGD significantly enhanced intratumoral accumulation and anti-tumor activities of free DOX in mice with peritoneal tumors. The iRGD system provides a simple way to potentiate IP chemotherapy and deserves further investigation as a possible companion to cytoreductive surgery and IP chemotherapy.
in 24 patients (16%), of which 21 patients had MMR mutations. All patients with MSI were C0 (P=.001). In our dataset, there was no C1 patient who tested positive for MMR wild type or microsatellite stability. Conclusion: KRAS mutations were twice as more common among C1 compared to C0 patients. All (100%) MSI-unstable and MMR mutated patients were found to have normal levels of pretreatment CEA, making CEA an unreliable prognostic indicator in this group of patients. If the above findings are consistently demonstrated in larger studies, high CEA levels could be used as a surrogate test to exclude MMR mutations and microsatellite instability.

PI17

Antero-posterior Perineal Approach for Sphincter Preservation in Ultra Low Rectal Cancer: Oncologic and Functional Outcome

W.M. Gawad,* O. Mansour, M. Lotief, M. Sakr. Surgical Oncology, National Cancer Institute-Cairo University, Cairo, Egypt.

Background: The perineal dissection through an Antero-Posterior perineal entry has been introduced to minimize the oncological drawbacks encountered with ultra-Low rectal tumours resection (2-5 cm) from anal verge as Circumferential Resection Margin (CRM) involvement, inadvertent intraoperative bowel perforation with subsequent increase in local recurrence rate & low overall survival. This approach confers better access to low seated rectal tumours enabling sphincter saving and bowel continuity with better life quality. Methods: Between 2008 and 2012, 35 consecutive patients with low rectal tumours (3-5 cm) from anal verge, underwent ultra low Anterior Resection with concomitant Antero-Posterior perineal entry, compared to 45 patients with conventional Low Anterior Resection. All patients received neoadjuvant Chemoradiation with R0 Resection. Patients data was prospectively collected from our colorectal data base. Rates of CRM involvement, bowel perforation and wound infection were compared. Continence was subjectively evaluated according to Kirwan Scale. The sphincter preservation and Colo-Anal Anastomosis (CAA) in the antero-posterior approach was achieved through either hand sown in 10 patients or double stapling technique in 25 patients with protective ileostomy in 15 patients. Results: The Rates of CRM involvement, bowel perforation and wound infection in such perineal approach versus conventional resection were 3.5% vs 10% (P=0.04), 5% vs 21.1% (P=0.521) and 11% vs 31% (P=0.518) respectively. Operative time was lower with the perineal entry than with conventional surgery (220.3 & 300min) respectively (P=0.04). Continence to stool & flatus was achieved in 48 patients (88%) Kirwan scale I, while 7 patients (12%) had control to stools only. Conclusion: This technique facilitates addressing ultra-low rectal tumours, with increased chances for sphincter preservation & bowel continuity concomitant with superior oncologic outcome compared to the conventional techniques suggesting its significance as a valid approach for low seated rectal tumours.

PI18

Cost Differential among Systemic Therapies for Colon Cancer

H. Nadeem, T.T. Jayakrishnan,* T.C. Gamblin, K.K. Turaga. Medical College of Wisconsin, Milwaukee, WI.

Introduction: According to the National Cancer Institute (NCI), national cancer care expenditures were an estimated $124.6 billion in 2010, of which a significant portion is attributed to chemotherapy costs. The National Comprehensive Cancer Network (NCCN) has outlined recommendations for the treatment of various cancers that incorporates alternative chemotherapeutic strategies presuposed to be of similar effectiveness. In the evolving economic climate with resource constraints, we hypothesized that there is a significant cost differential between possibly therapeutically equivalent systemic therapy regimens for colon cancer. Methods: Details of the chemotherapeutic regimens and dosages outlined in NCCN guidelines (2013) were acquired for colon cancer. Baseline costs (in US dollars US$/) were calculated based on the payment allowance for Medicare part-B drugs database (2013). Dosage amounts were calculated for an average American patient and additional costs (treatment time, pumps) were also added to the total regimen cost. The total costs were calculated for a treatment period of 6 months. Results: A total of 25 regimens (advanced/metastatic and adjuvant) were studied. The median cost for systemic treatment of advanced/metastatic colon cancer for a 6-month period was $34,840 (IQR $9,420 - $68,840; n=20 regimens) (Table 1). The median cost for adjuvant treatment alone was $13,870 (Range $2,600 - $33,230, n=5). The cost differential for a single patient between FOLFOX and Folfiliri+ziv-Aflibercept was $4.2 million for metastatic colon cancer. The addition of novel anti-neoplastics including biologics dramatically increased the price of treatment regimens. Conclusion: There is an economically significant cost differential between chemotherapeutic regimens that are prescribed as equally effective. Hierarchical adoption of equally effective regimens based on their therapeutic benefit, cost and patient specific toxicity profile may help reduce healthcare costs.

Table 1. Demonstrating the cost differential among systemic therapy regimens for metastatic colon cancer

<table>
<thead>
<tr>
<th>REGIMEN</th>
<th>COST (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-FU BASED</td>
<td></td>
</tr>
<tr>
<td>Rossowell Park regimen</td>
<td>770</td>
</tr>
<tr>
<td>Simplified Bi Weekly infusion 5-FU</td>
<td>3,421</td>
</tr>
<tr>
<td>Simplified Weekly infusion 5-FU</td>
<td>8,393</td>
</tr>
<tr>
<td>Capeoctxitin</td>
<td>33,229</td>
</tr>
<tr>
<td>Capeoctxitin+Bevacizumab</td>
<td>49,790</td>
</tr>
<tr>
<td>IRINOPEC TICAN BASED</td>
<td>69,392</td>
</tr>
<tr>
<td>Infotuxitin</td>
<td>2,790</td>
</tr>
<tr>
<td>IFOX</td>
<td>8,560</td>
</tr>
<tr>
<td>Folfox</td>
<td>10,286</td>
</tr>
<tr>
<td>Folferxitri</td>
<td>17,340</td>
</tr>
<tr>
<td>FolElit+Bevacizumab</td>
<td>47,369</td>
</tr>
<tr>
<td>FolElit+Pazitumab</td>
<td>68,783</td>
</tr>
<tr>
<td>FolElit+Avastincept</td>
<td>75,216</td>
</tr>
<tr>
<td>FolElit+ziv-Aflibercept</td>
<td>4,218,866</td>
</tr>
<tr>
<td>OXALAPAT BASED</td>
<td></td>
</tr>
<tr>
<td>Feltow</td>
<td>11,728</td>
</tr>
<tr>
<td>CapeOX</td>
<td>32,833</td>
</tr>
<tr>
<td>mFolfox+Pazitumab</td>
<td>30,450</td>
</tr>
<tr>
<td>CapeOx+Bevacizumab</td>
<td>66,896</td>
</tr>
<tr>
<td>mFolfox+ziv-Aflibercept</td>
<td>70,223</td>
</tr>
<tr>
<td>OXALAPAT BASED</td>
<td></td>
</tr>
<tr>
<td>Infotuxitin</td>
<td>58,495</td>
</tr>
<tr>
<td>Capeoctxitin</td>
<td>94,307</td>
</tr>
</tbody>
</table>

PI19

What is the Best Surgical Strategy for Low or Mid-rectal Cancer (LMMC) with Synchronous Liver Metastases (SLM)?


Objectives: LMMC with SLM is a challenging situation. Optimal treatment strategy is still discussed. Methods: Retrospective analysis of a prospective database of patients surgically treated for SLM from LMMC between 1991/01 and 2013/01. Patients' demographic data, operative morbidity, overall survival (OS) and disease-free survival (DFS) were analyzed. Combined surgery (CS) and sequential surgery (SS) were compared. Results: Among 110 patients surgically treated for SLM from rectal cancer, 47 had LMMC with SLM at diagnosis. 25 patients had combined rectal and hepatic surgery (CS group), and 22 patients had sequential surgery, that is liver-first surgery (2 patients) or rectal surgery first (20 patients) (SS group). All had received an induction chemofortherapy (n=28) and/or neoadjuvant chemoradiotherapy (n=44). There was no difference between groups in terms of age, sex and hepatic extent of disease. Median number of SLM was higher in the CS group than in the SS group (6 vs 3), as well as rate of major hepatectomy (72% vs 56%) and resected liver weight (785 g vs 695 g). Median number of procedures was 2 (1-4) in CS group and 3 (2-4) in SS group. Cumulative incidence of complications (at least one complication in all surgeries) was identical in both groups (76% vs 63.6% SS, p=0.524), but there was a significantly higher incidence of major complications in the SS group (16.0% CS vs 40.9% SS, p=0.033). No peri-operative death occurred. With a median follow-up of 73.3 months, median OS and DFS were respectively 56.5 months and 18.4 months, 3- and 5-year OS was 64% and 46%, and 3- and 5-year survival was 72.3% and 23.6%. There was no difference between groups. Conclusion: Combined surgery appears to be a good option with acceptable morbidity when treating patients with low or mid rectal cancer and synchronous liver metastases. This approach allows optimal metastatic disease treatment with integration of rectal cancer radiotherapy while limiting the number of surgeries.
P120
Identification of a Novel Biomarker Related to Lymph Node Metastasis in Colorectal Cancer through Gene Expression Analysis
H. Baba,1,2* T. Ishikawa,3 N. Ivata,1 H. Takahashi,4 A. Kikuchi,5 S. Okazaki,1 M. Ishiguro,1 H. Kobayashi,1 S. Iida,1 H. Uetake,5 K. Sugihara.1 1. Department of Surgical Oncology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan; 2. University of Maryland School of Pharmacology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan; 2. Department of Translational Oncology, Graduate School, Tokyo Medical and Dental University, Tokyo, Japan.

Background: Progression of Molecular Biology have developed identification of biomarkers for personalized cancer treatment. But there are few biomarkers used by clinical practice. Lymph node metastasis in colorectal cancer (CRC) is poor prognostic factor. Purpose: This study aimed to identify genes related to lymph node metastasis in colorectal cancer through gene expression analysis and to investigate the possibility of the candidate gene as a prognostic biomarker. Methods: mRNAs were extracted from 156 stage I-III CRCs by laser microdissection, which were resected from our institution from 2005 to 2009. We compared the expression profiles of mRNA expression in cancer cells of CRC patients with (Stage I+II, N=98) and without (Stage III, N=58) lymph node metastasis by oligonucleotide microarray analysis. We defined the gene which had highly expressed in integration analysis of copy number and gene expression as candidate gene. Then we analyzed protein expression level of the candidate gene by immunohistochemistry (IHC) using the same 156 colorectal cancer tissue and finally evaluated the correlation between the candidate gene expression and clinicopathological parameters. Results: Special AT-rich sequence-binding protein 1 (SATB1) was extracted from integrated microarray analysis (Fold change >2, P <0.05). The high expression of SATB1 protein was significantly related to lymph node metastasis in CRC (P<0.001). The high expression of SATB1 was also associated with short OS (P=0.038) and RFS (P=0.024). Conclusion: This study suggested that SATB1 may play an important role in lymph node metastasis of CRC. SATB1 would be a predictive biomarker of lymph node metastasis and recurrence after surgery of CRC. Further investigation is important.

P121
Does Chemotherapy/Biologies beyond Second Line Affect Colon Cancer? Specific and Overall Survival in Metastatic Colon Cancer: An Analysis of 5,129 Patients
N. Hanna,1* C. Woods,2 Z. Zheng,2 E. Onukwuha,2 B.S. Seal,1 C. Mullins.1 1. Surgery, University of Maryland, Baltimore, MD; 2. University of Maryland School of Pharmacy, Baltimore, MD; 3. Bayer Healthcare Pharmaceuticals, wayne, NJ.

Background: The purpose of this study was to investigate whether additional chemotherapy/biologic treatments after second line affect colon cancer-specific and overall survival in patients with metastatic colon cancer (mCC). Methods: Patients aged 66 to 105 years old diagnosed with mCC between 2003 and 2007 were selected for analysis from the Surveillance, Epidemiology and End Results SEER-Medicare data to determine the association between chemotherapy/biologic treatment lines and survival. We examined the survival benefits using Cox proportional-hazards regressions with inverse probability weighting method to adjust for the probability of receiving treatment lines. Results: Patients with no chemotherapy/biologic treatment had an adjusted median survival time of 6.8 months. Each chemotherapy/biologic treatment line received was associated with longer adjusted median survival times: 11.9 months, 23.2 months and 26.4 months for receipt of 1st-line treatment only, 2nd-line treatment and subsequent treatment, respectively. Colon cancer-specific mortality hazard ratios (HRs) were 0.637, 0.391 and 0.350 (p<0.001 for each) for 1st-line, 2nd-line and subsequent treatments, respectively. Overall mortality hazard ratios were 0.694, 0.398 and 0.364 (p<0.001 for each) for 1st-line, 2nd-line and subsequent treatments, respectively. Compared to receiving only first-line treatment, proceeding to second-line treatment was associated with longer colon cancer-specific survival (HR=0.614, p=0.001) and longer overall survival (HR=0.659, p=0.001). Patients with a low-grade tumor had longer colon cancer-specific and overall survival (HR=0.746, p=0.001; HR=0.762, p=0.001, respectively) and lived 5.6 months longer. Conclusions: Among mCC patients who survived at least 3 months from diagnosis, each of the 1st and 2nd chemotherapy/biologic treatment lines was independently associated with significantly longer survival. Additional treatment after the 2nd line showed neither benefit nor harm. Similar significant survival differences were seen in patients who survived at least 6 and 9 months from diagnosis.

P122
FTY720, a Sphingosine-1-phosphate Signaling Modulator, as a Novel Therapy for Colon Cancer Peritoneal Carcinomatosis

Introduction: Median survival of colon cancer peritoneal carcinomatosis (PC) remain dismal with only 6 months. Current treatment, 5-fluorouracil (5-FU) in combination with other drugs, is not effective for PC. Tumor associated macrophages produce Tumor Necrosis Factor-alpha (TNFa) that progress PC and cause cachexia. Sphingosine-1-phosphate (S1P), a bioactive lipid mediator produced by Sphingosine kinase (SphK1), is now known to play important roles in cancer progression by binding to S1PR1, suppress its progression. Here we demonstrate that FTY720 significantly suppress progression and prolong survival of colon cancer PC by decreasing both tumor associated and peritoneal macrophages, decreased TNFα levels, and prevent cachexia. Methods: PC was generated by ip of CT26-luc cells or HCT116-luc cells into mice. Tumor growth was measured live by a bioluminescence imaging system. Gene and protein expressions were analyzed by RT-qPCR, and immunohistochemistry. Angiogenesis and lymphangiogenesis were determined by microvessel density. Four cell lines were used for in vitro studies and cell viability were determined by WST-8 assay. Results: SphK1, S1PR1, TNFα and IL-6 levels are remarkably elevated in PC nodules compared from peritoneum. FTY720 suppress the growth and number of PC nodules and decrease Ki67 index and increase apoptosis in both PC models. FTY720 significantly
Abstracts: Poster Presentations

P123
Extended versus Segmental Resection for Colon Cancer of the Splenic Flexure: Short and Long-term Outcomes
N. Okkabaz,* H. Kessler, D. Dietz, F.H. Remzi, E. Gorgun. Department of Colorectal Surgery, Digestive Disease Institute, Cleveland Clinic, Cleveland, OH.

Background: Defining the best surgical approach for colon cancers located in the splenic flexure remains controversial. Our aim in this study was to compare short/long term outcomes and oncological results after extended resection for splenic flexure cancer with those of segmental colectomy. Methods: All patients who underwent colectomy for splenic flexure cancer between 1995 and 2010 were retrieved from an institutional review board approved, prospectively maintained cancer database. Palliative resections and patients with synchronous colon cancer were excluded. Patients who underwent limited resection with ligation of the left colic artery and left branch of the middle colic artery (group A) were compared to those who underwent extended resection, including main colic arterial ligation (group B). Perioperative variables and both short/long term and oncologic outcomes were compared between the groups. Results: 114 patients [77(67.5%) male; mean age: 66; 6A±14] underwent colon resection for splenic flexure cancer during the study period. There were 29 (25.4%) patients in group A and 85 (74.6%) patients in group B. Group A patients were older, had more cardiac disease and a higher ASA class (p<0.05). Intraoperative parameters including operative time, blood loss, rate of transfusion and adjunct organ involvement were similar between the groups. More laparoscopic resections were performed in group A (p<0.05). Postoperative complications and short-term outcomes were similar between the groups. Tumor stage and rates of both positive resection margins and lymphovascular invasion were similar. The median number of harvested lymph nodes was higher in group B. Local, distant and overall recurrence rates were comparable between the groups. Conclusion: Segmental or limited colonic resection that respects lymphovascular anatomy may be offered with acceptable oncologic outcomes to carefully-selected patients with colon cancer located in the splenic flexure.

Preoperative and Postoperative Characteristics Based on Resection Type

<table>
<thead>
<tr>
<th></th>
<th>Group A (n=29)</th>
<th>Group B (n=85)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>71±14.3</td>
<td>64±11.8</td>
<td>0.016</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>20 (68.9%)</td>
<td>77 (67.5%)</td>
<td>0.850</td>
</tr>
<tr>
<td>ASA Class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4 (13.8%)</td>
<td>28 (32.5%)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>16 (53.6%)</td>
<td>49 (57.6%)</td>
<td>0.098</td>
</tr>
<tr>
<td>3±</td>
<td>9 (31.0%)</td>
<td>8 (9.4%)</td>
<td></td>
</tr>
<tr>
<td>Operation type</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laparoscopic</td>
<td>11 (37.9%)</td>
<td>12 (14.1%)</td>
<td>0.006</td>
</tr>
<tr>
<td>Conventional</td>
<td>18 (62.1%)</td>
<td>73 (85.3%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal wall</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stoma</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Distal pancreate</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Spleen</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Diaphragm</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Operation time (min.)</td>
<td>153±60.3</td>
<td>148±56.3</td>
<td>0.725</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>350±3600</td>
<td>300±20000</td>
<td>0.343</td>
</tr>
<tr>
<td>Proctectomy (med)</td>
<td>0.0±0.0</td>
<td>0.0±0.0</td>
<td>0.234</td>
</tr>
<tr>
<td>Postoperative complications</td>
<td>18±21</td>
<td>40±41</td>
<td>0.163</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>8±10.0</td>
<td>7±14.0</td>
<td>0.519</td>
</tr>
<tr>
<td>Major (TNM)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>6 (20.7%)</td>
<td>17 (20.0%)</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>10±55.2</td>
<td>43±50.6</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>5 (17.2%)</td>
<td>25 (29.4%)</td>
<td>0.106</td>
</tr>
<tr>
<td>IV</td>
<td>2±6.9</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Recurrence</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local</td>
<td>0</td>
<td>12±14.1</td>
<td>0.377</td>
</tr>
<tr>
<td>Distant</td>
<td>3±10.3</td>
<td>13±15.5</td>
<td>0.758</td>
</tr>
</tbody>
</table>

ASA: American Society of Anesthesiology

P124
The Impact of Sarcopenia on Survival in Locally Advanced Rectal Cancer
A. Gamenthaler,* E. Siegel, W. Clark, X. Zhao, A. Chen, K. Maddox, D. Shibata. Surgical Oncology, Moffitt Cancer Center, Tampa, FL.

INTRODUCTION: The association between sarcopenia (or muscle loss) and worse oncologic outcomes has been documented in several different cancers and is thought to be a potential marker of a diminished host response to tumor. We sought to examine the impact of radiologically-defined sarcopenia on outcomes of RC patients treated by neoadjuvant chemoradiation (NCR) and radical resection. METHODS: Between 1998-2010, we identified 90 patients with Stage II/III RC treated by NCR and radical surgery. Sarcopenia was assessed using 3 CT-based measures derived at the L4-L5 level including mean psoas density (MPD; Hounsfield Units), total psoas area (TPA; mm²) and muscle mass index (MMI=TPA/height²; mm²/m²). Clinicopathologic data (age, gender, pretreatment and final tumor stage, treatment response and CEA level) were collected. Associations were analyzed by Wilcoxon Rank Sum while the Kaplan–Meier method, log-rank test, and Cox proportional hazards models were used to evaluate overall survival (OS) and disease-free survival (DFS).

RESULTS: Our population consisted of 50 males and 40 females with a median age at diagnosis of 61 (range 35-87). By univariate analyses, only age >61 was associated with the presence of sarcopenia by all 3 measures [MPD (p<0.0003), MMI (p=0.0001), and TPA (p=0.0006)]. Female gender was associated with increased muscle loss by MMI (p<0.0001) and TPA (p=0.0001). By multivariate analysis, MPD (range 14.5-77.3 HU) was independently associated with a worse OS (AHAR=0.94; 95%CI, 0.88-0.99; p=0.04) and marginally associated with DFS (AHAR=0.95; 95%CI, 0.89-1.00; p=0.056) when controlling for age, gender and pathologic response. This translates to a 28.5% reduction in risk of death with every 5 HU decrease in MPD. CONCLUSIONS: We have demonstrated that pre-treatment sarcopenia as measured by MPD is associated with worse OS and possibly DFS in patients with RC treated by NCR and radical surgery. Larger scale studies of sarcopenia and RC are warranted. Strategies targeting reversal of processes associated with muscle loss may play a potential future role in the multidisciplinary management of rectal cancer.

P125
Neoadjuvant Chemotherapy with Bevacizumab May Improve Outcome following Cytoreduction and Hyperthermic Intraperitoneal Chemosurgery HIPEC for Colorectal Carcinomatosis
W. Ceen,* P. Pattyn. GI Surgery, UZ Gent, Ghent, Belgium.

Objective: In selected patients with PC from colorectal origin, CRS and HIPEC may improve survival. At present, it is unclear whether neoadjuvant chemotherapy with or without targeted agents is indicated in this patient population. We aimed to define prognostic factors after cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemosurgery (HIPEC) for colorectal peritoneal carcinomatosis (PC). Methods Selected PC patients from colorectal origin without extra-abdominal disease were treated with cytoreductive surgery and HIPEC using oxaliplatin (200-460 mg/m²) or mitomycin C (35 mg/m²). Postoperative outcome and long term survival were prospectively recorded. The impact of clinical variables on overall survival (OS) was assessed using univariate analysis and Cox multivariate regression. Statistical significance was assumed whenever the probability of a type I error was <0.05. Results Between October 2002 and May 2012, 166 patients were treated with CRS and HIPEC. Neoadjuvant chemotherapy alone was administered to 21%, and neoadjuvant chemotherapy with bevacizumab to 16% of patients. Postoperative mortality and major morbidity were 2.4% and 35%, respectively. Half of the patients received adjuvant chemotherapy. After a median follow-up of 18 months, OS was 27 months (95% CI 19.8-35.2). On univariate analysis, OS was associated with extent of disease (P=0.001), completeness of cytoreduction (CC) (P<0.001), and neoadjuvant chemotherapy with bevacizumab (P=0.021), completeness of cytoreduction (CC) (P<0.001), and adjuvant chemotherapy (P=0.04) but not with primary site, synchronous presentation, or chemoperfusion drug. In multivariate Cox regression, independent predictors of OS were CC (HR 0.29, P<0.001) and neoadjuvant chemotherapy containing bevacizumab (HR 0.31, P=0.019). Conclusions Long term outcome after CRS and HIPEC for colorectal cancer is associated with CC and neoadjuvant therapy containing bevacizumab. This regimen merits prospective study in patients with resectable PC from colorectal origin.
P126
Robotic Extended Resections for Locally Advanced Anorectal Cancer
C.N. Clarke,1,* A.K. Agarwal,1 Y. You,1 B. Bednarski,1 M.A. Rodriguez-Bigas,1 J.M. Skibber,1 S. Nguyen,1 E. Schlette,1 G.J. Chang.1 Surgical Oncology, MD Anderson Cancer Center, Houston, TX. 2. University of Texas Medical School at Houston, Houston, TX.
Purpose: The robotic interface offers potential for expanding the therapeutic window of minimally invasive surgery (MIS) for patients with locally advanced anorectal cancer. This study evaluates the technical feasibility, safety, and short-term oncologic effectiveness of robotic extended resection for advanced anorectal cancer. Methods: We conducted a retrospective study of a prospective consecutive database of patients who underwent robotic resection for anorectal cancers from 1/09 to 9/13 at a tertiary cancer center. Patients who underwent robotic extended pelvic resection of extra-regional lymph nodes, en-bloc resection of involved adjacent organs or had a secondary additional procedure were identified. Operative parameters, pathologic findings, and perioperative outcomes were analyzed. Results: Among a total of 30 patients who met criteria, extra-regional lymph node dissection (LND) was performed in 11 (9 lateral pelvic, 2 aorto-caval) en-bloc resections in 12 (3 partial vaginectomy, 3 proctectomy, 3 small bowel, 2 cecoclygectomy, 1 bladder). 7 patients required additional procedures for associated pathology (6 oophorectomy, 1 uterine myomectomy). Median tumor location was 4 cm (interquartile range [IQR] 2-7) from the anal verge. Median BMI was 25.83 kg/m2 (IQR: 23.6-28.9). Twenty-four (80.6%) received neoadjuvant chemoradiation. There were 24-49 (median 33) radiation treatments of mean duration 49.5 (IQR:35-60) days. Median hospital stay was 4 (IQR: 3-5) days. Postoperative morbidity developed in 10 patients (33.3%), 4 pelvic abscesses, 3 ileus, 1 bowel obstruction, 1 ascites, 1 bleed requiring reoperation. Conclusions: MIS for locally advanced anorectal cancer can be safely performed using the surgical robot to include extended lymph node dissection or en-bloc multi-visceral resection. It is technically feasible with acceptable morbidity and short term oncologic outcomes. Further study of long term outcomes are ongoing.

P127
Nodal Involvement and Impact of Adequate Staging in Older Patients with Resectable Colon Cancer: A Population-based Analysis
H. Khan,1,* A. Olszewski,2 P. Somaundarir,1 1. Surgery, Roger Williams Medical Center, Providence, RI; 2. Memorial Hospital of Providence, Pawtucket, RI.
Background: The variation in nodal involvement between age groups has not been thoroughly studied in colon cancer, but it may affect strategies for extent of resection in geriatric patients (pts). The objective of our study was to compare nodal involvement in resectable colon cancer pts, with a focus on surgical staging practices in the elderly. Methods: We extracted data from the Surveillance, Epidemiology and End Results registry on 183,055 pts diagnosed with stage I-III colon adenocarcinoma between 2000 and 2010. Proportions of pts undergoing colon resection, pts with adequate staging with ≥12 lymph nodes examined (LNE, n=99,308) and with node-positive (N+) cancers were compared in age groups using chi-squared test. Relative risk (RR) of N+ cancer was compared in a multivariable linear-log model, and relative survival in a flexible parametric model, reporting excess hazard ratios (HR) with 95% confidence intervals (CI). Results: While the rates of colon resection were similar in all age groups, older pts were significantly less likely to have ≥12 LNE (P<0.0001, Table). When adequately staged, older pts had a significantly lower proportion of N+ cancers (P=0.0001), even after adjusting for multiple other variables. Survival was better in pts with ≥12 LNE, with no significant difference in the benefit between the age groups (P=0.25 for interaction). Conclusions: When adequately staged, older pts are less likely to have N+ cancer, which may help them avoid the recommendation for adjuvant chemotherapy. Since the survival benefit of ≥12 LNE is similar in every age group, the guidelines for extent of resection and pathological examination should be diligently adhered to in all pts undergoing curative surgery, regardless of age.

P128
Intralymphatic (IL) Infusion of Type 1 Polarized Dendritic Cells (dDC1) for the Treatment of Colorectal Cancer (CRC) M. Radomski,1* H.J. Zeh, A.H. Zureikat, J. Pingpang, J. Heather, E. Wieckowski, L. Butterfield, P. Kalinski, D.L. Bartlett. University of Pittsburgh, Pittsburgh, PA.
INTRODUCTION: The overall efficacy of dendritic cell-based vaccines has been disappointing. We hypothesize this is secondary to the delivery route of the cell-based vaccine and inadequate polarization of DCCs. Here, we describe a pilot study evaluating the feasibility of a semi-continuous IL infusion of a type 1 polarized DC (dDC1). Secondary endpoints consisted of overall survival (OS), as well as circulating immune reactivity to tumor antigens. METH- ODS: Patients were divided into three treatment arms and injected with dDC1’s (prepared with IL-1β, TNF-α, IFNγ, poly-I:C and IFNγ) loaded with autologous tumor (UV irradiated) and heterologous helper antigens (KLH protein or PADRE peptide) at a dose of 2x106 cells per course (4 courses). Routes of delivery were varied in each treatment arm. Arm A received 4 daily injections per course via intradermal delivery, arm B received a single intranalodial injection per course, and arm C received a semi-continuous IL infusion via an implanted subcutaneous port over 4 days. Blood samples were collected pre and post-treatment and analyzed for immune reactivity against survivin and CEA. RESULTS: Nine patients with stage IV CRC underwent R0 resection. Six patients received IL ports. Average port patency was 1.36±0.48 months. Only 4 patients (44%) successfully received 2 concurrent courses of IL vaccine. No patients received more than 2 concurrent courses of IL vaccine without having the port replaced due to catheter thrombosis. Of the 9 patients, 2 are still alive (66mo and 43mo after initial treatment date). Overall survival of the cohort was 23(±19) months. One patient with recurrent carminomatosis is still alive without evidence of disease at 66mo. We detected an increase in anti-survivin responses (IFNγ EILISPOT) following vaccination, especially in patients demonstrating prolonged OS, while no increase in anti-CEA responses were detected. CONCLUSIONS: Our study shows that prolonged IL delivery via an implantable port is not a feasible route for delivery of DCC’s due to loss of port patency. In 4 patients studied to date, immunological assays show a correlation between level of anti-survivin response and OS.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>N</th>
<th>Colon resection (%)</th>
<th>≥12 LNE after colon resection (%)</th>
<th>Node positive cancer (≥12 LNE) (%)</th>
<th>Relative risk of N+ cancer (≥12 LNE, 95% CI)</th>
<th>Excess mortality for pts with ≥12LNE, HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥20-49</td>
<td>20 (3, 0, 71)</td>
<td>94%</td>
<td>70%</td>
<td>47%</td>
<td>1</td>
<td>1 (0.64-0.79)</td>
</tr>
<tr>
<td>≥50-64</td>
<td>20 (6, 4, 51)</td>
<td>92%</td>
<td>62%</td>
<td>41%</td>
<td>0.95 (0.92-0.97)</td>
<td>1 (0.67-0.75)</td>
</tr>
<tr>
<td>≥65-74</td>
<td>65 (75, 62, 0)</td>
<td>93%</td>
<td>57%</td>
<td>37%</td>
<td>0.85 (0.83-0.88)</td>
<td>0.69 (0.65-0.73)</td>
</tr>
<tr>
<td>≥75-84</td>
<td>20 (5, 70, 52)</td>
<td>93%</td>
<td>56%</td>
<td>35%</td>
<td>0.80 (0.74-0.82)</td>
<td>0.65 (0.61-0.68)</td>
</tr>
<tr>
<td>≥85</td>
<td>15 (7, 22, 764)</td>
<td>91%</td>
<td>55%</td>
<td>34%</td>
<td>0.74 (0.71-0.76)</td>
<td>0.62 (0.58-0.67)</td>
</tr>
</tbody>
</table>

Graph showing survival specific effects at week 2x1

Overall Survival (months)
P129
Morbidity and Mortality following Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy in Patients with Diabetes
R.W. Randle,1 R.K. Svett,1 J.H. Stewart,1 P. Shen,1 E.A. Levine,1 K.I. Votanopoulos.1 1. General Surgery, Wake Forest University School of Medicine, Winston-Salem, NC; 2. Biostatistics, Wake Forest University School of Medicine, Winston-Salem, NC.

BACKGROUND: Patients with diabetes suffering from peritoneal surface disease (PSD) represent a challenging group to treat due to the effects of both processes on multiple organ systems. The impact of diabetes on outcomes following cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) remains undefined. METHODS: A retrospective analysis of a prospective database of 1065 CRS-HIPEC procedures was conducted. Patient demographics, comorbidities, type of primary tumor, hospitalization, morbidity, mortality, and distribution of complications were reviewed. RESULTS: CRS-HIPEC was performed in 91 diabetic and 844 non-diabetic patients from 1991 to 2013 for PSD originating from 452 (48%) appendiceal and 220 (24%) colorectal primaries. Patients with diabetes were older (p<0.005) and more likely to have lung disease (p<0.001), heart disease (p=0.009), higher BMI (p<0.001), and worse performance status (p=0.011) than non-diabetic patients. Diabetics and non-diabetics spent 6.8 and 3.1 (p=0.009) days in the ICU and 18.1 and 13.9 (p=0.074) days in the hospital, respectively. Thirty-day major morbidity was 48.9% and 43.2% (p=0.522) while 90-day major morbidity was 51.1% and 45.8% (p=0.526) in diabetics and non-diabetics, respectively. Despite similar major morbidity rates, diabetics had more infectious (p=0.001) and thrombotic complications (p=0.046), arrhythmias (p=0.007), renal insufficiency (p=0.002) and respiratory failure (p=0.002) than non-diabetics. Mortality was significantly worse for diabetic patients at 30-days (8.8% vs. 2.7%, p=0.007) and at 90-days (13.2% vs. 5.2%, p=0.008) and was predominantly attributed to older age (p=0.002), infectious complications (p=0.003), and enteric leak (p=0.007). CONCLUSION: Diabetes predicts a specific complication pattern associated with increased ICU stay and worse mortality in patients undergoing CRS-HIPEC. Diabetic patients deemed to be appropriate candidates for CRS-HIPEC should be treated with caution.

P130
Trends and Predictors of Resection of the Primary Tumor for Patients with Stage IV Colorectal Cancer: Operating Despite Guidelines
M. Shapiro,1 N.U. Rashid,2 E.E. Whang,3 V.A. Boosalis,4 Q. Huang,3 C.H. Yoon,3 M.S. Saund,3 J.S. Gold.1 1. VA Boston Healthcare Medicine Service, Boston, MA; 2. Dana-Farber Cancer Institute, Boston, MA; 3. Brigham and Women’s Hospital Department of Surgery, Boston, MA; 4. VA Boston Healthcare Pathology Service, Boston, MA; 3. Brigham and Women’s Hospital Department of Surgery, Boston, MA; 4. VA Boston Healthcare Pathology Service, Boston, MA.

Introduction: Approximately 20% of colorectal cancer patients have unresectable distant metastatic disease at diagnosis. Only a small percentage of these patients develop symptoms necessitating surgical intervention. Current guidelines recommend that patients with unresectable metastases receive chemotherapy without resection of the primary tumor. Our goal was to examine the trends and predictors of surgical resection in this group using a population-based database. Methods: Cases of colorectal cancer diagnosed with synchronous metastatic disease between 1988 and 2010 were identified using the SEER registry. Cases prior to 1988 were excluded as information regarding surgery was incompletely coded. Associations between surgical resection and available clinicopathological variables were sought using univariate and multivariate logistic regression. Results: 80,716 patients with Stage IV colorectal cancer diagnosed between 1988 and 2010 were identified. Of these, 68% underwent resection of the primary tumor. There was a trend toward the decreased use of surgical resection over time (Figure, p<0.001), however, in the most recent time period (2008-2010, n=13,120) 53% of patients with stage IV tumors who did not undergo resection of metastatic disease still had resection of the primary tumor. Variables associated with an increased rate of resection in this period were younger age (p=0.001), female gender (p=0.002), married status (p<0.001), private insurance status (p<0.001), earlier year of diagnosis (p<0.001), geographical region (highest in Southeast, p<0.001), right sided cancers (p<0.001), smaller tumor size (p<0.001), higher grade (p<0.001), and normal CEA (p<0.001). Race and urban location were not associated with the rate of surgery. Gender (p=0.015), marital status (p=0.001), insurance status (p=0.018), region (p<0.001), tumor site (p=0.001), grade (p=0.025), and CEA (p<0.001) were independent predictors in the multivariate analysis. Conclusions: Despite recommendations, surgical resection of the primary site is still common practice for patients with synchronous Stage IV colorectal cancer.

P131
Increased Incidence of Early Onset Colorectal Cancer in Arizona
R.M. DiGiovanni,1 E. Ohlson, V. Nfonsam. Department of Surgical Oncology, The University of Arizona, Tucson, AZ.

INTRODUCTION: Colorectal cancer (CRC) is the second leading cause of cancer related deaths in the United States. In the last three decades overall incidence of colorectal cancer in the United States has been declining. However, recent studies using the SEER database have shown an increasing incidence in younger age demographics. These studies were done using the SEER Cancer Database which Arizona does not participate in. The aim of this study is to investigate and analyze the incidence of CRC in Arizona, using the Arizona Cancer Registry. Methods: We performed a retrospective analysis of patients with colorectal cancer reported in the Arizona Cancer Registry from 1995-2010. Data obtained included age at diagnosis, gender, race, location of tumor, grade of tumor and stage of disease. The data was organized into 5-year increments from 0 to 4 years old to 85+ years old for incidence of colon, rectal, and overall CRC. Statistical analysis was performed using SPSS. Results – 39,623 cases of colorectal cancer were reported to the Arizona Cancer Registry from 1995-2010. There were 53.1% males and the average age at diagnosis was 69.5 years. There was a 3.1% decrease in the average age of diagnosis, 70.8 years to 68.1 years. Of the 39,623 cases 92% were >50 years. Overall, there was a 30% decrease in the incidence of CRC. However, there was a 22% increase incidence in patients aged 10-50. There was a 15% and 41% increase in the incidence of colon and rectal cancer respectively during that time frame. The most significant increase in overall CRC was seen in patients age 10-29, with a 102% increase. A 225% increase incidence of rectal cancer was seen in patients aged 30-34. For colon cancer, a 110% increase incidence was seen in patients 10-29. Conclusion: Overall, there is a decreasing incidence of colorectal cancer in Arizona. However there is increasing incidence of early onset CRC mirroring the national trend. We also saw a shift in mean age of diagnosis from 70.8 to 68.1. Rigorous screening and early detection have led to the overall decrease in the incidence of CRC. Increase in early onset CRC is likely multifactorial and further studies are necessary to better understand this trend.
Perforated Colon Cancer Increases the Risk of Metastases in Early Stage I and II Colon Cancer

C.J. Wai,1* T. Li,2 E.R. Sigurdson,2 J.M. Farma.2 1. Surgical Oncology, Hartford HealthCare Medical Group, Hartford, CT; 2. Fox Chase Cancer Center, Philadelphia, PA.

Introduction: Early stage colon cancer patients have a 5-year overall survival (OS) of up to 90% with poorer survival for those with later stage disease. There is a subset of early stage patients who will develop metastases. The aim of our study was to evaluate factors predictive of developing metastases in patients with early stage colon cancer. Methods: An IRB approved study was performed on stage I and II colon cancer patients operated on from 2005-2011 at our tertiary referral center. We compared age, gender, race, stage, location and surgical pathologic characteristics in patients that developed metastases to those that did not. Results: There were 94 patients identified with 43 males and 51 females (Table 1). The median age at diagnosis was 64.9 years (range 22-89). There were 34 stage I and 60 stage II patients. Seven developed metastases. All were stage II patients. Mean time to developing metastases was 17.4 months (range 5-58). Stage II patients were more likely than stage I patients to develop metastases (p = 0.038). Patients with T4 disease were more likely to develop metastases than T3 (p = 0.03) and T1/T2 (p = 0.0005). Patients with perforated cancer were more likely to develop metastases (p=0.027). The median number of lymph nodes excised in those with metastases was 17 and 12 in those who did not develop metastases (p=0.04). Metastases were located in the liver (2), abdominal wall (1), peritoneum (1), pelvic organs (2) and lymph nodes (1). Three-year OS was 91%. For those without metastases, the 3 year OS was 93% compared to an OS of 62% in those who developed metastases (p=0.001). Pathologic grade, histology, lymphovascular invasion and chemotherapy were not factors associated with developing metastases. On multivariate analysis, patients with perforated cancer were still more likely to develop metastases (p = 0.05). Conclusions: Patients with early stage I and II colon cancer have a high survival rate. However, a subset is more likely to develop metastases, such as those with perforated and thicker tumors. These patients should be treated aggressively with closer surveillance as they portend a subset of patients with a higher risk of recurrence.

Table 1. Early stage colon cancer patient characteristics.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age at Diagnosis</td>
<td>64.9 years</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>43 (45.7%)</td>
</tr>
<tr>
<td>Female</td>
<td>51 (53.6%)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>82 (87.2%)</td>
</tr>
<tr>
<td>African American</td>
<td>9 (9.6%)</td>
</tr>
<tr>
<td>Other</td>
<td>3 (3.2%)</td>
</tr>
<tr>
<td>Location of Primary Tumor</td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>37 (40.4%)</td>
</tr>
<tr>
<td>Transverse</td>
<td>51 (55.6%)</td>
</tr>
<tr>
<td>Left</td>
<td>6 (6.6%)</td>
</tr>
<tr>
<td>Signoid</td>
<td>41 (43.6%)</td>
</tr>
<tr>
<td>Pathologic Stage</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>34 (36.6%)</td>
</tr>
<tr>
<td>II</td>
<td>60 (65.8%)</td>
</tr>
<tr>
<td>T Stage</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>18 (19.1%)</td>
</tr>
<tr>
<td>T2</td>
<td>16 (17%)</td>
</tr>
<tr>
<td>T3</td>
<td>5 (93.5%)</td>
</tr>
<tr>
<td>T4</td>
<td>9 (9.6%)</td>
</tr>
<tr>
<td>Median Lymph Nodes Collected</td>
<td></td>
</tr>
<tr>
<td>Patients with Metastases</td>
<td>17</td>
</tr>
<tr>
<td>Patients without Metastases</td>
<td>12</td>
</tr>
<tr>
<td>Site of Recurrence</td>
<td></td>
</tr>
<tr>
<td>Lymph Node</td>
<td>1 (14.3%)</td>
</tr>
<tr>
<td>Liver</td>
<td>2 (25.6%)</td>
</tr>
<tr>
<td>Abdominal Wall</td>
<td>1 (14.3%)</td>
</tr>
<tr>
<td>Cecum/mesenteris</td>
<td>1 (14.3%)</td>
</tr>
<tr>
<td>Pelvis</td>
<td>2 (25.6%)</td>
</tr>
</tbody>
</table>

Appendicetal Carcinoid Tumors in Children: A Population-based Outcomes Study Involving 766 Patients from the Surveillance, Epidemiology, and End Results (SEER) Database (1973-2010)

K. Mahendraraj,* R.S. Chamberlain. St. Barnabas Medical Center, Livingston, NJ.

Introduction: Carcinoid tumors of the appendix (CT) is a rare disease in children, although it is the most common pediatric gastrointestinal neoplasm. Typically diagnosed incidentally following appendectomy for appendicitis, few studies compare clinical outcomes between pediatric (PP) and adult carcinoid patients (AP). This study examines a large cohort of adult and pediatric CT patients to identify differences in presentation and factors which affect clinical outcomes and may guide therapeutic decision making. Methods: Data on 766 patients with CT was abstracted from the Surveillance Epidemiology and End Result (SEER) database (1973-2010). PP was defined as age <20 and AP as ≥20. Standard statistical analyses were performed. Results: PP comprised 10.6% (n=81), and AP 89.4% (n=685) of the study cohort. Mean age was 15.3 in the PP and 45.6 among AP. CT in both PP and AP was significantly more common in Caucasians (81.6% and 85.2%, p<0.05), and females (76.5% and 66%, p<0.05). PP had more locoregional disease (93.3% vs 85.2%) and less lymph node involvement (9.9% vs 18.2%) than AP. PP had significantly more common in Caucasians (81.6% and 85.2%, p<0.05), and females (76.5% and 66%, p<0.05). PP had more locoregional disease (92.6% vs 85.8) and less lymph node involvement (9.9% vs 18.2%) than AP. Surgery was the primary treatment for both groups, however PP were treated with less aggressive surgical therapy for similar disease stage and presentation (29.8% received appendectomies and ileocecectomies vs 14.5% of AP). Conversely, 7.4% of PP had hemicolectomy vs. 17.8% of AP. PP had significantly better mean overall survival (36.7 years vs 27.3 years, p<0.05) and lower overall mortality (2.5% vs 23.9%; p<0.001). PP also had better 5- and 10-year survival (100% and 98%) than AP (84% and 78%); p<0.05. Conclusions: CT is a rare tumor in children which occurs most commonly in Caucasians and females. Surgery is the primary treatment modality in both AP and PP. AP present with more advanced disease and undergo more aggressive surgery. Compared to adults, CT in the pediatric population has better long term survival and excellent prognosis with surgical treatment.
P134

Disparities in Stage of Presentation and Treatment of Colorectal Cancer among Hispanic and Non-Hispanic White Patients


Background: Although incidence rates for colorectal cancer (CRC) for Hispanics are similar to non-Hispanic whites (NHW) in New Mexico, the cause-specific mortality is higher among the Hispanic population. Hispanics have also been shown to be less likely to be current with colorectal cancer screening guidelines as compared to NHW. The purpose of this study was to determine if there was a difference between Hispanics and NHW in stage at presentation and if the care provided was concordant with NCCN guidelines at our NCI Designated Cancer Center. Methods: A prospective database of all patients who presented with colorectal cancer between June 2009 and July 2013 was queried. A total of 197 patients were identified. Data was extracted that included: demographics, stage of CRC at first diagnosis, treatments given, and pathology results. Frequencies of stage at presentation and NCCN guideline concordance were recorded. Results: Table 1 shows the results. There were 107 (55%) Hispanics and 90 (45%) NHW. There was no statistical difference in Concordance among NHW (p=0.05). There was no statistically significant difference in concordance with NCCN guidelines for the 3 metrics analyzed. Conclusions: Hispanics and NHW with colon cancer presented with similar stage of disease and were concordant with NCCN guideline metrics. Hispanics with rectal cancer, however, presented at a more advanced stage of disease as compared to NHW patients.

The reason for this disparity remains to be elucidated. Future studies to include outreach, education, screening and molecular profiling of these disparate populations are planned.

Distribution by Ethnicity, Stage at Presentation and Treatment.

<table>
<thead>
<tr>
<th>Color</th>
<th>Stage</th>
<th>Adj Chi-Ind Treatment</th>
<th>Stage</th>
<th>Adj Chi-Ind Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic</td>
<td>Stage I</td>
<td>27 (26.3%)</td>
<td>22 (22.2%)</td>
<td>59 (58.3%)</td>
</tr>
<tr>
<td>NHW</td>
<td>54 (50.0%)</td>
<td>46 (46.1%)</td>
<td>28 (28.2%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>Stage II</td>
<td>27 (26.3%)</td>
<td>19 (19.0%)</td>
<td>32 (32.3%)</td>
</tr>
<tr>
<td>NHW</td>
<td>42 (40.0%)</td>
<td>37 (37.0%)</td>
<td>23 (23.2%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>Stage III</td>
<td>27 (26.3%)</td>
<td>22 (22.2%)</td>
<td>45 (44.5%)</td>
</tr>
<tr>
<td>NHW</td>
<td>42 (40.0%)</td>
<td>37 (37.0%)</td>
<td>23 (23.2%)</td>
<td></td>
</tr>
</tbody>
</table>

P135

Predictors of Postoperative Complications in Seniors Undergoing Colon Cancer Surgery

H. Alabbas,1* S. Krotneva,3 A. Ramjaun,3 T. Euqal,4 A. Meguerditchian. 1. Department of Surgery, McGill University, Montreal, QC, Canada; 2. Brigham and Women’s Hospital and Harvard Medical School, Boston, MA; 3. Clinical and Health Informatics Research Group, McGill University, Montreal, QC, Canada.

Introduction: The postoperative complication rate in seniors undergoing colon cancer surgery is nearly double that of the general population. While colon cancer incidence is high in seniors, there is a lack of an effective, accurate and time sensitive risk-profiling tools in seniors who may experience severe postoperative complications (SPCs). The aim of this study was to identify predictors of SPCs in seniors undergoing colon cancer surgery. Methods: A historical prospective study of colon cancer patients aged ≥65 years was assembled from administrative claims and hospitalization data provided by Quebec’s universal healthcare insurance provider between 2000 to 2006. The incidence and grades of SPCs were assessed using Clavien’s classification (grades III-V). A multivariate Cox model was employed to evaluate patient and various patient-related predictors of SPCs and to account for clustering of patients within surgeons. Results: 3789 patients (median age of 76) were included with 54.3% being female. Emergency admissions were encountered in 24.2%. SPCs were experienced by 29% of the cohort (median time to first complication of 6 days), with 17.3%, 12.6%, and 5% experiencing grade III, IV, and V complications, respectively. The incidence of emergency room visits and hospital readmissions were 17.8% and 11.3%, respectively. The multivariate analysis indicated that the following factors were associated with SPCs included: male (HR=1.28, 1.13-1.45), age ≥85 years (HR=1.25, 1.03-1.52), ≥10 different medications prescribed within 6 months preceding surgery (HR=1.17, 1.02-1.34) receipt of care for either renal insufficiency or cardiovascular disease (HR=1.43, 1.02-1.99) and emergency admissions (HR=1.39, 1.22-1.59). Conclusion: Recently prescribed medications, receipt of care for renal insufficiency or cardiovascular disease and emergency admissions, which can be identified through administrative databases, were associated with SPCs. These can potentially be tracked through administrative claims electronically to provide a risk assessment prior to the surgical intervention.
Factors associated with any post-operative complication (III-V) within 30 days of surgery in colon cancer patients (N=3789).

<table>
<thead>
<tr>
<th>Factors</th>
<th>No. of patients</th>
<th>% with complication</th>
<th>Univariate Cox model</th>
<th>Multivariate Cox model</th>
<th>α</th>
<th>Reference</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of unique drugs &lt;5</td>
<td>307</td>
<td>26.6</td>
<td>1.00 Reference</td>
<td>1.00 Reference</td>
<td>α</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.0</td>
<td>412</td>
<td>27.5</td>
<td>1.00 Reference</td>
<td>0.96(0.85,1.13)</td>
<td>0.082</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥10</td>
<td>320</td>
<td>35.0</td>
<td>1.00 Reference</td>
<td>1.24(1.03,1.49)</td>
<td>0.026</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Geriatric Co-morbidities

- Urinary Incontinence
- Anemia
- Arteritis
- Depression
- Osteoporosis
- Cardiac disorders
- Dementia
- Diabetes
- Renal Insufficiency
- Respiratory Illnesses
- Health Service Utilization

Adjusted for clustering of patients within physicians (N=390), year of surgery, rural residence and mean income in residence. The median cluster size was 6 patients, range: 1-53.

P136


Surgery, Washington University in St Louis School of Medicine, St Louis, MO.

INTRODUCTION: Despite meticulous surgical techniques, calcitonin levels remain detectable in 40% to 66% of patients following initial surgery for medullary thyroid carcinoma (MTC) and the optimal surgical management for persistent or recurrent disease remains controversial. Reoperative approaches range from targeted removal of detectable disease to comprehensive compartment-oriented lymph node clearance. Previous studies have suggested that biochemical cure, defined by normalization of post-operative calcitonin measurements, can be used to predict disease-free survival. To date, the surgical approach to reoperations for MTC varies widely and the reported rate of biochemical cure ranges from 0% to up to 45%. METHODS: A review of clinical case series with a proportional meta-analysis of postoperative calcitonin clearance following reoperation for MTC was performed. Studies were obtained from the following sources: PubMed, EMBASE, SCOPUS, and Cochrane Library. RESULTS: 27 articles capturing 984 patients met inclusion criteria and were included in the final meta-analysis. Overall, normalization of calcitonin following reoperation for MTC was achieved in 16.2% of patients (95% CI 10.0% to 22.5%). When stratified by operative procedure (see figure), targeted selective lymph node removal procedures had a normalization of calcitonin in 10.5% of patients (95% CI 6.4% to 14.7%), while compartment-oriented procedures had a higher rate of normalization of calcitonin at 18.6% of patients (95% CI 15.9% to 21.3%). Regardless of operative procedure, the percentage of patients with a 50% or greater decrease in calcitonin following reoperation for MTC was 65% (95% CI 55.1% to 76.3%). CONCLUSIONS: Our results indicate that while calcitonin reduction of 50% or greater is achievable through either compartment-oriented or selective reoperation approaches, the rate of calcitonin normalization and biochemical cure following reoperation for MTC is enhanced through use of a meticulous compartment-oriented lymph node dissection. Compartment-oriented node dissection should be the procedure of choice in reoperative MTC patients in whom the goal is disease-free survival.

P137


Cleveland Clinic, Cleveland, OH.

Introduction: An increasing number and higher rates of genetic mutations associated with pheochromocytoma and paraganglioma (PGL) have been identified, making genetic testing integral for optimal treatment. The aim of this study is to analyze patterns of referral and results of genetic testing in pheochromocytoma and PGL in a single institution. Methods: One hundred fifty six patients with pheochromocytoma or PGL who underwent surgery at a single institution by various subspecialties over 8 years were retrospectively reviewed. Clinical presentation, patterns of referral to genetic counseling, and results of genetic testing were analyzed. Results: At presentation, 12 (10%) of pheochromocytoma and 1 (3%) of PGL patients had known familial disease. Of pheochromocytoma patients, 41 (33%) met criteria for genetic testing (age <45, bilateral, multifocal, suspicious family history) and 26 of these (63%) were referred to genetics. Half (13 patients) were seen by genetics and a mutation was identified in 3 (23%). Of pheochromocytoma patients (n=85) not filling these criteria, 38 (38%) were referred to genetics at the time of diagnosis (17/32) or via a follow-up letter (15/32). Eleven patients (34%) were compliant with their appointment and none of these patients tested positive for mutations. Half of patients with PGL (n=15) were referred to genetics, and 11 (73%) attended the appointment. Two of these patients (18%) tested positive for an SDHB mutation, while the results are pending in another patient. Eighty-two percent of pheochromocytoma patients managed by endocrine surgery (46/56) were recommended genetic counseling compared to 14% of those treated by other specialties (10/70) (p<0.001). Among PGL patients, 73% of those treated by endocrine surgery (8/11) were referred to genetics versus 37% of those treated by other specialties (7/19) (p=0.05). Conclusions: A significant number of patients with pheochromocytoma and PGL do not undergo genetic testing due to patient incompliance and inconsistent physician referral across different subspecialties. Benefits of routine genetic testing are unproven within the limitations of the study.

P138


University of Miami Leonard M. Miller School of Medicine, Miami, FL.

Introduction: The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) includes atypia or follicular lesion of undetermined significance (AUS/FLUS) as an additional indeterminate classification to improve diagnostic accuracy of thyroid fine needle aspiration (FNA). This study evaluates
the impact of the BSRTC before and after its implementation at a single surgical referral center. Methods: A retrospective review of prospectively collected data of 1115 consecutive patients with index thyroid nodules who underwent FNA and thyroidectomy was performed. Records of these patients during pre-BSRTC (n=837) and post-BSRTC (n=278) periods were compared. FNA-cytology distribution was compared before and after BSRTC. Analysis of FNA diagnosis, malignancy within each category, AUS/FLUS utilization rates after BSRTC was performed using Student-T, Z and Pearson’s Chi-Square tests. A P-value <0.05 was considered significant. Results: In this surgical series, distribution of pre-BSRTC cytology included: insufficient, n=21 (3%); benign, n=279 (33%); indeterminate, n=291 (35%); suspicious for malignancy, n=87 (10%); malignant, n=159 (19%); and for post-BSRTC cytology: insufficient, n=8 (3%); benign, n=76 (27%); AUS/FLUS, n=80 (29%); follicular/Hürthle neoplasm, n=15 (5%); suspicious for malignancy, n=35 (13%); malignant, n=64 (23%). Overall, there was a significantly higher malignancy rate in the post-BSRTC compared to pre-BSRTC period (55% vs. 41%, p<0.001), respectively. AUS/FLUS was identified in 29% of post-BSRTC surgical patients with a high malignancy rate of 46%. There was a significant increase of malignancy rate in post-BSRTC III and IV (46% and 54%, respectively) categories compared to the pre-BSRTC indeterminate (27%) category (p<0.05 for both). Only 19% of patients with AUS/FLUS cytology underwent repeat FNA in 6 months, whereas the remaining 81% chose to directly undergo surgical resection. Conclusion: At this institution, pre-to post-BSRTC period correlation reveals a significant overall increase of malignancy among thyroidectomy patients. More frequent AUS/FLUS utilization was associated with higher than expected malignancy rates after BSRTC adoption.

P139 Can Surgeon Volume Mitigate Complications following Total Thyroidectomy? A. Hauch,1* Z. Al-Qurayshi,1 D. Slakey,1 G. Randolph,1 E. Kandil.1 1. Surgery, Tulane University School of Medicine, New Orleans, LA; 2. Harvard School of Medicine, Boston, MA.

Background: The extent of thyroid removal in cases of benign conditions or indeterminate nodules is still a matter of much debate. However, there has been an increase in the use of total thyroidectomy for management of benign thyroid diseases over the last fifteen years in US. We sought to compare the rates of complications between total/bilateral vs. unilateral thyroidectomy and whether surgeon experience had an effect. Methods: Cross-sectional analysis was performed using ICD-9 procedure codes included in the Nationwide Inpatient Sample (NIS) from 2003-2009 to identify all adult patients who underwent total/bilateral and unilateral thyroidectomy for benign or malignant conditions. Adjusted logistic regression models were used to control for confounders and to test for interaction between surgeon volume and risk of complications. Results: 62,722 procedures were included in this analysis. The majority of cases consisted of total/bilateral thyroidectomy in 57.9%, which was performed typically for benign disease. Overall there was a significant difference between the risks of complication following total/bilateral compared to unilateral thyroidectomy (20.4% vs. 10.8%; p<0.0001). High volume surgeons (performing >100 thyroid operations/year) performed only 4.96% of the procedures and 62.56% of them were total thyroidectomies. Low volume surgeons (performing <10 thyroid operations/year) were more likely to have postoperative complications following total/bilateral thyroidectomy compared to high volume surgeons (OR: 1.53, 95% CI: 1.12, 2.11), however, there was no difference in the risk of complications following unilateral thyroidectomy for benign or malignant conditions. Conclusion: Higher surgeon volume is associated with improved patient outcomes following total thyroidectomy. However, higher risk of complication associated with total/bilateral thyroidectomy compared to unilateral thyroidectomy is evident even among high volume surgeons. Thyroid surgeons should be mindful of the inherent risk of a total thyroidectomy.


Introduction: Thyroid nodules are common. The current gold standard, fine-needle aspiration biopsy (FNAB), yields 10-25% indeterminate results necessitating surgery for diagnosis. Elastic scattering spectroscopy (ESS) is a minimally invasive optical-biopsy technique, mediated by a fiberoptic probe. We hypothesized that by combining ESS with FNAB, we could improve the treatment of indeterminate thyroid nodules. Methods: We built a miniaturized ESS-integrated biopsy syringe that can fit through a 23-gauge biopsy needle and assessed the potential of ESS to pre-operatively differentiate benign from malignant thyroid nodules. An IRB approved protocol was conducted on patients undergoing ultrasound-guided FNAB of thyroid nodules. Cells and ESS data were collected from within the thyroid nodule. Post-surgical pathology was our gold standard for indeterminate cytology. Results: 140 patients were enrolled in the study, and 135 patients had usable data. All patients tolerated the procedure well; additional time to perform ESS measurements required less than 20 seconds. The average enrolled patient was an African American female in her early 50’s. Cytology resulted in 5 patients with malignant, 94 with benign, 32 with indeterminate and 4 with insufficient nodules. 35 patients underwent surgery, and 8 had histopathology-confirmed malignancy. Of the patients that underwent surgery, 17 had indeterminate thyroid nodules and only 3 of those patients had malignant pathology. Visual inspection revealed that an ESS waveform signature could discriminate benign from malignant disease. Analysis of spectra through an automated algorithm confirmed this finding. Preliminary results show a NPV of 0.99, a sensitivity of 0.92 and a specificity of 0.85. Conclusion: ESS can reduce the number of indeterminate nodules that require surgical treatment. With the collection of further data, an algorithm using cytology and ESS data could potentially be used as an in-situ real time minimally invasive adjunct to conventional FNA cytology to improve diagnosis and prevent unnecessary surgery.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female = 117, Male = 18</td>
</tr>
<tr>
<td>Age</td>
<td>Avg = 53 (Range = 22 - 84)</td>
</tr>
<tr>
<td>Race</td>
<td>White = 49</td>
</tr>
<tr>
<td>Black</td>
<td>52</td>
</tr>
<tr>
<td>Asian</td>
<td>8</td>
</tr>
<tr>
<td>Hispanic</td>
<td>22</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
</tr>
<tr>
<td>Cytology</td>
<td>Malignant = 5</td>
</tr>
<tr>
<td>Benign</td>
<td>94</td>
</tr>
<tr>
<td>Indeterminate</td>
<td>32</td>
</tr>
<tr>
<td>Insufficient</td>
<td>4</td>
</tr>
<tr>
<td>Histopathology</td>
<td>Malignant = 8</td>
</tr>
<tr>
<td>Benign</td>
<td>27</td>
</tr>
<tr>
<td>No Surgery Yet</td>
<td>100</td>
</tr>
</tbody>
</table>

P141 Preoperative Modified 4D-CT Reduces Unnecessary Opposite Side Exploration in Patients with Primary Hyperparathyroidism S. Singla,* P. Thirunavukarasu, M. Kukar, T. Platz, S. Kumar, W.G. Cance. Roswell Park Cancer Center; Buffalo, NY.

Background: 4DCT with volume rendering is a sensitive imaging modality for disease localization in primary hyperparathyroidism. Our aim was to determine whether the use of 4DCT reduces unnecessary opposite side exploration. Methods: We performed a retrospective review of 196 consecutive patients with primary hyperparathyroidism between 2010 and 2013. All patients
underwent 4DCT with volume rendering. Comparison was made to US and Sestamibi for preoperative localization, intra-operative correlation and pathology. Results: US, Sestamibi and 4DCT results were available in 176 (89.8%), 181 (92.3%) and 196 (100%) patients, respectively, and 163 patients had all three tests available. The US, Sestamibi and 4DCT were non-diagnostic in 50%, 43.1% and 6.1%, respectively. Among patients who had any diagnostic test, we calculated a usefulness rate based on its use in guiding non-unnecessary exploration, and a failure rate based on wrong side or unnecessary exploration, by correlating the results of investigations with final pathology results. The usefulness rate of US, Sestamibi and 4DCT were 48.3%, 53.5% and 92.3%, respectively for the entire cohort, and 46.6%, 54.6% and 93.1%, in patients who had all the three tests. The failure rates of US, Sestamibi and 4DCT were 3.4%, 5.8% and 2.7%, respectively for the entire cohort and 3.8%, 5.3% and 2.6%, for patients with all the three tests. In patients with all the three tests available, the 4DCT scan was non-diagnostic in 1 patient (0.6%), while US and Sestamibi were concordant in only 55 (33.7%) patients. In patients undergoing parathyroid surgery in re-operative necks (n=18), 4DCT was non-diagnostic in only 1 patient. In 12 patients where 4DCT was non-diagnostic, US and Sestamibi were concordant in only 1 patient, while in 5 patients who had unnecessary side exploration as guided by 4DCT, sestamibi and US were non-diagnostic in all. Conclusions: Modified 4DCT scan is superior to US and Sestamibi in diagnostic accuracy and reduces unnecessary side exploration in primary hyperparathyroidism. The concordant use of US and Sestamibi for preoperative localization may be safely replaced by 4DCT alone.

**P142**

**Histone Deacetylase Inhibitors Induce NF-kB Activity in Medullary Thyroid Cancer**

Y. R. Somnay,* X. Yu, S. Miyamoto, H. Chen. Surgery, University of Wisconsin, Madison, WI.

INTRODUCTION: Histone deacetylase inhibitors (HDACi) reduce medullary thyroid cancer (MTC) growth and invasion, but have failed to prolong long term survival (NCT01013597). Notably, Nuclear factor kappa B (NFkB) can be induced by genotoxic stress, driving tumorigenesis and extrinsic chemoresistance. Here, we examine the effect of HDACi treatment on NFkB activity and its modulation by targeted suppression of specific NFkB pathway intermediaries in MTC. METHODS: Two MTC cell lines (TT, MZ) were transfected with a luciferase-fused NFkB binding site or a mutant-kB (neg. control), and exposed to 1μM suberoylanilide hydroxamic acid (SAHA), 6mM valproic acid (VPA), or 4nM of the new HDACi Thailandepsin (TDPA) for up to 48hrs before luciferase reading. NFkB inhibitors were tested concomitantly with HDACi (5μM Ptc-210, 10μM Ku5593, 1-μM Withaferin A (WA), or 5-20μM bortezomib). RESULTS: SAHA, VPA and TDPA dose-dependently decreased TT and MZ cell growth and increased NFkB-dependent luciferase reporter activity over 48hrs. Activity peaked at 12hrs, w/ fold increases of 42.6±3.3±3 and 23.2±2 w/ SAHA, VPA and TDPA treatments respectively in MZ cells, and 428±4, 215±4, and 361±6 w/ SAHA, VPA and TDPA treatments respectively in TT cells (p<0.01, compared with non-treated induction). Wild type fold changes were significant w/ respect to mutants (p<0.01), except for among untreated cells (Mz; p=1.0; TT; p=0.08) underscoring the specificity of NFkB activity targeting and detection. HDACi-induced NFkB luciferase activity in the face of WA, PRC210, KU5593 and Bortezomib was dose-dependently reduced in MZ cells. While SAHA and VPA activated NFkB the most, WA (5μM), Prc210, KU5593 and Bortezomib (5μM and 20μM) significantly reduced NFkB activity (p=0.05). Since PRC210, a ROS scavenger, and KU5593, an ATM kinase blocker, deter NFkB activity specifically upstream genotoxic stimuli and not cytokine signals, HDACi may induce NFkB by oxidative stress. CONCLUSION: HDACi activate NFkB in MTC in vitro. Inhibition of HDAC-induced NFkB activity can be attained by targeting cytokine-induced pathway intermediates or reducing genotoxic stress. Thus, NFkB inhibition may potentiate HDACi induced cytotoxicity in MTC.

**P143**

**A Preoperative Diagnosis of Papillary Thyroid Cancer: Incidence and Implications**


Introduction: The aim of this study is to determine the incidence of patients with histologic PTC who were successfully identified preoperatively by current diagnostic modalities, and to evaluate if a preoperative PTC diagnosis has prognostic implications. Methods: We performed a retrospective single institution review of 1088 consecutive patients with histologic PTC from 2007-2012. Patients with incidentally identified microPTC (≤1 cm) were excluded. Preoperative PTC diagnosis was defined by a fine needle aspiration biopsy (FNAB) cytology classified as “Positive for PTC,” or the presence of BRAF V600E mutation or RET/PTC rearrangement after prospective mutational testing (MT) of cytologically indeterminate FNAB specimens. Results: A preoperative PTC diagnosis occurred in 50% of patients, and was diagnosed by cytology in 32% and by positive MT in 18%. When PTC was known preoperatively, patients were more likely to have a smaller primary tumor (1.8 ± 2.0 cm, p=0.03), extrathyroidal extension (ETA, 38% ± 10%, p<0.001), central compartment lymph node metastasis (CNLM, 47% ± 20%, p<0.001), and tall-cell variant PTC (15% ± 4%, p<0.001). TNM stage III/IV disease was more common in patients diagnosed preoperatively with a trend towards significance (28% ± 21%, p=0.05), yet no differences in distant metastasis or recurrence were observed. Patients with microPTC identified preoperatively were more likely to have ETA (21% ± 4%, p<0.001) or CNLM (46% ± 5%, p<0.001) compared to those who had a postoperative cancer diagnosis. ETA (34% ± 16%, p<0.001) was more common in patients diagnosed by cytology compared to those diagnosed by MT, but patients in both groups were equally likely to have CLNM (10% ± 5%) and TNM stage III/IV disease (p=0.6). Conclusion: A successful preoperative diagnosis of PTC occurred in only half of patients with histologic PTC. The use of routine preoperative adjunctive mutation testing successfully increased this likelihood by 40%. A preoperative diagnosis was associated with PTC with aggressive histopathologic features thus regardless of tumor size, at a minimum, total thyroidectomy should be considered in patients with a preoperative PTC diagnosis.

**P144**

**Outcomes after Subtotal Parathyroidectomy for Primary Hyperparathyroidism due to Hyperplasia: Significance of Whole versus Partial Gland Remnant**

M. Rajaei,* S.C. Olmann, D.F. Schneider, R.S. Sippel,* H. Chen. I. Wisconsin Institute for Medical Research, Madison, WI. 2. University of Wisconsin, Department of Surgery, Madison, WI.

Introduction: Primary hyperparathyroidism (PHPT) due to multi-gland hyperplasia has been traditionally managed by subtotal parathyroidectomy (PTX), with a partial gland left in situ, roughly the size of a normal gland. However, smaller, hyperplastic glands may be encountered at time of surgery, and it is unclear if leaving an entire, intact gland is an equivalent alternative. This study sought to evaluate the rates of permanent hyperparathyroidism and cure of PHPT with in patients with 4-gland hyperplasia that were left with either a whole or partial gland remnant after subtotal PTX. Methods: We reviewed the outcomes of PHPT patients with hyperplasia who underwent PTX at an academic institution. Surgeon intra-operative judgment determined remnant size (whole vs. partial gland), and patients were assigned one of these two categories. Results: Between 2002 and 2013, 189 patients underwent PTX for PHPT hyperplasia. 92 patients (49%) had a subtotal PTX with whole gland remnant while 97 (51%) had a partial gland remnant. Mean age was 58±1 years. 81.5% were female. Patients with a whole gland remnant had higher pre-operative serum phosphate (3.9±0.6 vs. 3.0±0.1, p=0.047) and PTH levels (87±5 vs. 78±7, p=0.047), and lower t-scores versus patients selected for partial gland remnant (−2.2±0.14 vs. −1.7±0.2, p=0.048). A family history for hyperparathyroidism (17.5% vs. 4.4%, p=0.004) was more prevalent in the partial gland remnant group. Both groups had similar pre-operative serum calcium, creatinine, alkaline phosphatase, and vitamin D levels. Only two patients were maintained on diuretics. Success rates, serum calcium and PTH levels at 6 weeks, and patient satisfaction were similar in both groups. However, a mean long term follow up of 21 ± 1.5 months revealed a recurrence rate of 5.3%. Disease persistence and recurrence rates were similar in patients with whole versus partial gland remnant. Conclusion: PHPT due hyperplasia can potentially be managed with subtotal PTX, leaving an intact gland as remnant without increased rates of disease persistence or recurrence. Older patients and those with smaller diseased glands may be the best candidates for this approach.
P145
Robotic Thyroidectomy for Cancer in the United States: Patterns of Use and Short-term Outcomes

M. Abdelgadir Adam,1,* P.J. Speicher,1 S. Reed,2 S. Roman,1 J.A. Sosa.1 1. Department of Surgery, Duke University Medical Center, Durham NC; 2. Duke Clinical Research Institute. Durham NC. 3. Department of Surgery & Duke Clinical Research Institute, Durham, NC.

Abstract: There are few studies analyzing adequacy of resection or utilization of robotic thyroidectomy in the U.S. Our aims were to determine patterns of use and short-term outcomes from robotic vs. open thyroidectomy for thyroid cancer. Methods Patients with thyroid cancer who underwent thyroidectomy in the National Cancer Database (2010-11) were included. Patients who underwent robotic surgery were compared to those who had open thyroidectomy. Descriptive statistics were used to analyze patterns of use, patient characteristics, and outcomes. Logistic regression was employed for factors associated with robotic surgery. Results 68252 patients with thyroid cancer underwent thyroidectomy; 225 had robotic surgery, and 57629 had open surgery. Compared to the open group, the robotic group was younger (47 vs. 51 yrs, p=0.0002), and had more Asian (8% vs. 4%, p=0.06) and privately insured patients (77% vs. 68%, p=0.01). Robotic thyroid surgery use increased by 30% from 2010 to 2011 (p=0.07). Robotic cases were reported from 93 centers, with just 4 centers performing one third of cases. There was significant regional variation, with 25% of cases reported from the Mid-Atlantic region; just 3% were done in New England (p<0.0001). In the robotic group, 39% had tumors <4cm, and 8% had tumors >4cm, but tumor size was similar to the open group (p=0.9). Total thyroidectomy was performed in 61% of patients in the robotic group vs. 80% in the open group (p=0.0001). The rate of conversion to open surgery was 4%. Patients were more likely to undergo robotic surgery if they were at an academic institution (OR 6.1) or ≤45 yrs (OR 2.2). After multivariable analysis, there were no differences in tumor margin status, number of lymph nodes removed, length of stay, or 30-day readmission rates between the two groups. Conclusion Use of robotic thyroid surgery for cancer is limited to a few high-volume institutions. While the overall number of cases remains small, robotic thyroid surgery appears to have short-term outcomes comparable to open thyroidectomy. Larger multi-institutional studies should be undertaken to determine thyroidectomy-specific complications and long-term outcomes.

P146
Patients Rely on Physicians to Inform Them about New Genetic Tests for Hereditary Cancer Syndromes

Introduction: New genetic tests may benefit former patients or their families; however no guidelines exist regarding physicians’ duty to inform patients about new genetic tests, and research on this topic is limited. To evaluate feasibility of disseminating information and patient expectations, we surveyed patients’ response to a notification about new genetic tests. Methods: We identified adult patients treated at a single institution from 1950 to 2010 for medullary thyroid cancer, pheochromocytoma, or paraganglioma. Patients were included if their history suggested high risk for a hereditary syndrome and never had a genetic test or had negative results on an outdated panel. We first notified 100 eligible patients, and continued to do so until we were notified by 100 patients. Once they were notified, we surveyed patients' willingness to obtain information about genetic tests, including clinical and ethical implications.

P147
Adrenocortical Carcinoma in Adults and Children: A Population-based Outcomes Study Involving 1,623 Patients K. Mahendraraj,* K. Sidhu, R.S. Chamberlain. St. Barnabas Medical Center, Livingston, NJ.

Introduction: Adrenocortical carcinoma (ACC) is a rare endocrine tumor that is typically aggressive in adult patients (AP), yet follows an unpredictable course in pediatric patients (PP) that has been little studied. This study examines a large cohort of adult and pediatric ACC patients to identify disease factors which affect clinical outcomes and that can be used to risk stratify patients from treatment and clinical trial accrual. Methods: Data on 1,623 patients with ACC was abstracted from the Surveillance Epidemiology and End Result (SEER) database (1973-2010). PP was defined as age <20 and AP as ≥20. Subgroups of PP were created as ‘< 5’, ‘5-9’ and ‘10-19’. Standard statistical analyses were performed. Results: PP comprised 6.2% (n=101) of ACC (n=1,623) while AP made up 93.8% (n=1,522). 2.8% were aged <5, 0.9% were 5-9, and 2.5% were 10-19. Mean age was 7.8 in PP and 55 in AP. Most ACC occurred in Caucasian females and presented with size >4 cm (p<0.001). PP had metastatic disease (7.1%; p<0.001) and lymph node (LN) involvement (2.9%) compared to other groups. Age 10-19 had the highest rates of metastasis and LN positivity. Mean overall survival (OS) was highest for PP (<5;7=0.001). The most common therapy for both PP and AP was surgery (77% and 66.4%). Surgical resection improved OS in both PP<10 and AP (30.6 and 13.6 years; p<0.001). PP<5 had lower overall mortality (13%) as well as better 2- and 5-year survival (90% and 90%) than all other groups; p<0.001. PP age 10-19 had the highest overall mortality (72.5%) and lowest 2- and 5-year survival (21% and 21%). Multivariative analysis identified age >10 (OR 46.6), distant disease (OR 13.7) and undifferentiated grade (OR 6.0) as independently associated with increased mortality, p<0.05. Conclusions: ACC is a rare tumor currently presenting in adult females and Caucasians with size >4 cm. PP age 10-19 and AP present with more advanced disease than PP<10. Surgical resection significantly improves OS in all groups, particularly PP<5. Older age and advanced disease are associated with increased mortality. PP<5 have the greatest ES and lowest mortality while PP age 10-19 have the worst outcomes.
P148
Loss of SMAD4 Results in Clinically Meaningful Differences in Overall Survival in Resected Gastrointestinal Neuroendocrine Tumors
C.L. Roland, * Y. Kang, D. Chatterjee, J. Estrella, A. Rashid, J.E. Lee, J.C. Yao, J.B. Fleming. MD Anderson Cancer Center, Houston, TX.

Background: Studies by comparative genomic hybridization have demonstrated that the 18q chromosomal region is frequently lost in gastrointestinal neuroendocrine tumors (GI-NET). However, the impact of DPC4/SMAD4 loss, which is located 18q21, in the pathogenesis of GI-NET remains controversial. In this study, we sought to determine the protein expression of SMAD4 in GI-NET and the impact on oncologic outcomes. Methods: To investigate the role of SMAD4 in GI-NET, a tissue microarray consisting of 33 GI-NET was constructed and analyzed by immunohistochemistry for SMAD4 expression. SMAD4 expression was classified as negative, SMAD4-low (<10% cells +) or SMAD4-high (>10% cells +). Staining results were correlated clinicopathologic features and overall survival. Results: Of the 33 tumors examined, 93% were low- or intermediate-grade and 7% high-grade. 35% of GI-NET were negative for SMAD4. 45% were SMAD4-low and 15% SMAD4-high. Expression of Chromogranin was observed in 91% of all tumors, synapto-physin in 94%, CDX2 in 64%, and CK19 in 55%. We were unable to identify any association between loss of SMAD4 and stage or tumor grade. There was an inverse correlation between loss of SMAD4 and CK19 expression, whereby 75% of SMAD4-neg tumors expressed CK19 and only 32% of SMAD4+ expressed CK19 (p=0.01). At a median follow-up of 123 months, median overall survival was 203 months. Survival differences related to SMAD4 status resulted in clinically meaningful, although statistically non-significant, differences in overall survival (SMAD4-low: 132 months vs. SMAD4-high: 203 months, p=0.058; Fig 1). Conclusions: Differences in SMAD4 expression result in clinically important differences in overall survival, although this cohort may be underpowered to detect a statistically-significant difference. Future studies with larger patient populations may be critical to evaluate the importance of SMAD4 in the pathogenesis of GI-NET.

P149
The Effect of Thyroiditis on the Yield of Central Compartment Lymph Nodes in Patients with Papillary Thyroid Cancer
T. W. Yen, S. Misustin, D. Evans, T.S. Wang. Medical College of Wisconsin, Milwaukee, WI.

Background: In patients undergoing thyroidectomy and central compartment neck dissection (CND) for papillary thyroid cancer (PTC), visualization of enlarged central compartment lymph nodes (LN) may lead to more extensive CND. We sought to determine the effect of patient age and the presence of thyroiditis on the number of malignant and total LN resected in patients undergoing CND for PTC. Methods: This is a retrospective review of a prospective database of patients with a preoperative diagnosis or suspicion of PTC who had a total thyroidectomy and CND between 4/09-6/13 who were noted to have thyroiditis on final pathology. Patients were categorized by age (18-29, 30-39, 40-49, 50-59, and ≥60 years) and compared to a control group of patients matched by age, gender, and tumor size. Results: In the cohort of 79 patients with thyroiditis, 66 (84%) were female and median age was 57 (range, 18-72) years. Overall, patients with thyroiditis had a higher median number of LN removed than those without thyroiditis (11 vs. 7; p=0.001); the median number of malignant LN was similar (0 vs. 1; p=0.095), resulting in a lower ratio of malignant:total LN (0 vs. 0.2; p=0.005). By age group, thyroiditis patients aged 18-29 and 40-49 years had statistically more LN removed; the ratio of malignant:total LN was lower in thyroiditis patients ages 18-29 and >60 (Table). For patients with or without thyroiditis, there was no difference between the age groups in the median number of LN removed (total or malignant) or in rates of recurrent laryngeal nerve injury or long-term hypoparathyroidism. Conclusions: Patients with thyroiditis and PTC who undergo CND have a greater number of LN removed but a lower proportion of metastatic LN, compared to those who do not have thyroiditis. The higher number of LN removed in the thyroiditis group may be attributed to a locoregional inflammatory process created by the thyroiditis. Although we have shown no difference in long-term complication rates, surgeons performing CND in patients with PTC and suspected thyroiditis should be aware that enlarged lymph nodes more likely represent an inflammatory, and not malignant, process.

P150
Discordance of Histological Grade between Primary and Metastatic Neuroendocrine Carcinoma

Introduction. The prognosis and management of neuroendocrine carcinoma is largely driven by histologic grade as assessed by mitotic activity or Ki67 expression. We reviewed our institutional experience to determine if the histological grade of neuroendocrine carcinoma changes between primary and metastatic tumors. Methods. We reviewed our institutional database to identify patients with metastatic neuroendocrine carcinoma. Specimens were independently reviewed and primary and metastatic tumors were categorized as low, intermediate, or high grade as determined by mitotic count or Ki-67 immunohistochemical staining. Results. We identified 18 patients with metastatic neuroendocrine carcinoma treated at our institution between 1997 and 2013 for whom complete pathological review of primary and metastatic tumors was possible. Primary lesions were found in the small intestine (n=9), pancreas (n=6), ampulla (n=1), stomach (n=1) and rectum (n=1). Metastatic lesions were hepatic (n=17) or peritoneal (n=1). Timing of metastasas was synchronous in 13 cases and metachronous in 5 cases. Histological grade was concordant between primary and metastatic tumors in 7 cases, and discordant in 11 cases. Among the discordant cases, 7 had a higher metastatic grade than primary grade, and 4 had a lower metastatic grade than primary grade. Metachronous presentation was associated with a higher likelihood of grade discordance (p=0.036); in this series, the histological grade of all metachronous metastases differed from that of primary tumors. Conclusions. There is a high prevalence of histological grade discordance between primary and metastatic foci of neuroendocrine carcinoma, particularly among patients with metachronous metastatic presentation. Given the importance of histologic grade in disease prognostication and treatment planning, this finding may be informative in the management of patients with metastatic neuroendocrine carcinoma.
Abstracts: Poster Presentations S95

P152
Surgeon and Staff Radiation Exposure During Radioguided Parathyroidectomy at a High Volume Institution S.C. Ottmann,* A. Brekke, J.D. Macatangay, D.F. Schneider, H. Chen, R.S. Sippel. Surgery, University of Wisconsin, Madison, WI.

