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SOCIETY OF SURGICAL ONCOLOGY
64TH ANNUAL CANCER SYMPOSIUM

March 2-5, 2011
Grand Hyatt San Antonio Hotel and Henry B. Gonzalez Convention Center
San Antonio, TX

The following is an outline of presentations and events scheduled during the Society of Surgical Oncology's 64th Annual Cancer Symposium, March 2-5, 2011, in San Antonio, TX.

Wednesday, March 2

8:00 am – 5:00 pm	A Comprehensive Breast Cancer Update for the Community Surgeon (includes hands-on workshops) Registration required.
8:00 am – 5:00 pm	An Update in HPB Surgery for the Community Surgeon (includes hands-on workshop) Registration required.
6:00 – 8:00 pm	*Dinner Symposium:* The Role of Physician Extenders in the Surgical Oncology Practice: From Diagnosis to Survivorship.
6:30 – 8:00 pm	*Dinner Symposium:* Diagnostic Accuracy in DCIS – National Crisis? Scientific Opportunity?

Thursday, March 3

8:00 – 10:00 am	Rectal Cancer Symposium
	Regional Perfusion Therapy
10:30 am – Noon	Intraductal Papillary Mucinous Neoplasms of the Pancreas: Controversies in Biology, Diagnosis, and Management
	Progress in Targeted Molecular Therapies
1:00 – 3:00 pm	Current Controversies in Endocrine Surgery
	Surgical Oncology in the Developing World
3:30 – 5:00 pm	Strategies to Reduce and Eliminate Disparities in Breast Cancer Outcomes
	Surgical Therapy for Solid Tumor Metastatic Disease
5:30 – 7:00 pm	New Techniques and Roles for the Surgical Oncologist: Optimal Multi-Disciplinary Care in Hepatocellular Carcinoma
	Clinical Innovation in Surgical Oncology: An International Perspective
7:00 – 8:30 pm	Welcome Reception at the Henry B. Gonzalez Convention Center

Friday, March 4

(With abstract numbers corrected from original printing)

6:30 – 7:30 a.m.	Meet the Professor Breakfasts *(Fee: $45)*
7:45 – 8:00 a.m.	Welcome/Opening Announcements
8:00 – 9:00 a.m.	Plenary Session I ..... Abstracts #1–4
9:00 – 9:45 a.m.	SSO Presidential Address: "It's Not the Destination, It's the Journey," Mitchell C. Posner, MD
10:15 – 11:00 a.m.	Plenary Session II ..... Abstracts #5–7
11:00 – 11:15 a.m.	Annual Heritage Presentation honoring Kirby I. Bland, MD
11:15 – 11:45 a.m.	2009–2011 Clinical Investigator Award Presentations
11:45 a.m. – 12:30 p.m.	American Cancer Society/SSO Basic Science Lecture: "Normalizing Tumor Vessels and Microenvironment for Cancer Treatment: From Bench to Bedside to Biomarkers," Rakesh K. Jain, PhD
1:30 – 4:00 p.m.	Parallel Sessions
	* Gastrointestinal Cancer ..... Abstracts #20–31 * Breast Cancer ..... Abstracts #32–43 * Melanoma/Sarcoma ..... Abstracts #44–55 * Endocrine/Head & Neck ..... Abstracts #56–67
3:00 – 3:30 p.m.	Poster Discussion Session
4:30 – 6:00 p.m.	*Susan G. Komen for the Cure® Symposium*: Management of the Clinically Negative Axilla – Time for a Change?
6:00 – 8:00 p.m.	Trainee Career Symposium

Saturday, March 5

(With abstract numbers corrected from original printing)

6:30 – 7:30 a.m.	Meet the Professor Breakfasts *(Fee: $45)*
7:45 – 8:30 a.m.	James Ewing Lecture: "Clinical Trials in Surgical Oncology: The Only Way Forward," Heidi Nelson, MD
8:30 – 9:30 a.m.	Breast Tumor Board
8:30 – 10:00 a.m.	21st Century Health Care Policy: What's Ahead for Surgical Oncologists?
9:30 – 10:00 a.m.	Clinical Trials in Clinical Practice – Breast Cancer 2010
10:30 – 11:15 a.m.	John Wayne Clinical Research Lecture: "Strategies for Improving the Quality of Cancer Surgery," John D. Birkmeyer, MD
11:15 a.m. – 12:30 p.m.	Breast-Focused Plenary Session ..... Abstracts #78–83
	Quality Improvement/Clinical Outcomes Plenary Session ..... Abstracts #84–89
1:30 – 4:00 p.m.	Cancer Forum..... Abstracts #8–19
	Gastrointestinal Focused Overview ..... Abstracts #68–77
4:00 – 5:00 p.m.	Town Hall/Annual SSO Business Meeting
5:00 – 6:30 p.m.	Great Debates in Surgical Oncology
7:30 – 10:30 p.m.	President's Reception and Banquet

ABSTRACTS

Accepted for
PLENARY and PARALLEL SESSIONS

64th Annual Cancer Symposium
Society of Surgical Oncology
March 2-5, 2011
San Antonio, Texas

1

Functional Analysis of microRNA-143 Tumor Suppressor Activity in Liposarcoma Identifies PLK1 as a Novel Therapeutic Target
S. Ugras,[1]* A. Jacobsen,[1] C. Angeles,[1] E. Brill,[1] P. DeCarolis,[1] R. O'Connor,[1] A. Crago,[1] R. Khanin,[1] N. Socci,[1] C. Sander,[1] T. Tuschl,[2] S. Singer.[1] *1. Memorial Sloan Kettering, New York, NY; 2. Rockefeller University, New York, NY.*

Introduction: microRNA-143 (miR-143) is significantly down-regulated in dedifferentiated liposarcoma (DDLS) relative to adipose tissue, and re-expression of miR-143 inhibits DDLS cell growth. We sought to determine the mechanism of this growth inhibition. Methods: A lentivirus-based system was used to re-express miR-143 in DDLS cells. The negative control was a non-specific scramble (Scr) sequence. Proliferation was assessed by measuring DNA content, and apoptosis assessed by the percentage of cells showing immunohistochemical staining of caspase-3. Microarray analysis was carried out to identify genes and signaling pathways regulated by miR-143. Inhibition of polo-like kinase (PLK1) was carried out by treating DDLS with BI 2536 (10 nM), a specific inhibitor. Results: Re-expression of miR-143, relative to Scr, decreased proliferation in DDLS cells by 57±11% (mean ± standard deviation) and induced apoptosis by >20 fold. Re-expression of miR-143 also significantly altered the expression of 268 genes ($p<0.05$, t-test). A computational analysis (NetBox) comparing these 268 genes to known pathways and protein-protein interactions identified one unexpectedly dense gene module ($p=0.04$) that included PLK1 and protein regulator of cytokinesis 1 (PRC1), binding partners mediating mitosis and cytokinesis. Both are predicted direct miR-143 targets. The effect of miR-143 re-expression on PLK1 and PRC1 expression was validated using quantitative PCR; PLK1 expression decreased by 42±1% and PRC1 expression by 51±1%. Immunoblotting demonstrated that PLK1 protein expression was also decreased. In DDLS cells relative to adipocyte controls, PLK1 and PRC1 were upregulated 66±7 and 43±4 fold, respectively. Treatment with the PLK1 inhibitor suppressed proliferation of DDLS cells by 49±8%. Conclusion: Functional analysis of microRNA-143 identified PLK1 and PRC1 as novel miR-143 targets in DDLS. PLK1 inhibition holds promise as a therapeutic for this disease.

2

Mechanisms of Improved Outcomes for Breast Cancer between Surgical Oncologists and General Surgeons W.C. Dooley,* J. Bong, J. Parker. *Breast Institute, University of Oklahoma, Oklahoma City, OK.*

Introduction: Prior multi-institutional studies have reported a survival benefit of breast cancer treatment by surgical oncologists over general surgeons. We investigated the mechanisms of such survival benefit within a single institution to better understand how to improve overall breast cancer care. Methods: This is a retrospective review of all breast cancer patients receiving primary treatment at a single institution from 1/1/1995 to 12/31/2008. Details of pathology and all therapies were compared between general surgeons and surgical oncologists. Additionally participation in clinical trials was recorded. Results: During the time period, there were 2192 patients who received primary breast cancer treatment at this institution. The mean age was 57 and mean follow-up >60 months. Stage distribution was similar between general surgeons(GS) and surgical oncologists (SO). Overall survival (SO 83.8% vs. GS 75.6%) and disease free survival (SO 80.7% vs. GS 72.0%) was highly statistically significant ($p<0.0001$). There were no statistical differences in overall or disease free survival for stage 0 patients. At 5 years follow-up there was a slight trend of higher disease free survival for SO related to higher radiation use in stage 0 lumpectomy cases and higher rates of hormonal chemoprevention use. For stages 1, 2a, 2b, 3a, and 3b there were statistically significant ($p<0.05$) differences for overall and disease free survival as seen in Table 1. Overall the use of breast conservation was more likely by SO – 52.6% vs. 38.3% all stages and 65.8% vs. 54.0% for stage 0-2. The compliance with all systemic therapies (chemo and hormonal) was more likely if being treated by SO - 77.3% vs. 68.5% ($p<0.02$). The use of radiation therapy for breast conservation and in stage 3 mastectomy patients was higher for SO ($p<0.002$). Participation in clinical trials was dramatically higher for SO patients – 56.2% vs. GS 7.0%. Conclusions : The value added by having primary breast cancer treatment by a surgical oncologist seems to arise from the more successful completion of multi-disciplinary care in a timely fashion and higher rates of clinical trial involvement.

Stage Specific Percent Survival

		Surgical Oncology	General Surgery
Overall Survival	Stage 1	95.0%	88.3%
	Stage 2a	87.6%	78.4%
	Stage 2b	83.1%	70.8%
	Stage 3a	79.9%	62.8%
	Stage 3b	70.6%	51.5%
Disease free Survival	Stage 1	92.4%	86.1%
	Stage 2a	86.3%	75.9%
	Stage 2b	79.1%	65.9%
	Stage 3a	72.6%	61.1%
	Stage 3b	62.9%	44.4%

3

Final results of the EORTC Intergroup Randomized study 40004 (CLOCC) evaluating the benefit of Radiofrequency Ablation (RFA) combined with chemotherapy for unresectable colorectal liver metastases (CRC LM) T. Ruers,[1]* C. Punt,[2] F. Van Coevorden,[3] J. Pierie,[4] I. Borel Rinkes,[5] J. Lederman,[6] G. Poston,[7] W. Bechstein,[8] M. Lentz,[9] M. Mauer,[10] B. Nordlinger.[11] *1. Surgery, NKI/AVL, Amsterdam, Netherlands; 2. University Medical Centre Nijmegen,, Nijmegen, Netherlands; 3. The Netherlands Cancer Institute, Amsterdam, Netherlands; 4. Medical Centre Leeuwarden, Leeuwarden, Netherlands; 5. Medical Centre Utrecht, Utrecht, Netherlands; 6. Middelsex Hospital – Meyerstein Institute,, London, United Kingdom; 7. Royal Liverpool University Hospital, Liverpool, United Kingdom; 8. Johann Wolfgang Goethe-University, Frankfurt, Germany; 9. EORTC Headquarters, Data Management Unit, Brussels, Belgium; 10. EORTC Headquarters, Statistics Department, Brussels, Belgium; 11. CHU Ambroise Paré, Boulogne-Billancourt, Paris, France.*