Introduction Radioguided parathyroidectomy (RGP) requires patient injection in technetium-99m (Tc-99m) sestamibi the day of procedure. Emitted gamma rays are detected during surgery to aid dissection, and confirm resected tissue is parathyroid tissue. Source (the patient) proximity and exposure duration are key determinants of exposure levels. The aim of this study is to quantify surgeon and staff radiation exposure during RGP. Methods Faculty surgeons and first assistants wore chest radiation safety badges to measure surface and deep dose exposure during RGP procedures at a high volume endocrine surgery practice. Area monitors were also used to measure personnel potential exposure. Patients were given 9-11 mCi of Tc-99m intravenously 1 to 2 hours prior surgery. Data was prospectively collected. To correct for duration of exposure and case volume, ratios were calculated per provider based on exposure in mrem. Institutional safety requirements has 100 mrem/hr as indicator for radiation training and monitoring, and 375 mrem/month (4500/yr) as maximum allowed exposure. Results 120 RGP were performed over 6 months. Badges were worn in 82 cases (68%), and involved 3 faculty and 4 trainee assistants. Primary hyperparathyroidism was the diagnosis for 95%. 10±2 mCi was given 11±16 minutes prior surgery. Directed RGP was performed in 64%, 36% required bilateral exploration. Median case volume per provider was 13 cases (6 to 45), with median exposure of 18hrs (9 to 70). Provider deep dose exposure (DDE) was 22±10 mrem, and surface dose exposure (SDE) was 23±10 mrem. Corrected for exposure duration, DDE was 0.6±0.2 mrem/hr and SDE 0.7±0.2 mrem/hr. Corrected for case volume, DDE was 0.8±0.2 mrem/case and SDE 0.9±0.2 mrem/case. Anesthesia exposure was minimal, while mayo stand exposure ranged from one to two thirds that of the operating surgeon and assistants. Based on institutional guidelines and above data, performing 63 to 143 RGP/yr warrants training and monitoring. >2800 RGP/yr would reach maximum allowable radiation exposure. Conclusion Surgeon and staff radiation exposure during RGP is minimal. High volume centers may warrant monitoring.

P153

Introduction: Rates of incidentally found cancer in benign goiter range from 10-35%. We analyzed our population of goiter patients undergoing surgery to determine the incidence of undetected thyroid cancer and to identify risk factors predictive of malignancy. Methods: A retrospective chart review was performed of consecutive patients undergoing thyroideectomy or lobectomy for goiter (2006-2012). Patients with preoperative fine needle aspiration (FNA) with pathology Bethesda level III-VI (FLUS, follicular neoplasm, suspicious, or positive for malignancy) were excluded. Thyroid cancer includes all histologic subtypes. Micropapillary carcinomas are reported separately (papillary tumors <1 cm). Clinical and histopathologic variables were collected pre- and intra-operatively. Univariate analysis was performed using the rank-sum test, Student’s t-test or Fisher’s exact test as appropriate, and a multivariate logistic regression model was developed. Results: Of 362 patients undergoing surgery for goiter, 290 patients met inclusion criteria. Incidence of thyroid cancer was 12% (n=35). Distribution of cancers by pathology was 80% (n=28) papillary carcinoma, 20% (n=7) follicular carcinoma, and 6% (n=2) thyroid lymphoma (two patients had multiple cancers). Among cases of papillary cancer, the most common subtype was follicular variant (n=26, 93%). An additional 20% (n=58) had micropapillary tumors. Thyroid cancer patients were younger (mean 49.7 vs. 55.1 years, p=0.014) and more likely to be male (31 vs. 17%, p=0.038) than non-cancer patients. In all patients under the age of 45, the incidence of cancer was 22% (n=67); in males it was 33% (n=6). Patients with nodules identified by a healthcare provider (17 vs. 7%, p=0.042), or incidentally (11 vs. 1%, p=0.002) were more likely to have thyroid cancer. On multivariate analysis, younger age (OR=96; p=0.009) and male gender (OR=2.9; p=0.011) remained significant. Conclusion: The incidence of thyroid cancer in male patients under the age of 45 undergoing thyroid surgery for goiter was quite high (33%). This association should influence the decision to refer for surgical intervention and the discussion regarding potential surgical findings.

Table 1: Characteristics of patients with goiter presenting for thyroid surgery with or without thyroid cancer on surgical pathology

<table>
<thead>
<tr>
<th>Total goiter population (290)</th>
<th>Goiter only (265)</th>
<th>Goiter with thyroid cancer (25)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years (n=290)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>54.4 (13.3)</td>
<td>54.1 (13.1)</td>
<td>0.614</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>49.9 (41.2)</td>
<td>49.7 (41.2)</td>
<td>0.636</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>236 (111%)</td>
<td>212 (83%)</td>
<td>0.009</td>
</tr>
<tr>
<td>Male</td>
<td>54 (19%)</td>
<td>43 (17%)</td>
<td></td>
</tr>
<tr>
<td>Ethnicity (n=287)</td>
<td></td>
<td></td>
<td>0.833</td>
</tr>
<tr>
<td>Caucasian</td>
<td>181 (63%)</td>
<td>150 (63%)</td>
<td></td>
</tr>
<tr>
<td>Non-Caucasian</td>
<td>106 (37%)</td>
<td>135 (37%)</td>
<td></td>
</tr>
<tr>
<td>Non-Caucasian cases years (n=278)</td>
<td>5.97 (21.2)</td>
<td>5.69 (21.3)</td>
<td>0.182</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>4.0 (2.1)</td>
<td>4.1 (2.2)</td>
<td>0.353</td>
</tr>
<tr>
<td>Symptoms (n=285)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papillary</td>
<td>200 (71%)</td>
<td>175 (74%)</td>
<td>0.519</td>
</tr>
<tr>
<td>Micropapillary</td>
<td>53 (19%)</td>
<td>40 (15%)</td>
<td></td>
</tr>
<tr>
<td>Multifocal</td>
<td>22 (8%)</td>
<td>19 (8%)</td>
<td></td>
</tr>
<tr>
<td>Anaplastic</td>
<td>3 (1%)</td>
<td>2 (1%)</td>
<td></td>
</tr>
<tr>
<td>Invasive</td>
<td>3 (1%)</td>
<td>2 (1%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.4%)</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>Histology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papillary</td>
<td>35 (12%)</td>
<td>29 (12%)</td>
<td>0.345</td>
</tr>
<tr>
<td>Micropapillary</td>
<td>3 (1%)</td>
<td>2 (1%)</td>
<td></td>
</tr>
<tr>
<td>Multifocal</td>
<td>3 (1%)</td>
<td>2 (1%)</td>
<td></td>
</tr>
<tr>
<td>Anaplastic</td>
<td>3 (1%)</td>
<td>2 (1%)</td>
<td></td>
</tr>
<tr>
<td>Invasive</td>
<td>3 (1%)</td>
<td>2 (1%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1 (0.4%)</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>Risk factors (n=12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbit polyclonal Abs.</td>
<td>30 (12%)</td>
<td>23 (11%)</td>
<td>0.345</td>
</tr>
<tr>
<td>Shortest of breath</td>
<td>30 (12%)</td>
<td>23 (11%)</td>
<td></td>
</tr>
<tr>
<td>Non-Caucasian cases years (n=278)</td>
<td>5.97 (21.2)</td>
<td>5.69 (21.3)</td>
<td>0.182</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>4.0 (2.1)</td>
<td>4.1 (2.2)</td>
<td>0.353</td>
</tr>
<tr>
<td>Risk factors (n=12)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabbit polyclonal Abs.</td>
<td>30 (12%)</td>
<td>23 (11%)</td>
<td>0.345</td>
</tr>
<tr>
<td>Shortest of breath</td>
<td>30 (12%)</td>
<td>23 (11%)</td>
<td></td>
</tr>
</tbody>
</table>

P155
Incidence and Spectrum of Gene Mutations in Primary Hürthle Cell Thyroid Carcinoma with and without Distant Metastases R. Petric,* B. Krhin,* V. Dolzan,* N. Bestic,* 1. Institute of Oncology, Ljubljana, Slovenia; 2. Institute of Biochemistry, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia.

Background and Objectives: Hürthle cell thyroid carcinoma (HCTC) is a rare type of thyroid cancer which represents 3 to 10 % of all thyroid cancers. Patients with Hürthle cell thyroid cancer have worse prognosis than patients with follicular thyroid carcinoma. The aim of our study was to test which mutations are present in primary tumor of patients with and without metastatic HCTC. In this manner, we would like to establish which biological drugs could be potentially used in the treatment of metastatic HCTC. Methods: Altogether six patients (4 females, 2 males; median age 68 y; range 47-48 y) were included in our study. Three patients had distant metastases (median age 76 y), while three patients had no metastases (median age 47 y). Genomic DNA was extracted from paraffin embedded samples of primary tumors. Commercially available cancer panel primers, ion library kit and ion sequencer were used in order to analyze a large number of target mutations. The library of PCR amplicons covering 739 different mutations in 46 target genes was constructed using multiplex PCR approach. The libraries were used for template preparation and sequenced on the sequencer. Results: All the primary tumors harbored mutations in APC, FGFR3, and PDGFRA genes. In primary tumors of patients with distant metastases we found mutations in the following genes: EGFR (all 3 of 3 samples), ATM (2 of 3), FGFR2 (2 of 3), RET (2 of 3), C-KIT (1 of 3), VEGF (1 of 3), MET (1 of 3), NRAS (1 of 3), PIK3CA (1 of 3), PTEN (1 of 3) and p53 (1 of 3). In primary tumors of patients without metastases we found mutations in the following genes: EGFR (2 of 3), ATM (1 of 3), FGFR2 (3 of 3), RET (2 of 3), C-KIT (1 of 3), VEGF (1 of 3), PIK3CA (1 of 3) and p53 (1 of 3). Conclusion: In our patients with distant metastases of HCTC the following genes need to be further investigated as potential targets for the treatment with targeted therapy: APC, FGFR3, PDGFRA, EGFR, ATM, FGFR2, RET, C-KIT, VEGF, MET, NRAS, PIK3CA, PTEN and p53 genes.
Is There a Survival Benefit with Total Thyroidectomy for Hurthle Cell Carcinoma? A 10-year Study

S. Anantha Sathyanarayana, 1,* G. Deutsch, 1 M. Beg, 1 S. Duhner, 2 A. Kadison, 1 L. Szyter, 1 C. Conte, 1 1. Surgery, Hofstra-NSLIJ School of Medicine, Manhasset, NY; 2. Hofstra-NSLIJ School of Medicine, New Hyde Park, NY.

Introduction: Hurthle cell carcinoma (HCC) is known to be an aggressive thyroid cancer seen in 3% of thyroid carcinomas. While the standard surgical treatment is total thyroidectomy, many patients undergo thyroid lobectomy. Previous studies have reported unclear survival benefit with partial thyroidectomy for HCC. The objective of our study was to analyze long term survival in HCC patients undergoing partial or total thyroidectomy. Methods: A retrospective analysis from 2000-2010 from a tertiary care hospital tumor registry was performed. Patient demographics, tumor characteristics including tumor size, type of surgery – thyroid lobectomy (TL) versus total thyroidectomy (TT), and post operative radioiodine therapy (RI) were collected. Kaplan Meir survival curves were plotted for survival analysis among the groups.

Figure 1: 5-year and 10-year Kaplan Meir survival curves

P156

Pediatric Thyroid Microcarcinoma
J. Lerner,* M. Goldfarb.

Pediatric Thyroid Microcarcinoma: A 10-year Study

S. Anantha Sathyanarayana, 1,* G. Deutsch, 1 M. Beg, 1 S. Duhner, 2 A. Kadison, 1 L. Szyter, 1 C. Conte, 1 1. Surgery, Hofstra-NSLIJ School of Medicine, Manhasset, NY; 2. Hofstra-NSLIJ School of Medicine, New Hyde Park, NY.

Background: The incidence of thyroid microcarcinomas (TMCs) is increasing in the general population and its characteristics are well documented in older individuals. However, the incidence pattern and features of TMCs in the pediatric population has not been well described. Methods: All pediatric patients ≤19 years of age with differentiated thyroid carcinoma (DTC) were identified from the SEER registry from 1988-2009. Patients were divided into 2 groups based on tumor size: TMCs and tumors >1cm. Demographic, tumor and treatment characteristics as well as overall (OS) and disease specific survival (DSS) were compared between the 2 groups. Results: Of 1831 pediatric DTC patients, 8.4% (n=154) had a TMC; the incidence decreased during the last decade (6.5% vs 14.5%, p < 0.001). Compared to patients with DTC >1cm, multivariate
Abstracts: Poster Presentations S97

P157
Healthcare Utilization in the Pre-diagnostic Period for Neuroendocrine Tumors J. Hallet,1* C. Law,2 S. Singh.1 1. Division of General Surgery, University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada.

Background: Despite being a rare malignancy, incidence of Neuroendocrine Tumors (NET) has increased. NET diagnosis (NETD) is often delayed, but limited data is available regarding the NET peri-diagnostic period. We sought to define the pre-diagnostic healthcare utilization for NET. Methods: We conducted a retrospective cohort study using the Ontario Cancer Database and ICD 9 and 10 codes to identify NETs in Ontario from 1994 to 2009. Patient demographics, physician encounters, and radiology imaging at 2-year, 1-year and 60-day prior to NETD were abstracted. We used the Andersen Behavioral Model framework to structure the results. Results: We retrieved 4,926 NET cases. Predisposing and enabling factors included age (mean 59.9 ± 14.9 years old), gender (49.7% males), income (41.7% 4th/5th quintiles), and Health Comorbidity Index (HCl) (202.8 ± 35.2). IL6 and IL17 are markers of inflammation and neutrophil expansion. High neutrophil:lymphocyte ratios (N:L) predict poor outcome in several malignancies. In contrast, IFN-γ is associated with anti-tumor immunity. We hypothesized that N:L and IFN-γ would be associated with responses to DTc HAI. Methods: Eight patients with unresectable, progressing LMs were enrolled and completed the protocol. The first three patients received anti-CEAdTc as an intrapatient dose escalation. The last three patients received 3 DTc doses (1e10) with low dose IL2 infusions. DTc HAI were given every 2 weeks and serum cytokines measured by ELISA. Results: The mean N:L for all patients was 13.9 (range 4.8-38.1). Four patients demonstrated increased N:L after treatment with a mean N:L fold change of 1.9. The mean peak IL6 level was 133.8 pg/ml (range 24.0-288.0) while the mean peak IL17 value was 436.4 pg/ml (range 0-1346.0). The patient with the highest peak N:L (88.9) had peak IL6 and IL17 levels of 120 pg/ml and 1204.6 pg/ml. Increased N:L and IL6 levels showed a trend toward a positive correlation (r=0.77, p=0.01), and patients with high N:L (≥20) demonstrated elevated IL6 levels (202.8 ± 48.5 vs 64.8 ± 35.2, p=0.08). IL2 levels correlated with IFN-γ (r=0.89, p<0.03) but not N:L (r=0.54, p=0.29). Increasing N:L was weakly associated with rising CEA level (r=0.67, p=0.18) while elevated IFN-γ level significantly correlated with a decrease in CEA in response to HAI dtc (r=0.94, p<0.02). Conclusions: N:L increased in most patients following dTc HAI in association with elevated IL6, which may reflect inflammation in response to treatment or disease progression. Elevated IFN-γ levels correlated with serum IL2 concentrations and a decrease in serum CEA, indicating that serum IFN-γ may be a surrogate of IL2 activity and response to dTc HAI. Sponsored by SSO Clinical Investigator Award

Figure 1. Framework for Pre-diagnostic Healthcare Utilization in NET using population-based data (n=4,926).

P158

Introduction: We recently completed the phase I Hepatic Immunotherapy for Metastases (HITM) trial testing the safety of genetically modified “designer” T cells (dTc) hepatic artery infusions (HAI) for patients with incurable CEA+ liver metastases (LM). IL6 and IL17 are markers of inflammation and neutrophil expansion. High neutrophil:lymphocyte ratios (N:L) predict poor outcome in several malignancies. In contrast, IFN-γ is associated with anti-tumor immunity. We hypothesized that N:L and IFN-γ would be associated with responses to dTc HAI. Methods: Patients with unresectable, progressing LMs were enrolled and completed the protocol. The first three patients received anti-CEAdTc as an intrapatient dose escalation. The last three patients received 3 DTc doses (1e10) with low dose IL2 infusions. DTc HAI were given every 2 weeks and serum cytokines measured by ELISA. Results: The mean N:L for all patients was 13.9 (range 4.8-38.1). Four patients demonstrated increased N:L after treatment with a mean N:L fold change of 1.9. The mean peak IL6 level was 133.8 pg/ml (range 24.0-288.0) while the mean peak IL17 value was 436.4 pg/ml (range 0-1346.0). The patient with the highest peak N:L (88.9) had peak IL6 and IL17 levels of 120 pg/ml and 1204.6 pg/ml. Increased N:L and IL6 levels showed a trend toward a positive correlation (r=0.77, p=0.01) and patients with high N:L (≥20) demonstrated elevated IL6 levels (202.8 ± 48.5 vs 64.8 ± 35.2, p=0.08). IL2 levels correlated with IFN-γ (r=0.89, p<0.03) but not N:L (r=0.54, p=0.29). Increasing N:L was weakly associated with rising CEA level (r=0.67, p=0.18) while elevated IFN-γ level significantly correlated with a decrease in CEA in response to HAI dtc (r=0.94, p<0.02). Conclusions: N:L increased in most patients following dTc HAI in association with elevated IL6, which may reflect inflammation in response to treatment or disease progression. Elevated IFN-γ levels correlated with serum IL2 concentrations and a decrease in serum CEA, indicating that serum IFN-γ may be a surrogate of IL2 activity and response to dTc HAI. Sponsored by SSO Clinical Investigator Award

P159

Introduction: Centrally located liver tumors (segments 4, 5 & 8) may require extensive resections due to their close relationship to major vascular and hilar structures and their deep location. Traditionally, these centrally located tumors are resected by hemi- or extended- hepatectomies (EH) because of technical ease relative to central hepatectomy (CH). The objective was to
compare the perioperative and long-term outcomes among patients undergoing CH and EH for malignant tumors of the liver. Methods: A 2:1 EH:CH case-control cohort was generated with propensity score matching on tumor size, location and pathology from a prospective database. Clinicopathological data were analyzed using chi-square, t-test and Kaplan-Meier methodologies were appropriate. Results: 49 CH patients were matched to 98 EH patients. There were no significant differences in demographics or tumor characteristics among the 98 EH and 49 CH, and underlying liver disease was present in 28% and 42% (p<0.09), respectively. There were no significant differences in mean operative and clamping time between EH and CH: 246 vs. 254 minutes and 31 vs. 34 minutes, respectively. Mean blood loss was 741 mL (EH) and 527 mL (CH) (p=0.1), with a mean 1 unit transfusion in each group. Clavien grade 2-5 complications occurred in 46% of EH and 31% of CH (p=0.08). R0 margins were achieved in 68% of EH and 88% of CH (p<0.01). Overall and recurrence-free survival did not differ by hepatocyte type (log-rank 0.14 and 0.18 respectively). Conclusion: CH is technically safe and not time consuming in patients with centrally located tumors that may otherwise require EH. Parenchymal preservation is critical in the presence of liver disease to minimize the risk of liver failure, or when recurrence may incur repeat resections. CH has the advantage of preserving parenchyma without oncological compromise, or increased blood loss or bile leaks despite two-planes of parenchymal transection.

P160 Novel Evaluation for Hepatic Functional Reserve after Liver Resection for Liver Tumors in Combination with 99mGSA Scintigraphy and 3D-CT M. Tamiguchi,* H. Furukawa. Division of Gastroenterology and General Surgery, Asahikawa Medical University, Asahikawa, Japan.

Background and Aim It is important to develop accurate diagnostic tools that can predict the risk of poor hepatic functional reserve (PHFR) after liver resections. In this study, the role of preoperative technetium-99m-diethylenetriaminepentaacetic acid-galactosyl human serum albumin (99mTc-GSA) liver scintigraphy and CT volumetric measurement of the liver in the preoperative risk assessment for PHFR was evaluated. Patients and method Sixty-four patients who were scheduled for liver resection more than sectionectomy were included. Preoperative functional tests, postoperative liver function, and PHFR were evaluated. Patients and method Sixty-four patients who were scheduled for liver resection more than sectionectomy due to hepatocellular carcinoma were included. Preoperative functional tests, postoperative liver function, and PHFR were evaluated. Results Significant correlations were observed between postoperative 99mTc-GSA studies, conventional liver function tests, and FLV × RLV was the only significant independent predictor of PHFR. No patients with FLV × RLV above 200 had manifest PHFR. Using a FLV × RLV of 160, it was possible to predict postoperative PHFR at a sensitivity of 92%, and specificity of 83%. Conclusion Preoperative measurement of 99mTc-GSA and the remnant liver volume on CT proved valuable in assessing the risk of liver failure after liver resection.


Background Approximately 5% of patients with breast cancer develop liver metastases as the only sign of disseminated disease. Well selected patients are candidates for local treatment of their breast cancer liver metastases (BCLM) with surgery or ablation. The aim of this study was to analyze prognostic factors associated with survival in patients undergoing liver resection or ablation for BCLM. Methods A review of metastatic breast cancer patients undergoing liver resection and/or ablation for BCLM at a single institution from 1993 to 2013 was performed. Survival was calculated from the time of either liver resection or ablation. Analysis of factors associated with outcome was performed with standard Kaplan-Meier and Cox-Regression methods. Results Seventy patients underwent local treatment for their BCLM; 52 patients had liver resections of which 4 had concomitant ablations and 18 patients had ablations as the sole treatment. The average age was 53±12.3 years at the time of BCLM treatment. The primary breast tumor was stage I in 28% of patients and the median recurrence-free interval (RFI) from breast surgery to diagnosis of BCLM was 4.86 years (range: 0.2-20.5). Most BCLM were solitary (62%), unilobar (70%), and smaller than 5cm (74%). Median follow-up was 36.2 months (range: 2-129). Overall 5-year survival was 37%, median overall survival was 49.6 months (range: 2-129), and median recurrence-free survival was 18.4 months (range: 1-118). Multivariate analysis identified 2 independent prognostic factors associated with improved overall survival: absence of adjuvant chemotherapy after breast surgery and RFI of more than 2 years. There were no significant prognostic factors associated with recurrence-free survival after liver-directed treatment of BCLM. (Table 1) Conclusions Liver-directed therapies (resection, ablation) are appropriate and may lead to prolonged survival in carefully selected patients. Absence of chemotherapy treatment after resection of the primary, likely a surrogate for early stage disease, and RFI of more than 2 years were the only independent predictors of outcome.


INTRODUCTION: Radiofrequency ablation (RFA) provides a viable therapeutic alternative to surgery in the treatment of hepatocellular carcinoma (HCC) in the setting of unresectable disease or poor patient physiology, including cirrhosis. Our study evaluates the short- and long-term outcomes of RFA when utilized as first-line therapy in patients with non-operative HCC. METHODS: In this dual-institutional retrospective review of prospectively maintained HCC databases, with institutional review board approval, all patients who received RFA as primary treatment for HCC from 1995 to 2008 were identified. Patient demographic and clinicopathologic characteristics were reviewed. Short-term peri-procedural outcomes were measured. Long-term outcomes, including disease-free and overall survival, were analyzed. RESULTS: 1,168 patients with 2,116 lesions were treated with RFA during the study period. Median age of the cohort was 58, with 57% of patients being male. 51.2% of patients had Child’s class A, 40.5% Child’s class B, and 8.3% Child’s class C cirrhosis. 62.8% of RFAs were performed percutaneously (pRFA) and 37.2% via an open approach (oRFA). Patients undergoing pRFA had fewer and smaller tumors than oRFA (median number of tumors 2 vs. 3, median size 2.7 vs. 4.0cm). Overall procedural complications and mortality rates were 2.5% and 1.5%, respectively. Causes of death included liver failure and hemorrhage.
sequelae. With a median follow-up time of 5 years, overall recurrence rate was 11%, whereas 49% of patients had developed new liver or extrahepatic lesions. 5-year disease-free survival (DFS) was higher in the pRFA group compared to their oRFA counterparts (44.8% vs. 24.1%); likewise, 5-year overall survival (OS) was higher in the pRFA group (57.5% vs. 47.0%). CONCLUSIONS: RFA is a safe and effective local treatment option for patients with non-operable HCC lesions. It can provide long-term local control and may achieve long-term survival, especially when transplant livers are not readily available.

**P163**
Defining the Benefit of Adjuvant Therapy following Resection for Intrahepatic Cholangiocarcinoma
H. In,1* S. Sharpe,1 M.S. Baker,2 R.R. Weichselbaum,1 M.S. Talamonti,2 M.C. Posner,1 1. Surgery, University of Chicago, Chicago, IL; 2. NorthShore University HealthSystems, Evanston, IL.

Background: The role of adjuvant treatment following resection of intrahepatic cholangiocarcinoma has not been well-defined. Methods: The National Cancer Data Base (NCDB) was used to identify patients from 1985 to 2011 diagnosed with non-metastatic intrahepatic cholangiocarcinoma who underwent surgical resection. Kaplan-Meier and Cox regression analyses evaluated differences in overall survival between patients who did and did not receive adjuvant therapy post-resection. Results: Of the 1,674 patients who underwent resection for cholangiocarcinoma, 1,191 (71.2%) had an R0 resection, 432 (25.8%) had an R1 resection and 51 (3.1%) had an R2 resection. In R0 resection patients, 194 (16.3%) patients received chemotherapy and 159 (13.4%) received chemoradiation. In R1 or R2 resection, 89 (18.4%) received chemotheraphy and 157 (32.5%) received chemoradiation. By multivariate regression, patients who were younger, had positive lymph nodes, had positive margins and diagnosed in more recent years were more likely to receive adjuvant therapy. The median overall survival after an R0 resection was 33.0 months (95% CI 30.3, 36.2), 17.0 months (95% CI 15.4, 20.0) after R1 resection and 7.7 months (95% CI 3.8, 12.9) after R2 resection. Cox regression analysis identified older age, higher Charlson score, lymph node positivity, higher tumor grade and positive margins as factors associated with decreased median overall survival. All patients, regardless of completeness of resection, had an overall survival benefit after adjusting for the above prognostic factors when they received chemotherapy (R0 resection: HR=0.68, p=0.002; R1/R2 resection: HR=0.65, p=0.006), however the benefit of chemoradiation therapy was limited to those with R1/2 resection (R0 resection: p=0.29; R1/2 resection: HR=0.61, p=0.0001). Conclusion: Positive lymph nodes, positive margins and high tumor grade are critical determinants of survival after resection for intrahepatic cholangiocarcinoma. Adjuvant chemotherapy had an overall survival benefit regardless of resection status. However, only those patients with positive margin resection benefited from the addition of postoperative radiation therapy.

**Benefit of adjuvant therapy according to margin status (adjusted model)**

<table>
<thead>
<tr>
<th></th>
<th>R0 resection patients (n=1191)</th>
<th>R1/R2 resection patients (n=883)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>p-value</td>
</tr>
<tr>
<td>No adjuvant therapy (n=1075)</td>
<td>ref</td>
<td>ref</td>
</tr>
<tr>
<td>Chemotherapy (n=238)</td>
<td>0.68</td>
<td>0.002</td>
</tr>
<tr>
<td>Chemoradiotherapy (n=316)</td>
<td>0.88</td>
<td>0.195</td>
</tr>
</tbody>
</table>

**P164**
Non-invasive Radiofrequency Field-induced Hyperthermia Inhibits Homologous Recombination Mediated Repair of Gemcitabine-Stalled Replication Forks
M. Raoel,1 C. Zhu,1 B. Ciminoja,1 H. Liu,2 S. Con,2 L. Wilson,2 S.A. Curley,3 1. University of Arizona, Tucson, AZ; 2. MD Anderson Cancer Center, Houston, TX.

Background: Hepatocellular carcinoma is a worldwide problem with rapidly rising incidence in the U.S. At diagnosis more than 75% of patients are not amenable to curative therapy. Conventional chemotherapy is highly toxic and resistance develops rapidly. Here we investigate the effect of non-invasive radiofrequency field (RF) induced-hyperthermia on repair of gemcitabine-stalled-replication forks in the DNA of liver cancer cells and tumors in vivo. Methods: Human liver cancer cell lines (Hep3B, SNU449 and HepG2) were evaluated. Reproductive viability was measured by clonogenic assay. Ther.

**P165**
Impact of Volume on Outcomes in Liver Surgery: Hospital Volume may Outweigh Surgeon Volume

Background: Favorable outcomes have been associated with institutions and surgeons that perform a high-volume of complex surgical procedures. However, there are limited data describing the impact of institutional volume on liver surgery outcomes performed by high- and low-volume surgeons. We used a statewide database to investigate the association between surgeon caseload, hospital volume, and outcome. Methods: Patients undergoing elective liver resection for malignancy between 1994 and 2000 were identified from the New York State Statewide Planning and Research Cooperative System (SPARCS) database. The SPARCS data system collects patient level data on patient characteristics, diagnoses, treatments, and charges for every hospital discharge in New York State. Centers with 3 or more liver surgeons were selected for analysis. Surgeons and institutions were considered high-volume if they performed greater than 15 and 30 cases per year, respectively. Outcomes including 30-day mortality were compared between high- and low-volume surgeons and institutions. Multivariate analysis was conducted to identify factors associated with improved outcome. Results: 2549 elective liver resections were performed at 35 institutions by 50 individual surgeons. A trend toward improved outcome was observed with high-volume centers (HVC, n=2) compared to low-volume centers (LVC, n=33) (mortality: 3.6% vs. 4.5%). Outcomes by high-volume surgeons (HVS, n=9) and low-volume surgeons (LVS, n=41) were comparable (mortality: 4.0% vs. 4.0%). LVS operating at HVC had a significantly lower mortality than HVS operating at LVC (3.4% vs. 5.3%; p<0.05). Multivariate analysis revealed extent of hepatic resection (p=0.01), presence of comorbid conditions (p=0.01), patient age (p=0.05), and hospital volume (p=0.05) were significantly associated with mortality. Surgeon volume was not associated with outcome (p=0.05). Conclusion: In this study, hospital volume was a significant predictor of mortality in hepatectomy performed for cancer while individual surgeon volume was not. Consideration should be given to referral patterns that favor performance of hepatic surgery in HVC over HVS in LVC.

**P166**
Prooperative CA 19-9 Kinetics as a Prognostic Variable in Radiographically Resectable Pancreatic Adenocarcinoma
E. Brown,* R. Canter, R. Bold. Department of Surgery, University of California, Davis, Sacramento, CA.

Introduction: Cancer antigen 19-9 (CA 19-9) is a well-studied marker of tumor burden in pancreatic cancer. Serial levels during chemotherapy correlate with treatment response and survival; a decrease following surgical resection is also correlated with survival. However, very little is known about the kinetics of CA 19-9 in the absence of therapy. We hypothesize that CA 19-9 kinetics in the preoperative period in the absence of any therapy predicts both...
resectable rates at time of surgery as well as survival. Methods: Retrospec-
tive review of an institutional database of patients with pancreatic adenocarci-
oma identified two groups of patients with two separate pre-operative CA 19-9
levels prior to planned pancreaticoduodenectomy. Primary outcome mea-
sures were resectability and overall survival. Univariate analysis was per-
formed using Chi-squared analysis. Survival analysis was performed with
Kaplan-Meier estimates. Results: Sixty-four percent of patients had resectable
disease (46 of 72 patients). Unresectable patients had a higher absolute change
in CA 19-9 than patients with resectable disease (median: 93 U/ml vs. −38
U/ml). A predictive threshold of ≥50 U/ml identified 58% of patients with
unresectable disease, while only 26% of patients who were resectable
exceeded this threshold (p=0.008). Unresectable patients also had a higher
rate of change in CA 19-9 than patients with resectable disease (median: 4
U/ml vs. −1 U/ml/day). When a predictive threshold of >10 U/ml/day for
rate of change in CA 19-9 was used, only 1% of resectable patients exceeded
this threshold, while 35% of unresectable patients had a rate ≥10 U/ml/day
(p=0.004). Survival analysis of the entire group revealed that a change in CA
19-9 ≥50 U/ml and a rate of change of CA 19-9 ≥10 U/ml/day each pre-
dicted improved survival (p=0.01, p<0.001); however, for patients with
resectable disease, CA 19-9 changes did not predict survival. Conclusions:
Preoperative change in CA 19-9 and the rate of change are useful tools to
predict resectable disease for pancreatic cancer. These variables also predict
overall survival; however, it does not predict survival for those with resectable
disease.

P167 Non-neoplastic Liver Fibrosis Staged by the Modified Ishak Method Predicts Two-year Recurrence for Patients with Early Hepatitis-B Associated Hepatocellular Carcinoma

Mount Sinai Medical Center, New York, NY.

Hepatocellular carcinoma (HCC) associated with hepatitis B (HBV) infec-
tion is a leading cause of cancer-related mortality worldwide, and there is a
need to identify factors in early HCC associated with poor outcomes. Ishak
fibrosis stage has been found to be an important prognostic indicator for HBV-HCC,
and the aim of this analysis was to investigate the role of Ishak fibro-
sis stage in prognosis among early tumors (<2cm in greatest diameter).
Data were obtained for patients with HBV-associated HCC treated by pri-
mary hepatic resection at a single Western institution between 1988 and 2013.
A dedicated liver pathologist blinded to patient outcomes performed a his-
tologic assessment of all liver resection specimens and evaluated fibrosis
according to the modified Ishak method (fibrosis stages 0-6) in addition to
other histopathologic variables. Other data were obtained via medical record
review. Cox proportional hazards regressions adjusted for vascular invasion
and histologic differentiation were used to compare disease-free survival and
short-term recurrence in these groups. Fifty-three resection patients with a
maximum tumor diameter <2cm were available for analysis. Median survival
for these patients was 50.7 months, and median disease-free survival was
30.0 months. Within five years of resection there were 4 deaths and 21 recur-
rences, and 14 recurrences occurred within two years of resection. Adjusted
Hazard Ratios (HR) and 95% confidence intervals for recurrence-free sur-
vival (time to recurrence or death) showed that each increase in stage of fibro-
sis was associated with a 40% increased risk of recurrence or death overall
[HR=1.40 (1.02-1.94)] and a 65% increased risk of recurrence within two
years [HR=1.65 (1.06-2.57)]. Results indicate that even among early HBV-
HCC, increased fibrosis and cirrhosis are associated with higher risk of early
recurrence. The significant impact of liver fibrosis on HCC progression is
established early on and is independent of tumor differentiation and vascu-
lar invasion.

A.D. Singhi, H.J. Zeh. University of Pittsburgh Medical Center, Pitts-
burgh, PA.

Introduction: Pancreatic intraepithelial neoplasias (PanINs) are well estab-
lished as a precursor lesion to pancreatic cancer. While PanINs at the tran-
ssection margin have not been shown to affect the dismal survival outcomes
for pancreatic cancer, it is not known whether the presence or grade of PanINs
in the gland may predispose patients who do achieve long-term survival to
having a localized recurrence or a second primary mass in the remnant gan-
creas. Methods: After IRB approval was obtained, a retrospective chart review
of patients with long term survival (defined as more than two years) from
pancreatic ductal adenocarcinoma (PDA) who underwent a margin negative
pancreatic resection between 2007 and 2010 was performed. Results: One hun-
dred and seven patients at a multi-site single academic institution were iden-
tified as having more than a two-year survival from a pancreaticoduodenec-
tomy or distal pancreatectomy for PDA. Forty-six patients had PanIN-3, 31
patients had PanIN-2, 10 patients had PanIN-1A or -1B, 2 patients had no
PanINs and PanIN status in the resected gland was noted for 18 patients.
There was no statistically significant difference in overall survival or time
to localized recurrence based on PanIN grade. Five patients developed a second
mass in the remnant pancreas with an average time to progression of 35.6
months (range 16.7 – 59.2 mo). Four patients have had resection of the rem-
nant pancreas and one has undergone chemotherapy treatment with plans for
re-resection. All five patients were alive at last follow-up. Of these five patients,
three patients had PanIN-3 in their original resected pancreatic specimen, one
patient had PanIN-2 and one patient had PanIN-1B. Conclusion: For patients
with a resected pancreatic ductal adenocarcinoma, the presence or grade of
PanIN lesions in the surgical specimen does not affect outcome or time to local-
ized recurrence.

The Positive Postoperative CEA is an Independent Predictor of Recurrence for Patients who underwent Curative-intent Treatment for Colorectal Liver Metastases

Memorial Sloan-Kettering Cancer Center, New York, NY.

INTRODUCTION: The importance of CEA for monitoring recurrence for Colorectal Liver Metastases (CRLM) after resection continues to be debated. The objective of this study is to assess the postoperative CEA as independent predictor of recurrence for patients with CRLM after hepatectomy with cura-
tive-intent treatment. METHODS: Patients were identified from a prospec-
tively maintained CRLM database and studied retrospectively. Patients who
had extrahepatic disease, initially unresectable CRLM, received intra-arterial
chemotherapy, exclusive tumor ablation or previous metastasectomies were
excluded. All patients in this study received adjuvant systemic chemotherapy
for CRLM including 5-fluorouracil, oxaliplatin or irinotecan. Post-operative
CEA is defined as the first CEA assessment performed within the first six
months after operation. Univariate and Cox regression models were developed
to determine factors independently associated with recurrence in two years.
RESULTS: Between 1997 and 2007, 318 consecutive patients were studied
and 168 patients (52.8%) experienced recurrence in two years. Among the post-
operative CEA cutoffs tested and identified as independent predictors, a post-
operative CEA ≥15 ng/ml obtained the highest HZ (1.87 – 95% C.I. 1.09 –
3.2; p=0.023) and it was chosen to be included in the survival analysis in the
multivariate model. The postoperative CEA ≥15 ng/ml presented specificity
of 96% and positive predictive value of 81.8% for recurrence. On multivari-
ate analysis, age ≥70 years, positive lymph node at primary tumor resection,
disease free interval ≥12 months, number of lesions ≥1, largest lesion ≥5
cm, presence of positive margins, and postoperative CEA ≥15 ng/ml were
independent predictors of recurrence in two years. Kaplan-Meier curves of
recurrence in two years were made according to Clinical Risk Score (CRS-
high [3 – 5] and low [0 – 2]), postoperative CEA ≥15 ng/ml or lower and
combining them (FIGURE). DISCUSSION: This study suggests that the post-
operative CEA is a worthwhile test for predicting recurrence in two years, and
being independently associated with recurrence.
Resistance to PI3K Inhibition in Pancreatic Cancer is Mediated through the ErbB Pathway


KRAS mutational activation plays a critical role in tumorigenesis, but exactly which downstream KRAS effector pathway is critical for this role remains less clear. One of the most studied downstream pathways is the phosphatidylinositol-3-kinase (PI3K) pathway which mediates cellular growth and survival. We evaluated the effect of BKM120 (a pan-class 1 PI3K inhibitor), currently in Phase I/II clinical trials, using cell lines and patient derived xenograft (PDX) models and assessed potential mechanisms of BKM120 resistance. Kinome reprogramming has been found as a mechanism of resistance to MEK inhibition in triple negative breast cancer. We hypothesized that kinome reprogramming may play a role in resistance to PI3K inhibition in pancreatic cancer. A panel of 10 pancreatic cancer cell lines were evaluated for response to BKM120 using a cell viability assay. A pancreatic cancer PDX mouse model, where actual tumors from patients are directly engrafted into mice, was used to assess BKM120 response in vivo. PDX were treated with vehicle or BKM120 (40mg/kg) daily for 28 days. Kinome reprogramming was evaluated using multiplexed inhibitor bead/mass spectrometry assays and receptor tyrosine kinase arrays. Combination indices were calculated using Compusyn. 20% tumor growth inhibition was observed in PDX (p=0.017) treated with BKM120 compared to surgery alone. Adjuvant RT versus S alone were younger (63 vs. 69 years, p<0.001), had more advanced tumors (69 vs. 53% T3/T4 tumors, p<0.001), and more frequent lymph node metastasis (73 vs. 40%, p<0.001). Multivariate analysis demonstrated that adjuvant radiation was not associated with improved overall survival (HR 0.88; 95% CI: 0.73-1.07, p=0.2). In PS matched cohorts, adjuvant RT failed to improve both overall survival (27 vs. 29 months, p=0.58) and disease specific survival (36 vs. 40 months, p=0.92) when compared to surgery alone. Adjuvant RT, in PS-matched multivariate models, was not associated with improved overall survival (Multivariate HR 0.84; 95% CI: 0.65-1.07, p=0.16). Conclusion: Adjuvant RT does not confer a survival benefit for patients with ampullary tumors. The lack of disease specific survival benefit suggests that it may also not be beneficial to prevent local recurrences and related mortality. Currently in practice adjuvant RT is administered for high risk ampullary adenocarcinoma, without proven benefit.

Table: Multivariate analysis of prognostic variables for overall survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.01</td>
<td>1.01-1.02</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Adjuvant XRT</td>
<td>0.88</td>
<td>0.73-1.07</td>
<td>0.20</td>
</tr>
<tr>
<td>Primary Tumor (T Stage)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>Ref</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>T2</td>
<td>0.57</td>
<td>0.71-1.33</td>
<td>0.86</td>
</tr>
<tr>
<td>T3</td>
<td>1.49</td>
<td>1.09-2.01</td>
<td>0.01</td>
</tr>
<tr>
<td>T4</td>
<td>1.67</td>
<td>1.22-2.18</td>
<td>0.02</td>
</tr>
<tr>
<td>Lymph Node Status, NO</td>
<td>2.17</td>
<td>1.78-2.64</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Tumor Grade</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Well differentiated</td>
<td>Ref</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>1.37</td>
<td>1.00-1.88</td>
<td>0.05</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>1.61</td>
<td>1.16-2.33</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Surgery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radical</td>
<td>1.02</td>
<td>0.86-1.22</td>
<td>0.82</td>
</tr>
</tbody>
</table>

Defining the Role of Adjuvant External Beam Radiotherapy on Resected Adenocarcinoma of the Ampulla of Vater

T.J. Miura,* A. Amini, T.T. Jayakrishnan, S. Tsai, K.K. Christians, F. Johnston, T.C. Gamblin, K.K. Turaga. Medical College of Wisconsin, Milwaukee, WI.

Introduction: The role of adjuvant radiotherapy in the treatment of ampullary carcinoma remains unclear. We hypothesized that adjuvant radiotherapy (RT) does not improve survival following resection for adenocarcinoma of the ampulla of Vater (AC). Methods: The Surveillance, Epidemiology, and End Results database was queried for all patients with nonmetastatic AC who underwent surgery (S) from 2004-2010. Propensity score (PS) modeling was applied to create balanced cohorts of patients that would be equally likely to receive radiation based on age, T-stage, N-stage, nature of surgery and grade of the tumor. Cox proportional hazards models were used to compare survival. Results: Of 1,287 patients identified, 329 (25.6%) patients received adjuvant RT. Unadjusted median overall survival for patients receiving adjuvant RT compared to surgery alone was 27 vs. 36 months (p=0.14). Patients receiving adjuvant RT versus S alone were younger (63 vs. 69 years, p<0.01), had more advanced tumors (69 vs. 53% T3/T4 tumors, p<0.01), and more frequent lymph node metastasis (73 vs. 40%, p<0.01). Multivariate analysis demonstrated that adjuvant radiation was not associated with improved overall survival (HR 0.88; 95% CI: 0.73-1.07, p=0.2). Disease specific survival (36 vs. 40 months, p=0.92) was also not improved by adjuvant RT. Conclusion: Adjuvant RT does not confer a survival benefit for patients with ampullary tumors. The lack of disease specific survival benefit suggests that it may also not be beneficial to prevent local recurrences and related mortality. Currently in practice adjuvant RT is administered for high risk ampullary adenocarcinoma, without proven benefit.
P172
**Molecular MR Imaging of Collagen to Diagnose Liver Fibrosis**

Introduction: The gold standard in diagnosing liver fibrosis remains biopsy despite its limitations, which include sampling error, and complications related to the invasiveness of the procedure. The goal of this study was to utilize a peptide probe targeted to type I collagen linked to gadolinium (Gd) with the goal of using magnetic resonance imaging (MRI) to non-invasively diagnose biliary fibrosis in a rodent model. Methods: Male CD Rats underwent bile duct ligation (BDL) or sham laparotomy. To assess liver fibrosis at different stages, rats were MR imaged on post operative day 4, 10, or 18 on a 1.5T clinical MRI system with a custom-built volume coil. A series of T1-weighted and T1-mapping images were acquired prior to and for one hour after injection of the collagen-targeted contrast agent, EP-3533. Following imaging, animals were euthanized and liver tissue was removed for hydroxyproline analysis (total collagen), Gd concentration (probe uptake) and Sirius red staining to determine an Ishak fibrosis score. Results: BDL in rats led to fibrous expansion of the bile ducts, which was evident after 4 days, and more dramatic after 10 days. By 18 days, the liver was cirrhotic as indicated by histology as well as markedly increased serum bilirubin levels. Injection of EP-3533 increased the relaxation rate enhancement (ΔR1 where ΔR1 = 1/T1 post – 1/T1 pre) of the liver and a significant difference was seen between sham controls and BDL rats at post operative day 18. These findings consistently correlated with measurements of Gd uptake, which was increased in animals that underwent BDL with a significant difference observed at post operative day 18. Conclusion: We have developed a non-invasive, collagen-enhanced MRI technique for the diagnosis of biliary fibrosis, and validated it in a rodent model. This technique may also be more broadly applicable to other forms of fibrosis, and may be especially useful in patients when biopsy is not feasible, as well as in clinical trials to monitor the efficacy of anti-fibrotic therapies over time.

P173
**Survival Benefit of Adjuvant Therapy for Resectable Pancreatic Cancer (PC) Patients Treated with Neoadjuvant Therapy**

Background: Adjuvant therapy has been shown to offer a survival benefit to patients (pts) with PC as compared to surgery alone. For pts who receive neoadjuvant therapy and then surgery, the benefit of adjuvant therapy is unknown. Methods: We identified all pts with PC who completed all intended neoadjuvant therapy and surgery from 2008-2013. Data regarding demographics, neoadjuvant treatment history, surgical outcomes, pathologic, and survival data were abstracted from electronic medical records. Results: We identified 67 pts; 42 (63%) received additional postop adjuvant therapy and 25 (37%) did not. Pts who did not receive adjuvant therapy were more likely to be age 75 or older (10 [71.4%] of 14 vs. 13 [25.0%] of 52, p =0.002), have a higher Charlson Comorbidity Index (mean 3.56 vs. 2.46, p =0.003), and require more days in hospital during neoadjuvant therapy (2.75 vs. 7.12 days, p =0.22). Pts were also less likely to receive adjuvant if they were discharged to a skilled nursing facility (SNF) after surgery (p = 0.001). The receipt of adjuvant therapy was associated with node positive disease status; 18 (42.9%) of 42 vs. 5 (20.0%) of 25, p = 0.04. Overall median survival for the entire cohort was 36.5 months. The median survival for node positive pts who received adjuvant vs. no adjuvant therapy was 26.2 vs. 10.3 months, (log rank p = 0.08) respectively. Median survival for node negative pts who received adjuvant therapy was 31.4 months and was not met by the pts who did not receive adjuvant (p = 0.54). Conclusion: As expected, a significant proportion of pts who receive neoadjuvant therapy and surgery do not receive adjuvant therapy. As shown for the experience with surgery alone, older age and greater comorbidities are associated with failure to receive adjuvant therapy. Node positive disease after neoadjuvant therapy is a powerful predictor of poor outcome especially in the absence of additional systemic therapy. Our translational research laboratory is focusing on this patient population where novel approaches to systemic therapy are needed.

P174
**Squamous Cell Carcinoma of the Pancreas: A Population-based Clinical Outcomes Study with 357 Patients**
K. Mahendraraj,* J.A. Di Como, R.S. Chamberlain. St. Barnabas Medical Center, Livingston, NJ.

Introduction: Squamous cell carcinoma of the pancreas (SCP) is a very rare and aggressive exocrine pancreatic neoplasm. Clinical information relating to SCP is scant and is derived primarily from small retrospective studies. This study sought to examine a large cohort of SCP in order to determine demographic, clinical, and pathologic factors characteristic of SCP patients, and to compare SCP clinical outcomes to pancreatic ductal adenocarcinoma (PDAC). Methods: Demographic and clinical data on 174,515 patients with pancreatic cancer were abstracted from the SEER database (1973-2010). 347 SCP and 102,735 PDAC formed the study groups. Standard statistical analyses were performed. Results: SCP comprised 0.3% and PDAC made up 58.9% of all pancreatic cancers identified. The mean age of the SCP and PDAC patients was similar (68.7±12 vs. 68.2±12). Both SCP and PDAC was more common in Caucasians (73.7% and 74.6% (PDAC)) and in the head of the pancreas (44.3% and 50.9% (PDAC)). SCP were more often poorly differentiated, >4cm, and presented with distant disease compared to PDAC, p<0.05. The majority of SCP and PDAC patients were not treated with surgery or radiation therapy (67.5% and 68.8%). SCP mean survival was significantly lower than PDAC (70.4 vs 0.85 years), however SCP patients benefited more from both surgery (3.8 years) and a combination surgery and radiotherapy (3.8 years) than PDAC patients (2.2 years and 3.0 years), p<0.001. Multivariate analysis identified age over 65 (OR 1.4), pancreatic ductal origin (OR 1.5), metastatic disease (OR 2.3), and poor grade (OR 2.3) as associated with mortality for SCP, p<0.005. Conclusions: Pancreatic SCP is a rare malignancy that presents with poorer grade, larger tumor size, with a higher rate of metastatic disease than PDAC. Despite these aggressive features, SCP patients amenable to surgical or combined surgery/radiation therapy derive greater survival advantage than similarly treated PDAC. Surgical resection should be considered in all SCP patients with resectable disease. Older age, pancreatic ductal origin and advanced stage or grade are associated with increased mortality among the cohort studied.
**P175**

**Short and Long-term Outcomes for Transarterial Radioembolization with Yttrium-90 Microspheres for Hepatocellular Carcinoma**

H.F. Schoellhammer, 1* P.H. Ituarte, 1 Y. Chen, 2 J. Park, 3 H. Marx, 4 J. Kessler, 4 G. Singh, 1 J.J. Park, 4 J. Kim. 1

1. Division of Surgical Oncology, City of Hope Comprehensive Cancer Center, Duarte, CA; 2. Department of Radiation Oncology, City of Hope Comprehensive Cancer Center, Duarte, CA; 3. Department of Diagnostic Radiology, City of Hope Comprehensive Cancer Center, Duarte, CA; 4. Division of Interventional Radiology, City of Hope Comprehensive Cancer Center, Duarte, CA.

**Introduction:** Selective internal radioembolization treatment (SIRT) with yttrium-90 (Y-90) microspheres has been shown to be safe and efficacious for unresectable hepatocellular carcinoma (HCC). Our goals were to report our clinical experiences and survival outcomes with SIRT at a non-transplant center. Methods: Patients with unresectable HCC who underwent SIRT from 2007-2012 were reviewed. Patient demographics were evaluated and complications graded with Common Terminology Criteria for Adverse Events. Kaplan-Meier (KM) survival curves were constructed and compared with the log-rank test. Predictors for survival in KM models were tested with multivariable Cox proportional hazards analysis. Results: During the study period 53 patients (n=37, male) underwent 89 SIRT treatments. Mean age was 68 (range 16-86); mean follow-up time from first treatment was 12.7 months. Overall, 24 patients received one treatment, and 29 patients received ≥2, with 95% outpatient treatments. SIRT was well tolerated; fatigue, upper quadrants abdominal pain, and nausea were the most common adverse effects (55% of patients), all resolving over 1-2 weeks. Serious complications included pancreatitis (n=1, Grade 3), radiation pneumonitis (n=1, Grade 5), and hepatic decompensation (n=2, Grade 1 and 3). Median overall survival (OS) for the cohort was 13.4 months. Twenty-four patients previously underwent other liver-directed therapies; however, no difference in OS was seen compared with patients receiving SIRT de novo (15.4 vs. 12.4 months, respectively; p=NS). Patients undergoing ≥2 SIRT had significantly longer OS than those undergoing 1 treatment (18.8 vs. 5.7 months, respectively; p=0.015). On multivariable analysis, receipt of ≥2 SIRT significantly predicted OS at 3 years (HR 0.43, 95% CI 0.22-0.87, p=0.018). Conclusion: Patients with unresectable HCC can be safely and effectively treated with Y-90 microspheres SIRT in a non-transplant center. Our experience verifies the safe application of SIRT and suggests that patients who undergo multiple SIRT treatments may have biology of disease or treatment response that results in prolonged survival.

**P176**

**Differential Hepatic MicroRNA Expression in an Animal Model of Intrahepatic Cholangiocarcinoma**

J. Rose, 1* E. Nearing, 1 Y. Li, 2 J. Nelson, 1 J. Kowdley, 3 F. Rocha. 1

1. Virginia Mason Medical Center, Seattle, WA; 2. Benaroya Research Institute, Seattle, WA.

**Introduction:** Intrahepatic cholangiocarcinoma (IHC) is a rare, often difficult to treat primary malignancy of the liver with a median survival of 6-12 months for unresectable disease. MicroRNA (miR) is a class of non-coding RNA molecules known to regulate oncogenic gene transcription. We aimed to identify differentially expressed miRs in a drug-induced rat model of IHC.

**Methods:** Fischer rats were administered 300 mg/L of thioacetamide in drinking water ad libitum to induce IHC. Tumor-bearing and control livers were harvested at 22 weeks and next generation RNA sequencing was utilized to compare hepatic miR profiles between thioacetamide treated rats and age-matched controls in triplicate. Resultant miR counts were normalized using Kernel Density Estimation. MiRs with a greater than twofold change and a read count of at least 4 per million were considered for further analysis.

**Results:** All thioacetamide treated animals developed IHC by 22 weeks confirmed with histology. At a median read depth of 6.6 million per sample, 547 unique miRs were detected between all samples. Based on cut-off criteria, 112 miRNAs were included for analysis with a median fold change of 2.5 (See Figure). Of these, mir-200, mir-215, mir-130, and mir-181 were amongst the most significantly overexpressed in tumor tissue; while let-7 and mir-29 were amongst the most underexpressed when compared to control livers (FDR <0.05). These six miRs have previously been demonstrated to regulate genes associated with the development of human hepatocellular and cancer. The most abundant miR in IHC was mir-21, however its expression was less than 2 fold compared to normal liver. **Conclusion:** mir-200, mir-215, mir-130, and mir-29 are differentially expressed in a drug-induced rat model of IHC. This model may serve to study miR gene targets for design of novel therapeutic strategies in IHC.
**P177**

Impact of Repeat Resection for Borderline Colorectal Liver Metastases


Background: Liver resection is the only treatment of potential cure, however, recurrence rate is extremely high especially in patients of borderline resectable colorectal liver metastases (CLMs). Although repeat resection is the only curative therapy, the outcome after repeat resection is unclear. This study analyzed the impact of repeat resection for borderline resectable CLMs.

METHODS: Between 1999 and 2008, a total of 274 patients underwent hepatectomy resection for CLMs and 251 were liver limited CLMs. In this study, 5 nodules or >5cm is defined as borderline CLMs (BL-CLMs). Of 251 patients, the number of non BL-CLMs and BL-CLMs were 251 and 97. Predictors of survival were analyzed focusing on BL-CLMs. RESULTS: After median follow up of 50 months, 5-year overall and recurrence free survival after liver resection were 41%, 13% in the BL-CLMs, which were significantly poorer compared with the non BL-CLMs (68%, p=0.0003, 32%, p=0.00001), respectively. Among 97 patients with BL-CLMs, 86 (88%) developed recurrence. Repeat resection underwent in 36 (37%) patients including 35 patients with repeat liver resections (2nd; n=24, 3rd; n=8, 4th; n=3) and one patient with pulmonary resection. In 86 patients with recurrence, 5-year survival is significantly improved in repeat resection group compared with non-resection group (55% vs. 12%, p<0.001). The recurrence free survival in patients with repeat resection is the similar compared with those of non resectable recurrence (4 months vs. 5 months, p=0.873). Univariate and multivariate analysis revealed the repeat resection was the only favorable prognostic factor (55% vs 35%, p=0.035). Five or more nodules (p=0.013) and positive resection margin at liver resection (p=0.029) were identified as a poor prognostic factor for recurrent free survival in univariate and multivariable analysis. Thirty seven patients (38%) survived more than 5 years, 18 of 37 (48%) underwent single or multiple repeat resections. CONCLUSION: Recurrence rate after liver resection for BL-CLMs with numerous metastases is especially high. Repeat resection plays a key role for a long term survival and cure.

**P178**

Sarcopenia in Preoperative Therapy for Resectable Pancreatic Cancer: Does It Matter?


Background: Sarcopenia (loss of muscle mass) predicts perioperative complications and delayed recovery after cancer surgery, and poor survival following de novo pancreatectomy in patients with pancreatic adenocarcinoma. However, the association between sarcopenia and outcomes following treatment with neoadjuvant therapy is unknown. We sought to characterize changes in body composition of pancreatic cancer patients treated with preoperative chemoradiation to determine the prevalence and impact of baseline and treatment-associated sarcopenia when neoadjuvant therapy is employed. METHODS: We examined the pretreatment and preoperative CT scans of all 90 patients with potentially resectable pancreatic cancer enrolled on a previously-reported phase II trial of neoadjuvant gemcitabine-based chemoradiation. We computed normalized cross-sectional areas (CSA) of skeletal muscle (SKM), visceral adipose tissue (VAT), and subcutaneous adipose tissue (SAT) at the L3 vertebral level. Sarcopenia was defined using gender-specific norms and evaluated in the context of prospectively-acquired clinical data. Results: At enrollment, 46 (52%) patients were sarcopenic, 59 (59%) were overweight or obese, and 21 (24%) were both. After neoadjuvant therapy (median 4.2 months), CSA (cm^2/m^2) decreased for each compartment [SKM 47.6 vs. 46.3 (p=0.004), VAT 45.1 vs. 41.2 (p=0.01), and SAT 53.0 vs. 15.9 (p<0.001)] and 9 (25%) patients without baseline sarcopenia developed sarcopenia. Neither pretreatment nor preoperative sarcopenia were associated with either successful pancreatectomy or progression free or overall survival (all p>0.05). Conclusion: From this first study of changes in body composition of patients receiving preoperative therapy for pancreatic cancer, we conclude that sarcopenia is not a poor prognostic factor and that neoadjuvant chemoradiation is associated with a further decline in skeletal muscle mass. However, sarcopenia alone may not portend a poor prognosis when nonoperative therapy is delivered prior to pancreatectomy. Further studies of anthropometric changes that occur during curative therapy for pancreatic cancer are needed to develop perioperative strategies and optimize outcomes.

**P179**


Introduction: A favorable response to induction therapy may allow a subset of patients with locally advanced pancreatic cancer (LAPC) to be considered for resection. We sought to assess our early experience with such patients who traditionally would not have been considered for surgery. Methods: We identified all patients (pts) with LAPC who were well enough to receive either chemotherapy or chemoradiation from 2008-2012. Criteria for LAPC included encasement of the celiac axis (CA) or SMA, lack of a venous target for SMV-PV reconstruction, or invasion of adjacent structures (other). Demographics, treatment data, and survival outcomes were abstracted. Results: We identified 31 pts with LAPC due to arterial encasement (CA [n=12, 39%], SMA [n=12, 39%], both CA and SMA [n=2, 6%]), lack of venous target (n=2, 6%), or other (n=3, 10%). Chemotherapy and chemoradiation was given to 28 (90%) pts; 8 (26%) had gemcitabine monotherapy, 6 (18%) had gemcitabine-based combinations, and 14 (44%) had 5-fluorouracil-based therapy. Three pts (10%) received only chemoradiation. Of the 31 pts, 12 (39%) developed disease progression; 10 (32%) local and 2 (6%) distant. Of the remaining 19 (61%) pts, 1 refused surgery, 3 (15%) had metastases at laparoscopy, and 15 (48%) were resected. Operations included pancreaticoduodenectomy (n=6, 33%), distal pancreatectomy (n=7, 39%), central pancreatectomy (n=1, 5%), and total pancreatectomy (n=1, 5%). Vascular resections were performed in 9 (60%) of the 15 pts (6 arterial, 1 venous, and 2 arterial and venous). R0 resections were achieved in 14 (93%) of the 15 pts; 1 pt had an R1 resection. No demographic or chemotherapeutic regimen was associated with surgical resection. Pts with CA encasement were more likely to undergo resection than pts with SMA encasement (OR 7.0, P=0.05). Median survival was significantly greater in pts who completed all therapy including surgery (45 mo vs. 14 mo; P<0.005) (Fig 1). Conclusion: Induction therapy may identify a subset of pts with LAPC in whom a complete resection of the primary tumor is both technically possible and of potential oncologic benefit. The survival duration for this subset of patients is quite favorable.
Abstracts: Poster Presentations S105

2. Radiology and Imaging Sciences, Emory University, Atlanta, GA.

 Sequences compared to Standard MRI

**P180**

Effect of Adjuvant Chemotherapy with S-1 or Uracil-Tegafur compared to Surgery Alone for Patients Undergoing Curative Resection of Biliary Tract Cancer O. Itano,* M. Shinoda, M. Kitago, Y. Ache, T. Hibi, H. Yagi, M. Ishii, Y. Kitagawa. Department of Surgery, Keio University School of Medicine, Tokyo, Japan.

Introduction: Although the surgical resection rate of advanced biliary tract cancer (BTC) has increased, it has not achieved satisfactory improvements in survival. These findings indicate the limitations of surgical resection and emphasize the need for adjuvant treatment. The purpose of this study is to evaluate the effect of postoperative adjuvant chemotherapy with S-1 or uracil-tegafur (UFT) versus surgery alone on 2-year survival and disease-free survival (DFS) for resected BTC patients. Methods: Between January 1995 and April 2013, a total of 117 patients with carcinomas of gallbladder (Stage III/IV) (n=22), or bile duct (n=95) undergoing resection with curative intent were analyzed retrospectively and compared among surgery alone (n=63), UFT (n=41) (400 mg/m2/day) and S-1 (n=13) (80 mg/m2/2 days; 1-28, given orally daily for 4 weeks, followed by a 2-week rest, repeated every 6 weeks). Results: Compared of clinicopathological characteristics among three groups, there were no differences in patient's factors. As to tumor factors, there were no differences in T factor and Stage, however the number of lymph node metastasis is more in adjuvant groups than those in surgery alone group. Toxicity was generally mild in both adjuvant groups. UFT was administered for 3-36 months (mean 18 months) and no grade 3 or 4 toxicity was diarrhea (2.4%), and leucopenia (2.4%). S-1 was administered for 2-19 months (mean 11 months) and grade 3 or 4 toxicities were diarrhea (7.7%) and skin rash (7.7%). There were no treatment-related deaths. The 2-year survival and DFS rates in patients of the UFT group (51.2% and 48.8%) and the survival rate in the S-1 group (59.3%) were not statistically different from those in the surgery alone group (39.7% and 33.3%, respectively). However, the 2-year DFS rate was significantly better in the S-1 group (69.2%) than that in the surgery alone group (33.3%) (p=0.047). Conclusion: Postoperative adjuvant therapy with S-1 improved the DFS rate (7.7%) compared to Standard MRI imaging in up to 35% of patients. This technique may allow earlier detection of occult liver metastases and potential intervention at the time of imaging. Further studies on the recurrence rate and overall survival of patients undergoing breath-hold MRI compared to Standard MRI are needed.

**P181**

Improved Detection of Liver Metastases with Breath-hold MRI Sequences compared to Standard MRI F.A. Adeshoko,1,* S.G. Nour,2 J. Li,3 M.H. Squires,1 S.K. Mattheil,1 K. Cardona,1 M.C. Russell,1 D.A. Kooby,1 1. Surgical Oncology; Emory University, Atlanta, GA; 2. Radiology and Imaging Sciences, Emory University, Atlanta, GA.

INTRODUCTION: Standard Magnetic Resonance Imaging (MRI) may not reliably identify subtle liver metastases. High resolution MRI with controlled breath suspension under general anesthesia (breath-hold) is employed for precise targeted ablation of liver metastases. We assessed the value of breath-hold MRI for the detection of additional subtle metastatic liver lesions not seen on pre-procedural imaging. METHODS: Patients with known liver metastases detected on standard MRI not deemed appropriate for resection were referred for MRI-guided ablation with breath-hold technique. Prior to planned ablation, preliminary imaging was performed during suspended breathing to obtain TSE T1, TSE T2, and VIBE images with EOVIST contrast in 3 planes. Pre-procedure standard MRI findings were compared with breath-hold MRI results for number of hepatic lesions detected. RESULTS: Between 2011-2013, 37 patients with liver metastases underwent both standard and breath-hold MRI. Median age was 61 and 22 were men. 15 patients (41%) had colorectal cancer (CRC) and 10 patients (27%) had neuroendocrine tumor (NET) primary pathology; a total of 98 liver lesions were detected on standard MRI in all 37 patients. Additional hepatic metastases not seen on standard MRI were found in 13 patients (35%) with similar frequency among the most common pathologies studied [CRC: 6 of 15 (40%) vs NET: 5 of 10 (50%)]. Among these 13 patients, an average of 5 additional hepatic metastases per patient were detected. CONCLUSION: Utilizing MRI controlled breath suspension under general anesthesia enables detection of additional liver metastases not visible on standard MRI imaging in up to 35% of patients. This technique may allow earlier detection of occult liver metastases and potential intervention at the time of imaging.

**P182**

The Impact of Pancreaticojejunostomy versus Pancreaticogastrostomy Reconstruction on Pancreatic Fistula after Pancreateoduodenectomy: Meta-analysis of Randomized Controlled Trials F.S. Zih,1,* J. Hallet,2 R. Deobald,1 A.S. Scheer,1 N. Coburn,2 P. Karanicolas,1 1. Division of General Surgery, University of Toronto, Toronto, ON, Canada; 2. Division of Surgical Oncology, Sunnybrook Health Sciences Centre - Odette Cancer Centre, Toronto, ON, Canada.

Introduction: Pancreatic fistula (PF) remains a common source of morbidity following pancreatectoduodenectomy (PD). Despite numerous prospective studies, the optimal conduit for pancreatic remnant reconstruction is controversial; we sought to compare the impact of pancreaticojunostomy (PJ) with pancreaticogastrostomy (PG) on PF. Methods: We systematically searched Medline, EMBASE, Scopus, Web of Science, Cochrane Central and the grey literature for randomized controlled trials (RCTs) comparing PJ and PG after PD. Two reviewers independently selected the studies, extracted data, and assessed the risk of bias using the Cochrane Risk of Bias tool. Primary outcome was clinically significant PF, defined as International Study Group on Pancreatic Fistula (ISGPF) grades B and C, or based on authors' definition. Secondary outcomes included bile leak, delayed gastric emptying (DGE), overall morbidity and mortality. We pooled results from the studies using a random-effects model, evaluated the degree of heterogeneity, and explored potential explanations for heterogeneity. Results: From 2212 citations, we identified 6 RCTs including 1010 patients. All studies presented moderate risk of bias. Patients who underwent PG experienced significantly less PF (Relative Risk (RR)=0.65, 95% Confidence Interval (CI) 0.47-0.92), and bile leak (RR=0.19, 0.04-0.88). Delayed gastric emptying, overall post-operative morbidity, and mortality did not differ between the groups. When assessing PF, moderate heterogeneity was present (I2 35%). When considering only the subgroup with soft pancreas/small pancreatic duct the summary risk ratio was slightly lower (RR=0.61, 0.38-0.97). Conclusion: PG reconstruction decreases the rate of PF when compared to PJ. Surgeons should consider reconstructing the pancreatic remnant following PD with PG, particularly in patients at high risk of PF.

![Figure 1. Overall Survival](image-url)
P183

Prognostic Factors and Long-term Outcomes of Resected Pancreatic Adenocarcinoma: A Comparison between Two Decades


Background: There have been improvements in short and long-term survival rates for patients with resected pancreatic adenocarcinoma over time. The main objective of this study was to evaluate differences in long-term survival in a cohort of patients with resected pancreatic adenocarcinoma. Methods: This is a retrospective cohort study of patients who underwent pancreatic resection for pancreatic adenocarcinoma over 2 decades at a high volume academic center. Univariate and multivariate analysis using Cox proportional hazards model were performed to evaluate prognostic factors associated with long-term survival. Time trend analyses were performed to evaluate differences between decades. Results: There were 489 patients identified, 179 patients during the early (1991-2000) and 310 during the recent decade (2001-2010). Main differences between early and recent decade were: node-positive disease rate (39% vs. 69%), number of lymph nodes collected (median 7 vs. 17), perioperative mortality (6.7% vs. 1.6%) and percentage of patients receiving adjuvant therapy (33% vs. 68%), respectively. There were no differences in sex distribution, age, margin positivity rate or tumor grade. In the multivariate analysis, node, margin status, tumor grade, adjuvant therapy and decade of resection were independently associated with overall survival for the entire cohort. Patients who received adjuvant therapy had better median overall survival: 17 [95% confidence interval (CI): 14-22] vs. 26 months (95% CI: 24-31). Median overall survival for the early and recent decade were 16 months (95% CI: 14-20) and 27 months (95% CI: 24-30), P<0.001, respectively. Conclusions: Factors associated with improved long-term survival remain comparable over time: low tumor grade, node and margin negative disease. Short and long-term survival for patients with resected pancreatic adenocarcinoma has improved in the recent decade. This is due to decreased perioperative mortality and increase use of adjuvant therapy.

P184

Robotic Assisted Pancreatoduodenectomy may be Associated with an Increased Likelihood of Receiving Adjuvant Chemotherapy


Introduction: One of the potential advantages to the minimally invasive approach to the pancreaticoduodenectomy is improved time to recovery and decreased physiologic stress. Multiple prospective randomized trials have shown that adjuvant chemotherapy (AC) after pancreaticoduodenectomy for pancreatic ductal adenocarcinoma (PDA) improves survival compared to surgery alone. However, data from the National Cancer Database shows only 16-32% utilization of AC at teaching hospitals. We hypothesized that patients who undergo robotic pancreaticoduodenectomy (RPD) have a higher chance of receiving AC, completing AC, and faster time to AC than those who undergo open pancreaticoduodenectomy (OPD). Methods: We retrospectively reviewed the records of all patients who underwent RPD for PDA between 2009-2012. We compared these results to our cancer registry data of OPD performed for PDA between 2005-2008. Results: 236 patients with PDA were analyzed: 47 underwent RPD and 189 underwent OPD. There was no statistical difference between groups in terms of: age, sex, stage, clinical trial participation, R0/R1 resections, or 30/90 day peri-operative mortality. However, RPD patients were more likely to receive AC than OPD patients (81.8 vs 50.8%, P<0.001). Only 6.5% of RPD did NOT receive chemotherapy (neoadjuvant chemotherapy [NAC] and AC) compared to 30.2% in OPD (P<0.001). More RPD than OPD patients underwent NAC (46.8 vs. 19.1%, P<0.001). In addition, in the RPD group, there was a trend in patients who received NAC to faster AC than those who did not (57 vs 71.5 days, P=0.067). There was also no difference in time to AC (63 vs 69 days, P=0.356), and no difference in utilization of XRT (23.4 vs 35.1%, P=0.164). Conclusion: Patients undergoing minimally invasive robotic pancreaticoduodenectomy were more likely to receive adjuvant chemotherapy than a historical control cohort undergoing open pancreaticoduodenectomy.

P186

Does Preoperative Transperitoneal Biopsy Affect Long-term Outcome of Patients with Resectable Hilar Cholangiocarcinoma?


Introduction: Hilar cholangiocarcinoma is an uncommon hepatobiliary malignancy with an overall poor prognosis. Complete resection provides the only potential for cure. Although several clinicopathological factors have correlated with survival, the impact of various preoperative interventions has not been widely evaluated. We previously showed that preoperative transperitoneal biopsy of cholangiocarcinoma by FNA was associated with a greater frequency of peritoneal metastases in patients undergoing liver transplantation. Whether similar findings occurred in patients undergoing non-transplant resection is unknown. We sought to determine if preoperative transperitoneal biopsy in patients undergoing resection would affect their long term outcome and pattern of recurrence. Method: A retrospective chart review of 89 patients with resected hilar cholangiocarcinoma from 1993-2013 was performed. Data review included perioperative imaging, pathology findings of transperitoneal biopsies, and operative pathology. The primary endpoint of the study was disease-free survival. Survival was estimated using Kaplan Meier method. Result: Preoperative transperitoneal biopsy was performed in 50 of 89 patients with resected cholangiocarcinoma. FNA biopsy was positive in 30 (62.5%) patients and negative in 18 (37.5%) patients. Two patients had a non-diagnostic result. An R0 resection was performed in 85 of 89 patients. Disease recurred overall in 21 of 50 patients after preoperative biopsy. Among patients with a biopsy +, biopsy -, and no biopsy recurrence rates were 53%, 28%, and 49% respectively. Five year recurrence free survival for biopsy +, biopsy -, and no biopsy was 36%, 24%, and 41% respectively (P<0.02). (See Figure). Conclusion: Transperitoneal biopsy does not impact long-term outcome in patients undergoing resection of hilar cholangiocarcinoma. However, difference in recurrence rates between biopsy positive and biopsy negative patients warrants broader study for corroboration and impact on survival.

P187

Erlotinib Sensitizes Hepatocellular Cancer Cells to TRAIL-induced Cell Death

V. Dudeja, R. Chugh, S. Banerjee, V. Sangwan, O. Alsaidi, S. Vickers, A. Saluja. University of Minnesota, Minneapolis, MN.

Introduction: TRAIL (Tumor Necrosis Factor-Related Apoptosis Inducing Ligand) is emerging as a promising anti-cancer therapy by virtue of its strong anti-tumor activity in wide range of cancer cells. Unfortunately, Hepatocellular cancer is resistant to TRAIL. Development of strategies to overcome this resistance will lead to emergence of novel therapies for this difficult to treat malignancy. EGFR dependent signaling pathways are up-regulated in multiple cancer cells and induce resistance to chemotherapy and apoptosis. In this study we evaluated whether erlotinib, an inhibitor of EGFR signaling, sensitizes hepatocellular cancer cells to TRAIL induced cell death. Methods: Hepatocellular cancer cell line HUH-7, which is very resistant to TRAIL was treated with TRAIL(0-40ng/ml), Erlotinib(0-25uM) or a combination of the two and the effect on the viability and caspase-3 and 8 activation was measured. The effect of the combination therapy was also evaluated in Capan-1 pancreatic cancer cell line and HT29 colorectal cancer cell line to ascertain whether these effects are limited to the hepatocellular cancer only or are observed in other
malignancies as well. Results: Combination of Erlotinib and TRAIL was markedly more effective in killing hepatocellular cancer cells when compared with either drug alone (Table). Similarly, combination therapy led to higher level of caspase-3 activation as compared to either drug alone (Table). Analogous results were observed in colon cancer and pancreatic cancer cell lines. Conclusion: Erlotinib sensitizes cancer cells to TRAIL induced apoptosis and cell death. Combination of Erlotinib and TRAIL has immense potential to emerge as novel therapeutic strategy for cancer.

Effect of TRAIL, Erlotinib or combination of the two on the viability and caspase-3 in hepatocellular and pancreatic cancer cell lines.

<table>
<thead>
<tr>
<th>Viability (%) of Control</th>
<th>Caspase-3 (%) of Control</th>
<th>Caspase-3 (%) of Control</th>
<th>Caspase-3 (%) of Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>HUH-7 100.0± 90.0</td>
<td>100.0± 90.0</td>
<td>000.0± 90.0</td>
<td>100.0± 90.0</td>
</tr>
<tr>
<td>123±12</td>
<td>123±12</td>
<td>123±12</td>
<td>123±12</td>
</tr>
</tbody>
</table>

*p<0.05, Data expressed as mean±SEM

P188

The Safety and Efficacy of Minimally Invasive Approaches to Liver Resection: A Meta-analysis

N.R. Jackson,* A. Hauch, T. Hu, J. Buell, E. Kandil. Tulane University School of Medicine, New Orleans, LA.

Introduction Minimally invasive surgical approaches for liver surgery are gaining popularity. The aim of this study is to compare the safety and efficacy of conventional laparotomy with that of robotic and laparoscopic approaches to liver resection. Methods Two independent reviewers conducted a systematic review on publications in PubMed and EMBASE identified from the following keyword searches: robotic liver, laparoscopic hepatic, and open hepatectomy. Clinical trials and observational studies in an adult population were included. Searches were limited to comparative articles of laparoscopic hepatectomy with either conventional or robotic liver approaches. Outcomes included total operative time, estimated blood loss, length of hospitalization, resection margins, postoperative complications and perioperative mortality. Outcome comparisons were calculated using random effects models to pool estimates of mean net differences or of the relative risk between group outcomes. Results Eight hundred thirty-three abstracts were identified by our search criteria. Forty-nine manuscripts met the inclusion criteria and were included in analysis. Of the 3155 patients represented in this analysis, 1582 (50.1%) underwent a laparoscopic approach, 1572 (49.8%) an open approach, and 60 (1.9%) a robotic approach. There was no difference in total operative times, surgical margins, or perioperative mortality rates between groups. Across all outcome measures, laparoscopic and robotic approaches showed no difference. As compared with the minimally invasive groups, patients undergoing laparotomy had a greater estimated blood loss (pooled mean net change: 152.0mL, 95% CI: -1.78, 2.66), and a higher total complication rate (OR: 0.51, 95% CI: 0.22 to 0.87; p = 0.018). Multivariate analysis revealed that adherence did not independently affect survival when stage and aggressiveness of treatment were included in the model (HR, 1.3; 95% CI, 0.76 to 2.2, p = 0.34). Conclusions: Although the BCLC guidelines serve as a practical guide to the management of patients with HCC, they are not universally practiced. These results indicate that survival of patients with hepatocellular cancer is determined by stage and aggressiveness of treatment, not adherence to BCLC guidelines.

P189

Adherence to BCLC Guidelines and Impact on Overall Survival


Background: Multiple studies exist that validate the prognostic value of the Barcelona Clinic Liver Cancer (BCLC) staging. However, none have established a survival benefit. The aim of this study was to evaluate the adherence to the BCLC guidelines at a rural tertiary care center, and to determine the effect of following the treatment recommendations on overall survival. Methods: A retrospective chart review was conducted for 97 patients newly diagnosed with hepatocellular carcinoma (HCC) from 2000 to 2012. The treatment choice was compared with the BCLC guidelines and percentage adherence calculated. Overall survival was estimated using the Kaplan-Meier method and the log rank test was used to test the difference between the two groups. Cox regression tests were used to determine independent effects of stage, treatment aggressiveness, and guideline adherence on survival. A p-value < 0.05 was considered statistically significant. Results: Of 97 patients, 75% (n = 73) were male. Median overall survival was 12.9 months. In 59.8% (n = 58) of the patients, treatment was adherent to stage specific guidelines proposed by the BCLC classification. There was no significant difference in overall survival between the adherent and non-adherent groups (11.2 vs 14.1 months, p > 0.98). However on stage specific survival analysis, we noted a significant survival benefit for adherence to the guidelines for early stage HCC (27.9 vs 14.1 months, p < 0.05), but a decrease in survival for adherence in the end stage (20 days vs 9.3 months, p = 0.01). On univariate analysis, more aggressive treatment was associated with increased survival (hazard ratio [HR], 0.4; 95% confidence interval [CI], 0.22 to 0.87; p = 0.018). Multivariate analysis revealed that adherence did not independently affect survival when stage and aggressiveness of treatment were included in the model (HR, 1.3; 95% CI, 0.76 to 2.2, p = 0.34). Conclusions: Although the BCLC guidelines serve as a practical guide to the management of patients with HCC, they are not universally practiced. These results indicate that survival of patients with hepatocellular cancer is determined by stage and aggressiveness of treatment, not adherence to BCLC guidelines.

P190

Pretreatment Neutrophil/Lymphocyte Ratio versus Platelet/Lymphocyte Ratio as a Predictor of Survival in Pancreatic Cancer Patients

B. Azab,* M. Shariff, N. Shah, W.K. Von Waagner, A. Alam, A. Picon, S.W. Bloom. Staten Island University Hospital, Staten Island, NY.

Background: The aim of our study was to assess the predictive value of pretreatment platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR) in terms of survival in pancreatic cancer patients. Methods: A retrospective study of a prospectively maintained database of 367 pancreatic cancer patients treated between January 2004 and December 2011. Exclusion criteria included those with hemoproliferative disorders, leukopenia
(WBC<4k/cc, leukocytosis (WBC >12k/cc) and unavailable blood count before surgery or chemotherapy. Those patients expired within 60 days of blood count draw were also excluded. Six patients were excluded from our cancer registry and social security death index. Results: Total of 157 patients were qualified for the study. The average follow-up period was 14 months (range 30-3 month). There were 57 patients underwent pancreatectomy and 86 received chemotherapy. According to Kaplan-Meier survival curves, the patients in the highest 4th NLR quartiles had worse survival compared to lower NLR quartiles (p=0.029), whereas the highest PLR quartile did not (p=0.356) (Figure 1). Conclusion: Pretreatment NLR is a significant predictor of mortality in pancreatic cancer patients, whereas pretreatment PLR was not.

Figure 1: Kaplan Meier curves of the survival among the pancreatic cancer patients according to their pretreatment neutrophil / lymphocyte ratio (NLR) and platelet / lymphocyte ratio (PLR) quartiles.

**P191**

**Post-treatment Serum CEA Levels May Determine Response to Yttrium-90 Microspheres in Patients with Refractory Hepatic-only mCRC**

- R. Aimaq,* G. Singh, Y. Chen, L. Lai. *City of Hope, Duarte, CA.*

Introduction: Yttrium-90 (Y-90) is a radioisotope that can be used to treat tumors while sparing surrounding healthy tissues. In particular, Y-90 resin microspheres is FDA approved for selective internal radiation therapy (SIRT) of unresectable hepatic metastatic colorectal cancer (mCRC). The purpose of this study was to evaluate our institutional experience using Y-90 SIRT in the mCRC patient population. Methods: Patients with liver-only mCRC who received Y-90 SIRT from 2008 – 2012 were identified from a prospectively maintained database. Demographic, treatment and outcome variables were analyzed. Overall survival (OS) was calculated using the Kaplan-Meier method and differences compared using the log rank test. Chi-square and multivariate analysis were used to evaluate prognostic factors. Results: In the study period, 19 patients with hepatic only mCRC refractory to systemic therapy and ablative techniques underwent Y-90 SIRT. These patients were mostly male (n=11) with predominantly bilobar (n=9) or right lobe disease (n=8) and had failed a median of two regimens of systemic chemotherapy (range 1-4) and liver-directed therapies. Fifteen patients underwent one treatment; four were treated twice. The most common complication was transient nausea and abdominal pain (63%). Post-procedure CT at 2 months demonstrated stable disease in 5/22 (23%) and progression in 17/22 (77.3%). OS in the patients with stable disease compared with patients with progression was 18 vs. 10 months (p=0.06). Multivariate analysis age, sex, race, prior treatment, and baseline serum CEA levels were not predictive of response; however, initial post-treatment CEA levels were significantly lower in the stable disease group compared with the group who progressed (p=0.02). Conclusions: Patients with refractory hepatic mCRC may be treated with Y-90 SIRT with minimal morbidity. The treatment may confer a possible survival advantage in those patients who have stable disease on post-treatment imaging. Post-treatment CEA levels may be a surrogate for response and assist in the determination of treatment benefit.