Background: In patients with unresectable CRC LM there is an increasing tendency to combine systemic chemotherapy (CT) with local tumour destruction by RFA. However, the benefit of this combined treatment has not yet been demonstrated. Methods: This randomised phase II study (ClinicalTrials.gov NCT00043004) evaluated the benefits of adding RFA to systemic CT in patients with ≤9 unresectable CRC LM and no extrahepatic disease. Between 2002 and 2007, 119 pts were randomised between CT alone (59) or RFA plus CT (60) In both arms, CT consisted of 6 months FOLFOX (oxaliplatin 85mg/m2 and LV5FU2) plus, since October 2005, bevacizumab. The primary objective was to exclude a 30-months overall survival (OS) rate ≤38% with RFA+CT (Fleming Design). Safety and progression free survival (PFS) were secondary endpoints. Results: Baseline characteristics were similar between arms: 60% had ≥ 4 LM. 51 patients (85%) received CT in the RFA+CT arm and 59 (all) in the CT arm. The median number of CT cycles for patients who started CT was 10 in both arms. Toxicity profiles for CT were comparable between both arms. At a median follow up of 4.4 years, the 30-month OS rate was 61.7% (95% CI,48.21-73.93) in the RFA +CT arm and 57.6% (44.07 – 70.39) in the CT arm. In eligible patients (RFA + CT; 57 pts, CT; 58 pts) these figures were 64.9% (95% CI, 51.13 – 77.09) and 56.9% (43.23 -69.84), respectively. The median PFS was 16.8 months in the RFA + CT arm (95% CI, 11.7-22.1) and 9.9 months (9.3-13.7) in the CT arm ($p=0.025$. On a lesion basis, 6.5% of the lesions treated by RFA showed local recurrence. Conclusion: This is the first study that prospectively investigates the efficacy of RFA in combination with CT. The primary endpoint (30-months OS > 38%) was met, but also 30 months OS in the CT arm was much higher than 38%. PFS was significantly longer in the RFA + CT arm compared to the chemotherapy alone arm.

4

Predicting Adherence to Stage-specific Treatment Guidelines for Adenocarcinoma of the Colon R. Chagpar,* Y. Xing, Y.N. You, Y. Chiang, B.W. Feig, G.J. Chang, J.N. Cormier. *Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Treatment guideline adherence has been proposed as a measure of cancer care quality. The purpose of this study was to determine popu-

lation-based rates of and factors associated with adherence to the National Comprehensive Cancer Network (NCCN) treatment guidelines for adenocarcinoma of the colon. Methods: All patients within the National Cancer Database (NCDB) who were diagnosed with colonic adenocarcinoma (2003-2007) formed the study cohort. Adherence to stage-specific NCCN guidelines was based on pathologic assessment. Multivariate analyses were performed to determine clinicopathologic and socioeconomic factors that were predictive of adherence. Non-adherence was based on whether chemotherapy was not recommended for stage I and low-risk stage II, or recommended for high-risk stage II, and stages III and IV as indicated by the guidelines. Results: A total of 220,406 patients were identified, 148,016 (67.1%) of whom were treated in accordance with NCCN guidelines. Patients with stage I disease were most likely to receive guideline-based treatment (96.1%), relative to those with stage II (low risk: 75.5%, high risk: 24.7%), stage III (62.6%) and stage IV (66.8%) disease, respectively (p<0.0005). Lack of recommended chemotherapy was largely responsible for non-adherence in high-risk stage II (91.9%) and stage III (82.1%). Using stage-specific multivariate models, factors associated with adherence across all stages included age, race, Charlson-Deyo Comorbidity Index, later year of diagnosis, and insurance status. Conclusion: Significant variability exists particularly for the treatment of high-risk stage II and stage III colon cancer. Although adherence to consensus-based guidelines has increased in recent years, older patients with pre-existing comorbidities, certain ethnicities, and those with lower socioeconomic status are less likely to be offered systemic therapy within these high risk groups. Young, healthy patients with early stage disease (stage I and low-risk stage II) were more likely to have been recommended chemotherapy, which is not in accordance with NCCN guidelines. The impact of non-adherence on patient outcomes needs to be further elucidated.