**P192**

**Survival after Resection For Pancreatic Cancer at a High Volume, Academic, Community-based Hospital does not Differ from Outcomes Seen in University Hospitals and Specialty Cancer Centers**

- C. Anderson, P. Santoro, R.Z. Abdel-Misih, N.J. Petrelli, J.J. Bennett. *Surgical Oncology, Helen F. Graham Cancer Center, Newark, DE.*

Introduction: Outcomes in pancreatic cancer treatment in community-based settings remain understudied. The aim of our study is to evaluate survival after resection for pancreatic ductal adenocarcinoma (PDAC) in a high-volume, community-based teaching hospital. Most of the literature on pancreatic cancer outcomes is derived from University based medical centers and specialty cancer centers. Since most cancer care in the country is provided through community hospitals, it is imperative to evaluate outcomes in this setting. Methods: The study was designed as a retrospective review of medical records for patients who underwent curative surgical resection for PDAC between 2006 and 2012. Patient and tumor characteristics were evaluated. Overall survival was determined using Kaplan-Meier analysis. Data was compared to the pancreatic cancer nomogram, derived from a high volume, specialty cancer center. Results: Between 2006 and 2012, 295 patients were brought to the operating room for resection of various pancreatic neoplasms, 118 had PDAC, and 69 underwent successful resection. These patients are the focus of the study. Median overall survival was 19 (±4) months. Median N-stage specific survival was: N0 = 25 (±5.6) months, N1 = 18 (±3.5) months. Median survival stratified by margin resection status: Margin(-) = 24 (±3.5) months, Margin(+) = 11 (±2.8) months (p=0.07). For our patient population, the pancreas cancer nomogram predicted survival rates of 64%, 30% and 16% at 1, 2 and 3 years. The actual survival for our patient population was 55%, 35% and 23% at 1, 2 and 3 years, respectively, with a 5 year overall survival of 17%. Conclusion: Post-resection survival outcomes for pancreatic adenocarcinoma treated at a high-volume community cancer center are similar to data published from University hospitals and specialty cancer centers. In an era where performance metrics for complex surgeries are being scrutinized, this study shows that specialized community hospitals can provide comparable outcomes and patients don’t need to travel far to obtain optimal care.

**P193**

**A Single Institution Experience with Irreversible Electroporation for Pancreatic Cancer**


Background: Irreversible electroporation (IRE) is an ablative technique in which short, high-voltage pulses are applied to tissues to permeabilize the cell membranes. As no thermal energy is created it can be used close to vital structures. Here we report our initial experience with this novel technique in a series of unresectable pancreatic cancer patients. Methods: We performed a retrospective data review of all IRE cases performed at our institution for pancreatic cancer from July 2011 to September 2013. These patients were evaluated for peri-operative morbidity, mortality and oncologic outcome. A total of 7 open pancreatic cases were performed. Results: Seven patients (4 women and 3 men) underwent IRE with a median age of 68 years (51 to 76 years) and a median BMI of 34 (22 to 40). One patient underwent margin accentuation with IRE in combination with a distal pancreatectomy. One patient was treated for a recurrence at the root of the SMA one year after a Whipple followed by CHT and CRT. The remaining five patients were found unresectable at time of surgery and ablation of the tumor was performed instead. In one of the patients the final pathology was benign, the other four received perioperative CHT or CRT. We encountered no intra-operative complications with a median blood loss of 100 ml (50 – 1500 ml). The overall 30-day mortality was 0%. Median length of...
stay was 8 days (3-31). Procedure related complications included one gastric hematoma and one gastric outlet obstruction due to post-ablation edema. Two patients died of disease at 6 and 12 months after IRE ablation, the remaining patients are alive with no evidence of disease progression (1 – 21 months). Conclusion: Our comprehensive early experience suggests that IRE for unresectable pancreatic cancer is safe and feasible. Other small series have suggested a survival benefit. A randomized trial including IRE in the treatment regimen for pancreatic cancer should strongly be considered to truly understand the possible benefits of the novel technique.

P194
Efficacy and Cost-effectiveness of Robotic Hepatectomy

Introduction: Robot-assisted surgery is increasingly utilized in many specialties and becoming the standard for select procedures. However, its use in hepaticolobar surgery has only recently been explored at a handful of institutions. Concerns around safety, as well as a perceived increase in cost, are often cited as barriers to adopting this technology. Methods: Between May 2011 and March 2013, forty-six laparoscopic robot-assisted hepatectomies were performed at a single institution. Clinical data from the surgical procedures and postoperative outcomes were reviewed retrospectively. For cost analysis, 41 patients who underwent open hepatectomy during the same fiscal year were selected as controls. Results: Of the 46 robotic hepatectomies, 16 (35%) were performed for metastatic colorectal cancer and 15 (33%) for hepatic cell carcinoma. Median patient age was 57 and 48% were female. Thirty-two (70%) patients had undergone prior abdominal surgery and median BMI was 26. Median largest tumor size was 3.5 cm and a median of 2 hepatic segments were resected. Median operative time was 229 minutes with a median blood loss of 250 ml. Four (8.7%) patients required intraoperative blood transfusion and three (6.5%) were converted to an open procedure. Median length of stay was 3 days. All-cause 30-day mortality was 0%.

For patients in whom 1-2 hepatic segments were removed, direct costs were 34% lower compared to open procedures (p=0.04). No difference in direct costs was observed in patients undergoing more extensive liver resection (≥3 segments).

Conclusions: Our institution’s preliminary experience demonstrates that hepatectomy can be safely and effectively performed via robotic approach. Operative length, blood loss, conversion rate, intraoperative transfusion rate, complication rate, and mortality for these cases are equivalent or superior to those reported in open and robotic series from other institutions. Direct costs are not higher in robotic hepatectomy, particularly in smaller resections, likely due to the decreased length of stay. As surgeons gain more experience with this technology, further studies are needed to effectively compare its outcomes with traditional surgical approaches.

P195
Outcomes of Microwave Ablation for Colorectal Cancer Liver Metastases
O.S. Eng,1 S. Narayanan,1 A. Tsang,1 D. Moore,1 C. Chen,1 C.J. Gannon,1 D.A. August,1 D.R. Carpio,1 L.G. Melstrom,1 1: Rutgers Cancer Institute of New Jersey, Rutgers-Robert Wood Johnson Medical School, New Brunswick, NJ; 2: Advanced Surgical Associates of New Jersey, Capital Health Management, Pennington, NJ.

Introduction: The surgical management of colorectal cancer liver metastases continues to evolve to optimize oncologic outcomes while maximizing parenchymal preservation. Although long term results after hepatectomy and radiofrequency ablation are well reported, follow-up data after microwave ablation are limited. This study investigates outcomes and patterns of recurrence in patients who underwent intraoperative microwave ablation of colorectal cancer liver metastases. Methods: Thirty-three consecutive patients who underwent intraoperative microwave ablation with or without concomitant hepatectomy of colorectal cancer metastases from 2009-2013 at our tertiary care center were identified. Clinical and pathologic variables were recorded and analyzed. Perioperative and long-term data were reviewed to determine outcomes. Results: In the patient cohort, 73% (24) were male, and the median age was 61 (range 42-89). A total of 49 tumors were treated with ablation, with 70% (34) of ablations in conjunction with a concomitant hepatectomy. Most tumors were ≤3 cm (42, 86%). Median preoperative CEA was 4 ng/mL (range 0.7-9.6). Nearly all patients received either preoperative (32, 97%) and/or postoperative (30, 90%) chemotherapy. Median length of stay was 6 days (range 1-32). Median Clavien-Dindo classification was 1 (range 0-5). Forty-two (42%) of patients had no complications. Median follow-up was 301 days (range 13-1035), with 45% (15) of patients presenting with a recurrence. Median time to first recurrence was 259 days (range 64-956). In those patients, 15% (2) presented with an isolated local recurrence in the liver. The majority of recurrences included either a local or hepatic component (12, 80%) or distant disease alone (2, 7%). On univariate analyses, there were no perioperative variables to predict local recurrence alone. Conclusion: Intraoperative microwave ablation is a safe and effective modality for use in the treatment of colorectal cancer liver metastases. Recurrences in these patients most often included distant disease. Therefore, microwave ablation alone or in conjunction with hepatectomy is a reasonable approach for the management of metastatic colorectal cancer to the liver.

P196
Depth of Invasion is Predictive of Sentinel Lymph Node Status and Overall Survival in Merkel Cell Cancer

Introduction: Unlike melanoma, the impact of primary tumor depth in predicting the risk of a positive sentinel lymph node biopsy (SLNB) and survival in Merkel Cell Cancer (MCC) is not well characterized. We sought to identify factors associated with SLNB status, disease-specific survival (DSS) and overall survival (OS) in patients with MCC. Methods: An IRB-approved retrospective review of pts with MCC treated between 1988 and 2012 at a single center. Pts were categorized into 5 groups based on nodal status: 1) SLNB negative, 2) SLNB positive, 3) SLNB not done, 4) MCC of unknown primary origin (MCCUP), and 5) Primary MCC with synchronous clinically evident regional nodal disease (MCC + RLN). Logistic regression, proportion hazard models, and competing risk regression methods were used to analyze factors associated with SLNB status and survival. Results: 391 pts were identified. 274 (70%) were male and median age was 75 years (range 13-96). Median tumor diameter was 1.5 cm (range 0.2 – 12.5 cm) and median tumor depth was 4.8 mm (range 0.3 – 45.0 mm). 194 pts had SLNB performed; the rate of SLN positivity was 31% (61 pts). Age, gender and presence of lymphovascular invasion were not associated with SLNB positivity. Increasing tumor diameter and depth were associated with an increased risk of SLN positivity (p=0.024 and 0.016, respectively) Table 1. Presence of immunosuppression, increasing tumor diameter and tumor depth were associated with overall survival (p<0.01, <.001 and <.001 respectively). Primary location was associated with OS (p=0.032), truncal primary had a 1.92 fold-increased risk vs. head and neck. The DSS differed by patient group (p=0.021), being best in pts with negative SLNB and worst in pts with MCC + RLN at presentation. SLNB positive and SLNB not done patients had the worst DSS and OS. Pts with negative SLNB fared marginally better than patients with a positive SLNB (85 months vs. 59.5 months, p=0.062). Conclusions: Increasing tumor diameter and depth are independently associated with the probability of positive SLN and worse OS in MCC. Additional data is required to analyze the impact of tumor depth in the staging of MCC.

Table 1. Clinopathological features vs. Risk of Positive Sentinel Lymph Node Biopsy and Overall Survival in Merkel Cell

<table>
<thead>
<tr>
<th>Variable</th>
<th>Risk of Positive SLNB (n=194)</th>
<th>Overall Survival (n=391)</th>
<th>Disease Specific Survival (n=388)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M vs F)</td>
<td>0.95 (CI 0.94-0.96)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Age (per 10 year increase)</td>
<td>0.96 (CI 0.91-1.01)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Presence of immunosuppression (n=349)</td>
<td>0.97 (CI 0.94-0.99)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Tumor diameter (cm)</td>
<td>1.05 (CI 1.03-1.07)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Tumor depth (mm)</td>
<td>1.02 (CI 1.01-1.03)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Location of Primary</td>
<td>1.00 (CI 0.99-1.01)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>1.00 (CI 0.99-1.01)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Lower Extremity</td>
<td>1.00 (CI 0.99-1.01)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Unknown</td>
<td>0.99 (CI 0.98-1.00)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Trunk</td>
<td>1.00 (CI 0.99-1.01)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
<tr>
<td>Upper Extremity</td>
<td>1.00 (CI 0.99-1.01)</td>
<td>1.2 (CI 1.11-1.30)</td>
<td>1.2 (CI 1.11-1.30)</td>
</tr>
</tbody>
</table>

Patients with distant metastatic disease were removed from the association testing between nodal status and OS.
The Effect of the AJCC 7th Edition Definition of T1 Melanoma on Utilization of Sentinel Lymph Node Biopsy for Thin Melanoma

T.J. Hiiken, T.E. Grof, N.I. Comfere, J.W. Inselman, E.B. Habermann; Mayo Clinic, Department of Surgery, Rochester, MN; Mayo Clinic, Department of Dermatology and Pathology, Rochester, MN; Mayo Clinic, Department of Health Sciences Research, Rochester, MN

Introduction: Practice guidelines suggest that sentinel lymph node biopsy (SLNB) be offered to select patients with “high risk” thin melanomas. While the majority have an excellent prognosis and low prevalence of lymph node metastasis, 25% of melanoma deaths are attributable to T1 tumors. Earlier guidelines recommending reclassification of SLNB for T1b tumors, implemented in 2010, changed the definition of T1 melanoma to reflect mitogenicity rather than level of invasion, based on prognostic models, not the likelihood of occult lymph node metastasis. We assessed the effect of this 2010 staging change on SLNB rates for T1 melanoma patients. Methods: Using Surveillance, Epidemiology, and End Results (SEER) Registry data from 2004-2010, we identified 32,527 cases of T1 melanoma and compared pre-2010 (N=27,170) with 2010 (N=5,357) data on a year to year basis. Logistic regression models were used to analyze SLNB rates in 2004-2009 vs 2010 T1 melanoma patients. Results: 40.9% of 2004-2009 T1b melanoma patients (prior to staging change) vs 33.3% of 2010 T1b patients (after staging change) had a SLNB, while the overall SLNB rate for T1 patients increased from 12.1% in 2004 to 14.4% in 2010 (p<0.001 for both). SLNB was performed for 38.3% of 2004-2009 melanomas ≥0.7 mm vs 39.3% post-staging change (p=0.556). \( T \) stage, tumor thickness, level, ulceration, SEER registry and patient age were associated with the performance of SLNB, all \( p<0.001 \). Conclusions: Overall SLNB rates for T1 melanoma patients increased from 2004 to 2010 along with SLN positivity rates, while performance of SLNB for T1b patients decreased. This may be a function of T-stage reclassification, from 2004 to 2010 along with SLN positivity rates, while performance of SLNB, all \( p<0.001 \). The proportion of SLN+ T1 patients was 6.1% pre-2010 and 7.8% in 2010, \( p=0.07 \). Conclusions: Overall SLNB rates for T1 melanoma patients increased from 2004 to 2010 along with SLN positivity rates, while performance of SLNB for T1b patients decreased. This may be a function of \( T \)-stage reclassification, as SLNB rates were stable for patients with melanomas \( \geq 0.7 \) mm. These data suggest that mitogenic rate may not be the best predictive marker for occult lymph node disease. Improved definition of and treatment guidelines for “high-risk” T1 melanoma patients most likely to benefit from lymph node surgery are needed.

---

CXCL10 Expression by Melanoma Cells is Associated with Metastatic Ability and Tumor Cell Adhesion

S.C. Wightman, S. Bagaria; Mayo Clinic, Jacksonville, FL; Mayo Clinic, Scottsdale, AZ

Introduction: Oligometastasis is a state of limited metastasis with the potential for cure by surgery or radiotherapy. We designed a syngeneic mouse melanoma model with stable tumor clones representing oligo- (<5 lesions) and polytomastatic (>30 lesions) pulmonary disease. After evaluating transcriptomic and proteomic differences between oligo- and polytomastatic tumor cells, we found CXCL10 consistently elevated in polytomastatic tumor clones. To understand potential functions of CXCL10 in the metastatic phenotype we generated stable knockdowns (KD) of this chemokine in oligo- and polytomastatic clones of B16 murine melanoma. Methods: Stable CXCL10 KDs of oligo- and polytomastatic B16F1 clones (P2M5B and P2M3C respectively) were generated by lentiviral transfection. CXCL10 expression was assessed by Western blot and ELISA (R&D Systems, MN). Cell adhesion was measured in 96-well plates coated by Matrigel and assayed by Cell Titer-Blue. Results: The oligo- and polytomastatic CXCL10 KDs demonstrated more than 10-fold suppression of CXCL10 expression by Western analysis relative to controls. Secretion of CXCL10 was suppressed 4.60-fold \( (p=0.0005) \) and 1.35-fold \( (p=0.0003) \) in P2M5B and P2M3C KDs respectively by ELISA. The oligotomastatic parental clone P2M5B had reduced adhesion compared with the polytomastastic P2M3C clone (1.49-fold \( p=0.00006 \)); this indicates that adhesion may be responsible for oligo- versus polytomastatic developent of metastases. Suppression of CXCL10 led to a 1.33-fold \( (p=0.04) \) and 1.27-fold \( (p=0.001) \) decrease in adhesion of P2M5B and P2M3C KDs respectively when compared to the non-targeting vector. Conclusion: Our data indicate that colonization of the lung microenvironment by melanoma cells is associated with matrix adhesion properties of tumors. Our data also demonstrate for the first time that CXCL10 plays an important role in the regulation of tumor cell adhesion to cellular matrix, and therefore may act as previously unrecognized regulator of melanoma metastases development.

---

Does Increasing Wait Time to Surgery for Cutaneous Melanoma Increase the Risk for Nodal Metastases? B. Rawal, S. Bagaria

Introduction There are no standardized recommendations for how long a patient can wait from time of diagnosis to definitive surgery for cutaneous melanoma without increasing the risk of nodal metastases. In this study we investigate the impact of wait-time to surgery for cutaneous melanoma on the risk for sentinel node metastases. Methods A retrospective review of a single-institutional database was performed to identify patients diagnosed with clinically node negative cutaneous melanoma undergoing sentinel node biopsy between 1995 and 2013. Wait-time to surgery was calculated from the date of diagnosis to date of definitive surgery. The primary outcome measured was the presence of sentinel nodal metastasis. Results Our study population consisted of 1,037 patients with cutaneous melanoma. Median age was 63 years. There were 487 (47%) T1 lesions, 317 (31%) T2 lesions, 163 T3 (16%) lesions, and 70 (7%) T4 lesions. Sentinel node metastases were found in 116 (11%) of all cases and in 39 (8%) T1, 229 (9%) T2, 31 (19%) T3, and 19 (27%) T4 lesions. The number of cases with wait-times of 1-14, 15-42, and >42 days were 115 (11%), 685 (66%), 237 (23%), respectively. The mean wait-time for those with negative sentinel nodes was similar to those with positive sentinel nodes (34 vs. 32, respectively). The rate of sentinel node metastasis did not differ for wait-times of 1-14, 15-42, and >42 days (12%, 11%, 11%, respectively; \( p=0.94 \)). Patients were then stratified into low-risk melanomas (T1 and T2 lesions) and high-risk melanomas (T3 and T4 lesions). Once again, no difference in the rate of sentinel node metastases was seen for wait-times of 1-14, 15-42, and >42 days for low-risk melanomas (10%, 8%, and 8%, respectively; \( p=0.80 \)) and high-risk melanomas (21%, 22%, and 19%, respectively; \( p=0.91 \)). Conclusion When compared to a wait-time of <2 weeks, wait-times of 6 weeks for sentinel node surgery are not associated with an increased incidence of sentinel node metastasis in patients with cutaneous melanoma. Review of our single-institutional database suggests that wait-times of 6 weeks for sentinel node surgery are not associated with an increased incidence of sentinel node metastasis in patients with cutaneous melanoma, review of a single-institutional database suggests that wait-times of 6 weeks for sentinel node surgery are not associated with an increased incidence of sentinel node metastasis in patients with cutaneous melanoma.
P200

Ipilimumab Combined with Isolated Limb Perfusion (ILP) for Extremity Melanoma
M. Kim, C. Wilfong, A. Blum, A. Alosi, D. Fisher, J. Skitzki. Roswell Park Cancer Institute, Buffalo, NY.

Background: Ipilimumab (IPI) an anti-CTLA-4 antibody has shown significant activity against metastatic melanoma. T cell-CTLA-4 receptors inhibit immune activation and systemic IPI promotes anti-tumor immunity. The combination of systemic IPI prior to regional therapy was explored with a novel mouse model of ILP. Methods: Female C57BL/6 mice were injected with 1 × 106 B16-OVA cells subcutaneously in the leg. After 5 days of tumor establishment, 3 doses of IPI (100 μg intraperitoneal) were delivered over 7 days. In the ILP group, tumor bearing legs were perfused with 90 μg melphalan for 30 minutes through the superficial femoral artery using a non-oxygenated circuit. Using immunohistochemistry and flow cytometry, CD8+ and OVA-specific CD8+ T cells within the tumor microenvironment were analyzed at 1, 7, and 14 days following ILP. Tumor growth was measured every other day. Result: Administration of IPI by itself had no effect on tumor growth compared to controls. ILP treatment significantly delayed tumor growth with no additive effect when combined with IPI. Local and systemic toxicity was not increased after ILP with the addition of IPI. However, increased numbers of CD8+ T cells were seen in tumors treated with IPI compared to untreated controls at 1 and 7 days (p<0.05). Antigen-specific tumor infiltrating cells were also noted to be increased with both IPI and IPI+ILP treatments (p<0.05 vs. untreated control and ILP alone respectively). At 2 weeks post limb perfusion, the IPI+ILP mice continued to trend towards increased tumor infiltrating CD8+ and OVA-specific cells compared to ILP alone. Conclusion: The addition of IPI to ILP produced equal inhibition of tumor growth with no added toxicity. Importantly, tumor infiltrating CD8+ and OVA-specific cells were increased and were indicative of a brisk immune response that may be exploited during regional therapy.

P201

Yield of Radiologic Studies for Identifying Distant Disease in Clinical Stage IIB and IIC Melanoma
C. Angeles, D. De Blasi, M.S. Brady, C.E. Ariyan, D.G. Coit. Surgical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY.

Introduction: The diagnostic value of radiologic studies for patients with newly diagnosed stage II melanoma is unknown. This study sought to determine the yield of radiologic imaging at presentation in the highest risk patients with Stage IIB or Stage IIC melanoma. Methods: Clinical stage IIB/C (cIIB, cIICC) patients diagnosed between 1998-2008 were identified from a prospective single institution database. Patients were included if radiologic studies were completed within 3 months of diagnosis in image naïve patients prior to sentinel lymph node biopsy (SLNB). Studies included were CT or MRI of the chest, CT or MRI of the brain, CXR, CT or MRI of the neck, chest, abdomen, or pelvis, PET scan, or bone scan. Results: A total of 495 patients were included in the analysis: 300 stage cIIB and 195 stage cIICC. Median follow-up was 55 months. Among stage cIIB patients, imaging studies resulted in indeterminate findings in 30% and true positive (TP) in 0.7%. Among stage cIICC patients, imaging studies resulted in indeterminate findings in 27.7%, TP in 9.2%, and FP in 4.1%. The true positive findings are 4 non-melanoma cancers and 16 melanoma metastases. Median recurrence free survival (RFS) for all patients with negative and indeterminate findings was 88 and 36 months, respectively (p<0.001). Of patients who subsequently underwent SLNB (299/495), those with indeterminate imaging findings were more likely to have a positive SLN than those with negative findings (45% vs 32%, Z-score -2.1, p<0.03). Conclusion: Radiologic studies obtained during initial staging workup for clinical stage IIB and IIC melanoma patients generate indeterminate findings in 29% of patients and identify true positive disease in only 4%. Patients with indeterminate findings are more likely to have a positive SLN and worse RFS than patients with negative studies.

P202

Necessity of Completion Pelvic Lymph Node Dissection after Positive Inguinal Sentinel Lymph Node Biopsy in Cutaneous Melanoma

Introduction: In patients with melanoma metastatic to an inguinal sentinel lymph node (SLN), the decision to complete a pelvic lymph node dissection including external iliac and obturator nodes in addition to an inguinal dissection, is controversial. We reviewed our experience with inguinal SLN’s to evaluate the role of pelvic lymph node dissection in an attempt to identify those patients at risk for iliac recurrence. Methods: We retrospectively reviewed patients at our institution that underwent inguinal SLN biopsy for melanoma between 1996 and 2012. Patients were evaluated for tumor characteristics, SLN status, surgical treatment, and recurrence patterns. Results: 301 patients underwent inguinal SLN biopsy from 310 groins: 188 (63%) were women, the median Breslow depth of primary tumors was 1.4mm, and 58 (19%) were ulcerated. Fifty-nine patients (20%) had metastatic melanoma identified in a SLN, and their median Breslow-depth was 2.1mm. Fifty-three SLN positive patients (90%) underwent further lymph node dissection; all of these were inguinal dissections without pelvic lymph node dissection. Over a median follow up of 38.4 months, 46 of the 301 patients (15%) developed recurrent melanoma, with a median time to recurrence of 17.2 months. Fifteen patients recurred in an iliac lymph node, 7 of whom (47%) previously had a positive inguinal SLN. Only 1 of the 7 met current guidelines for pelvic lymph node dissection. Thirteen of 15 patients (87%) who went on to recur in an iliac node, had eventual distant metastases, and 11 of them (73%) have died of their disease. The median time from development of iliac disease to the development of distant metastases was 3.1 months. Conclusions: Only one of 15 patients that developed iliac nodal recurrence who subsequently underwent SLNB (299/495), those with indeterminate imaging findings were more likely to have a positive SLN than those with negative findings (45% vs 32%, Z-score -2.1, p<0.03). Conclusion: Radiologic studies obtained during initial staging workup for clinical stage IIB and IIC melanoma patients generate indeterminate findings in 29% of patients and identify true positive disease in only 4%. Patients with indeterminate findings are more likely to have a positive SLN and worse RFS than patients with negative studies.

P203

Therapy With Hedgehog Inhibitors for Locally Advanced or Metastatic Basal Cell Carcinoma
R.I. Neves, B. Anderson, J. Drabick. Penn State Hershey Cancer Institute, Hershey, PA.

Basal cell carcinoma (BCC) may occasionally progress to an advanced state that is no longer amenable to surgery, radiation therapy or, more rarely, may spread to distant sites. Genetic studies have shown that almost all BCC’s contain aberrant Hedgehog signaling pathway activation and uncontrolled proliferation of basal cells. Vismodegib is an inhibitor of the Hedgehog pathway that binds to and inhibits SMO, a transmembrane protein involved in Hedgehog signal transduction. We present a series of patients from a single institution with locally advanced BCC (LABCC) or metastatic BCC (MBCC) that were treated with Vismodegib in a 16-month period. From April 2012 to August 2013 twenty adult patients with LABCC or MBCC not candidates for surgery or radiation therapy received Vismodegib 150 mg daily until disease progression, unacceptable side effects or discontinuation of the treatment. When applicable, objective response rate was assessed by RECIST 1.0 and defined as decrease of 30% or more in the externally visible or radiographic dimension.
or complete resolution of ulceration present at baseline. Progressive disease was defined as increase of 20% or more in the externally visible or radiographic dimension, new ulceration, or new lesion. Patients who had a response underwent tumor biopsy during treatment and pathological evaluation was used to determine whether the response was partial or complete. The most common side effects from treatment were loss of taste, cramps, hair loss, weight loss and fatigue. Patients with LABCC (n=19) had objective response rate above 80%. As of the data-cutoff point 13 patients had complete response confirmed by absence of residual BCC on biopsy and had not disease progression. The only MBCC to the axillary lymph nodes (n=1) had only clinical objective response by assessment of cessation of pain, weeping and shrinkage of axillary wound by 2 months of treatment. The totality of patients with LABCC had tumor shrinkage. Visible reductions in tumor size and improvement in appearance were noted for the majority of patients. Conclusions: Vismodegib is a new treatment alternative and associated with tumor responses in patients with LABCC or MBCC.

P204
Prognosis of Acral Lentiginous Melanoma compared to Sun Induced Melanomas: An Analysis of 1,039 Cases

Introduction: Of the four major histologic subtypes of cutaneous melanoma, Acral Lentiginous Melanoma (ALM) is the most frequent in Latin America and Asia. Some studies indicate that ALM has a worse prognosis when compared with other subtypes. This study report the analysis of ALM compared with sun-induced melanomas. Methods: Review of Melanoma prospectively revised database from 1982 to 2012. All patients with subungueal, palmar or plantar melanoma and histologically confirmed was recorded as ALM. The other subtypes were clinically and pathologically identified. A total of 1,603 patients were diagnosed with melanoma and includes melanous melanoma, Acral Lentiginous Melanoma (ALM) is the most frequent in Latin America and Asia. Some studies indicate that ALM has a worse prognosis when compared with other subtypes. This study report the analysis of ALM compared with sun-induced melanomas. Results: A total of 1,039 patients were ALM or Sun-induced melanoma. The median age was 63.8 and 56 years respectively (p=0.01). The 66.7% of ALM patients were older than 60 years while only 47.9% of SIM (p=0.0001). The median Breslow thickness was 5.79 mm for ALM patients and 4.23 mm for SIM (p=0.0001). The distribution according to Breslow thickness was 16.04% (T1), 15.86%(T2), 23.06% (T3) and 45.05% (T4) of ALM versus 29.55% (T1), 20.45% (T2), 20.25% (T3) and 29.75% (T4), reflecting thicker melanomas in ALM patients (p=0.0001). Most of the ALM was ulcerated more than SIM (70.27% vs 41.2% p=0.000). The stage distribution was shown in table 1. We do not find significant differences in terms of gender distribution (p=0.281) or sentinel node biopsy result (p=0.79). The median survival time was 55 months versus 82 months for ALM and SIM respectively (p=0.0001). The 5 and 10 years overall survival (OS) was 46.8% and 27.3% for ALM and 57.9% and 45.4% for SIM (p=0.000). No differences were found in median survival or OS when ALM and SIM were stratified by disease stage. Conclusion: ALM have more aggressive features, clinically and pathologically, that results in lower survival rates compared to sun-induced melanomas.

P205

Introduction: We previously presented a Type I Polarized dendritic cell (DC)-based vaccine capable of eliciting antigen-specific CD8+ T cell response to BRAF V600E and preventing tumor formation in mice challenged with B16V600E melanoma. We have subsequently tested the ability of our vaccine to treat established B16 tumors in conjunction with a BRAF inhibitor (PLX4720). Methods: Our DC1 vaccine was prepared from bone marrow precursors matured to DC1 phenotype. Cohorts of 10 C57Bl/6 mice were injected with 5x10^4 B16 cells transplanted with lentiviral vector to express the BRAF V600E mutation. On day 15, when tumors were palpable, treatment was initiated with DC1s pulsed either with affinity modified BRAF peptide or OVA control peptide with or without PLX4720. Another group received no treatment. Vaccinations were administered via intradermal injection twice weekly. Tumors were measured with a digital caliper and volume was calculated using the formula: (L x W^2) / 2. Antigen specific CD8+ responses were assessed by IFN-γ ELISA and differences determined by two-tailed t-test. Group survival was compared with the log rank test; differences in tumor growth were determined by comparing tumor doubling times. Results: CD8+ T cells isolated from mice vaccinated with DC1s pulsed with BRAF or Ova peptide demonstrated increased antigen specific IFN-γ secretion (p=0.05). Mice treated with DC1s pulsed with mutated BRAF peptide with and without PLX4720 demonstrated improved survival compared to control mice who received no treatment (p=0.0002 and p=0.0008, respectively) or treatment with PLX4720 alone (p=0.0006 and p=0.0177, respectively). Mice vaccinated with DC1s pulsed with Ova control peptide with PLX4720 demonstrated increased survival compared to PLX4720 alone (p=0.3302). Addition of the DC1 BRAF vaccine to PLX4720 decreased tumor burden over time, causing a significant slowing of tumor doubling time (p=0.0199). Conclusions: Types of mice with established B16V600E+ melanomas with BRAF-pulsed DC1s in combination with PLX4720 prolonged survival and slow tumor growth superior to those treated with PLX4720 alone.
P206
Sentinel Node Biopsy is Indicated for Thick Clinically Node-negative Melanoma

M. Yamamoto,1* J.Y. Wong,1 K.J. Fisher,2 J. Kosco,2 M. Konstantinovic,3 N. Govsyeyev,3 J.L. Messina,1 A.A. Sarnaik,1 C.W. Cruse,1 C.A. Puleo,1 R.J. Gonzalez,1 V.K. Sondak,1 J.S. Zager,1 1. H Lee Moffitt Comprehensive Cancer Center, Tampa, FL; 2. University of South Florida, Tampa, FL.

Introduction: Sentinel lymph node biopsy (SLNB) is considered standard of care and a useful staging procedure for intermediate thickness melanoma. Since the ASCO guidelines do not definitively recommend SLNB for thick melanoma, we sought to determine if there is a prognostic survival benefit to SLNB in these pts. Methods: From 1999 to 2012, 571 pts with melanoma whose primary tumors were ≥ 4mm in Breslow depth were evaluated from a single institution. Pts who presented with distant disease were excluded from this study. Associations between survival and clinicopathologic characteristics were explored using stratified Kaplan Meier curves and log rank p-values. Results: Of 571 pts, 401 (70.2%) were male and median age was 66. The median Breslow depth was 6.2 mm (range 4-25) with the predominant histology being nodular type (45.5%). 412 pts (72%) underwent SLNB and 46 (8%) underwent a complete node dissection due to clinically positive nodal disease at presentation. An additional 113 pts (20%) did not have a SLNB (i.e. medical comorbidities, patient preference, failure to map on lymphoscintigraphy). A positive SLN was seen in 161 of 412 pts (39.1%). Nineteen pts presented with nodal recurrence in the mapped basin despite a negative SLNB (false negative rate [FNR] 10.6%). The median overall (OS) and disease-specific survival (DSS) for the entire cohort was 42.5 and 62.1 months, respectively. The median DSS for pts with a negative SLN was 82.4 months, 41.2 for positive SLN and 26.8 for those with clinically positive nodal disease at presentation. Based on these data, we consider SLNB to be indicated for pts with thick clinically node negative melanoma.

P207
Tanning Beds: How Harmful are they in Young Patients with Melanoma?

C. Farley, Y. Alimi, S. Perez, W. Kneckt, A. Hestley, G.W. Johnson, M.C. Russell, K. Delman, M. Rizzo,* Emory University, Atlanta, GA.

BACKGROUND: An increase in the incidence of melanoma has been observed over the past decade, particularly in young women ages 19-35 years. Recent data has shown a link between tanning bed use and melanoma risk. This study sought to determine the incidence and frequency of tanning bed use among young patients diagnosed with melanoma at a single institution. METHODS: A retrospective case-control design analyzed the incidence and frequency of tanning bed use among melanoma patients ages 18-50 years and diagnosed between 1991 to 2011 compared to controls (randomly selected general surgery patients ages 18-50 years). A telephone survey investigated family history of skin cancer and/or melanoma, hair color, eye color, skin type, tanning bed use (absolute and frequency), and patient awareness of risks and/or dangers associated with tanning bed use. RESULTS: 611 melanoma cases were identified. 267 (44%) completed the telephone survey as did 96 controls. Of these 363 subjects, 192 were female. Females were 4.2 times more likely to have used a tanning bed than males (OR 4.18; 95% CI, 2.69-6.51). Melanoma patients were 2.5 times more likely to have used a tanning bed than controls (OR 2.48; 95% CI, 1.51-4.07). Melanoma patients were more likely to have natural light color hair and blue-green eyes than controls. Of 171 tanning bed users, 75% were younger than 25 years of age at first use. Among the tanning bed users, 90% were aware of a danger or risk associated with tanning bed use as shown in the Table. CONCLUSION: Melanoma diagnosed between the ages of 18-50 is associated with increased tanning bed use. In this study population, tanning beds were most commonly used at a young age and, more specifically, by females reinforcing the need to advocate for legislation to restrict access to tanning beds.

P208
Evaluating Sentinel Lymph Node Biopsy in Thin (<1mm) Melanoma


Introduction: The role of sentinel lymph node biopsy (SLNB) in T1(<1mm) melanomas remains controversial. Numerous relatively small retrospective studies have identified factors associated with SLN metastasis, but there is a lack of consensus as to when biopsy should be pursued. The purpose of this study is to assess the role of sentinel node biopsy in T1 melanoma patients using a large population database to identify high-risk patients and assess the prognostic value of the procedure. Methods: Using the Surveillance Epidemiology and End Results (SEER) database, T1 melanoma patients who underwent SLNB from 2004-2009 were identified. Clinicopathologic data based on the 2002 TNM staging system and overall survival (OS) were compared among patients with positive(+) and negative(-)
and negative (−) SLNs. Logistic regression was used to estimate odds ratios (OR) and 95% confidence intervals (CI) for tumor specific factors, adjusted for demographic factors. Results: Of the T1 melanoma patients identified, 8867 (14.3%) underwent SLNB. The overall SLNB(+)* rate was 3.6%. The SLNB(−)* rate for patients with ulceration was 9%, associated with a 5-fold increased likelihood of positive biopsy (95% CI: 2.9 - 9.8, p<0.001). Rates of nodal positivity for CL 4-5 and thickness >0.75mm were 4.8% and 4.1%, respectively. For melanomas with both CL 4-5 and ulceration, the SLNB(−)* rate was 14.8%, associated with a 14-fold increased odds of a SLNB(−)* versus having neither high risk feature (95% CI: 8.4 – 23.0, p<0.001). Survival distributions stratified by SLNB status were significantly different (p<0.001; log-rank test). 5-year OS was 91.2% for SLNB(+) patients (95% CI: 90.2% - 92.2%) and 75.6% for SLNB(−) patients (95% CI: 69.2% - 82.6%). Conclusions: The present study represents the largest series of T1 melanoma patients studied and demonstrates the strong prognostic value of SLNB in this population. Although the overall node positivity rate was low, high risk factors such as ulceration, CL 4-5, and increased thickness were associated with a significantly increased rate of nodal spread. Ulceration is the factor most strongly associated with nodal positivity. Mitotic rate should be critically assessed in the future.

**P209**

Intratumoral Immune Environment in Patients with Advanced or Metastatic Melanoma before and after Ipilimumab. C.V. Angeles,1,4 D. Gyorki,2 M. Pulitzer,1 C.E. Ariyan.1

Introduction: While ipilimumab (IPI) has a clinical benefit in patients with advanced or metastatic melanoma, the response rate is low. Efforts to identify biomarkers of response have identified an increase in HLA-DR expression in the blood and an inflammatory gene signature in the tumor, but there is little understanding about the routine changes within the tumor. This study sought to identify changes in immune infiltrate and alterations in antigen expression in tumors removed after treatment with IPI. Methods: From a prospective single institution database, patients with matched pre- and post-IPI tumor specimens were selected. Tumors were de-identified and labeled immunohistochemically for immune markers as well as tumor antigens. Slides were analyzed and quantified for staining (0-3) and intratumoral location in a blinded fashion by a melanoma dermatopathologist. Results: Thirteen patients were identified with matched pre- and post-IPI specimens (13 and 15, respectively). At the start of IPI treatment, patients were either stage IIB or stage IV. Median time between start of IPI treatment and surgery was 61wk (range 12-123wk). 77% of patients showed clinical benefit with partial response or stable disease at 24wk. There were no complete responders. The causes for surgery were progressing disease (46.7%), only remaining site of disease (26.7%) or symptoms (26.7%). All patients but one had T-cell infiltration in tumor prior to IPI treatment. Post treatment, 71.4% of patients had an increase in CD8. Only 6.7% of patients had an increase in HLA-DR. The majority of patients had a decrease or stable expression of tumor antigens S-100 and HMB-45. The 5-year overall survival was 51%. Conclusion: In this small cohort of selected patients, we saw a survival benefit with ipilimumab even in patients with isolating progressing lesions. Contrary to previous data, we did not see a marked post-treatment increase in HLA-DR. The intratumoral immune environment did demonstrate an increase in CD8, but no other striking changes. These observations underscore the importance of considering additional immune therapy as well as surgery for patients with advanced melanoma.

**P210**

Expansion of Pharmacologically Activated Melanoma-specific Lymphocytes in Alternate Gamma Chain Cytokines: Gene Expression Variances between T Cells and T Cell Subsets Exposed to IL-2 versus IL-7/15. C.K. Zoon,1,4 E. Seitelman,2 L. Graham,2 C.I. Dumur,2 H. Bear.1 1. General Surgery, Virginia Commonwealth University, Richmond, VA; 2. Virginia Commonwealth University - Department of Surgical Oncology, Richmond, VA; 3. Virginia Commonwealth University - Department of Pathology, Richmond, VA.

Introduction: We have previously demonstrated that culturing tumor-sensitized T cells in interleukin (IL)-7/15 after activation by bryostatin/ionomycin (B/I) surpassed T cells cultured in IL-2 in both expansion and anti-tumor activity. Our present study sought to determine whether B/I-activated T cells exposed to IL-7/15 exhibited gene expression patterns that were distinct from T cells cultured in IL-2. Methods: Lymphocytes were harvested from the lymph nodes of Pmel-1 mice whose footpads were previously injected with B16-GMCSF melanoma cells. Sensitized lymphocytes were then activated with B/I, washed and cultured in IL-2 or IL-7/15 for 1, 3 or 6 days. Lymphocytes were either directly analyzed by microarray or by real time quantitative polymerase chain reaction (RT-QPCR), or sorted into T cell subsets and analyzed for gene expression. Results: We demonstrated a significant difference in the gene expression patterns for T cells cultured in IL-7/15 vs. IL-2, starting at day 3 of culture and remaining consistent on day 6. Interestingly, we found that even when divided into T cell subsets, the central memory (TCM), effector memory (TEM) and effector (TE) T cells cultured in the same cytokine more closely resembled each other than their identical subset phenotype exposed to a different cytokine regimen. Conclusions: Our study suggests that the global changes in gene expression seen between unsorted T cells grown in IL-2 or IL-7/15 do not merely reflect the difference in frequency of TCM cells vs. TEM cells vs. TE cells that are enriched when cultured, but rather reflect that the genetic expression of those T cell subsets, when exposed to different cytokines, are fundamentally different, independent of T cell differentiation markers.
Abstracts: Poster Presentations

P211
The Immunologic Profile of Cutaneous Squamous Cell Carcinoma
D.J. Cucher, D. Bradley-Dunlop, R.S. Krouse.

Background: Immunosuppressed (IC) state may contribute to the increased development of cutaneous squamous cell carcinoma (CSCC). This may be related to changes in dermal immunologic cell presence and activity. This study is an initial evaluation of the immunologic difference of CSCC arising in IC and non-IC patients. Methods: Twenty cases of CSCC were included in this study (10 IC and 10 non-IC). Internal controls were from adjacent normal skin, and patients matched by site of tumor and age. IC state was due to medications or disease. Mononuclear cell populations were characterized by quantitative immunohistochemistry (IHC). Markers included: CD4 and CD8 (T cell markers), CD1a (antigen presenting cell marker), CD207 (Langerhans cell marker), CD 83 (dendritic cell activation markers), and Granzyme B (activated cytotoxic T cell marker). Statistical analysis was via a paired student t-test. Results: CSCC in IC patients had an average size of 1.9 cm vs 1.5 cm in non-IC patients. Tumors in the IC group invaded deeper (6 mm vs 3 mm). 7 of 10 tumors in the IC group were moderately to poorly differentiated, 3 were well differentiated. 6 of 10 tumors in the non-IC group were well differentiated, 4 moderately differentiated. Tumor tissue trended towards increased CD4 and CD8 (p=0.056) and CD8 (p=0.0489) T cell counts compared to normal skin in both groups (Fig. 1). The CD4:CD8 ratio in IC tumor was almost half of that in non-IC tumor. CD1a dendritic cells were modestly increased in tumor and adjacent skin of non-IC patients, and CD207 Langerhans cells in the tumors of both groups were decreased. CD83 was minimal and correlated with the absence of Granzyme B staining in all tissue groups. Conclusion: CSCC in IC individuals are larger, invade more deeply, and are less well differentiated compared to non-IC tumors. IHC suggests a lack of T cell anti-tumor function at the tumor site in both groups that may contribute to tumor progression. The immunologic differences in CSSC versus normal skin may be intensified in IC patients. Further study is needed to determine the entirety of immunologic changes in IC versus non-IC patients. This may lead to the development of local preventative measures for potentially aggressive SCC.

Fig. 1

P212
Isolated Limb Infusion with Melphalan and Actinomycin D for Melanoma: A Meta-analysis for Response and Toxicity

Introduction: Isolated limb infusion (ILI) has been developed as a simplified and minimally invasive alternative to isolated limb perfusion (ILP) to treat irresectable limb melanoma. An increasing number of centers around the world have reported their results using this procedure. For the current study we conducted this, to date, first ILI meta-analysis. Methods: A literature search was carried out according to the guidelines for diagnostic meta-analysis in order to select eligible papers reporting limb toxicity and response rates following ILI using melphalan and actinomycin D for irresectable limb melanoma. A total of 576 patients from 7 publications could be included. Results: Regional toxicity following ILI was low: no visible effect of the treatment or slight erythema and/or oedema was seen in 79% of the patients while considerable erythema and/or oedema with blistering was experienced by 19%. In 2% a threatened or actual compartment syndrome was seen while no procedure-related amputation has been reported. A complete response was seen in 33% of the patients and a partial response in 40%, resulting in an overall response of 73%. Stable disease and progressive disease was seen in respectively 14% and 13% of the patients. Conclusion: This first meta-analysis of ILI using melphalan and actinomycin D shows that regional toxicity was generally low. The procedure resulted in a satisfactory overall response rate of 73%. When comparing ILI and ILP one should bear in mind that ILI is usually applied to significantly older patients and patients suffering from higher stages of disease, which both have been shown to decrease the chance of a favorable response.

P213
miR-21 Inhibition Slows Disease Progression and Improves Survival in a Marine Metastatic Melanoma Xenograft Model
E. Paulus,* M.D. Fleming, C.H. Yang, L. Pfeffer. University of Tennessee Health Science Center, Memphis, TN.

Background: Advanced melanoma is an aggressive malignancy with a dismal prognosis. Interferon (IFN) is a biological agent that regulates cell proliferation and apoptosis. IFN also induces the expression of microRNA (miR)-21, which plays an important role in the oncogenic process. This study examines the role of miR-21 on human melanoma growth, invasion, metastatic potential, and sensitivity to IFN. Methods: Human melanoma cell line SK-MEL 188 was cultured and transduced with an antagonist-21 lentivirus (miR-21 KD) or an empty vector (EV) lentivirus, and subjected to various in vitro and in vivo biological assays. Results: Knockdown of miR-21 reduced SK-MEL 188 cell proliferation compared to EV and IFN (mean cell count ratio 0.52). When cell invasion was measured by transwell migration assays, the mean number of migrating cells (MMC) of miR-21 KD was decreased when compared to EV (p=0.035) and EV and IFN (mean cell count ratio 0.52). When cell invasion was measured by tranwell migration assays, the mean number of migrating cells (MMC) of miR-21 KD was decreased when compared to EV (p=0.035). Immunocompromised mice were injected via tail vein with EV and miR-21 KD SK-MEL 188 cells expressing luciferase for bioluminescence imaging. At 14 days, mice injected with EV-transduced cells had a statistically higher average
bioluminescence compared to mice with miR-21 KD. Mice injected with EV cells (n=7) had a median survival of 14 days, whereas mice injected with miR-21 KD (n=7) had a median survival of 21 days (p=0.037). Upon necropsy, mice injected with EV exhibited large melanocytic tumors in the liver and lungs, whereas mice injected with miR-21 KD exhibited smaller, often non-melanocytic nodules. Conclusion: These results indicate that miR-21 KD enhances the sensitivity of SK-MEL 188 cells to basal and IFN-induced inhibition of cell proliferation and migration. A significant increase in the median survival was found in mice injected with miR-21 KD cells. This study identifies a linkage between miR-21 and the metastatic behavior of human melanoma cells.

P214
Do Tumor-infiltrating Lymphocytes in Melanoma Metastasectomy Specimens Change after Ipilimumab Treatment? J. Ozao-Choy,1* R.R. Turner,1 T. Ly,1 O. Hamid,1 H. Torisu-Itakura,1 D.L. Morton,1 M.B. Faries.1 1. John Wayne Cancer Institute, Santa Monica, CA; 2. St. John’s Hospital Center, Santa Monica, CA; 3. Angeles Clinic, Santa Monica, CA.

Background: Ipilimumab is now an FDA-approved treatment for patients with metastatic melanoma. We examined whether tumor-infiltrating lymphocytes (TIL) in metastasectomy specimens differ before and after treatment with ipilimumab. Methods: Our cancer center’s database was queried for patients who had metastasectomy before and after ipilimumab treatment; paired specimens from the same patients were sought. Nine pairs of paraffin-embedded metastasectomy specimens were stained by immunohistochemistry for CD3+, CD8+ and CD4+ TIL. A blinded pathologist selected three separate areas of the tumor edge and within the tumor with the most immune infiltrate to photograph and to perform semi-quantitative assessments on the specimens. The image analysis of the percent area of staining was also performed with Image J. Both analyses were then analyzed by paired t-test. Results: The semi-quantitative pathology assessments of CD8+ TIL of the entire specimens showed an increase which approached a statistically significant difference (p=0.08); however, there were no differences in CD3+ or CD4+ TIL. The mean percent area of staining of CD3+, CD8+, CD4+ TIL at the tumor edge all decreased after treatment while the mean CD8+ TIL within the tumor increased; however, these changes were not statistically significant (Table 1). When a ratio of within tumor to edge (W:E) percent area was analyzed, the mean CD8+ TIL W:E ratio increased from 0.54 to 0.85 (p=0.05). Conclusions: This is the first study, to our knowledge, to evaluate paired whole metastasectomy specimens rather than biopsies from the same patients before and after ipilimumab treatment as well as the first to assess the location of TILs. Interestingly, all patients had significant numbers of TIL in their pre-ipilimumab specimens mostly concentrated at the periphery of the tumor. After treatment, the W:E ratio of CD8+ TIL appears to increase suggesting that ipilimumab enables a redistribution of CD8+ TIL from the edge to the center of the tumor. Further studies will be necessary to evaluate how this redistribution effect occurs and possible use as a prognostic factor to predict response and survival.

TIL % area before and after ipilimumab treatment

<table>
<thead>
<tr>
<th></th>
<th>Pre-ipilimumab mean % area</th>
<th>Post-ipilimumab mean % area</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD3+</td>
<td>11.0</td>
<td>7.4</td>
<td>0.10</td>
</tr>
<tr>
<td>CD8+</td>
<td>7.5</td>
<td>3.5</td>
<td>0.20</td>
</tr>
<tr>
<td>CD4+</td>
<td>8.5</td>
<td>3.1</td>
<td>0.27</td>
</tr>
<tr>
<td>CD8+ Within</td>
<td>5.3</td>
<td>4.0</td>
<td>0.35</td>
</tr>
<tr>
<td>CD8+ Edge</td>
<td>4.2</td>
<td>4.4</td>
<td>0.89</td>
</tr>
<tr>
<td>CD8+ Within</td>
<td>6.4</td>
<td>8.8</td>
<td>0.53</td>
</tr>
<tr>
<td>W:E ratio</td>
<td>0.55</td>
<td>0.58</td>
<td>0.84</td>
</tr>
<tr>
<td>W:E ratio</td>
<td>0.54</td>
<td>0.63</td>
<td>0.05 **</td>
</tr>
<tr>
<td>W:E ratio</td>
<td>0.72</td>
<td>0.90</td>
<td>0.87</td>
</tr>
</tbody>
</table>

**statistically significant

P215
Immunotherapeutic Intra-arterial Adoptive Transfer In a Murine Model C. Wilfong,* A.B. Blum, M. Kim, D. Fisher, J. Skitzki. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.

Background: Adoptive transfer of CD8 T cells by the standard intravenous (IV) route is a promising treatment for metastatic melanoma. We hypothesize that intra-arterial (IA) adoptive transfer avoids cell trapping within the pulmonic and splenic vasculatures, resulting in greater delivery of adoptively transferred cells to the tumor and improved anti-tumor effect. Methods: Female C57BL/6 mice were injected with 1 x 10^6 B16-OVA cells s.i. in the distal thigh. 1x106 activated, OVA-specific OT1 cells were labeled using two different fluorescent cell labels (CFSE or CTO). After 7 days of tumor growth, mice were injected IA with 1x107 CTO cells via common femoral artery and IV with 1x107 CFSE cells via tail vein. Trafficking of adoptively transferred cells was examined by flow cytometry at 1 and 24 hours post injection in liver, spleen, lymph nodes, lungs, and tumor. Tumor growth studies were performed via IV and IA injection of 5x106 OT1 cells with caliper measurements every 2 days. Results: At 1 hour, there were significantly more CFSE versus CTO labeled OT1 cells within the lymph nodes and tumors. There was no significant difference observed in the remaining tissues. At 24 hours there were significantly more CTO versus CFSE labeled cells within all tissues. Tumor growth studies showed no significant differences. Tumor sections 1 hour following adoptive transfer demonstrated no significant difference between the ratio of CFSE and CTO cells; however, at 24 hours there were significantly more CTO cells within the tumors. CTO cells accounted for 75% of the adoptively transferred cells seen within the tumor tissue at 24 hours (p<0.05). Conclusion: After 24 hours the amount of adoptively transferred OT1 cells using the IA route was greater in the tumor than using the IV route. Despite non-significant differences in tumor growth data between IV and IA groups, flow cytometry data suggests that intra-arterial delivery of adoptively transferred cells may result in a greater number reaching the tumor, which may translate to improved long-term outcomes.


Introduction: Merkel cell carcinoma (MCC) is a cutaneous neuroendocrine tumor that occurs on sun-damaged skin, may spread via lymphatics, and can therefore be staged with sentinel lymph node biopsy (SLNB). MCC is radiosensitive and chemo-sensitive, although the role of adjuvant therapy is still unclear. We
examined the impact of different treatments on the outcome of MCC. Methods: We performed a retrospective review of state cancer registry data from California, Oregon and Washington of patients diagnosed with pathologically confirmed primary skin MCC between 1988 and 2012 (n = 4,038). Data was analyzed using Cox-regression and Kaplan-Meier methods. Results: Mean tumor size was 27.7 mm. Head and neck primaries were the most frequent (47%), followed by extremity (37%) and truncal (9%). Male gender, age > 60 years, and tumor size > 21 mm were predictors of lower overall survival. Patients with positive nodes or no documented nodal evaluation had worse 5-year disease-specific survival compared to patients who were node negative. No nodal evaluation had decreased survival (Hazard Ratio = 1.72, 95% CI [1.18, 2.15]) compared to lymph node evaluation by SLNB. Complete lymph node dissection conferred improved survival in patients with a positive SLNB. In clinically node negative patients who had a positive SLNB, radiation and chemotherapy did not affect survival. Conclusions: Negative prognostic factors for MCC include male gender, age > 60 years, tumor size > 21 mm, and positive nodal status. Lymph node evaluation is an important component to MCC treatment. The role of adjuvant radiation and chemotherapy needs further evaluation.

P217

Clinical Significance of Ornithine Decarboxylase Activity in Melanoma K.A. Brueske, Y. Zhang, G. Peng, E.C. Hsueh.* Surgery, Saint Louis University, St. Louis, MO.

We have observed variable expression of ornithine decarboxylase (ODC), a key enzyme for polyamine synthesis, in human melanoma cell lines and tissues. Inhibition of ODC had negative growth and migration effect on human melanoma cells in vitro. We evaluated the expression of ODC and its regulatory molecules in human melanoma specimens and the clinical significance of their expression. Snap-frozen tumor specimens from 29 metastatic melanoma patients were evaluated. Total RNA was extracted and reverse transcribed into cDNA using random hexamers primer. Quantitative real-time PCR was performed using TaqMan Gene Expression Assay (Applied Biosystems) with the probe and primer set for ODC, antizyme-1 (AZ-1), antizyme-2 (AZ-2), antizyme-3 (AZ-3) and antizyme inhibitor (AZI). All experiments were repeated three times. GAPDH was used as an internal control. Clinical variables and follow-up disease status were obtained under a Saint Louis University IRB-approved protocol. Disease-free and overall survival was calculated from time of diagnosis to the time of recurrence or death, respectively. Log-rank test was used for survival analysis. Spearman test was used for correlation between laboratory and clinical variables. P < 0.05 was considered to be statistically significant. Variable expressions of ODC, AZI, AZ-1, AZ-2, and AZ-3 were observed in human melanoma tissues. There was an inverse correlation between ODC expression and AZ-1 expression, p < 0.05. However, there was no correlation between any of the antizyme isoform expression and the expression level of AZI, the antizyme inhibitor. On log-rank analysis comparing the marker expressions and clinical variables, significant correlation of AZ-3 expression and disease-free survival was noted (P = 0.0075). There was a trend for significant correlation between AZ-3 and Breslow thickness (P = 0.1). No significant correlation between the marker expressions and overall survival was observed. Significant correlation of disease-free survival with antizyme-3 was observed in this small cohort of metastatic melanoma patients. Validation of this finding is on-going in a larger dataset. Antizyme-3 may be a promising target for melanoma treatment and surveillance.

P218


Background: Despite evidence-based guidelines supporting sentinel lymph node biopsy (SLNB) and completion lymphadenectomy (CLND), national data suggests compliance is suboptimal. Advanced age is one of the most commonly cited reasons for failure to comply with standard guidelines. We therefore investigated the prognostic significance of SLN and non-SLN status in the elderly population Methods: Single institutional retrospective review of patients ≥ 65 with melanoma who underwent SLNB biopsy. Wilcoxon tests were used to compare continuous variables and chi-square or Fisher’s exact tests were used to compare categorical variables between groups. Univariable and multivariable Cox regressions were used for analysis of time-to-event variables. Results: 169 elderly patients underwent SLN biopsy. The median age was 76 (65-97) years; 134 (80%) had an ECOG performance status of zero, 31 (18%) one, and 3 (2%) two. Lymphatic mapping failed in 1 (1.8%) patients all with head and neck primaries. 63 (38%) patients had a positive SLN and 53 (84%) underwent CLND. Reasons for omission of CLND included patient refusal in 4 (40%), surgeon recommendation in 4 (40%) and postoperative complication in 1 (10%). Additional nodal disease was identified on CLND in 9 patients (17%) with a positive SLN. 5 patients (5%) with a negative SLN had a regional nodal basin recurrence after median follow-up of 82 months. SLN+ patients were younger (p < 0.0001), had thicker (p = 0.005) and more often ulcerated (p = 0.003) melanomas. In univariate analysis male sex (p = 0.04), Breslow depth (p < 0.001), ulceration (p < 0.02), positive SLN (p < 0.001) and positive non-SLN on CLND (p = 0.03) were all associated with poor disease-specific survival as well as disease-free survival. In multivariable analysis the presence of microsatellites (p = 0.02) and a positive SLN (p = 0.02) were associated with worse disease-specific survival. Conclusions: Lymphatic mapping and SLN biopsy with CLND for SLN+ patients provide important prognostic information. Lymphatic mapping failure in the elderly was uncommon. Age alone should not be a contraindication to SLN biopsy and CLND for SLN+ disease.

P219

Generation of Induced Pluripotent Stem Cells from Tumor-infiltrating Lymphocytes H. Saito,1 K. Okita, N. Fusaiki,1 M.S. Sabel,1 A. Chang,1 F. Ito,1* 1. University of Michigan, Ann Arbor, MI; 2. Kyoto University, Kyoto, Japan; 3. Keio University, Tokyo, Japan.

Human induced pluripotent stem cells (iPSCs) derived from somatic cells of patients hold great promise for autologous cell therapies. One of the possible applications of iPSCs is to use them as a cell source for producing autologous lymphocytes for cell-based therapy against cancer. Tumor-infiltrating lymphocytes (TILs) were found to have tumor-reactive T cells and have been used for adoptive cell therapy for metastatic melanoma. The objective in this study is to generate iPSCs from TILs and assess their pluriplasticity. Under the approved protocol by the Institutional Review Board and the Human Pluripotent Stem Cell Research Oversight Committee, we obtained tumor from a patient who provided informed consent for tissue procurement and generation of iPSCs. TILs were reprogrammed by Sendai virus (SeV) vector encoding four pluripotency transcription factors (Oct3/4, KIF4, Sox2 and c-Myc). TIL-derived iPSCs (TIL-iPSCs) were characterized by their pluriplasticity. Within 3 weeks of infection with SeV to deliver pluripotency transcription factors, we identified colonies that resembled embryonic stem cells (ESCs) among the T cell derivatives. TIL-iPSCs displayed typical stem cell morphology and had a normal karyotype. Alkaline phosphatase and immunofluorescence staining with stem cell surface marker, OCT3/4, SSEA3, SSEA4, TRA1-81 and TRA1-60 proteins suggested pluripotency of colonies. RT-PCR analyses revealed that TIL-iPSCs expressed pluripotent stem cell markers such as NANOG, OCT3/4 at levels comparable to those in ESCs. T cell receptor (TCR) gene rearrangement analysis in TIL-iPSCs confirmed that they originated from mature T cells and retained diversity of TCR gene rearrangement. In conclusion, human iPSCs with diverse TCR gene rearrangement can be generated from TILs efficiently by SeV encoding four pluripotency transcription factors. Future work will explore their differentiation potential to T cells for cancer immunotherapy. We acknowledge Dr. Mamoru Hasegawa in DNA Vec Corporation for kindly providing Sendai virus vectors.
**P220**

**Sentinel Lymph Node Biopsy is Less Frequently Performed in Melanoma Patients with a Low Socioeconomic Status**


1. University Medical Center Groningen, Groningen, Netherlands; 2. Comprehensive Cancer Centre the Netherlands, Groningen, Netherlands.

Background: Sentinel lymph node biopsy (SLNB) is recommended for patients with a cutaneous invasive melanoma AJCC stage Ib and II. In the US, whether a SLNB is performed depends on patient factors including high socioeconomic status and possession of a private health care insurance. We analyzed whether socioeconomic status and other patient and tumor characteristics influenced the chance of having a SLNB performed in a country where every patient has equal access to healthcare. Material and Methods: Patients diagnosed with a cutaneous invasive melanoma of ≥1 mm between 2004 and 2011 from the northeastern part of the Netherlands were selected from the Netherlands Cancer Registry. An estimate of the socioeconomic status (SES) was defined by income, employment, and level of education. Patients were equally divided over five groups based on SES score. Regression analysis was performed to assess the association of patient and tumor characteristics and SLNB use. Results: SLNB was performed in 1009 of the 2413 included patients (42%). The frequency of performing SLNB increased from 24% in 2004 to 55% in 2011 (P<0.001). Patients were less likely to undergo SLNB if they had a low SES (P=0.03), a melanoma located in the head and neck area (P<0.001) or when they were older than 55 years (P=0.001). SLNB use was more likely when the diagnosis of melanoma was made in a university hospital (P=0.045) or when the Breslow thickness was 2.01-4.0 mm (P=0.03). Conclusions: The use of SLNB has increased significantly between 2004 and 2011. However, although SLNB is a worldwide accepted staging procedure for patients with invasive cutaneous melanoma, in 2011 it was still only performed in 55% of the Dutch patients with a melanoma ≥1 mm. SLNB was less frequently performed in patients with melanoma in the head and neck region, patients older than 55 years and in patients with low socioeconomic status. The final MSLT-I results should reveal whether this also has impact on the survival of these subgroups of patients.

**P222**

**Cervical Sentinel Node Melanoma Metastases: When is Parotidectomy Indicated?**


Introduction: Current standard of care in head and neck (H&N) melanoma includes completion lymph node dissection (CLND) for patients with cervical sentinel node (SN) metastases. Although superficial parotidectomy is indicated for parotid SN metastases, it is unclear whether a parotidectomy is required in the setting of cervical SN metastases alone. Methods: We performed a retrospective review of our prospectively maintained melanoma database. We queried for patients with H&N melanoma, age at diagnosis, sex, primary tumor site, Breslow, histologic subtype, ulceration, procedure type, location of SN lymph node (LN) positivity, size of SN metastasis, and disease recurrence. Results: We identified 70 patients with parotid SN metastases who underwent CLND for cervical SN positivity. Five underwent initial parotidectomy at the time of CLND and 65 did not. Parotid LN metastases were found in two of the five undergoing initial parotidectomy. Of those without initial parotidectomy, six (9%) developed subsequent parotid LN metastases and were treated with parotidectomy. Compared to patients without parotid involvement (n=62), patients with parotid LN metastases (n=8) were significantly more likely to have anterior scalp primary lesions (Fisher’s exact test p=0.001) and thicker primary lesions (t test p=0.02, mean Breslow with parotid involvement 4.05 mm, without 2.55 mm). Cervical SN location did not predict parotid involvement. No significant differences were identified in histologic subtype, ulceration, or size of SN metastases. However, parotid LN metastases were identified even in patients with isolated tumor cells in cervical sentinel nodes. Conclusions: The rate of parotid nodal involvement with a positive cervical SN is similar to that of involvement of non-sentinel nodes in other areas. Pending the results of ongoing clinical trials, parotidectomy should be considered at the time of CLND in patients with cervical SN metastases, particularly patients with anterior scalp lesions and thicker primary tumors.

**P223**

**Small Bowel Metastasectomy for Adoptive Immunotherapy in Metastatic Melanoma: A Single Institution Experience**


Introduction: Prolonged survival has been demonstrated in select patients (PT) with metastatic melanoma (MM) receiving adoptive cell therapy (ACT). Procurement of tumor infiltrating lymphocytes (TIL) for ACT requires metastasectomy. Prior studies have demonstrated benefit in PT with MM undergoing thoracic or hepatic metastasectomy for TIL procurement. Small bowel is the most common gastrointestinal site of MM (SBM) and carries a poor prognosis with median survival of 6 to 8 months (m). We evaluate the outcome of PT with SBM who underwent resection in preparation for TIL therapy. Methods: A retrospective analysis of a prospective database identified 102 PT with patients treated with ILBCG. Stage/extent of disease, demographic data, and outcome (overall and melanoma-specific survival) were analyzed to assess treatment patterns and efficacy of ILBCG in a general melanoma population. Results: 593 patients received ILBCG. At the time of ILBCG 93 patients were Stage I or II, 326 were Stage III and 172 were Stage IV. Five-year overall survival (OS) and melanoma-specific survival (MSS) for the entire cohort were 51.0% and 54.5%, respectively with median survivors not yet reached. MSS for patients with Stage I/II, Stage III, and Stage IV at time of ILBCG were 64.7%, 56.1%, and 46.2%, respectively. Surprisingly, patients older than 60 exhibited improved post-BCG outcomes relative to younger patients (p=0.012). On multivariable analysis, stage of disease and female sex carried significant survival advantages. Unexpectedly, patients with head and neck sites of disease had significant survival advantage relative to truncal lesions (p=0.026) and equivalent to extremity melanoma. Conclusions: ILBCG remains a valuable therapy for superficially accessible metastatic melanoma. Patients with head and neck sites of disease and older patients, both of which are normally adverse prognostic groups, enjoyed significantly improved outcomes and may be particularly good candidates for this therapy. Ongoing research will investigate mechanisms of action for this inexpensive and non-toxic therapy.
SBM from 2,313 PT treated for MM from December 1989 to June 2011. Results: The incidence of SBM was 4%. At initial diagnosis, AJCC stage was I (23%), II (27%), III (25%), and IV (25%), 11% classified as M1c. Mean time to development of SBM was 48m (0.5-346m). Eighty-two (80%) presented with symptoms of fatigue (59%), pain (40%), obstruction (23%) and acute GI bleeding (3%). The 102 PT underwent 125 operations. Eighty (78%) underwent single segmental small bowel resection (SBR), 22% required multiple SBR, and 17% required multi-visceral resection. Following resection 21% had no evidence of disease (NED) and 79% had residual disease (RD). Post-operative morbidity and mortality was 19% and 2% respectively. Sixty-one (60%) went on to receive ACT. Median overall survival (OS) for all PT having surgery was 12.3 m. PT resected to NED had a median OS of 5.5 years, vs. 10.0 m in PT with RD (p <0.0001). Median OS was superior for those PT with ≥ 3 lesions resected vs. ≤ 4 lesions resected, 13.1 m vs. 9.4 m respectively (p = 0.049). Actuarial 1-Y, 3-Y and 5-Y OS from resection was 52%, 21% and 17%. Overall comparison of actuarial 1-Y, 3-Y and 5-Y OS for PT NED vs. RD was significant (85%, 68% and 60% vs. 42%, 10% and 7%). Conclusions: Prolonged OS can be achieved in a select group of PT who undergo resection of SBM in preparation for immunotherapy.

**P226**

Melanoma and Sarcoidosis: An Unusual and (or) Confounding Relationship? R. Tuttle,* N. Khashalani, S. Singla, J. Skitzki, V. Francescutti, J. Kane. Roswell Park Cancer Institute, Buffalo, NY.

Introduction: Sarcoidosis is a very rare inflammatory disease (<40 cases per 100,000) of unknown etiology, primarily involving the lungs/lymph nodes. We observed a higher than expected incidence of sarcoidosis in our melanoma patients. Methods: Retrospective review of all melanoma patients at our institution from 2003-2013 who also had an ICD-9 diagnosis of sarcoidosis. Patients, tumor, treatment, and follow-up information were collected/analyzed. Results: Out of 3912 melanoma patients, 21 also had a diagnosis of sarcoidosis (calculated incidence 537 cases per 100,000). All patients were Caucasian and 48% were male. Melanoma stage at diagnosis: I-43%, II-24%, III-29%, and unknown-4%. The relationship of sarcoidosis to melanoma diagnosis: 33% prior to, 14% synchronous, and 48% subsequent. For patients diagnosed with melanoma first, the median time to the sarcoidosis diagnosis was 22.8 months. The site of sarcoidosis was 48% lymph node only, 14% lung only, 14% lymph node and lung, and 14% unknown. Sarcoidosis was asymptomatic in 29% of patients; 10% received steroids. Eleven patients with sarcoidosis diagnosed simultaneously or subsequently to melanoma were found on surveillance imaging. Melanoma immunotherapy was administered to 9 patients; 4 prior to the sarcoidosis diagnosis (3 received Interferon and 1 Iplimunumab). During melanoma follow-up, sarcoidosis led to an initial incorrect diagnosis of recurrent melanoma in 48%. This resulted in 12 additional procedures (10 mediastinal biopsies, 2 lung/endothoracic biopsies) to make the correct diagnosis. A diagnosis of metastatic melanoma was delayed in 1 patient due to the presence of known sarcoidosis. Conclusions: The incidence of sarcoidosis in melanoma appears to be significantly higher than for the general population. Lung and lymph node involvement confounded melanoma surveillance, leading to additional workup for “false positive” findings or a delay in the diagnosis of metastatic disease. The etiology of this unusual relationship requires further investigation.

**P225**


Purpose Surgical outcomes in melanoma surgery need to be assessed on the basis of both oncological outcome and surgical complications. Currently there is no meaningful data on complication rates for common procedures or validation of quality assurance parameters in melanoma surgery. These procedures include wide excision (WE), sentinel node biopsy (SNB) and regional lymph node dissection (RLND). There is only minimal data available whereby individual surgeons can audit their practice. Methods Surgical performance indicators were determined from a review of the literature and expert opinion. Audit data has been collected against these parameters since 2008 and is presented in a quarterly ‘parameters’ meeting. Key performance indicators (KPI) include death, unplanned intensive care unit admission, DVT/PE, return to theatre and readmission to hospital for complications. Melanoma surgery specific performance indicators (MSSPI) were developed and assessed. Proposed standards for MSSPIs were determined. For wide excision primary closure (WE-PC) wound infection and dehiscence should occur in <2% of cases, for wide excision skin graft (WE-SG) failure of >20% of the grafted area should occur in <5% of cases and for wide excision flap repair (WE-flap) flap necrosis should occur in <5% of cases. In SNB procedures wound infection and seroma requiring intervention should occur in <5% of cases and the procedure should aim to remove all the sentinel nodes identified on the lymphoscintigram. In RLND cases involving the neck (a four levels), axilla, inguinal and ilioinguinal fields at least 20, 10, 7 and 11 lymph nodes should be retrieved >90% of the time respectively. The rates of wound complications requiring intervention in the neck, axilla and groin should be <5, <10 and <30% respectively. Results Complications classified as KPIs were uncommon. MSSPI targets were generally achieved though for WE-SG the benchmark was exceeded in 2011. Data for 2011 and 2012 are shown in the table below. Conclusion The data presented provide a standard by which melanoma surgeons can audit their surgical performance with the ultimate aim of improving patient outcomes.

**P224**

Factors Associated with Sentinel Node Positivity in Patients with Thick Cutaneous Melanoma (≥4mm) J.Y. Wong,1 K.J. Fisher,1 J. Kosco,2 M. Konstantinovic,2 N. Gvosseyev,2 J.L. Messina,1 A.A. Sarnaik,1 C.W. Cruse,1 C.A. Puleo,1 R.J. Gonzalez,1 V.K. Sondak,1 J.S. Zager,1 1. H Lee Moffitt Comprehensive Cancer Center, Tampa, FL; 2. University of South Florida School of Medicine, Tampa, FL.

Introduction: Although sentinel lymph node biopsy (SLNB) is standard of care for patients (pts) with intermediate thickness melanoma, controversy remains on its utility and prognostic value in thick melanoma. We sought to identify the pt and tumor related factors that are predictive for clinically occult nodal metastasis and whether SLNB has prognostic implications in pts with thick melanoma. Methods: From 1999 to 2012, 419 pts with thick melanoma (≥4 mm) who underwent SLNB from a single institution were retrospectively reviewed. Pts who presented with clinically positive nodal or distant disease were excluded from the study. Demographic and clinicopathologic characteristics were correlated with nodal status based on SLNB. Univariate (UV) and multivariate (MV) logistic regression analyses were performed. Results: Of 419 pts, 292 (69.7%) were male and the median age was 64. Median Breslow thickness was 6 mm (range 4-25 mm). Overall, 161 pts (38.4%) had a positive sentinel node (SNL), 251 (59.9%) had a negative SNL, and 7 (1.7%) failed to map on lymphoscintigraphy with no SLNB was performed. On UV analysis, ulceration, trunk and extremity location, and presence of satellitosis were predictive of SNL status. Mitotic rate, tumor regression, and Breslow thickness, however, were not predictive of SNL status. On MV analysis, truncal (odds ratio [OR] 4.0, p =0.0003) and extremity (OR 3.17, p=0.008) melanoma, and presence of satellitosis (OR 10.31, p =0.006), were significant predictors of a positive SNL. Desmoplastic histology had a decreased likelihood (OR 0.09, p=0.001) for a positive sentinel lymph node on UV and MV analysis. Conclusions: In thick melanoma, factors historically associated with SNL status (ulceration, Breslow thickness, mitotic rate) were not found to be predictive of positive SNL. However, truncal or extremity primary tumors were more...
commonly found to have positive SLNB. Satellitosis was the strongest predictive factor for a positive SLNB and hence appears to indicate patients with thick melanoma at particularly high risk of regional spread.

<table>
<thead>
<tr>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR (95% Wald CI) p-value</td>
<td>OR (95% Wald CI) p-value</td>
</tr>
<tr>
<td>Age (≥ 66 vs. ≤ 65)</td>
<td>0.73 (0.47-1.10)</td>
</tr>
<tr>
<td>Sex (Female vs. Male)</td>
<td>1.10 (0.79-1.58)</td>
</tr>
<tr>
<td>Location</td>
<td></td>
</tr>
<tr>
<td>Trunk vs. Head/Neck</td>
<td>4.00 (2.07-7.85)</td>
</tr>
<tr>
<td>Extremities vs. Head/Neck</td>
<td>2.83 (1.56-5.12)</td>
</tr>
<tr>
<td>Breslow Thickness (≥ 6 vs. &lt; 6 mm)</td>
<td>1.21 (0.51-3.60)</td>
</tr>
<tr>
<td>Histology</td>
<td></td>
</tr>
<tr>
<td>Desmoplastic vs. Superficial spreading</td>
<td>0.07 (0.02-0.29)</td>
</tr>
<tr>
<td>Acral Lentiginous vs. Superficial spreading</td>
<td>0.80 (0.32-2.25)</td>
</tr>
<tr>
<td>Nodular vs. Superficial spreading</td>
<td>0.80 (0.44-1.48)</td>
</tr>
<tr>
<td>Vertical growth phase</td>
<td>0.78 (0.08-6.67)</td>
</tr>
<tr>
<td>Tumor regression (Absent vs. Present)</td>
<td>0.58 (0.22-1.44)</td>
</tr>
<tr>
<td>Mitotic rate (≥ 5 vs. &lt; 5)</td>
<td>1.00 (0.69-1.65)</td>
</tr>
<tr>
<td>Satellitosis</td>
<td>4.03 (1.75-9.21)</td>
</tr>
</tbody>
</table>

* dichotomized at median value

A Pilot Study of CXCL12/CXCR4 Chemokine Expression in Sentinel Lymph Node Tracts in Cutaneous Melanoma: An Often Overlooked Signaling Pathway

Introduction: The chemokine signaling environment of the sentinel lymph node (SLN) tract is an often overlooked but clinically important pathway for tumor metastasis. Our hypothesis is that the CXCR4/CXCL12 receptor/ligand pair, implicated in metastatic melanoma, is present in the lymph node tract of subjects with cutaneous melanoma. Methods: We designed a prospective pilot study of consecutive patients with cutaneous melanoma as the indication for SLN biopsy. Following IRB approval, study subjects were consented, enrolled, and SLN tracts were collected intraoperatively. Immunohistochemical (IHC) staining of the tissue was then used to identify the presence of CXCR4 and CXCL12. IHC images were analyzed by multiple observers in a standardized fashion to determine the degree of receptor/ligand and control staining. Clinicians, investigators and graders were blinded to the subject’s clinicopathologic status. Results: At this interim evaluation 10 subjects were enrolled in this study. The median age of subjects was 65 (Range 41-84), 90% were male (n=9). In terms of location, 65% of lesions were truncal, and 40% of lesions involved an extremity. Review of pathologic factors showed mean Breslow thickness of 2.20 (SD=3.10), mean mitotic figures were 1.67/mm² (SD=2.25). A single subject (10%, n=1) had a positive sentinel node with 90% (n=9) negative on SLNB. IHC images showed expression of CXCR4 in 50% of SLN tracts with an average IHC image score of 2.0 (SD=0.816). CXCL12 was expressed in 100% of SLN tracts with an average IHC image score of 2.50 (SD=0.527). Of note, the one subject with a positive SLN had IHC images identifying only positivity of CXCL12, with negative CXCR4 staining. Conclusion: CXCL12 was identified via IHC images in all SLN tracts. Contrary to our initial hypothesis, CXCR4 was identified in only 50% of tracts. Receptor/ligand interactions of the SLN tract with respect to CXCR4/CXCL12 is a novel field of study that is essential to future understanding of chemokines and their role in melanoma metastasis.

Immunohistochemical (IHC) Images of Sentinel Lymph Node Tract Specimens: A) 4',6-Diamidino-2-phenylindole (DAPI) Nuclear Stain B) IHC Image of Positive Sentinel Lymph Node, +CXCL12 C) IHC Image of Negative Sentinel Lymph Node, +CXCL12, -CXCR4

P227

Keystone Flaps can be Performed Safely by Surgical Oncologists without Specific Plastic Surgery Training

R.K. Orr, N. White, R.B. Hird, C. Nguyen, Gibbs Regional Cancer Center, Spartanburg, SC.

Introduction: Behan has popularized the Keystone Design Island Perforator flap as an alternative to skin grafting for cutaneous defects from oncologic resection and as an excellent cosmetic alternative to extensive primary closure. Following a publication by the Sydney Melanoma Unit (Ann Surg Oncol 2008:15:2867-73) we began using the Keystone flap and are reporting this prospective experience. Methods: Beginning October 2008, one surgeon performed 88 keystone flaps in 86 patients. The surgeon has experience in cutaneous oncology, but has no formal plastic training and learned the Keystone technique by extensive study of publications. Data were prospectively collected including indications for the procedure, size of the cutaneous defect, and complications. The results during the first half of the experience (through June 2011) were compared to the later experience. Results: Average age 61.4 (20-92), 59% were men. 79% had melanoma, 9% basal cell carcinoma, 8% squamous cell, carcinoma, and 1 each Merkel cell and extensive condyloma. 33% trunk, 34% upper extremity, 30% lower extremity, and 3% neck, Mean thickness for melanomas was 1.4 mm (0.3-4.2). Sentinel node biopsies were performed in 55 (14.5% positive). The average cutaneous defect for all patients was 21.4 cm² (3-88); 25% were greater than 25 cm². There were no flap losses, returns to the OR, nor hospitalizations related to procedural complications. One major complication occurred: a 50% wound separation that required prolonged healing by secondary intention (15th patient in series). Minor complications occurred in 9 additional patients (9.8%): 5 minor wound defects that healed easily, 2 infections, and 2 that required resuturing of a portion of the wound. 36 flaps were performed during the first half of the experience, with a 22% complication rate, as compared to 2 complications in the last 52 flaps (4%). Conclusions: Keystone flaps may be performed safely by a surgeon without specific plastic surgery training. Major complications are rare, but minor wound complications were frequent during the “learning curve” phase.
using the harmonic scalpel was significantly shorter (208 vs. 261 minutes, \( p = 0.02 \)) than the cases using the LigaSure. There was no difference in the mean lymph node retrieval 13 (9-19) compared to 15 (7-26) (\( p = 0.4 \)), the incidence of wound infections, including cellulitis (11% vs. 22%, \( p = 1.0 \)) and the median length of stay (23 hours vs. 23 hours, \( p = 0.66 \)), for the harmonic and LigaSure, respectively. Although the median drain duration was shorter for the harmonic scalpel technique (22 vs. 35 days) it did not reach significance \( p = 0.5 \). Similarly, there was a higher incidence of seromas using the harmonic scalpel technique (44% vs. 22%) but again it did not reach significance, \( p = 0.6 \).

Conclusion: Lymphorrhea and seroma formation remain a major morbidity of inguinal lymphadenectomy, and a minimally invasive approach does not resolve this problem. Some animal models have suggested that alternative energy sources coapt lymphatic vessels compared to electrocautery. This has not been our experience in clinical practice and neither tissue sealing devices were associated with high incidence of seromas and prolonged drain days. Further investigation is warranted in techniques to limit seroma formation following inguinal lymphadenectomy.

**Comparison of alternative energy sources for minimally invasive inguinal lymphadenectomy**

<table>
<thead>
<tr>
<th>Energy Source (N)</th>
<th>Operative Time</th>
<th>Conversion</th>
<th>Number of LN</th>
<th>SS1</th>
<th>Drain Days</th>
<th>Seroma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harmonic Scalpel (9)</td>
<td>280</td>
<td>123</td>
<td>113%</td>
<td>22</td>
<td>41%</td>
<td></td>
</tr>
<tr>
<td>LigaSure (9)</td>
<td>261</td>
<td>0</td>
<td>15</td>
<td>22</td>
<td>35</td>
<td>22%</td>
</tr>
<tr>
<td>p-value</td>
<td>0.02</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

**P230**

**Sentinel Node Biopsy under Local Anesthesia: The European Institute of Oncology Experience** E. Pennacchioli,* A. Intelsiano, F. Verrecchia, G. Tosti, F. Baldini, G. Spadola, M. Mosconi, A. Testori. European Institute of Oncology, Milan, Italy.

Background: Sentinel node biopsy is an important staging procedure in several tumors like melanoma. We decided to evaluate feasibility, safety and satisfaction of both patient and surgeon about sentinel node biopsy performed under local anesthesia and with single-day hospitalization. Materials and Methods: Since 1999 at EIO Melanoma division a questionnaire about SNB performed under local anesthesia has been submitted to patients and surgeons. SNB is performed at the same time of the wide excision of primary tumor and the local anesthesia approach was proposed only on patients with a single site sentinel node localization, excluding neck and poplite sentinel nodes. We recorded data about the previous primary lesion, the preoperative medical information given to patients about the procedure to be planned, any symptomatology of pain during the procedure through a scale from 0 to 10, patient’s satisfaction, hospitalization setting, drugs used and drugs dosage, availability of anesthetist during the procedure in the event of a patient requiring a sedation and duration of surgery. Results: Since 1999 498 forms were collected. 80% of patients were dismissed the same day and 87% of them were satisfied of the day-hospital setting. Duration of surgery was less than 30 minutes in 53% of cases but 35% of patients expected an even shorter surgery. 50% of patients felt pain during the surgery but the average value from 0 to 10 was 3.8 and the median value was 4. 82% would repeat it again under local anesthesia and 86% would suggest to do so to other patients. Conclusions: SNB can be performed under local anesthesia and in a day surgery setting safely and with patients satisfaction. It can also reduce costs of hospitalization and reach a better impact under local anesthesia and in a day surgery setting.

**P231**

**Two Decades Single-center Experience of Melphalan-based Isolated Limb Perfusion (ILP) with or without TNF for In-transit Melanoma Metastases** K. Veerman, B.L. Van Leeuwen, H.J. Hoekstra, R. Van Ginkel.* Surgery, UMCG, Groningen, Netherlands.

Background In-transit metastases (ITMs) develop in 5-8% of all melanoma patients, often preceding systemic disease and thus influencing survival. This accentuates the importance of ITMs management. In case of rapid recurrence or numerous ITMs, ILP is preferred. This study reports the Groningen perfusion experience with Melphalan (M-ILP) and TNF-Melphalan (TM-ILP) for ITMs. Methods Between 1992 and 2012 57 perfusions (18 M-ILPs; 39 TM-ILPs) were performed and included in this study. Patients with ‘limited’ ITMs received M-ILP (10-13 mg Melphalan/L limb volume) and patients with ‘bulky disease’ TM-ILP (1-4 mg TNF). Cox-regression analysis was used to determine variables with significant impact on time to local progression (TLP) and systemic progression (TSP) and melanoma-specific survival (MSS). For clinical response logistic regression was used. Survival curves were constructed by the Kaplan Meier-method and compared with the log-rank test. Results In 87 ILPs overall response was 90%; 27 complete responses (47%), 27 partial responses (47%), 3 no responses (6%). In 18 M-ILPs complete responses (33%) were observed and in 39 TM-ILPs 21 complete responses (54%), \( p = 0.124 \). Age below 65 years and low tumor load (≤ 5 ITMs) were independent prognostic favorable factors for developing complete response to ILP (resp. \( p = 0.003 \); \( p = 0.038 \)). After a median follow-up of 15 (range, 1-144) months local recurrence or disease progression occurred in 36 patients (63%). Absence of CR (\( p = 0.101 \)) and Stage IIIC disease (\( p = 0.002 \)) were independent prognostic factors for progression to systemic disease. Non-ulcerating primary melanoma and complete response to ILP are favorable to MSS (Fig 1, resp. \( p = 0.021 \), \( p = 0.018 \)). Conclusion Melphalan-based Isolated Limb Perfusion is an effective regional treatment for in-transit melanoma metastases, in case of bulky disease Isolated Limb Perfusion with TNF and Melphalan is preferred.

**Figure 1**

Melanoma Specific Survival. A: MSS vs. Ulceration; B: MSS vs. Complete response

**P232**

**Indocyanine Green and Fluorescence Lymphangiography for Sentinel Lymph Node Identification in Melanoma** J.M. Cloyd,* I.L. Wapnir, B.M. Read, R.S. Greco. Surgery, Stanford University, Stanford, CA.

Assessment of the sentinel lymph node (SLN) has been established as a reliable method of determining regional lymph node involvement, one of the most important prognostic indicators in melanoma. SLN mapping with Indocyanine green (ICG) fluorescent lymphangiography is an attractive alternative to technetium-99m sulfur colloid (Tc-99m) and isosulfan blue dye (ISB). We sought to determine the effectiveness of ICG-guided SLN mapping compared to other modalities. Thirty-two consecutive patients with cutaneous melanoma undergoing SLN biopsy were retrospectively reviewed. All patients underwent preoperative lymphoscintigraphy with Tc-99m. After induction of general anesthesia, peritumoral intradermal injections of 4mL ISB and 2mL of ICG were performed. Real time fluorescence imaging was performed using the SPY infrared imaging system (Novadaq Technologies Inc; Bonita Springs, FL). Concordance of the three modalities with histopathology was recorded. ICG was defined as successful if fluorescence was detected in situ and guided the LN dissection. A total of 46 lymph nodes were identified from the 32 patients (range 1–3). The majority of melanomas were extremity based (n=19), were superficial spreading type (n=25) and had SLN localized to the axilla (n=24). Rates of successful in situ detection per lymph node were 43/46 (93.5%) for Tc-99m, 31/46 (67.4%) for ISB and 42/46 (91.3%) for ICG. All but one LN was fluorescent ex vivo. Percentage of patients with at least one LN detected was 32/32 (100.0%) for Tc-99m, 22/32 (68.8%) for ISB and 28/32 (87.5%) for ICG. On univariate logistic regression, age, gender, body mass index, melanoma subtype, Breslow depth, location of primary, histological status of LN, location of LN, radioisotope count, and uptake of blue dye were not associated with failure of ICG fluorescence. There were no complications related to ICG administration. In conclusion, fluorescence lymphangiography with intraocular ICG injection facilitates SLN identification and is more effective than blue dye in melanoma staging.
P233
Malignant Adnexal Tumors of the Skin: A Single-institution Experience

T. Oyasuji, W. Tan, J. Kane, J. Skitzki, V. Francescutti, N. Khushalani. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.

INTRODUCTION: MATS are rare tumors with no consensus on management guidelines. We aimed to examine the natural history of MATS, define treatment paradigms, and identify predictors of improved survival.

METHODS: A retrospective review of all MATS treated at our institution from 1990 through 2012 RESULTS: Fifty patients (pts), median age 59.5 yrs (range 22-95), 56% males were identified within the time period. Nearly half (48%) of the pts were > 60 yrs. Primary site was head and neck (52%), upper extremities (16%), lower extremities (16%) & trunk (16%). The histologic sub-types by frequency are outlined in the table. Pts most commonly presented with early stage disease (Stage I, 32%) & were mostly nodal-negative (N0, 88%). The vast majority were T1 (44%) tumors. T2, T3 and T4 tumors were 18%, 2% and 10% respectively (Tx, 26%). Forty-nine pts (98%) had surgical treatment with wide local excision (30%), Mohs (22%) and local excision (46%). Four pts (8%) received adjuvant chemotherapy (CT), and 7 pts received radiation therapy. Six pts (12%) experienced recurrence (3 local, 1 regional and 2 distant recurrences). Median OS was 158 months (95% CI, 52-255). OSS at 5 yrs was 62%, and at 10 yrs was 57%. Age > 60 years (HR 12.9, P = 0.00008) was an unfavorable predictor of OS. The 5-yr and 10-yr disease-specific survival was 63%. No association was found between the primary tumor stage and pathologic nodal positivity, though the sample size was small. CONCLUSIONS: In our small series for MATS, prognosis was better for younger patients. While surgery remains the mainstay of therapy, the role of surgical nodal basin staging and adjuvant chemotherapy in MATS needs further investigation.

Histologic subtypes of MATS and their distribution in our series

<table>
<thead>
<tr>
<th>Histologic Subtype</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eccrine adnexocarcinoma</td>
<td>16 (30%)</td>
</tr>
<tr>
<td>Sebaceous adnexocarcinoma</td>
<td>9 (18%)</td>
</tr>
<tr>
<td>Maliginant eccrine poroma</td>
<td>6 (12%)</td>
</tr>
<tr>
<td>Schaudinn’s duct adenocarcinoma</td>
<td>2 (12%)</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>5 (10%)</td>
</tr>
<tr>
<td>Malignant eccrine spiradenoma</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Malignant nodular hidradenoma</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Pronecrocarcinoma</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Apocrine adnexocarcinoma</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

P234
Lymph Node Staging for Mucosal Melanoma


Introduction: Mucosal melanomas of the vulva and anorectum are rare and have more aggressive biology than the more common cutaneous melanoma. Because of their rarity, no specific staging system or guidelines exist to prognosticate or aid in therapeutic decision making. This study describes our experience with lymph node (LN) staging for these melanomas by sentinel lymph node biopsy (SLNB) or lymphadenectomy (LAD) and their clinical outcomes. Method: A retrospective chart review was carried out for adult patients diagnosed with melanoma from January 1990 to April 2013, treated at our tertiary referral center. Those with cutaneous, ocular, head and neck, unknown primaries, or metastatic disease at time of diagnosis were excluded. Patient management was at the discretion of the attending physician. Survival curves were generated using the Kaplan-Meier method and compared using the log-rank test. Results: A total of 2195 melanoma patients were identified; 26 (1.2%) had melanoma of the vulva, cervix, vagina, or anorectum. Of these, 19 (73%) patients had gynecologic mucosal melanoma (GMM) and 7 (27%) had anorectal mucosal melanoma (ARMM). Median age was 67.5 (range 49-91 years); 92% were females. The majority (84.6%) underwent a wide local excision of the primary. Ten (38.5%) patients did not undergo any nodal staging procedure; 9 (34.6%) had SLNB and 7 (26.9%) had initial elective LAD. Four patients (44.4%) had positive LN on SLNB; 2 went on to have completion LAD with no further positive LN. Two of seven elective LAD (28.6%) yielded positive LN. There was no difference in median post-surgical recurrence without SLNB, thereby hastening definitive treatment.

P235
PET-CT Identifies Regional Nodal Metastasis in Cutaneous T4 Melanoma

Melanoma M.S. Jones,* M. De Guzman, M. Riveria, J.L. Baynosa, C.R. St Hill, D.M. Kirtan. General Surgery, University of Nevada School of Medicine, Las Vegas, NV.

Introduction: Positron Emission Tomography-Computed Tomography (PET-CT) has been investigated as an adjunct to more accepted methods of cutaneous melanoma staging. There is a paucity of literature investigating the concordance of sentinel lymph node biopsy (SLNB) findings and PET-CT results in T4 melanoma patients. The objective of this study was to investigate the utility of PET-CT in the preoperative workup of patients with T4 melanoma. Methods: According to our IRB approval, a retrospective review was conducted of consecutive subjects having received SLNB for cutaneous T4 melanoma from 2007-2012. Regression analysis was performed to identify clinicopathologic factors associated with PET-CT positivity. Statistical analyses were performed using IBM SPSS Statistics, Version 20 software (Armonk, NY). Results: Our review resulted in analysis of 35 subjects. Median age was 61 (Range 34-89) with 40% female subjects (n=14). Median follow-up for the study was 11 months (Range 0-40 months). Pathologic findings for the overall cohort showed 46.4% (n=13) with positive sentinel nodes, 63.6% (n=21) ulcerated, 33.3% (n=8) lymphovascular invasion, and 20% (n=4) perineural invasion. In follow-up, 32.1% (n=9) had recurrence, 22.2% with local recurrence (n=2). Mean Breslow thickness was 7.4mm (SD=3.5), while mean mitotic figures/mm2 was 5.4 (SD=4.9). None of these factors were significantly different between positive vs. negative PET-CTs. On univariate analysis positive PET-CT was associated with 88.9% positive SLNB compared to 22.2% if PET was negative (p=0.003). Positive PET-CT was also associated with 41.7% positive non-SLN compared to 5.6% with negative PET-CT. Additionally, 54.5% of patients with positive PET-CT had a recurrence vs. 12.5% recurrence with negative PET-CT (p=0.033). Multivariable regression showed only SLNB positivity to be significantly associated with PET-CT positivity (OR 44.0 p=0.004). Conclusions: Patients with cutaneous T4 melanoma appear to be a niche group for whom PET-CT may be of utility. T4 melanoma patients with regional nodal metastasis identified on PET-CT may benefit from immediate lymphadenectomy without SLNB, thereby hastening definitive treatment.

The overall survival of anorectal mucosal melanoma versus gynecologic mucosal melanoma from time of diagnosis.
The Natural History of Primary Cutaneous Endocrine (Merkel Cell) Carcinoma: 20-year Experience from a Canadian Perspective

A. Pooni, S.S. Brar, A.M. Easson. Department of Surgery, University of Toronto, Toronto, ON, Canada.

Introduction: Merkel Cell Carcinoma (MCC) is a rare, aggressive primary cutaneous neuroendocrine carcinoma. First described in the early 1970s, its natural history remains poorly characterized. Much of what is known about MCC is derived from few single institution series. To date, a Canadian experience has not been described. Methods: A retrospective analysis of our institution’s prospective cancer registry was performed to identify all patients diagnosed with MCC between 1988 and 2010. Patient, tumor and treatment variables were collected. Cases were staged using the AJCC 7th edition criteria and analyzed to determine MCC specific outcomes. Results: One hundred and fifty two cases were identified, 19 were excluded due to incomplete staging data. In the remaining 133 cases, the mean age at diagnosis was 71 years (range 38-95) with an average follow up of 33 months. The head and neck (42%) followed by the extremities (36%) were the most common sites of disease. Thirty percent of patients presented with stage I disease, 22% with stage II, 25% with stage III and 19% with stage IV. The 5-year overall survival rates were 57%, 46%, 33% and 7% for stages I,II,III,IV respectively (p=0.01). Thirty six percent of patients who presented with local or regional disease recurred, with an average disease free interval of 461 days. In node positive disease the recurrence rate was 47%. Lymph nodes (52%) followed by distant disease (26%) were the most common sites of recurrence. 107 (81%) patients were treated with wide local excision. Twenty-four percent of node negative patients received radiotherapy compared to 85% of patients with stage III disease. Chemotherapy was reserved for metastatic disease. Conclusion: This study represents the largest series to date describing the Canadian experience with Merkel Cell Carcinoma. The data describes the stage specific natural history of MCC and confirms its aggressive nature. Disease stage at presentation was a predictor of overall survival (p<0.01). To improve patient outcomes, research to clarify stage specific predictors of survival and progress adjuvant therapies is required.

Sentinel Node Biopsy as a Staging Procedure for Head and Neck Melanoma


1. Vanderbilt University Medical Center, Department of General Surgery, Nashville, TN; 2. Vanderbilt University Medical Center, Division of Surgical Oncology, Nashville, TN; 3. Vanderbilt University Medical Center, Division of Hematology-Oncology, Nashville, TN.

Introduction Sentinel lymph node biopsy (SLNB) is an effective staging procedure for melanoma of the trunk and extremities. The accuracy and safety of SLNB for melanomas with lymphatic drainage to the parotid nodes has been questioned. We evaluated the long term outcome of patients undergoing parotid SLNB to determine the safety and efficacy of this procedure. Methods Sixty one patients underwent wide excision and parotid SLNB for clinical stage I and II head and neck melanoma between 07/01/1997 and 06/30/2008. Tc-99m sulfur colloid, lymphoscintigraphy, and a gamma probe were used. Clinical and pathological data were collected through a prospective, IRB-approved data repository. Results Most patients were older (mean age 62), males (88%) with melanomas of the ear (32%), cheek (19.7%), forehead (19.7%), neck (11.5%), scalp (9.8%), or eyelid/brow (6.6%). Mean tumor thickness was 2.0 +/- 1.9 mm; 23% were ulcerated, 54% had a mitotic rate >1/mm². SLNB were identified in 59/61 (97%) patients. 119 basins were mapped (60 parotid, 54 cervical, 5 other), with 3.4 +/-1.6 SN per basin. Twelve of 61 (19.7%) had tumor-positive parotid SLN. One false negative (FN) result (Accuracy 99%, FN rate 7%) was confirmed after 5 years actuarial follow-up. Seven (11.5%) patients experienced complications, (2 temporary facial nerve paresis). Long-term follow-up was available for 50 patients; 34 (56%) were alive with median overall survival of 83 months. 15 of 50 (30%) developed recurrence with median disease-free survival of 32 months. Conclusion With careful attention to technical details, parotid sentinel node biopsy can be performed with a low rate of serious complications. The procedure is associated with a low long-term false negative rate and is the procedure of choice for staging the parotid nodes in head and neck melanoma.
Surgery for Gastrointestinal Metastasis in Stage IV Melanoma


Introduction: The prognosis of patients (pts) with gastrointestinal (GI) metastasis from melanoma is poor. Surgery remains a therapeutic option to render them NED. Patients rendered NED have close to a 2 year median OS after surgery for palliation. Conclusion: Surgery for GI metastasis in melanoma could be safely performed in selected pts with excellent symptom relief and little morbidity. Patients rendered NED have close to a 2 year median OS after surgery. Since rendering pts NED appears to be associated with a prolonged OS, strategies using neoadjuvant targeted or immunotherapies with the goal of reducing tumor burden and number of organs involved followed by surgery should be considered.

Gastrointestinal Metastasis in Stage IV Melanoma

P240
Clinical Utility of Combining PLX4032, a BRAF Inhibitor, with a Multivalent Melanoma Immunotherapeutic Vaccine M. Wallack,1 R. Suriano,2 N. Tuli,1 A.L. George,2 J. Geliebter,3 R.K. Tiwari.1 1. New York Medical College, Valhalla, NY; 2. Metropolitan Hospital, New York, NY.

Introduction: Successful melanoma vaccines require the use of multiple melanoma associated antigens (MAA). We have developed a vaccinia virus based vaccine using multiple primary cell lines, which express a plethora of antigens such as MART-1, tyrosinase, and gp100. This oncolysate vaccine has been tested in a human clinical trial and generated an immunologic response. Further, the BRAF genetic lesion is one of the most common mutations and inhibition of its signaling pathway has demonstrated clinical efficacy in melanoma patients. The objective of this study is to examine the possible development of a combinatorial therapeutic approach to treat melanoma combining our MAA rich vaccinia based melanoma vaccine with BRAF inhibitors. Methods: The primary cell lines used in our study were characterized based on the expression of the mutated BRAF gene as well as to their responsiveness upon treatment with PLX4032, a BRAF inhibitor. In addition, the MAA expression of our five primary melanoma cell lines was characterized in vitro upon treatment with PLX4032. The expression of various MAAs was assayed for both at the protein and gene levels. Results: The primary melanoma cell lines used in our study were determined to be either homozygous or heterozygous for the mutated BRAF gene. In addition, the cell lines harboring the mutated BRAF were responsive to treatment with PLX4032 such that inhibition of phosphorylation was observed for the various proteins present in the BRAF cell signaling pathway, namely Mek and Erk. Interestingly, upon treatment with PLX4032, the MAA expression profile of our primary melanoma cells was altered such that we observed increased expression of various antigens such as MART-1, gp100, and tyrosinase both at the protein level and gene level. Conclusion: Our results conclude that treatment of our primary cells with PLX4032, the MAA expression profile of our primary melanoma cells was altered such that we observed increased expression of various antigens such as MART-1, gp100, and tyrosinase both at the protein level and gene level.
Abstracts: Poster Presentations

**S125**

**Complete surgical resection should be recommended for patients with unicentric disease.** Compared to multicentric disease (100% vs 84%, P=0.623), patients with PC histology had worse 5-year OS compared to unicentric disease (100% vs 80%, P=0.012). There was no difference in 5-year disease free survival (DFS) for all patients at 37.94 months (SE=6.75 months), and mean overall survival (OS) for all patients is 39.31 months (SE=6.97 months). Mean DFS for pelvic node negative patients is 43.5 months (SE=8.32 months), whilst mean DFS for pelvic node positive patients is 30.1 months (SE=10.39 months). There was a trend of better survival in the pelvic node negative patients compared to the node positive patients. However, this was not statistically significant (Log rank test p=0.244). Conclusion: Cloquet’s node was shown to be superior to radiological imaging and should be preferentially used to decide on the extent of nodal dissection.

**Lymph Node status and correlation with pathological and radiological findings**

<table>
<thead>
<tr>
<th>No</th>
<th>FNAC of palpable lymph node</th>
<th>Sentinel LN biopsy findings</th>
<th>Cloquet’s Node frozen section</th>
<th>Radiological suspicion of pelvic node involvement</th>
<th>Extent of dissection</th>
<th>No. of positive nodes</th>
<th>Pelvic Lymph Node involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Positive</td>
<td>Not done</td>
<td>Negative</td>
<td>No CIGD</td>
<td>Yes</td>
<td>1</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>Negative</td>
<td>Not done</td>
<td>Negative</td>
<td>No CIGD</td>
<td>Yes</td>
<td>4</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>Positive</td>
<td>Not done</td>
<td>Positive</td>
<td>No CIGD</td>
<td>No</td>
<td>3</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td>Not done</td>
<td>Not done</td>
<td>Positive</td>
<td>No CIGD</td>
<td>No</td>
<td>3</td>
<td>NA</td>
</tr>
<tr>
<td>5</td>
<td>Negative</td>
<td>Not done</td>
<td>Negative</td>
<td>No CIGD</td>
<td>No</td>
<td>4 NA</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>Negative</td>
<td>Not done</td>
<td>Indeterminate / Negative</td>
<td>No CIGD</td>
<td>No</td>
<td>1</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>Positive</td>
<td>Not done</td>
<td>Positive</td>
<td>No CIGD</td>
<td>No</td>
<td>3</td>
<td>Yes</td>
</tr>
<tr>
<td>8</td>
<td>Not done</td>
<td>Not done</td>
<td>Positive</td>
<td>No CIGD</td>
<td>No</td>
<td>3</td>
<td>NA</td>
</tr>
<tr>
<td>9</td>
<td>Not done</td>
<td>Not done</td>
<td>Positive</td>
<td>No CIGD</td>
<td>No</td>
<td>4 NA</td>
<td>NA</td>
</tr>
<tr>
<td>10</td>
<td>Not done</td>
<td>Not done</td>
<td>Indeterminate / Negative</td>
<td>No CIGD</td>
<td>No</td>
<td>1</td>
<td>No</td>
</tr>
<tr>
<td>11</td>
<td>Not done</td>
<td>Not done</td>
<td>Negative</td>
<td>No CIGD</td>
<td>No</td>
<td>1</td>
<td>NA</td>
</tr>
<tr>
<td>12</td>
<td>Not done</td>
<td>Not done</td>
<td>Positive</td>
<td>Yes CIGD</td>
<td>Yes</td>
<td>10</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**Comparison between clinical features of unicentric and multicentric Castleman’s Disease**

**P242**

**Feasibility of 18FDG-directed Lymph Node Surgical Excisional Biopsy for Appropriate Diagnostic Tissue Sampling in Patients with Suspected Lymphoma**

S.P. Povoski, 1 N.C. Hall, 2 D.A. Murrey, Jr., 1 S. Nichols, 1 C.L. Wright, 1 E.W. Martin, Jr. 1. The Ohio State University, Division of Surgical Oncology; Department of Surgery, Columbus, OH; 2. The Ohio State University, Division of Nuclear Medicine, Department of Radiology, Columbus, OH.

**Background:** 18FDG PET/CT imaging is widely utilized in the clinical evaluation of patients with suspected or documented lymphoma. The aim was to describe our cumulative experience with 18FDG-directed lymph node surgical excisional biopsy in patients with suspected lymphoma. Methods: From 06/2007 to 11/2010, 13 patients (mean age 51 (±16; 22-76) years), with suspected new or recurrent lymphoma suggested by 18FDG-avid lesions seen on diagnostic patient PET/CT (pPET/CT) imaging, were injected IV with 18FDG prior to undergoing same-day (S-D) diagnostic lymph node surgical excisional biopsy in the operating room. Various 18FDG detection strategies were used: S-D pre-resection pPET/CT; intraoperative gamma probe (IGP) assessment; clinical scanner PET/CT (pPET/CT) imaging, of whole surgically excised tissue specimens (WSETS); specimen gamma well counts (SGWC); and/or S-D post-resection pPET/CT. Results were expressed as mean (±SD; range). Results: S-D 18FDG injection dose was 14.8 (±2.4; 12.5-20.6) mcI. Sites of 18FDG-avid lesions were 4 inguinal, 3 cervical, 3 abdominal/retropitoneal, 2 axillary, and 1 inguinal region subcutaneous tissue. S-D pre-resection pPET/CT was performed on 4 patients. IGP assessment was performed on 13 patients. pPET/CT imaging of WSETS was performed in 10 cases. SGWC was performed in 6 cases. S-D post-resection pPET/CT imaging was performed on 8 patients. Time from 18FDG injection to S-D pre-resection pPET/CT; IGP assessment, and S-D post-resection pPET/CT were 76 (±8; 64-84), 240 (±63; 168-304), and 487 (±104; 331-599) minutes, respectively. Time from 18FDG injection to pPET/CT of WSETS was 363 (±60; 272-446) minutes. Time from 18FDG injection to GWC was 591 (±96; 420-689) minutes. IGP assessment successfully identified 18FDG-avid lesions in 12/13 patients. Histopathologic evaluation confirmed lymphoma in 12/13 patients and benign disease in 1/13 patients. Conclusions: 18FDG-directed lymph node surgical excisional biopsy for suspected lymphoma is technically feasible for guiding appropriate diagnostic tissue sampling of lymph nodes seen as 18FDG-avid lesions on diagnostic 18FDG PET/CT imaging.

**P243**

**The Clinical Presentation and Management of Castleman’s Disease**

C. Bailey, 1 L. Fayad, W. Lea, B. Feig. University of Texas, MD Anderson Cancer, Houston, TX.

**Background:** Castleman’s Disease (CD) is a rare lymphoproliferative disorder characterized by lymph node hyperplasia. There is limited data on the role of surgery in patients with CD. The primary aim of this study is to analyze the clinical features, treatment approaches and outcomes in patients with CD. Methods: A retrospective review of patients with a histologic diagnosis of CD between 1990 and 2012 was performed. CD was characterized as unicentric or multicentric and further divided according to histologic variant: hyaline vascular (HV), plasma cell (PC) or mixed. Chi-square and Mann-Whitney U test were used to compare clinical variables. Kaplan-Meier method and log-rank test were used for survival analysis. Results: Records from 53 patients were analyzed: 23 had unicentric disease and 30 had multicentric disease. Patients were evenly matched for age, sex and race. There were more patients with plasma cell histology (P<0.001) in the multicentric group (Table). The mean follow-up for the entire cohort was 64 months (median 57 months). Nineteen (82.6%) patients with unicentric disease underwent surgical resection, 1 with recurrent disease after complete surgical resection. Only 1 (3.3%) patient with multicentric disease underwent surgical resection, 25 (83.3%) received systemic therapy and 3 (10%) did not undergo any treatment. Three (10%) developed recurrent disease after complete surgical resection. Complete surgical resection should be recommended for patients with unicentric CD, whereas the role of surgery for patients with multicentric CD needs to be evaluated in prospectively designed studies.

**P244**

**Recurrence in Oral Squamous Cell Carcinoma**

S. Nichols, 1 C.L. Wright, 1 E.W. Martin, Jr., 1 C.R. Anderson, 1*. 1. Norwich Medical School, University of East Anglia, Norwich, United Kingdom; 2. Norfolk and Norwich University Hospital, Norwich, United Kingdom.

**Background:** Excision margins for oral squamous cell carcinoma (OSCC) are poorly understood, and evidence about the effect of margin size on outcome characterized by lymph node hyperplasia. There is limited data on the role of surgery in patients with CD. The primary aim of this study is to analyze the clinical features, treatment approaches and outcomes in patients with CD. Methods: A retrospective review of patients with a histologic diagnosis of CD between 1990 and 2012 was performed. CD was characterized as unicentric or multicentric and further divided according to histologic variant: hyaline vascular (HV), plasma cell (PC) or mixed. Chi-square and Mann-Whitney U test were used to compare clinical variables. Kaplan-Meier method and log-rank test were used for survival analysis. Results: Records from 53 patients were analyzed: 23 had unicentric disease and 30 had multicentric disease. Patients were evenly matched for age, sex and race. There were more patients with plasma cell histology (P<0.001) in the multicentric group (Table). The mean follow-up for the entire cohort was 64 months (median 57 months). Nineteen (82.6%) patients with unicentric disease underwent surgical resection, 1 with recurrent disease after complete surgical resection. Only 1 (3.3%) patient with multicentric disease underwent surgical resection, 25 (83.3%) received systemic therapy and 3 (10%) did not undergo any treatment. Three (10%) developed recurrent disease after an initial complete radiographic response to systemic therapy. Patients with unicentric disease had higher 5-year overall survival (OS) compared to multicentric disease (100% vs 80%, P=0.012). There was no difference in 5-year disease free survival (80% vs 84%, P=0.623). Patients with PC histology had worse 5-year OS compared to patients with mixed and HV histology (87% vs 91% vs 100%, P=0.031). Conclusion: Unicentric and multicentric CD are clinically distinct disorders. Complete surgical resection should be recommended for patients with unicentric CD, whereas the role of surgery for patients with multicentric CD needs to be evaluated in prospectively designed studies.

**P245**

**Too Close for Comfort? A Meta-analysis of Margin Size and Local Recurrence in Oral Squamous Cell Carcinoma**

C. Bailey, 1* L. Fayad, W. Lea, B. Feig. University of Texas, MD Anderson Cancer, Houston, TX.
come is conflicting. Close (<5mm) and involved (~1mm) pathological margins, as defined by national guidance, are key indicators of the need for adjuvant treatment, despite these definitions not being based on easily identifiable evidence. This review aimed to assess the impact of pathological margin size on local recurrence rates in patients treated with surgery alone. Methods MEDLINE, EMBASE and citation lists were searched for studies that looked at local recurrence following excision of primary OSCC without adjuvant therapy. Five studies met the inclusion criteria, of which four compared recurrence rates in patients with pathological margins clear by less than 5mm with those who had pathological margins clear by 5mm or greater. Results: The included studies were sufficiently homogeneous for meta-analysis. Recurrence rates were pooled to give a 21% absolute risk reduction (95% confidence interval 12% to 30%, \( p=0.00001 \)) in local recurrence with margins clear by more than 5mm. The pooled odds ratio was 0.34 (95% confidence interval 0.21 to 0.54, \( p=0.00001 \)) for clear margins as compared to close margins. However, unweighted pooled recurrence rates were 20% in patients with margins clear by more than 5mm, suggesting a 5mm margin is not sufficient in a subset of patients, who may have an intrinsically higher risk of recurrence. Subgroup analysis of T1/2 stage tumours compared to T3/4 stage tumours showed no significant increase in local recurrence with later stage tumours, regardless of margin status. Conclusions: The findings of this review corroborate guidance that suggests margins clear by less than 5mm are inadequate and suggest that a 5mm pathological margin should be used as the minimum acceptable margin size in oral squamous cell carcinoma. The 20% recurrence rate in patients with clear margins is significant and suggests further research into this ‘high risk’ group is needed, to facilitate improvements in outcomes.

P246

Infiltrative Borders Predict a Poor Prognostic Phenotype in Oral Squamous Cell Carcinoma

C.R. Anderson,1,2 M. Moncrieff,1 R. James,3,4 K. Sisson.4 1. University of Minnesota Department of Diagnostic and Biological Sciences, School of Dentistry, Minneapolis, MN; 2. University of Minnesota Department of Diagnostic and Biological Sciences, School of Dentistry, Minneapolis, MN.

Background: The invasive border of oral squamous cell carcinomas is known to be prognostically relevant, but methods of assessment vary widely within the literature. Furthermore, standard histopathological assessment covers a minority of the actual tumour border, calling in to question the efficacy of systems that look at the ‘predominant’ pattern of invasion. Methods: This study reports the retrospective analysis of a cohort of 180 patients with primary T1/2 OSCC. All patients were treated with curative intent by surgery with or without adjuvant radiotherapy between 1997 and 2011, and all pathology was reviewed for this study by one head and neck pathologist. This study assessed a simple categorisation of infiltrative or cohesive borders, based on the worst pattern of invasion seen. The relationship between the tumour border and both outcome and markers of aggressive disease were explored. Results: On univariate analysis, an infiltrative invasive front was significantly associated with poor outcome in terms of recurrence, disease specific and overall survival (\( p<0.01 \) for all outcome measures). On multi-variate analysis, adjusting for adjuvant radiotherapy and all standard pathological variables, an infiltrative invasive front was significantly associated with locoregional recurrence (HR 2.19, 95%CI 1.14 to 4.22, \( p=0.019 \)), and predicted poor disease free (\( p=0.033 \)) and disease specific (\( p=0.048 \)) survival. We also found that infiltrative borders were strongly associated with more traditional markers of aggressive disease, such as perineural (\( p<0.001 \)) and lymphovascular (\( p=0.001 \)) invasion. Infiltrative borders were also associated with an increased tumour burden, with infiltrative tumours being significantly greater in diameter (\( p<0.001 \)) and depth (\( p<0.001 \)) than those with cohesive borders. Conclusion: We have demonstrated using a simple, reproducible method of assessing invasive borders that allows prediction of prognosis, and that infiltrative borders are an important marker of poor prognosis. We suggest that this is used, along with other clinical and pathological markers, as an indication for adjuvant therapy.

P247

Oncolytic Adenoviruses Targeting HPV Positive Head and Neck Squamous Cell Carcinomas

C.J. LaRocca,1,2 A. Emery,3 J. Han,1 J. Davydova,2 M. Herzberg,2 R. Gopalakrishnan,3 M. Yamamoto.2 1. University of Minnesota Department of Surgery, Minneapolis, MN; 2. University of Minnesota Department of Diagnostic and Biological Sciences, School of Dentistry, Minneapolis, MN; 3. National Cancer Centre Singapore, Singapore, Singapore.

Introduction: The percentage of head and neck squamous cell carcinomas (HNSCC) that are Human Papilloma Virus (HPV) positive has increased in recent years. The HPV E6 and E7 oncoproteins are attractive therapeutic targets for conditionally replicative oncolytic adenoviruses (CRAds). The adenovirus (Ad) E1a CR1 region and HPV E6 are both involved in p53 degradation. Similarly, both the Ad E1a CR2 region and HPV E7 are known to dissociate the Rb-E2F complex. We hypothesized that CRAds with these deletions can replicate selectively in HPV positive cells where the E1a functions are compensated by the expression of HPV E6 and E7 thereby resulting in a therapeutic agent for HPV positive HNSCCs. Methods: Two CRAds were tested both in vitro and in vivo. Crystal violet and MTS assays were used to determine the cytocidal effect of the viruses in multiple HNSCC cell lines. Also, a luciferase assay was used to determine the transduction efficiency of the viruses. Using the UPCI SCC 090 cell line (HPV positive), subcutaneous tumor xenografts were generated in athymic nude mice and subsequently treated with one dose of the CRAds. Results: Two CRAds were generated with infectivity enhancement via a 5/3 fiber modification (5/3 A24 with a partial deletion in CR2 and 5/3 CB016 with deletions in CR1 and CR2). The viral cytocidal effect seen by crystal violet staining and transduction analysis with luciferase expressing vectors indicated that this infectivity enhancement maximized the efficiency of the vectors. In vitro, both viruses demonstrated significant oncolytic effects. The 5/3 CB016 virus was selective for only HPV positive cells, while the 5/3 A24 virus lysed cells regardless of their HPV status. In vivo, both viruses demonstrated anti-tumor effects until eight days after inoculation, which was as strong as the wild type virus. These data indicate that both viruses show anti-tumor effects in vitro and in vivo, although the 5/3 CB016 virus is more specific to HPV positive HNSCC cells. Conclusion: We have shown that CRAds targeted to HPV positive HNSCCs demonstrate in vivo and in vitro oncolytic effects and have the potential to become an effective treatment modality.

P248

Statin Use is Associated with Increased Survival in Patients with Advanced Epithelial Ovarian Carcinoma


Background: Statins are the most common lipid-lowering agents used for the treatment of dyslipidemias. Recent studies have shown that statins improve the prognosis of several epithelial neoplasms. The aim of this study was to analyze the relationship between statin use with progression free survival (PFS) and overall survival among patients diagnosed with epithelial ovarian cancer. Methods: One hundred and twenty one patients who underwent cytoreductive surgery (CRS) for epithelial ovarian carcinoma were analyzed retrospectively. Patients with active statin use at diagnosis or during treatment were compared with a control group. Clinical and pathological factors were described. PFS and overall survival were analyzed with Kaplan Meier method. Significance was considered at \( p<0.05 \). Results: Thirty patients (10.7%) were actively receiving statin therapy at diagnosis or during treatment. The mean age observed for statin users was 55 ± 9.7 vs. 54 ± 12.2 years for non-users (\( p<0.05 \)). Most patients were diagnosed in a clinically advanced stage: 55.5% were stage IIIC and 21% were stage IV. Most patients had an optimal CRS (68%). Subgroup analysis of patients who were on stage IIIC showed that median PFS and overall survival were 40.6 and 36.8 months, respectively for non-users (\( p<0.05 \)). Cox regression analysis demonstrated that prognostic factors for improved survival were optimal CRS, statin use and normal albumin levels prior to the surgical intervention. Conclusions: Statin use in patients with stage IIIC ovarian cancer is associated with improved PFS and overall survival.

P249

A Retrospective Analysis of Kidney Injury after Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

E. Sin,1* C. Chia, M. Teo. National Cancer Centre Singapore, Singapore, Singapore.

Background: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have been found to prolong survival in patients with malignant peritoneal disease. Kidney injury is a potentially serious morbidity. We looked at the rate of acute kidney injury (AKI) and chronic renal failure (CRF) in 47 patients and aim to identify predisposing risk factors. Methods: During 2005-2013, we performed CRS and HIPEC on patients with ovarian primaries and peritoneal metastasis. Retrospective data was collected on the patient’s demographics, clinical details, peri-operative creatinine levels, peri-operative chemotherapy details, etc. AKI was defined as an increase in creatinine of 2 or more times the baseline. CRF was defined as a creatinine level of 2 or more times the baseline.
in serum creatinine of $\geq 26.5 \, \mu\text{mol} / \text{L}$ over 48h; CRF was defined as persistent deranged renal function for $\geq 3$ months. Results Our 47 patients had a median age of 52(34-74) years. The mean baseline creatinine was 55 $\mu\text{mol} / \text{l}$ (38-102) and mean baseline albumin was 35 g/l(13-45). All underwent preoperative chemotherapy with mainly carboplatin/paclitaxel for an average of 7 cycles(3-17) with a mean of 11 months between chemotherapy cessation and operation date. All received intraoperative cisplatin at a median dose of 60 mg/kg at a median temperature of 40 degrees (40-41.5) for a duration of 60 min. Intraoperative blood loss averaged at 1500 ml(200-4600). 76% received post-operative chemotherapy with mainly carboplatin/paclitaxel. 17(36%) experienced postoperative AKI, of which 24(4%) required postoperative inpatient dialysis;10(21%) show resolution of AKI with conservative management within a median of 11 days. 6(13%) had deranged renal function on discharge, and 1(2%) needed long term dialysis. Univariate analysis showed that risk factors for AKI development included preoperative albumin, intraoperative temperature, duration of chemotherapy and blood loss. Risk factors for CRF included the age of the patient and intraoperative blood loss. Conclusion Kidney injury is a significant HIPEC morbidity and identification of risk factors helps improve pre-operative patient selection and optimization, and facilitate closer perioperative monitoring and fluid management in at-risk patients.

### P250

**Ocular Melanoma When You've Seen One, You haven't Seen Them All: A Clinical Outcomes Study of 8,165 Patients (1973-2010)**

K. Mahendraraj, Jr. S. Shrestha, R.S. Chamberlain. *St. Barnabas Medical Center, Livingston, NJ.*

Introduction: Ocular melanoma (OM) comprises less than 5% of all melanomas, with uveal melanoma (UM) being the most common subtype and the most common primary intraocular cancer. Conjunctival melanoma (CM) is a very rare form of OM that differs from UM in both location and clinical behavior. This study examines a large cohort of OM patients and compares demographic and clinical factors affecting outcomes to identify ideal treatment approaches for both UM and CM. Methods: Demographic and clinical data on 277,120 patients with melanoma was abstracted from the Surveillance, Epidemiology, and End Results (SEER) database (1973-2010). Standard statistical analyses were performed. Results: 8,165 OM cases represented 2.9% of all melanomas. UM cases accounted for 92.1% (N=7,516) and CM cases 7.9% (N=649). Mean age-adjusted CM incidence was significantly lower than UM (0.4 per million vs 5.1 per million; p<0.001). UM patients presented with localized disease more often than CM. CM had a longer mean overall survival (OS) (15.4 vs. 14.6 years) and lower overall mortality (38.8% vs 46.1%); p<0.05. Primary radiotherapy was associated with prolonged survival compared to surgery for UM (15.8 vs 13.6 years), while surgery resulted in prolonged survival for CM (15.4 vs 6.4 years); p<0.001. Multivariate analysis identified male gender (OR1.1), age over 50 (OR4.0) and distant metastases (OR8.6) as independently associated with increased mortality for OM, p<0.005. In UM, surgery alone (OR2.6) was associated with increased mortality while radiotherapy (OR0.5) was associated with reduced mortality. Conclusions: CM presents more often with localized disease and is associated with a better OS and lower mortality than UM. Surgery is the primary therapy for CM, while radiotherapy is the primary treatment and prolongs survival in UM. Males, older age, and distant disease are all associated with an increased risk of mortality in OM, with primary surgical treatment being an additional risk factor in UM.

### P251

**Intraoperative Utilization of a Portable Large Field of View Gamma Camera for Improved Radioguided Surgery**

A. Terando, Jr. N.C. Hall, S.P. Povoski, J. Phay, S. Nichols, C.L. Wright, E.W. Martin, Jr. *The Ohio State University Wexner Medical Center, Columbus, OH.*

Background: Radioguided surgery (RS) is generally used for breast and melanoma sentinel lymph node biopsy (SLN) procedures and for parathyroid adenoma resection. Historically, RS involves preoperative administration of a radiopharmaceutical followed by intraoperative utilization of a handheld gamma detection probe (GDP) for detecting and resecting radioactive foci. We present our experience with a portable large field of view gamma camera (LFOVGC) for improved real-time intraoperative localization and verification of resection of radioactive foci. Methods: A portable LFOVGC was used for imaging during RS. For most cases, intraoperative imaging of the surgical field was acquired prior to incision. Likewise, a handheld GDP was used during the surgical procedure. Intraoperative imaging of the resected specimen and the post-resection surgical field were subsequently acquired. Results: Over a 26 month period, a total of 90 patients underwent LFOVGC imaging. This consisted of 58 99mTc SLN biopsy procedures (28 breast, 27 melanoma, 2 vulvar, and 1 head/neck), 22 99mTc sestambi parathyroid adenoma resection procedures, 4 111In pentetreotide guided surgeries, 3 99mTc DTPA ureter identification studies, 2 99mTc-labeled red blood cells limb perfusion monitoring cases, and 1 111In-labeled white blood cell radioguided surgery. LFOVGC imaging provided clinically-relevant information to the surgeon by: (a) assisting the surgeon in localizing areas of increased radiopharmaceutical accumulation with the handheld GDP, (b) verifying complete resection of targeted radioactive foci, (c) identifying key anatomic structures, and (d) monitoring effectiveness of surgical procedures in real-time. Conclusions: Portable LFOVGC imaging can provide useful information as an adjunct to a handheld GDP during RS. Our experience is that LFOVGC imaging assists with localization and verification of resection of radioactive foci beyond the capabilities of a handheld GDP alone. The portable LFOVGC can be used to globally assess the entire surgical field and resultantly direct the surgeon for more precise targeting of radioactive foci with a handheld GDP.
P252
En-bloc Multivisceral Pelvic Resection for Locally Advanced Primary and Recurrent Ovarian Cancer: A Single-Centre Experience

D. Ng,* C. Chia, G. Tan, M. Teo. Department of Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore.

Aim: A review of a single-centre experience of en-bloc multivisceral pelvic resection as a treatment modality for patients with locally advanced primary and recurrent ovarian cancer. The perioperative outcomes, morbidity and long-term oncological outcomes are reviewed. Materials & Methods: Patients undergoing en-bloc multivisceral pelvic resection for recurrent and locally advanced ovarian cancer between January 1993 to March 2013 were identified from a retrospective database. All patients underwent pre-operative staging investigations with CT scan of chest, abdomen and pelvis and pelvic MRI. Locally advanced ovarian cancers is defined as tumours that require a multivisceral resection and all of which have tumors that are clinically bulky with adherence, fixation or invasion into adjacent critical structures on imaging. En-bloc multivisceral pelvic resection is defined as en-bloc removal of pelvic organs to which the primary tumour was adherent to. Structures such as the rectosigmoid, urinary bladder, ureters, and sigmoid colon were resected en-bloc where indicated with the lesion. Urological or plastic reconstructions were employed where indicated. Patients were followed up according to a standard protocol of Ca 125 measurements and imaging modalities CT/MRI/PET. The primary outcome measured was overall survival (OS) and secondary outcome measured was disease free survival (DFS). OS was examined by the Kaplan-Meier Method. Results: En-bloc multivisceral pelvic resections were performed in 18 patients with a median age of 59.5. The rate of major postoperative complications was 6% (n=1). There were no mortalities in the perioperative period. All patients were operated with curative intent and negative circumferential margins were achieved in all patients. The 5-year OS for patients with primary and recurrent disease is 60% and 40% respectively (p=0.754). The median survival for patients with recurrent disease is 35 months. The DFS for all patients is 18 months. Conclusion: An aggressive approach with en-bloc multivisceral pelvic resection provides survival benefit to patients with locally advanced primary and recurrent ovarian cancer at acceptable morbidity.

P253
Peroneal Flap: A Versatile and Viable Option for Head and Neck Reconstruction

Y. Lin,* K. Yang. Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

Introduction: The mainstream flaps of choice for head and neck reconstruction are ALT, radial forearm, fibula, jejunum flaps. Each option is preferred by different surgeons or institutions. For the past 15 years, peroneal flap has been the workhorse in our institution. The goal of this study is to present the peroneal flap as a versatile and viable option for head and neck reconstruction. Materials and Methods: Between 1995 and 2012, there were 189 peroneal flaps and 70 ALT flaps used in the head and neck reconstruction by Dr. Kuo-Chung Yang. We retrospectively reviewed the medical records from those surgeries, looking for all the patients’ characteristics and perioperative complications. All the applications using peroneal flap to different classifications of defects will be demonstrated for its versatility. The flap failure rates of the peroneal flaps carrying various components were used to evaluate the reliability of its “chimeric” characteristic. The perioperative complications rate of ALT flap was used as a comparison to assess the viability of the peroneal flap. Fisher’s exact test was conducted to compare the percentages of different groups. A P value less than 0.05 was considered statistically significant. Results: In terms of the versatility of a peroneal flap, it could be reliably harvested as a single-paddle flap, a double-paddle flap, or a “chimeric” flap composed of skin paddles and a muscle bulk to fill a wide variety of defects, e.g. a buccal defect, a through-through defect, a hemiglossectomy defect, or a hypopharyngeal defect. An aesthetically pleasing and salvia-leakage preventing neo-ommissure could be easily created due to its pliability. The flap failure rates of the peroneal flaps carrying various components are not statistically significantly different (p=0.69), revealing the reliability of its chimeric characteristic. In terms of the viability, there is no statistically significant difference between ALT and peroneal flap in perioperative complications (10% vs 18.5%, p=0.128). Conclusions: Due to its reliable chimeric characteristic and comparable complications rates, peroneal flap is a versatile and viable option in the head and neck reconstruction.
Patients With Advanced Cancer: Comparing End-of-life Preference between those Undergoing Curative Intent Surgery versus Non-curate Intent Treatment J.R. Schubart, M.J. Green, B. Levi, A.N. Kulaayat, N.J. Gusani.* Section of Surgical Oncology, Department of Surgery, Penn State College of Medicine, Hershey, PA.

INTRODUCTION We analyzed data from a clinical trial examining the impact of an online decision aid for advance care planning. Our hypothesis was that patients with advanced cancer who had initial curative intent surgery (CIS) would report higher levels of hope, less hopelessness, and would prefer more aggressive end-of-life treatment than those who had non-curate intent treatment (non-CIT). METHODS Hope and hopelessness were measured at baseline and post-intervention using the 12-item Herth Hope Index and 7-item Beck Hopelessness scale, respectively. A treatment aggressiveness scale (0-40, higher=more aggressive) was created by summing responses to questions within the decision aid that asked about patient wishes for 8 different treatments (e.g., CPR, ventilation, etc.) under 5 clinical scenarios (e.g., stroke, dementia, etc.). Wilcoxon Rank Sum test was used to compare medians for treatment aggressiveness between groups, and a linear mixed effects model was used to compare mean change in hope and hopelessness from baseline to post-intervention within and between groups. RESULTS Of 159 patients with stage IV non-CNS and non-hematologic cancer, 95 had CIS and 64 had non-CIT. There was a slight increase in hope for the CIS group (41.4 to42.1, p=0.08) and a slight decrease for the non-CIT group (40.6 to 40.4, p=0.68), but no significant difference between groups (p=0.15). Hopelessness decreased slightly in both groups (CIS: 0.5 to 0.4, p=0.50; non-CIT: 0.8 to 0.6, p=0.16) but there was no significant difference between groups (p=0.51). For patients who used the online decision aid (n=79), there was no significant difference in median treatment aggressiveness score between groups. CONCLUSION Patients with advanced cancer who undergo initial CIS do not experience greater hope or less hopelessness than patients who undergo non-CIT. Both report similar desires for aggressiveness of end-of-life treatment. This finding supports the notion that advance care planning should be undertaken for both patients whose treatment is with curative intent and for those whose cancer treatment is palliative.

Baseline Health-related Quality of Life in Elderly Patients with Cancer G.M. Barden,1* A.D. Naik,2 J.N. Cormier,1 A. Artinyan,1 S. Sangsury,3 N.J. Petersen,4 D.A. Anaya,1 1. Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX; 2. Houston VA Center for Innovations in Quality, Effectiveness and Safety (IQuEST), Houston, TX; 3. Department of Medicine, Baylor College of Medicine, Houston, TX; 4. Department of Surgical Oncology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX.

Introduction: Global graying will result in a growing number of elderly cancer patients requiring surgical treatment. Given the physical and psychosocial transitions experienced by elderly patients, characterization of baseline HRQoL is critical to understand the challenges faced by the elderly and its impact on postoperative outcomes. The goal of this study was to examine preoperative HRQoL of elderly cancer patients, and to identify specific deficits by comparing HRQoL to the young and non-cancer elderly US population. Methods: This is a prospective cohort study of cancer patients scheduled for surgery at a tertiary referral center (2012-2013). The primary outcome examined was baseline HRQoL, measured using the SF-36 survey. Domain-specific, and Physical Component (PCS) and Mental Component Summaries (MCS) were compared between the young (<65y) and old (≥65y) cancer patients, and between old cancer patients and US elderly patients without cancer (n=599), age and sex-adjusted. The X2 and t-tests were used for descriptive analysis and comparisons. Results: 232 patients were included; 107 (46%) in the old group. The majority of patients had gastrointestinal malignancies (n=161, 69%). Elderly patients with cancer reported better HRQoL than young cancer patients, with better mean domain-scores in bodily pain (46.8 vs. 43.2; p<0.03), vitality (47.4 vs. 43.8; p=0.04), emotional well-being (52.6 vs. 46.7; p<0.001), and overall better mean MCS scores (51.2 vs. 45.9; p<0.001). Elderly cancer patients, however, reported worse HRQoL than the US elderly healthy population with worse mean domain-scores in physical functioning...
### P259

**3-year Recurrence and Survival Outcomes after Sentinel Lymph Node Biopsy with [99mTc] Tilmanocept in Clinically Node-negative Breast Cancer and Melanoma Patients**

S.P. Povoski, J. Kim, S. Schneebaum.

**1. The Ohio State University, Columbus, OH; 2. University Hospitals Case Medical Center, Cleveland, OH; 3. Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.**

**INTRODUCTION:** Sentinel lymph node biopsy (SLNB) has been shown to be a suitable alternative to full lymph node dissection in clinically node-negative (N0), early-stage breast cancer and melanoma (NSABP B-32, ACOSOG Z-0011, MSLT-1). A phase 3, prospective, multi-institutional, open-label, single arm trial assessed receptor-targeted [99mTc]tilmanocept for intraoperative identification of SLNs in clinically N0 breast cancer and melanoma patients (ClinicalTrials.gov/NCT00671918). As many regional and local recurrences occur in the first 2 years, a voluntary 3-year follow-up study was conducted to assess recurrence and survival outcomes following SLNB in these patients.

**METHODOLOGY:** Patients were asked to participate in a 3-year follow-up study following their participation in the [99mTc]tilmanocept Phase 3 trial. Voluntary enrollment was open to patients with or without (pN+) SLN metastases. Recurrence and survival data were to be collected at 6 to 36 months after primary tumor excision and SLNB. The primary objective was to determine regional (i.e., draining lymph node basin) recurrence-free rate after SLNB with [99mTc]tilmanocept. Secondary endpoints were overall recurrence-free rate (including primary tumor excision site, regional, and distal recurrence), disease-specific survival, and overall survival. RESULTS: Of 169 patients completing the Phase 3 trial and eligible for the follow-up study, 109 (64 breast cancer, 45 melanoma) participated and completed a planned follow-up visit. Table 1 summarizes 3-year recurrence and survival results. Notably, in patients confirmed pN0 after SLNB (n=88; 39 melanoma, 49 breast cancer), the regional recurrence-free rate was 98.8% and the disease-specific survival was 98.6%. CONCLUSIONS: Low regional recurrence rates and high disease-specific survival rates of pN0 patients after 3 years identify [99mTc]tilmanocept accurately identifies SLNs (false negative rate <2%) 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.

**Table 1: Summary of 3-year recurrence and survival results**

<table>
<thead>
<tr>
<th>Recurrence free rate</th>
<th>Breast Cancer</th>
<th>Melanoma</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pN0</td>
<td>100% (9)</td>
<td>93.0% (9)</td>
<td>97.1% (9)</td>
</tr>
<tr>
<td>pN+</td>
<td>100% (9)</td>
<td>97.4% (1)</td>
<td>98.8% (1)</td>
</tr>
<tr>
<td>Overall</td>
<td>96.8% (9)</td>
<td>96.1% (6)</td>
<td>97.3% (6)</td>
</tr>
<tr>
<td>Disease-specific survival rate</td>
<td>97.8% (1)</td>
<td>92.1% (5)</td>
<td>95.6% (4)</td>
</tr>
<tr>
<td>Disease-specific survival rate</td>
<td>93.3% (1)</td>
<td>400% (3)</td>
<td>79.4% (4)</td>
</tr>
<tr>
<td>Overall survival</td>
<td>96.8% (9)</td>
<td>96.1% (6)</td>
<td>97.3% (6)</td>
</tr>
<tr>
<td>Disease-specific survival rate</td>
<td>97.8% (1)</td>
<td>100% (9)</td>
<td>98.0% (1)</td>
</tr>
<tr>
<td>Disease-specific survival rate</td>
<td>93.3% (1)</td>
<td>600% (3)</td>
<td>84.3% (4)</td>
</tr>
<tr>
<td>Overall survival</td>
<td>96.8% (9)</td>
<td>96.1% (6)</td>
<td>97.3% (6)</td>
</tr>
</tbody>
</table>

Two of the 3 regional recurrences in melanoma patients were regional-only recurrences. One patient (pN+) had both a regional and a distant recurrence.

### P260

**Establishment of a Voice Messaging System is Associated with Improved Clinical Outcome in Hepatocellular Carcinoma**

A. El Mokdad, A. Singal, J.C. Mansour, G.C. Balch, A. Yopp.* U T Southwestern Medical Center, Dallas, TX.

**Therapeutic delays after HCC diagnosis is multifactorial and associated with worse outcomes.** Voice messaging systems (VMS) communicate follow-up telephone calls to patients for clinic visits. However, conventional imaging findings to both the ordering physician and HCC clinic were initiated. The VMS notified physicians of abnormal studies ordered on outpatient basis. Prior, the ordering physician relied on electronic reports without notification. We conducted a retrospective review of a prospective HCC database to identify patients diagnosed on outpatient imaging studies two years following and two years prior to initiation of the VMS. Demographics, tumor characteristics, treatment, and survival were compared between the two groups of patients with one-way ANOVA and Chi-squared tests. Survival curves were generated using Kaplan-Meier with log rank test. Results: 44 patients were identified in the two years following initiation of VMS and 46 patients in the 2 years prior. There was no difference in age at diagnosis, gender, or race/ethnicity between the groups. Patients had a predominant HCV etiology (74% vs 66%, p=ns) and preserved liver function (Child-Pugh Class A, 66% vs. 61%, p=ns). AJCC (stage 1, 61% vs. 57%, p=ns) and BCLC classification (BCLC A, 56% vs. 48%, p=ns) were similar. Patients receiving treatment was similar in both groups (82% vs 76%, p=ns) with no difference in modalities. Time from study confirming HCC to subsequent clinic visit (0.6 vs. 3.2 months, p=0.003) and time from clinic visit to treatment (1.5 vs. 2.8 months, p=0.003) was shorter following VMS initiation. Median overall survival following VMS initiation was significantly longer than in the prior period (37.1 vs. 16.6 months, p=0.04). Conclusions: Establishment of a VMS to communicate abnormal imaging findings consistent with HCC is associated with improved survival, most likely due to shorter time to treatment and more streamlined care.
The Impact of Perioperative Blood Transfusions on Cancer Recurrence and Survival following Oncologic Resection

C. Peeples, 1 C. Jenkins, 1 T. Mangla, 1 T. Riggs, 1 F. Ivaska, 1 J. Robbins, 1 1. Beaumont Health System, Royal Oak, MI; 2. Beaumont Research Institute, Royal Oak, MI.

Background: Blood transfusions have been associated with immunologic suppression. Cancer patients undergoing definitive oncologic resection may require blood transfusion during the peri-operative period. A relationship between transfusions, cancer recurrence, and survival has been proposed but not well established. Objectives: The objective was to investigate the association of peri-operative blood transfusions with cancer recurrence and overall survival in patients undergoing definitive oncologic resections. We also evaluated the correlation of timing of the transfusion with recurrence rates. Methods: We did a retrospective review of the tumor registry at a single institution from January 2004 through November 2010. All patients with a diagnosis of brain, colorectal, esophageal, kidney, lung, ovarian, uterine, pancreatic, and stomach cancers who underwent a definitive oncologic resection were included. Peri-operative blood transfusion was defined as the receipt of blood transfusion within 30 days preoperatively, during surgery, or during the first 30 days post operatively. Multivariate analysis adjusted for age, gender, and oncologic stage. Results: A total of 2836 patients were included in the analysis. Oncologic stage was associated with proportion of patients transfused (p=0.0001). Overall, 19.2% of patients received at least one transfusion, and 14.4% had recurrence. Transfusion was associated with shorter time to recurrence (30 vs. 36 months, p < 0.001) and risk of recurrence increased with each unit transfused (hazard = 1.09, p < 0.005). Median length of follow up was 37 months. After adjustment for oncologic stage, age, gender, and cancer type, a significant association between cancer recurrence and perioperative blood transfusion remained (hazard = 1.40, p < 0.009). Conclusion: We identified a significant association between peri-operative blood transfusion, cancer recurrence, and mortality following definitive oncologic resection. In addition, risk of recurrence increased with each unit transfused. While our study demonstrated an association, rather than causation, prudence suggests judicious transfusion use.

Underuse of Tri-modality Treatment Impacts Survival for Patients with Inflammatory Breast Cancer: An Analysis of Treatment and Survival Trends from the National Cancer Database

N. Rueth, * 1. Beaumont Health System, Royal Oak, MI; 2. Beaumont Research Institute, Royal Oak, MI.

Decision Making and Recommendation for Management Change

Level of Curativity (%) Total No. of Patients Change p-value

<table>
<thead>
<tr>
<th>Level of Curativity</th>
<th>Total</th>
<th>No. of Patients</th>
<th>Change p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uncertain</td>
<td>55(8)</td>
<td>30(60)</td>
<td></td>
</tr>
<tr>
<td>Somewhat certain</td>
<td>39(6)</td>
<td>21(42)</td>
<td></td>
</tr>
<tr>
<td>Certain</td>
<td>44(7)</td>
<td>21(42)</td>
<td></td>
</tr>
</tbody>
</table>


The use of tri-modality therapy fluctuated annually (58.4%-73.4%). Patients associated survival trends over time. Logistic regression and Cox proportional hazards models were used to examine factors predicting treatment and survival, respectively. Results: We identified 10,197 patients who fulfilled the entry criteria. The use of tri-modality therapy fluctuated annually (58.4%-73.4%). Patients who were older than 54 years, diagnosed earlier in the study period, lived regions of the country outside of the Midwest, or had a higher comorbid score were significantly less likely to receive tri-modality therapy (all p<0.05), with a negative impact on survival. 5- and 10-year survival rates were highest among patients receiving tri-modality treatment (55.4% and 37.3%) compared to patients who got the combination of surgery + chemotherapy, surgery + XRT, or surgery alone (Figure 1). After adjusting for potential confounding variables, use of tri-modality therapy remained a significant predictor of survival. Conclusions: Our analysis demonstrates that underutilization of tri-modality therapy negatively impacts survival for patients with IBC. The use of tri-modality therapy has increased only marginally with time, and there remain significant patient factors associated with differences in use of guideline compliant tri-modality treatment. We have identified potential barriers to care that may be used to target tri-modality treatment delivery and potentially improve patient outcomes.

The Role of Preoperative Comprehensive Geriatric Assessment to Predict HRQoL in Elderly Cancer Patients

G.M. Barden, * A.D. Naik, J.N. Corrimer, A. Artinyan, S. Sansgiry, N.J. Petersen, D.A. Anaya. 1. Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX; 2. Houston VA Center for Innovations in Quality, Effectiveness and Safety (QuEEST), Houston, TX; 3. Department of Medicine, Baylor College of Medicine, Houston, TX; 4. Department of Surgical Oncology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX.

Introduction: Preoperative comprehensive geriatric assessment (CGA) is advocated to help with patient selection and improve the decision-making process for elderly cancer patients. However, the utility of CGA for predicting patient-centered outcomes such as HRQoL, which are particularly relevant to this population, is unknown. The goal of this study was to evaluate the role of using preoperative CGA to examine the association of geriatric conditions with HRQoL in an elderly cancer surgery population. Methods: This is a prospective cohort study of elderly cancer patients (≥65y) scheduled for surgery at a tertiary referral center (2012-2013). Baseline clinical information and CGA data were collected preoperatively; patients were administered validated surveys to examine 8 domains within the CGA (functional status, fatigue level, cognitive function, depression, comorbidities, operative risk, nutrition and social support). The primary outcome was baseline HRQoL, measured using the Physical Component (PCS) and Mental Component Summaries (MCS) of the SF-36 survey. Univariate and stepwise multivariate linear regression were used to examine the association of geriatric conditions with worse HRQoL, while adjusting for important patient and tumor-related factors. Results: 107 elderly cancer patients were included; the majority had gastrointestinal malignancies (71%). CGA identified geriatric conditions in all domains, ranging from 12% for depression to 96% for high-operative risk (Figure 1). After MV linear regression, poor functional status by ADLs 11.3(4.6-18.1), by IADLs 6.4(0.4-12.4), high fatigue level 8.5[3.3-13.8], and high comorbidity index 6.0[0.7-11.3] were associated with worse PCS HRQoL, and decreasing age 4.0[0.2-0.7], poor functional status by IADLs 5.4[0.6-10.3], and depression 12.0[4.1-18.9] were associated with worse MCS HRQoL.

P263

Underuse of Tri-modality Treatment Impacts Survival for Patients with Inflammatory Breast Cancer: An Analysis of Treatment and Survival Trends from the National Cancer Database

N. Rueth,* 1. Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX; 2. Beaumont Research Institute, Royal Oak, MI; 3. Department of Medicine, Baylor College of Medicine, Houston, TX; 4. Department of Surgical Oncology, Division of Surgery, The University of Texas MD Anderson Cancer Center, Houston, TX.

Introduction: Despite sophisticated advances in breast cancer therapy, guidelines for inflammatory breast cancer (IBC) remain largely unchanged, and studies evaluating contemporary treatment trends are lacking. In this study, we analyzed patient factors that predicted the use of guideline recommended tri-modality treatment (chemotherapy, surgery, and radiation therapy [XRT]) and studied the impact that treatment delivery had on survival. Methods: Using the National Cancer Data Base (NCDB), patients who underwent surgical treatment of non-metastatic IBC from 1998-2010 were identified. We collected patient, tumor, and treatment data and analyzed treatment delivery and associated survival trends over time. Logistic regression and Cox proportional hazards models were used to examine factors predicting treatment and survival, respectively. Results: We identified 10,197 patients who fulfilled the entry criteria. The use of tri-modality therapy fluctuated annually (58.4%-73.4%). Patients who were older than 54 years, diagnosed earlier in the study period, lived regions of the country outside of the Midwest, or had a higher comorbid score were significantly less likely to receive tri-modality therapy (all p<0.05), with a negative impact on survival. 5- and 10-year survival rates were highest among patients receiving tri-modality treatment (55.4% and 37.3%) compared to patients who got the combination of surgery + chemotherapy, surgery + XRT, or surgery alone (Figure 1). After adjusting for potential confounding variables, use of tri-modality therapy remained a significant predictor of survival. Conclusions: Our analysis demonstrates that underutilization of tri-modality therapy negatively impacts survival for patients with IBC. The use of tri-modality therapy has increased only marginally with time, and there remain significant patient factors associated with differences in use of guideline compliant tri-modality treatment. We have identified potential barriers to care that may be used to target tri-modality treatment delivery and potentially improve patient outcomes.
predictors of worse HRQoL for both physical and mental health in elderly cancer patients, and should be incorporated as part of the preoperative information to guide decisions targeted at improving postoperative HRQoL for this population.

Figure 1. Baseline Presence of Geriatric Conditions, Identified by Comprehensive Geriatric Assessment (CGA) in 167 patients.

Weight Loss and Postoperative Outcomes in Patients with Advanced Cancer

S. Singla,* P. Thirunavukarasu, S.S. Sanghera, S. Nair, Roswell Park Cancer Center, Buffalo, NY.

Background: Nutritional status is considered a predictor of post-operative complications in patients undergoing surgery. However, the impact of weight loss as an independent predictor of poor outcome has not been extensively studied in patients with advanced cancer. Methods: Using the American College of Surgeons-National Surgical Quality Improvement Project’s (ACS-NSQIP) participant-use file from 2005 until 2011, patients were identified who underwent elective surgery in the setting of disseminated cancer. Patients that had preoperative weight loss (WL) were then compared to non-weight loss patients (NWL). Data on demographics, comorbidities, clinical preoperative and intraoperative variables and 30-day morbidity and mortality were collected and reviewed. A multivariate analysis was conducted to evaluate the association between weight loss and morbidity, serious morbidity and mortality while adjusting for other variables. Results: We identified 30,669 patients with disseminated cancer; of these 3,514 patients (11.5%) had weight loss prior to surgery. Compared to NWL patients, WL patients were more commonly men than women (12.6% vs 10.3%, p<.001), black than white (14.6% vs 11.0%, p<.001), and had a lower BMI (23.4 vs 26.7, p<.001). Compared to NWL patients, WL patients had a significantly longer median length of stay, higher rate of surgical site infections, and higher rate of re-intubation, pneumonia, renal insufficiency and failure, cardiac arrest, septic shock, overall morbidity (37.5% vs. 28.4%, p<.001), serious morbidity (23.8% vs. 17.5%, p<.001) and mortality (13.8% vs 6.0%, p<.001). On multivariate analyses, weight loss was an independent predictor of postoperative morbidity (OR 1.3, 95% CI: 1.19-1.42) serious morbidity (OR 1.2, 95% CI: 1.13-1.37) and mortality (OR 1.75, 95% CI: 1.54-1.98). Conclusions: Patients with advanced cancers presenting with weight loss are at a significantly higher risk for post-operative morbidity and mortality. Optimizing nutritional status in these patients is critical before undergoing elective surgical procedures.

Learning Curve and Outcomes of Cytoreduction Surgery and Hyperthermic Peritoneal Chemoperfusion for Peritoneal Malignancies


Introduction: Cytoreduction Surgery (CRS) and hyperthermic chemoperfusion (HIPEC) may improve oncologic outcomes in some peritoneal surface malignancies. This complex procedure may be associated with high complication rates, prolonged hospital length of stay (LOS) and potential mortality. Our objective was to determine the learning curve (LC) of CRS/HIPEC for postoperative and surgical outcomes in a high-volume center. Methods: 370 patients with peritoneal carcinomatosis from mucinous appendiceal neoplasms (MAN=282), malignant peritoneal mesothelioma (MPM=65) and gastrointestinal cancer (GC=23) were identified from a prospective database between 2001-2010. Multivariate logistic regression analysis was used to identify independent risk factors for complete cytoreduction and major morbidity (grades 3-5). Risk-adjusted sequential probability ratio test (RA-SPRT) was employed to assess the LC of CRS/HIPEC for incomplete cytoreduction and major morbidity using pre-specified odds ratio boundaries derived from previously published data. Moving average (MA) analysis was used to trend hospital and ICU LOS. Results: Complete cytoreduction, major morbidity and 60-day mortality were 83.5%, 30% and 1.9% respectively. Higher SPCI was the major independent risk factor for incomplete cytoreduction, while high-grade histology, incomplete cytoreduction and diagnosis of MPM and GC (when compared to MAN) were predictors of major complications after CRS/HIPEC (p<0.05). RA-SPRT chart for incomplete cytoreduction started to decrease after 20 cases and breached the lower boundary (-5.2) at case 96 with subsequent stability; while major morbidity showed a steady decrease after 96 cases, breached the lower boundary (-8.9) at case 188 and remained stable after that. MA analysis revealed a drop followed by stability after initial 100 cases in hospital LOS (+15 d) and after initial 200 cases in ICU LOS (+3.5 d). Conclusions: Completeness of cytoreduction, morbidity and mortality rates for CRS/HIPEC at our institution are comparable to previously reported data. Our learning curve analysis reveals that approximately 180 procedures are required to improve operative outcomes.

Multidisciplinary Education for Surgical Oncology Trainees: Results of a National Needs Assessment

S. Ganai,* A.S. Akthar,1 O.M. Hahn,1 R.J. Maggiore,3 E.E. Cohen,1 S.J. Chhumara,1 A. Howard,1 M.C. Posner,2 D.W. Golden.1 1. The University of Chicago Medicine, Chicago, IL; 2. Southern Illinois University School of Medicine, Springfield, IL; 3. University of Missouri - Kansas City School of Medicine, Kansas City, MO; 4. Oregon Health Sciences University, Portland, OR.

Introduction: Several training paradigms generate surgeons capable of addressing cancer care, including the new fellowship pathway towards subspecialty certification in Complex General Surgical Oncology. While multidisciplinary oncology curricula (MDOC) have been advocated as an optimal approach to help surgeons gain understanding of associated disciplines, it is uncertain how MDOC have been implemented into training. This study is part of a needs assessment of MDOC focusing on the attitudes of surgical trainees. Methods: In April 2013, a web-based survey was sent to 316 surgical fellowship program directors (PDs) including surgical oncology (SO, n=19), breast oncology (BO, n=32), colorectal (CR, n=57), hepatobiliary (HPB, n=19), and subspecialties (SS: urologic, n=32; gynecologic, n=46; head/neck, n=29; musculoskeletal, n=11; thoracic, n=66). Program response rate was at least 28% based on voluntary site identification (SO 42%, BO 44%, CR 14%, HPB 37%, SS 28%). Responses from 160 trainees were received, including 27 SO, 19 BO, 13 CR, 9 HPB, and 92 SS trainees. Results: Multidisciplinary tumor board

Introduction: The Institute of Medicine’s report on improving cancer care, along with collaborative efforts of national organizations including the National Quality Forum, has resulted in the development of “accountability measures” which are being increasingly used for hospital accreditation, managed care contracts and Center for Medicare and Medicaid Services quality monitoring. To understand potential coding pitfalls related to the application of these measures, we evaluated adherence at a tertiary care cancer center to determine reasons for non-compliance. Methods: A retrospective review was performed of all eligible cases of breast and colon cancer reported to the American College of Surgeons Commission on Cancer (ACS) at a single institution from 2008 – 2012. Coding for compliance was performed using the ACS standards for accountability measures for breast and colon cancer. Timing-based quality indicators for stage I-III breast cancer include radiation therapy administered within 1 year (BCS), hormonal therapy within 1 year (HT), and adjuvant chemotherapy within 120 days of diagnosis (MAC); for stage III colon cancer, the measure is adjuvant chemotherapy within 120 days of diagnosis (ACT). Results: Identified cases included 897 BCS, 1,433 HT, 312 MAC, and 122 ACT, with adherence rates of 95.1%, 94.1%, 87.2%, and 86.9%, respectively. The reasons for non-adherence included patient-centered factors such as patient choice to delay or obtain treatment elsewhere (Table). Other factors coded as non-adherent included delays at outside facilities, lost to follow-up, designation of date of diagnosis based on suspicion rather than biopsy, insurance approval, need for other procedures, diagnosis of a second malignancy, and complications. Conclusions: Our center averaged an annual compliance with the adjuvant measures of 97% and 94%, respectively. Among those receiving some instruction in MO or RO, significantly more SO/BO trainees (97% and 93%) were taught via dedicated clinical rotations compared to CR/HPB (0% and 14%) and SS trainees (56% and 50%); p<0.001. Perceived utility of MO/RO rotations was greatest in BO trainees; p<0.01. Conclusions: Differing philosophies towards MDOC may be reflected by training paradigms, with SO/BO programs placing more value on dedicated clinical rotations over didactics or relying solely on MDTBs for oncology instruction. Further survey of PDs may be warranted.

P269 Credit where Credit is Due: Using Population-based Registries to Identify Treating Hospitals A.C. Saunders,1* L. Ji,2 A. Cupino,2 C. Dyke,3 J.W. Morgan,3 C.R. Morris,3 S.S. Lum,3 N.L. Solomon.5 1. Loma Linda University Medical Center, Loma Linda, CA; 2. Loma Linda University School of Public Health, Loma Linda, CA; 3. SEER Cancer Registry of Greater California, Sacramento, CA; 4. California Cancer Registry, Sacramento, CA; 5. Loma Linda University School of Medicine, Loma Linda, CA.

Introduction: Population-based cancer registries are often used to assess care received by cancer patients. These registries consolidate information on treating hospitals using the class of case schema developed by the Commission on Cancer, where patients receiving definitive cancer treatment at the reporting hospital are assigned a class of 10 or 20. This study investigates whether the consolidation process has led to inaccuracy in identifying hospitals where the most definitive cancer-directed surgery is performed. Methods: With IRB approval, consolidated data in the California Cancer Registry (CCR) was cross-referenced with raw admission and treatment data provided by California hospitals, using records from 2004-2009 of gastric cancer patients undergoing definitive surgical resection. Results: A total of 3,055 records were reviewed. A class of 10 or 20 was assigned in 2,932 cases, but 345 of these received their definitive surgical treatment at a hospital other than the reporting hospital. Incisional biopsy had been performed at the reporting hospital in 344 of the 345 cases, and this procedure was incorrectly coded in the consolidated data as definitive surgical treatment. A class other than 10 or 20 was assigned in 123 patients, and found to be correct in 121 cases. Thus, coding for a class of 10 or 20 in the CCR carried a positive predictive value of 88%, or 12% error, for correctly identifying the hospital where the most definitive surgical resection was performed (see Table 1). Conclusions: The 12% error seen in the assignment of class of case 10 or 20 has the potential to cause inequitable assignment of risk and reward to hospitals involved in the treatment of gastric cancer. Accurate identification of hospitals where the most definitive cancer-directed surgery is performed is of particular importance when considering quality improvement programs and pay-for-performance models of reimbursement. These findings in a subset of patients should prompt further investigation into the occurrence of similar errors across the CCR and other important cancer databases.

Table 1: Raw Hospital Data

<table>
<thead>
<tr>
<th>Class of Case</th>
<th>CCR</th>
<th>Definitive Surgery performed at reporting hospital</th>
<th>Definitive Surgery performed at other hospitals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class of Case</td>
<td>10 or 20</td>
<td>2,876</td>
<td>345</td>
</tr>
<tr>
<td>PPV%</td>
<td>88%</td>
<td>Sp%</td>
<td>98%</td>
</tr>
</tbody>
</table>

P270 Predictive Factors of Peritoneal Carcinomatosis from Appendiceal Cancer Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy W.A. Jimenez, A. Sardi,5 C. Nieroda, M. Sitrig, M.F. Nunez, R. MacDonald, V. Milovanov, N. Aydin, V. Guschin. Surgical Oncology, Medical Center, Baltimore, MD.

Introduction: Cytoreductive surgery (CRS) associated with hyperthermic intraperitoneal chemotherapy (HIPEC) is the standard of care for peritoneal carcinomatosis (PC) from appendiceal cancer in selected patients. This study evaluates the predictive factors for long term survival of patients with PC from appendiceal cancer treated with CRS/HIPEC in a medical center specializing in peritoneal surface malignancies. Methods: A retrospective analysis of a prospective database of 358 CRS/HIPEC procedures performed identified 202 patients with PC from appendiceal cancer, in whom 233 CRS/HIPECs were performed February 1998 and February 2013. Kaplan-Meier survival curves were used to analyze the survival related to the peritoneal cancer index (PCI), complete cytoreduction (CC 0-1), lymph node status (LN), and tumor histopathology. Results: One-hundred-twenty-nine (64%) women and 73 (36%)...

Introduction Optimal cytoreduction is fundamental in the treatment of peritoneal carcinomatosis (PC) often requiring debulking of the diaphragm. However, the outcome of diaphragmatic stripping and resection during cytoreductive surgery (CRS) followed by Heated Intraperitoneal Chemotherapy (HIPEC) is unknown. The aim of this study is to assess the short-term outcomes of patients undergoing CRS/HIPEC with diaphragmatic involvement. Methods A retrospective chart review from April 2007 to October 2013 of all patients undergoing CRS/HIPEC with curative intent for PC was conducted. Groups 1 and 2 consisted of patients with and without diaphragmatic disease respectively. Univariate and Propensity Score Analysis were used to compare both groups. Results Of a total of 199 patients undergoing CRS/HIPEC, 89 (45%) presented with diaphragmatic disease. Most common diagnoses included appendiceal and colorectal (50%), pseudomyxoma peritonei (12%), gastric (7%), and ovarian cancers (5%). Characteristics of both groups are summarized in Table 1. The majority of patients had right diaphragmatic involvement 97.7% and 31.8% had bilateral disease. Full thickness resection was performed in 62.5% and was repaired with mesh in 4%. Thoracostomy tubes were used in 51% of patients undergoing full thickness diaphragmatic resection at the time of CRS/HIPEC for an average of 5 days (range 2-12days). Postoperative thoracostomy tubes were placed in 6.8% of cases. Major complications corresponding to Clavien-Dindo Classification 3-5 were significantly higher in Group 1 (OR 3.7, CL 95% 1.2-11.1; P=0.023), as was the length of hospital stay (9 vs 7 days, =0.0394). Conclusion Patients with diaphragmatic involvement present with higher tumor burden, requiring prolonged procedures and are less likely to achieve optimal debulking. Although 90 day mortality was not different, once correcting for baseline differences, Group 1 had a 3.7 higher risk of major complications and significant increase in length of stay. Both surgeon and patient should consider the presence of diaphragmatic implants in their preoperative decision making process.

Table 1. Preoperative, Operative and Postoperative Variables

Abbreviations- yrs:years, SD: Standard Deviation, #:Number, PCI: Peritoneal Carcinomatosis Index, EBL:Estimated blood loss, surg: surgery, min:minute, CCR:complete cytoreduction, ICU:Intensive Care Unit, +: Clavien-Dindo Classification types 3-4-5, *: P values derived from Propensity Score Analysis, other P values result from univariate analysis.

P273 Port Site Metastases is an Independent Prognostic Factor in Patients with Peritoneal Carcinomatosis M.F. Nunez, A. Sardi,* C. Nieroda, W.A. Jimenez, M. Sittig, R. MacDonald, V. Gushchin. Surgical Oncology, Mercy Medical Center, Baltimore, MD.