Table 1: Multivariate Analysis of Factors Associated with Stage-specific Adherence to NCCN Treatment Guidelines for Colon Cancer

Factor	Stage I	Stage II		Stage III	Stage IV
	OR	OR (Low Risk)	OR (High Risk)	OR	OR
Age					
<50	Referent	Referent	Referent	Referent	Referent
50-64	1.73	1.88	0.63	0.92	0.67
65-74	1.75	3.13	0.42	0.76	0.50
>75	2.36	10.02	0.14	0.28	0.20
Race					
Caucasian	Referent	Referent	Referent	Referent	Referent
African American	0.91	1.24	0.92	1.02	0.78
Hispanic	0.81	1.10	0.81	0.79	0.79
Charlson-Deyo					
0	Referent	Referent	Referent	Referent	Referent
1	1.17	1.23	0.85	0.92	0.84
2	1.30	1.66	0.67	0.68	0.60
3	1.69	1.77	0.54	0.58	0.43
Insurance Status					
Private	Referent	Referent	Referent	Referent	Referent
Medicare	1.23	1.22	0.84	0.95	0.73
Medicaid	0.83	1.06	0.86	0.800	0.75
Uninsured	0.45	1.02	0.99	0.89	0.62

*OR = Odds Ratio. Bolded values indicate significance for a 95% confidence interval

5

Disease-free and Overall Survival of 277 Early Stage Breast Cancer Patients with Negative Sentinel Lymph Node Status in the Presence of Bone Marrow Micrometastases I. Langer,[1]* B. Kocaoglu,[2] U. Guller,[3] C.T. Viehl,[4] G. Sauter,[5] O.R. Koechli,[7] G. Berclaz,[8] M. Zuber.[6] *1. Lindenhofspital Bern, Department of Surgery, Bern, Switzerland; 2. Kantonsspital Bruderholz, Department of Surgery, Bruderholz, Switzerland; 3. University Hospital Bern, Department of Surgery, Bern, Switzerland; 4. University Hospital Basel, Department of Surgery, Basel, Switzerland; 5. University Hospital Basel, Institute of Pathology, Basel, Switzerland; 6. Kantonsspital Olten, Department of Surgery, Olten, Switzerland; 7. Bethanien Clinic, Gynecology, Zurich, Switzerland; 8. Sonnenhof Clinic, Gynecology, Bern, Switzerland.*

Introduction: The sentinel lymph node (SLN) procedure has proven to accurately detect axillary lymph node metastases and represents the most important prognostic factor. Bone marrow micrometastases (BMM) are thought to predict the prognosis in breast cancer even as an independent factor. This study examined the disease-free and overall survival of node-negative patients in correlation to their BMM status. Methods: We analyzed 410 patients with early stage breast cancer (pT1 and pT2 <=3cm, cN0) who were prospectively enrolled in the Swiss multicenter study between 1/2000 and 12/2003. All patients underwent SLN biopsy as well as bone marrow aspiration from both iliac crests. The SLN were identified with blue dye and technetium labelled colloid. The histological examination of the SLN consisted of serial sectioning (250 µm) with H&E and immunohistochemistry (Lu-5, CK 22). The mononuclear cells of the BM aspirates were isolated by density gradient centrifugation through Ficoll. Cancer cells were stained with monoclonal antibodies A45-B/B3 against cytokeratin 8, 18 and 19 and counted by an automated computerized digital microscope. All results were reviewed by one pathologist. Results: SLN negative patients were found in 67.6% (277/410) of those undergoing BM aspirations. Their BMM status was negative in 75.8% (210/277), whereas in 24.2% (67/277) BM micrometastases were identified. The median follow-up was 60 months for both groups. The 5-year overall survival was 92.7% for the BMM negative and 92.5% for the BMM positive group (p=0.85). The 5-year disease-free survival reached 93.6% in the BMM negative group versus 92.2% in the BMM positive group (p=0.50). Conclusion: This is the first prospective study to examine the long-term disease-free and overall survival in SLN negative patients in correlation to their BMM status. Although BMM are identified in one of four SLN negative patients, they are not a prognostic factor regarding disease-free and overall survival in SLN negative breast cancer patients.

6

Expression profiling of difficult to diagnose thyroid histologic subtypes show distinct expression profiles and identify candidate diagnostic microRNAs M. Kitano,[1]* R. Rahbari,[1] E.E. Patterson,[1] Y. Xiong,[1] S.M. Steinberg,[1] N.B. Prasad,[2] M.A. Zeiger,[2] E. Kebebew.[1] *1. National Institutes of Health, Bethesda, MD; 2. The Johns Hopkins University School of Medicine, Baltimore, MD.*

Introduction: Thyroid cancer diagnoses are increasing worldwide with incidentally discovered thyroid nodules encompassing a large number of cases. Although fine-needle aspiration (FNA) is still the gold standard for diagnosis of a thyroid nodule, up to 30% of cases have inconclusive cytologic features, and this limitation is primarily due to several thyroid histologic types with overlapping cytologic features. MicroRNAs (miRNAs) are small endogenous noncoding RNAs which post-transcriptionally regulate gene expression and have been implicated in carcinogenesis. We hypothesized that there are miRNAs that are differentially expressed between benign and malignant thyroid tumors that are difficult to distinguish by FNA biopsy. Methods: The expression of 1,263 human miRNAs were profiled in 47 tumor samples representing difficult to diagnose histologic subtypes of thyroid neoplasm (21 benign, 26 malignant). Differentially expressed miRNAs were validated using quantitative real time-PCR (qRT-PCR). The area under the receiver operating characteristic curve (AUC) was used to determine the diagnostic accuracy of differentially expressed miRNAs. Results: Hierarchical clustering demonstrated grouping of 2 histologies – papillary thyroid carcinoma and follicular thyroid carcinoma. We found that 34 miRNAs were differentially expressed (14 upregulated, 20 downregulated) in malignant thyroid neoplasm compared to benign thyroid neoplasm (p<0.05). 25 of the 34 miRNAs were selected for validation using qRT-PCR. 15 of the 25 miRNAs were found to be differentially expressed between benign and malignant samples with p-value <0.05 and 7 had AUC values > 0.7. miR-7 and miR-126 had the highest diagnostic accuracy (AUC = 0.81 and 0.77, respectively). Conclusion: To our knowledge, this is the first study to evaluate the diagnostic accuracy of miRNAs in thyroid histologies that are difficult to distinguish as benign or malignant by FNA biopsy. Mir-126 and miR-7 had high diagnostic accuracy and could be helpful adjunct markers to thyroid FNA biopsy in tumor types which are inconclusive.