INTRODUCTION: Port site metastases (PSM) have been reported after laparoscopy in patients with peritoneal carcinomatosis. We hypothesize that
they are an independent predictor of overall survival in patients undergoing Cytoreductive Surgery and Hyperthermic Intra-peritoneal Chemotherapy (CRS/HIPEC). METHODS: A retrospective review of a prospective database of 350 patients revealed 65 patients who underwent laparoscopy prior to CRS/HIPEC. The origin of primary tumors is detailed in Table 1. Previous port sites were excised regardless of tumor involvement. Patients with PSM in the final histopathology were divided into two groups: patients with positive PSM and patients without PSM. Overall survival (OS) was estimated by Kaplan-Meier curves and the Log-Rank Test. Cox regression (hazard ratios (HR) and 95% CIs) was used to test for independent effects of the LN metastases and positive port site involvement on survival. RESULTS: Sixty-five (28%) patients had laparoscopy before CRS/HIPEC. In 45 (69%) patients, diagnostic laparoscopy was performed for suspected malignancy and in 20 (31%) patients the tumor was found incidentally. One hundred and forty-four ports were resected, 41 (29%) ports were positive for malignancy in a total of 22 (34%) patients. Mean overall survival at 1, 3, and 5 years was 86%, 62%, and 57%, respectively. Survival at 1 and 3 years in PSM was 72% and 20%, respectively, compared with patients without PSM, 95% and 79%, respectively (p<0.001). Positive LN were detected in 13/22 patients with PSM and in 1/43 without PSM. Independent effects on survival shows HR=3.1, CI=1.07-8.82, p=0.001 for LN metastases and HR=3.4, CI=1.18-9.65, p=0.001 in patients with positive PSM. CONCLUSION: Port site metastases are common in patients with peritoneal carcinomatosis and independently confer a worse prognosis. It may reflect the tumor biology or potential consequences of laparoscopy.

Table 1. Primary tumor origin, port site metastases and lymph node positivity

<table>
<thead>
<tr>
<th>TYPE OF TUMOR</th>
<th>PREVIOUS LAPAROSCOPY</th>
<th>PSM&lt;20</th>
<th>+/+LN N Total</th>
<th>+/+LN N PSM</th>
<th>+/+LN N (PSM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendix</td>
<td>29</td>
<td>8</td>
<td>12</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Colon</td>
<td>8</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Small bowel</td>
<td>5</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>4</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Gastro</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Primary Peritoneal</td>
<td>8</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Ovarian</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Fallopian Tube</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>65</td>
<td>18</td>
<td>24</td>
<td>13</td>
<td></td>
</tr>
</tbody>
</table>


P274 Significance of Diaphragmatic Resections and Thoracic Chemoperfusion on Outcomes of Peritoneal Surface Disease Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (CRS/HIPEC)


Background: Diaphragmatic resection (DR) during CRS/HIPEC exposes the thorax into direct contamination from the peritoneal cavity. It is unknown if synchronous thoracic chemoperfusion should be a part of the operative management of these patients. Methods: A prospective database of 1,078 procedures was analyzed. Type of malignancy, chest perfusion, resection status, comorbidities, morbidity, mortality and overall survival were reviewed. Results: 103 CRS/HIPEC procedures were performed with synchronous DR with a median follow-up of 52 months. 57(55%) were performed for appendiceal and 23 (22%) for colon cancer. DR was related with higher volume of disease as indicated by more organ resections (3.7 vs 2.8 p=0.001) and higher incidence of R2 resections (66 vs 52%, p=0.006). Patients with and without DR had similar 30 day grade III/IV morbidity of 23 vs 17%, with 30-day readmission of 11% to 15%. Length of ICU care (6 vs 3 days, p=0.15) and hospitalization (17 vs 14 days, p=0.008) were longer with DR. 90 day mortality was 7.7% for patients with DR vs 3.6% for those without (p=0.05). Comorbidities predicted death (p=0.03). 19 (20%) of DR patients underwent synchronous abdominal and chest chemoperfusion with an associated 30.8% grade III/IV morbidity without mortality. Failure in the chest post DR followed by perfusion was 26% (5/19) vs 5% (4/78) when the thorax was not perfused (p=0.01). Median survival for complete cytoreduction for low-grade appendiceal cancer was 175 months without DR and not reached with DR (p=0.17). Median survival for colorectal cancer patients post complete cytoreduction was 23 months following DR vs 31 without DR (p=0.76). Conclusions: Diaphragmatic resection during CRS/HIPEC is an independent predictor of surgical mortality, incomplete cytoreduction and increased length of hospitalization. Surgical mortality was not related to synchronous thoracic perfusion. Chest perfusion was performed selectively in patients with higher disease burden and was associated with more thoracic recurrence, with unknown impact on overall survival.

P275 Using Implementation Methodology to Develop a Virtual Tumor Board Program Regionally

G.M. Barden,1* A.D. Naik,3 J.A. Davila,2 A. Arintyn,1 A. Walder, N.J. Petersen,2 D. Albo,1 D.H. Berger,1 D.A. Ana,1 1. Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX; 2. Houston VA Center for Innovations in Quality, Effectiveness and Safety (QuESt), Houston, TX; 3. Department of Medicine, Baylor College of Medicine, Houston, TX.

Introduction: Multidisciplinary evaluation (MDEval) is the current standard for cancer care. Tumor board (TB) conferences are designed to provide such standard. Limited availability of TBs locally hampers the ability to accomplish MDEval, with Virtual TB (VTB) as a possible solution to overcome this limitation. The goal of this study was to implement a Virtual Tumor Board (VTB) Program regionally, using a TB implementation framework, and to examine its success with an implementation model. Methods: A VTB was implemented within a regional network (10 medical centers) in the Veterans Affairs healthcare system (2011-2013). The implementation process focused on developing standardized constructs within a TB implementation framework using a web-based platform: Policy, Organizational, TB structure, TB function. The VTB implementation was examined using the RE-AIM model (reach, proportion of target intervention delivered), Efficacy (proportion of complex cases accomplishing appropriate MDEval, by NCCN guidelines), Adoption (VTB utilization rates and website hits), Implementation (proportion of cases successfully presented) and Maintenance (Implementation measure beyond 12 months). Descriptive statistics were used to examine each measure and the X2 and t-test were used to compare institutions. Results: 164 VTB cases were presented. The VTB program was successfully implemented in 7 of 9 referring institutions (78% reach). Among selected complex cases (HCC, liver metastasis, pancreatic, and rectal cancer, n=110), appropriate MDEval was accomplished in 102 (93% efficacy). Adoption was fair with 35% utilization of available VTB settings and 294 website hits during the study period. Implementation was good with 97.5% of all requested cases presented successfully; with no difference beyond 12 months (maintenance). There were no differences in any of the measures by institution. Conclusions: Development of a regional VTB program using established implementation methodology is feasible and improves access to MDEval of complex cancers. Future studies should focus on using this information to develop VTB program performance measures and examine its impact on treatment and long-term outcomes.

P276 Patient Satisfaction with GI Cancer Multidisciplinary Care and GI Cancer Nurse Navigation L.E. McCahill,4, J. Kokko.1 1. Surgical Oncology, Metro Health Hospital, Wyoming, MI; 2. Lacks Cancer Center, Grand Rapids, MI.

Background: Health care reform, including the Affordable Care Act, calls for increased care coordination and evaluation of patient satisfaction with multidisciplinary care. Various methods to enhance coordination of cancer care have included both nurse navigators and multidisciplinary clinics (MDC). MDCs can be very inefficient for surgeons and navigational services add additional costs to cancer care. While both are widely heralded, there exist no reports of patient satisfaction evaluating their impact on quality of cancer care. Methods: Patients were eligible if newly diagnosed with a GI Cancer (pancreas, liver, colorectal, esophageal/gastric) within the prior 12 months, and they received cancer treatment from at least two cancer specialists (surgical oncology, medical oncology, radiation oncology) and underwent initial evaluation...
in MDC clinic. A 36-item survey using a 5 point Likert scale (1=strongly agree to 5=strongly disagree) was developed after extensive literature review to evaluate patient satisfaction with 1) timeliness and coordination of initial evaluation 2) coordination of multidisciplinary cancer care 3) effectiveness of MDC evaluation format 4) understanding of initial treatment plan and involvement with treatment decision making and 5) Nurse navigation services. Two survey mailings were performed. Results: Sixty two patients diagnosed between Jan 2010 and July 2012 were mailed surveys, and 26 (42%) were completed. Results of highlighted survey items are shown in Table 1. Conclusion: Patients with newly diagnosed gastrointestinal cancers requiring multi-modality cancer therapy expressed high satisfaction with coordination and quality of cancer care as well as good understanding of treatment and self-involvement with decision making when their initial care utilized both nurse navigation and a multidisciplinary clinic. While this cancer delivery model has additional costs and some inefficiencies for care providers, goals of health care reform appear to be met. This survey can serve as a platform to evaluate care coordination and patient satisfaction for multidisciplinary cancer care.

### Patient Satisfaction with Multidisciplinary Cancer Care

<table>
<thead>
<tr>
<th>Aspect of Multidisciplinary Cancer Care</th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Lower satisfaction rating (3-5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse Navigation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helpful in coordinating initial care</td>
<td>19 (73%)</td>
<td>10 (38%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Listened to health concerns</td>
<td>17 (65%)</td>
<td>7 (27%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Addressed symptoms</td>
<td>15 (58%)</td>
<td>9 (35%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Kept me informed during treatment</td>
<td>14 (54%)</td>
<td>10 (38%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Available during treatment for questions</td>
<td>13 (50%)</td>
<td>10 (38%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Important part of my cancer care</td>
<td>15 (55%)</td>
<td>8 (31%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Multidisciplinary Clinic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Studies were available at Clinic visit</td>
<td>16 (62%)</td>
<td>10 (38%)</td>
<td>0%</td>
</tr>
<tr>
<td>Staging studies well coordinated and convenient</td>
<td>12 (48%)</td>
<td>7 (27%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Adequate time with each doctor</td>
<td>18 (69%)</td>
<td>7 (27%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Know who to contact of questions</td>
<td>16 (64%)</td>
<td>7 (28%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Liked seeing all doctors in one clinic visit</td>
<td>13 (51%)</td>
<td>6 (26%)</td>
<td>4 (17%)</td>
</tr>
<tr>
<td>Would recommend GI MDC clinic to others</td>
<td>19 (73%)</td>
<td>4 (15%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Understanding and Involvement in Treatment decision making</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doctors addressed emotional needs</td>
<td>13 (50%)</td>
<td>10 (38%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>Doctors explained Treatment in understandable way</td>
<td>19 (73%)</td>
<td>6 (23%)</td>
<td>1 (4%)</td>
</tr>
<tr>
<td>Doctors involved in treatment decisions</td>
<td>19 (73%)</td>
<td>5 (19%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Doctors sought to communicate with each doctor</td>
<td>15 (58%)</td>
<td>9 (35%)</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Primary Care doctor well informed about cancer plan</td>
<td>13 (50%)</td>
<td>6 (23%)</td>
<td>7 (29%)</td>
</tr>
<tr>
<td>Understood treatment plan at clinic conclusion</td>
<td>13 (52%)</td>
<td>11 (44%)</td>
<td>1 (4%)</td>
</tr>
</tbody>
</table>

### P277

**The Marriage Defense for Cancer: A National View**

N.M. Burrish,1 Z. Chau,1 M. Eckander,1 J.K. Smith,1 L. Bliss,2 S. Ng,1 J.F. Tseng,1,3
1. Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; 2. University of Massachusetts Medical School, Worcester, MA.

Marriage has a reputed association with better outcomes in various diseases including individual malignancies. We investigated the effect of marriage in the top 5 solid tumor cancers in combined lethality and incidence. Methods: Prostate, breast, colon, pancreas and lung cancer patients diagnosed 1998-2009 were identified using Surveillance, Epidemiology and End Results (SEER). Univariate analysis performed using chi-square; Kaplan-Meier for survival; multivariate analyses using Cox proportional hazards. To determine whether any marriage effect was due to early diagnosis, sensitivity analysis was performed, constructing multivariate model with locoregional patients only. Results: 466,259 prostate, 519,893 breast, 311,318 colon, 80,748 pancreas and 461,937 lung cancer patients were identified. Marriage was associated with earlier stage and younger age, and increased likelihood of radiation therapy expressed high satisfaction with coordination and quality of cancer care as well as good understanding of treatment and self-involvement with decision making when their initial care utilized both nurse navigation and a multidisciplinary clinic. While this cancer delivery model has additional costs and some inefficiencies for care providers, goals of health care reform appear to be met. This survey can serve as a platform to evaluate care coordination and patient satisfaction for multidisciplinary cancer care.

### P278

**Palliative Local Wound Control in Advanced Malignancy**

A. Blakely,* W.G. Cioffi, T.J. Miner. Brown University, Providence, RI.

Introduction: Surgical palliation of cancer is best defined as procedures performed with non-curative intent to improve quality of life or control symptoms of advanced malignancy. Soft tissue involvement of advanced malignancies may produce symptoms that significantly reduce quality of life, such as pain or bleeding. Literature on outcomes of palliative resection of soft tissue malignancy for local control is lacking. Methods: Soft tissue resections performed with palliative intent for local control were identified from a prospectively maintained palliative surgery database at a tertiary care center from January 2004 to July 2013. Tumor type, presenting symptom, procedure performed, need for skin graft, and symptom recurrence were recorded. Patients were followed for at least 60 days or until death. Results: 31 patients who underwent palliative soft tissue resection for local control were identified. Primary tumor types included melanoma (n=9, 29.0%), squamous cell carcinoma (n=9, 29.0%), sarcoma (n=5, 16.1%), breast (n=3, 9.7%), and other (n=5, 16.1%). 16 of 31 patients (51.6%) underwent resection for pain, 2 (6.5%) for bleeding, and 13 (41.9%) for local control or other symptoms. Procedures were performed on the trunk (n=17, 54.8%), extremities (n=7, 22.6%), head/neck (n=3, 16.1%), or multiple areas (n=2, 6.5%). 11 of 31 patients (35.5%) underwent axillary, inguinal, or neck lymph node dissection, 17 (54.8%) radical resection, and 3 (9.7%) wound excision. Split-thickness skin graft was performed in 6 of 18 radical resections (33.3%). 5 patients (16.1%) had symptom recurrence at the site of initial palliative procedure, of whom 3 (9.7%) underwent a second palliative procedure. 6 patients (19.4%) had new disease-related symptoms develop during follow-up. 30-day morbidity was 19.4%; mortality was 3.2%, which was due to progression of disease. Conclusions: Palliative surgery for local control of advanced soft tissue malignancy can provide durable symptom relief and improved quality of life. These procedures positively impact patients regardless of primary tumor type or tumor extent. Careful patient selection is important in order to maximize benefit of surgical palliation and minimize morbidity and mortality.

### P279

**The Detrimental Impact of Intact Primary Tumors in Patients with Metastatic Midgut Carcinoid Tumors**

J. Harris,1 K. Campbell,1 D. Huang,1 M. Evers,1 S.P. McKenzie.1 General Surgery, University of Kentucky, Lexington, KY; 2. Surgical Associates of Austin, Austin, TX.

Background: Single Institution studies have suggested that patients with metastatic midgut carcinoid (MCT) may benefit from resection of the primary tumor regardless of symptoms. We sought to determine if resection of the primary tumor alone in patients with metastatic MCT provided a survival advantage across a national patient sample. Methods: Using the Surveillance Epidemiology and End Results (SEER) database, all patients with American Joint Cancer Committee (AJCC) Stage IV MCT during the years 1992-2009 were identified and stratified by surgical resection of the primary tumor alone in patients with metastatic MCT provided a survival advantage across a national patient sample. Results: Over a 17 year period, we identified 724 patients with stage IV MCT. Of this group 80.1% (n=583) underwent surgical resection their primary tumor regardless of symptoms. We sought to determine if resection of the primary tumor may benefit from resection of the primary tumor. In the non-surgical group, 21.3% (n=20) had surgical resection and the impact on cancer outcomes remain relevant and warrant investigation.
vs. 25 months; p<0.0001). When compared to both the non-surgery—not recommended and surgical resection groups, SRNP patients had significantly worse overall (MS 29 vs. 83 vs. 14 months, respectively; p<0.0001) and disease specific survival (35 vs. 100 vs. 14 months, respectively; p<0.0001). Independent predictors of both decreased overall survival and disease specific survival included were no surgical resection, advanced age, and worse tumor grade (all p values <0.001). Conclusions: Based on this large, national patient sample, and aggressive surgical approach to the primary tumor is warranted in patients with stage IV MCT. Despite its relatively indolent biology, most patients with primary tumors in place succumb to disease within three years.

**P280**

**Using Mobile App Technology for Point of Care Cancer Surgery Risk Assessment**

P. Thirunavukarasu,* S. Singla, S. Nurkin. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.

**INTRODUCTION:** Accurately assessing surgical risk is difficult. Procedure-specific and patient related factors such as age and comorbid status make the prediction of operative outcomes subjective, and often inaccurate. Previous scoring systems, while more reliable, are time consuming - making them impractical for clinical use. The purpose of this project was to create a mobile solution for fast, point-of-care surgical risk assessment in patients undergoing cancer surgery. **METHODS:** We extracted data on demographic, clinical, operative and postoperative outcome variables on patients undergoing common surgical oncology procedures for cancer from the National Surgical Quality Improvement Project (NSQIP), 2005 to 2011 database. These include but are not limited to Esophagectomy, gastrectomy, hepatectomy, pancreaticoduodenectomy, colectomy and proctectomy. These data were used to design a mobile application, which allows input of patient/disease related information such as the surgical procedure, age and the American Society of Anesthesiology (ASA) class. **RESULTS:** This “Cancer Surgery NSQIP App” was developed for mobile devices to predict postoperative outcomes based on selected preoperative NSQIP variables. The application generates instant output to display surgical risks such as mortality, overall morbidity and serious morbidity (sMorbidity). The application also analyses stored NSQIP data to calculate the accuracy of the generated result to the specified patient parameters. Our next steps will be validating this application prospectively in patients undergoing surgery for cancer at our institution. **CONCLUSION(S):** Mobile communication devices are increasingly key tools for clinicians. Uniting the NSQIP data set with this technology creates a powerful tool for surgical clinical care. It provides a surgeon the ability to give an objective, immediate, point of care risk assessment for patients and their families. This information may be able to help guide physicians and patients in their surgical management, by providing realistic expectations of postoperative outcomes.

**P281**

**Neoadjuvant Pelvic Perfusion may Facilitate Resection of Pelvic Recurrent Rectal Cancer**

H. Wanebo,1* G. Begossi,2 E. Gustafson,3 J. Belliveau.1 1. Landmark Medical Center, Woonsocket, RI; 2. Alta Bates Summit Medical Center, Oakland, CA; 3. Providence College, Providence, RI; 4. Charlton Memorial Hospital, Fall River, MA.

**Introduction:** Pelvic recurrence of rectal cancer is a persisting therapeutic challenge in spite of widespread use of adjuvant/neoadjuvant chemo radiation and wide resection isolated pelvic perfusion (IPP) may facilitate pelvic resection in selected high-risk patients. **Patients:** IPP was done in 42 patients with locally advanced previously irradiated rectal cancer, 26 as a preoperative therapy and 16 for palliation. A comparative larger non-perfused group included 63 patients with pelvic resection only for recurrent rectal cancer. **Method:** Isolated pelvic perfusion (60 min) using pump oxygenation (Temp>41 degrees c), chemo agents – 5 FU 1500mg/m2, Cisplatin/Oxaliplatin 100/130mg/m2, Mitomycin 10-20- mg/m2, was done in 42 patients (67 IPP). Results (Follow up surgery): Palliative IPP in 16 advanced rectal cancer patients induced significant relief (1-4 months) of narcotic resistant pain (in 70%). Preoperative IPP in 26 locally advanced rectal cancer achieved a clinical path (CR) in 2 patients, and significant regression in 11 patients rendering them resectable. 7 had R0 pelvic resections; of 6 other patients, 4 refused surgery, 2 were medically excluded. Median survival was 24 months in 12 resectable and 30 mos in resected pts (2 pts were 5 year survivors). This is compared to outcome in 63 patients amenable to having pelvic resection alone: 57% had R0 resection (median OS 36 mos), 28% had R1 resection (med OS = 15 mos) and 15% had R2 resection (med OS 21 mos). Conclusion: Neoadjuvant IPP may facilitate selection of recurrent rectal cancer by identifying therapeutic responders likely to benefit from major pelvic resection and excluding non-responders most likely to benefit from non-surgical therapy. The potential to induce regression and facilitate R0 resection merits further exploration.
Abstracts: Poster Presentations

P282
Comparison of Sizes of Sentinel and Non-sentinel Lymph Nodes in Colorectal Cancers

S. Saha,† U. Koduru,‡ J.M. Burke,§ A. Korant,† S. Saha,&& V. Dhar,§ G. Johnston,¶ M. Arora,¶ T. Singh,¶ D. Wiese,* 1. McLaren Regional Medical Center, Flint, MI; 2. Michigan State University College of Human Medicine, East Lansing, MI; 3. McLaren Macomb Medical Center, Mount Clemens, MI; 4. Dana-Farber Cancer Institute, Boston, MA.

Background: Sentinel lymph node (SLN) mapping (M) in colorectal cancer (CRCa) with ultrastaging of SLNs find more nodes per patient (Pt) and more metastasis in the SLNs than non-SLNs (NSLNs) compared to conventional method of examination of the specimen. We hypothesized that SLNs may represent a subset of nodes smaller than those detected by routine pathological exam, and hence missed by conventional method of examination. Hence, we compared the sizes of SLNs and NSLNs in CRCa pts undergoing SLNMD.

Methods: SLNMD was done in 365 pts by subserosal peritumoral injections of blue dye for SLNMD. Blue stained nodes were tagged as SLNs followed by oncologic resection. SLNs were sectioned at 5 levels, 4 stained with H & E, one with cytokeratin (CK-IHC). The non-SLNs were sectioned at one level and stained with H & E. Greatest diameter of the nodes for sizes were measured on glass slides or from gross examination. Results: Of the total of 5601 LNs (Average 15.3/pt) included, 912 (16%) were SLNs and 4689 (84%) non-SLNs. Of the total lymph nodes removed, 77% were 5mm or less; 69% of positive LNs and 97% of negative LNs were less than 9mm (Table 1). On average, the size of the SLN was bigger (5.7mm) than NSLN (4.0mm). Both positive and negative SLNs were also bigger than positive and negative NSLNs (Table 1).

Conclusions: Our study confirms that on average, SLNs are bigger than NSLNs whether positive or negative or as a whole. This also highlights diligent efforts needed by the pathologists, as 77% of all lymph nodes were examined on glass slides or from gross examination. We hypothesized that SLNs may represent a subset of nodes smaller than those detected by routine pathological examination. Hence, missed by conventional method of examination. Hence, we compared the sizes of SLNs and NSLNs in CRCa pts undergoing SLNMD.

Table 1: Comparison of SLN† and NSLNç sizes(mm) in CRCa pts.

<table>
<thead>
<tr>
<th>Size of lymph node (mm)</th>
<th>Number of all lymph nodes</th>
<th>Positive lymph nodes</th>
<th>Negative lymph nodes</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-5</td>
<td>430 (77%)</td>
<td>215 (37%)</td>
<td>215 (37%)</td>
<td>N/A</td>
</tr>
<tr>
<td>6-9</td>
<td>932 (17%)</td>
<td>182 (32%)</td>
<td>182 (32%)</td>
<td></td>
</tr>
<tr>
<td>10-40</td>
<td>339 (6%)</td>
<td>176 (31%)</td>
<td>176 (31%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>5601</td>
<td>537 (9.5%)</td>
<td>537 (9.5%)</td>
<td></td>
</tr>
</tbody>
</table>

**Fisher's exact test and Chi-square with Yates’ correction**
† SLN: Sentinel Lymph Node
ç NSLN: Non-Sentinel Lymph Node

P283
Outcomes of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Mesothelioma: A Peritoneal Surface Malignancy Center Experience


Introduction: Peritoneal mesothelioma is an uncommon malignancy which can be difficult to treat. Cytoreductive surgery (CRS) and hyperthermic Intraperitoneal Chemotherapy (HIPEC) have evolved as treatment of choice when complete cytoreduction is achieved. This study reports the experience of a peritoneal surface malignancy center on the outcomes of CRS/HIPEC for peritoneal mesothelioma. Methods: A retrospective analysis of a prospective database of 389 CRS/HIPEC procedures identified 23 patients who underwent CRS/HIPEC for peritoneal mesothelioma from 1999-2013. One patient underwent CRS/HIPEC twice. Gender, age at diagnosis, age at surgery, previous surgeries, follow up time, peritoneal cancer index score (PCI), completeness of cytoreduction (CC), pathology and overall survival (OS) were analyzed. Results: There were 11 males and 12 females. Mean age at the time of diagnosis was 55.3 years (range=25.7-71.2) with a mean age at surgery 57.5 years (range = 31.5-74.7). Mean follow up time from surgery was 33.6 months (range=0.5-215). The median PCI score was 30.5, 79% had PCI >20. Complete cytoreduction (CC 0-1) was achieved in 78% of cases. Pathology included 21 epithelioid, 1 sarcomatoid and 1 mixed type. At present, 9 patients have no evidence of disease (NED), six are alive with disease. Eight patients are dead, 4 of mesothelioma and 4 of other conditions. Patients with epithelioid mesothelioma without evidence of disease had the highest survival rate (60.8%). Post operative morbidities were experienced in 11 patients (48%), only 3 were grade III. There was one in hospital mortality. One and 5 year OS rates from diagnosis were 86.7 and 65.3%, respectively (95% CI: 64.3-95.5 and CI 35.4-80.6). One and 5 year OS from HIPEC was 71.5 and 65.5%, respectively, (95% CI: 46.9-86.2 and CI 40.4-82.1). Conclusion: Patients with peritoneal mesothelioma may achieve long term survival when treated with CRS/HIPEC with best results seen in patients with epithelioid histopathology. CRS/HIPEC is strongly recommended for peritoneal mesothelioma.

P284
The Effects of Neoadjuvant Chemotherapy and Radiation Therapy on Outcomes of Pancreaticoduodenectomy


Introduction - The purpose of this study was to investigate the effects of preoperative chemotherapy and radiation therapy on postoperative outcomes of pancreaticoduodenectomy (PD). Methods - The ACS-NSQIP Participant User File (PUF) from 2005 to 2010 was used to analyze the outcomes of patients who underwent chemotherapy and radiation therapy prior to PD. Their outcomes were compared to those who underwent PD without neoadjuvant therapy. Preoperative variables and postoperative complications were compared between the two groups. We performed a multivariate binomial logistic regression to analyze factors associated with 30-day mortality and major complications. Results - We identified 4,305 patients who underwent PD for pancreatic malignancies without neoadjuvant therapy and 60 patients who received neoadjuvant therapy. Patients who received neoadjuvant therapy were significantly younger (61.9 ± 9.8 years vs 65.9 ± 11.3 years; p = 0.007) and were more likely to have had weight loss in the last six months compared to those who did not (22.8% vs 53.8%; p = 0.027). The preoperative cardiovascular, pulmonary, renal, endocrine and hematologic co-morbidities were similar between the two groups. The average operative time for patients undergoing PD after neoadjuvant therapy was significantly longer, with a higher rate of intra and postoperative transfusion requirements. However, the mortality rate, the average length of stay, and the rate of major complications between the two groups were similar (Table 1). On multivariate regression analysis, neoadjuvant therapy was associated with a higher likelihood of receiving intra or postoperative transfusion (OR 2.4, 95% CI: 1.1-5.0, p = 0.020). Other factors associated with need for transfusion were hematocrit < 30% (OR 1.9, 95% CI: 1.4-2.8, p = 0.001), history of myocardial infarction (OR 3.4, 95% CI: 1.0-11.2, p = 0.042), and hypertension (OR 1.5, 95% CI: 0.9-2.4, p = 0.003). Conclusion - Operative time and transfusion requirements were significantly higher for patients who underwent neoadjuvant chemotherapy and radiation therapy. Neoadjuvant therapy was not associated with an increase in mortality or major complications.
P286
Adjuvant Intraoperative Post-dissection Tumor Bed Chemotherapy: A Novel Approach in Treating Malignant Neuroendocrine Tumors

Y. Wang,1* M.A. Hall, P. Boudreaux, E. Woltering, L. Anthony.
LSUHSC - New Orleans, Kenner, LA.

Background: Malignant neuroendocrine tumor (NET) patients are often diagnosed at an advanced stage with extensive mesenteric lymph node and liver metastasis. Even with skillful surgical dissection, macro and microscopic residual disease at the dissection site remains a possibility. We hypothesized these potential tumor residuals in mesenteric lymph node dissection beds can be eliminated safely by a local application of 5-fluorouracil (5-FU). Methods: Retrospectively, charts of 62 consecutive midgut NET patients with bogy mesenteric lymphadenopathy underwent cytoreductive debulking surgeries from 1/2007 to 12/2009 were reviewed. Thirty-two (32) patients received an intraoperative application of 5-FU saturated gelfoam strips secured into the mesenteric defect following the extensive lymphadenectomy. Thirty (30) untreated patients served as a control. Results: 3-year survival after cytoreductive surgery was 22/32 (68.8%) for the treated group, versus 20/30 (66.7%) for the control. 6 patients (6/32, 18.8%) among the study group required additional debulking surgeries, versus 16 patients (16/30, 53.3%) in the controlled group. Upon reoperation, locoregional recurrence was noted in 9 of the 16 patients (56.3%) in the control group, versus only 2/6 (33.3%) of treated patients. Post-op complication rates are similar in the two arms. Conclusion: Intraoperative application of chemotherapy is a safe and effective adjuvant for eliminating any potential microscopic residual disease after extensive cytoreductive surgeries in advanced stage NET patients with mesenteric lymph node metastasis. It provides patients with sustained, slow releasing, high dose of 5-FU within the surgical bed with a negligible side effect profile, whereby reducing local recurrence rates and decreased the need of reoperation. Further study is required to evaluate its effect on long term survival.

P285
The Impact of Comorbidity on Costs and Effects of Second-line Treatment among Elderly Metastatic Colon Cancer Patients

A. Woldemichael,1 E. Onukwugha,2 Z. Zheng,1 N. Hanna,3* B.S. Seal,3 C. Mullins.1* Surgery, University of Maryland, Baltimore, MD; 2. Bayer Healthcare Pharmaceuticals, Wayne, NJ.

Background: The Charleston Co-morbidity Index (CCI) was developed as in hospital mortality indicator and subsequently used to both predict and adjust survival differences in cancer patients. Comorbidity is also known to influence the cost of providing treatment. We therefore examined how the incremental cost effectiveness of treating metastatic colon cancer (mCC) patients with 2nd line treatment (Tx2) will vary based upon their baseline CCI. Methods: We identified 2,897 elderly (age 66+) mCC patients who received NCCN recommended first-line treatment (Tx1) between 2003 and 2009 in the SEER-Medicare dataset. Approximately 6% and 1% of patients with missing CCI and outlier costs (above $579,621.9), respectively, were excluded. We categorized patients by their CCI for 12 months prior to diagnosis into three categories: low (CCI=0), medium (CCI=1) and high (CCI=2+). We calculated and compared 5-years incremental costs and effects on patients who received and those who did not receive Tx2. Costs are inflation adjusted to January 2009 dollars using US Medical Price Index (MPI). We adjusted for censoring using Inverse Probability Weighting (IPW) method and selection bias on observables using Propensity Score Bin Bootstrapping method. Results: Among patients who received Tx1, 56% proceeded to receive Tx2. Of those who received Tx2, 67%, 23%, and 10% have low, medium and high comorbidities, respectively. Compared to those who did not receive Tx2, patients who received Tx2 with low, medium, and high baseline comorbidity levels of patients increase.
P288
Quality of Life after Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy: A Prospective Study from an Asian Cancer Centre


Background Although Cytoreductive surgery with hyperthermic intra-peritoneal chemotherapy (CRS+HIPEC) has gained acceptance for the treatment of peritoneal carcinomatosis, the data on quality of life (QOL) after treatment remains scarce, particularly among the Asian population. This study assesses the QOL post CRS and HIPEC in an Asian cancer centre. Methods 40 consecutive patients who underwent CRS+HIPEC were enrolled in the study. QOL was measured via the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaires pre-operatively and at three, six and twelve months post-operatively. Changes in quality of life scores of 5 or more were considered significant. Results 40 patients were analysed of which 31 (78%) were females. Median age was 51 years (15 – 89 years). 34 patients had pre-operative ECOG status of 0 while the remaining 6 had ECOG status of 1. CRS + HIPEC were performed for ovarian cancer in 15 patients (38%), colorectal carcinoma in 14 patients (35%) and appendiceal carcinoma in 5 patients (13%). The median intra-operative Peritoneal Carcinomatosis Index (PCI) score was 12 (2 – 34) while the Completeness of Cytoreduction (CC) Score was 0 and 1 in 33 and 7 patients respectively. 3 patients died from progressive disease 3 to 6 months post CRS + HIPEC during the entire study period. The QOL scores of the cohort pre-operatively and at various time points post CRS+HIPEC is illustrated in Table 1. Global health status was non inferior to pre-operative scores after CRS + HIPEC. Significant improvements were seen in physical functioning, emotional functioning and social functioning scores, with the improvement in social functioning score being the most marked. CRS + HIPEC was associated with an improvement in symptoms of nausea/vomiting and loss of appetite. However, patients tend to be more symptomatic from constipation post CRS + HIPEC compared to pre-operatively. Conclusion CRS and HIPEC does not significantly impair QOL and may instead lead to improvement in parameters such physical functioning, emotional functioning and role functioning.

Table 1

<table>
<thead>
<tr>
<th>QOL Parameter</th>
<th>Pre-Op (n=40)</th>
<th>3 months (n=30)</th>
<th>6 months (n=21)</th>
<th>12 months (n=23)</th>
<th>Net Change from Pre-Op</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global Health Function Score</td>
<td>68</td>
<td>63</td>
<td>71</td>
<td>66</td>
<td>-2</td>
</tr>
<tr>
<td>Physical functioning</td>
<td>87</td>
<td>76</td>
<td>96</td>
<td>81</td>
<td>+6</td>
</tr>
<tr>
<td>Role functioning</td>
<td>85</td>
<td>74</td>
<td>85</td>
<td>85</td>
<td>0</td>
</tr>
<tr>
<td>Emotional functioning</td>
<td>80</td>
<td>78</td>
<td>90</td>
<td>88</td>
<td>+8</td>
</tr>
<tr>
<td>Cognitive functioning</td>
<td>85</td>
<td>81</td>
<td>89</td>
<td>85</td>
<td>0</td>
</tr>
<tr>
<td>Social functioning</td>
<td>78</td>
<td>81</td>
<td>85</td>
<td>97</td>
<td>+19</td>
</tr>
</tbody>
</table>

Symptom Score

Fatigue: 23 24 22 22 +2

Nausea and vomiting: 6 8 3 0 -6

Pain: 18 17 9 18 0

Diarrhoea: 14 12 15 15 4

Appetite Loss: 17 14 11 6 -11

Constitution: 10 10 10 23 15

Diarrhoea: 9 10 15 6 -3

Financial Difficulty: 30 26 32 33 +3

P289
Outcomes after Emergency Surgery for Colorectal Cancer
C. Luu,* J. Velasquez, B.A. Petrie, R. Kumar, B. Lee. Surgery, Harbor-UCLA Medical Center, Torrance, CA.

Introduction: Emergency surgery (ES) for colorectal cancer (CRC) has been associated with a poor prognosis. The purpose of this study is to evaluate short and long term outcomes after emergency vs. elective surgery for CRC patients at a large urban county hospital setting. Methods: A retrospective review of 279 patients who received surgery for CRC from 2005 to 2012 was performed. Patient demographics, tumor characteristics, surgical morbidity and mortality, and survival were analyzed. Univariate and multivariate analyses and Cox regression were performed for cohort comparisons and to evaluate overall survival. Results: 29 of 279 patients (10.4%) required ES. Indications for ES included peritonitis, complete bowel obstruction, and intra-abdominal abscess. Of the entire cohort, there were 153 male patients (54.8%) and 126 female patients (45.2%). The average age was 55.5 years. There were 37 (13.3%), 136 (48.7%), and 106 (38%) stage I, II, and III patients, respectively. Age, race, and body mass index were similar in patients who did and did not undergo ES. Both groups were also similar in stage, total lymph nodes retrieved, positive lymph node status, and receipt of chemotherapy. All but one patient in each group underwent resection of their primary tumor. There were 12 (4.8%) Clavien grade III or higher post-operative complications in the non-ES group compared to 4 (13.8%) in the ES group (p=0.071). There was only one 30-day mortality, which occurred in a patient who presented with bowel perforation. Average length of stay was 12.1 vs. 19.7 days (p=0.001) for the non-ES vs. ES group, respectively. Five-yr survival was 74.3% vs. 67.7% for the non-ES vs. ES groups, respectively (p=0.102). On Cox regression, only stage and race were predictive of survival. Median length of follow-up was 33 months. Conclusions: Our study indicates that long term survival is comparable between patients undergoing ES vs. elective resection for CRC. The need for emergency surgery should not preclude an attempt at aggressive oncologic resection.

P290
Resources and Safety Associated with Developing a Peritoneal Surface Malignancy Program in a Community Hospital
R.A. Hofer,* J.P. Wilson. Surgery, Sentara Careplex Hospital, Newport News,, VA.

Introduction: In 2005 a peritoneal surface malignancy program was developed, providing cytoreductive surgery and heated intraperitoneal chemotherapy to patients with abdominal carcinomatosis within a community hospital. This study was performed to identify the resources expended treating these patients, as well as the safety of performing these procedures in this setting. Methods: A retrospective chart review was performed from 8/2005 to 1/2013 with IRB approval. Results: 63 patients underwent cytoreductive surgery with heated intraperitoneal chemotherapy from 8/2005-1/2013. 10 disease entities were treated, with 68% of patients (43/63) having carcinomatosis from colon, ovary or appendicular cancers. The average length of procedures was 10.23 hours. 30% of patients underwent a bowel resection (21/63). The average blood loss was 436.3 ml, and 69.8% of patients (44/63) had an average of 1.8 units of blood transfused intra-operatively. 90.5% of patients achieved a complete cytoreduction (57/63). The 30 day operative mortality was 1.6% (1/63). 12.7% of patients required ICU stays (8/63), with 87.3% (55/63) managed within an Oncology Specialty Unit with hemodynamic monitoring. The average hospital stay was 18.7 days, with 6 (10.5%) patients hospitalized for more than 20 days. 4.8% of patients required readmission (3/63). There were 39 significant complications with 2 patients requiring re-operation. (Table 1) Cost analysis was available from 2007-2012, and the overall direct cost to provide care was $1,708,660.00 with a direct margin of $621,085.00. Average supply cost per case was $4,823.00. Conclusions: The authors conclude that these procedures can be done safely in the community hospital setting, but with significant morbidity and expenditure of hospital resources. The use of a specialized Oncology Unit with monitoring capability, reduced the need for use of the ICU. This significant expenditure of resources did not result in a financial loss to the hospital.

Morbidity Following Cytoreductive Surgery with Heated Intraperitoneal Chemotherapy

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative Infection</td>
<td>12</td>
</tr>
<tr>
<td>Bowel Obstruction</td>
<td>2</td>
</tr>
<tr>
<td>Anastomotic Leak</td>
<td>3</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>1</td>
</tr>
</tbody>
</table>

Complications in 63 consecutive patients
P291
Does First-line Treatment Impact the Cost Effectiveness of Second-line Treatment for Elderly Metastatic Colon Cancer Patients?
C. Mullins,1 A. Woldemichael,1 Z. Zheng,2 E. Onukwugha,2 B. S. Seal,1 N. Hanna.1,4 J. Surgery, University of Maryland, Baltimore, MD; 2. Bayer healthcare Pharmaceuticals, Wayne, NJ.

Background: Randomized clinical trials for second-line treatment (Tx2) of metastatic colon cancer (mCC) often have strict inclusion/exclusion criteria regarding prior treatment, yet in the real world there is significant variation. This study aims to determine whether cost effectiveness estimates of Tx2 for mCC patients varies by the regimen they received in first-line treatment (Tx1). Methods: We identified 3,211 elderly (≥66) mCC patients in the SEER-Medicare dataset who received NCCN recommended Tx1 between 2003 and 2009. Patients were categorized by Tx1 based on a previously published algorithm as fluorouracil and leucovorin (5-FU/LV), irinotecan (IRI), oxaliplatin (OX), or “other,” which included IROX or biologics without OX or IRI. Separate 5-year incremental cost-effectiveness of Tx2 were calculated for each Tx1. Approximately 1% of patients with outlier costs were excluded. Patients enrolled in HMOs, lost Part A and/or B, and died of causes other than colon cancer are censored. We adjusted for censoring using the Inverse Probability Weighting (IPW) method. Costs were inflation-adjusted to 2009 dollars using the national monthly medical price index. Results: Among patients who received Tx1, 34% received 5FU, 17% received IRI, 46% received OX, and 3% received other (IROX or Biologics) regimens; 44.5% proceeded to Tx2. Compared to those who do not receive Tx2, patients who received Tx2 following IROX or Biologics, IRI and 5FU in Tx1 live 292 (se = 4), 224 (se = 2), and 191 (se = 2) days longer and incur added costs of $49,096 (se = $7,137), $83,784 (se = $12,322), and $91,686 (se = $10,312), respectively. Recipients of OX in Tx1 did not receive a survival benefit from Tx2, despite additional costs of $46,849 (se = $10,468). Conclusions: The real-world survival benefit of Tx2 for elderly mCC patients in SEER-Medicare varied based on Tx1 from potential harm to a mean of 292 days of incremental survival. Similarly, the costs and cost effectiveness of Tx2 varied by Tx1. These results underscore the importance of considering prior treatment when evaluating the benefit of subsequent treatment for elderly mCC patients.

P292
Comprehensive Outcomes Assessment in Patients with Incurable Cancer and Small Bowel Obstruction
W.H. Tseng,1 J.N. Cormier,2 B. Badgwell. Surgical Oncology, MD Anderson Cancer Center, HOUSTON, TX.

BACKGROUND: There is a paucity of data comparing surgical to non-operative management for patients with malignant small bowel obstruction (MSBO) and optimal outcome measures have not been defined. We sought to define the utilization of procedural and non-procedural management of MSBO and report survival and symptom improvement. METHODS: Utilizing a tertiary cancer center database of patients with advanced, incurable malignancy from 2000-06, we identified patients requiring acute surgical consultation for MSBO. Treatment strategies were compared and analyses were conducted to identify variables associated with 90-day survival and ability to resume oral intake. RESULTS: 122 patients with MSBO were identified; 63(52%) received non-procedural management, 29(24%) received procedural (PRO)-based management, and 30(25%) received surgical palliation. The most common cancer types overall were colorectal (27%), genitourinary (12%), and sarcoma (10%). Patients with radiologic evidence of ascites (p=0.002) or carcinomatosis/sarcomatosis (p=0.02) were less likely while patients with an intact primary tumor or recurrence (p=0.03) were more likely to receive surgery. Among patients undergoing surgery, there was one perioperative mortality (3.3%) and 53% of patients had at least one perioperative complication. 63% of patients undergoing surgical palliation were tolerating an oral diet at the time of discharge compared to 65% in the non-procedural and 52% in the PRO group (p=NS). 67% of patients receiving surgical palliation survived >90 days compared to 49% in the non-procedural and 35% in the PRO group (p=0.05). Death within 90 days was associated with the presence of ascites (p=0.03) and/or carcinomatosis/sarcomatosis (p=0.03) while the ability to tolerate oral intake at discharge was associated with albumin level (p=0.002). CONCLUSIONS: Survival outcomes, although clearly related to patient selection, should be included as outcome measures in palliative surgery studies. Symptom improvement is obtained in the majority of patients with MSBO regardless of treatment strategy and there is a need for additional observational studies and clinical trials for these patients.

P293
Long-term Functional Decline in Geriatric Oncology Patients after Treatment is a Major Problem: Instituting a Geriatric Oncology Program to Stabilize Functional Decline
P. Somasundar,* H. Khan, N. Reis, K. Perry, J. Stoukides. Surgery, Roger Williams Medical center, Providence,. RI.

Hypothesis: Sixty percent of cancer incidence is in ≥65 years of age. Long term functional decline after treatment is not unusual in these patients (pts) and not well addressed. The goal of the geriatric oncology program is to assess, appropriately intervene during pre-treatment phase and decrease the functional decline. Methods: At the cancer center, pts with newly diagnosed solid cancers (≥65 years) are placed in the program to improve quality. The geriatric oncology program assesses the pts activities of daily living (ADL), instrumental activities of daily living (IADL), PHQ9 survey for depression, Montreal cognitive assessment scale (MOCA), polypharmacy (≥7 drugs), timed up and go test, nutritional survey and comorbidities. Interventions are placed accordingly with an automatic trigger to geriatrician, dietitian, pharmacist, social worker; psychiatry is initiated if issues are identified with assessment. The progress of pts is monitored by an inter-disciplinary team. Pts were assessed at 0, 30, 90 and 180 days for functional decline. Results: The program started November 2012, Recruited 71 pts, male =30. There were 21 surgical pts and 50 non-surgical, 5 pts completed the program. Initial visit 21/71 pts, at 30 days 7/16, at 90 days 9/15 and at 180 days 3/5 pts had interventions done (table 1). During initial visit interventions were done on 17 pts for polypharmacy, 8 pts for nutrition, 6 pts by social worker, 2 pts underwent prophylactic interventions, 2 pts treated for depression. Severe functional decline identified in 1/5 pts at 180 days. Conclusion Interventions in cancer pts have been addressed during or after treatment with surgery, chemotherapy or radiotherapy. Pre-treatment pt factors are important to address in improving pts tolerability to treatment. The treatment of elderly cancer patients is a challenge for primary care physicians, oncological physicians including surgeons. A multi-disciplinary team with focus on the needs of the elderly is important to decrease the long term functional decline effectively and help complete the multi-disciplinary treatment modality.

Assessment for functional decline and Interventions done during the multiple visits

<table>
<thead>
<tr>
<th>Geriatric Assessment, (Days and Interventions)</th>
<th>Pharmacy/Nutrition</th>
<th>Social Work</th>
<th>Probability/Psychiatry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial visit</td>
<td>17</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>30 days</td>
<td>6</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>90 days</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>180 days</td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
**P294**

**Hepatic Artery Infusion (HAI) for Recurrent or Chemor Resistant Hepatic Malignancy**
H. Vanebo,1,6,5, S. Redy Sanikommu,4, C. Taneja,3, G. Begosia,1, F. Cummings,1, J. Belliveau,1. 1. Landmark Medical Center, Woonsocket, RI; 2. Hurley Medical Center, Flint, MI; 3. Roger Williams Medical Center, Providence, RI; 4. Alta Bates Summit Medical Center, Oakland, CA.

Introduction: Colorectal Hepatic metastases occur as synchronous (20-25%) or metachronous (60%) lesions with most (75%) being unresectable. Combination chemotherapy is considered to have increased Overall Survival (OS) from 6 months to 21 months as well as enhancing resectability. Addition of biologics (EGFR inhibitors) has shown increased responsiveness ~60% in KRAS wild type (Crystal Study) but less than 30% if KRAS mutated. HAI may provide benefit in patients with resistant hepatic metastases. Methods: We reviewed survival outcome in chemo resistant/high risk patients following hepatic artery infusion (HAI) in 21 CRC pts, 10 HCC pts and 6 pts with miscellaneous hepatic metastases. Patients resided by clinical and lab exam (LFT, Tumor markers), CT, MRI and angiography had operative placement of HAI catheter with infusion pump. Selected resections were done (if reasonable) to augment oncologic outcome. Results: A pilot study of HAI in 36 pts with untreated hepatic metastases showed a measurable volumetric radiologic response in 13 (36%) with > 50% volumetric regression in 7 patients (54% and >50% regression in 6 patients (46%). Disease progression occurred in 7/36 (20%) and stable disease was observed in 44%. The current study included colorectal cancer 22 pts, primary liver cancer 9 pts, and a miscellaneous group (6 pts). The colorectal cancer group consisting of 22 pts, 5 with synchronous cancer and 16 with metachronous lesions had a post HAI median overall survival (OS) of 18 mos. Primary liver cancer in 9 pts (HCI in 8 and cholangio CA in 1 pt) included failure of resection in 4 pts, and TACE/RFA in 3 pts. Post HAI median OS was 9 months. A third group of pts had been resected for meso- cccellular Ca from lung, breast, bladder or carcinoid. Survival post HAI was >60 mos in 2 pts with resected GB ca and 23/9 mos post HAI in 2Bca pts and 11 mos/9 mos in Lung Ca/Carcinoid pts. Conclusion: HAI alternating with systemic chemo therapy has apparent survival benefit in selected patients with persistent chemo resistant malignancy from metastatic CRC, HCC or selected miscellaneous cancers (breast, lung, liver, gallbladder cancer) and warrants further study.

**P295**

**Mortality in Surgical Oncology Patients Visiting the Emergency Room (ER)**
M.R. Bosscher,1 B.L. Van Leeuwen, H.J. Hoekstra. University Medical Center Groningen, Groningen, Netherlands.

Aims: To investigate 30-day and long term mortality in surgical oncology patients visiting the ER. Methods: Retrospective chart review of all surgical oncology patients visiting the ER of the University Medical Center Groningen between 01-10-2012 and 01-04-2013. Results: 206 cancer patients. Median age 63 (range 18-89) yrs, 112 males (54.4%) and 94 females (45.6%) visited the ER for surgical consultation. Thirty seven pts (17.6%) presented with prolapse. Of 609 patients identified, 537 underwent resection for primary or metastatic GIST. Median age was 9 months. A third group of pts had been resected for meso- cellular Ca from lung, breast, bladder or carcinoid. Survival post HAI was >60 mos in 2 pts with resected GB ca and 23/9 mos post HAI in 2Bca pts and 11 mos/9 mos in Lung Ca/Carcinoid pts. Conclusion: HAI alternating with systemic chemo therapy has apparent survival benefit in selected patients with persistent chemo resistant malignancy from metastatic CRC, HCC or selected miscellaneous cancers (breast, lung, liver, gallbladder cancer) and warrants further study.

**P296**

"**Getting My Life Back**: Complex Abdominal Wall Hernias as a Barrier to Quality of Life in Cancer Survivors**
R. Nenshi,5 C. Bensimon,5 F. Wright,1 A. Smith,1 F. Brennan.1 1. University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Health Sciences, Toronto, ON, Canada.

Introduction: Increasingly more cancer patients achieve long-term survival following multimodal, complex therapeutic regimens involving extensive surgery as well as chemo-radiotherapy. This has increased the number of cancer survivors living with complex abdominal wall hernias (CAWH). Incisional hernias following surgery are common and can occur in up to 20% of patients. Hernias are known to have significant physical, social and emotional repercussions on patients. Study Objective: This qualitative study proposes to explore cancer survivors’ experiences before and after the repair of CAWH. Our primary goal is to offer insight into the impact of CAWH on the quality of life of cancer survivors with the view of identifying and addressing gaps in cancer survivorship care. Methods: Data was collected through one-on-one, in-depth semi-structured interviews. Ten pre-operative and eleven post-operative patients were interviewed. Participants met the following inclusion criteria: completed surgery +/- multimodal therapy for cancer; had the presence of a post-operative abdominal wall hernia; were English-speaking; and able to provide consent. Analysis of interviews via comparative analysis techniques and coding strategies were used to identify themes. Results: Participants’ views were organized according to the following emerging themes: 1) Struggling to find a sense of normalcy post-cancer treatment; life is described as being restricted/interrupted (on hold/hell); 2) Feeling abandoned; and having few resources or supports to help them manage living with a hernia; 3) Experiencing distress, loss of self-confidence, feeling hopeless about their situation, and hopeful for their future post successful hernia repair. Conclusions: Our findings demonstrate the all-encompassing impact of hernias on the quality of life of cancer survivors. This strongly suggests that hernia management should be viewed as a part and parcel of cancer treatment to improve quality of life in cancer survivors.

**P297**

**Surgical Management of Gastrointestinal Stromal Tumors: An International Multi-institutional Analysis**
D. Bischoff,1 Y. Kim,1 F. Quereshy,2 P. Karanicolas,3 C. Law,4 D.G. Blazer III,5 S.K. Mathiel,5 T. Bauer,2 T.C. Gamblin,2 T. Pawlik,1* 1. Surgery, Johns Hopkins Hospital, Baltimore, MD; 2. Duke University Medical Center, Durham, NC; 3. Winship Cancer Institute, Emory University, Atlanta, GA; 4. Medical College of Wisconsin, Milwaukee, WI; 5. University of Virginia, Department of Surgery, Charlottesville, VA; 6. Odette Cancer Centre, Sunnybrook Health Sciences Centre; University of Toronto, Toronto, ON, Canada; 7. Princess Margaret Hospital, University of Toronto, Toronto, ON, Canada.

Background: Gastrointestinal stromal tumors (GIST) are the most common mesenchymal tumors of the gastrointestinal tract. The aim of this study was to characterize outcomes after resection of GIST in the imatinib era. Methods: 609 patients who underwent surgical resection of GIST from 1998 to 2012 were identified from a multi-institutional database. Clinicopathological characteristics, operative details, and oncologic outcomes were analyzed and defined. Results: Of 609 patients identified, 537 underwent resection for primary, non-metastatic GIST. Median age was 63; 49% were female. Median tumor size was 4.4 cm (IQR 3.0-8.0 cm) and 65% were symptomatic. The majority of tumors (39%) arose in the stomach. A small subset of patients (44%, 8%) underwent neoadjuvant therapy with a tyrosine kinase inhibitor (TKI) for patients requiring surgical oncology consultation and treatment have a 30-day mortality of 26.9% and a long term mortality of 51.9%.
abstracts: poster presentations s143

including only patients with complete data (n=113), age vs. 63%), and present metastases (2-yr DSS=10% vs. 56%) were each sig-
ificant (OR=4.5, 95% CI=1.3-15.7) remained significantly associated with 2-yr DSS.

CI=2.0-17.3), size>5cm (OR=7.8, 95% CI=2.9-21.2), and metastases
were associated with 2-yr DSS. Kaplan-
Meier curves were generated. Results: 287 patients with angiosarcoma were
identified from the Surveillance Epidemiology and End Results (SEER) tumor
registry. Given their low incidence, we hypothesized they contributed little to
the formulation of the AJCC staging system. We thus sought to identify other
factors that could improve risk stratification in a contemporary cohort of
patients with angiosarcoma. Methods: Angiosarcomas (ICD-O=9120) were
included in the study. The majority of tumors arose on the trunk (58%), fol-
lowed by extremity (28%), and visceral sites (15%). The median age at diag-
nosis was 65 years, and the median DSS was 17 months. 46% of tumors were
low (201, 37%), intermediate (101, 19%) or high risk for recurrence (135, 25%). 112 patients (21%) had adjuvant TKI therapy for a median duration of
56 weeks (IQR 9-56 weeks). Factors associated with receipt of adjuvant TKI
included tumor size and site, symptomatic presentation and mitotic rate (all
p<0.01). Median follow-up was 30 month and 5-year recurrence-free and over-
all survival were 75% and 66%, respectively. Factors associated with recur-
rence included tumor size and site and mitotic rate (all p<0.05). Patients with
GIST tumors characterized by a high mitotic rate had a worse recurrence-free
(HR=5.0) and overall survival (HR=2.6)(both p<0.05)Figure. Conclusion:
In this large multi-institutional cohort of GIST patients, roughly 20% of patients
received TKI therapy in the peri-operative period. At 5-years, 25% of patients
experienced a recurrence. Although high-risk patients were the most likely to
receive TKI therapy, this subset of patients remained at the highest risk for poor
long-term recurrence-free and overall survival.

Figure demonstrating overall survival and recurrence free survival for
primary non-metastatic GIST by mitotic rate

P298
Prognostic Factors for Angiosarcoma: Analysis of a Rare Histology Utilizing the SEER Registry

Introduction: Angiosarcomas represent a rare subtype of soft tissue sar-
comas that have been associated with an aggressive behavior and poor
 prognosis. Given their low incidence, we hypothesized they contributed little to the calculation of the AJCC staging system. We thus sought to identify other
factors that could improve risk stratification in a contemporary cohort of
patients with angiosarcoma. Methods: Angiosarcomas (ICD-O=9120) were
identified from the Surveillance Epidemiology and End Results (SEER) tumor
registry (2004-2009). Tumors arising in the central nervous system were
excluded. Univariate and multivariate logistic regression were used to iden-
tify factors associated with 2-yr disease-specific survival (DSS). Kaplan-
Meier curves were generated. Results: 287 patients with angiosarcoma were
included in the study. The majority of tumors arose on the trunk (58%), fol-
lowed by extremity (28%), and visceral sites (15%). The median age at diag-
nosis was 65 years, and the median DSS was 17 months. 46% of tumors were
>5cm, 76% were intermediate/high grade, 7% had nodal involvement, and
35% had metastases at presentation. Age ≥70 (2-yr DSS=19% vs. 43%),
size ≥5cm (2-yr DSS=20% vs. 65%), intermediate/high grade (2-yr DSS=37% vs.
63%), and present metastases (2-yr DSS=10% vs. 56%) were each sig-
nificantly associated with decreased DSS (each p<0.05), but nodal metas-
tases (2-yr DSS=27% vs. 37%, p=0.58) was not. In a multivariate analysis
including only patients with complete data (n=113), age ≥70 (OR=5.9, 95%
CI=2.0-17.3), size ≥5cm (OR=7.8, 95% CI=2.9-21.2), and metastases
(OR=4.5, 95% CI=1.3-15.7) remained significantly associated with 2-yr DSS.
The 2-yr DSS was 76% (95% CI=65%-87%) for age ≥70 and ≤5cm compared
with 52% (95% CI=37%-67%) for age ≥70 and >5cm, 47% (95% CI=31%-63%)
for age ≥70 but ≤5cm, 20% (95% CI=7%-33%) for age ≥70 and >5cm, and
14% (95% CI=7%-21%) for those with metastases. Figure 1. Conclusion:

Age, size, and metastatic presentation were found to be important prognos-
tic factors for the risk stratification of patients with angiosarcoma. Neither
grade nor nodal status were associated with 2-yr DSS in this aggressive his-
tologic subtype.

Figure 1. Survival of Patients with Angiosarcoma by Prognostic Factors

P299
Neoadjuvant Radiation does not Increase Morbidity following Resection of Retroperitoneal Sarcoma
D.P. Nussbaum,* P.J. Speicher, A.M. Ganapathi, J.E. Keenan, D.G. Kirsch, D.S. Tyler, D.G. Blazer III. Department of Surgery, Duke University Medical Center, Durham, NC.

Introduction: Neoadjuvant radiation therapy (XRT) has several theoret-
ical benefits in the treatment of retroperitoneal sarcoma (RPS), but wide-
spread use has not been adopted, in part secondary to concerns about treat-
ment toxicity and perioperative morbidity. There are limited data regarding
its effect on short-term postoperative outcomes, most of which come from small, single-institution series. Methods: The 2005-2011 NSQIP partici-
 pant user files were queried for patients undergoing resection of RPS. Sub-
jects were stratified by the use of neoadjuvant XRT. Perioperative variables
and outcomes were compared between groups. Groups were then propen-
sity matched using a 2:1 nearest-neighbor algorithm and multivariable logis-
tic regression was performed to assess neoadjuvant XRT as a predictor of
outcomes. Results: A total of 786 patients underwent resection of RPS. Neoadjuvant XRT was administered to 72 patients (9.2%). Patients who
received neoadjuvant XRT were slightly younger (56.5 vs. 61.5 years,
p<0.01), but otherwise the groups were similar with regard to demograph-
ics and preexisting comorbidities. After propensity matching, all baseline
characteristics between groups were highly similar. Although there was no
difference in the rate of contiguous organ resection (61.1 vs. 63.9%, p=0.80)
or intraoperative radiation therapy (1.4 vs. 1.1%, p=0.58), median opera-
tive time was longer in the neoadjuvant XRT group (278 vs. 219 min,
p<0.01). There were no differences in mortality (2.8 vs. 3.1%, p=0.99), major
complications (29.2 vs. 25.2%, p=0.55), overall complications (36.1 vs.33.2%, p=0.71), early reoperation (5.6 vs. 7.4%, p=0.81), or length of
stay (7 vs. 7 days, p=0.56). Following further adjustment with multivariable
logistic regression, we confirmed that there were no differences in 30-day mortality or postoperative morbidity (Figure 1) between patients who did
and did not receive neoadjuvant XRT. Conclusions: Neoadjuvant XRT may
contribute to increased operative time, but does not appear to increase short-
term morbidity or mortality following resection of RPS. Continued investi-
gation is needed to better define the role for neoadjuvant XRT in the man-
agement of RPS.


**P300**

Extremity Sarcoma: An Epidemiologic Study of the Use of Adjuvant Radiotherapy in High-Risk Patients S.D. Kachare,* N.A. Vohra, E.E. Zervos, J.H. Wong, T.L. Fitzgerald. East Carolina University, Brody School of Medicine, Greenville, NC.

Introduction: Landmark clinical trials on the use of radiotherapy for high-risk sarcomas ushered in the era of limb preservation. Further studies assessing the timing of radiotherapy established the superiority of neoadjuvant regimens in long-term functional outcomes. In order to determine clinical integration of these data we analyzed a national cancer registry. Methods: All patients undergoing limb preserving surgery for stage Ila, Iib and III extremity soft tissue sarcomas from 1988-2010 were identified in the SEER tumor registry. Results: A total of 6,574 patients were identified. The median was age of 58y (range <1-105y). A majority patients were male (53%), white (83%), underwent radiotherapy (66%), had lower extremity tumors (73%), and were stage III (46%). The most common histologic subtype (WHO) was fibrohistiocytic (27%) followed by sarcoma NOS (17.5%), liposarcoma (16.9%), leiomyosarcoma (11.6%), myxofibromyoblastic (9.4%), other (6.9%), synovial (6.4%), and nerve sheath (4.0%). On univariate analysis location, stage, and histologic subtype were associated with a greater likelihood of undergoing radiotherapy, yet gender, race, and year of diagnosis were not. On logistic regression significant association with radiotherapy persisted for stage (IIa OR 1.2, Iib OR 1.26, and III OR 2.74) and histologic subtype. For those treated with radiotherapy, a neoadjuvant approach was associated with African American race (p=0.002), younger age (p=0.005), lower extremity location (p=0.007), stage III tumors (p=0.0001), histologic subtype (p=0.0001), and more recent year of treatment (<0.0001). On logistic regression age (p=0.0001), year of diagnosis (1.04, p=0.0005), stage (p=0.0001), race (other OR 1, white OR 1.24, AA OR 1.58), and histologic subtype remained significantly associated with neoadjuvant treatment. In 1988 8% of those receiving radiotherapy had neoadjuvant compared to 33% in 2010. Conclusions: A substantial number of patients with high-risk extremity sarcomas fail to receive recommended radiotherapy which has changed little over the last 22 years. However, there has been a steady increase in the use of a neoadjuvant approach in those treated.

**P301**

Accuracy of Percutaneous Biopsy for Retroperitoneal Liposarcoma

N. Ioma, N.W. Tseng, K. Torres, K.K. Hunt, J.N. Cormier, N. Somaiah, B. Feig. 1 University of Texas MD Anderson Cancer Center, Houston, TX; 2 University of Texas health science Center at Houston, Houston, TX.

Introduction: Liposarcoma is the most common histologic subtype of retroperitoneal soft tissue sarcoma. Surgery is the primary treatment, but neoadjuvant therapy (chemotherapy and/or radiotherapy) may be considered in cases of dedifferentiated liposarcoma (DDLs) due to the increased risk of recurrence. Therefore, subtype-specific diagnosis of retroperitoneal liposarcoma is vital for appropriate treatment planning. Methods: We retrospectively reviewed the medical records of patients registered in our retroperitoneal liposarcoma database. Pathology reports from the operative resection and preoperative biopsy were compared, and the accuracy of the subtype-specific preoperative biopsy assessed. Results: We extracted the records of 120 patients who underwent 137 preoperative biopsies followed by operative resections between 1993 and 2013. Pathological examination following final operative resection revealed 74 cases of well-differentiated liposarcoma (WDLs) and 63 of DDLs. The overall diagnostic accuracy of percutaneous biopsy for identifying liposarcoma subtype was 63.5% (87/137; 83.8% [62/74] for WDLs and 39.7% [25/63] for DDLs, p < 0.01; Table 1). Among 63 DDLs patients, 19 (31%) were diagnosed as WDLs by preoperative biopsy; 56% (14/25) of patients who were correctly diagnosed as DDLs by preoperative biopsy received neoadjuvant therapy; only 21% (8/38) of patients who were not diagnosed as DDLs underwent neoadjuvant therapy (p < 0.01). Among the 74 WDLs patients, 62 patients were correctly diagnosed as WDLs, 7 (11%) received neoadjuvant treatment. Of 5 patients who were incorrectly diagnosed as DDLs by preoperative biopsy, 4 (80%) underwent neoadjuvant therapy (p < 0.01). Conclusion: The accuracy of percutaneous biopsy in the diagnosis of DDLs is extremely low (39.7%). It is important that this low sensitivity of percutaneous biopsy to detect DDLs is taken into account when developing treatment strategies for patients with retroperitoneal liposarcoma. Lack of pathological confirmation of DDLs by percutaneous biopsy should not rule out the potential use of neoadjuvant therapy when other clinical and radiographic findings are suggestive of dedifferentiation.

**P303**


Introduction: Although unplanned excision of soft tissue sarcomas (STS) is a potential quality of care issue, not all patients will harbor residual disease at re-excision. We sought to determine predictors of residual disease. Methods: We identified 264 patients between January 2008 and July 2012 from a prospectively-maintained academic database with a diagnosis of primary STS of all anatomic sites. Patients with fibromatosis were excluded. 72 patients (32%) were referred after an initial unplanned excision. We evaluated predictors of residual STS following repeat resection, sensitivity/specificity of interval MRI to predict residual STS, and predictors of oncologic outcome. Univariable and multivariable logistic regression was used as appropriate. Results: Mean age was 52, 62% were male, and 70% of tumors were located on the extremity. 34 patients (47%) had the primary tumor excised in fragments at unplanned excision. 54 patients (76%) underwent repeat excision, and 42 (72%) were found to harbor residual STS. Univariable analysis identified only fragmented excision as a significant predictor of residual STS (OR 4.3, 95% CI 1.08 – 15.09, P=0.04), but on multivariable analysis, no variables were significantly associated with residual STS. With a median follow-up of 29 months, multivariable analysis identified final margin, and not fragmented excision, as a significant predictor of local recurrence. If interval MRIs which showed “non-specific enhancement” were considered negative, the sensitivity and specificity of MRI for predicting residual STS were 67% (95% CI 49 – 81%) and 86% (95% CI 57 – 98%), respectively. Conclusion: Approximately 1/3 of STS patients are referred to an academic center after an initial unplanned excision. 72% of patients undergoing repeat excision are found to harbor residual
Abstracts: Poster Presentations S145

P304

Background: The prognostic value of the current staging scheme is limited for retroperitoneal sarcomas (RS). The aim of this study was to identify prognostic factors that may influence survival in RS. Methods The SEER registry was queried to identify patients diagnosed with RS. Kaplan Meier analysis was performed to estimate cancer-specific survival. Multivariate survival analysis using Cox’s regression model was performed to identify prognostic factors for survival in RS, adjusting for age, histology, tumor size, lymph node evaluation, radiation therapy, extent of disease (EOD), and tumor grade. Results A total of 2,537 RS cases were identified between 1988-2010. Most common histologic subtypes were liposarcoma (LPS) (56.2%), leiomyosarcoma (LMS) (29.4%), and malignant fibrous histiocytoma (MFH) (9.2%). LPS was associated with longer 5-year survival rates compared to LMS and MFH; 72% vs. 50.8% vs. 37.6%, respectively (p=0.001). With respect to tumor size, LPS tumors greater than 20cm were associated with worse survival compared to smaller tumors (p=0.026), LMS tumors less than 10cm were associated with longer survival (p=0.003), and MFH tumors less than 15cm were associated with improved 5-year survival (p=0.017). Lymph node evaluation did not affect survival in RS. With the exception of MFH, EOD was associated with a significant effect on 5-year survival in RS (p=0.001). Well-differentiated LMS and LPS tumors were associated with longer 5-year survival compared to poorly differentiated tumors. Tumor grade did not affect survival in MFH. Conversely, only MFH was associated with a significant effect on survival with radiation therapy (p=0.002). On multivariate analysis, strong predictors of survival for LMS and LPS were tumor grade, tumor size, and EOD. Predictors of survival in MFH included EOD and radiation therapy. Conclusion Histology, tumor size, and EOD are important global prognostic factors for survival in patients with RS. Lymph node evaluation did not influence survival. Given the variable behavior of histologic subtypes and prognostic predictors within each category, incorporating histology when staging RS may improve our ability to prognosticate survival.

P305

Objectives: Surgical resection of gastrointestinal stromal tumors (GISTs) remains the cornerstone of treatment for non-metastatic disease. Multivisceral resection (MVR) for locally advanced tumors is often required to achieve negative margins. The aim of this study was to review the peri-operative and long-term oncologic outcomes for patients who required MVR versus single organ resection (SOR) for GISTs. Methods: All patients who underwent surgical resection for GISTs from 2001 to 2011 at a large, tertiary cancer center were identified. Short-term and peri-operative outcomes, disease-free survival (DFS) and overall survival (OS) were analyzed. Patient outcomes were evaluated using the Fisher’s exact test for categorical variables and the Student’s t-test for continuous variables. Survival rates were analyzed using the Kaplan-Meier’s product-limit method. Results: Of the 110 patients who underwent surgical resection for GISTs, 33 (30%) underwent MVR while 77 (70%) required SOR. Patients within the two study arms had similar demographic profiles. Tumors in the MVR group were significantly larger (14.98 cm vs. 8.27 cm, p=0.0424) and had a higher mitotic index (51.52% >5/50 vs. 16.88%, p=0.0001). The MVR group had a significantly longer OR duration (359 mins., p=0.0021), higher operative blood loss (1148 mL vs. 309 mL, p=0.0111) and increased number of peri-operative complications (54.55% vs. 33.77%, p=0.0207). There was no significant difference in the final margin status between the two groups (R0 resection: SOR 92.2%, MVR 81.8%, p=0.13). While the 5-year DFS was significantly lower in the MVR group (52.7% vs. 82.8%, p=0.0092), there was no difference in 5-year OS between the two study arms (80.0% vs. 90.5%, p=0.2559). Discussion: Patients in the MVR group had tumors with more aggressive malignant behavior and a significantly higher rate of peri-operative complications. In spite of these factors, there was no difference in the 5-year OS between the two arms. These findings support the use of MVR in the appropriately selected patient. Further studies are necessary to fully define its clinical application.

P306
Use of Neoadjuvant Tyrosine-kinase Inhibitors can Aid in Resection of Gastrointestinal Stromal Tumors A. Cocieru, K.N. Shah, P.J. Speicher, D. Bischoff, D.S. Tyler, T. Pawlik, D.G. Blazer III, 1. Duke University Medical Center, Division of Surgical Oncology, Durham, NC; 2. Johns Hopkins University, Department of Surgery, Baltimore, MD.

Background: The introduction of tyrosine-kinase inhibitors represents an important advance in the management of gastrointestinal stromal tumors
(GIST), but the role of neoadjuvant tyrosine-kinase inhibitor therapy (NTKIT) in the surgical management of these tumors has not been well established. The goal of this study is to explore the ability of NTKIT to downstage GISTs and/or facilitate organ-sparing surgery. Methods: We performed a retrospective bi-institutional analysis of surgically treated GIST patients. Among all GIST patients operated between 2004-2011, we identified 47 patients who were treated preoperatively with NTKIT. Results: The median patient age was 58 years old, and median size of the largest tumor was 9.4 cm (range, 1-24 cm). Patients were symptomatic in 82.9% of cases, and the most common presenting symptoms were pain (44.7%), bleeding (27.7%), and obstruction (21.3%). Primary tumor location included 28 gastric (59.5 %), 13 rectal (27.7%), 3 duodenal (6.4%) and 3 (6.4 %) small bowel tumors. Preoperatively, localized disease was observed in 55.3%, locally advanced in 23.4 %, and metastatic GISTs in 21.3 %. The median duration of NTKIT was 8.5 months, and 89.5% of patients completed neoadjuvant therapy. The main indications for preoperative NTKIT were: large size/difficult location (63.8%), multivisceral involvement (14.8 %) or metastatic disease (21.3 %). Using RECIST criteria, 51.3 % of patients had partial response, 46% had stable disease and 2.5 % had progressive disease. The response to NKIT impacted surgical management in 34% by facilitating one of the following: 1) organ-sparing resection; 2) more limited multivisceral resections for locally advanced tumors; 3) minimally invasive approach to resection; 4) R0 resection in metastatic GIST. R0, R1 and R2 resection was achieved in 78.7%, 6.38 % and 13.2 % of cases respectively. A recurrence rate of 42.6% was observed with median follow up of 27.3 months. Median survival was 102.7 months. Conclusions: NTKIT results in radiographic and clinical response in a substantial number of patients with GISTS, allowing for less extensive and less invasive operations for some of these patients.

**P308**

**A Prospective Multicenter Trial for Limb Sparing with Mild Hyperthermic Isolated Limb Perfusion with Low Dose TNF Alfa and Melphalan in the Treatment of Locally Advanced Soft Tissue Sarcoma of the Extremities**


Introduction: Because there is no benefit of amputation for locally advanced soft tissue sarcoma of the extremities, limb-sparing surgery has become the gold standard. TNF based isolated limb perfusion (TNF-ILP) has been reported as high efficient treatment to achieve function-preserving surgery in patients candidates to amputation. Most of the experiences with this approach come from single centers of Europe. We report the first prospective multicenter trial in Latinamerica with this approach. Material and Methods: Prospective multicenter trial with analysis of 45 patients with locally advanced soft tissue sarcoma diagnosed histologically, who underwent to TNF-ILP, and the application of training program in Mexico. Results: 47 TNF-ILP were done in 45 patients (20 male – 25 female). Median of age was 44.6 years and median follow up of 14.8 months was reached. Most patients had stage III tumors (86.7%), lower extremity (73.3%), and femoral perfusion was the most common with 19 cases (42%). The major histology was synovial sarcoma and liposarcoma. Four patients was perfunded with recurrent agressive fibromatosis with no other option than amputation. The global response rate was 77.8%, five patients with complete response included. The limb-sparing rate was 89.9%. The Overall survival for 12, 24 and 36 months was 78%, 58% y 49%, respectively. Conclusion: TNF-ILP is a high effective treatment, and can be done safe in major centers of Mexico.

**P307**

**Spindle Cell Tumors of the Colon and Rectum**

N. Ikoma, Y. Chiang, J.N. Cormier, K. Torres, K.K. Hunt, Y. You, B. Feig. 1 University of Texas MD Anderson Cancer Center, Houston, TX; 2 University of Texas at Houston, Houston, TX.

Introduction: Spindle cell tumors of the colon and rectum are rare, representing 0.1% of all tumors of the colon and rectum. While the treatment and outcome of patients with Gastrointestinal Stromal Tumors (GIST) are well documented, non-GIST tumors of the colon and rectum are poorly defined. Methods: 1062 histologically confirmed cases of spindle cell tumors of the colon and rectum (1998-2010) were identified from the National Cancer Database. Data collected included: site (colon vs. rectum), tissue of origin, sex, race, age, insurance status, adjuvant treatment, treatment type. Multifactorial survival analysis was performed using a Cox regression model; differences in overall survival (OS) were calculated using a Log-Rank test. Results: 654 (62%) tumors originated in the colon and more colon patients were over 75 compared to patients with rectal tumors (27% vs. 18%, p=0.002). Colon tumors were larger (49% vs. 38% >5cm p=0.001), more likely to be poorly differentiated (31% vs. 18%, p=0.001), and less likely to undergo a local surgical procedure (5% vs. 31%, p<0.001). OS was significantly better for rectal tumors (p=0.001). Risk of death was significantly lower for patients <50 (HR 0.38, 95%CI 0.21-0.70) and 50-64 compared with patients >75 (HR 0.55, 95% CI 0.35-0.86). Patients who underwent locoregional surgery had a risk reduction of death compared to patients that did not have any surgery (HR 2.34, 95% CI 1.51-3.64). For colon tumors, locoregional resection was associated with improved outcomes compared to no surgery (p=0.0005, HR 2.91) or local surgical resection (p=0.05). Rectal tumors patients <50 (p=0.009) and 50-64 (p=0.02) had a reduction in risk of death compared to those >75. In contrast to colon tumors, rectal tumors did not benefit from more extensive surgery (p=0.16). Conclusions: Non-GIST spindle cell tumors of the colon and rectum are a rare clinical entity. In this series, primary site of origin in the rectum was associated with a better survival. More extensive surgery did not confer a survival advantage for rectal tumors. It may be appropriate to spare ano/rectal function if a spindle cell tumor of the rectum can be completely removed with a more limited resection.
P309
Impact of the Peritoneal Surface Disease Severity Score in Patients with Sarcomatosis Undergoing Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy
G. Salti,1* S. Undevia,2 The University of Illinois at Chicago, Chicago, IL; 2. Edward Hospital, Naperville, IL.

Introduction: The Peritoneal Surface Disease Severity Score (PSDSS) staging was introduced as a basis of scoring patients into prognostic groups to improve selection of colorectal cancer patients with peritoneal metastases. It incorporates three categories comprising clinical symptoms, extent of carcinomatosis, and tumor histopathology. This study aims to determine the impact on survival of PSDSS in patients with peritoneal sarcomatosis (PS) undergoing cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Methods: A retrospective review of patients with CRS and HIPEC for PS was performed to score patients. Survival was analyzed using the Kaplan-Meier method. Univariate and multivariate analyses were also performed. Overall survival (OS) and disease-free survival (DFS) were evaluated. Results: There were 16 patients with PS who underwent CRS plus HIPEC for PS from 3/2007-7/2013. Of these, 5 (31.3%) were PSDSS stage I; 2 patients (12.5%) were PSDSS stage II; 2 patient (12.5%) were PSDSS stage III; and 7 patients (43.8%) were PSDSS stage IV. Median follow-up was 12 mo (4-75). Overall survival (OS) was 39 months. When stratified into two groups (PSDSS I/II vs. PSDSS III/IV), univariate analysis demonstrated PSDSS affecting OS (median not reached vs. 12 mo, p=0.033) and disease-free survival (median 38 mo vs. 8 mo, p=0.004). This impact on survival persisted by multivariate analysis. Conclusion: The PSDSS staging system developed for peritoneal metastases of colorectal does have prognostic impact in patients with PS undergoing CRS and HIPEC and may be utilized in selecting patients undergoing this aggressive treatment approach.

P310
Resection for Recurrent or Residual Retroperitoneal Sarcoma: Is It Worth It?
T.D. Hamilton,1* A.J. Cannell,1 K. Minji,1 C. Catton,1 M.E. Blackstein,1 B.C. Dickson,2 R.A. Gladdy,1 C.I. Swallow,1 University of Toronto, Toronto, ON, Canada; 2. Radiation Oncology, University of Toronto, Toronto, ON, Canada; 3. Medical Oncology, University of Toronto, Toronto, ON, Canada; 4. Pathology, University of Toronto, Toronto, ON, Canada.

Introduction: Population-based data show that by 5yrs after resection of primary retroperitoneal sarcoma (RPS), over 50% of patients have recurred. Many patients are candidates for re-resection, but morbidity may be high and disease control is uncertain. A related entity is gross residual disease following incomplete primary resection. We reviewed our experience with both recurrent (RC) RPS and residual (RD) RPS, referred to our center for consideration of surgical management. Methods: Patients seen from 1996 through 2012 who had resection of primary RPS at outside institutions were identified from a prospective database. Survival curves were generated by the Kaplan-Meier method and compared by log rank analysis. Results: 45 patients referred with RC (33) or RD (12) disease comprise the study cohort. Median age was 61 (30-85). 69% had liposarcoma. Prior to primary surgery, cross-sectional imaging (CT/MRI) had been obtained in 30/45 patients, 24 (73%) of those with RC and 6 (50%) of those with RD RPS; core biopsy had been obtained in 6 (18%) of RC and 2 (17%) of RD RPS patients. Of the 45 patients assessed, 15 were deemed inappropriate for resection due to distant metastases (7), multifocality (4), poor performance status (2) or technical unresectability (2). 7 received palliative chemo- and/or radio-therapy (XRT). The median overall survival (OS) in this group was 15mos, and the 5-yr OS was 29%. 30 patients were managed surgically with at least one resection (range 1-3); 22 of the RC and 8 of the RD group. 23 of the 30 (77%) who had re-resection at our center received pre-op XRT and 5 also received post-op brachytherapy. One patient had pre-op chemotherapy. 30-day peri-op mortality was 0 in the RC group, and 13% (1/8) in the RD group. In the 30 who had re-resection, median post-op follow-up was 42mos; median OS was 35mos. OS was worse in the RD vs. RC groups (41 vs. 77mos, see Figure, p=0.02). Median time to re-recurrence was 35mos and 49mos in the RD and RC groups, respectively (p=ns). Conclusions: Durable disease control and prolonged survival can be achieved in selected patients with RC RPS. RD RPS after initial incomplete gross resection represents a challenging problem.

P311
Bowel Obstruction as a Predictor of Poor Survival in Patients Undergoing Cytoreductive Surgery (CS) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC)
S. Singla,* P. Thirunavukarasu, R. Tuttle, J.A. Alosi, V. Francescutti, J. Skitzki. Roswell Park Cancer Center, Buffalo, NY.

Background: CS combined with HIPEC is a treatment option with potential curative intent for select patients with peritoneal carcinomatosis. Despite pre-operative optimization, patients presenting with bowel obstruction often perform worse than their non-obstructed cohorts. Methods: We performed a single institution retrospective review on 112 consecutive patients presenting with peritoneal carcinomatosis between January 2003 and November 2011. All patients who underwent CS and HIPEC were included in the analyses. These patients were divided into two groups; patients with bowel obstruction (BO) and patients without bowel obstruction (NBO). Results: There were 45 males and 67 females with a median age of 53 years (range, 16-79 years). For all patients, the most common site of origin was appendix (n=51, 45.5%), while the most common histology subtype was adenocarcinoma (n=65, 58%). In patients presenting with BO (n=8) at the time of CS/HIPEC, the most common site of origin was colon (n=4), followed by appendix (n=2), small bowel (n=1) and peritoneum (n=1). Three-fourths of these patients (n=6, 75%) were found to have adenocarcinoma on histology. Prior to CS/HIPEC, 4 patients (50%) had presented with bowel obstruction at the time of initial intervention. Further, while 5 (62.5%) patients with BO received pre-operative chemotherapy, 6 (75%) patients required more than one bowel resection during the operation. The median survival in the BO group was 7.7 (95% CI, 0-16.1) months as compared to 66 (95% CI, 40.7-92.4) months in patients with NBO (p<0.005). Conclusions: CS with HIPEC is prolongs survival in select patients with peritoneal carcinomatosis. However, in patients presenting with bowel obstruction the survival appears poor and CS/HIPEC may be considered as palliative in nature in this sub-group.
P312
The Accuracy of Predictive Models in the Evaluation of Recurrence Rates for Gastrointestinal Stromal Tumors

Surgical Oncology, University of Toronto, Toronto, ON, Canada.

Objective: The incidence and outcome of gastrointestinal stromal tumors (GISTs) continues to evolve with improvements in detection, surgical technique, and adjuvant therapy. Treatment decisions are frequently guided by tumour characteristics related to malignant potential. The purpose of this study was to review the outcomes of patients undergoing surgical resection for GISTs, and to compare the observed with predicted recurrence rate based upon three validated risk stratification systems. Methods: All patients who underwent surgical resection for GISTs from 2001 to 2011 at a large, tertiary cancer center were identified. Demographic profile, clinicopathologic variables and recurrence rates were analyzed. Survival rates were evaluated using the Kaplan-Meier’s product-limit method. Concordance indices were calculated for the three risk stratification systems. Results: 110 patients were included in the analysis (median age 59.2, range 28.3 – 92.1 years). Of these patients, 78 (70.9%) underwent surgical resection alone and 28 (25.5%) also received adjuvant therapy. The majority of patients had tumors that were rated very low (4.5%), low (32.7%) or intermediate (22.7%) with respect to malignant behavior. An R0 resection was achieved in 89.1% of patients. Observed 2-year and 5-year recurrence rates in our study were significantly lower than those predicted by the MSKCC nomogram (9.0% vs. 19.65% and 20.2% vs. 27.6%, respectively). The concordance index of the NIH-consensus classification was superior to both the modified NIH-consensus classification and the MSKCC nomogram (0.9216 vs. 0.9127 and 0.8075, respectively). Conclusions: The recurrence rates in our study were significantly lower than those predicted by the MSKCC nomogram. Of the validated nomograms studied, the NIH-consensus classification was the most concordant with our observed recurrence rates. The relatively low recurrence rate observed in our study may be due to the quality of surgical resection. A novel predictive model that includes margin status may help stratify recurrence-risk for patients with GISTs. Further research is needed to validate this clinicopathologic tool.

P313
Why Go Wide? Outcomes of Marginal Oncologic Surgery in Atypical Neurofibroma and Low-grade MPNST

N. Berthalm,* K. Jones,* A. Putnam,* D. Viskochil,* R. Randall.1 1. UCLA Medical Center, Santa Monica, CA; 2. Huntsman Cancer Institute, University of Utah, Primary Childrens Medical Center, Salt Lake City, UT.

Intro: While malignant peripheral nerve sheath tumors (MPNST) are among the most aggressive soft tissue sarcomas and benign pleomorphic neurofibromas pose no metastatic threat, little is known about the natural history of the intermediate nerve sheath lesions: atypical neurofibroma and low-grade MPNST. The present investigation is the first dedicated to the clinical outcomes of atypical neurofibroma and low-grade MPNSTs exclusively. The study also reviews the impact of surgical margins on survival and local recurrence in these lesions.

Methods: Retrospective review of 23 consecutive patients with surgically treated atypical neurofibroma and low-grade MPNSTs (N=11) and low-grade MPNSTs (N=12) and more than one year follow-up at a pediatric hospital between 1998 and 2012. Clinical outcomes including patient survival, presence of metastatic disease, and local recurrence were reviewed.

Histology was reviewed to confirm diagnosis and classify surgical margins. Results: Twelve patients with low-grade MPNST and 11 with atypical neurofibroma were identified. Median age at time of surgery was 14 years old (range 2-21) and 52% (12/23) of patients were female. Median follow-up was 47 months (range 14-198 months). Nineteen of 23 patients carried an underlying diagnosis of neurofibromatosis type 1 (NF1). Nineteen of 23 patients had positive margins on resection, with an additional three showing pleomorphic neurofibroma at the surgical margin. Six patients underwent re-resection – three immediately after surgery for “positive margins” and three distant for painful recurrence (2 low-grade MPNST, 1 atypical neurofibroma). Zero patients died of metastatic MPNST. Discussion: This is the first study dedicated to clinical outcomes in low-grade MPNST and atypical neurofibroma exclusively. In a series in which 19 of 23 patients with intermediate nerve sheath tumors – 11 atypical neurofibromas and 8 low-grade MPNSTs – had frankly positive surgical margins treated with observation, none has died of metastatic MPNST. While further studies are needed, this suggests that wide surgical margins may not be necessary for intermediate nerve sheath tumors and may carry unnecessary surgical morbidity.

P314
Analysis of Factors Affecting Outcome in De-differentiated and Well-differentiated Retroperitoneal Liposarcomas

M. Choi,* F. Amersi, B. Balzer, C. Forscher, A.W. Silberman. Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, CA.

Introduction: Retroperitoneal (RP) liposarcomas are rare tumors with high local recurrence rates and poor survival. Surgical resection has been shown to improve outcomes. Our aim was to determine predictors of outcome following surgical resection of well differentiated (WDSL) vs de-differentiated (DDLS) liposarcomas. Methods: We performed a retrospective review of 65 patients who underwent surgical resection for a RP or pelvic WDSL or DDLS between 1987 and 2012. Clinical and pathological variables were used to create univariate and multivariate models for both survival and recurrence. Results: Of the 65 patients, 40 had WDSL and 25 had DDLS. Patients with WDSL were older than patients with DDLS (63 vs. 59.8, p=0.39). Median tumor size was 14.5 cm (range: 10-23 cm) in the WDSL vs. 17.5 cm (range: 10.5-30 cm; p=0.63) in the DDLS group. Patients in the DDLS had significantly more high-grade tumors (80% vs. 37.5%, p=0.002). Although multi-organ resection was more common in the DDLS group (64% vs. 43%, p=0.004), more patients with DDLS had positive margins compared to WDSL patients (76% vs. 32.5%, p=0.0009). Overall survival at 5 and 10 years for patients with WDSL was 64.6% and 53.3% whereas overall survival for DDLS was 57.5% and 30.7%, respectively. Median survival was 10 yrs vs. 6 yrs (p=0.71) for WDSL vs. DDLS, respectively. Median time to recurrence was 2.9 yrs vs. 2.3 yrs (p=0.62) for WDSL vs. DDLS, respectively. In a multivariate analysis, tumor grade was the only significant predictor of survival (p=0.01) in both groups. Resection of multiple (>1) organs did not affect survival regardless of margin status (p=0.65). Finally, tumor grade was the only significant predictor of recurrence on multi-variable analysis (p<0.01 for low/intermediate vs. high). Conclusion: Patients with DDLS have biological differences with larger, higher grade tumors requiring multi-organ resection. Although median time to recurrence was not statistically significant between both groups, higher grade was a significant predictor of mortality and recurrence. Our study suggests that DDLS should be treated with a more aggressive multi-modality approach.
Factors Associated with Improved Prognosis after Pulmonary Resection for Metastatic Sarcoma

A. Perhacek, M. Sok, J. Zgajnar, M. Hoeveer, N. Besic

1. Institute of Oncology, Ljubljana, Slovenia; 2. University Clinical Center Ljubljana, Ljubljana, Slovenia.

Introduction: The lungs are the most common organ targeted by sarcoma and resection remains the only treatment that could provide a cure for such patients. The aim of this study was to evaluate factors that are associated with better disease free survival (DFS) and overall survival (OS) after pulmonary resection (PR) for metastatic sarcoma. Patients and methods: Altogether 37 consecutive patients underwent PR at our institution with intention to treat lung metastases originating from sarcoma from January 2000 to December 2009. Clinicopathological data were retrospectively collected and prognostic factors associated with DFS and OS after the first PR were evaluated using univariate and multivariate analysis. Results: Altogether 54 procedures were performed in 37 patients. The mean age of patients was 48 years, 15 were men and 22 women. In nine patients staged procedure was performed for bilateral disease, five patients had one operation and one patient had three operations for recurrent lung metastases. Of 54 procedures performed, 44 were metastasectomies, six lobectomies, one bilobectomy and three pneumonectomies. The 5-years DFS and OS were 19% and 35%, respectively. In univariate analysis factors associated with longer DFS were complete resection (R0) [p=0.025], unilateral disease [p=0.04], no extrapulmonary disease [p=0.001], and number of lung metastases (1-3) [p=0.004]; while complete resection (R0) [p=0.001], no extrapulmonary disease [p=0.003] and no discrepancy between the number of lung metastases radiologically and histologically [p=0.046] were associated with longer overall survival. According to multivariate Cox regression model, only complete resection (R0) [HR 0.368, 95% CI 0.148-0.916, p=0.032 for DFS; HR 0.218, 95% CI 0.088-0.541, p=0.001 for OS] and no extrapulmonary disease [HR 0.154, 95% CI 0.054-0.445, p=0.001 for DFS; HR 0.309, 95% CI 0.120-0.799, p=0.015 for OS] were independent prognostic variables for both DFS and OS. Conclusion: In our retrospective analysis of PR for metastatic soft tissue and osteogenic sarcoma, we found that only complete resection and no extrapulmonary disease were associated with better prognosis.

Multimodality Management of Synovial Sarcoma: A Review of Single Institution Experience

M. N. M. L., S.S. Dee, N. K. Shukla, S. Bakhshi, D. Sharma

1. Surgical Oncology, Dr BRAIRCH, All India Institute of Medical Sciences, New Delhi, Delhi, Delhi, India; 2. Medical Oncology, Dr BRAIRCH, All India Institute of Medical Sciences, New Delhi, Delhi, Delhi, India; 3. Radiation Oncology, Dr BRAIRCH, All India Institute of Medical Sciences, New Delhi, Delhi, Delhi, India.

Introduction: Soft tissue sarcomas (STS) constitute only 1% of all solid tumors. Synovial sarcoma (SS) constitutes 5-10% of all sarcomas and categorized as a high-grade sarcoma. There is paucity of literature pertaining to SS from developing countries. Methods: Study population was identified from a prospectively maintained STS database of the Surgical Oncology department at a tertiary cancer center. All patients with Histological diagnosis of SS were included for the analysis. Results: A total of 446 cases of STS were treated between 1995 and 2009 and 80 patients had pathologically proven SS. Median age at diagnosis was 33 years (13-65 years). There were 53 males (66.3%) and 27 females (33.8%). Most common site was proximal lower limb (thigh). Sixty patients presented with prior interventions mainly in the form of margin positive surgery/trauma at the site of the DFSP was noted in 34% of patients. The median operative time was 594 min (495-820) in the D+P group and 837 min (315-1270) in the D group. Sixty patients presented with symptoms (84%) and underwent a biopsy (88%). Prior surgery/trauma at the site of the DFSP was noted in 34% of patients. The median duration of the lesion prior to excision was 24 months. Overall, primary, and recurrent group 5 year LRFS was 87%, 85% and 80%, with a median follow up of 3.75 years. On univariate analysis, mitotic rate of >5/10 HPF was unfavorable. Age, margin status, size, FS variant, taking fascia or more than fascia were not found to be significant prognostic factors. The median time to LR was 31 months for patients (9%). Although 4 patients developed metastatic disease, no patient died of DFSP in the study period. Reconstruction was used in 46% and 3% were treated with surgery alone. Radiotherapy was given to 18 patients and was given more often when margins were positive or close. One patient was treated with a TKI. CONCLUSION: The treatment of DFSP in the primary or recurrent setting is surgical excision. Without negative margins or when further surgical excision is not possible, adjuvant XRT is effective. High mitotic index is predictive of a worse RFS. The overall prognosis with complete excision is good.

Abstracts: Poster Presentations S149

All India Institute of Medical Sciences, New Delhi, Delhi, India; 3. Radiation Oncology, Dr BRAIRCH, All India Institute of Medical Sciences, New Delhi, Delhi, India; 2. Medical Oncology, Dr BRAIRCH, All India Institute of Medical Sciences, New Delhi, Delhi, Delhi, India.

Introduction: Dermatofibrosarcoma protuberans (DFSP) is a rare, slow-growing soft tissue malignancy associated with a chromosomal translocation. Initial treatment options include wide local excision or Mohs micrographic surgery. Tumors are known to recur locally. Adjuvant options include radiotherapy and tyrosine kinase inhibitors (TKI). Current guidelines on surgical margins and recurrence rates vary. METHODS: A retrospective study was done of 77 patients with primary or recurrent DFSP treated between 1985-2012. Data was collected from clinical, operative and pathological reports. Clinico-pathological and treatment data were analyzed using the log rank test for univariate analysis. Local recurrence free survival (LRFS) was assessed by the Kaplan-Meier method. RESULTS: Of the 77 patients, 55% were female with a median age of 40. The fibroblastic (FS) variant was present in 16%. The trunk was the most common site (43%). The majority of patients presented with symptoms (84%) and underwent a biopsy (88%). Prior surgery/trauma at the site of the DFSP was noted in 34% of patients. The median duration of the lesion prior to excision was 24 months. Overall, primary, and recurrent group 5 year LRFS was 87%, 85% and 80%, with a median follow up of 3.75 years. On univariate analysis, mitotic rate of >5/10 HPF was unfavorable. Age, margin status, size, FS variant, taking fascia or more than fascia were not found to be significant prognostic factors. The median time to LR was 31 months for patients (9%). Although 4 patients developed metastatic disease, no patient died of DFSP in the study period. Reconstruction was used in 46% and 3% were treated with surgery alone. Radiotherapy was given to 18 patients and was given more often when margins were positive or close. One patient was treated with a TKI. CONCLUSION: The treatment of DFSP in the primary or recurrent setting is surgical excision. Without negative margins or when further surgical excision is not possible, adjuvant XRT is effective. High mitotic index is predictive of a worse RFS. The overall prognosis with complete excision is good.

Does a Multidisciplinary Approach Improve Outcomes in Sacral Chordoma?


1. Surgical Oncology, Mount Sinai Hospital, Department of Surgery, University of Toronto, Toronto, ON, Canada; 2. Department of Radiation Oncology, Princess Margaret Hospital, Toronto, ON, Canada; 3. Department of Pathology, Mount Sinai Hospital, Toronto, ON, Canada; 4. Orthopedic Oncology, Mount Sinai Hospital, Toronto, ON, Canada.

INTRODUCTION: Chordomas are slow-growing notochordal sarcomas traditionally treated with surgery alone. Complete resection may require removal of adjacent pelvic organs. Our centre has developed a multidisciplinary approach including pre-operative radiation with resection and reconstruction involving multiple surgical specialties. The goal of this study is to report the short- and long-term outcomes of this comprehensive approach METHODS: All patients with a histologically confirmed diagnosis of sacral chordoma from 1989 to 2012 were identified in our prospective database and a retrospective chart review was performed. Data were analyzed using SPSS. RESULTS: Thirty-one patients with a median age of 64.5 years were identified. Eight patients were unresectable or refused surgery; 23 patients were treated with curative intent, including radiotherapy in 78% (18; 15 pre- and 3 post-operatively). Median resected tumor size was 8.8 cm (4.5-15.8), which required sacrectomy at 52% or above in 76%. Median follow up was 60 months (5-261). Early in the series, the operative approach was from the retroperitoneum with the patient in the decubitus position, followed by sacrectomy in prone (D+P group; n=6). This was modified to a combined anterior/posterior approach (A+P group), beginning in 2002. Conclusions: moving to prone for sacrectomy (n=17). Median operative time was 594 min (495-820) in the D+P group and 837 min (315-1270)
in the A+P group (p=0.1). Median intra-operative transfusions were 21 and 9 units of pRBCs, respectively (p=0.003). Rate of re-operation tended to be higher in the D+P group (75% vs 25%, p=0.06). Rates of image-guided percutaneous drain (25% D+P vs 19%) and administration of TPN (25% D+P vs 24%) were similar. Median length of stay (LOS) was 38.5 days for D+P (17-103) and 29 days (16-88) in the A+P group (p=0.7). Overall survival (OS) and local recurrence free survival (LRFS) at 5 yrs were 85% and 60% in the D+P group compared to 100% and 70% in the A+P group, respectively (OS p=0.24, LRFS p=0.42). CONCLUSIONS: Adjuvant radiation with multi-disciplinary abdomino-sacral resection of sacral chordoma resulted in excellent OS and LRFS, with acceptable peri-operative morbidity and LOS.

P319

BACKGROUND: In esophageal cancer (EC) patients not eligible for surgery definitive chemoradiation (dCRT) with curative intent using cisplatinum (5-FU) is the standard regime. Nowadays carboplatin and paclitaxel are also often used. In this study we compare survival and toxicity rates between both regimens. METHODS: This multicentre study included 102 patients treated in five centres in the North Netherlands from 1996 till 2008. Forty-seven patients received cisplatinum / 5-FU and 55 patients carboplatin / paclitaxel. RESULTS: Overall survival (OS) was not different between the cisplatinum / 5-FU and carboplatin / paclitaxel group (P=0.879, Hazard Ratio [HR] 0.97 confidence interval [CI] 0.62-1.51), with a median survival of respectively 16.1 (CI 11.8-20.5) and 13.8 (CI 10.8-16.9) months. Median disease free survival (DFS) was comparable (P=0.760, HR 0.93 CI 0.60-1.45) between the cisplatinum / 5-FU group (11.1 months, CI 6.9-15.3) and the carboplatin / paclitaxel group (9.7 months, CI 5.1-14.4). Groups were comparable except clinical T-stage was higher in the carboplatin / paclitaxel group compared to cisplatinum / 5-FU as dCRT treatment in EC patients. Toxicity rates were lower in the carboplatin / paclitaxel group together with a higher treatment compliance. Carboplatin / paclitaxel as an alternative treatment for cisplatinum / 5-FU is a good candidate regimen for further evaluation.

P320
A Comparative Analysis of the Efficacy of Surgical and Non-surgical Modalities for Nodal Staging in Potentially Resectable Non-small Cell Lung Cancer P. Shoot,† D. Hillman, R.S. Chamberlain. 1. Surgery, Saint Barnabas Medical Center, Livingston, NJ; 2. Saint George’s University, True Blue, Grenada.

There have been an increasing number of studies comparing the use of computed tomography, positron emission tomography, or a combination of these imaging modalities for suspected non-small cell lung carcinoma (NSCLC). Additional studies have also been completed comparing minimally invasive diagnostic methods such as endoscopic ultrasonic-fine needle aspiration (EUS-FNA) and endobronchial ultrasound-transbronchial needle aspiration (EBUS-TBNA) to mediastinoscopy (MS) for staging NSCLC. Accurate staging of NSCLC is essential for correct clinical management and to avoid unnecessary surgical procedures. This review examines all published reports on the efficacy of imaging, minimally invasive methods and surgical methods for staging NSCLC. A comprehensive search of PubMed and Google Scholar was performed looking at the use of CT, PET, EUS-FNA, EBUS-TBNA, and MS in the staging of NSCLC. Keywords searched included PET/CT, EBUS, EUS, mediastinoscopy and NSCLC. 38 studies involving 6,869 patients were included. Criteria for inclusion were N>20, publication date after 1995, NSCLC only, and sufficient data to permit calculation of the sensitivity and specificity. Thirty eight distinct studies reported data on various techniques for staging NSCLC. 14 studies (N=2,177) compared CT and PET, demonstrating a sensitivity (Sn) and specificity (Sp) of 27-75%, 34-98% and 25-100%, 76-98% respectively. 5 studies (N=1,280) reported that CT/PET was superior, with a Sn and Sp of 47-94% and 60-92% respectively. 17 studies involving 1,873 patients reported on the efficacy of minimally invasive staging showing that EBUS-TBNA and EUS-FNA were more sensitive than MS, and that EBUS-TBNA was more specific than MS. Overall, minimally invasive staging methods were equivalent to MS, but more accurate that PET/CT. PET/CT staging of NSCLC has a higher Sn and Sp than each study performed alone and a negative PET/CT may avoid unnecessary surgical intervention. Minimally invasive procedures (EUS-FNA/EBUS-TBNA) are equivalent to MS for identifying mediastinal metastases and may effectively replace MS in NSCLC staging in the near future.

P321
Actual 5-year Survival after Neoadjuvant Chemotherapy and Resection for Esophageal Adenocarcinoma S. Yeluri,* P. Jose, A. Saha, O. Rotimi, S.L. Dexter, H. Sue-Ling, A.I. Sarela. Upper GI Surgery, St. James’s University Hospital, Leeds, United Kingdom.

INTRODUCTION: In the UK, potentially curable oesophageal adenocarcinoma is treated with neo-adjuvant chemotherapy (NC) and radical surgery. We compared the pathological characteristics of actual 5 year survivors and non-survivors, following such treatment, in order to identify prognostic
markers for long survival. METHODS: A database of 356 esophagectomies [adenocarcinoma, 236(66%); squamous cell carcinoma, 66(19%); other cancers, 54(15%); NC, 226(63%)] performed by 3 surgeons between January 2001 and Sept 2012 was used. All patients with adenocarcinoma, NC and a minimum interval of 5 years following surgery were identified. TNM version 7 was used. Circumferential resection margin (CRM) was considered positive if tumour cells were present within 1 mm of the margin. RESULTS: There were 102 patients (81 men, 79%), with median age 61 years (range, 37-69), 97 patients had an Ivor Lewis operation, 4 had laparoscopically assisted trans-hiatal resection and 1 had a 3-incision procedure; there was one post-operative mortality, with median retrieval of 34 nodes (range, 10-82), 41 (40%) patients were alive at 5 years after surgery; median survival, 90 months (range, 60-144). The remaining 61 patients had median survival of 19 months (range, 3-58). Differences in T and N characteristics between the two groups are shown in Table. As compared to non-survivors, 5-year survivors had significantly lower incidence of ypT3/T4 disease [49(81%) vs. 23(56%), p=0.002], node-positive disease [52 (87%) vs. 17 (42%), p=0.001], CRM positive status [38(67%) vs. 14(35%), p=0.002], vascular invasion [50(91%) vs. 17(46%), p=0.001] and lymphatic invasion [33(100%) vs. 13(54%), p=0.001] respectively. Tumour differentiation (p=0.13) was not significantly different in the two groups. On multivariate analyses, ypN1 status (p=0.02, HR=2.34, 95%CI: 1.14, 4.81) and vascular invasion (p=0.006, HR=3.76, 95%CI:1.45, 9.75) independently predicted for long term survival. CONCLUSIONS: 40% of patients with locally advanced esophageal adenocarcinoma actually survive for at least 5 years following NC and surgery. Achieving a node negative status remains a major predictor of long term survival.

### P322

**Impact of Pre-treatment Imaging on Survival of Esophagectomy after Induction Therapy for Esophageal Cancer: Who Should Be Given the Benefit of Doubt?**


Purpose: The benefit of esophagectomy for patients with locally advanced esophageal cancer and possible distant metastatic disease present on initial imaging that is no longer seen after chemoradiation treatment (CRT) is unclear. We examined survival of patients with this clinical scenario who are given “the benefit of doubt” and undergo resection. Methods: A prospective database of patients who underwent esophagectomy after CRT between 2003 and 2009 was queried. A multivariable logistic regression model was developed to predict the impact of preoperative and post-therapy staging characteristics on survival. Survival of patients with and without possible metastatic disease on initial imaging was compared with the log-rank test. Results: During the study period, 70 (32%) of 220 patients who underwent CRT followed by esophagectomy had possible metastatic disease on initial CT or PET imaging. Of the 63 patients who had PET evidence of suspicious metastatic disease, 23 (37%) had possible disease in the lung, 11 (18%) in the liver, 4 (6%) in the pleura and 24 (39%) in other locations. Mean follow-up was 24 months for all patients and 37 months for surviving patients. Overall, survival of patients with and without possible metastatic disease on initial imaging was not significantly different (p=0.4). However, pretreatment PET evidence of a liver lesion (p=0.003, OR 3.2, CI 1.5-6.8) significantly predicted worse survival in multivariable analysis, and patients with PET positive liver findings had worse survival compared to all other patients (Figure). In addition none of 10 patients with pathologic metastatic disease at resection, which also predicted significantly worse survival (p=0.01, OR 3.1 CI 1.3-7.4), lived longer than 2.5 years. Conclusions: Patients with possible liver metastases on pre-treatment PET and patients with unexpected metastatic disease found at the time of surgery do not benefit from resection. However, patients with pre-treatment imaging that shows possible metastatic disease in sites other than the liver still have reasonable long-term survival after resection.

### P323

**Micro-RNAs Up-regulated in Oligometastatic Pulmonary Metastases Decrease Adhesion and Integrin Expression in vitro**


Introduction: Patients may develop tumors that produce only a few metastases over the course of years (oligo-metastatic tumors), or develop multiple metastases in a short time (poly-metastatic tumors). We identified micro-RNAs (miRNAs) increased in lung metastases of oligo-metastatic patients relative to poly-metastatic patients. These miRNAs may play a role in determining metastasis number and rate of progression by reducing cell adhesion through suppression of integrins involved in binding to extracellular matrix. These findings may help identify means for controlling metastatic spread. Methods: miRNAs up-regulated in oligo-metastatic pulmonary metastasectomy samples were analyzed with the Diana mirPath pathway prediction algorithm. The TargetScan and Diana-microT algorithms identified eight miRNAs with multiple predicted integrin targets involved in cell adhesion. Matrigel adhesion assays and qPCR quantification of miRNA and target mRNA levels were performed on MDA-MB-435 cells transiently transfected with an miRNA mimic or a negative control. Results: We identified Integrin α2, α4, αv, β1, β3, and β8 as cell adhesion molecules that are potential targets of eight differentially regulated micro-RNAs identified from patient samples. Four of the eight micro-RNAs (miR-135a, -369, -544 and -655) decreased cell adhesion by 31%, 72%, 37%, and 29% vs. negative control (all p<0.01). These 4 miRNAs decreased expression of integrin α4 mRNA by 20-66% (all p<0.05), integrin αv mRNA by 25-50% (all p<0.05) and integrin β8 mRNA by 30-60% (all p<0.05) compared to a negative control. Integrin α2, α3 and β3 mRNA levels were not significantly decreased. Conclusions: Individual miRNAs over-expressed in clinical samples of oligo-metastases are able to suppress cell adhesion and multiple integrin mRNAs in vitro. Suppression of integrins by these miRNAs may be partially responsible for decreased adhesion. Over-expression of these miRNAs or suppression of their targets may play a role in novel metastasis prevention therapies.

### P324

**Post-neoadjuvant Treatment Staging with PET and EUS is Not Necessary in the Management of Resectable Esophageal Adenocarcinoma (EAC)**


Introduction: EAC is a devastating diagnosis with poor long-term survival. Most patients are treated with neoadjuvant chemoradiation. Modalities used to diagnose, stage, and re-stage EAC have been studied without clear evidence of a superior protocol. Positron emission topography (PET) and endoscopic ultrasound (EUS) are common diagnostic staging tools. In
the present study, we wished to determine whether PET and/or EUS were predictive of tumor response and long-term survival. Methods: We reviewed all patients with the diagnosis code for esophageal cancer in the University of Alabama at Birmingham University Hospital tumor registry from 2000-2010 who underwent surgery following staging PET scans and EUS. Survival data was calculated using Kaplan-Meier analysis. Results: 402 patients were treated for EAC at our institution from 2000-2010. 100 patients underwent attempted therapeutic resection after staging PET and EUS. 32 patients were found to have no cancer on final pathology. Patients with complete pathological response had better long-term survival than patients with residual disease (median survival 33.5 months vs. 16.6 months, 5-year survival 44.0% vs. 23.3%, P=0.026). EUS did not correlate to final pathology in regards to T-stage (R²=0.09, 33% accuracy) or N-stage (sensitivity 30%, specificity 85%, positive predictive value 47%, negative predictive value 28%, accuracy 67%). Change in avidity on PET scan was also unable to predict final pathological diagnosis (change in SUVmax 30.6% complete responders vs. 46.6% non-responders, P=0.65). The absolute avidity on PET scan did not differ between the two groups (mean, complete responders 4.89 SUV vs. incomplete responders 5.30 SUV, P=0.55). Conclusions: Patients with complete pathological response after neoadjuvant therapy for EAC have better long term outcomes than those with residual cancer. Neither PET scan nor EUS was predictive of response following neoadjuvant therapy. We recommend obtaining PET and EUS for evaluating loco-regional response after therapy and advocate that all appropriate patients undergo resection for curative intent.

P325
Actual 5-year Survival after Esophagectomy for Squamous Cell Carcinoma following Neoadjuvant Chemotherapy

INTRODUCTION: We compared the pathological characteristics of actual 5 year survivors and non-survivors, following neo-adjuvant chemotherapy and radical surgery for squamous cell carcinoma (SCC) of the oesophagus, in order to identify prognostic markers for long survival. METHODS: A database of 356 oesophagectomies [adenocarcinoma, 236(66%); squamous cell carcinoma, 66(19%); other cancers, 54(15%); neoadjuvant chemotherapy, 226(63%)] performed by 3 surgeons between January 2001 and Sept 2012 was used. All patients with SCC, neo-adjuvant chemotherapy and a minimum interval of 5 years following surgery were identified. TNM version 7 was used. Circumferential resection margin (CRM) was considered positive if tumour cells were present within 1 mm of the margin. RESULTS: There were 41 patients (20 men, 49%), with median age 61 years (range, 41-77).36 patients had an Ivor Lewis operation, and 5 had a 3-incision procedure; median retrieval of 34 nodes (range, 11-104). 22 (54%) patients were alive at 5 years after surgery; median survival, 83 months (range, 60-140). The remaining 19 patients had median survival of 14 months (range, 4-57). Differences in T and N characteristics between the two groups are shown in table below. As compared to non-survivors, 5-year survivors had significantly lower incidence of ypT3/T4 disease [17(90%) vs.11 (50%), P=0.009] and lympho-vascular invasion [14(78%) vs. 8(38%), P=0.013]. CRM positive status (p=0.07), node positive status (p=0.1), and tumour differentiation (p=0.85) were not statistically significant between the two groups. Node positive status (p=0.006) and T3/T4 stage (p=0.046) predicted for poor long term overall survival across the group of patients. CONCLUSIONS: T and N stage remain important determinants of long term survival after radical treatment for oesophageal SCC. Even after curative resection, overall survival in patients with adverse pathological variables is a sixth of the survival seen in patients with favourable pathological features.

P326
Freedom from Recurrence after Induction Cisplatin/5-FU/RT versus Carboplatin/paclitaxel/RT in Patients with Esophageal Cancer

Background: The optimal neoadjuvant treatment regimen for esophageal cancer has yet to be defined. Methods: We analyzed a prospective database of esophageal cancer patients treated with cisplatin/5-FU/RT (A) or carboplatin/paclitaxel/RT (B) then esophagectomy. Endpoints were pathologic response (pCR), recurrence, and overall survival. Covariates (age, gender, clinical stage, Charlson comorbidity index (CCI), and ECOG PS) were adjusted via propensity score weighting from logistic regression. Differences in survival curves were compared using weighted Kaplan-Meier methods and Wilcoxon tests. Landmark analysis compared differences in outcomes at least 6 months after surgery. Results: From January 2008 to June 2013, 71 patients received induction RT (50.4 Gy), with 38 and 33 patients in groups A and B, respectively. Patient demographics were similar. Operative procedure, R0 resections, and operative complications did not differ (operative mortality 1/71, 1.4%; anastomotic leak rate 10% A vs. 9% B, p=1.0). Median follow-up was 18.2 and 9.1 months for groups A and B, respectively. There was no difference in overall survival (p=0.88) or total number of recurrences (11/38, 29% A vs. 10/33, 30% B). Landmark analysis revealed a difference in recurrence at least 6 months after surgery: time to recurrence was shorter in group B (median time to recurrence 31 mos A vs. 18 mos B, p=0.02). pCR was seen in 13/38 (34%) A and 9/33 (27%) B (p=0.53). In patients with pCR, there was a trend toward more recurrences in group B (2/13, 15% A vs. 4/9, 44% B, p=0.14). Conclusions: Six months after surgery patients receiving induction carboplatin/paclitaxel/RT had shorter time to recurrence compared to cisplatin/5-FU/RT. In those with pCR a trend towards increased distant recurrences was seen with carboplatin/paclitaxel/RT, which may have less systemic efficacy in esophageal cancer than cisplatin/5-FU/RT. This should be evaluated in larger series.

P327
Circular-stapled Esophagogastric Anastomoses and Need for Dilatation in Patients Undergoing Minimally Invasive (MIS) Ivor Lewis Esophagectomy after Induction Chemoradiation for Esophageal Cancer

Background: Concern exists that circular-stapled anastomoses are associated with a higher rate of stricture formation after MIS Ivor Lewis esophagectomy than either linear-stapled or hand-sewn techniques. Methods: Retrospective analysis identified 45 patients who received induction chemoradiation and MIS Ivor Lewis esophagectomy. Operations were performed by a single surgeon from October 2010 through July 2013. Analyzed variables included

<table>
<thead>
<tr>
<th>Survival</th>
<th>ypT Stage</th>
<th>ypN Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 months</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>6-12 months</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>12-18 months</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>18-24 months</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>24-30 months</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30-36 months</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>36-42 months</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>42-48 months</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>48-54 months</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>54-60 months</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
age, sex, race, comorbidity index, ECOG PS, nutritional status, intra-operative technique, complications, recurring, and survival. Results: Mean age 63 years, 91% white, 82% male, 67% GE junction tumors, adenocarcinoma (91%), and 89% stage IIB or above. 76% presented with dysphagia; 42% had associated weight loss (mean 12%). All 45 received induction chemotherapy (platinum based), with 41 patients receiving concomitant radiation (median 50.4 Gy, range 45.6-57 GY). 98% had R0 resections with a mean of 26 LNs harvested. An EEA stapler was utilized for all anastomoses, the final 28 via transoral method. The majority of anastomoses were covered with omentum (82%). Pyloric injection of botulinum toxin was utilized for gastric emptying (91%). Median length of hospital stay was 11 days. Perioperative complication rate was 64% (Table 1). Pathologic complete response rate was 38%. Median follow-up was 11.8 months (range 2.2-32.8) and demonstrated 7 deaths (3 cancer related), 6 patients with distant recurrences and no local recurrences. 7 patients (15.6%) developed strictures requiring dilation. Conclusions: Minimally invasive Ivor Lewis esophagectomy after chemoradiation is safe, with acceptable morbidity and desirable oncologic outcomes. Using the circular-stapled approach, the rate of anastomotic leak is low, while the rate of stricture requiring dilation is similar to that reported for linear-stapled and hand-sewn anastomoses.

Table 1 - 30-Day Morbidity and Mortality by Clavien Classification.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Grade I (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common Metastatic Disease</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Common Morbidity</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Recurrent Nerve Injury</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Nasoethmoid Sinusitis</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Minor - Grade II</td>
<td>21 (44)</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>10 (22.2)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>Necrosis Sinusitis</td>
<td>3 (6.7)</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>0 (0)</td>
</tr>
<tr>
<td>DVT</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Cytolymphorhea (without intervention)</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Major - Grade III</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Anastomotic Leak</td>
<td>3 (6.7)</td>
</tr>
<tr>
<td>Pericardial Tamponade</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>2 (4.4)</td>
</tr>
<tr>
<td>Major - Grade IV</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Renal Failure</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Myocardial Infarction</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Ischemic Stroke</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Respiratory Failure</td>
<td>1 (2.2)</td>
</tr>
<tr>
<td>Major - Grade V</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

P328
Implementation of a Tobacco Cessation Program in a Thoracic Surgical Oncology Clinic


Many patients in a thoracic surgery oncology clinic smoke. Impaired wound healing and increased respiratory complications are linked to smoking, and long term survival may be impacted by cardiovascular disease, emphysema and metachronous tumors. Although quitting smoking has proven benefits, nicotine addiction is challenging to overcome, leading to a nihilistic view of cessation. Unaided cessation has a poor success rate (<5%), while a combination of physician recommendation, counseling by certified tobacco treatment specialists (TTS), individualized pharmacotherapy and follow up can improve cessation. A multidisciplinary team from thoracic surgery, nursing and respiratory therapy was assembled to provide multifaceted, evidence-based tobacco treatment in our thoracic oncology surgery clinic. After institutional board review approval, all patients were queried for tobacco use, and any patient actively smoking underwent brief intervention by the surgeon (who is a TTS) and referred for more in depth counseling to a dedicated in-clinic TTS. For convenience, the counseling was done in a private room adjacent to the clinic rooms. Demographic data, smoking data, drug/alcohol use and medication use were prospectively recorded. Follow up visits were in the hospital, upon return to clinic and/or by phone. Exhaled breath carbon monoxide confirmed initial active use and successful cessation. Over the initial seven months, 60 active smokers received brief intervention by the surgeon and referral to an in-clinic TTS counselor. Despite physician recommendation, the convenience, and the free service, 23/60 patients refused to meet the TTS counselor. Of the patients who agreed to meet with the TTS, consented to enroll in the program, and agreed to follow up contact (24/60), 17/24 (70.8%) quit and remained abstinent at last contact. Integrating TTS in a surgery oncology clinic can be done. For those who enroll and consent to follow up, our pilot data demonstrates excellent short-term cessation. Ongoing enrollment, follow up, and expansion within our institution will allow better understanding of tobacco cessation services integrated into clinical settings.

P329
The Impact of Surveillance after Lobectomy for Stage IA Non-small Cell Lung Cancer

A.R. Shoffner, I.A. Naqvi, T.A. D’Amico, M.W. Onaitis, M.F. Berry. Duke University Medical Center, Durham, NC.

OBJECTIVE: The purpose of this study was to determine reintervention rates that result from surveillance after lobectomy for stage IA non-small cell lung cancer (NSCLC). METHODS: The incidences of recurrent disease and metachronous primaries were determined for all patients who underwent lobectomy for stage IA NSCLC without induction or adjuvant therapy from 1996 to 2010 at a single institution and were followed for at least two years or until the development of new or recurrent disease. Disease free intervals and Kaplan-Meier survival curves were compared using Mann-Whitney and log-rank tests, respectively. RESULTS: Of 316 patients who met the inclusion criteria during the study period, 50 patients (16%) developed recurrent disease (15 local only, 35 distant) and 45 patients (14%) had new primaries. Surveillance with CT scan was performed on 260 patients, and found 18/50 recurrences (7 local, 11 distant) and 37/45 new primaries in asymptomatic patients. Surveillance with chest x-ray was performed on 53 patients and found 5 recurrences (3 local, 2 distant) and 6 new primaries in asymptomatic patients. In contrast, 26 recurrences (4 local, 22 distant) and 6 new primaries were discovered due to symptoms. Recurrence was incidentally found in one patient who had stopped pursuing follow up. On average, recurrent disease was found 22.1 ± 8.8 months and new primaries were found 52.2 ± 11.1 months after lobectomy (p < 0.001). Repeat surgery alone was utilized in 58% (20/45) of new primaries but only 27% (4/15) of local recurrences. Chemotherapy or radiotherapy was administered to 68% (34/50) of patients with recurrent disease. Five-year survival after discovery of new primary disease was 50.8 ± 9.6% and five-year survival after discovery of recurrent disease was 4.5 ± 3.1% (p < 0.0001, Figure). CONCLUSIONS: Surveillance after lobectomy for stage IA NSCLC frequently finds either recurrent or new primary disease. Most patients with recurrent disease can be treated but survival is poor. Most patients with new primary disease can undergo surgical resection with reasonable survival.
cases after surgery, monitored 48 LC patients (LCP) (m=40, f=8; lobectomy)

Methods: In trial (1987-2013) consecutive 14 to 28 days after first imaging.

Conclusions: Anastomotic leakage was demonstrated in 7% of patients

Follow-up Imaging for Radiologically-detected Anastomotic Leakage after Oesophagectomy

Introduction The mainstay of management of late presenting or radiologically detected leaks after oesophagectomy in our unit is non-operative with water-soluble contrast swallow tests until the leak has healed. This study aimed to describe our experience with radiologically detected leaks. Methods From January 2008 to August 2013, 192 patients underwent oesophagectomy for oesophageal cancer. Standard practice within our unit is to perform a water-soluble contrast swallow test within a week after surgery. 10 patients had incomplete data and 7 patients did not have any post-operative imaging and were excluded. A radiological leak was defined as one only detected on post-operative imaging with no adverse clinical signs. Results Of 175 patients included in this study, there were 3 clinical leaks (1.7%) and 12 radiological leaks (6.7%). 74 patients had a sutured anastomosis (42%) and 120 patients had a stapled anastomosis. Median time between surgery and first swallow was 7 days (range, 4-22). Six patients had other imaging prior to first planned swallow; in all of these patients, computed tomography of the chest and abdomen with oral contrast was performed for clinical reasons (suspected intra-abdominal or thoracic sepsis) within 7 days of surgery. All radiological leaks healed with non-operative management comprising radiological drainage of any collections, total parenteral nutrition and a strict ‘nil-by-mouth’ policy; none required operative re-intervention. Of the 12 patients with radiologically-detected leaks, 2 had no further swallows. The remaining 10 patients received weekly swallow tests until the leak had healed. Only two patients’ leaks had healed within 14 days with a further 4 patients healing within 28 days and 2 patients within 35 days. Conclusions: Anastomotic leakage was demonstrated in 7% of patients by routine post-operative water-soluble contrast and none required operative re-intervention. Only two patients had healed within 14 days. These data suggest that routine post-operative swallow assessment is important to detect leakage and that further swallow tests should not be performed until at least 14 to 28 days after first imaging.

Precise Early Detection of Lung Cancer and Immune Circuit

Objective: Significance of immune circuit in terms of early detection of lung cancer (LC) was investigated. Methods: In trial (1987-2013) consecutive cases after surgery, monitored 48 LC patients (LCP) (m=40, f=8; lobectomy=48 with pathologic stage IA (tumor size = 1.6±0.4 cm; squamous=21, adenocarcinoma=25, large cell=2; T1N0M0=48; G1=16, G2=21, G3=11, 5-year survival=100%), 282 patients with lung non-malignant pathology (NMP) (m=188, f=94; pneumonectomy=5, lobectomy=179, segmentectomy=98; non-malignant tumors=100; abscess=112; tuberculosis=70) and 120 healthy donors (HD) (m=69, f=51) were reviewed. Variables selected for study were input levels of immunity blood parameters, sex, age, TNMG. Blood samples were evaluated for IgG, IgM, IgA, natural antibodies, circulating immune complexes. The percentage, absolute count and total population number (per human organism) of CD3, CD19, CD4, CD8, CD16, CD26, monocytes, CD4+2H, CD8+V, leukocytes, lymphocytes, polymorphonuclear and stick-nuclear leukocytes were estimated. The laboratory blood studies also included input levels of NST (tests of oxygen dependent metabolism of neutrophils stimulated and non-stimulated by Staphylococcus aureus or by Streptococcus pyogenes, index of stimulation of leukocytes by Staphylococcus aureus or Streptococcus pyogenes, index of thymus function, phagocytic number, phagocyte index, index of complete phagocytosis. Differences between groups were evaluated using discriminant analysis, clustering, nonlinear estimation, structural equation modeling, Monte Carlo, bootstrap simulation and neural networks computing. Results: It was revealed that early detection of LC from NMP and HD (n=402) significantly depended on: CD4+2H, CD8+VV, CD4, B, CD16, monocytes (P<0.001-0.017). Neural networks computing, stepwise selection and bootstrap simulation revealed relationships of early detection of LC and monocytes (rank=1), CD4+2H (rank=2), CD19 (3), CD8+VV (4), CD4 (5), CD16 (6). Correct detection of early LC was 100% by neural networks computing (error=0.000; area under ROC curve=1.0). Conclusion: Early detection of LC from NMP and HD significantly depended on immune cell circuit.

MicroRNA-133a Regulates the mRNAs of Two Invadopodia-related Proteins, FSCN1 and MMP14, in Esophageal Cancer

Background: FSCN1 and matrix metalloproteinase 14 (MMP14) are both invadopodia-related proteins. We herein elucidate the tumorigenicity of these proteins and identify novel therapeutic agents in esophageal squamous cell carcinoma (ESCC). Methods: FSCN1 and MMP14 were evaluated by immunohistochemistry (IHC) in 140 surgically resected ESCC specimens. The role of FSCN1 and MMP14 and the role of miR-133a were established using knockdown and transfection strategies in ESCC cells, respectively. The expressions of FSCN1, MMP14 and miR-133a were evaluated in 84 specimens. Results: Neither FSCN1 nor MMP14 was detected in the normal epithelium by IHC staining. Patients with positive FSCN1 staining showed significantly higher T and clinical stages and a higher rate of recurrence. Patients with positive MMP14 staining showed significantly higher T, N and clinical stages, a higher level of lymphatic invasion and vascular invasion and higher rates of recurrence. A multivariate analysis of the IHC findings revealed the expression of either of these proteins to be an independent poor prognostic factor. The co-expression of these proteins correlated with the worst overall survival (OS) rate out of all the examined factors. The knockdown of FSCN1 or MMP14 led to a significant decrease of the mRNA or protein and decrease in the proliferation and invasion of ESCC cells. However, the knockdown of FSCN1 did not lead to a decrease in MMP14 mRNA or protein. Similarly, the knockdown of MMP14 did not affect the expression of FSCN1 mRNA or protein. Transfection of a miR-133a mimic decreased the mRNA and protein levels of both FSCN1 and MMP14 and led to a significant decrease in proliferation and invasion. An RNA analysis in 84 specimens revealed a significant correlation between FSCN1 and MMP14 expressions, and significant inverse correlations between FSCN1 and miR-133a and between MMP14 and miR-133a. A significantly poorer OS was observed among patients with a lower miR-133a expression. Conclusions: The combined expression of FSCN1 and MMP14 is associated with a poor prognosis, and miR-133a, which regulates their mRNAs, can serve as a strong tumor suppressor of ESCC.
P333

Is it Time to Abandon the 5cm Margin Rule during Resection of Distal Gastric Adenocarcinoma? A Multi-institution Study of the U.S. Gastric Cancer Collaborative

Background A proximal margin distance of 5cm is advocated for resection of gastric adenocarcinoma (GAC). We assessed the prognostic value of proximal margin (PM) distance and a positive PM on survival after resection of distal GAC. Methods All pts who had resection of GAC from 2000-2012 at 7 institutions of the U.S. Gastric Cancer Collaborative were included. Pts with positive distal margins or 30-day mortality were excluded. The prognostic value of PM distance (assessed in 0.5cm increments) and a positive PM on survival after resection of gastric adenocarcinoma (GAC). We assessed the prognostic value of margin distance (assessed in 0.5cm increments) and a positive PM on survival after resection of distal tumors overall (OS) and recurrence-free survival (RFS) after resection of distal tumors. Multivariate (MV) regression was used to assess the prognostic value of the proximal margin distance and a positive PM on survival after resection of distal gastric cancer and stage-specific. In Stage I, a >3cm proximal margin is associated with the same improved overall survival as a 5cm margin. In Stage II-III disease, neither the distance of the proximal margin nor a negative proximal margin impact survival, due to other adverse pathologic factors. This may affect intraoperative decisions regarding extent of resection.

Multivariate Regression Analysis for Overall Survival, Stratified by Tumor Stage

<table>
<thead>
<tr>
<th>Variable</th>
<th>Stage I tumors (n=141)</th>
<th>Stage I-III tumors (n=224)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA Class</td>
<td>HR (95% CI) p-value</td>
<td>HR (95% CI) p-value</td>
</tr>
<tr>
<td>T Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>1.33 (0.30-6.66) 0.77</td>
<td>1.05 (0.42-2.67) 0.86</td>
</tr>
<tr>
<td>T2</td>
<td>1.84 (0.47-7.24) 0.38</td>
<td>3.16 (0.69-13.99) 0.14</td>
</tr>
<tr>
<td>T3</td>
<td>--</td>
<td>3.14 (0.74-13.21) 0.12</td>
</tr>
<tr>
<td>T4</td>
<td>--</td>
<td>4.40 (1.04-18.01) 0.04</td>
</tr>
<tr>
<td>N Stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>N1</td>
<td>2.05 (0.42-7.77) 0.29</td>
<td>1.09 (0.51-2.02) 0.79</td>
</tr>
<tr>
<td>N2</td>
<td>--</td>
<td>1.19 (0.67-2.09) 0.96</td>
</tr>
<tr>
<td>N3</td>
<td>--</td>
<td>1.82 (1.32-2.56) 0.04</td>
</tr>
<tr>
<td>N4b</td>
<td>--</td>
<td>2.27 (1.69-4.23) 0.03</td>
</tr>
<tr>
<td>Tumor Size ≤5cm</td>
<td>0.39 (0.25-2.52) 0.70</td>
<td>0.89 (0.60-1.23) 0.57</td>
</tr>
<tr>
<td>Perioperative Transfusion</td>
<td>2.59 (1.84-6.49) 0.04</td>
<td>1.09 (0.69-1.72) 0.71</td>
</tr>
<tr>
<td>Proximal Margin ≤3cm</td>
<td>0.33 (0.16-0.70) 0.01</td>
<td>0.88 (0.60-1.28) 0.90</td>
</tr>
</tbody>
</table>

P334

BCAR3 is Important for Peritoneal Dissemination in Pancreatic Cancer
S.R. Cader, E. Flate, Y. Heakal, R.A. Moffitt, J.M. Anderson, M.A. Hollingsworth, R. Miller, J. Yeh, I. UNC, Chapel Hill, NC; 2. University of Nebraska Medical Center, Omaha, NE.

Introduction: Nearly all patients with pancreatic cancer die of metastatic disease. In order to improve patient survival, it is imperative to understand the molecular mechanisms underlying metastasis. BCAR3 (breast cancer antiestrogen resistance-3) has been previously shown to contribute to aggressive breast tumor phenotypes. Microarray analysis of normal pancreas, primary and metastatic tumors, suggested a role for BCAR3 in metastatic pancreatic cancer. Here we report a novel role for BCAR3 in pancreatic cancer. Methods: BCAR3 knockdown was achieved using shRNA and transwell migration and invasion assays performed in pancreatic cancer cell lines. Tissue microarrays (TMA) 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. Fluorescence immunohistochemistry (IHC) was performed using an antibody against BCAR3 and high resolution acquisition of fluorescently stained slides was performed in Spectrum (Aperio) and automated quantitative analysis (AQUA). Results: Microarray analysis of 54 normal pancreas, 195 tumor and 53 metastatic samples demonstrated that BCAR3 gene expression was significantly upregulated in metastatic tumors compared to either normal pancreas (p=0.0001) or primary tumors (p=0.0086). Resected patient tumors with high BCAR3 expression correlated with poor survival (p=0.005). Knockdown of BCAR3 significantly decreased the ability of cell lines (SW1990 and CFPAC) to migrate and invade (p=0.01). BCAR3 staining was cytoplasmic, with higher concentration in tumor epithelium compared to stroma (p<0.001). BCAR3 expression was significantly greater in peritoneal metastases compared to primary pancreatic tumors (p=0.036). Conclusion: BCAR3 is critical for pancreatic cancer cell line migration and invasion, and is associated with poorer survival in patients with resectable pancreatic cancer. BCAR3 also appears to be most important for peritoneal dissemination in patients, a common mode of spread in pancreatic cancer.
**P335**

**Combined Proteasome and MEK Inhibition Results in Enhanced Growth Inhibition of Patient-derived Pancreatic Ductal Adenocarcinoma**

T. Newhook,1,* J.M. Lindberg,1 S.J. Adair,1 AJ. Kim,1 J. Parsons,1 T. Bauer.1 1. University of Virginia, Department of Surgery, Charlottesville, VA; 2. University of Virginia, Department of Microbiology, Immunology, and Cancer Biology, Charlottesville, VA

Background: Survival for patients with pancreatic ductal adenocarcinoma (PDAC) remains dismal and more effective therapeutic strategies for these patients are needed. As mutations in the KRAS oncogene are important drivers of PDAC progression, rational therapeutic strategies for patients include targeting the RAS pathway. We hypothesized that MEK inhibition results in a unique dependence on a functioning proteasome and that combination treatment with MEK inhibitor plus proteasome inhibitor will result in enhanced growth inhibition in orthotopic patient-derived xenografts (PDX) from pancreatic cancer. Results and Methods: Gene expression profiling was performed on 15 early passage orthotopic PDX tumors and bioinformatic analysis revealed that expression of genes comprising components of the 26S proteasome were upregulated in tumors from patients with shorter survival (data not shown). Patient-derived KRAS-mutant (Tumor 608 and 366) and KRAS-wild type (Tumor 738) PDAC cell lines were treated with MEK1/2 inhibitor trametinib and escalating concentrations of the proteasome inhibitor bortezomib. In all three cell lines, trametinib inhibited cell proliferation and all tumor cell lines were sensitive to bortezomib exhibiting sub-micromolar IC50s (Fig. 1A). To assess the in vivo consequences of proteasome inhibition, mice were engrafted with patient-derived tumors orthotopically and treated with control, trametinib, bortezomib, and combination therapy. Combination therapy with trametinib and bortezomib was more effective than either treatment alone (Fig. 1B) indicating that blocking RAS-MEK-ERK signaling potentiates the sensitivity of tumor cells to proteasome inhibition. Conclusions: Combination therapy with a proteasome inhibitor plus MEK inhibitor results in significant growth inhibition of patient-derived PDAC tumors. Our observations support the idea that inhibition of RAS signaling with FDA approved inhibitors of MEK1/2 reveals a window of therapeutic vulnerability, that in pancreatic cancer cells are more sensitive to inhibition of a functioning proteasome.

---

**P336**

**Pancreatic Circulating Tumor Cells as a Diagnostic Adjunct in Pancreatic Cancer**

J.S. Ankeny,1,* S. Hou,1 M. Song,1 M.M. Rochefort,1 M.D. Girgis,1 W.H. Isacoff,1 H. Tseung,2 J.S. Tomlinson.1 1. Department of Surgery, University of California, Los Angeles, Los Angeles, CA; 2. Department of Molecular and Medical Pharmacology, University of California, Los Angeles, Los Angeles, CA

Background: Circulating tumor cells (CTCs) may improve our ability to diagnose pancreatic ductal adenocarcinoma (PDAC), obtain pure molecular information uncontaminated by stromal cells, and accurately stage patients at the time of diagnosis. Therefore, we evaluated CTCs as an adjunctive diagnostic biomarker for PDAC. Methods: We performed a prospective analysis on 50 consecutive, pre-treatment patients with either suspicion for, or recent diagnosis of PDAC. Venous blood samples (2 mL) were evaluated for the presence and number of CTCs utilizing a novel microfluidic NanoVelcro “chip” enhanced by anti-EpCAM enrichment. CTCs were defined by size ($\geq 10 \mu m$) and by immunocytochemistry staining pattern (DAP1+/CK+/CD45-). Additionally, KRAS mutational status was assessed in 3 patients to confirm PDAC origin of CTCs. Results: Of the 50 patients, 32 had PDAC and 18 had non-malignant pathology on tissue biopsy. CTCs were detected in 20 of 32 (62.5%) patients with PDAC, and in 1 of 18 (5.5%) patients with non-malignant pathology. CTC numbers were significantly higher in PDAC versus non-malignant patient groups (p $< 0.001$). Receiver operating characteristic (ROC) curve analysis determined optimal ability for CTCs to distinguish between PDAC and non-malignant disease with detection of $\geq 1$ CTC. At this cut-off, the specificity of CTCs for the diagnosis of PDAC was 94.4%, PPV 95.2%, and NPV 58.6%. The area under the ROC curve (AUROC) was 0.795 (95% CI = 0.671-0.916, p $< 0.001$), indicating overall ability for CTC detection to discriminate PDAC from non-malignant disease. Additionally, in patients with a diagnosis of PDAC, CTC number correlated with stage and patients with $\geq 2$ CTCs were 11.6 times more likely to harbor systemic disease. Conclusions: In this study, CTCs were a useful adjunct for diagnosis of PDAC. Additionally, $\geq 2$ CTCs strongly correlated with stage IV disease. Longer follow-up and addition of outcomes data is needed to firmly establish CTCs as a predictive biomarker in PDAC.

---

**P337**

**Primary Tumor in the Pancreas Potentiates the Formation of Liver Metastasis in a Murine Model of Pancreatic Cancer**

R. Panni,* D. Sanford, T. Nywening, B. Belt, P. Goedegebuure, D. DeNardo, D. Linehan. Washington University in St. Louis, St. Louis, MO.

Introduction: Pancreatic cancer (PC) is currently the fourth leading cause of death and the mortality rate approaches 100% due to early metastatic spread. Metastasis is a multistep process; the tumor cells acquire mesenchymal features, enter the circulation and extravasate into the parenchyma of distant organs, and develop macro metastasis. Our group and others have shown that PC induces changes at the cellular level in the liver long before the establishment of metastasis. Based on our preliminary experiments, we hypothesized that primary tumor in the pancreas primes the liver to augment implantation of metastatic tumor cells. Methods: In order to study the impact of primary tumor on systemic mechanisms that might facilitate metastatic progression, we implanted a mouse PC cell line, KCKO, orthotopically in the tail of the pancreas, in wild type (WT) mice. Ten days later, we compared changes in the liver by flow cytometry and RT-PCR and injected an mCherry+ luciferase expressing, murine PC cell line (Pan02) in the inferior pole of the spleen and performed hemi-splenectomy. Results: Mice with primary tumor in the pancreas had a significant increase in monocyte and macrophage populations in the liver at day 6 after tumor implantation. RT-PCR was also conducted for the quantification of gene expression level, for genes associated with macrophage mobilization and changes in the microenvironment i.e. CCL2, CSF1, s100a4, s100a8, CXCL12, LOX, VEGFa (p=0.01) (Fig.1A). Our results showed that all mice with primary tumor acquired liver metastasis after splenic injection of Pan02 however, only 40% of mice without primary tumor developed liver metastasis (p=0.0016), by day 15 (Fig 1B&C). Conclusion: We demonstrate that primary tumor in the pancreas significantly increases the incidence and burden of liver metastasis in a murine model of PC. Our results suggest that PC primes the microenvironment in the liver, which plays a key role in implantation of tumor cells, and establishment of metastasis.
P338

Functional BRM Promoter Polymorphisms, Pancreatic Adenocarcinoma Risk and Survival

M. Segedi,1* L. Anderson,2 O. Espin-Garcia,1 A. Borgida,1 T. Bianco,1 D. Cheng,1 Z. Chen,1 P. Devalben,1 M. Brown,1 R. Hung,1 M. Cotterchio,2 S. Gallinger,1 W. Xu,1 D. Reisman,3 G. Liu,1 S.P. Cleary.1
1. Princess Margaret Cancer Centre-University Health Network-Ontario Cancer Institute, University of Toronto, Toronto, ON, Canada; 2. Mount Sinai Hospital-Lunenfeld Research Institute, Toronto, ON, Canada; 3. University of Florida, Gainsville, FL.

Background: Variant alleles of two promoter polymorphisms in the BRM gene (BRM-741, BRM-1321), create MEF2D transcription binding sites that lead to epigenetic silencing of BRM, the key catalytic component of the SWI/SNF chromatin remodeling complex (PMID:23524580). BRM suppression can be reversed pharmacologically (PMID: 21478905). Our group and others have reported associations with lung, head & neck, and hepatocellular cancer risk (PMIDs: 21478907, 23322154, 23359823). We have also reported associations with lung and esophageal cancer prognosis (ASCO 2013; abstr 11057 & 4077). In this analysis, we assessed risk and survival associations with pancreatic cancer.

Methods: A population-based case-control study was conducted in Ontario with 623 histologically-confirmed pancreatic adenocarcinoma cases and 1192 age/gender distribution-matched controls (PMID: 23908141). Survival of cases was obtained through the Ontario Cancer Registry. Logistic and Cox proportional hazard regression models were fitted, adjusting for relevant covariates. Results: Median age was 65 years; 52% were male; 53% had received a curative resection; Stage I (8%), II (55%), III (14%), IV (23%); 79% received chemotherapy; 83% had died. In the risk analysis, the adjusted odds ratios were 1.01 (95%CI:0.1-2.0) and 0.96 (95%CI:0.7-1.3) for the homozygous variants of BRM-741 and BRM-1321, respectively, when each was compared to wildtype; adjusted odds ratio of double-homozygotes was 1.11 (95%CI:0.80-1.53) when compared to the double-wildtype. In contrast for the survival analysis, the hazard ratios (adjusted for age, stage, receipt of curative surgery, receipt of chemotherapy, and packyears) were 2.19 (95%CI: 1.9-2.5) for BRM-741 and 1.94 (95%CI: 1.7-2.2) for BRM-1321, per each unit increase in variant alleles. Compared with the double-wildtype, the adjusted hazard ratio for carrying no, one, and two homozygous (double-homozygous) variants were 2.14 (95%CI:1.6-2.8), 4.17 (95%CI:3.0-5.7), and 8.03 (95%CI: 5.7-11.4), respectively. Conclusions: Two functional promoter BRM polymorphisms were not associated with pancreatic adenocarcinoma risk, but are strongly associated with survival.

P340

Tumor-induced STAT3 Activation in Monocytic-Myeloid Derived Suppressor Cells Enhances Cancer Stem Cells in Human Pancreatic Cancer


Introduction: Pancreatic cancer (PC) is associated with a dense, fibrotic stroma & infiltration of leukocytes that provide an immune privileged tumor microenvironment. Aldehyde dehydrogenase-1 activity in PC identifies cancer stem cells (CSCs) that are responsible for tumor initiation and its activity has been correlated with poor overall prognosis in human PC. Myeloid cells have been shown to impact tumor stemness but the impact of tumor infiltrating monocyctic myeloid derived suppressor cells (Mo-MDSC) on ALDH1 Bright CSCs and epithelial to mesenchymal transition (EMT) is not well understood. Methods: Mo-MDSC (Mouse: CD11b+/Gr1+/Ly6G-/Ly6Chi & Human: CD14+/HLADR-/low) were isolated and co-cultured with mouse and human PC cell lines, respectively. Flow-cytometry, RT-PCR, western blotting and functional studies including invasion assays were performed to study the phenotypic and functional changes in the tumor cells after co-culture with Mo-MDSC. Results: Human PC promotes conversion of CD14+ monocytes to Mo-MDSC (Fig 1A). RT-PCR revealed significant upregulation of markers associated with EMT in tumor cells co-cultured with MDSC (Fig 1B). Invasion assays showed that PC cells co-cultured with Mo-MDSC were more invasive, confirming the EMT phenotype. Flow cytometry revealed that the ALDH1 Bright population increases in PC cell lines after co-culture with Mo-MDSC (Fig 1C) & results in increased spheroid formation. We further found that Mo-MDSC co-cultured with tumor cells upregulated pSTAT3. A STAT3 inhibitor diminished ALDH1 Bright CSC populations (Fig 1C) & function, confirming the importance of this pathway in Mo-MDSC dependant enhancement of tumor plasticity. Conclusion: Our data suggest that the PC tumor microenvironment transforms monocytes to Mo-MDSC by STAT3 activation which increase the frequency of ALDH1 Bright CSCs and promote EMT. Therefore, targeting STAT3 activation may be an effective therapeutic strategy in combination with conventional chemotherapy in PC.
P341
Clinical Significance in the Diagnosis Lymph Node Metastasis in Patients with Gastric Cancer by Intraoperative RT-PCR System with Multiple Markers S. Yanagita,* Y. Uenosono, T. Aritgami, T. Hagiwara, S. Ishigami, S. Noguchi, Department of Digestive Surgery, Breast and Thyroid Surgery, Field of Oncology, Kagoshima University, Kagoshima, Kagoshima, Japan.

INTRODUCTION: The results of two multicenter trials for the clinical application of sentinel node (SN) navigation surgery (SNNS) in patients with gastric cancer in Japan pointed out that the sensitivity of intraoperative diagnosis of SN metastasis to be improved (sensitivity 48.8-79.7%) (J Clin Oncol 2013, Gastric Cancer 2013). And the sensitivity of OSNA (one-step nucleic acid amplification) with CK19 as a single marker in diagnosis of lymph node metastasis was reported to be 83.3% (Gastric Cancer 2013). We investigated the clinical utility of intraoperative RT-PCR system with multiple markers. METH-OIDS: 143 cases (cT1=122, cT2=21) were enrolled in this study. All patients received surgical resection with lymphadenectomy. A total of 1568 lymph nodes were harvested (cT1; n=1273, cT2; n=298). All dissected lymph nodes were divided into two pieces and one was submitted for hematoxylin and eosin (HE) staining and the other was submitted for intraoperative RT-PCR assay (total process time 40 minutes) with CK19 and CEA as markers. The sensitivity of RT-PCR was estimated based on the pathological diagnosis. RESULTS: 10.6% and 19% in patients with cT1 (n=13) and cT2 (n=4) were diagnosed as pN+ by HE staining, respectively. 34 lymph nodes in cT1 and 7 lymph nodes in cT2 were diagnosed as pN+ by HE staining. 1) Patients-based results, the sensitivity of RT-PCR with positivity in CK19 only and CEA only was 88.9% (cT1; 84%, cT2; 100%) and 83.3% (cT1; 84%, cT2; 80%), respectively. The sensitivity of RT-PCR with positivity in CK19 or CEA was 88.9% (cT1; 84%, cT2; 100%), respectively. 2) Lymph node-based results, the sensitivity of RT-PCR with positivity in CK19 only and CEA only was 78% (cT1; 73%, cT2; 100%) and 19% in patients with cT1 (n=13) and cT2 (n=4) were diagnosed as pN+ by HE staining.

P342
No Survival Benefit with Multimodality Adjuvant Therapy for Margin Negative T2N0 Gastric Adenocarcinoma with Optimal Lymphadenectomy H. In,* S. Sharpe, M.S. Baker, M.S. Talamonti,* M.C. Posner, Department of Surgery, University of Chicago, Chicago, IL. 2. NorthShore University HealthSystem, Evanston, IL.

Background The benefit of adjuvant therapy following resection of early stage, node-negative gastric adenocarcinoma following an R0 resection is unclear. Methods The National Cancer Data Base (NCDB) was used to identify patients with a T2N0 gastric adenocarcinoma who underwent an R0 resection. Patients treated with neoadjuvant therapy and those for whom lymph node count was unavailable were excluded from the analysis. Kaplan-Meier and Cox regression analyses were used to evaluate differences in overall survival among patients who received postoperative chemotherapy, chemoradiation or no further treatment, while adjusting for age, race, Charlson score, tumor size, grade, tumor location, type of surgery and whether ≥ 15 lymph nodes were examined. Results 8,039 patients underwent margin negative resection for T2N0 gastric cancer between 1985 and 2011. Eighty-six percent received no adjuvant therapy, 5.6% received chemotherapy only and 8.9% received chemoradiation. 72.5% had fewer than 15 nodes examined. With a median follow-up of 42.1 months, the 5-year overall survival was 53.2% for all patients, 64.5% for those who received adjuvant therapy and 51.4% for those who did not (p < 0.0001). Multivariate Cox regression identified higher Charlson score, < 15 lymph nodes examined, higher tumor grade and tumor location in the gastric cardia as factors associated with significantly decreased overall survival. Among patients who had <15 lymph nodes examined, there was a 5-year overall survival benefit for adjuvant chemotherapy (HR=0.84, p=0.046) and adjuvant chemoradiotherapy (HR=0.77, p=0.001) over no additional therapy. However, for patients who had ≥ 15 nodes examined, neither adjuvant chemotheraphy (p=0.315) nor adjuvant chemoradiotherapy (p=0.494) provided an overall survival benefit compared to resection alone. Conclusions Adequate lymph node dissection and staging is critical in directing optimal treatment of patients with T2N0 gastric cancer. Under-staging orsuboptimal resection of regional lymph nodes may explain the benefit of adjuvant therapy after an R0 resection for patients with T2N0 gastric cancer.

P343
Early Postoperative Intrapelritonal Chemotherapy (EPIC) after Cytoreductive Surgery (CRS) for Patients with Peritoneal Carcinomatosis Results in Greater Morbidity G.H. Tan,* C. Chia, W. Ong, K. Soo, M. Teo. National Cancer Centre Singapore, Singapore, Singapore.

Introduction: Peritoneal carcinomatosis (PC) is increasingly being treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemothera-apy (HIPEC) with or without early postoperative intraperitoneal chemotherapy (EPIC). Since January 2000, we have performed 140 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. Methods: A prospective database of consecutive patients undergoing CRS + HIPEC in a single institution between January 2000 and July 2013 was reviewed. Patients included in the study were treated between January 2008 to July 2013, in order to eliminate learning curve bias. Our primary end point was postoperative complication rates. Results: 72 patients who underwent CRS + HIPEC for OC of ovarian, colorectal, appendiceal, mesothelioma and primary peritoneal origins were included in the study. 48 patients received EPIC after CRS + HIPEC, and 34 patients did not receive EPIC. HIPEC was with mitomycin C or cisplatin, and EPIC was with 5-FU or oxaliplatin, depending on the primary tumour. Overall, 29 of 72 patients (40%) suffered postoperative complications, however the rate of high-grade complications was significantly higher in the EPIC group (56% vs. 15%, p=0.014). Hospitalization duration was also significantly longer in the EPIC group (16 days vs. 12 days, p=0.002). Conclusion: The use of EPIC after CRS + HIPEC for PC is associated with a significantly increased rate of high-grade complications, and results in longer hospitalization.

P344

Introduction: Laparoscopic (lap) resection is widely accepted for early, dis-tal gastric cancer, but remains controversial for locally-advanced and proximal tumours, which are more common in Western patients (pts). This study aimed to compare outcomes following lap versus open gastrectomy in West-een pts with gastric adenocarcinoma. Methods: Ninety consecutive pts who underwent lap gastrectomy from Nov 2005 to April 2013 were compared with 90 pts who had open resection during the same time period. Pts were matched for age, stage, body mass index, and procedure (distal versus total gastrectomy). Endpoints were short and long term perioperative outcomes. Results: Overall, 68 pts (38%) had locally-advanced disease (stage II or III), and 54 (30%) had proximal tumors. Total gastrectomy was performed in 56 pts (31%). There was no difference in the use of neoadjuvant therapy between the groups (26% lap vs 36% open). In the lap group, operative time was longer (median 240 vs 165 minutes; p < 0.01), and blood loss was less (100 vs 150 mL; p < 0.01). There was no difference in number of lymph nodes retrieved (median 20 in both groups). Duration of epidural use was less in the lap group (3 vs 4 days; p = 0.02). Minor complications were less in the lap group in the early (27% vs 16%) and late (17% vs 7%) postoperative periods. There were no dif-ferences in major complications or 30-day mortality. Length of stay was less in the lap group (5 versus 7 days) but this was not statistically-
significant. Adjuvant therapy was given to 40% of pts in the lap group vs 26% in the open (p = 0.01). Median follow-up for survivors was 18.8 months (31.1 for open, 11.0 for lap). There was no difference in RFS or DSS. In a subset analysis of 68 pts with stage II/III disease, lap resection was associated with a higher likelihood of receiving adjuvant therapy than open (82% versus 76%; p < 0.01). Conclusions: Lap gastrectomy for gastric adenocarcinoma was associated with decreased blood loss, pain, and morbidity, and a greater likelihood of receiving adjuvant therapy compared to open. These data suggest that the lap approach is safe and effective for select pts with locally-advanced and proximal tumors.

**Categorical variables expressed as median (range).**

---

**P345**

**Ethnicity is the Strongest Predictor of Lymph Node Status in Patients with Early Gastric Cancer**


**INTRODUCTION:** Ethnicity has long been suspected to affect survival in patients with gastric adenocarcinoma. However, the clinicopathological impact of ethnicity on early gastric cancer (EGC) is not known. This study aims to assess if ethnicity carries sufficient prognostic implication to influence current treatment strategies for EGC. METHODS: From 2000 to 2013, 1010 patients were registered in the Gastric Cancer Tumor Registry. Of these, 280 underwent gastrectomy performed by US surgeons and 102 patients (10.1% of all gastric cancer patients) had pathological confirmation of EGC by US pathologists. A retrospective analysis of pathological and clinical prognostic indicators was performed. RESULTS: The study population consisted of 37 (36%) Asians and 65 (64%) non-Asians (26 (26%) Caucasians, 25 (25%) Hispanics, 13 (13%) African-Americans, and one (1%) Pacific Islander). Of these, one (4.4%) Asian and 3 (9.3%) non-Asians with T1a lesions had lymph node metastasis (LNM) (p = 0.47), while one (7.1%) Asian and 16 (48.9%) non-Asians with T1b lesions (p = 0.007). Overall, 2 (5.4%) Asians and 19 (29.2%) non-Asians had LNM (p = 0.004). The mean number of lymph nodes retrieved was 15.7 in Asians and 17.6 in non-Asians (p = 0.473). Univariate analysis comparing the clinicopathological characteristics in each group did not reveal significant difference regarding histotype, size, grade, location, morphology, or lymph-vascular invasion, except for the LNM rate and mean body mass index (23.2 in Asian versus 26.6 in non-Asian, p = 0.0001). Multivariate analysis showed that age (OR, 0.901; 95% CI, 0.82-0.99; p = 0.03), Asian ethnicity (OR, 0.0001; 95% CI, 0.0001-0.49; p = 0.03), tumor size (OR, 2.24; CI, 1.13-4.45; p = 0.02), presence of lymphovascular invasion (OR, 31.1; CI, 12.4-774; p = 0.04) were significant predictors for LNM. CONCLUSIONS: This unique study demonstrated that Asian ethnicity in EGC is associated with a significantly decreased rate of LNM in comparison to non-Asians, despite similar histopathological characteristics of each group, suggesting that non-Asian ethnicity may be an independent predictor for LNM, possibly due to more aggressive tumor biology.
**P347**

Loss of 5-Lipoxygenase Reduces Pancreatic Neoplasia with Low and High Levels of Omega-6 Fatty Acids through a Pro-survival Mechanism


Introduction: High omega-6 (ω-6) diets yield elevated serum levels of arachidonic acid and are metabolized to leukotrienes by 5-lipoxygenase (5-LO), an enzyme that is upregulated in human pancreatic cancer. Diets rich in ω-6 fatty acids have been shown to increase proliferation in pancreatic cancer (PC) and neoplastic cells both in vitro and in vivo. This study aims to determine the effect of 5-LO deletion on pancreatic lesions in a mouse model, including mice fed high ω-6 diets, and in human pancreatic duct epithelial (HPDE) cells treated with fatty acids (FA) with and without the 5-LO activating protein (FLAP) inhibitor, MK-886. Methods: EL-Kras/5-LO null and wild type mice were sacrificed at age 6-9 months of age and evaluated for number of pancreatic lesions. Some mice were fed high fat diets with varying ω-3:ω-6 FA ratios: 1:125 (high ω-6), 2.5:1 (high ω-3), or 1:15 (control). In vitro, HPDE cells were treated for 48 hours either with FA alone or FA with MK-886. Cells lysates were analyzed for pAKT, a pro-survival marker, expression using Western blot analysis. Results: The EL-Kras/5-LO-/- mice were found to have significantly fewer lesions compared to heterozygous and wild-type mice. Among the EL-Kras/5-LO-/- mice, those fed a high ω-6 diet were found to have significant increase in lesions compared to the group fed a high ω-3 diet. In vitro, HPDE cells treated with FA and MK-886 were found to have decreased levels of pAKT compared to those cells treated with FA alone. Conclusions: Complete loss of 5-LO in a preclinical setting led to reduced frequency of mutant Kras-induced pancreatic lesions, implying a similar response in developing neoplastic lesions in human pancreas. Furthermore, a high ω-6 diet resulted in increased pancreatic lesions compared to a high ω-3 diet in the presence of a 5-LO knockout, suggesting that 5-LO contributes to pancreatic tumorigenesis, though this is not solely responsible for lesion formation (Cox-2). Finally, human pancreatic ductal cells recapitulated in vivo findings and suggest that the effects of 5-LO may function through pAKT.

**P348**

Syndecan-1 Liposomes Specifically Target Pancreatic Adenocarcinoma


Introduction: Nanoparticles that target extracellular receptors have emerged as a novel approach in the treatment and imaging of solid tumors. However, most current imaging modalities have limited resolution to study nanoparticle accumulation within tumors. Multispectral Optoacoustic Tomography (MSOT) is a recent imaging advance that promises tissue resolution up to 150 μm. In this study, we hypothesized that Syndecan-1 ligand would effectively target insulin-like growth factor 1 receptors (IGF1-R) overexpressed in pancreatic tumors, and using MSOT we evaluated Syndecan-1 liposomes as vehicles for targeted drug delivery. Methods: IGF1-R expression on multiple pancreatic cell lines was demonstrated with Western blot, with cell binding of Syndecan-1 labeled liposomes confirmed in vitro by flow cytometry. Luciferase-expressing S2VP10 cells were then orthotopically injected into the pancreas of SCID mice. At day 14 post-implantation, the mice were systemically injected with Syndecan-1 labeled liposomes encapsulating CF-750 dye. Delivery and uptake of Syndecan-1 liposomes was evaluated in vivo with MSOT at 6 hour intervals and confirmed with fluorescent imaging. Tumor uptake of liposomes was confirmed ex vivo and compared to off-target accumulation. Results: IGF1-R was well expressed on S2VP10 cells on western blot compared to controls. Flow cytometry of S2VP10 cells incubated with Syndecan-1 liposomes demonstrated increased dye uptake compared to cells exposed to naked liposomes alone (79.0% vs 27.6%), indicating successful cell binding in vitro. Upon in vivo injection of Syndecan-1 liposomes, accumulation within the pancreatic tumor was observed using MSOT as early as 6 hours after injection, with peak accumulation at 12 hours (Fig. 1). Ex vivo fluorescent imaging of the pancreatic tumors confirmed dye uptake within the tumor (4100 counts/sec) and decreased uptake within the liver (36 counts/sec) and kidney (670 counts/sec). Conclusion: High-resolution axial imaging using MSOT demonstrates preferential accumulation of Syndecan-1 liposomes throughout pancreatic tumors. These targeted liposomes show promise as a drug delivery system for treating pancreatic adenocarcinoma.

**P349**

Serum MMP7 as a Preoperative Prognostic Marker for Patients with Pancreatic Ductal Adenocarcinoma


Introduction: Elevated serum matrix metalloproteinase 7 (MMP7) has been reported to be associated with metastatic pancreatic ductal adenocarcinoma (PDA). We evaluated preoperative serum MMP7 level as a prognostic marker in PDA patients with potentially resectable disease and compared its utility with preoperative levels of cancer antigen 19-9 (CA 19-9). Methods Preoperative MMP7 were measured from 134 consecutive patients from 2004-2008 who had available serum samples. These patients had resectable disease as determined by preoperative imaging. CA 19-9 results were available for 92 patients. Patients were stratified into a poor outcome group (PG) defined by unresectable disease at operation or recurrence-free survival (RFS) <12 months or a favorable outcome group (FG) where RFS >12 months. Wilcoxon rank-sum test and receiver operating characteristics (ROC) curve were used for analysis. Results Advanced T stage, nodal disease, and the presence of vascular invasion were associated with higher MMP7. Area under ROC for MMP7 as a prognostic marker for PG was 0.60 (0.496 to 0.70). When MMP7 was >13.5 ng/mL, the result was 97% specific for PG and the positive predictive value (PPV) was 95%. Twenty of 134 patients (15%) had MMP7 >13.5 ng/mL. At operation, 3 patients had distant disease and 5 had locally unresectable (LU) tumors. Of the 12 patients resected, 11 had RFS <12 months. When CA 19-9 was >700 U/mL, it was 96% specific for PG and the PPV was 95%. Twenty-one of 92 patients (23%) had CA 19-9 >700 U/mL. At operation, 3 had metastases and 3 had LU disease. Of the 13 patients resected, 14 had RFS >12 months. Using both assays (either MMP7 >13.5 ng/mL or CA 19-9 >700 U/mL), the sensitivity for PG increased from 19% and 30%, respectively, to 46%. MMP7 >13.5 ng/mL correctly predicted PG in 8 of 16 patients who had preoperative CA 19-9 <155 U/mL and in 3 of 16 patients with normal CA 19-9 (<37 U/mL). Conclusion Elevated serum MMP7 was associated with poor outcomes in patients who presented with radiographically resectable disease. MMP7 and CA19-9 may be used together to more accurately stratify patients prior to operation.
Very Elevated Serum MMP7 and CA 19-9 Are Highly Specific in Predicting Poor Outcomes in PDA patients

<table>
<thead>
<tr>
<th>MMP7 Cut-Off</th>
<th>CA 19-9 Cut-Off</th>
<th>Combined Cut-Off</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;13.5 μg/mL</td>
<td>&gt;35.5 μg/mL</td>
<td>&gt;13.5 μg/mL</td>
</tr>
<tr>
<td>700 U/mL</td>
<td>&gt;1700 U/mL</td>
<td>&gt;700 U/mL</td>
</tr>
<tr>
<td>557 (40%)</td>
<td>851 (60%)</td>
<td>557 (40%)</td>
</tr>
</tbody>
</table>

Patients: Sensitivity 99%, Specificity 96%
PMP: 99%, PNP: 95%
PPV: Positive Predictive Value; NPV: Negative Predictive Value


Background: The purpose of this study is to evaluate the impact of a multidisciplinary clinic (MDC) on the treatment of patients with pancreatic ductal adenocarcinoma (PDA). We hypothesized that early multidisciplinary input into clinical decision making might improve the time to treatment, clinical trial participation, utilization of multi-modality therapy, increase utilization of neoadjuvant therapy, and survival. Methods: Using cancer registry data, patients with PDA from 2008-2012 were analyzed. Outcomes of patients evaluated at the MDC were compared to patients not evaluated at the MDC (non-MDC). Results: 1408 patients were identified: 557 (40%) MDC and 851 patients (60%) non-MDC. MDC were younger than non-MDC (68 vs 70; p=0.0045). MDC were more likely to be an earlier stage than non-MDC (p=0.0005): I – 4% vs 4%, II – 54% vs 43%, III – 11% vs 9%, and IV – 32% vs 44%. MDC were more likely to participate in a clinical trial than non-MDC (28% vs 14%; p<0.0001). MDC were more likely to receive treatment than non-MDC (90% vs 71%; p=0.0001). More MDC received neoadjuvant therapy than non-MDC (16% vs 8%; p=0.0001). MDC were more likely to receive 2 (38% vs 24%; p<0.0001) or 3 (12% vs 9%; p=0.018) types of therapy than non-MDC. No difference in median time from diagnosis to first treatment in MDC than non-MDC (0.95 vs 0.92 mos; p=0.69). After adjusting for age, stage, and therapy, no statistical difference in median DFS (17 vs 12 mos; p=0.11), time to recurrence (38 vs 34 mos; p=0.075), or OS (41 vs 35 mos; p=0.134) was seen. Conclusions: Patients evaluated in a MDC were more likely to receive treatment, multimodality therapy, neoadjuvant therapy, and participate in a clinical trial. Evaluation in an MDC did not delay treatment or change survival.