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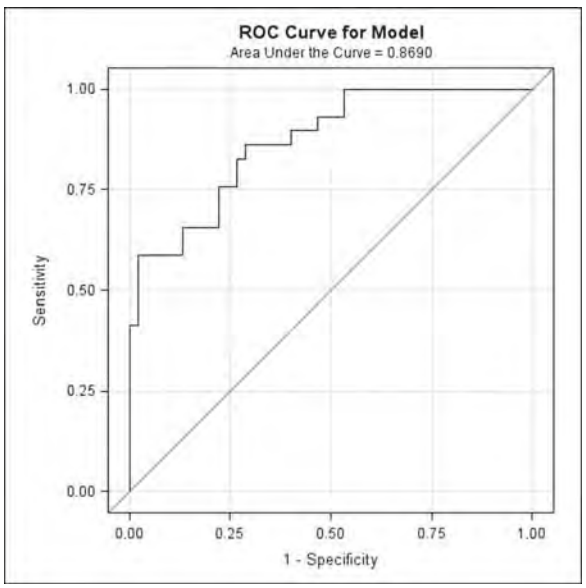
Serum Autoantibody Profiling Using a Protein Microarray for the Prognosis of Melanoma M.S. Sabel,* Y. Liu, J. He, X. Xie, D.M. Lubman, K.A. Griffith. *Surgical Oncology, University of Michigan, Ann Arbor, MI.*

As the functional proteins ultimately determine phenotype of the melanoma cell, changes in serum protein expression may demonstrate prognostic or predictive value, with the added benefit of not requiring primary tumor. We utilized a subproteome of melanoma glycoproteins for autoantibody discovery to discover novel serum markers for melanoma. Methods. Glycoproteins extracted from melanoma cells using dual-lectin affinity chromatography and RP-HPLC separation were spotted on a microarray. These were exposed to serum from newly diagnosed melanoma patients and controls, using anti-human

IgG to detect response. Outlier-sum and Wilcoxon Rank-Sum test were used to select fractions differentiating nodal status, mass spectrometry was used to identify candidate protiens. Results were validated using a larger sample set for extracted and recombinant proteins. Results. Among the 79 patients in our validation set, autoantibody response to ASAH1, CTSD, & LDHB had significant negative associations with the presence of regional disease, while response to GRP94 had a positive association. 22 (27.9%) patients had over-expression of ASAH1, CTSD or LDHB, strongly associated with being node negative (HR 0.173 [.045-.663], p<.0001). Anti-GRP94, detected in 9 (11%) of patients, was significantly associated with being node positive (HR 3.043 [2.177-4.254], p<.0001). Among the 4 antibodies, there was minimal correlation to each other or known melanoma prognostic factors. After adjustment for age, gender, Breslow thicknes, ulceration, and mitotic rate, all 4 proteins remained highly significant (ASAH1, CTSD or LDHB; HR 0.45 [0.007-0.309], p=.0016, GRP94; p<.0001). Multivariable model for prediction of regional metastasis included Breslow thickness, anti-ASAH-1, LDHB or CTSD and anti-GRP94, with an ROC area under the curve of 0.8690 (Figure 1). Conclusions. A microarray of melanoma glyocoproteins led to the discovery of 4 serum antibodies present in a substantial fraction of patients and strongly correlated with nodal status independent of known prognostic factors. Antibody-array proteomics show strong potential for discovering proteins critical to the development and progression of melanoma.



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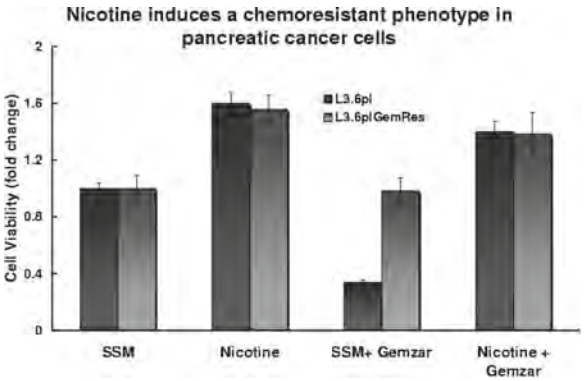
Gemcitabine Chemoresistance is Regulated by Nicotine-induced Id1 Expression in Pancreatic Adenocarcinoma Cells J.G. Trevino,* S.P. Chellappan. *Tumor Biology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL.*