The Effect of Perioperative Transfusion on Recurrence and Survival following Gastric Cancer Resection: A 7-institution Analysis of 765 Patients From the U.S. Gastric Cancer Collaborative


Background: Whether perioperative blood transfusion has a negative prognostic effect on recurrence and survival in patients undergoing resection of gastric adenocarcinoma (GAC) is unknown. Methods: All patients who underwent resection for GAC from 2000-2012 at 7 institutions were identified. The effect of transfusion on recurrence-free (RFS) and overall survival (OS) in the context of adverse clinicopathologic variables was examined by univariate (UV) and multivariate (MV) regression analyses. Results: Out of 765 patients, 765 underwent curative intent, R0 resection. Median follow-up for survivors was 44 months; 30-day deaths were excluded. Median estimated blood loss (EBL) was 250cc and 166 patients (22%) received perioperative RBC transfusions. 5-yr RFS was 51% in transfused and 61% in non-transfused patients (p=0.01). Median OS was decreased in patients receiving transfusions (19 vs 50 months, p=0.001). On MV analysis, transfusion remained an independent risk factor for decreased RFS (HR 2.8; 95% CI: 1.2-6.5; p=0.01) and decreased OS (Table), regardless of EBL or need for splenectomy. Timing (intraoperative vs postoperative) and volume (number of units) did not alter the effect of transfusion on survival. Non-transfused patients were more likely to receive adjuvant therapy (56% vs 44%; p=0.01). Conclusion: Perioperative blood transfusion is associated with decreased recurrence-free and overall survival following resection of gastric cancer, independent of adverse clinicopathologic factors. This supports the judicious use of perioperative transfusion during resection of gastric cancer.

Fluorescence-guided Surgery of Pancreatic Cancer using Activatable Cell Penetrating Peptides (ACPPs) in Orthotopic Mouse Models

C.A. Metildi,1 S. Kaushal,1 C.N. Felsen,1 Q.T. Nguyen,2 R.Y. Tsien,3 R.M. Hoffman,2 M. Bouvet,1,4 1. Surgery, University of California San Diego, La Jolla, CA; 2. University of California San Diego and Anti-Cancer, Inc., San Diego, CA.

Introduction: We have previously developed fluorescence guided surgery (FGS) of pancreatic cancer using GFP and fluorescent antibodies. In this report, we evaluated the efficacy of activatable cell penetrating peptides (ACPPs), cleavable by MMP-2 and MMP-9, conjugated to Cy5 fluorophores to label primary pancreatic cancer for FGS in orthotopic mouse models. Methods: We established orthotopic mouse models of human pancreatic cancer using tumor fragments of the human Mia PaCa-2-GFP pancreatic cancer cell line. Two weeks after tumor implantation, the tumors were resected with bright light surgery (BLS) or FGS. FGS was performed with a fluorescence-dissecting microscope two hours after periorbital injection of ACPPs. Completeness of resection was assessed at the time of surgery by visualizing GFP-expressing cells in the surgical site. Postoperatively, whole body imaging of the mice was used to assess for recurrence. At eight weeks, mice were sacrificed to evaluate pancreatic tumor burden, as well as local and distant recurrence. Results: Cy5-conjugated ACPPs permitted clear visualization of tumor margins for FGS. With FGS, no residual tumor was detected in the postoperative surgical site in all 16 mice. One mouse out of 16 undergoing BLS had evidence of residual tumor postoperatively. At eight weeks, mice in the BLS group demonstrated larger primary tumors compared to mice in the FGS group (1.72 g vs 0.58 g; p=0.02). Mean disease-free survival (DFS) was significantly lengthened from 5.33 weeks in the BLS group to 7.38 weeks in the FGS group (p=0.02). Furthermore, recurrence rates were lower in the FGS group (38% vs 73%, p=0.049). This translated into a lower local and distant recurrence rate for FGS compared to BLS (31% vs 67% and 25% vs 60%, respectively). Conclusions: We have shown that ACPPs can effectively label primary pancreatic tumors for improved resection results and improved outcomes post-resection. ACPPs have potential to improve surgical outcomes in patients...

Introduction: Staging laparoscopy (SL) can improve accuracy of staging in pancreatic head adenocarcinoma (PHAc) and can help avoid unnecessary laparotomies in patients with occult metastatic or unresectable disease. However, the added value of staging laparoscopy in the modern era of high-quality cross-sectional imaging is not well defined. Methods: Patients undergoing treatment with curative intent for PHAc between 2005 and 2012 were reviewed, including patients who underwent pancreaticoduodenectomy with or without SL or failed laparotomy (FL) with or without SL. Only imaging performed at our institution was reviewed. Pancreatic protocol CT (PPCT) was defined as oral and IV contrast-enhanced thin-slice helical CT obtained in arterial, pancreatic parenchymal and portal venous phases. High-quality preoperative imaging (HQPI) was defined as either PPCT or MRI/MRCP. Results: Between 2005 and 2012, 528 patients with potentially resectable PHAc went to the OR for staging and/or resection, of which 473 patients (90%) had HQPI (Figure). One hundred and forty-one patients (30%) underwent laparoscopy, which showed unresectable disease in 44 patients (31%). The rate of unresectable disease was significantly higher among patients who underwent SL as a separate procedure (n=30/37, 81%; p<0.0001) when compared with those who underwent SL as an add-on to planned laparotomy (n=14/105, 13%; p=0.0001). The most common findings on positive SL were liver metastases (38%), locally-advanced unresectable disease (25%), and positive cytology (7%). Of the 97 patients (69%) with negative SL, 19 (20%) went on to failed laparotomy. Among these patients, the most common reasons for failure were unresectable vascular involvement (47%), liver metastases (21%), and lymph node metastases (16%). Conclusions: In the era of high-quality cross-sectional imaging, SL identified occult unresectable disease in 31% of patients with pancreatic head adenocarcinoma who were selected to undergo the procedure. Therefore, SL remains a valuable tool in identifying advanced disease and preventing laparotomy in select patients with pancreatic head adenocarcinoma.

Risk Factors for Non-infectious Wound Complications following Open Upper Gastrointestinal Surgery: Subset Analysis of a Phase 3 RCT A. Takeno,1* F. Junya,2 H. Hirao,3 H. Hatano,4 S. Endo,3 J. Kawada,5 M. Yamasaki,6 S. Kobayashi,7 Y. Akamaru,7 T. Mizushima,8 J. Shimizu,9 K. Umeshita,7 T. Tsujinaka,10 T. Ito,3 M. Mori,3 Y. Doki.7 1. Surgery, Kansai Rosai Hospital, Amagasaki, Hyogo, Japan; 2. Surgery, NTT West Osaka Hospital, Osaka, Japan; 3. Surgery, Osaka National Hospital, Osaka, Japan; 4. Surgery, Toyonaka Municipal Hospital, Osaka, Japan; 5. Surgery, Higashiosaka City General Hospital, Osaka, Japan; 6. Surgery, Osaka General Medical Center, Osaka, Japan; 7. Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Osaka, Japan; 8. Surgery, Osaka-Koseinenkin-Hospital, Osaka, Japan; 9. Surgery, Osaka Rosai Hospital, Osaka, Japan; 10. Surgery, Katsuragi City Hospital, Osaka, Japan; 11. Complementary and Alternative Medicine, Graduate School of Medicine, Osaka University, Osaka, Japan.

Introduction: A phase 3 RCT with the incidence of wound complications (WCs) following open gastrointestinal (GI) surgery, depending on whether subcuticular sutures or staples are used, as a primary endpoint was performed. (UMIN000002480) We investigated risk factors for non-infectious WCs following open upper GI surgery as a subset analysis of the main trial. Methods: We assessed WCs of 789 patients undergoing elective open upper GI surgery out of 1080 patients enrolled in the main trial. Risk factors for non-infectious
WC were investigated by univariate and multivariate analysis in several clinical factors. Results: The types of diseases were 771 gastric cancers, 14 gastrointestinal stromal tumors, and 4 others. The types of procedures were 402 distal gastrectomy, 289 total gastrectomy, 35 proximal gastrectomy, and 54 other. WC occurred in 68 of 789. Forty-three were superficial surgical site infections, and 25 were non-infectious WCs (14seroma, 7 wound separation, 1 hematoma, and 3 others). Types of wound closure (subcuticular sutures 6/376, stapler 19/413, RR: 0.336, 95%CI: 0.133-0.851, p=0.022) and drain insertion (drain insertion 14/661, no drain 11/128, RR: 0.230, 95%CI: 0.102-0.518, p=0.0004) showed significant differences in the incidence of non-infectious WCs in univariate analysis. These factors were also identified as independent risk factors in multivariate analysis (subcuticular sutures RR: 0.337, 95%CI: 0.132-0.861, p=0.023, drain insertion RR: 0.223, 95%CI: 0.092-0.543, p=0.001)

Conclusions: Subcuticular sutures and drain insertion are useful to reduce the risk of non-infectious WCs following open upper GI surgery.

P357

The Effect of Postoperative Morbidity on Survival after Resection for Gastric Adenocarcinoma: Results from the U.S. Gastric Cancer Collaborative L.X. Jin, 1* L.E. Moses, 1 Y. Yan, 1 M.H. Squires, 1 S.M. Weber, 2 M. Bloomston, 2 G. Poulshides, 1 K.J. Votanopoulos, 1 T. Pawlik, 1 W.G. Hawkins, 1 D. Linehan, 1 S.M. Strasberg, 2 A.W. Archer, 1 A. Ejaz, 1 D.A. Kooby, 2 C.R. Schmidt, 2 D.S. Swords, 2 D.J. Worhunsky, 1 S.K. Maithel, 1 R.C. Fields, 1 1. Washington University in St. Louis, St. Louis, MO; 2. Emory University, Atlanta, GA; 3. Stanford University, Palo Alto, CA; 4. The Ohio State University Comprehensive Cancer Center – The Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH, 5. Johns Hopkins University, Baltimore, MD; 6. University of Wisconsin School of Medicine and Public Health, Madison, WI; 7. Wake Forest University, Winston-Salem, NC.

Background: The negative impact of postoperative complications (POCs) on survival is well documented for many cancer types, but has not been well described in gastric cancer. Here, we evaluated the effect of POCs on survival after surgery for gastric cancer in a cohort of patients from a multi-institutional database. Methods: Patients who underwent surgery with curative intent for gastric adenocarcinoma between 2000-2012 from participating institutions of the U.S. Gastric Cancer Collaborative were analyzed. Patients who died within 30 days of surgery were excluded. Ninety-day postoperative complication data were collected. Survival probabilities were estimated by Kaplan-Meier analysis and compared using the log-rank test. Results: A total of 853 patients from seven institutions met inclusion criteria. Median follow-up was 28 months. The overall complication rate was 40% (n=344). The most frequent complications were infectious (25%, including surgical site infection [8%]), and anastomotic leak (6%). Seven percent of patients underwent reoperation during the same hospitalization. Five-year overall survival (OS) for patients without postoperative complications was 54%, compared with 39% for patients with POCs (p=0.001). Disease free survival (DFS) at five years was 61% for patients without POCs compared to 49% in patients with POCs (p=0.002). Patients without POCs were significantly more likely to receive adjuvant therapy (55% vs 42%; p=0.001). Conclusions: In a large, multi-institutional cohort, POCs were associated with decreased survival in patients undergoing surgery for gastric adenocarcinoma. This may be due, in part, to the negative impact of complications on the receipt of adjuvant therapy. Efforts aimed at reducing perioperative morbidity are important not only for short-term surgical outcomes, but also for enhancing long-term oncologic outcomes in patients with gastric cancer.

P358

Central Pancreaticectomy and Distal Pancreatectomy for Pancreatic Neck Lesions Result in Equivalent Long-term Pancreatic Function and Fistula Formation M.P. Kim, 1* H. Tran Cao, 1 M.H. Katz, 1 F.W. Pisters, 2 S.A. Curley, 1 J. Vauthey, 1 T. Aloia, 2 D. Evans, 1 J.E. Lee, 1 J.B. Fleming, 1 1. The University of Texas M.D. Anderson Cancer Center, Houston, TX; 2. Medical College of Wisconsin, Milwaukee, WI.

Introduction: The surgical management of pancreatic neck or proximal body lesions is controversial and consists of either central pancreaticectomy (CP) or distal pancreatectomy (DP). Compared to DP, advocates of CP cite potential benefits as spleen conservation and putative long-term preservation of endocrine and exocrine pancreatic function. We compared the incidence of postoperative pancreatic fistulae (POPF) and endocrine/exocrine insufficiency among patients who underwent CP versus DP. Methods: A retrospective review of a prospectively maintained database identified patients who underwent CP or DP for primary lesions of the pancreas between 1994 and 2012. Clinicopathologic data from both patient groups were analyzed for long-term utilization of pancreatic enzyme replacement therapy (PERT) and insulin/oral hypoglycemic agents. Patients were assessed for POPF formation based on clinical grade B or C criteria. Results: Indications for CP (n=20) included pancreatic neuroendocrine tumor (PNET, n=9), intraductal papillary mucinous neoplasm (IPMN, n=6), solid pseudopapillary neoplasm (SPN, n=3), and serous cystadenoma (SC, n=1). Indications for DP (n=195) included PNET (n=105), mucinous cystic neoplasms (MCN, n=54), SPN (n=15), IPMN (n=9), and other (n=12). Median follow-up times for CP and DP patients were 25.6 and 50.3 months, respectively. The incidence of POPF in the CP patient group was 18% compared to 20% in the DP group (p=0.41). Postoperative exocrine insufficiency as determined by long-term use of PERT and DP groups were 15% and 18.5%, respectively (p=0.35). Postoperative endocrine insufficiency managed with insulin and/or oral hypoglycemic agents was 25% in the CP group compared to 32.3% in the DP group (p=0.25). All patients who experienced POPF were successfully managed by percutaneous drainage. Conclusion: DP permits successful oncologic resection of pancreatic neck lesions in appropriately selected patients without an added risk of long-term exocrine and endocrine insufficiency. The incidence of POPF is comparable among patients who underwent CP or DP and can be managed non-operatively.

P359

Bi-specific T Cell Therapy for Pancreatic Cancer S. Mohammed, 1* U. Anurathapan, 1 R. Chan, 1 R. Mucharl, 1 H. Heslop, 1 C. Rooney, 1 M.K. Brenner, 1 A. Leen, 1 J. Vera, 1 1. Department of Surgery, Baylor College of Medicine, Houston, TX; 2. Center for Cell and Gene Therapy, Baylor College of Medicine, Houston, TX.

Background: Adoptive T cell therapy directed to tumor-associated antigens (TAAs) by transgenic expression of chimeric antigen receptors (CARs) can produce tumor response, even in patients with resistant disease. However, targeting a single TAA may lead to selection of the nontargeted TAA population (TAAs) by transgenic expression of chimeric antigen receptors (CARs) can produce tumor response, even in patients with resistant disease. However, targeting a single TAA may lead to selection of the nontargeted TAA population. Bi-specific T-cell therapy targeting two distinct TAAs, MUC1 and PSCA, both overexpressed in pancreatic cancer, may enhance the potency of adoptive immunotherapy. Methods: Peripheral blood mononuclear cells were transduced with retroviral vectors encoding CAR-MUC1 or CAR-PSCA. Short and long-term anti-tumor activity was assessed by chromium release and co-culture assay, respectively, using the tumor cell lines CAPAN1, K562 and DU145. Results: After retroviral transduction, T cells stably expressed CAR-MUC1 (83±4%) and specifically killed MUC1+ cell lines, CAPAN1 and DU145, but not MUC1- 293T cells (35±5%, 23±4% and 3±2% specific lysis, respectively, 10:1 Effector:Target). When MUC1+ targets were cultured with either MUC1/mOrange+ or PSCA/GFP+, which illustrated exquisite specificity of T-cells but a weakness when targeting a heterogeneous tumor. There-
respectively, 10:1 E:T). Finally, we assessed anti-tumor activity when both CAR-modified products were combined. When tumor cells expressing both TAAs were treated with CAR-MUC1 and CAR-PSCA T-cells, we saw additive anti-tumor effects with 76±6% killing of CANP1 versus only 35±6% and 54±6% killing of CANP1 and CAR-PSCA T-cells individually. Conclusion: The combination of CARs that target two distinct TAAs expressed on cancer cells (PSCA and MUC1) may prevent tumor immune escape and enhance the potency of adoptive T cell transfer.

P360 Immune Response in Metastatic Regional Lymph Nodes from Pancreatic Adenocarcinoma may Predict Patient Outcome E. Nizi, N. Sternbach, F. Gerstenhaber, G. Lahat, J. Klaueunser. Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel.

Background: Regional lymph nodes (RLNs) may be considered the first site for metastasis from primary tumor. As RLNs are exposed to tumoral antigens and contain all immunological machinery to mount an effective immune response, we hypothesized that tumor-immune interaction in RLNs could suggest tumor escape or immunity. Methods: Histological sections from metastatic RLNs of 55 pancreatic ductal adenocarcinoma (PDAC) patients were retrospectively evaluated for architectural parameters, peritumoral T, B and dendritic cells, and T helper lineage markers by immunohistochemistry. Histological data was correlated with overall survival (OS) expressed in months. Results: Primary tumor size and perivascular invasion did not correlate with OS in patients with RLN metastases, however, perineural invasion did; 29±2.3 vs. 13.9±1.5 (p<0.001). Preserved RLN architecture was associated with longer OS vs. tumor-induced architectural changes; 39±9.6 vs. 23.5±2.0 (p<0.05), respectively. The presence of desmoplasia in RLN did not confer adverse outcome (OS=21 vs.3.5±2 for patients without vs. OS=19±1.87 for those with desmoplasia, p=0.66). High number of peritumoral CD8+ cells in RLN was associated with longer survival; 22±7.15 vs. 14.8±2.0 (p=0.05). Accordingly, T helper skewing toward Th1, as measured by T-bet expression, had the same effect on OS. The number of CD20+ and CD4+ peritumoral cells in RLN was not associated with prognosis, possibly due to the large number of the latter in intact LN s. Conclusions: CD8+ tumor-infiltrating cells and Th1-deviated immune response in RLN may point to a subgroup of PDAC patients with protective immune response. These findings may indicate that tumor immunity in RLN affects prognosis.


Background: Use of perioperative chemotherapy (CTx) alone versus chemoradiation therapy (cXRT) in the treatment of resectable gastric cancer remains varied. We sought to define the utilization and effect of CTx alone versus cXRT in the treatment of resectable gastric cancer. Methods: Using the U.S. Gastric Cancer Collaborative database, we identified 505 patients between 2000 and 2012 with gastric cancer who received perioperative CTx alone whereas the remaining 294 (58%) patients received 5-FU based cXRT. Patients between 2000 and 2012 with gastric cancer who received perioperative CTx alone whereas the remaining 294 (58%) patients received 5-FU based cXRT. Conclusion: receipt of cXRT was associated with improved long-term OS (CTx alone: 21 months vs. cXRT 45 months; p=0.001). In the propensity-matched multivariate model that adjusted for tumor size, T-stage, and nodal status, cXRT remained associated with an improved long-term disease-free (HR 0.43) and overall (HR 0.41) survival (both P<0.001). Conclusions: XRT was utilized in 58% of patients undergoing curative-intent resection for gastric cancer. Using propensity-matched analysis, cXRT was an independent factor associated with improved recurrence-free and overall survival.

P362 Usefulness of Laparoscopic Narrow-band Imaging for the Diagnosis of Peritoneal Metastasis in Patients with Gastric Cancer H. Kikuchi, K. Kaniwa, S. Miyazaki, I. Iino, H. Yoshihiro, M. Ohta, T. Sakaguchi, H. Konno. Second Department of Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan.

INTRODUCTION: The peritoneum is one of the most frequent and lethal locations of recurrence in patients with advanced gastric cancer. Accurate diagnosis of peritoneal metastasis is important for improving outcomes, but it is difficult using conventional modalities. Staging laparoscopy is often used to diagnose peritoneal metastasis in patients with advanced gastric cancer, but accurate detection of metastasis can be difficult. We evaluated the usefulness of laparoscopic narrow-band imaging (NBI) versus conventional laparoscopic white-light imaging (WLI) for the diagnosis of peritoneal metastasis. METHODS: We excised 25 white nodules from the parietal peritoneum of 17 patients with gastric cancer and suspected peritoneal metastasis. The WLI and NBI findings were compared with the pathological findings. RESULTS: All the peritoneal lesions examined were observed as white nodules on WLI. Intraluminal vessels were evaluated by WLI and NBI for: (1) vessel dilatation, (2) vessel tortuosity, (3) vessel heterogeneity, and (4) brown spots. Each individual abnormal finding had a diagnostic accuracy of less than 76% with or without NBI. Detection of any one abnormal finding had a sensitivity, specificity, and accuracy of 50%, 84.6%, and 68%, respectively, on WLI and 91.7%, 69.2%, and 80%, respectively, on NBI, for detection of peritoneal metastasis. Detection of any one abnormal finding on NBI plus clear demarcation of the nodule on WLI had a sensitivity of 91.7%, specificity of 92.3%, and accuracy of 92.3% for detection of peritoneal metastasis. Pathological examination showed that a brown spot detected on NBI correlated with dilated vessels around cancer cells. CONCLUSIONS: NBI was more sensitive for the detection of dilated microvessels than WLI. We developed a new diagnostic strategy for accurate detection of peritoneal metastasis using four NBI findings (vessel dilatation, vessel tortuosity, vessel heterogeneity, and brown spot), and clear demarcation of WLI NBI could be an important tool for the diagnosis of peritoneal metastasis during staging laparoscopy.

P363 A Novel AMP Kinase Activator Sensitizes Pancreatic Cancer to Radiation L.A. Shirley, M. Yang, C. Chou, A. Estrada-Bernal, T. Williams, M. Bloomston, C. Chen. 1. The Ohio State University Wexner Medical Center, Columbus, OH; 2. The Ohio State University College of Pharmacy, Columbus, OH.

Background: Metformin, through activation of adenosine monophosphate kinase-α (AMPKα), inhibits the mTOR pathway, resulting in radiosensitization in various cancer types, including breast, lung, and sarcoma. We used a newly derived small molecule activator of AMPKα, OSU-53D, to assess its role as a radiosensitizer in pancreatic cancer. Methods: We calculated in vitro radiation dose response of OSU-53D in three pancreatic cancer cell lines (MiaPaCa-2, BxPC-3, AsPC-1). Sub-therapeutic concentrations of either OSU-53D or metformin were combined with increasing doses of radiation and survival determined by clonogenic assay. Cells treated with increasing concentrations of OSU-53D for 24 hours followed by 4 Gy of radiation were lysed at multiple timepoints for immunoblotting. We used immunostaining to analyze foci of the DNA damage marker γ-H2A.x in a concentration-depend
ent manner. Immunocytochemical analysis at various timepoints after combined treatment showed increased γ-H2A.X foci at 1 hour after radiation, with persistence of foci at up to 24 hours, which was not seen with radiation alone, suggesting delayed DNA damage repair. Western blot analysis revealed increased expression of the apoptosis marker cleaved PARP and autophagic marker LC3-B with increasing concentrations of OSU-53D combined with radiation. Of note, pre-treatment of pancreatic cancer cell lines with therapeutic doses of metformin followed by radiation could not recapitulate the radiosensitization observed with OSU-53D. Conclusions: Pre-treatment with a novel AMPKα activator OSU-53D increased pancreatic cancer cell killing when combined with radiation. This combination led to increased expression of markers of DNA damage, apoptosis, and autophagy, revealing possible mechanisms of action. Taken together, we demonstrate that OSU-53D is a novel radiosensitizer which could improve therapeutic response in pancreatic cancer.

### P364

*C6 Ceramide Potentiates Paclitaxel and Gemcitabine-mediated Anti-tumor Effects against Pancreatic Cancer in vivo and in vitro via Inhibition of Pro-survival PI3K/AKT/mTOR and ERK/MAPK Pathways*

H. Wanebo, S. Lu, C. Cao, D. Shrayer, W. Bowen.

1. Landmark Medical Center, Wentzowos, RI; 2. Brown University, Providence, RI.

Introduction: Survival of pancreatic cancer is about 5%, emphasizing need to develop new treatment strategies. Our studies suggest C6 Ceramide (C6Cer) may be a useful chemotherapeutic adjunct. Methods: Cell culture, MTT assay, Western Blot, SCID mouse xenograft. Results: Co-administration of Gemcitabine (Gem) or Paclitaxel (Taxol) and C6Ceramide (C6Cer) significantly increased cell death/apoptosis in pancreatic cancer (PanCa) cells (L3.6, PANC-1 and MIA PaCa-2) in vitro, compared to chemo or C6-Cer alone. Similar synergism was seen with Cetuximab (Cetux) in spite of common KRAS mutations which induce Cetux resistance. Cetux had no cytostatic effect alone in PanCa cell lines, but this was markedly enhanced by C6Cer. Combination of C6-Cer with Gem or Taxol significantly decreased p-AKT and p-GSK3α/β (PI3K/AKT pathway), p-S6 and p-4E-BP1 (mTORC1 pathway, and p-ERK (Ras/MET/ERK pathway) in L3.6 PanCa cells. Inhibitors of PI3K/Akt (LY294002), mTORC1 (rapamycin), and MEK/ERK (U0126) mimicked cytotoxic effect of C6-Cer on L3.6 cell when combined with Taxol or Gem. This was also reflected on levels of p-AKT, p-S6/p-4E-BP1, and p-ERK, where Gem alone had no effect in contrast to the combination with respective inhibitor which significantly decreased levels of target phosphoprotein. This indicates an association of effect on cell signaling pathways, including inhibition of pro-survival PI3K/AKT/mTOR and ERK/MAPK/KRAS mutant pathways enhancing cytotoxicity by Gem or Taxol. Similar in vivo results occurred in SCID mouse xenograft model growing L3.6 cell line cancers, C6 Cer with Gem or Taxol induced significant tumor regression and survival vs. chemo or C6 Cer alone. Conclusion: Results suggest that inhibition of pro-survival pathways by C6 Cer significantly enhances chemotherapeutic activity of Gem, Taxol, and Cetuximab, in vitro and in vivo. This regimen may have value in therapy against PanCa, and possibly other aggressive cancers and also suggests value of C6Cer with Taxol (not used for PanCa) or Cetuximab which is ineffective in KRAS mutant cancer.

### P365

*Does Inadequate Lymph Node Staging Impact Survival in Resected Gastric Cancer?*


1. Department of Surgery, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; 2. Department of Medicine, Veteran Affairs Medical Center, Philadelphia, PA; 3. Department of Radiation Oncology, Veteran Affairs Medical Center, Philadelphia, PA.

Introduction: Survival of gastric adenocarcinoma (GA) is significantly impacted by the number of lymph nodes (LN) examined at resection. The goal of this study was to determine whether inadequate LNS (≤15 LN) is associated with worse survival. Methods: We performed a matched cohort study using the Surveillance, Epidemiology, and End Results (SEER) database to compare patients with GA (AJCC stage I-III) with adequate LNS (≥15 LN) to those with inadequate LNS (≤15 LN). We used propensity score matching to select controls for each case leading to a matched cohort of 9,189 patients. The primary endpoint was overall survival (OS). Results: The median age for all cases was 70 years and the median follow-up was 40 months. Median OS was 36.5 months for patients with adequate LNS compared to 21.7 months for patients with inadequate LNS (log-rank p<0.001). Patients with inadequate LNS had significantly higher rates of positive surgical margins, but this did not affect OS. Multivariate analysis confirmed that inadequate LNS was associated with lower OS (HR 1.26, 95% CI 1.17–1.35; p<0.001). Of note, patients with inadequate LNS had significantly more patients with AJCC stage III (p=0.04) and more patients with lymphovascular invasion (p<0.001). Conclusion: Inadequate LNS is associated with worse OS, independent of AJCC stage and pathologic factors. Counseling patients and providers before surgery about the importance of performing adequate LNS is warranted.

*Does Inadequate Lymph Node Staging Impact Survival in Resected Gastric Cancer?*
S166 Abstracts: Poster Presentations

### P366
**Nasoenteric Catheter or Jejunostomy as a Route for Nutrition after Major Upper Gastrointestinal Operations**

**F.A. De Vasconcellos Santos,1* L.T. Lacerda,2 M. Kansaon,2 A.J. Wainstein,1 A. Drummond-Lage,1 L.J. Torres,1 M.D. Correia.3**

1. Surgery, ONCAD, Belo Horizonte, Minas Gerais, Brazil; 2. Mater Dei Hospital, Belo Horizonte, Minas Gerais, Brazil; 3. Clinics Hospital - UFMG, Belo Horizonte, Minas Gerais, Brazil.

**INTRODUCTION:** Curative treatment of upper gastrointestinal tract neoplasms is complex and associated with high morbidity and mortality. In general, the patients are already malnourished, and early postoperative enteral nutrition is recommended. However, there is no consensus concerning the best enteral access route in these cases. METHODS: A prospective randomized trial was performed from 2008 to 2012 with 59 patients who underwent esophagec-

tomy, total gastrectomy or pancreaticoduodenectomy. Four of the patients did not agree to the randomization, and 13 were excluded. Thus, of the 42 included patients, 21 received nasoenteric tubes, and 21 received jejunostomy tubes.

**RESULTS:** The two groups were similar in demographic and clinical aspects. The nasoenteric (NE) and jejunostomy groups received early enteral therapy in 71.4% and 61.9% of cases (p>0.05), respectively. The median length of enteral therapy use was lesser in the NE group (8.5 vs. 15.3 days), but the difference was not statistically significant. The NE group required the introduction of parenteral therapy more often compared with the jejunostomy group (p<0.05). Complications related to the enteral route occurred in 38% and 28.5% of patients (p>0.05) in the NE and jejunostomy groups, respectively. In the NE group, there were four losses and four tube obstructions, and in the jejunostomy group, there were two losses, four obstructions and two cases of leakage around the tube. In the latter group, patients who used the therapy for a longer time had tube complications (p<0.05) and had longer ICU and hospital stays (p<0.05).

**CONCLUSION:** In conclusion, both enteral routes are associated with the same number of complications. However, the presence of jejunostomies allows enteral therapy for longer time periods, especially when patients have complications, thus avoiding the need for parenteral nutrition.

### P367
**What is the Optimal Multimodality Approach to Siewert II/III Gastroesophageal Junction Adenocarcinoma? A Population-based Analysis**

**J. Harris,1* B. Huang,1 P.C. McGrath,1 S.P. McKenzie.2**

1. General Surgery, University of Kentucky, Lexington, KY; 2. Surgical Associates of Austin, Austin, TX.

Introduction: Despite intensive investigation, the optimal multimodal approach (MMA) to proximal gastric adenocarcinoma (PGC) remains controversial. The purpose of this study was to determine if an optimal surgical and MMA to PGC could be determined through population based analysis.

**Methods:** Using both the Surveillance, Epidemiology, End Result(SEER) and Kentucky Cancer Registries(KCR), all patients with surgical resected PGC captured from 2004-2010 were analyzed. Results: 2079 patients with resected PGC were identified from SEER and 175 patients from KCR. In both groups, the vast majority (>93%) had cancer of the cardia. Based on SEER, 285 patients underwent proximal esophagogastrectomy, 1484 patients underwent total gastrectomy with distal esophagectomy, and 310 patients underwent total gastrectomy with en bloc resection of other organs. Adjuvant radiation occurred in 44% of patients. (504 neoadjuvant, 408 adjuvant). Adjuvant radiation therapy provided a clear survival advantage in stage II/III disease (all p values <0.005). Radiation sequence and surgery type provided no clear benefit in survival. Based on the KCR analysis, inclusion of chemotherapy, alone or in concert with radiation, or as a neoadjuvant or adjuvant approach, provided no clear optimal strategy to effect survival. When all adjuvant strategies were considered, only neoadjuvant chemoradiation predicted improved survival (HR 0.46, CI 0.26-0.84).

**Conclusion:** Based on these population analyses, no optimal surgical approach to PGC impacts survival. While strategies including chemoradiation improve survival, optimal sequencing of multimodality therapy is yet to be determined.

### P368
**Evaluation of PET Response to Neoadjuvant Therapy for Patients with Gastric and GEJ Adenocarcinoma**

**J. Hernandez,1* V. Beylerli,1 D. Goldman,1 L.H. Tang,1 D.H. Ilson,1 R. Downey,1 V.E. Strong,1 M. Shah,1 M. Gönen,1 H. Schoder,1 D.G. Coit.1**

1. Memorial Sloan-Kettering Cancer Center, New York, NY; 2. Cornell University, New York, NY.

**Background:** Although neoadjuvant therapy is commonly utilized to treat localized gastric and gastro-esophageal junction (GEJ) adenocarcinoma, the implications of response to therapy as measured by PET imaging remain poorly understood.
defined. Our aims in undertaking the study were to determine if changes in PET avidity correlate with histologic response, and to determine the best predictor(s) of disease-free and overall survival. Methods: We reviewed a prospective database to identify patients with gastric and GEJ adenocarcinoma who were evaluated with PET imaging prior to and following neoadjuvant treatment. Spearman rank correlation was used to analyze the relationship between changes PET scans and histologic response. Cox proportional hazards regression was used to assess the relationship between imaging and pathologic parameters, and disease-free and overall survival. Results: Since 2002, 216 patients of median age 63 years met our criteria. At last follow-up (median 22 months, range: 0 - 119), 118 patients recurred or died. The median DFS and OS for expired patients were 7.5 months (range: 0-62) and 14 months (range: 0 - 69), respectively. Between baseline and follow-up PET imaging (median 63 days, range: 15 - 454), 170 patients were treated with chemotherapy and 46 patients with chemoradiotherapy. The median change in SUV was 43% (range: -300 - 100.0%) and the median histologic tumor response was 50% (range: 0 - 100%). No association was identified with the use of chemoradiation (as compared to chemotherapy alone) and change in SUV (p=0.8). We identified a significant relationship between change in SUV and histologic response (r=0.32, p<0.01). Furthermore, the change in SUV was related to both DFS and OS on univariate analysis, as was tumor response and pathologic stage (Table). On multivariate analysis only pathologic stage, and specifically the presence of lymph node metastases, was related to DFS (p<0.01) or OS (p<0.01). Conclusions: Following neoadjuvant therapy for gastric and GEJ adenocarcinoma, PET response is prognostic, although pathologic nodal status is the best predictor of outcome.

### Table

<table>
<thead>
<tr>
<th>OUTCOME</th>
<th>VARIABLE</th>
<th>HR (95% CI)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall Survival</td>
<td>SUV Change</td>
<td>0.95</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Tumor Response</td>
<td>0.94</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Radiation</td>
<td>1.10</td>
<td>0.71</td>
</tr>
<tr>
<td></td>
<td>Stage</td>
<td>0.70</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Disease-free Survival</td>
<td>SUV Change</td>
<td>0.96</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Tumor Response</td>
<td>0.94</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Radiation</td>
<td>1.20</td>
<td>0.42</td>
</tr>
<tr>
<td></td>
<td>Stage</td>
<td>0.23</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

P370

Clinicopathologic Characteristics and Prognostic Predictors of Survival in Patients with Stage IV Gastric Cancer: A Single Institutions Experience with Cytoreductive Surgery (CS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) C. Ihemelandu,* P. Sugarbaker.

Surgery, MedStar Washington Hospital Center, Washington, DC.

Introduction: - Most stage IV gastric cancer patients present with non-operable disease, and even in those with operable disease, rates of relapse are high and prognosis is poor. Our aim was to analyze the clinicopathologic characteristics, prognostic factors, and overall survival associated with stage IV gastric cancer Methods: - A retrospective analysis of a tumor registry for all patients treated for stage IV gastric cancer between 1991-2012 at a tertiary institution. Results: - Of 231 patients there were 127(55.0%) males vs. 104(45.0%) females. The mean age at diagnosis was 66 years. Seventy-eight (33.8%) patients presented with a signet ring vs. 153(66.2%) with an intestinal histology. Twenty-six (11.3%) patients were treated with CS and HIPEC vs. 64(27.7%) and 141(61%) respectively who were treated with surgery and systemic chemotherapy, and no surgical intervention. In univariate analysis signet ring tumors had a better overall median survival 5 vs. 3 months (p= 0.04). Amongst the cohort of patients treated with CS and HIPEC the median survival was 40 months for the signet ring histology vs. 8 months for the intestinal. Median survival time was 14 months for patients treated with CS and HIPEC vs. 6 and 2 months respectively for those treated with surgery and systemic chemotherapy or no surgery. One, 3 and 5 year survival was 51%, 38% and 29% respectively for patients treated with CS and HIPEC vs.39%, 16% and 9%, and 14%, 2% and 0% for surgery and no surgery. Significant predictors of an improved survival in multivariate analysis were a young age at diagnosis (p=0.000), treatment with CS and HIPEC (p=0.000). Gender, race, tumor pathology, use of radiation therapy and systemic chemotherapy did not achieve significant status. Conclusion: - Young age at diagnosis and use of CS and HIPEC are independent predictors for an improved overall survival in patients diagnosed with stage IV gastric cancer. Paradoxically signet ring pathology demonstrated an improved survival over the intestinal pathology when treated with CS and HIPEC.
P371
A Comprehensive Assessment of Neoadjuvant Therapy for Pancreatic Adenocarcinoma: Results from the National Cancer Database (NCDB) R.S. Lewis,* J.A. Drebik, D.L. Fraker, C.M. Vollmer. Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA.

Introduction: Limited, early experience from specialty centers suggests neoadjuvant therapy for pancreatic adenocarcinoma (PDAC) holds promise for enhancing patient selection, improving survival, or both. A comprehensive, contemporary assessment of its utilization on a national scale is lacking. Methods: Surgical patients with diagnoses of invasive PDAC between 1998-2010 were identified from the NCDB. Neoadjuvant patients (NA) were defined as those who received chemotherapy and/or radiation before surgery. NA and surgery-first patients (SF) were compared and survival analysis was conducted on patients treated between 1998-2005. Results: Among 232,539 PDAC patients overall, 43,724 were SF. 2,680 NA cases (5% of surgeries) were contributed by 532 institutions, 10 of which provided 31% of the cases. The use of NA doubled (6-12% of surgical PDAC) between 2006-2010. One-third of NA patients had chemotherapy only. When compared to SF patients, NA patients were treated in academic centers more often (66.4% vs. 51.9%; P<0.001). Charlson comorbidity scores did not differ. Only 17% of NA patients were clinical T4, suggesting few were locally advanced. Median days from diagnosis to surgery were 122 in NA patients. Mean postoperative stay was shorter in NA patients (11.0d vs. 12.0d; P<0.001). 30-day mortality for NA was 2.8% vs. 4.9% for SF (P<0.001). Additional systemic therapy was applied to 29.3% of NA patients postoperatively. NA patients had median survival from diagnosis of 19.9 vs. 15.3m in SF (P<0.001); however, long-term survival was equivalent (5-year=14% in both). Survival benefit was observed for NA in all stages except Stage I. There was significant regional and institutional variation in NA survival rates. Conclusion: National utilization of NA therapy has increased significantly in recent years, and now represents a common treatment path for patients with PDAC. Although this does not reflect an intention-to-treat analysis, NA functions well as a patient selection technique, as it improves postoperative outcomes. Furthermore, NA therapy appears to improve survival in advanced stage disease but not in earlier tumors.

P372

Introduction: The need for radical resection and extensive lymphadenectomy for early adenocarcinoma of the distal esophagus and GEJ has recently been challenged. We aimed to evaluate outcomes of limited esophagectomy with jejunal interposition (EG+JI) and compare it with our data for more radical esophagectomies. Methods: A retrospective review of prospective database of limited EG+JI procedures performed between 2007 and 2011 was done. Only patients with GEJ adenocarcinomas (Siewert I, II and III) were included. End points were short- and long-term perioperative outcomes and 2 year survival. Comparison was made with trans-thoracic (TTE) and transhiatal esophagectomy (THE) done for the same type of tumors. Results: Out of 148 patients with GEJ tumors, 123 had THE, 12 had TTE and 13 had EG+JI. There was no differences between groups as measured by Charlson comorbidity index. For those who had EG+JI, 11 were males and mean age was 62 (range: 42-82). One patient had Stage 0, 5 had stage I, 2 had stage II and 5 had stage III. Neoadjuvant chemotherapy was used in 4 patients and chemoradiation was used in one, while 8 received neither. R0 resection was achieved in all patients. Between 3 and 19 lymph nodes were harvested. Mean postoperative length of stay was 9.3 days (range 7-17 days). Overall morbidity was 46%, anastomotic leakage (15%), pulmonary, cardiac complications and wound infection (7.7%) each. Two highly comorbid patients died within 30 days because of acute myocardial infarction and pneumonia sepsis. Otherwise, all other patients fitted into survival curves predicted by their disease stage. Two year survival was 54%. There were no significant differences in perioperative outcomes in patients with stages I and II compared to those with stage III disease. There was no significant difference in perioperative outcomes and overall survival when compared to THE and TTE. Conclusion Limited EG+JI is a valid replacement technique for early GEJ tumors with comparable overall morbidity and mortality to more radical procedures. It may also be considered for select locally advanced tumors.

Table 1. Comparative data for GEJ adenocarcinoma patients undergoing surgical resection with curative intent.

<table>
<thead>
<tr>
<th>Variable</th>
<th>EG+JI (n=13)</th>
<th>THE (n=12)</th>
<th>TTE (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Mean ±SD)</td>
<td>62±12.1</td>
<td>62±21.5</td>
<td>63±12.1</td>
</tr>
<tr>
<td>Pathological Stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>(7/13)</td>
<td>0</td>
<td>18(14/6)</td>
</tr>
<tr>
<td>I</td>
<td>5(38.5%)</td>
<td>6(50.0%)</td>
<td>2(16.7%)</td>
</tr>
<tr>
<td>II</td>
<td>3(23.1%)</td>
<td>4(33.3%)</td>
<td>2(16.7%)</td>
</tr>
<tr>
<td>III</td>
<td>5(38.5%)</td>
<td>2(16.7%)</td>
<td>2(16.7%)</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>0</td>
<td>2(16.7%)</td>
</tr>
<tr>
<td>Histological Grade</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well differentiated</td>
<td>0</td>
<td>0</td>
<td>6(49.0%)</td>
</tr>
<tr>
<td>Moderately differentiated</td>
<td>8(61.5%)</td>
<td>4(33.3%)</td>
<td>6(49.0%)</td>
</tr>
<tr>
<td>Poorly differentiated</td>
<td>3(23.1%)</td>
<td>2(16.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Neoadjuvant therapy</td>
<td>None</td>
<td>8(61.5%)</td>
<td>2(16.7%)</td>
</tr>
<tr>
<td>Chemotherapy alone</td>
<td>5(38.5%)</td>
<td>4(33.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Chemoradiation</td>
<td>0</td>
<td>0</td>
<td>4(33.3%)</td>
</tr>
<tr>
<td>Lymph nodes (Mean ±SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrieved</td>
<td>10±5.4 (8±6.9)</td>
<td>14±8.5 (6±6.9)</td>
<td>15±8.6 (6±6.8)</td>
</tr>
<tr>
<td>Length of stay (Mean±SD in days)</td>
<td>9.5±3.6</td>
<td>17±5.1</td>
<td>12.9±3.3</td>
</tr>
<tr>
<td>Overall mortality</td>
<td>4(30.8%)</td>
<td>5(41.7%)</td>
<td>6(49.0%)</td>
</tr>
<tr>
<td>Leakage</td>
<td>2(15.4%)</td>
<td>1(8.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>7(53.8%)</td>
<td>2(16.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac</td>
<td>1(7.7%)</td>
<td>2(16.7%)</td>
<td>0</td>
</tr>
<tr>
<td>Sepsis</td>
<td>2(15.4%)</td>
<td>1(8.3%)</td>
<td>0</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1(7.7%)</td>
<td>2(16.7%)</td>
<td>0</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>3(23.1%)</td>
<td>1(8.3%)</td>
<td>0</td>
</tr>
<tr>
<td>2-years survival (%)</td>
<td>51</td>
<td>41</td>
<td>60</td>
</tr>
</tbody>
</table>

P373
Unique Cellular Interactions between Pancreatic Cancer Epithelial Cells and the Omentum G. Lahat,* V. Feygenczon, S. Lowenstein, J. Mazereky, J. Klaunser. Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.

Background: Omental spread is not uncommon in pancreatic ductal adenocarcinoma (PDAC), reflecting end-stage disease and short survival. The aim of the present study was to investigate cellular interactions between PDAC epithelial cells and the omentum. Methods: A xenograft nude mouse model was used to evaluate the potential in-vivo effect of human omentum on PDAC tumor growth. H&E stain of all human omental samples was utilized to determine their exact compounds. Condition medium (CM) of non-cancerous human omental cells, incubated for 24h, was used to investigate its in-vitro effects on PANC-1 and Mia PaCa-2 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 tumor growth rate of PANC-1 cells co-localized with human omentum as compared to cancer cells only (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 cellular growth and reduced apoptosis induced by Gemcitabine. In addition, omental CM enhanced PDAC cellular migration and invasion capacities. Our data depict that omental CM significantly enhanced endothelial cells tube formation, suggesting its role as a proangiogenic factor in the microenvironment of PDAC omental metastases. Using a robust proteomic approach we compared non-cancerous omental samples (n=5) to same patients subcutaneous samples (n=5). In this analyses we identified numerous distinctive omental proteins related to high metabolic activity and increased cellular stress, potentially involved in the formation and progression of PDAC omental metastasis. Conclusion: These findings provide several insights into the cellular interactions between the omentum and PDAC cells. Understanding the molecular mechanisms of this lethal event can provide knowledge of PDAC progression and metastasis which may eventually identify novel diagnostic, prognostic, and therapeutic targets.

P374
Intraoperative Assessment of the Pancreatic Neck Margin during Pancreatoduodenectomy for Adenocarcinoma is Unlikely to Benefit the Patient Y.M. Hashim,* K.M. Trinkaus, D. Linehan, S.S. Strasberg, R.C. Fields, W.G. Hawkins. 1. Washington University School of Medicine - Department of Surgery, St. Louis, MO; 2. Washington University School of Medicine - Division of Biostatistics, St. Louis, MO.

Introduction: Pancreas cancer is the fourth leading cancer death in the United States. Surgery is considered the only potential cure. A positive surgi-
Cochran-Armitage test was used for trends. Logistic regressions were used to model inpatient mortality, complications and laparoscopy. Results: From 1998 to 2011, 120,527 and 25,540 patients (nation-wide weighted records) underwent gastrectomies and esophagectomies for cancer. From early (1998-2002) to late (2008-2011) study years, inpatient mortality decreased from 6.69% to 3.88% ($<0.0001$) and complications increased from 27.41% to 31.63% ($<0.0001$) for gastrectomy. Similarly, inpatient mortality decreased from 9.75% to 5.53% ($<0.0001$) and complications increased from 37.69% to 43.07% ($<0.0001$) for esophagectomy. Use of laparoscopy in gastrectomy increased from 1.64% to 5.89% ($p<0.0001$) and in esophagectomy from 0.80% to 5.74% ($p<0.0001$). Patients undergoing laparoscopy had lower inpatient mortality (3.13% vs. 5.96%, $p=0.0010$) and were less likely to experience complications (26.20% vs. 31.47%, $p=0.0121$). After adjustment, independent predictors of the use of laparoscopy included elective admission, female sex, resection after 2003 and resection at a large (vs. medium), urban, teaching high volume center (vs. low volume center) in the Northeast (vs. Midwest and South). Conclusions: Inpatient mortality and complications for gastrectomy and esophagectomy have improved over the past decade. Use of minimally invasive techniques is expanding with associated superior patient outcomes. Resection hospital characteristics drive which patients undergo laparoscopy for esophagus and stomach cancers.

**P375**

Routine Cyst Fluid Cytology is not Indicated in the Evaluation of Pancreatic Cystic Lesions.

L.A. Shirley,* J. Walker, S. El-Dika, S. Krishna, P. Muscarella, C. Ellison, C.R. Schmidt, M. Bloomston. *The Ohio State University Wexner Medical Center, Columbus, OH.

**Background:** The diagnostic workup of cystic lesion of the pancreas often involves endoscopic ultrasound (EUS) with fine-needle aspiration (FNA) of cyst contents. In addition to CEA and amylase measurement, fluid is routinely sent for cytologic examination. We evaluated the diagnostic utility of these cytologic findings in clinical decision-making. Methods: A retrospective review was performed of patients who underwent EUS-guided pancreatic cyst aspiration. Findings from axial imaging and EUS were reviewed and compared to cyst fluid cytology. Results: A total of 167 patients were reviewed. In the 48 patients who had suspicious findings on ultrasound, such as combined solid and cystic lesions, presence of enhanced or thickened cyst walls, confluence of thin septations, or intramural nodules, cytology yielded diagnostic information in 89.6% of cases (43 patients). However, in the 119 patients where no solid or suspicious components were revealed on ultrasound, fluid cytology yielded no significant diagnostic results in any case. In all cases where mucin was noted on cytologic review, thick fluid was also seen at the time of aspiration. Conclusions: In the absence of suspicious radiologic or EUS findings, cytologic analysis of pancreatic cyst fluid yields no benefit. In such cases, fluid that would otherwise be sent for cytologic evaluation would be better served for other purposes, such as molecular analysis or banking for future research.

**P376**

Utilization of Laparoscopy for Resections of Stomach and Esophagus Cancers: Is Hospital the Deciding Factor?

L. Bliss,1* Z. Chau,2 C.J. Yang,3 J.K. Smith,4 E.R. Witkowski,5 E. Ragulin-Coyne,6 S. Ng,7 J.F. Critchlow,8 A.J. Moser,1 J.F. Tseeng,9 1. Beth Israel Deaconess Medical Center, Cambridge, MA; 2. University of Massachusetts Medical School, Worcester, MA.

**Background:** Foregut surgery is technically complex. Outcomes for such high-stakes operations receive increasing scrutiny and the use of minimally invasive approaches has been further adopted. This study aims to determine national trends in laparoscopy utilization and patient outcomes for potentially curative cancer resections of the esophagus and stomach. Methods: Retrospective review of all esophageal and gastric cancer resections in the Nation-wide Inpatient Sample during 1998 to 2011. Univariate analyses of sex, race, admission status, Elixhauser comorbidity score, year, insurance, hospital characteristics, procedure, and center volume were performed by chi-square.
pancreatitis to pancreatic cancer. Thus, ILK inhibition may provide a way to specifically target the tumor microenvironment while sparing normal stroma. Additionally, in patients with cancer, balanced expression in tumor and stroma was associated with worse survival, revealing a possible role of ILK in the crosstalk between tumor and stroma and progression of disease.

P378
Morbidity and Mortality Associated with Gastrectomy: National Surgical Quality Improvement Project Review

W. Papenfuss,* M. Kukar, K. Attwood, S. Nurkin, N. Wilkinson. Roswell Park Cancer Institute, Buffalo, NY.

Background: Gastrectomy for the treatment of gastric cancer remains a mainstay of therapy and may be curative in early stage disease. Unfortunately, surgery alone is inadequate for advanced stage disease and as such more aggressive surgery (en bloc resection or extended lymphadenectomy) are often advocated. Unfortunately, surgical complications may delay or make impossible the delivery of adjuvant therapy. Understanding the actual measured incidence of these complications is needed for multidisciplinary planning and patient counseling. Material and Methods: The American College of Surgeons-National Surgical Quality Improvement Project (ACS-NSQIP) database was queried for patients who underwent gastrectomy for malignancy (ICD-9-151.X) at participating NSQIP hospitals from 2005-2010. Thirty day mortality and morbidity were evaluated. Results: 2,580 patients underwent gastrectomy for malignancy divided as total gastrectomy (TG) 999 (38.7%) and partial gastrectomy (PG) 1581 (61.3%). Overall, serious morbidity occurred in 23.6% and the 30 day mortality 4.1%. Patients receiving a TG where younger and healthier than those receiving a DG for the following measured criteria: age, diabetes, COPD and HTN. Serious morbidity and mortality were significantly higher in the TG group than PG group, 29.3% vs. 19.9%, p<.001 and 5.4% vs. 3.4%, p<.001, respectively. The inclusion of additional procedures increased the risk for serious morbidity and mortality for the following: splenectomy (ORs = 2.1 and 2.9), pancreatectomy (ORs = 2.0 and 3.5), esophagectomy (ORs = ns and 3.5) or colectomy (ORs = 2.3 and 3.6). All were statistically significant. Abdominal lymphadenectomy decreased the risk of mortality; OR = 0.468 and p= 0.028. Conclusions: Gastrectomy for cancer as currently practiced carries a high morbidity and mortality. Inclusion of additional major procedures further increases these risks. The addition of lymphadenectomy was not associated with increased morbidity or mortality.

P379
Elevated Neutrophil to Lymphocyte Ratio (NLR) in Gastric Cancer Portends Poor Prognosis Regardless of Stage

N.D. Saunders,* M. Michel, L. Stevens, A. Saha,* S. Yeluri, H. Sue-Ling, S.L. Dexter, A.I. Sarela. St. James's University Hospital, Leeds, United Kingdom.

Introduction Identification of biologic factors associated with recurrence and survival after curative resection N0 gastric adenocarcinoma may extend the role and utility of adjuvant therapy for some patients. This study aimed to describe pathological characteristics and patterns of recurrence of patients with node-negative gastric cancer and outline prognostic factors for survival. Methods A database of all gastrectomies for cancer performed by 3 surgeons from September 2001 to September 2013 contained 381 patients and was used to identify patients with a minimum follow-up interval of 5 years and N0 disease. The standard practice included D2 lymphadenectomy. Results From September 2001 to September 2008, 236
patients had gastrectomy for gastric cancer of which 75 (32%) had nodenegative disease. 8 patients received neo-adjuvant chemotherapy and 6 patients had incomplete data and were excluded from this study. Of the remaining 61 patients, 36 had subtotal gastrectomy; the other 25 patients had total gastrectomy. Median lymph node yield was 35 nodes (range, 7-48); more than 15 nodes were retrieved in 52 patients (85%). T-stage was T0 (4 patients, 7%), T1 (24, 38%), T2 (24, 39%) or T3 (9 patients, 16%). Six patients (10%) developed recurrent disease; 5 had T2 disease and 1 had T3 disease; 4 had poor differentiation and 3 had vascular invasion. At least 15 lymph nodes were retrieved from all patients. Sites of metastases were in the peritoneum (2 patients; disease-free intervals, DFI, 2 years and 8 years), liver (2; DFI, 16 months and 18 months), breast (1; DFI, 9 months) and pancreas (1; DFI, 25 months). Overall actual 5-year survival was 76%. Conclusions Chemotherapy naïve patients with adequately staged (> 15 nodes) N0 gastric adenocarcinoma had actual 5 year survival of 76%. The risk of recurrence was predicted by poorly differentiated tumours.

P381
Significance of Anatomic Site on Prognosis in Gastrointestinal Stromal Tumors (GIST) M. Kukar,' A. Groman,2 A. Kapil,1 S.R. Grobmyer,3 S.N. Hochwald.1. Roswell Park Cancer Institute, Surgical Oncology, Buffalo, NY; 2. Roswell Park Cancer Institute, Biostatistics, Buffalo, NY; 3. Cleveland Clinic, Section of Surgical Oncology, Cleveland, OH.

Introduction: Several series of resected GISTs have identified tumour size and mitotic rate as prognostic variables and have indicated that GISTs in uncommon locations have worse survival. Our large database analysis aims to determine the prognostic significance of GISTs in the esophagus, colon and rectum. Methods: The Surveillance Epidemiology and End Results (SEER) database was queried from 1990 to 2009 using CS SCHEMA v0203 and histology codes 33, 37, 39, 40, 41. Using site specific surgery codes, patients undergoing surgical resection were identified. Characteristics of esophageal, small intestine, colon and rectum GISTs were each compared to gastric GISTs using univariate and multivariate analysis. Results: 4817 GISTs (34 Esophageal, 2933 Gastric, 1555 Small intestine, 139 Colonic and 156 rectal) were identified. There was a 24% increase in overall incidence in 2005-2009 as compared to 2000-2004 (3.9 to 4.8/10,000/year). Univariate and multivariate predictors of worse survival in all patients and in surgical resection group include age, race, gender, advanced stage, tumor size >10cm, no surgical intervention and anatomical location. Overall median survival was 99 months in all patients vs. 113 months in surgical resection group (Esophageal 61 vs. 97 months, Gastric 101 vs. 124 months, Small intestine 103 vs. 107 months, Colonic 52 vs. 68 months, Rectal 105 vs. 131 months respectively). Survival for surgical resection group was worst in colonic GIST group—small intestine—gastric-esophageal—rectum. Figure 1. Conclusions: Our results show a rising incidence in GIST and challenges previous findings by demonstrating that esophageal, rectal and gastric GISTs have similar survival. In addition, this is the first study to demonstrate that colonic GISTs have decreased survival compared to rectal GISTs.

Figure 1: Overall survival in resected GIST patients based on anatomical location.

P382
Factors Predictive of Survival in Patients with Node-negative Pancreatic Cancer: Implications for Selective Treatment A.R. Cyr, A. Asghar, S.L. Mott, H. Hoshi, J.R. Howe, J.J. Mezir.1 Surgical Oncology and Endocrine Surgery, University of Iowa Hospitals and Clinics, Iowa City, IA.

Introduction: Prognostic variables in patients with node negative pancreatic cancer may be different than those with node positive disease, which is the dominant predictor of survival in patients with pancreatic cancer following resection. Since data on this subgroup of patients are limited, the objective of this study is to evaluate variables associated with survival following resection in patients with node negative disease. Methods: A retrospective review of a pancreactectomy database was performed and survival was evaluated and compared between patients with node negative (N-) and node positive (N+) pancreatic cancer. Patients who died within 90 days of resection or who had gross residual disease (R2/M1) were excluded. Results: There were 201 patients who met criteria for analysis; 136 patients (67.7%) had a margin negative resection (R0) and 65 (32.3%) had microscopic positive disease (R1). There were 87 patients (43.9%) with N- disease, and 123 (69.9%) were treated with adjuvant therapy. At a median follow-up of 28 months (range 3.3-194.7), 140 patients died (75.3%). On univariate analysis, factors associated with worse survival included resection, advanced T stage, and N+ disease. Independent predictors of survival on multivariate analysis included R1 resection and N+ disease. Adjuvant therapy was not associated with improved survival for the entire cohort. When evaluated separately in a univariate analysis, patients with N- disease had worse survival with R1 resection, which was not significant in N+ patients. Adjuvant therapy was associated with a significant improvement in survival in patients with N+ disease, however patients with N- disease had equivalent survival whether or not they received adjuvant therapy (Figure). Conclusions: In this study, patients with N- pancreatic cancer had different factors that predict outcome compared to those with N+ disease. These include the significance of negative margins and the lack of improvement in survival from adjuvant therapy. These data highlight the biologic differences in behavior of N- vs. N+ pancreatic cancer, which have important implications for patient specific treatment.

Figure. Overall survival following resection in patients with N- and N+ pancreatic cancer with and without adjuvant therapy.

P383
Metabolomic Profiling of Gastrointestinal Stromal Tumor (GIST) and its Response to Imatinib Therapy D. Yakoub,1* V. Marks,2 A. Paz Mejia,3 J. Walls,3 J. Trent,3 A.S. Livingston.1. University of Miami-Division of Surgical Oncology, Miami, FL; 2. University of Miami-Division of Chemistry, Miami, FL; 3. University of Miami-Division of Medical Oncology, Miami, FL.

Background: There is a growing need for novel drugs to treat resistant GIST. The goal of this study was to evaluate the time course of metabolic changes in GIST cells treated with the tyrosine kinase inhibitor imatinib mesylate. Methods: Human GIST T1 cells were incubated with imatinib 0.5 mM. 1H-NMR spectra were acquired using a 500MHz NMR spectrometer equipped with a cryoprobe head at 298 K. One-dimensional NOESY 1yr1D pre-saturation pulse program was used. Spectra were imported into the NMR Suite Processor. Effect was measured in extracted cell pellets and media at 24 and 48 hours and compared with controls to assess global metabolic profiles including drug effect on glucose metabolism, energy state and lipid metabolism. Results: By 48 hours, cells shifted from cytosolic glycolysis towards the mitochondrial Krebs cycle, as indicated by glucose initial increase then significant decrease with lactate production and minimal changes in pyruvate; in addition to elevated glutamine and glutamate synthesis. Proline, alanine, AXP, glutathione,
sarcopenia mildly increased denoting initial cellular stress response. Aspartate, isoleucine, leucine, myoinositol, tyrosine, valine and especially cell membrane phospholipids as phosphocholine, mildly increased while glycerophosphocholine significantly decreased denoting inhibited growth and invasiveness. Creatine, choline, phenylalanine and taurine showed minimal changes. Volatile molecules as formate increased of unclear significance. Conclusion: Metabolomic profiling of GIST cells exposed to signal transduction modulators supplements molecular findings and provides further mechanistic insights into longitudinal changes of the mitochondrial and glycolytic pathways of oncogenesis, it can potentially provide novel as well as complementary therapeutic targets.

Figure 1. GIST cell extracts metabolite concentration trends over time when incubated with imatinib mesylate (spectra referenced to DSS, normalized data)

**P384**
CT-based Assessment of Sarcopenia as an Outcome Predictor in Patients Undergoing Pancreaticoduodenectomy

J.P. Namm, J.P. Namm,1* W. Dale,2 A. Palakodeti,1 J.A. Hemmerich,1 S.J. Stocker,1 R. Rothman,1 A. Kamm,1 E.C. Poli,1 M.S. Baker,3 M.S. Talamonti,3 E. Choi,1 M.C. Posner,1 J.B. Matthews,1 K.K. Roggin.1 1. Department of Surgery, University of Chicago, Chicago, IL; 2. Section of Geriatrics and Palliative Medicine, Department of Medicine, University of Chicago, Chicago, IL; 3. Department of Surgery, NorthShore University HealthSystem Center, Evanston, IL.

Objective: Pancreaticoduodenectomy (PD) is associated with high perioperative morbidity. Up to 35% of older patients undergoing PD demonstrate characteristics of frailty according to geriatric assessments. Sarcopenia, characterized by decreased muscle mass and strength, is an important component of frailty and is associated with adverse clinical outcomes. We investigated whether pre-operative, standardized CT-based assessments of sarcopenia independently predicted surgical outcomes following PD. Methods: An analysis of pre-operative, pre-contrast phase abdominal CT scans was performed on surgical outcomes in a prospective cohort of patients undergoing a PD from 2007 to 2013 (n=99). Blinded to outcomes, the psoas muscle cross-sectional area was measured at the level of the L3 vertebra and normalized to the subject’s height as the total psoas area (TPA) index to assess muscle mass. The attenuation of the psoas muscle was measured in Hounsfield units (HU) to assess muscle strength. Multivariate logistic and linear regressions were used to analyze the impact of sarcopenia on outcomes which include complications, length of stay (LOS), return to ICU, and discharge to a skilled nursing facility (SNF) while controlling for age, body mass index (BMI), comorbidities, American Society of Anesthesiology score (ASA), and serum albumin. Results: The sample was 86% men with a median age of 67 years (range 28-88). The mean TPA index was 5.88 ± 1.53 cm²/m² and the mean psoas muscle HU was 47 ± 7. TPA index correlated with return to ICU (OR 2.00, p=0.07) and discharge to a SNF (OR 0.69, p=0.084). Psoas muscle HU was an independent predictor for LOS (β -0.33, p=0.047) and return to ICU (OR 0.82, p=0.022). BMI was predictive of pancreatic fistula (OR 1.17, p=0.021), return to ICU (OR 0.79, p=0.041), and wound dehiscence (OR 1.2, p=0.031). Conclusion: TPA index and psoas muscle HU are CT-based measures of sarcopenia which are easily measured on pre-operative scans of patients undergoing PD. In addition to other pre-operative clinical assessments, TPA index and psoas muscle HU can be used to predict PD complications including return to ICU and LOS.

**P385**
The Causes for Readmissions after Pancreatic Resections which are Preventable


Background: As an effort to decrease healthcare expenditure, hospital readmission rates have recently been brought to the forefront of policymakers’ attention. Our goal was to clarify the extent and identify reversible factors for readmission after pancreatic resections in a dedicated high volume center. Methods: Medical records of patients who underwent pancreatic resection between 2008-2012 were reviewed. Results: A total of 400 patients were reviewed. The 30-day and 90-day readmission rates were 23% and 30%, respectively. Whipple procedure was performed in 59% of patients and distal pancreatectomy in 31%. Most of the indications were neoplastic tumors (94.3%) which originated mainly from the pancreas (88.2%). The most common causes for 30-day readmissions were surgery related infections and anastomotic leaks (50%), and then drain malfunction (12%). The average interval between discharge and 30-day readmission was 9.4±6.77 days. Multivariate analysis identified the following risk factors: complication grade 3 (OR=2.3; CI: 1.3-5.2; P=0.009), discharge with drain (OR=3.5; CI: 1.7-7.5; P=0.001), total pancreatectomy (OR=6.8; CI: 1.4-32; P=0.02), and preoperative bilirubin (OR=1.1; CI: 1.02-1.2; P=0.01). The independent risk factors for 90-day readmissions were: malignant tumor (OR=2.6; CI: 1.2-5.4; P=0.01), delayed gastric emptying (OR=3.6; CI: 1.1-11; P=0.03), and anastomotic leak (OR=4.7; CI: 2.3-9.5; P=0.001). The leading causes for admissions of patients between 31-90 days after discharge were: non specific symptoms (41%) and non surgical infections (21%). Twenty-eight patients visited our Urgent Care Center (UCC) at a range of 1-60 days after discharge but were not admitted.

Analysis of factors associated with 30-day readmissions:

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Readmitted (n=30)</th>
<th>Not Readmitted (n=307)</th>
<th>p-value</th>
<th>Multivariate analysis (OR, CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in Surgery, year (a)</td>
<td>65±13 (91)</td>
<td>67±11 (307)</td>
<td>0.13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin total (preoperative), (g/dL)</td>
<td>2.52±4 (90)</td>
<td>2.5±2 (304)</td>
<td>0.01</td>
<td>1.1; 1.02-1.2</td>
<td>0.01</td>
</tr>
<tr>
<td>Operative Procedure</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whipple</td>
<td>65% (59)</td>
<td>57% (176)</td>
<td>0.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total pancreatectomy</td>
<td>23% (21)</td>
<td>34% (105)</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total pancreatectomy (n)</td>
<td>5% (5)</td>
<td>6% (13)</td>
<td>8.3</td>
<td>1.4-3.2</td>
<td>0.02</td>
</tr>
<tr>
<td>Central pancreatectomy (n)</td>
<td>5% (5)</td>
<td>5% (11)</td>
<td>0.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multivisceral resection (n)</td>
<td>1% (1)</td>
<td>7% (6)</td>
<td>0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Pancreatic resection (n)</td>
<td>1% (1)</td>
<td>4% (14)</td>
<td>0.12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant Tumor (n)</td>
<td>72% (65)</td>
<td>67% (206)</td>
<td>0.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive Margin (n)</td>
<td>11% (50)</td>
<td>9% (307)</td>
<td>0.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AJCC T4 (n)</td>
<td>51% (57)</td>
<td>50% (134)</td>
<td>0.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Node Positive (n)</td>
<td>35% (34)</td>
<td>39% (130)</td>
<td>0.68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discharge with Drain (n)</td>
<td>33% (31)</td>
<td>8% (25)</td>
<td>&lt;0.001</td>
<td>3.5; 1.7-7.5</td>
<td>0.001</td>
</tr>
<tr>
<td>Discharge (Day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home (n)</td>
<td>60% (35)</td>
<td>76% (232)</td>
<td>0.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with VNS (n)</td>
<td>37% (34)</td>
<td>23% (78)</td>
<td>0.009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>to rehab (n)</td>
<td>2.2% (2)</td>
<td>1.6% (5)</td>
<td>0.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative Complications</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any Complication (n)</td>
<td>67% (60)</td>
<td>46% (142)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complication G1-G2 (n)</td>
<td>30% (27)</td>
<td>25% (108)</td>
<td>0.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complication G3 (n)</td>
<td>37% (34)</td>
<td>11% (34)</td>
<td>&lt;0.001</td>
<td>2.6; 1.3-5.2</td>
<td>0.009</td>
</tr>
<tr>
<td>Any Anastomotic Leak (n)</td>
<td>29% (28)</td>
<td>7% (23)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic leak (n)</td>
<td>25% (23)</td>
<td>6% (19)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra-abdominal abscess (n)</td>
<td>12% (11)</td>
<td>4% (13)</td>
<td>0.006</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative transfusions (n)</td>
<td>33% (30)</td>
<td>6% (205)</td>
<td>0.009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU stay, grade 4 complication</td>
<td>7% (7)</td>
<td>7% (24)</td>
<td>0.07</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
P386
Radiographic Response to Neoadjuvant FOLFIRINOX for Advanced Non-metastatic Pancreatic Cancer is not Required to Proceed with Resection
J. Onesti,1* M. Blazer,2 T. Williams,3 R.M. Goldberg,3 T. Bekaii-Saab,4 M. Bloomston.1 1. Surgical Oncology, The Ohio State University Wexner Medical Center, Columbus, OH; 2. Pharmacy, The Ohio State Wexner Medical Center, Columbus, OH; 3. Radiation Oncology, The Ohio State Wexner Medical Center, Columbus, OH; 4. Medical Oncology, The Ohio State Wexner Medical Center, Columbus, OH.

Background: Response to neoadjuvant therapy in advanced pancreatic cancer is notoriously difficult to assess. We sought to determine if radiographic response (or lack thereof) following neoadjuvant FOLFIRINOX in advanced non-metastatic pancreatic cancer was predictive of true resectability. Methods: Patients treated with neoadjuvant FOLFIRINOX for borderline resectable (BR) or locally advanced (LA) pancreatic adenocarcinoma were reviewed. Imaging before and after chemotherapy were compared to operative findings and, when applicable, the final pathology. Results: Seventeen patients were included (10 LA and 7 BR). FOLFIRINOX was given for an average of 2.8 (range 1-6) months. Radiographic response was seen in 5 (29%), stable disease in 6 (35%), and progression in 6 (35%) patients. Three were not offered resection due to metastatic disease (N=1) or unresectable vascular invasion (N=2). The remainder (N=14) were explored, despite the anticipated need for vascular resection (N=11). Twelve (71%) were resected with 10 having negative margins. Major vascular resection was only required in 3 (1 venous, 2 arterial). There were no postoperative deaths. Conclusions: Lack of radiographic response to neoadjuvant FOLFIRINOX for advanced non-metastatic pancreatic cancer does not predict unresectability. Major vascular involvement (suitable replacement) should not deter the surgeon and will often not be required. Patients with traditionally unresectable disease who have undergone neoadjuvant FOLFIRINOX can still be considered for potentially curative surgery regardless of the degree of radiographic response.

<table>
<thead>
<tr>
<th>Radiographic Assessment</th>
<th>Progressed</th>
<th>Stable</th>
<th>Improved</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>36</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>LA/BR</td>
<td>4/2</td>
<td>50</td>
<td>1/4</td>
</tr>
<tr>
<td>Exploded</td>
<td>3 (50%)</td>
<td>6 (100%)</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Resected</td>
<td>2 (33%)</td>
<td>5 (87%)</td>
<td>5 (100%)</td>
</tr>
<tr>
<td>Vascular Resection</td>
<td>1</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>R9</td>
<td>2 (100%)</td>
<td>4 (80%)</td>
<td>4 (80%)</td>
</tr>
</tbody>
</table>

LA: Locally Advanced
BR: Borderline Resectable

P387
Factors Associated with Recurrence in Lymph Node-negative Gastric Adenocarcinoma: Results from the U.S. Gastric Cancer Collaborative L.X. Jin,1* M.H. Squires,2 G. Poultsides,3 K.I. Votanopoulos,4 S.M. Weber,5 M. Bloomston,6 T. Pavlik,7 W.G. Hawkins,4 D. Linehan,6 S.M. Strasberg,8 A.W. Archer,3 K. Cardona,3 C. Cho,3 D.A. Kooby,3 E.A. Levine,5 E. Winslow,6 N.D. Saunders,6 G. Spolverato,7 S.K. Mathiel,6 R.C. Fields,3 1. Washington University in St. Louis, St. Louis, MO; 2. Emory University, Atlanta, GA; 3. Stanford University Medical Center, Palo Alto, CA; 4. Wake Forest School of Medicine, Winston-Salem, NC; 5. University of Wisconsin School of Medicine and Public Health, Madison, WI; 6. The Ohio State University Comprehensive Cancer Center – The Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, OH; 7. Johns Hopkins University, Baltimore, MD.

Background: Lymph node (LN) status is a predictor of recurrence after gastrectomy for gastric adenocarcinoma. Clinicopathologic predictors of recurrence in patients with node-negative disease are less well established. Methods: Patients who underwent surgery with curative intent for gastric adenocarcinoma from between 2000 and 2012 from participating institutions of the U.S. Gastric Cancer Collaborative were analyzed. Patients who died within 30 days of surgery were excluded. Univariate and multivariate analysis of clinicopathologic factors associated with recurrence was performed. Results: Nine-hundred sixty-five patients from seven institutions were included in the analysis. Three-hundred forty-five (36%) had LN(-) disease, of whom 63 (18%) had disease recurrence after a median follow-up of 24 months. The most common patterns of recurrence were: peritoneal alone (44%), liver (22%), or combined liver/peritoneal (9%). This distribution did not differ significantly from LN(+) disease. Univariate analysis identified tumor size, limits plastic, diffuse histology, poor differentiation, signet ring histology, T stage ≥3, perineural invasion, and lymphovascular invasion as risk factors for recurrence. On multivariate analysis, T stage ≥3 (OR 3.6, 95% CI=1.7-7.5) and poorly differentiated histology (OR 2.4, 95% CI=1.2-4.9) were independent predictors of recurrence (Table). Conclusions: Despite the presence of negative lymph nodes, patients with T stage ≥3 and poorly differentiated histology are at high risk of recurrence after gastrectomy for adenocarcinoma of the stomach. These factors, along with other patient and treatment-related variables, may be used to select patients who may benefit from more aggressive adjuvant therapy and to guide subsequent surveillance for disease recurrence.

<table>
<thead>
<tr>
<th>Clinicopathologic risk factors for recurrence after resection with curative intent in patients with lymph node negative gastric cancer (n=345)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>T Stage</td>
</tr>
<tr>
<td>T1a</td>
</tr>
<tr>
<td>T1b</td>
</tr>
<tr>
<td>T2</td>
</tr>
<tr>
<td>T3*</td>
</tr>
<tr>
<td>T4a</td>
</tr>
<tr>
<td>T4b</td>
</tr>
<tr>
<td>Grade</td>
</tr>
<tr>
<td>Well</td>
</tr>
<tr>
<td>Poor*</td>
</tr>
<tr>
<td>Limits plástica</td>
</tr>
<tr>
<td>Diffuse histology</td>
</tr>
<tr>
<td>Signet ring histology</td>
</tr>
<tr>
<td>LVI</td>
</tr>
<tr>
<td>PNI</td>
</tr>
</tbody>
</table>

* T stage ≥3 and poorly differentiated histology are independent predictors of recurrence.

P388
Sarcopenia does not Accurately Predict Outcomes in Patients Undergoing Pancreatic Resections J. Onesti,* G. Weight,1 S.E. Kennig,1 M.T. Tierney,2 M.G. Doherty,3 M.H. Chung.4 1. General Surgery, Grand Rapids Medical Education Partners/Michigan State University College of Human Medicine, Grand Rapids, MI; 2. Radiology, Grand Rapids Medical Education Partners/Michigan State University College of Human Medicine, Grand Rapids, MI; 3. Advanced Radiology Services, Grand Rapids Medical Education Partners/Michigan State University College of Human Medicine, Grand Rapids, MI; 4. Surgical Oncology, Spectrum Health Medical Group, Grand Rapids Medical Education Partners/Michigan State University College of Human Medicine, Grand Rapids, MI.

Background: Recent studies have suggested that core muscle area and density may aid in predicting outcomes from major abdominal surgeries. Pancreatic resections, including those for patients with adenocarcinoma, have not been analyzed independently. Methods: A total of 272 consecutive pancreatic resections from July 2005 to July 2011 were reviewed. Lean psoas muscle area (LPMA) was calculated by measuring the area and density of the psoas muscles at the level of the fourth lumbar vertebra, then correcting for fatty infiltrate. Preoperative risk factors including LPMA, comorbidities, albumin (g/dl), weight loss, age and gender were analyzed with a primary endpoint of overall survival as determined by Cox proportional hazards regression. Secondary endpoints, including complications, hospital length of stay, discharge destination and readmission, were evaluated using multiple and logistic regression analysis, as appropriate. Statistical analyses were then repeated to include only patients with adenocarcinoma. Results: The study sample included 53% males, 63% proximal pancreatic resections, and 52% adenocarcinoma. The mean age was 64 years, and the mean preoperative albumin was 3.4 g/dl. Complications were noted in 42% of patients, with 23% developing a Clavien-Dindo...
P389
Practice Patterns and Outcome Differences for Distal Pancreatectomy in Surgeons with and without Fellowship Training S. Wu,* S. Woo, Y. Akmal. Kaiser Permanente Los Angeles, Los Angeles, CA.

INTRODUCTION: Recent data show that pancreatic cases account for a small percentage of general surgery training and that outcomes for major pancreatic resections are improved when performed by high-volume surgeons. Fellowship training provides additional experience for these complex procedures, but fellowship training exists, many patients undergo pancreatic resections by non-fellowship trained surgeons. OBJECTIVE: To compare operative approaches and postoperative outcomes of distal pancreatectomy performed by surgeons with and without Surgical Oncology/Hepatobiliary fellowship training. METHODS: A retrospective review of all patients who underwent distal pancreatectomy between 2005 and 2011 at twelve Southern California Kaiser Permanente Foundation Hospitals. Patients who had concurrent major organ resection or underwent surgery for trauma were excluded. RESULTS: A total of 231 patients underwent distal pancreatectomy among 52 surgeons; 16 (31%) were fellowship trained and 36 (69%) were not. Of 105 cases performed by fellowship trained surgeons, 44 (42%) were performed laparoscopically compared to 35 of 126 (28%) cases by the non-fellowship trained group. There was a significantly higher rate of the laparoscopic approach with fellowship trained surgeons (p = 0.0266). There was also a higher rate of spleen preservation in the fellowship trained group (36% vs 11%, p = 0.0001). There was no difference in rate of complications (52% vs 52%, p = 1.0) or rate of pancreatic leak (34% vs 25%, p = 0.1489) for the non-fellowship trained versus fellowship trained groups. CONCLUSION: Surgical Oncology/Hepatobiliary fellowship trained surgeons are more likely to use a laparoscopic approach and to preserve the spleen during distal pancreatectomy compared to non-fellowship trained surgeons. The rates of short-term postoperative complications and pancreatic leak were similar for both groups. However, advanced training does influence surgical approach but it is unclear if impacts long-term outcomes.

P390

BACKGROUND: Pancreatic adenocarcinoma (PDAC) typically presents in an older population and little is known about its prognosis in younger patients. The current study sought to evaluate the epidemiology, treatments, and outcomes in a cohort of PDAC patients under 50. METHODS: All PDAC patients aged 50 years or younger at diagnosis evaluated at a single institution from 1980-2012 were identified from administrative databases and medical records. Clinico-pathologic parameters including demographics, staging, surgical management, and oncologic therapy was collected. Survival analysis was performed using the Kaplan-Meier method. RESULTS: Two hundred twenty-six patients were identified, 59% male and 41% female. The distribution by ages 30-34, 35-39, 40-44, 45-50 was 8, 22, 49, and 147 respectively. Fifty-four percent of patients had a family history of adenocarcinoma, and 61% had a history of alcohol use. Primary tumor location was 83% in the head and/or uncinate process, and 17% in the neck, body, or tail of the gland. The median overall survival (OS) was 11.0 months (95% CI 6.4-16.7) and 7.3 months (95% CI 5.6-8.8) respectively. Of the resected patients, 21.7% were treated with neoadjuvant chemotherapy, 84.7% received adjuvant chemotherapy, and 63.0% underwent adjuvant chemoradia-
tion. CONCLUSIONS: The majority of PDAC patients younger than 50 present with inoperable disease. Survival data suggest that these patients have a similar prognosis to the general PDAC population despite their younger age, ability to undergo pancreatectomy and tolerate (neo)adjuvant therapy.

P391

Background: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS and HIPEC), has led to improved outcomes for patients with malignant peritoneal mesothelioma (MPM) over the last decade. Recent literature published has demonstrated varied outcomes with regards to survival benefit. A systematic review was undertaken to synthesize the survival outcomes from recently published literature. Methods: Using Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines a pre-specified search strategy was used to abstract data from PubMed, CINAHL, the Cochrane Library, and EMBASE databases. Mortality rates were calculated by the DEALE method, and random effects modeling was used to synthesize the data. Publication bias was assessed using Beggs plot. Results: Of 6528 citations, we identified 86 articles for full text review and 13 articles were included. Outcomes were available for 373 patients with a median age of 54 years (IQR 51-55). The predominant histology was epithelioid mesothelioma (75%, 189 of 253 reported), while sarcoma-
toid/biphasic occurred in 12.6% (32 of 253). CRS+HIPEC was performed using cisplatin based regimens in 12 studies, and mitomycin only based regimen in 1 study (12 patients). Almost 22% (8-38%) of patients received systemic chemotherapy in addition to HIPEC. Complete macroscopic cytoreduction was achieved in 67% (±33%), with a median PCI score of 20 (±7). The summarized mortality rate was 0.19 (±0.04, 0.42), with a pre-
dicted 1 and 5 year survival of 83% and 39% respectively. Studies showed substantial heterogeneity in regimens utilized, variables assessed, and reporting of toxicity. Quality of studies varied significantly with many stud-
ies possessing high risk of bias. Conclusions: CRS+HIPEC offer patients promising 1 and 5 year survival compared to historical controls. The increased emphasis on completeness of cytoreduction and incorporation of systemic chemotherapy, especially for aggressive histology is novel over the previous decade. Our data is limited by the heterogeneity of the included studies.
P392
Factors Associated with Failure to Operate for Localized Pancreatic Adenocarcinoma
M. Strohl,1,** S. Raigani,1 J. Hardacre,1 J. Ammori,2 J. Kim,1 1. Case Western Reserve University School of Medicine, Cleveland, OH; 2. Division of Surgical Oncology University Hospitals Case Medical Center, Cleveland, OH.
Background: Surgery is potentially curable for patients with early stage pancreatic cancer. The primary aim of this study was to identify factors that are associated with not receiving surgery in patients with localized pancreatic adenocarcinoma using the Surveillance, Epidemiology and End Results (SEER) database. A secondary aim was to evaluate the effect of receiving surgery on disease-specific survival. Methods: The study population included patients diagnosed with SEER historic stage A localized pancreatic adenocarcinoma between 1988-2010 in 17 SEER registries from across the United States. Exclusion criteria included unknown site-specific surgery status, multiple primary malignancies, unstaged, non-invasive, regional, or distant disease at diagnosis, non-cancer directed surgery, and biopsy only. Univariate and multivariate methods were employed to determine which factors were associated with the failure to undergo surgery. Kaplan-Meier log-rank tests and cox proportional hazards regression modeling were used to determine factors associated with disease-specific survival. Results: Of 6,742 patients diagnosed with localized pancreatic adenocarcinoma, 1,715 patients (25.4%) received surgical treatment. There was no significant difference in the utilization of surgery over time. On multivariate analysis, patients were less likely to undergo surgery if they were older than 50 years, black, unmarried, located in regions outside the East, had pancreatic head or body lesions, had higher tumor grades, or had tumor size >2 cm (P<0.0001). Patients who did not undergo surgery had significantly worse disease-specific survival than patients who underwent surgery (6 vs 27 months, P<0.0001). Factors independently associated with survival were surgical treatment (HR 3.09 95% CI 2.82-3.38), age, sex, year of diagnosis, marital status, tumor grade and size. Discussion: These results are the first to use the SEER database to analyze factors associated with surgery as a treatment for localized pancreatic cancer. While not all patients with localized disease are candidates for curative resection, there is an opportunity for educating patients and physicians about the potential benefits of surgery.

P393
Does Age Affect Clinical Presentation, Treatment, or Outcomes in Gastric Adenocarcinoma? A Multi-institutional Study of the U.S. Gastric Cancer Collaborative
J.W. Etra,1,* M.H. Squires,1 G. Poultsides,1 S.M. Weber,1 M. Bloomston,3 R.C. Fields,7 T. Pawlik,7 K.I. Votanopoulos,1 C.R. Schmidt,7 A. Ejaz,4 A.W. Acher,4 D.J. Worhunsky,7 N.D. Saunders,4 D.S. Sowards,1 L.X. Jin,7 C. Cho,2 E. Winslow,2 M. Russell,1 C.A. Staley,6 D.A. Kooby,1 S.K. Maithel,7 K. Cardona,7 1. Department of Surgery, Emory University School of Medicine, Atlanta, GA; 2. Stanford University, Stanford, CA; 3. University of Wisconsin School of Medicine and Public Health, Madison, WI; 4. The Ohio State University Wexner Medical Center, Columbus, OH; 5. Washington University in Saint Louis, St. Louis, MO; 6. Johns Hopkins University, Baltimore, MD; 7. Wake Forest University, Winston-Salem, NC.
Background: The relationship of presentation and treatment variables to survival in young gastric adenocarcinoma (GAC) patients is not well defined. The aim of this study was to determine survival differences across various age groups and to evaluate clinical, pathologic, and treatment factors that may influence survival. Methods: All pts undergoing curative intent gastrectomy for localized gastric cancer between 2000-2012 from the U.S. Gastric Cancer Collaborative were analyzed. Pts who died within 30 days of operation and those who went curative resection of GEJ adenocarcinoma from 2000-2012 at 7 academic institutions within the U.S. Gastric Cancer Collaborative were identified. Pts with Siewert type 1 tumors and those who died within 30 days were excluded. Survival was assessed according to the E7 and G7 staging systems. RESULTS: Fifty-one pts underwent resection of GEJ tumors. Median age was 63 with 63% of pts having poorly-differentiated tumors. Rates of adjuvant chemoradiation (65% vs 46% vs 36%; p<0.031) were also higher in pts <40yo. On MV analysis for survival, diffuse GAC, N2/N3 disease, T3/T4 status, receipt of neoadjuvant chemotherapy, and receipt of adjuvant chemoradiation were associated with OS (Table). Conclusion: In those patients undergoing curative surgical resection for gastric cancer, patients <40yo present with more advanced disease but receive more aggressive operations and are more likely to receive adjuvant therapy. Given these findings, their overall survival is equivalent to that of older patients, supporting continued aggressive treatment in young patients with advanced disease.

Multivariate Regression Analysis for Overall Survival in All Resected GAC Patients (N=810)

<table>
<thead>
<tr>
<th>( p )-value</th>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>0.706</td>
<td>0.79-0.90</td>
</tr>
<tr>
<td>Diffuse Type</td>
<td>0.079</td>
<td>1.63</td>
</tr>
<tr>
<td>Poorly or Undifferentiated</td>
<td>0.611</td>
<td>1.0-1.68</td>
</tr>
<tr>
<td>Signet Ring</td>
<td>0.508</td>
<td>0.38-0.68</td>
</tr>
<tr>
<td>N2/N3</td>
<td>0.012</td>
<td>1.51-4.11</td>
</tr>
<tr>
<td>T3 or T4</td>
<td>&lt;0.001</td>
<td>2.49</td>
</tr>
<tr>
<td>Tumor Grade</td>
<td>0.071</td>
<td>1.64-3.76</td>
</tr>
<tr>
<td>Positive Lymph Nodes</td>
<td>0.077</td>
<td>1.27</td>
</tr>
<tr>
<td>Neoadjuvant Chemotherapy</td>
<td>0.034</td>
<td>1.64-2.71</td>
</tr>
<tr>
<td>Adjacent CXRT</td>
<td>0.014</td>
<td>1.99-10.99</td>
</tr>
<tr>
<td>Adjacent Chemotherapy</td>
<td>0.410</td>
<td>1.64-2.71</td>
</tr>
</tbody>
</table>

CXRT = chemotherapy & radiation therapy

P394
A Multi-institutional Study Comparing the use of the AJCC 7th Edition Esophageal versus Gastric Staging System for Gastro-esophageal Junction Cancer in a Western Population
F.A. Adeshukho,1** M.H. Squires,1 G. Poultsides,1 T. Pawlik,7 S.M. Weber,7 C.R. Schmidt,7 K.I. Votanopoulos,7 R.C. Fields,7 A. Ejaz,4 A.W. Acher,4 D.J. Worhunsky,7 N.D. Saunders,4 D.S. Sowards,1 L.X. Jin,7 C. Cho,2 E. Winslow,2 M. Russell,1 C.A. Staley,6 D.A. Kooby,1 S.K. Maithel,7 K. Cardona,7 1. Department of Surgery, Emory University School of Medicine, Atlanta, GA; 2. Department of Surgery, Stanford University, Stanford, CA; 3. Department of Surgery, Johns Hopkins University, Baltimore, MD; 4. Department of Surgical Oncology, University of Wisconsin, Madison, WI; 5. Division of Surgical Oncology, Ohio State University, Columbus, OH; 6. Department of Surgery, Wake Forest University, Winston-Salem, NC; 7. Department of Surgery, Washington University, St. Louis, MO.
INTRODUCTION: Controversy exists over the staging of gastroesophageal junction (GEJ) adenocarcinomas within the esophageal system of the AJCC 7th edition. Studies from the East suggest that GEJ tumors are better stratified within the gastric system. The aim of our study was to assess the adequacy of the AJCC 7th esophageal (E7) vs gastric (G7) staging systems for GEJ tumors in a Western population. METHODS: All pts who underwent curative resection of GEJ adenocarcinoma from 2000-2012 at 7 academic institutions within the U.S. Gastric Cancer Collaborative were identified. Pts with Siewert type 1 tumors and those who died within 30 days were excluded. Survival was assessed according to the E7 and G7 systems. RESULTS: Fifty-one pts underwent resection of GEJ tumors. Median age was 63 with 63% of pts having poorly-differentiated tumors. The median follow-up was 18mos. The E7 staging system did not adequately stratify patients by T or N stage with a loss of distinctiveness between T1-3(T1vsT2, p=0.58; T2sT3, p=0.08) and N0-3 (N0vsN1, p=0.09; N1vsN2, p=0.66; N2vsN3, p=0.29) tumors. Similarly, the G7 system was not able to appropriately stratify patients by T or N stage with a loss of distinctiveness between T1-3(T1vsT2, p=0.58; T2sT3, p=0.13) and N0-3(N0vsN1, p=0.09; N1vsN2, p=0.66; N2vsN3, p=0.37; N3a vs N3b, p=0.39) stages. On final stage analysis (Figure), the outcomes were similar between both systems and neither the E7 nor G7 systems, with the exception of the G7 stage I vs II, adequately stratified pts by stage(E7: IvsII, p=0.07; IIvsIII, p=0.23; G7:
S176 Abstracts: Poster Presentations

**P395**
Morbidimt in Long-term Survivors after Pancreatoduodenectomy for Pancreatic Adenocarcinoma
1. Fox Chase Cancer Center, Philadelphia, PA; 2. St. Luke’s Hospital, New Bedford, MA.

Background: Because the focus of pancreatoduodenectomy for pancreatic adenocarcinoma is placed on disease-free and overall survival, morbidity in long-term survivors is not well described. We sought to evaluate outcomes of long-term survivors of pancreatic cancer after pancreatoduodenectomy. Methods: We identified 30 patients from our prospectively collected database of patients with pancreatic adenocarcinoma who had undergone pancreatoduodenectomy, and who were without evidence of disease with at least 40 months of follow-up. Demographics, treatment and pathologic characteristics were collected for review. Data with regards to long-term sequelae were also collected, particularly those complications requiring additional procedures and the development of metachronous cancers. Results: The median length of follow up was 83 months, with 60% of patients still alive. Half the patients were male, and the median age at diagnosis was 70 years. With regard to treatment, 80% of patients received chemoradiation, with half of these patients receiving it in the neoadjuvant setting. All patients received an R0 resection, although two patients required at least partial resection of the superior mesenteric or portal veins. Thirty-three percent of patients had N1 disease. Forty-four percent of patients did not have any significant subsequent sequelae. In the remainder, four patients (13%) developed ascites requiring repeated paracentesis or Denver shunt, with median time to development (MTD) of 63 months. Six patients (20%) developed a biliary stricture requiring stent placement (MTD 56 months), one patient developed portal venous thrombosis requiring a venous stent (MTD 52 months), and 3 patients (10%) experienced clinically significant anastomotic ulcers (MTD 47 months). With regards to metachronous cancers, 2 patients developed subsequent lymphomas (MTD 92 months). Conclusions: Long-term survivors of patients who undergo pancreatoduodenectomy for pancreatic adenocarcinoma will develop significant late sequelae, which often can manifest more than three to five years after surgery. Continued follow-up and counseling is warranted.

**P396**
Preoperative Staging of Gastric Adenocarcinoma with CT Gastrography and 3-D Reconstruction: Report of a Pilot Study

Background: Accurate staging is important to determine the sequence of treatment options for patients with gastric adenocarcinoma. In this study we evaluate the accuracy of CT gastrography with 3D reconstruction (CTG) in predicting the stage of gastric adenocarcinoma. Methods: A pilot study was conducted on patients with biopsy-proven gastric adenocarcinoma who underwent preoperative CTG. Patients consumed effervescent granules and pre and post contrast CT was performed in multiple positions. This allowed distention of different regions of the stomach while excluding local invasion of adjacent organs. CTG findings were used to determine extent of disease, as measured by T and N stage. Staging results from both CTG and endoscopic ultrasound (EUS) were compared, with concordance rates measured against final pathologic stage. Results: A pilot cohort of 7 patients with a mean age of 66 years underwent preoperative CTG. In addition, EUS and complete surgical resection were performed in 6 of 7 patients (86%); one patient had EUS and CTG but did not undergo surgery, while another patient had CTG and surgery but not EUS. Both CTG and EUS accurately predicted surgical stage in 5 of 6 patients (83%). CTG was 100% accurate in predicting T stage in tumors ≤T2, whereas EUS understaged a T4 lesion noted on CTG. When examining N stage, CTG correctly predicted surgical N stage in 5 of 5 (100%) patients, however EUS correctly predicted nodal disease in 4 of 5 patients (80%). In the single non-surgical patient, CTG and EUS both staged the patient as T3N2, however only CTG was able to further stage this patient as M1. Conclusion: This pilot study demonstrated that CTG with 3D reconstruction accurately predicts staging in patients with gastric adenocarcinoma. Although its use in early gastric cancers (T1) may be limited, it compares favorably to EUS in tumors T2 or greater. In addition, CTG appears superior to EUS in detecting nodal and distant metastases. The use of CTG may be an effective tool in guiding pre-operative treatment decisions and could also reduce medical expenses in patients who would otherwise receive both a standard staging CT and EUS.

**P397**
Irreversible Electroporation and Pancreatic Cancer Surgery: Long-term Outcomes from a Single Institution
N. Ali,* M.M. Shah, K.M. El-Hayek, J. Wey, M. Walsh, S. Chatikonda. Digestive Disease Institute, Cleveland Clinic Foundation, Cleveland, OH.

Introduction: Irreversible electroporation (IRE) is a newer ablation technology that has evolved and is being utilized worldwide for many oncologic purposes. Typically it is used in the setting of pancreatic cancer for lesions that are deemed unresectable or margin accentuation for borderline resectable lesions. We present our long term outcomes with IRE since our institutions utilization in 2010. Methods: Retrospective review of a prospectively maintained database of patients undergoing surgery with inter-operative use of IRE at a single institution from December 2010 until July 2013. Results: IRE was performed in 26 patients. All ablations were performed inter-operatively. IRE was part of the treatment strategy for borderline resectable pancreatic tumors, and a majority of these patients underwent neoadjuvant chemotheraphy and radiation therapy (NCR). IRE was utilized for margin accentuation for resected lesions, and was primary treatment for tumors found to be unresectable due to mesenteric vascular involvement. Of the 26 patients, 12 (46%) underwent pancreatoduodenectomy (PD), 3 (12%) distal pancreatectomy (DP), 8 (31%) biliary and enteric bypass for unresectable pancreatic head tumors, and 3 (12%) IRE alone for unresectable body and tail lesions. Mean survival for resected patients (both PD and DP) was 372 days (range 32-728). Mean survival for unresected lesions was 222 days (range 24-648). Kaplan-Meier survival curve for all patients undergoing IRE shows 81% of patients survive for 1 year, with drop-off as seen(Figure 1). Comparison of those receiving NCR with IRE showed 1.3 times longer survival than those with IRE alone. 96% of patients treated were recurrence free at 6 months. There were no morbidity or mortality attributed to IRE during the study period. Conclusion: IRE is can be used for both margin accentuation and primary treat-
ment for unresectable lesions. Our outcomes show good disease free and overall survival for both borderline resectable and unresectable lesions. We believe that IRE should be part of treatment algorithm for patients with borderline resectable disease and can be safely performed in the majority of patients.

Figure 1: Overall survival for IRE patients, with number at risk above the x-axis.

P398
Neutrophil-lymphocyte Ratio as Predictor of Surgical Mortality and Survival in Complex Surgery of Upper Gastrointestinal Tract

INTRODUCTION: The neutrophil-lymphocyte ratio (NLR) has been proposed as a marker of systemic inflammatory response and as prognostic tool in various malignant neoplasms. We evaluate the impact of elevated neutrophil-lymphocyte ratio (NLR) as predictor of outcome in patients with upper gastrointestinal tract resection for malignant neoplasms in a tertiary referral center in Mexico City. METHODS: A retrospective study was carried out on patients with upper gastrointestinal tract resection for malignant neoplasms from January 2007 to December 2012. Patient demographic, clinical, and laboratory data were collected at the time of hospital admission and during follow-up. Comorbidities were registered with the Charlson score and complications were recorded according to Clavien score. NLR was considered high when >5. Variables associated with morbidity and mortality were analyzed using the chi square test for categorical variables and the Student’s t test for the continuous variables. Survival was calculated with the Kaplan-Meier method and curves were compared with the log-rank test. Statistical significance was considered at p<0.05. RESULTS: A total of 397 patients (52% women) with a mean age of 56 years were included. The most common surgical procedures were Whipple (50.9%) followed by gastrectomy (35%). Surgical morbidity was 41.3% and mortality 7.1%. Factors associated with significant surgical complications (Clavien > 3) were: low body mass index (<18), AJCC stage > III, ASA > III, Charlson >4 and transfusion requirement. Factors associated with mortality were old age (> 70), high NLR, AJCC stage > III and Charlson >4. On multivariate analysis, only high NLR ratio and Charlson >4 remain significant. High NLR was associated with lower survival rate at three years (69.1 vs. 57.3%; p=0.014). CONCLUSION: High NLR could be a predictor of surgical mortality and survival in cancer resection of upper gastrointestinal tract.

P399
Morphometric Predictors of Morbidity following Pancreatectomy

BACKGROUND: Pancreas cancer is the fourth leading cause of cancer related death in the United States. Surgical therapy for pancreas cancer has high risk of complication, even at high volume centers, and is associated with significant morbidity. The objective of this study was to compare different clinical and morphometric features of patients undergoing pancreatectomy in order to predict associated morbidity. METHODS: This is a retrospective review of all patients undergoing pancreatectomy at a tertiary care institution from December 2004-April 2012. Demographics, comorbidities, body mass index (BMI), and albumin levels were examined at time of diagnosis. Morphometric parameters on pre-operative computed tomography (CT) scan were measured, including measurement of psoas muscle cross sectional area, perinephric fat, and abdominal wall fat. Patients were placed into quartiles for each of these morphometric parameters for comparison. Thirty day morbidity and mortality were compared between groups. RESULTS: One hundred five patients underwent pancreatectomy during the study period (52 men, 53 women; average age 66). Median BMI was 28.4 kg/m2, and average albumin level was 3.77 g/dL. Psoas muscle area correlated with risk of surgical complication with the lowest quartile having a 46% complication rate, compared to 18% in the highest (p<0.04). Perinephric fat also correlated with surgical complications with the lowest quartile having a 7.6% complication rate versus 37% in the highest (p<0.02). Abdominal wall fat did not correlate with surgical complications. Finally, comparison was made between groups with different degrees of muscle mass linked with degree of obesity based on BMI. There was a strong statistically significant correlation between high psoas muscle mass and low BMI for low surgical complications compared to the group with low muscle mass and high BMI (p<0.0001). CONCLUSIONS: Patients undergoing pancreatic surgery with pre-operative sarcopenia in combination with high fat content have higher rates of major surgical complications. The results of this study suggest noninvasive pre-operative testing can be used to quantify post-operative risk in pancreatic surgery.

P400
Interobserver Variability in Contrast-enhanced CT and Whole-body FDG-PET in the Staging of Gastric Adenocarcinoma: A Single Institution 12-year Review

INTRODUCTION: The role of 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography (FDG-PET) in the staging work-up of gastric adenocarcinoma has not been clearly defined. The aim of this study was to assess the interobserver variability between contrast-enhanced computed tomography (CT) and FDG-PET in the staging of gastric adenocarcinoma. METHODS: We performed a retrospective chart review of all patients treated at our institution for gastric adenocarcinoma between 2000 and 2012. We identified all patients who had undergone a contrast-enhanced CT and FDG-PET before initiating treatment. The CT scans were evaluated by an experienced blinded body radiologist and the PET scans were independently evaluated by 2 experienced blinded nuclear physicians. Disease stage was assessed, looking at tumor, locoregional and distant lymph node disease, and metastasis. The results were analyzed using 2x2 contingency table analysis and the variability between modalities was determined by kappa-statistics. RESULTS: At our institution we identified 897 patients who had biopsy-proven gastric adenocarcinoma and 202 (22.5%) had a contrast-enhanced CT and an FDG-PET as part of their staging work-up. Of these, imaging from 123 patients was available for independent review. There appeared to be greater variability between CT and FDG-PET for the detection of primary tumor (kappa = 0.097) and distant lymph node disease (kappa = 0.175) while there seemed to be a fair agreement for the detection of locoregional lymph nodes (kappa = 0.335) and metastatic disease (kappa = 0.237). CONCLUSIONS: In the staging of patients with gastric adenocarcinoma, FDG-PET serves as a valuable adjunct to CT, especially when evaluating lymph node disease.
P401
A Qualitative Study of Patient and Clinician Attitudes regarding Surveillance following Resection of Pancreatic and Peripancreatic Cancer
R. Deobald,* E. Cheng, Y. Ko, F. Wright,* P. Karranicas.1
1. University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Odette Cancer Centre, University of Toronto, Toronto, ON, Canada.

Background: Pancreatic carcinoma is the fourth leading cause of cancer death in the USA. Following surgical resection, most patients will develop recurrence within two years. Intense follow-up is often recommended; however, the impact on survival is unknown. We sought to qualitatively assess patient and clinician attitudes towards follow-up and the perceived benefits and challenges. Methods: The research team developed a semi-structured interview guide. Purposive sampling identified patients who had undergone curative attempt resection and were in active surveillance or had developed recurrence. Clinicians involved in patient care were also interviewed. Themes were derived using standard qualitative methods. Results: Fifteen patients and seven clinicians were interviewed. Patient themes included (1) Limited understanding of disease prognosis; (2) Desire for reassurance through follow-up; (3) Desire to know when recurrence occurred; (4) Challenging treatments; (5) Minimal difficulties with the follow-up protocol; and (6) Limited role of family doctors in pancreatic cancer follow-up. Clinician themes included (1) Expectation that patients are aware of recurrence risk; (2) Desire to provide reassurance to patients; (3) Support for intense follow-up protocol despite lack of supporting evidence; (4) Secondary goals for surveillance; (5) Perceived patient challenges in follow-up; (6) Openness to family doctors doing follow-up. Overall, the dominant theme was one of disconnect between patients and clinicians in the understanding of the disease and its prognosis. Conclusion: Patients with pancreatic or peripancreatic cancer have an intense need for reassurance and obtain this through the follow-up process. Consequently they express few difficulties with follow-up despite the intensity of testing. Oncologists recognize this desire for reassurance and provide it through follow-up despite the lack of evidence to show benefit. There appears to be a disconnect between patients and clinicians in the understanding of the disease and its prognosis suggesting further work is needed to improve patient-physician communication.

P402
Outcomes of Laparoscopic Resection of Gastrointestinal Stromal Tumors Stratified by Tumor Size

Introduction: The safety of minimally invasive techniques has been described for the resection of gastric gastrointestinal stromal tumors (gGIST). However, few studies have examined the outcomes of laparoscopic (lap) GIST resection stratified by tumor size. We hypothesized that lap GIST resection would be associated with favorable perioperative and postoperative outcomes and that no differences in perioperative outcomes will be noted in resections of larger tumors compared to smaller ones. Methods: Retrospective review of patients who underwent lap GIST resection at our institution from 2000–2013 was performed. Cases converted from lap to open were not included in analysis. Mean continuous outcome variables were compared between T2 (2-5cm tumor size) and T3 (5-10cm) resections using student’s t-test. Margin status, pre-discharge mortality, and recurrences were compared between T2 and T3 resections with two-tailed z-tests. P<0.05 was considered the threshold for significance. Results: 75 patients were identified, comprising the largest lap GIST series in the literature. 5 lap to open conversions (6.25% of attempted lap cases) occurred during this period of time. Mean follow-up (±SEM) was 33.0±3.6 months. 10 of 14 T1 GIST specimens resected (71%) were incidentally discovered lesions from specimens from various laparoscopic operations, and this group was therefore excluded from comparison. T3 tumors were significantly larger than T2 tumors in our series. No significant differences were noted in patient age, gender, ASA score, or operative time between the T2 and T3 groups (Table 1). The recurrence rate was higher in T3 tumors, though this difference did not reach significance (p=0.08). No lap resections were attempted on tumors >10cm. Conclusions: Our group performed a retrospective review of lap gGIST resections stratified by tumor size. Pre-discharge mortality and recurrence were rare in our series. We did not detect any differences in perioperative or long term outcomes when comparing T2 and T3 resections. Our data suggest that lap resection of selected tumors up to T3 is a safe and effective treatment modality at a high volume center.

---

Table 1. Tumor <2cm Tumor 2-5cm Tumor 5-10cm
n 14 42 20
Age (y) 65.7 63.2 61.0
Gender (M/F) 43% 59% 45%
Follow-up (m) 19.0 35.2 37.5
ASA Score 2.8 2.3 2.5
Operative Time (min) 162.5 121.9 141.1
EBL (cc) 49.6 61.3 93.0
Tumor Size (cm) 1.1 3.3 6.1*
Positive Margins (%) 18.0% 2.5% 5.6%
Return to Reg Diet (d) 1.9 3.6 2.8
LOS (d) 2.7 4.1 3.3
Pre-Discharge Mortality (%) 7.10% 0% 0%
Recurrences (per 100 person-years) 0.00 0.86 5.03
*p<0.05

P403
Neoadjuvant Therapy for Pancreatic Cancer in Patients over Age 75

Introduction: Multiple treatments in series may be difficult for older patients (pts) to tolerate. We sought to examine the outcomes associated with neoadjuvant therapy in older pts with resectable (R) or borderline resectable (BLR) pancreatic cancer (PC). Methods: Pts ≥75 years (O) with those <75 (Y) with R or BLR PC receiving neoadjuvant therapy from 2008–2012 were identified. Clinicopathologic and treatment data were abstracted. Completion of all therapy was defined as the receipt of neoadjuvant therapy followed by surgical resection. Results: We identified 181 pts; 20.8% (n=16) of R and 12.5% (n=13) of BLR were ≥75 years. Older pts had higher Charlson Comorbidity Index (CCI) (median: 4 vs. 2, p<0.01), more hospitalizations during neoadjuvant therapy (50% vs. 28%, p=0.04) and were less likely to complete all therapy as compared to Y pts (72.4 vs. 89.5%, p=0.01). Poor performance status was the most common reason for failure to complete all therapy in O vs. Y pts (17.2% vs. 0.7%, p<0.01). Higher CCI (OR 0.25; 95% CI: 0.08-0.74, p=0.01) and advanced clinical stage (OR 0.17; 95%CI: 0.06-0.48, p=0.01) were associated with failure to complete all therapy. Among pts who completed all therapy, no significant differences in complication rates (15.0% vs. 15.3%, p=0.33), median length of hospital stay (10 vs. 9 days, p=0.29), or 30 day readmission rates (10% vs. 11%, p=0.81) were observed. Median overall survival of the 181 pts was 19.7 and 26.4 months (p=0.04) for O and Y pts respectively. In contrast, of 138 pts who completed all therapy, there was no difference in survival between O vs. Y pts (24.3 mo vs. 36.7 mo, p=0.20). Conclusions: After neoadjuvant therapy, 25% of pts≥75 years of age will not undergo surgical resection. The most common reason for not completing all therapy is a decline in performance status. Whether neoadjuvant therapy improves the selection of older pts who should not undergo an operation or prevents successful resection of pts who may have tolerated an operation is unclear. With evolving paradigms of treatment sequencing, the management of PC pts with advanced age will require further assessment.
Abstracts: Poster Presentations

P404
A Population-based Cohort Study of Factors Predicting Treatment Management Strategy in Metastatic Gastric Cancer
J. Vasilevska-Ristovksa,1 R. Seevaratnam,1 R. Cardoso,1 B. Zagorski,1
Population-based Study
1. Public Health Sciences, Queen’s University, Kingston, ON, Canada; 2. Dalhousie University, Halifax, NS, Canada; 3. Maimonides Medical Center, Brooklyn, NY; 4. Sunnybrook Research Institute, Toronto, ON, Canada; 5. University of Toronto, Toronto, ON, Canada.

Background: The majority of gastric cancer (GC) patients present with metastatic disease, for whom the benefit of aggressive treatment is unclear. Understanding factors predicting treatment choice may help future decision-making. Methods: A population-based cohort study of patients diagnosed with M1 stage IV (6th Ed) GC in Ontario 04/01/2005-03/31/2008 was performed. Patients who received treatment were categorized as 1) chemotherapy or chemoradiation, 2) surgery alone, 3) surgery with either chemotherapy or radiation and 4) all treatments. Characteristics compared among treatment groups included patient, disease and health system factors. Polytomous logistic regression using backward selection identified independent predictors of treatment strategy. Odds ratios (OR) and 95% confidence intervals (CI) were reported. Results: 898/1433 M1 patients received oncologic management. Among treatment strategies, the distribution of the number and type of metastatic sites, primary tumor locations, Charlson scores, number and type of symptoms and receipt of care from a high volume physician differed significantly. On multivariate regression, patients with a tumor located in the gastroesophageal junction (OR: 0.37 [95%CI 0.20-0.66], proximal (OR 0.41 [95%CI 0.04-0.64]) and entire stomach (OR 0.30 [95%CI 0.1-0.79) were less likely than those with a tumor in the distal stomach to receive all three treatment modalities. Patients with bleeding (OR 2.00 [95%CI 1.26-3.18]) or symptoms of major obstruction (OR 1.49 [95%CI 0.91-2.44]) had increased odds of receiving all three treatment modalities compared to chemotherapy or chemoradiation. Patients who saw a high volume physician had a significantly increased odds of receiving all three treatments versus chemotherapy or chemoradiation alone compared to those who did not see a high volume physician (OR 2.49 [95%CI 1.58-3.93]). Additional factors significantly associated with decreased odds of receiving all three treatments included symptoms of malnutrition, signs of advanced disease and liver metastases. Conclusion: Disease, patient and system characteristics all played a role in determining which oncologic strategies were provided.

P405
Gastric Cancer Outcomes and Survival: Findings from a Large Population-based Study
A. El-Sedfy,2* M. Dixon,3 A. Mahar,4 J. Vasilevska-Ristovksa,1 R. Seevaratnam,1 R. Cardoso,1 B. Zagorski,1 L. Paszat,1 L. Helyer,5 J. Heather,2 S. Ahrendt, M.P. Holtzman, J. Pingpank, A.H. Zureikat,1 A. Mahar,3* L. Helyer,5

1. Sunnybrook Research Institute, Toronto, ON, Canada; 2. Department of Surgery, Saint Barnabas Medical Center, Livingston, NJ; 3. Department of Surgery, Maimonides Medical Center, Brooklyn, NY; 4. Department of Public Health Sciences, Queen’s University, Kingston, ON, Canada; 5. Department of Surgery, Dalhousie University, Halifax, NS, Canada; 6. Department of Surgery, University of Toronto, Toronto, ON, Canada; 7. Division of Surgical Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

BACKGROUND: Although the incidence of gastric cancer (GC) has declined, it still remains one of the most common causes of cancer-related mortality worldwide. The aim of this study is to describe the demographic, tumor and clinical characteristics at a population-level. METHODS: We performed a primary chart review for all GC patients diagnosed April 2005 to March 2008 in Ontario. Survival analysis was performed using Kaplan-Meier analysis. RESULTS: During the study period, 2516 patients were diagnosed with GC. The reported demographic data included the following: 65% men, 35% women, 88.4% urban population, 11.6% rural population, 52.4% of patients were over the age of 70 years and 9.2% were below age 50 years. Although 52.7% of this cohort had no previous hospitalization, the majority of patients had major symptoms (61.4%) at the time of diagnosis and had AJCC Stage IV disease (66.9%). Early GC was found in 11.2% of patients. Tumors were located at the gastroesophageal junction in 26.1% of cases and distal stomach in 37.4% of cases. Of the patients that underwent surgery, 16.5% had positive proximal margins, while 21.7% had positive distal margins. Median length of hospitalization (interquartile range) was 12 days (9-20 days). Median number of lymph nodes (LN) harvested (interquartile range) was 13 LNs (8-19 LNs). The median overall survival times for AJCC stage 0, II, IIIa, IIIb and IV were 72, 58.5, 29.8, 18.4 and 6.9 months, respectively. CONCLUSIONS: While this data confirms the fact that the Province of Ontario has a low prevalence of GC, it also demonstrates that different stages of GC have distinct demographic, tumor and clinical characteristics. Our population-level assessment reveals an elevated proportion of diagnosis at AJCC stage IV and an elevated positive margin rate after resection.

P406
Pancreatic Fistulae in Patients Undergoing Hyperthermic Intraperitoneal Chemoperfusion (HIPEC) and Distal Pancreatectomy
A. El-Sedfy,2* M. Dixon,3 A. Mahar,4 J. Vasilevska-Ristovksa,1 R. Seevaratnam,1 R. Cardoso,1 L. Paszat,1 L. Helyer,5 J. Heather, S. Ahrendt, M.P. Holtzman, J. Pingpank, A.H. Zureikat,1 A. Mahar,3* L. Helyer,5

1. Sunnybrook Research Institute, Toronto, ON, Canada; 2. Department of Surgery, Saint Barnabas Medical Center, Livingston, NJ; 3. Department of Surgery, Maimonides Medical Center, Brooklyn, NY; 4. Department of Surgery, Saint Barnabas Medical Center, Livingston, NJ; 4. Department of Public Health Sciences, Queen’s University, Kingston, ON, Canada; 5. Department of Surgery, Dalhousie University, Halifax, NS, Canada; 6. Department of Surgery, University of Toronto, Toronto, ON, Canada; 7. Division of Surgical Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

Introduction: We compared the rate of pancreatic fistulae in patients undergoing distal pancreatectomy and HIPEC to patients undergoing distal pancreatectomy alone. Methods: Between 2001 and 2012, demographics, clinicopathologic and perioperative details, including pancreatic fistula rates, and long-term outcomes were reviewed in patients undergoing distal pancreatectomy as a component of cytoreductive surgery and HIPEC for peritoneal carcinomatosis of appendiceal (n=31) or colorectal (n=23) origin and compared to patients undergoing minimally invasive or open distal pancreatectomy without HIPEC (n=66) for locally resectable pancreatic adenocarcinoma. Pancreatic fistulae were graded according to the International Study Group of Pancreatic Surgery system. Results: Overall pancreatic leak rate was not different between the two groups however the severity of leak was different between the HIPEC cohort and both the distal pancreatectomy cohort (table) and open distal pancreatectomy cohort. Patients in the HIPEC group were younger, had a higher rate of ICU admission and longer hospital length of stay (19.4 vs. 8.3 days). HIPEC patients with leak did not differ in their extent of debulking, length of stay or post-operative complications including wound infection, cardiac and pulmonary complications, ileus and delayed gastric emptying compared to HIPEC patients without leak. Conclusion: When they occur, pancreatic fistulae in patients undergoing distal pancreatectomy and HIPEC are more severe than in those undergoing distal pancreatectomy alone however there is no difference in life-threatening type C leaks.

Leaks by type in patients undergoing distal pancreatectomy in setting of HIPEC vs distal pancreatectomy alone

<table>
<thead>
<tr>
<th>Type of Leak</th>
<th>No HIPEC</th>
<th>HIPEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Leak</td>
<td>10 (12.5%)</td>
<td>46 (39.7%)</td>
</tr>
<tr>
<td>Type A Leak</td>
<td>12 (15.0%)</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Type B Leak</td>
<td>31 (37.5%)</td>
<td>13 (11.2%)</td>
</tr>
<tr>
<td>Type C Leak</td>
<td>0 (0.0%)</td>
<td>4 (3.4%)</td>
</tr>
</tbody>
</table>

Fisher’s exact test p-value < 0.0001

P407
Population-based Outcomes of Laparoscopic and Open Gastroctomy
A. El-Sedfy,2* A. Mahar,4 J. Vasilevska-Ristovksa,1 R. Seevaratnam,1 R. Cardoso,1 B. Zagorski,1 L. Paszat,1 L. Helyer,5 J. Heather,2 S. Ahrendt, M.P. Holtzman, J. Pingpank, A.H. Zureikat,1 A. Mahar,3* L. Helyer,5

1. Sunnybrook Research Institute, Toronto, ON, Canada; 2. Department of Surgery, Saint Barnabas Medical Center, Livingston, NJ; 3. Department of Surgery, Maimonides Medical Center, Brooklyn, NY; 4. Department of Surgery, Saint Barnabas Medical Center, Livingston, NJ; 4. Department of Public Health Sciences, Queen’s University, Kingston, ON, Canada; 5. Department of Surgery, Dalhousie University, Halifax, NS, Canada; 6. Department of Surgery, University of Toronto, Toronto, ON, Canada; 7. Division of Surgical Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

BACKGROUND: Curative intent treatment for gastric cancer (GC) involves a gastrectomy with lymphadenectomy. A laparoscopic approach may offer benefits, however large multi-center studies are lacking. The aim of this study is to examine short and long term outcomes of laparoscopic gastrectomy (LG) vs. open gastrectomy (OG) for GC on a population-level. METHODS: A retrospective, provincial chart review of GC patients diagnosed April 2005 to March 2008, for whom an operative note existed, was performed. Outcomes measured were tumor-node-metastasis stage at presentation, location
of tumor, number of lymph nodes (LN) retrieved, specimen margins, length of operation, length of stay (LOS), postoperative blood-product transfusions (BPT) and overall survival (OS). RESULTS: A total of 392 patients underwent a resection of which 337 (86.0%) were an OG and 55 (14.0%), a LG. There was no significant difference in 30-day mortality (5.6% OG; 7.3% LG; p=0.547). Median operative time (interquartile range [IR]) was longer for LG compared to OG (280 min (230-245 min) vs. 255 min (210-305 min); P=0.0251). Median LOS (IR) for OG was 12 days (9-19) compared to 8 days (6-19) for LG (p=0.126). Proximal margins were positive in 9.9% of OG, compared to 3.7% of LG (p=0.284). Distal margins were positive in 8.8% of OG, compared to 11.1% of LG (p=0.422). Median number of LNs harvested (IR) in OG was 14 LNs (8-20 LNs) compared with 10 LNs (6-13 LNs) in LG (p=0.0034). BPTs occurred in 142 (42.1%) and 17 (30.9%) patients from OG and LG, respectively (p=0.116). The 5-year OS for OG is 45.6% vs. 50.5% for LG (p=0.837). CONCLUSIONS: Our population-level assessment reveals similar 30-day mortality rates in both OG and LG. Although non-significant, LG had a trend towards shorter LOS and fewer BPTs. In regards to oncological principles, while both groups had similar margin status results, LG had significantly less LNs harvested during lymphadenectomy. Significant selection bias likely exists for patients chosen for LG.
Disclosures Policy and Disclosures
As required by the Accreditation Council for Continuing Medical Education (ACCME) and in accordance with the Society of Surgical Oncology (SSO) policy, all educational planners, presenters, instructors, moderators, authors, reviewers and other individuals in a position to control or influence the content of an activity must disclose all relevant financial relationships with any commercial interest that have occurred within the past 12 months. This includes the disclosure of all financial relationships with a commercial interest of a spouse or partner. A commercial interest is any entity producing, marketing, reselling, or distributing health care goods or services consumed by, or used on, patients. ACCME does not consider providers of clinical service directly to patients to be commercial interests. The ACCME considers financial relationships to create conflicts of interest when individuals have both a financial relationship with a commercial interest and the opportunity to affect the content of CME about the products or services of that commercial interest. All identified conflicts of interest must be resolved and the educational content thoroughly vetted for fair balance, scientific objectivity, and appropriateness of patient care recommendations. It is required that disclosure be provided to the learners prior to the start of the activity. Individuals with no relevant financial relationships must also inform the learners that no relevant financial relationships exist. Learners must also be informed when off-label, experimental/investigational uses of drugs or devices are discussed in an educational activity or included in related materials. Disclosure in no way implies that the information presented is biased or of lesser quality. It is incumbent upon course participants to be aware of these factors in interpreting the program contents and evaluating recommendations. Moreover, expressed views do not necessarily reflect the opinions of the SSO. (Please note that Posters were not certified for credit.)

The following Oral Abstract and Poster Main Authors and Presenters have disclosed financial relationships with commercial interests:

**Andtbacka, Robert 52**
Advisory Board: Amgen Inc.; Consultant: Amgen Inc.

**Faries, Mark 54**
Advisory Board: Amgen; Other: Unpaid Proctor, Decatur Systems

**Martin, Robert 1, 44**
Consultant: Bayer/Onyx

**Martinez Said, Hector P204, P308**
Advisory Board: Boehringer Ingelheim, Bristol Myers Squibb, Roche, Merck Sharp & Dohme

**Mullins, C. Daniel P291**
Advisory Board: Amgen, Bayer, Genentech, Pfizer; Grant: Amgen, Bayer, Pfizer; Research, Bayer, Pfizer; Consultant, Speaker Honorarium: Pfizer

**Saiura, Akio P177**
Honorarium: Bristol Myers, Chugai, Merk Serono

**Schwarz, Roderich 84**
Speaker: Genentech, Novartis

**Wagman, Lawrence 23**
Speaker: Bristol-Myers-Squibb
The following Oral Abstract and Poster Main Authors and Presenters have reported that they have no relevant financial relationships with commercial interests to disclose:

Aalders, Kim P10
Abbott, Andrea P237
Abbott, Daniel 82
Abdelgadir Adam, Mohamed P145
Abdelsattar, Zaid 24, 63
Abe, Shoko 10
Abramowitz, Dan P305
Adeshuko, Folashade P181, P394
Adesoye, Taiwo P150
Adkisson, Cameron P143
Ahmed, Shuja P274
Aimaq, Rahim P191
Ajkay, Nicolas P5
Akanuma, Naoki P332
Alabbas, Haytham P135
Alakus, Hakan 20
Al-Azhri, Jamila P65
Alemi, Farzad P390
Ali, Noaman P397
Alsaied, Osama 43
Amini, Albert P179
Anantha Sathyanarayana, Sandeep P154, P155
Anderson, Caroline P192, P245, P246, P254
Angeles, Christina P209, P201
Ankeny, Jacob P336
Aoyagi, Tomoyoshi P122
Araujo, Raphael P169
Arena, Elizabeth P222
Arora, Tania P317
Artinyan, Avo V6
Aukema, Tjerd 86
Awad, Ziad V8
Aydin, Nail P283
Azab, Basem P190
Baba, Hironobu P120
Bagaria, Sanjay P199
Bailey, Christina P102, P243
Barbie, Thanh P89
Barden, Gala P258, P264, P275
Bartlett, Edmund P298
Bates, Benjamin P193
Beane, Joal 4
Beasley, Georgia 49
Bedrosian, Isabelle P18
Bennett, Adam 61
Bennett, Joseph P192
Bennett, Sean 28
Bergquist, John P76
Bernthal, Nicholas P313
Besic, Nikola P12, P153
Bilchik, Anton 21
Bischof, Danielle 69, P297
Blakely, Andrew P278
Blank, Sima P167
Blansfield, Joseph P399
Bliss, Lindsay P376
Bloomquist, Erica P14
Bloomston, Mark 2
Boland, Genevieve 53
Boone, Brian 5, P346
Bosscher, Marianne P259
Boughey, Judy P59
Bouvet, Michael P353
Bowles, Tawnya P239
Brahmbhatt, Rushin P55
Braun, Josef P103
Broussard, Brett P324
Brown, Daniel P40
Brown, Erin P166
Brueske, Kevin P217
Budde, Cristina P95
Buijs, Maria P114
Bulte, Joris P44
Burga, Rachel P97
Burrish, Nikki P277
Cader, Sonia P334
Calata, Jed P98
Canter, Robert P303
Carpenter, Kendall P202
Ceelen, Wim P105, P125
Chan, Carlos P47
Chawla, Akhil P21
Chen, Kathryn P395
Chikman, Bar P66
Choi, Michael P314
Choudry, Mohammad Haroon P113
Chow, Oliver P111
Cintolo-Gonzalez, Jessica P205
Clarke, Callisia P126
Cloyd, Jordan P232
Cocieru, Andrei P306
Condren, Audree P85
Cooper, Amanda P178
Coopey, Suzanne P11
Corona-Cruz, J. Francisco 87, V1
Cucher, Daniel P211
Cyr, Anthony P382
Datta, Jashodeep 15, P365
De Andrade, James P71
Conflict of Interest Disclosures
Kim, Michael P358
Kim, Minhyung P200
Kimbrough, Charles P348
Kirane, Amanda P36
Kirchoff, Daniel P221
Kluger, Michael 78, P159
Knab, Lawrence P347
Kobayashi, Hirotoshi P96
Koh, Ye Xin P242
Koslow, Starr P32
Krell, Robert P256
Kroon, Hidde P50, P212
Kshivets, Oleg P331
Kukar, Moshim 37, 80, P381, V2
Lahat, Guy 74, P373
Lai, Lily P54
Lai, Victoria P149
Lancaster, William P208
LaRocca, Christopher P247
Laronga, Christine P35, P88
Lautner, Meeghan P70
Lavy, Ron P66
Lee, David P284
Lerner, Jonathan P156
Leung, Anna P8
Lewis, Russell P371
Li, Pamela P92
Liederbach, Erik P58
Lin, Ying-Sheng P253
Lindberg, James 96
Look Hong, Nicole 56
Lubezky, Nir 74
Luna-Perez, Pedro P107
Lushaj, Entela 85
Luu, Carrie P289
Luyimbazi, David P34
Mackey, Aimee 14
Madden, Jesse P239
Maffuz-Aziz, Antonio P68
Mahar, Alyson P404
Mahendraraj, Krishnaraj P90, P133, P147, P174, P250
Mallipeddi, Mohan P329
Maloney, James 85
Mann, Gregory P49
Mansour, John 61
Margenthaler, Julie P41, P89
Mathew, Jesna P189
McAuliffe, Priscilla P40
McCahill, Laurence P276
Medina-Franco, Heriberto P39, P248, P398
Metildi, Cristina P353
Mezhir, James P382
Michel, Martin P380
Milgrom, Sarah 19
Miller, Marian P50
Miura, John P171, P355, P403
Miyashita, Tomoharu 83
Mohamed, Hossam 36
Mohammed, Somalia P83, P359
Mongiu, Anne P84
Muilenburg, Diego 51
N M L, Manjunath P316
Nadeem, Hasan P118
Nagahara, Makoto P31
Nagahashi, Masayuki P3
Nakhlis, Faina P57, P84
Namm, Jukes P82, P384
Nason, Katie 79
Nathan, Hari 60
Nenshi, Rahima P296
Neves, Rogerio P203
Newhook, Timothy 95, P335
Ng, Deanna P252
Nguyen, Trang P168
Niebling, Maarten P220
Nizri, Eran P360
Nunez, Maria P273
Nussbaum, Daniel P299
Nywening, Timothy P340
O'Connor, Victoria 70
Ojo, Adewuni P75
Okkabaz, Nuri P123
Okumura, Hiroshi 81
Oltmann, Sarah P151
Onesti, Jill P386, P388
Orr, Richard P228
Oxenegg, Jacqueline P261
Oyasiji, Tolutope P233
Ozao-Choy, Junko P214
Pandalai, Prakash P223
Panni, Roheena P337
Papenfuss, Wesley P378
Parikh, Alexander 31
Park, Do Jong 90
Parvez, Elena P81
Paulus, Elena P213
Pawlik, Timothy 39, 69, P297
Pennacchioli, Elisabetta P230
Peeples, Claire P262
Perhavic, Andraz P315
Petric, Rok P153
Philips, Prejesh 98
Platt, Jennica P29
Plukker, John P319
Pockaj, Barbara P56
Polanco, Patricio P266
Pooni, Amandeep P236
Porembka, Matthew P165
Porter, Geoffrey P80
Portsch, Pamela P69
Povoski, Stephen P244, P259
<table>
<thead>
<tr>
<th>Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prabhakaran, Sangeetha</td>
<td>P241</td>
</tr>
<tr>
<td>Press, Danielle</td>
<td>P137</td>
</tr>
<tr>
<td>Proctor, Erica</td>
<td>P52</td>
</tr>
<tr>
<td>Qadan, Motaz</td>
<td>P304</td>
</tr>
<tr>
<td>Racz, Jennifer</td>
<td>P305, P312</td>
</tr>
<tr>
<td>Radomski, Michal</td>
<td>P128</td>
</tr>
<tr>
<td>Rajaei, Mohammad</td>
<td>P144</td>
</tr>
<tr>
<td>Randle, Reese</td>
<td>P129</td>
</tr>
<tr>
<td>Raooof, Mustafa</td>
<td>P164</td>
</tr>
<tr>
<td>Rashid, Omar</td>
<td>P268</td>
</tr>
<tr>
<td>Read, Rebecca</td>
<td>P225, V5</td>
</tr>
<tr>
<td>Reyna, Chantal</td>
<td>P24</td>
</tr>
<tr>
<td>Rickles, Aaron</td>
<td>P17</td>
</tr>
<tr>
<td>Rivard, Justin</td>
<td>P287</td>
</tr>
<tr>
<td>Rizzo, Monica</td>
<td>P207</td>
</tr>
<tr>
<td>Robinson, Kristin</td>
<td>P7</td>
</tr>
<tr>
<td>Rodriguez, Rodrigo</td>
<td>P134</td>
</tr>
<tr>
<td>Roland, Christina</td>
<td>P148</td>
</tr>
<tr>
<td>Romero Arenas, Minerva</td>
<td>P146</td>
</tr>
<tr>
<td>Rose, J. Bart</td>
<td>P176</td>
</tr>
<tr>
<td>Rosen, Jennifer</td>
<td>P140</td>
</tr>
<tr>
<td>Rowland, Kathryn</td>
<td>P136</td>
</tr>
<tr>
<td>Rubio, Isabel</td>
<td>P25</td>
</tr>
<tr>
<td>Rueth, Natasha</td>
<td>P263</td>
</tr>
<tr>
<td>Ruszczyk, Melanie</td>
<td>P22</td>
</tr>
<tr>
<td>Sadot, Eran</td>
<td>P161, P385</td>
</tr>
<tr>
<td>Saha, Arin</td>
<td>P330, P380</td>
</tr>
<tr>
<td>Saha, Sukamal</td>
<td>P282</td>
</tr>
<tr>
<td>Saied Calvino, Abdul</td>
<td>P158</td>
</tr>
<tr>
<td>Saigal, Anupama</td>
<td>P87</td>
</tr>
<tr>
<td>Saito, Hidehito</td>
<td>P219</td>
</tr>
<tr>
<td>Salti, George</td>
<td>P309</td>
</tr>
<tr>
<td>Samples, Jennifer</td>
<td>P9</td>
</tr>
<tr>
<td>Sanford, Dominic</td>
<td>97</td>
</tr>
<tr>
<td>Sardi, Armando</td>
<td>P270, P273, P283</td>
</tr>
<tr>
<td>Saunders, Aaron</td>
<td>P269</td>
</tr>
<tr>
<td>Saunders, Neil</td>
<td>P379</td>
</tr>
<tr>
<td>Schiffman, Suzanne</td>
<td>P350</td>
</tr>
<tr>
<td>Schmidt, Hank</td>
<td>P26</td>
</tr>
<tr>
<td>Schneble, Erika</td>
<td>P6</td>
</tr>
<tr>
<td>Schoellhammer, Hans</td>
<td>P175</td>
</tr>
<tr>
<td>Schubart, Jane</td>
<td>P257</td>
</tr>
<tr>
<td>Segedi, Maja</td>
<td>P338</td>
</tr>
<tr>
<td>Sepesi, Boris</td>
<td>88</td>
</tr>
<tr>
<td>Serrano, Oscar</td>
<td>P400</td>
</tr>
<tr>
<td>Serrano Aybar, Pablo</td>
<td>P183</td>
</tr>
<tr>
<td>Shahabang, Mohsen</td>
<td>P78, P189</td>
</tr>
<tr>
<td>Shah, Anushi</td>
<td>P186</td>
</tr>
<tr>
<td>Shah, Kevin</td>
<td>P306</td>
</tr>
<tr>
<td>Sham, Jonathan</td>
<td>P146, P194</td>
</tr>
<tr>
<td>Shapiro, Mia</td>
<td>P130</td>
</tr>
<tr>
<td>Sharpe, Susan</td>
<td>P20</td>
</tr>
<tr>
<td>Sherman, Scott</td>
<td>29</td>
</tr>
<tr>
<td>Shirley, Lawrence</td>
<td>P363, P375, P377</td>
</tr>
<tr>
<td>Shoor, Priya</td>
<td>P320</td>
</tr>
<tr>
<td>Showalter, Shayna</td>
<td>P1</td>
</tr>
<tr>
<td>Sin, Eliza</td>
<td>P249</td>
</tr>
<tr>
<td>Singla, Smit</td>
<td>P141, P265, P311</td>
</tr>
<tr>
<td>Smith, Franz</td>
<td>P196</td>
</tr>
<tr>
<td>Smith, Roger</td>
<td>V6</td>
</tr>
<tr>
<td>Snyder, Rebecca</td>
<td>64</td>
</tr>
<tr>
<td>Soares, Kevin</td>
<td>P109</td>
</tr>
<tr>
<td>Somasundar, Ponnamdai</td>
<td>P293</td>
</tr>
<tr>
<td>Somnay, Yash</td>
<td>P142</td>
</tr>
<tr>
<td>Spahnz, Philip</td>
<td>17</td>
</tr>
<tr>
<td>Speicher, Paul</td>
<td>94</td>
</tr>
<tr>
<td>Spillane, Andrew</td>
<td>V5</td>
</tr>
<tr>
<td>Squires, Malcolm</td>
<td>32, 89, P333, P351</td>
</tr>
<tr>
<td>Stavrou, Eleni</td>
<td>P94</td>
</tr>
<tr>
<td>Steinman, Jennifer</td>
<td>P16, P45</td>
</tr>
<tr>
<td>Steliga, Matthew</td>
<td>P328</td>
</tr>
<tr>
<td>Stevens, Lewis</td>
<td>P330</td>
</tr>
<tr>
<td>Strohle, Madeleine</td>
<td>P392</td>
</tr>
<tr>
<td>Sugahara, Kazuki</td>
<td>P115</td>
</tr>
<tr>
<td>Sun, Susie</td>
<td>P8</td>
</tr>
<tr>
<td>Sutton, Jeffrey</td>
<td>66</td>
</tr>
<tr>
<td>Swistel, Alexander</td>
<td>V3</td>
</tr>
<tr>
<td>Tabrizian, Parissa</td>
<td>P108</td>
</tr>
<tr>
<td>Takeno, Atsushi</td>
<td>P356</td>
</tr>
<tr>
<td>Tan, Grace</td>
<td>P343</td>
</tr>
<tr>
<td>Tan, Winson Jinhong</td>
<td>P288</td>
</tr>
<tr>
<td>Taniguchi, Masahiko</td>
<td>P160</td>
</tr>
<tr>
<td>Terando, Alicia</td>
<td>P251</td>
</tr>
<tr>
<td>Terhune, Julia</td>
<td>P93</td>
</tr>
<tr>
<td>Teshome, Medidget</td>
<td>3</td>
</tr>
<tr>
<td>Thirunavukarasu, Pragathee</td>
<td>22, P116, P280</td>
</tr>
<tr>
<td>Thomay, Alan</td>
<td>P326, P327</td>
</tr>
<tr>
<td>Thorn, Mitchell</td>
<td>42</td>
</tr>
<tr>
<td>Tignanelli, Christopher</td>
<td>P170</td>
</tr>
<tr>
<td>Tran Cao, Hop</td>
<td>62, P162</td>
</tr>
<tr>
<td>Tran, Thuy</td>
<td>P304</td>
</tr>
<tr>
<td>Trappey, Alfred</td>
<td>16</td>
</tr>
<tr>
<td>Tsai, Susan</td>
<td>P173</td>
</tr>
<tr>
<td>Tsang, Melanie</td>
<td>P318</td>
</tr>
<tr>
<td>Tseng, Jennifer</td>
<td>P216, P277</td>
</tr>
<tr>
<td>Tse, Warren</td>
<td>P292</td>
</tr>
<tr>
<td>Tummel, Evan</td>
<td>8</td>
</tr>
<tr>
<td>Tuttle, Rebeca</td>
<td>P224</td>
</tr>
<tr>
<td>Uehara, Keisuken</td>
<td>P104</td>
</tr>
<tr>
<td>Uenosono, Yoshikazu</td>
<td>91</td>
</tr>
<tr>
<td>Ugras, Stacy</td>
<td>P19</td>
</tr>
<tr>
<td>Untch, Brian</td>
<td>34</td>
</tr>
<tr>
<td>Uppal, Abhineet</td>
<td>P323</td>
</tr>
<tr>
<td>Van Broekhoven, Danique</td>
<td>75</td>
</tr>
<tr>
<td>Van Ginkel, Robert</td>
<td>P231</td>
</tr>
<tr>
<td>van Rooijen, Stefanus</td>
<td>P106</td>
</tr>
<tr>
<td>Veerman, Kelly</td>
<td>P231</td>
</tr>
<tr>
<td>Verberne, Charlotte</td>
<td>2</td>
</tr>
<tr>
<td>Villescas, Victoria</td>
<td>P62</td>
</tr>
<tr>
<td>Voci, Amy</td>
<td>P86</td>
</tr>
<tr>
<td>Vos, Elvira</td>
<td>P4</td>
</tr>
</tbody>
</table>
Votanopoulos, Konstantinos P255
Vu, Huan P91
Wachtel, Heather 38
Wai, Christina P132
Wallace, Anne P46
Wallack, Marc P240
Wanebo, Harold P281, P294, P364
Wang, Bo P138
Wang, Sam P349
Wang, Yi-Zarn P286
Warren Peled, Anne P60
Wasif, Nabil 65
Weissler, Julie P64
Weiss, Matthew 93
Weixler, Benjamin 18
Wexelman, Barbara P74
Wightman, Sean P198
Wikholm, Lauren P30
Wilfong, Chandler P215
Wilson, Gregory P271
Wilson, Niamey P27
Woldemichael, Andinet P285
Worhunsky, David 77
Wright, G. Paul P13
Wu, Daniel P2
Wu, Susana P389
Yakoub, Danny P372, P383
Yamamoto, Maki P206, P226
Yamaoka, Yusuke P112
Yanagita, Shigehiro P341
Yeluri, Sashidhar P321, P325
Yopp, Adam 45, P260
Zih, Francis P182
Zihni, Ahmed P402
Zoon, Christine P210
AUTHOR INDEX

67th Annual Cancer Symposium
Society of Surgical Oncology
March 12–15, 2014
Phoenix, Arizona
Boone, E.L.  P328  Cance, W.G.  37, P141
Boosalis, V.A.  P130  Cannell, A.J.  P310, P318
Borger, D.  39  Canter, R.  P166
Borgida, A.  P338  Canter, R.J.  P303
Bosch, S.L.  P106  Cao, C.  P364
Bosch, M.R.  P295  Capano, M.  P344
Boudreaux, P.  P286  Caravan, P.  172
Boutin, R.D.  P303  Cardoso, R.  P405, P407
Bouton, M.  P30  Carlson, G.W.  P207
Bouvet, M.  P353  Carpenter, K.  10, P202
Bowen, W.  P364  Carpio, D.R.  P195
Bowles, T.  P239  Carr, J.C.  17
Bowser, I.  48  Carty, S.E.  P143
Boyd, T.  P63  Casali, P.  72
Braam, H.J.  P106  Cate, S.  P92
Bradley-Dunlop, D.  P211  Catton, C.  P101
Braley, M.S.  P201  Caudle, A.  53
Brahmbhatt, R.D.  P55  Cauley, C.E.  P11
Brar, S.S.  P236, P305, P312  Cavallo, J.A.  P402
Braun, J.  P103  Ceelen, W.  27, P105, P125
Brekke, A.  P151  Cerullo, I.  38, P152
Breken, R.  45  Chabaud, S.  P119
Brennan, M.F.  14, 34, 71, P344, P349  Chabot, J.  78
Brenneman, F.  P296  Chadha, M.  P92
Brenner, M.K.  P359  Chappar, A.B.  13, P48
Brock, J.  P57  Chappar, R.  P137
Brod, A.M.  15  Chakikonda, S.  P397
Broome, J.T.  35  Chamberlain, R.S.  P90, P133
Broussard, B.L.  P324  Chan, C.H.  P47
Brower, S.T.  P345  Chan, K.  56
Brown, D.D.  P40  Chan, R.  P359
Brown, E.  P166  Chan-Nuc, C.  P398
Brown, M.  P338  Chang, A.  P219
Brown, R.  16  Chang, G.J.  62, P102, P126
Brueske, K.A.  P217  Chang, K.K.  71
Brusse-Keizer, M.  P114  Chatterjee, D.  P148
Budde, C.N.  P95  Chau, Z.  P277, P278
Buell, J.  P188  Chawla A.  P21
Buiks, M.M.  P144  Chen, A.  P124
Bulle, J.  P44  Chen, C.  19, P111, P195, P363, 377
Burga, R.A.  40, 42, P97, P158  Chen, H.  21, 58, P142, P144, P151
Burgerhoff, H.G.  P319  Chen, K.T.  P395
Burgers, S.  86  Chen, L.  P2, P2
Burke, E.E.  P69  Chen, P.  P72
Burke, J.M.  P282  Chen, S.  12, P50
Burnish, N.M.  P277  Chen, Y.  71, P119, P175, P191
Burtness, B.  P326  Chen, Z.  P111, P338
Busaidy, N.L.  P146  Cheng, D.  P338
Butterfield, L.  P128  Cheng, E.  P401
Buysse, M.  23  Cheng, J.  P81
Byrne, M.  P65, P73  Cherui, D.  45
Cader, S.R.  P334  Cheria, C.  P249, P252, P288, P343
Cai, L.  P347  Chiang, Y.  P307
Calata, J.F.  P98  Chikman, B.  P66
Callegaro, D.  72  Chin-Lenn, L.  P287
Calverley, V.  P80  Chmieleowski, B.  58
Cameron, J.  93  Chmura, S.J.  P267
Camp, E.R.  P208  Cho, C.  98, P150, P333, P361, P387, P393, P394
Campbell, K.  P279  Cho, C.S.  89, P351
Campbell Jr, D.A.  63, P256  Choe, E.  37, 68
Choe, E.  P384  Choi, M.  P314
Choi, A.  P242  Chot, M.  93
Chopra, K.  P242  Chou, C.  P363
Chou, J.  P1  Choudry, M.A.  P113, P266
Chou, S.  P154  Choy, O.S.  P101
Chowdary, K.K.  P171, P173, P179, P355, P403
Christina, N.A.  79  Chow, D.Y.  P164
Chugh, R.  43, P187  Chung, M.H.  P13, P388
Chung, P.W.  P318  Cintolo-Gonzalez, J.  P205
Cioffi, W.G.  P278  Cisneros, B.  P164
Clara, J.  P237  Clark, K.  P42
Clark, W.  P124  Clarke, C.N.  P126
Clary, B.M.  94  Cleary, R.K.  63
Cleary, S.P.  P183, P338  Clemente-Gutierrez, U.E.  P39
Clemente-Gutierrez, U.E.  P248  Clifton, G.T.  P6, P16
Cloyd, J.M.  P232  Coburn, N.  P182, P404, P405, P407
Cocieru, A.  P306  Codrington, H.  86
Cohen, A.  P26, P85  Cohen, E.E.  P267
Cohen, S.J.  P326  Coit, D.G.  34, 90, P201, P344, P368
Cole, D.  P208  Coleman, J.A.  34
Colett, A.E.  P5  Collins, J.P.  P43
Colombo, C.  72  Comfere, N.I.  P197
Condran, A.  P85  Conrad, C.  P178
Conte, C.  P154, P155  Contreras, C.M.  P324
Cooper, A.  P178  Coopey, S.  P11
Coopey, S.B.  P47, P74  Coppola, S.  72
Corben, A.  9  Cormier, J.N.  3, 53, 76, P258, P264, P292, P301, P307
DeAndrade, J.P.  17  De Blasi, D.  P201
De Bock, G.H.  2  De Gusman, M.  P227, P355
De la Garza-Salazar, J.  P204  De Smet, L.  P105
De Vasconcellos Santos, F.A.  P366
De Vill, J.H.  P44, P99, P106  Deelderick, P.  P167
DeGnim, A.C.  P23, P55, P59  Dekkh, N.  P72
Delaney, T.F.  71  Delman, K.  P52, P207
DeMatteo, R.  41, P97, P161, P169, P349, P385  DeNardo, D.  P337, P340
Dengel, L.T.  9  DeNitto, P.C.  P62
DeNitto, P.C.  P62  Deniwar, A.  36
Denlinger, C.S.  P326  Deo, S.S.  P316
DePeralta, D.K.  P172  Deobald, R.  P182, P401
Dering, J.  58
Gonzalez, S.J. P67
Gooch, J. 9
Goodman, K.A. 19, 90
Gopalakrishnan, R. P247
Gorgun, E. P123
Govsseyev, N. P206, P226
Gracey, E.J. P55
Graham, L. P210
Granata, V. P182
Grant, M.D. P53
Gratian, L. 30
Gray, R.J. P7, 65
Greco, R.S. P232
Green, M.J. P257
Greene, A. 78
Greenup, R. 14
Greenup, R.A. P37
Gregory, L.Y. P172
Greig, P.D. P183
Gremponrez, F. 27
Grierson, J. 46
Griffin, A.M. P318
Grills, P. P72
Gripp, P. P347
Grobymyr, S.R. P381
Groeger, J. P385
Groeschl, R.T. 39
Grorman, A. 68, P381
Gronchi, A. 72
Gross, M.E. P101
Grossmann, I. 2, P114
Grotz, T.E. V4, P197, P218, P229
Grove, S. P1
Grubbs, E.G. P146
Grünhagen, D. 75
Gueller, U. 18
Guidi, A.J. P11
Guilec, S. 48
Gupta, M. 77, P365
Gupta, S. 44
Gusani, N.J. P257
Gushchin, V. P270, P273, P283
Gustafson, E. P281
Guyton, F. 59
Gyorki, D. P209

H
Habermann, E.B. P197
Haghhi, T. 91, P341
Hahn, O.M. P267
Hahn, S. 6
Hale, D.F. P6, 16
Haley, A. P66
Hall, M.A. P286
Hall, M.J. P326
Hall, N.C. P244, P251
Halle, D. 21
Hallet, J. P157, P182
Hamid, O. P214
Hamilton, T.D. P310
Hammer, J.B. P396
Hamrahan, A. P137
Han, E. P34
Han, J. P247
Han, S. 6
Han, Y. 10
Han-Kwang, Y. 6
Hansde, P234
Hanna, N. P121, P285, P291
Hansemann, D.J. 66, 82
Hansen, H.J. P101
Haraguchi, N. 91, P112
Hardacre, J. P392
Hardee, M. P79
Harismendy, O. 20
Harmon, J.W. 83
Harris, J. P279, P367
Hartmann, L.C. P55
Hashim, Y.M. P374
Hatanato, H. P356
Hauch, A. 33, P139, P188
Haverick, E. P379
Hawkins, W.G. P354, P257, P374, P387, P402
Hayes, B. 13
He, J. 93
Heakal, Y. P334
Heather, J. P128, P266, P406
Heiferman, J. P347
Heiferman, M. P347
Hembach, J.K. P186
Hellen, M. P193
Hel, J. 6
Helston, S. P390
Helyer, L. P80, P404, P405, P407
Hemmerich, J.A. P384
Henderson, M. 50
Hendren, S. 63, P256
Hendrix, A. P28
Henry, L.R. 18
Henry-Tillman, R. P79
Herman, J. 93, P381
Hernandez, J. P368
Hernandez Izarrary, R.C. P4
Herrera Loexa, S.G. P170
Herrera-Gomez, A. V1, 87
Herzberg, M. P247
Herzig, D.O. P95
Heslin, M. 59, P324
Heslop, H. P359
Hestley, A. P207
Hetu, J. P119
Hewitt, K. P239
Hibi, T. P180
Hicken, W. 26
Hicks, D.G. P17
Hieken, T.J. P23, P59, P61, P76, P197, P218
Hilchey-Pye, A. P80
Hill, E. P208
Hill, J.S. 10, P202
Hilliard, E. P9
Hillman, D. P320
Hilots, S. P167
Hiramatsu, K. P104
Hirao, M. P112, P356
Hird, R.B. P228
Hirshfield, K.M. P94
Hocevar, M. P315
Hochwald, S.N. V2, 80, P381
Hodak, S.P. P143
Hodgson, N. P81
Hoefner, R.A. P290
Hoeekstra, H.J. P220, P231
Holman, J.P. P395
Holfman, R.M. P353
Hofstetter, W.L. 88
Hogg, M.E. P184, P266, P346, P350
Hollander, L. P63
Hollenbeck, C. P8
Holingsworth, M.A. P334
Holmes, H.M. P178
Holland, M.P. P113, P266, P406
Hong, C. P22
Hong, T.S. 47, P110
Honig, J. P319
Hori, H. P382
Hoshino, I. P332
Hoskin, T.L. P23, P55, P59
Horton, J. 14
Hosper, G.A. P319
Hostetter, R. 48
Hou, S. P336
Howard, A. P267
Howard, J.H. P222, P379
Howe, J.R. 29, P382
Howell, G.M. P143
Hsu, C. P30
Hsueh, E. 52
Hsueh, E.C. P217
Hu, C. 62, P102
Hu, M.I. P146
Hu, T. P148
Hu, Y. 57
Huang, B. P279, P367
Huang, K. P400
Huang, Q. P130
Huang, W. P3, P122
Huang, X. 45
Hudis, C. P161
Huerta-Bahena, J. P68
Hugen, N. P99
Hughes, K.S. P11, P47, P74
Hughes, M.S. P223
Hui, J. P234
Huismans, A.M. P212, P322
Huisinger, M. P78, P399
Hunt, K.K. 3, 76, P301, P307
Hunt, J. P36
Hwang, E.S. P14, P37
Hwang, H. P22
Hyngstrom, J. P239
Hyung, W. 6
Idrees, K. 31
Idemianlu, C. P370
Idemienlu, C. P370
Ili, S. P120
Iino, I. P362
Ikeda, M. P112
Ikenaga, M. P112
Ikoma, N. V7, P301, P307
Ilson, D.H. 90, P368
Inmazde, M. 34
In, H. P163, P342
Inchausti, S.M. P223
Ingram, D. 76
Inoue, Y. P177
Inselman, J.W. P197
Intelisano, A. P230
Iordanescu, G. P77
Isacoff, W.H. P336
Ishigami, S. 81, 91, P341
Ishiguro, M. P120
Ishii, M. P180
Ishikawa, T. P120
Ismo, C. P238
Isozaki, Y. P345
Itagaki, S. P332
Itano, O. P180
Ito, F. P219
Ito, T. P218
Ito, T. 17
Itarte, P.H. P175
Ivasscu, F. P262
Iwasa, Y. P190
Iwata, N. P120
Izner, A. 27, P105
Izzo, F. P162
J
Jaap, K. P399
Jab, F. 80
Jackson, M. P17
Jackson, N.R. P188
Jackson, R. P186
Jackson, T. P305, P312
Jacobs, S.A. 23
Jaffe, E. P109
Jakub, J.W. V4, P59, P229
Jakubowski, C.D. 34
James, R. P246, P254
Janjigian, Y.Y. 90
Jaramillo, K. P398
Jarnagin, W. 41, P161, P165, P169, P349, P385
Jawad, M.S. P72
Jayakrishnan, T.T. P108, P118, P171, P355, P391
Jayaraman, S. P98
Jenkins, C. P262
Jensen, E.H. 43
Jespken, J. 20
Ji, L. P269
Jiagge, E. P52
Jiang, B. 54
Jimenez, C. P146
Jimenez, M. P305, P312
Jimenez, R. P63
Jimenez, W.A. P270, P273, P283
Jimenez-Fuentes, E. V1, 87
Author Index

S

Sabel, M.S. P219
Saclarides, C. P65
Sadot, E. P161, P385
Saha, A. P321, P325, P330, P336, P340
Saha, S. P282
Sahi, S. 28
Saied Calvino, A. P158
Saigal, A. P87
Sailo, H. P219
Saiura, A. P177
Sakaguchi, K. P104
Sakaguchi, T. P362
Sakamoto, E. P104
Sakr, M. P117
Sakr, R. P32
Salem, B. P82
Salmans Lacross, J. P83
Salo, J.C. P202
Sali, G. P309
Saluja, A. 43, P187
Samiei, A. P347
Samples, J. P9
Samuels, M.L. 20
Sanchez-Galvez, X. P204
Sanchez-Garcia, S. 26
Sanfilippo, R. 69, P337, P340
Sanford, D. P192
Sanghera, S.S. P285
Sangwan, V. 43, P187
Sansigry, S. P258, P264
Santoro, P. P192
Santos, E. P97
Sarantou, T. P202
Sardi, A. P270, P273, P283
Sarela, A.I. P321, P325, P330
Sarraf, M. P216
Sarmiento, J.M. 32
Samaa, A.A. P196, P206, P226
Sarfel, U. P108, P272
Sasaki, K. 81
Sasako, M. 6
Sato, T. 44
Saul, R. P107
Saunders, M.S. P130
Saunders, A.C. P269
Saunders, N. P333, P351
Saunders, N.D. P361, P379, P387, P393, P394
Sblitany, H. P60
Scaife, C.L. P101
Schaeke, E. 86
Schedin, P. P22
Scheer, A.S. P182
Schiffman, S.C. P350
Schette, E. P126
Schmidt, C.R. P351, P357, P361, P375, P379, P383, P394
Schmidt, H. P26, P85
Schmied, B.M. 18
Schnebel, E. P6, 16
Schneebaum, S. P259
Schneider, D.F. P144, P151
Schneider, R. 11
Schoder, H. P368
Schollerhammer, H.F. P175
Schreeder, M. 1
Schubart, J.R. P257
Schuster, D.M. 32
Schuurman, M. P220
Schwaib, R.B. 20
Schwarz, J. P284
Schwarz, R.E. 48, 84
Scodeller, P. P115
Scoggins, C.R. 44, 55, 98
Scott, W.J. P326, P327
Seal, B.S. P121, P285, P291
Sears, A. P6, 16
Seervarathnam, R. P405, P407
Segedi, M. P338
Seitelman, E. P210
Sekimoto, M. P112
Sekino, N. P332
Selby, L. P344
Semple, J. P29
Sempoux, C. 39
Sener, S. P64
Sepesi, B. 88
Ser Yee, L. P161, P385
Serpel, J. 50
Serrano, O.K. P400
Serrano Aybar, P. P183
Shabahang, M. P78, P189, P399
Shah, A. P186
Shah, A.R. P76
Shah, D. P303
Shah, F.A. 83
Shah, K.N. P306
Shah, M. P368
Shah, M.M. P397
Shah, N. P190
Shah, P.C. P326, P327
Shah, S.A. 66, 82, P271
Shah, S.S. P61, P76
Shaitelman, S.F. P70, P263
Shakir, A. P184
Sham, J.G. P46, P194
Shapiro, M. P130
Sharrif, M. P190
Sharma, A. P75
Sharma, D. P316
Sharma, R. 61
Sharer, S. P58, P163, P342
Sharpe, S.M. P20
Shea-Budjell, M. P287
Shellito, P.C. P110
Shen, P. P129
Shen, P.W. P255, P274
Shen, Y. P70, P263
Sherman, S.K. 29
Sheny, R.M. P223
Shibata, D. P124, P268
Shimizu, J. P356
Shinoda, M. P180
Shirley, L.A. P363, P375, P377
Shoemaker, R. P91
Shoffner, A.R. P339
Shoor, P. P320
Showalter, S.L. P1
Shrayer, D. P364
Shrestha, S. P250
Shuai, Y. P350
Shuddhahek, R. P402
Shukla, N.K. P316
Siamakpour-Rehiani, S. P9
Sidhu, K. P147
Siegal, E. P124
Sigurdsson, E.R. P132
Silberfein, E.J. P83
Silberman, A.W. P314
Sim, M. P44, 67, 70, P221, P222
Sin, E. P249, P288
Singhal, A. P260
Singer, S. 71, 73
Singh, C.P. P175, P191, P396
Singh, S. P157
Singh, T. P282
Singh, A.D. 5, P168
Singla, S. 22, P141, P224, P265, P280, P311
Sipperstein, A. P137
Sippe, R.S. P144, P151
Sisco, M. P58
Sisson, K. P245, P246, P254
Sittig, M. P270, P273, P283
Skibber, J.M. 62, P126
Skinner, K.A. P17
Slack, R. P178
Slakey, D. 33, P139
Slamon, D.J. 21, 58
Slinkluff, C.L. 57
Slipak, S. P189
Slump, C.H. P114
Smedley, W. 59
Smidt, M. P10
Smit, J.K. P319
Smit, A. P296
Smith, B.L. P11, P74
Smith, D. 12
Smith, D.D. P84
Smith, F. P196
Smith, J. 19
Smith, J.K. P277, P376
Smith, M.M. P77
Smith, R.A. P66
Smithers, B. 50
Smolkin, M.E. 57
Snow, R. P35, P88
Snyder, R.A. 64
Snyder, S. P9
Soares, K. 93
Soares, K.C. P109
Sobel, H. P13
Soclosieve, C. P161
Sok, M. P315
Solit, D. P180
Solomon, N.L. P269
Solomon, S. P161
Solorzano, C.C. 35, P51
Somai, N. P19
Somassundar, P. P127, P293
Somassundaram, R. P205
Somnay, Y.R. P142
Sonik, V.K. P196, P206, P226, P237, P241
Song, M. P336
Sonnenblick, E. P26, P85
Soo, K. P242, P288, P343
Soon, A. P49
Soran, A. P16, P45
Sosa, J.A. 30, P145
Somas, J.A. P238
Spadola, G. P230
Spanheimer, P.M. 17, P71
Specchi, M. P11, P74
Speicher, P.J. 49, 94, P145, P226, P299, P306
Spiegel, S. P3, P122
Spillage, A.J. P5, P225
Spleithoff, J.W. P114
Spolverato, G. P361, P387
Squires, M.H. 32, 89, 98, P181, P333, P351, P357, P361, P387, P393, P394
Srereamaloj, P. P36
St Hill, C.R. P227, P235
Stacchiotti, S. 72
Stager, V. P222
Stainken, B.F. 40, P158
Staley, C.A. 32, 89, P333, P351, P393, P394
Stallings Mann, M.L. P55
Stang, M.T. P143
Wang, F. P60
Wang, J. 11
Wang, L. 31, 40
Wang, Q. P167
Wang, S.C. P349
Wang, T. P324
Wang, T.S. P149
Wang, W. 76, P288
Wang, Y. P286
Wang-Gillam, A. 97
Warpnir, I.L. P232
Wargo, J. 47
Warneke, C. 53
Warschkow, R. 18
Warshaw, A.L. 47
Wasif, N. P7, 65, P199
Weber, J.S. P290
Wecsler, J. P64
Weerasinghe, R. P216
Weese, J.R. P354
Wei, A.C. P183
Weichselbaum, R.R. P163, P198, P323
Weigel, R.J. 17, P71
Weinberg, A. P272
Weiss, B. P30
Weiss, M. 93
Weixler, B. 17, 18
Weksler, B. 79
Weltz, C. P26
Wenham, R. P237
Wevers, K. P220
Wexelman, B. P74
Wey, J. P397
Whang, E.E. P130
White, D. 4
White, E.J. 57
White, N. P228
White, R. 10
White, R.R. 94
White, Jr, R.L. P202
Whiteside, M. P51
Whiting, C.K. P101
Wicha, M. P52
Wieckowski, E. P128
Wiese, D. P282
Wiggers, T. 2
Wightman, S.C. P198, P323
Wikholm, L. P30
Wolkin, G. P200, P215
Wilkinson, N. P378
Williams, P. P91
Williams, S.J. P227
Williams, T. P363, P386
Wilson, C. P33
Wilson, F. P27
Wilson, G. P82, P271
Wilson, L. P184
Wilson, N. P27
Wima, K. 66, 82, P271
Winchester, D.J. P20, P58
Winger, D. 79
Winslow, E. 89, 98, P150, P333, P351, P357, P361, P387, P393, P394
Wecluser, J. P64
Weerasinghe, R. P216
Weese, J.R. P354
Weil, A.C. P183
Weichselbaum, R.R. P163, P198, P323
Weigel, R.J. 17, P71
Weinberg, A. P272
Weiss, B. P30
Weiss, M. 93
Weixler, B. 17, 18
Weksler, B. 79
Weltz, C. P26
Wenham, R. P237
Wevers, K. P220
Wexelman, B. P74
Wey, J. P397
Whang, E.E. P130
White, D. 4
White, E.J. 57
White, N. P228
White, R. 10
White, R.R. 94
White, Jr, R.L. P202
Whiteside, M. P51
Whiting, C.K. P101
Xie, X. P28
Xin, W. 95
Xing, Q. P34
Xu, S. 15, P205, P242
Xu, W. P338
Xie, X. P28
Xin, W. 95
Xing, Q. P34
Xu, S. 15, P205, P242
Xu, W. P338
Yabe, M. P345
Yagi, H. P180
Yakoub, D. P372, P383
Yamada, A. P3, P122
Yamamoto, K. P112
Yamamoto, M. P206, P226, P247
Yamaoka, Y. P112
Yamasaki, M. P356
Yan, J. P34
Yan, M. 48
Yan, Y. P357
Yanagita, S. 91, P341
Yang, C.H. P213
Yang, C.J. P376
Yang, J.C. 4
Yang, K. P253
Yang, M. P363
Yang, R.L. 15
Yao, J.C. P148
Yao, K. P20, P58, P77
Yates, R.B. P238
Ye, H. P72
Yeh, A. P116
Yeh, J. P170, P334
Ye, H. P72
Yeh, A. P116
Yeh, J. P170, P334
Yeh, M. 46
Yeluri, S. 321, P325, P330, P380
Yen, T.W. P149
Yen, R. 46, P194
Yin, J. 12, P34
Ying, A.K. P146
Ying, J. P18
Yip, L. P143
Yip, R. P34
Yoon, C. 90
Yoon, C.H. P130
Yoon, S.S. 71, 90
Yost, S. 20
You, Y. 62, P102, P126, P307
Young-Woo, K. 6
Yue, B. P196
Zacharias, A.J. P108
Zager, J.S. 49, 51, 52, P196, P206, P226, P237, P241
Zagorski, B. P405, P407
Zahoor, H. 79
Zaydfudim, V. P186
Zeh, H.J. 5, P113, P128, P168, P184, P266, P346, P350, P406
Zeldov, B. P298
Zenati, M.S. P184, P346
Zervos, E.E. P300
Zetti, A. 18
Zgajnar, J. P315
Zhang, J. 28
Zhang, M. 46
Zhang, Y. P217
Zhang, Z. P85
Zhao, D. P33
Zhao, X. P124
Zheng, H. P242
Zheng, L. P93, P109
Zheng, Z. P121, P285, P291
Zhu, A. 39, P167
Zhu, C. P164
Zhu, L. P347
Zhu, W. P64
Zhi, F.S. P182
Zihni, A. P402
Zoon, C.K. P210
Zuber, M. 18