The signaling pathways contributing to DNA-binding protein inhibitor Id1 expression and chemoresistance in pancreatic cancer remain unknown. Id1 plays a role in pancreatic tumor progression with tumor promoting effects of nicotine regulating protein tyrosine kinase Src activation and Id1 expression, both associated with chemoresistance in other systems. We hypothesize Id1 expression regulates chemoresistance in pancreatic cancer through a nicotine promoting Src-dependent pathway. To test our hypothesis, we probed pancreatic cancer cell lines, L3.6pl, PANC-1, and Mia-PaCa-2, for innate gemcitabine chemoresistance with cell viability MTT assay and western blot analysis of PARP cleavage programmed cell death. Gemcitabine sensitive cells were exposed to rising gemcitabine concentrations to establish a resistant subtype, L3.6plGemRes. Protein analysis and mRNA expression were determined by western blot analysis and RT-PCR respectively. Induction of Src phosphorylation or Id1 expression was performed with nicotine (1 μM). Specific inhibition of c-Src expression was performed with short-interfering RNA (siRNA). We determined nicotine induced Src phosphorylation and Id1 expression. Inhibition of Src by siRNA resulted in decreased nicotine-induced Id1 expression. Inhibition of Src and Id1 expression by siRNA in innate or established gemcitabine resistant pancreatic cancer cells resulted in gemcitabine sensitization. To determine if nicotine contributes to gemcitabine chemoresistance, we exposed gemcitabine-sensitive cells to nicotine with subsequent exposure to gemcitabine IC50, 250 ng/ml, and cell viability assays confirmed a 2-fold increase in cell proliferation and a 4.5-fold reduction in apoptosis. Further, nicotine induced phosphorylation of key signaling enzymes involved in proliferation and apoptosis, Erk1/2 and Akt respectively. In summary, we demonstrate that Id1, through a nicotine promoting Src-dependent pathway, is necessary for establishment of a chemoresistant phenotype in pancreatic cancer cells. Understanding the signaling pathways involved in pancreatic tumor chemoresistance will lead to therapies resulting in improved tumor responses.



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Differential Expression of Colon Cancer Associated Transcript-1 (CCAT1)in the Adenoma-Carcinoma sequence of the colon and rectum B. Alaiyan,[1] N. Elyaiev,[1] H. Pan,[4] M. Izadjoo,[4] M. Roistacher,[1] V. Tzivin,[1] A. Stojadinovic,[3] D. Halle,[1] B. Trink,[5] A.O. Gure,[2] A. Nissan.[1]* *1. Surgery, Hadassah-Hebrew University Medical center Mount Scopus, Jerusaelm, Israel; 2. Bilkent University, Ankara, Turkey; 3. Walter Reed Army Medical Center, Washington, DC; 4. Armed Forces Institute of Pathology, Washington, DC; 5. Johns Hopkins University Meidcal Center, Baltimore, MD.*

Introduction: The transition from normal epithelium to adenoma and carcinoma in human colon is associated with acquired molecular events taking 5-10 years for malignant transformation. We discovered CCAT1, a non-coding RNA over-expressed in CRC, but not in normal tissues, thereby making it a potential disease-specific biomarker. We aimed to define and validate CCAT1 as a CRC-specific biomarker, and to study the expression range of CCAT1 in the adenoma-carcinoma sequence of CRC tumorigenesis. Methods: Tissue samples were obtained from patients undergoing surgical or colonoscopic resection of adenomas or CRC. Normal colonic tissue (n=11), adenomatous polyps (n=18), primary tumor tissue (n=22), normal mucosa adjacent to primary tumor (n=16), lymph node(s) (n=10), liver (n=8), and peritoneal metastases (n=14) were studied. RNA was extracted from all tissue samples, and CCAT1 expression studied using Quantitative PCR (qRT-PCR) with confirmatory in-situ hybridization. Results: Low expression of CCAT1 was identified in normal tissue obtained from patients with benign conditions. Significant CCAT1 upregulation was observed in adenomatous polyps, primary tumor tissue, and normal mucosa adjacent to primary tumor, lymph node, as well as distant metastases to liver and peritoneum (Table 1). In order to rule out contamination of adjacent tissues by cells released from the primary tumor during surgery, the qRT-PCR results were confirmed by in-situ hybridization demonstrating significant correlation between CCAT1 up-regulation measured by qRT-PCR and in-situ hybridization. Conclusion: CCAT1 is upregulated in the adenoma-carcinoma sequence of CRC. This up-regulation is evident in pre-malignant conditions and through all disease stages including advanced metastatic disease. Therefore, CCAT1 may serve as a biomarker for diagnosis, staging and follow-up of CRC.

Table 1: Mean, standard deviation (SD), and percentage CCAT1 relative quantity (RQ) as measured by qRT-PCR

	Normal colonic tissue	Adjacent normal colonic tissue	Adenomatous Colonic Polyp	Primary Colonic Adenocarcinoma	Lymph node metastasis	Liver metastasis	Peritoneal metastasis
Mean RQ	5.94	17.68*	178.65**	61.26***	11,414.5****	119.18	816.29
SD	5.83	21.50	156.96	59.76	12, 022.5	138.89	2,736.12
%	27.3	37.5	89.5	80.95	100%	66.67	57.14

* p<0.09 (Vs normal), ** p=0.0012, *** p=0.0048, ****p<0.0001

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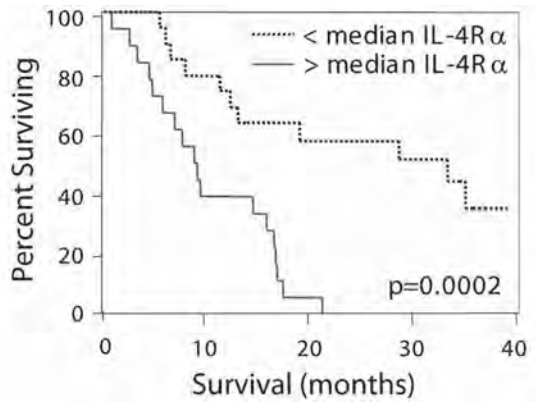
Expression of the major subunit of the IL-13 receptor, IL-4Rα, is highly predictive of poor survival in human pleural malignant mesothelioma B.M. Burt,* D. Winter, A. Bader, W. Richards, R. Bueno, D.J. Sugarbaker. *Division of Thoracic Surgery, Brigham and Women's Hospital, Boston, MA.*

OBJECTIVE IL-13 is a pleotropic cytokine whose role in tumor immunity is unfolding. The main subunit of the IL-13 receptor is the IL-4Rα. We set out to determine the functional relevance and clinical importance of IL-13 and the IL-4Rα in human malignant pleural mesothelioma (MPM), a tumor arising in a background of smoldering inflammation. METHODS Quantitiative PCR and immunohistochemistry for the IL-4Rα was performed on tumor samples from patients with MPM undergoing extrapleural pneumonectomy (EPP). Flow cytometry was used to quantify the expression of the IL-4Rα on 7 human MPM cell lines. ELISA was used to determine the quantity of IL-13 in fresh MPM patient tissue samples and to determine the quantity of TGF-β in MPM cell culture supernatants. RESULTS High mRNA expression of the IL-4Rα in the tumors of 38 patients with MPM undergoing EPP was associated with a marked reduction in overall survival (Figure 1), and this was independent of age (p<0.001), stage (p<0.001), and histologic type (p=0.002) in proportional hazards models. Immunohistochemistry of tumor sections revealed that the IL-4Rα was expressed mainly on MPM tumor cells and that significant membrane expression of this protein was found in 52 of 54 patients. Similarly, high surface expression of the IL-4Rα was found on 7 human MPM cell lines by flow cytometry. The IL-4Rα is the main subunit of the IL-13 receptor. IL-13 was found in high quantities in fresh MPM tumor tissue (56±6 ng/ml) and in the pleural effusions (84±22 ng/ml) and serum (50±4 ng/ml) of MPM patients. To determine the effect of IL-13 on MPM tumor cells, we cultured the human MPM cell line JMN-1B in the presence of IL-13. This resulted in a significant increase in tumor cell production of the fibrogenic and immunosuppressive cytokine, TGF-β [737±137 (IL-13 treated) vs. 341±64 ng/ml (untreated), p=0.03]. CONCLUSIONS High expression of the IL-4Rα predicts a marked decline in overall survival in human MPM. We surmise that signaling through this subunit of the IL-13 receptor by MPM tissue-derived IL-13 and the resultant production of TGF-β is one mechanism that fuels aggressive tumor biology.



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High Tumor PDGFR-α and PDGFR-β Expression Is Associated With Decreased Survival in Patients Selected for Resection of Hepatocellular Carcinoma S. Patel,[1]* P.J. Kneuertz,[1] M. Delgado,[2] C. Cohen,[2] J. Sarmiento,[3] C.A. Staley III,[1] D.A. Kooby,[1] A.B. Farris III,[2] S.K. Maithel.[1] *1. Department of Surgery, Division of Surgical Oncology, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Pathology, Emory University, Atlanta, GA; 3. Department of Surgery, Division of General Surgery, Emory University, Atlanta, GA.*

Background Hepatocellular carcinoma (HCC) is a vascular tumor that proliferates through angiogenic pathways mediated, in part, by vascular endothelial growth factor receptor 2 (VEGFR2), and platelet derived growth factor receptor (PDGFR) α and β. We hypothesized that overexpression of these proteins is associated with decreased survival after resection. **Methods** 57 patients, with available tissue for analysis, who underwent liver resection for HCC between 8/00-3/08 at one institution were identified from a prospectively maintained database. Tumors were assessed by immunohistochemistry for VEGFR2, PDGFR-α, and PDGFR-β expression and were graded by a single pathologist. Primary outcome was overall survival (OS). **Results** Median patient age was 64 years; 65% (n=37) were male. Median F/U was 24.5 mo, and median OS was 25.5 mo. Median tumor size and number were 7 cm and 1, respectively. Macro and microvascular invasion was present in 9% (n=5) and 42% (n=24) of patients, respectively. 25% of patients had tumors that met Milan criteria. 9% had positive resection margins. 35% of patients had cirrhosis, and the median non-adjusted MELD score was 7.5. Tumors exhibited differential expression of VEGFR2 (low: 79%, high: 21%), PDGFR-α (low: 93%, high: 7%), and PDGFR-β (low: 96%, high: 4%). After excluding all 30-day deaths (n=7), high PDGFR-α and PDGFR-β expression were independently associated with decreased overall survival (8.7 vs 29.1 mo, p=0.01; 2.8 vs 28.8 mo, p<0.001; respectively). High VEGFR2 expression displayed a trend toward decreased OS (20.8 vs 27.5 mo, p=0.2). When adjusted for tumor burden, margin status, and MELD score on independent multivariate analyses, both PDGFR-α and β expression were predictive of decreased survival (Table). **Conclusion** High expression of PDGFR-α and PDGFR-β are independently associated with decreased overall survival even when accounting for margin status and standard criteria used to select patients for resection such as MELD score and tumor extent. This finding may help to select patients who would benefit from targeted inhibitor therapy in the adjuvant setting.

Multivariate Analyses for Decreased Overall Survival after HCC resection (n=50)							
PDGFR-α				PDGFR-β			
Variable	HR	95% CI	P-value	Variable	HR	95% CI	P-value
Tumor > Milan	0.48	0.13-1.86	0.29	Tumor > Milan	1.11	0.34-3.62	0.87
Positive Margin	3.71	0.88-15.69	0.08	Positive Margin	3.87	0.88-17.0	0.07
MELD Score	1.07	0.92-1.23	0.37	MELD Score	1.06	0.93-1.20	0.39
High PDGFR-α	**6.30**	**1.42-28.02**	**0.02**	**High PDGFR-β**	**36.04**	**4.28-303.69**	**0.001**

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Increased miR-21 Activity Enhances Invasion and Directly Targets TIMP3 in Melanoma V. Grignol,* E.T. Fairchild, V.I. Karpa, A. Chan, G.B. Lesinski, W.E. Carson, III. *Ohio State University, Columbus, OH.*

Background: Understanding the pathogenesis of melanoma is critical to developing new therapies. MicroRNAs (miRs) bind to target mRNAs and alter their translation. In this study we evaluated the effects of increased miR-21 expression on melanoma cell line behavior. Methods: The miR expression pattern in melanoma was evaluated by microarray, PCR and in-situ hybridization (ISH). Melanoma cell lines WM1552c, WM793b, MEL 39, and A375 were transfected with a pre-miR-21 expression vector and evaluated for proliferation (MTT assay), doubling time (total cell number), migration (scratch test), and invasion (Boyden chamber assay). Target proteins of miR-21 were measured by immunoblot. Luciferase constructs linked to the 3'UTR of putative mRNA targets of miR 21 were used to determine miR binding. Results: Upregulation of miR-21 was identified by microarray. Real-time PCR of patient tissue samples showed miR-21 to be significantly over expressed in malignant melanoma as compared to benign nevi (mean fold increase 8.5 ± 7.4, p < 0.0001). ISH confirmed these results. Over-expression of miR-21 in 4 melanoma cell lines did not affect proliferation, doubling time or migration. miR-21 over-expression led to a significant increase in melanoma invasiveness

($p < 0.05$). Immunoblots on 24 hour post-transfection lysates revealed a decrease in tissue inhibitor of metalloproteinase-3 (TIMP3), a putative target of miR 21, as compared to controls, but not PDC4, PTEN or TM1. siRNA knockdown of TIMP3 in cell lines significantly enhanced their invasiveness, mimicking the effects of miR-21 ($p < 0.05$). To determine if miR-21 repression of TIMP3 was mediated through direct binding of miR-21 to the 3'UTR of TIMP3, luciferase constructs under the control of the wild-type TIMP3 3'UTR or a TIMP3 3'UTR mutant (mutated miR-21 binding sites) were generated. Wild-type luciferase 3'UTR empty vector was used as a control. A 25% reduction in luciferase activity was seen in cells co-transfected with pre-miR-21 and TIMP3 3'UTR as compared to controls ($p < 0.05$). Conclusion: miR-21 enhances the invasive potential of melanoma cell lines through TIMP3 inhibition. Inhibition of miR 21 may result in a less invasive phenotype.

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ErbB3 targeting with MM-121 monoclonal antibody, inhibits tumorigenesis in a murine model of human pancreatic adenocarcinoma A. Frolov,* J. Liles, L. Azih, A. Mikhailina, J. Arnoletti. *University of Alabama at Birmingham, Birmingham, AL.*

We have previously described ligand-induced cross-activation between the epidermal growth factor receptor (EGFR) and the ErbB3 receptor as a major contributor to pancreatic cancer tumor progression. In that context, we have identified neuregulin-1 (NRG-1) as an ErbB3 ligand that induces pancreatic cancer cell proliferation and resistance to the effects of EGFR-targeted therapy. MM-121 is a novel monoclonal antibody that inhibits ErbB3, disrupting the activation of the ErbB3-Pi3K-AKT signaling axis. MM-121 is currently undergoing clinical trials in other tumor types. We sought to investigate the effects of MM-121 treatment on pancreatic cancer cells both in vitro and in vivo while analyzing its potential synergy with EGFR inhibitors such as erlotinib. Our results indicate that MM-121 rapidly inhibited the NRG-1-mediated activation of ErbB3 receptors in AsPC-1 pancreatic cancer cells and partially inhibited AKT phosphorylation. Interestingly, when combined with erlotinib, MM-121 completely abolished the activation of ErbB3-AKT cascade, a result that could not be achieved by either agent alone. In vivo, we tested the anti-proliferative effects of MM-121 (75-600 mg, q3d for 4 weeks) in BxPC-3 and AsPC-1 pancreatic cancer cell subcutaneous xenografts. MM-121 displayed a dose-dependent anti-tumorigenic effect in both types of xenografts. The degree of pancreatic cancer xenograft growth inhibition ranged from 20% (75mg) to 100% (600mg) when compared to placebo-treated tumors. These pre-clinical results identify ErbB3 as a molecular target in pancreatic cancer treatment. MM-121 inhibition of Erb3, either alone or in combination with anti-EGFR agents, should be validated in clinical trials as a therapeutic approach for pancreatic adenocarcinoma patients.

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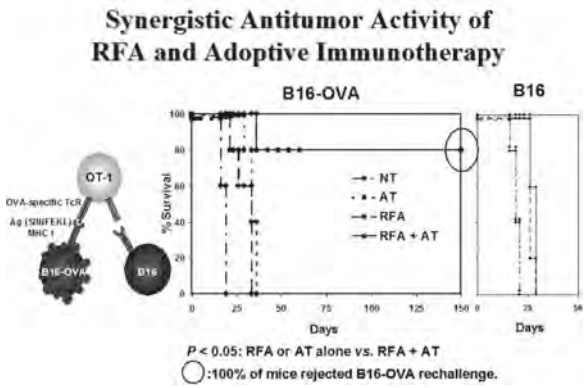
Radio-frequency Ablation Augments Antitumor Activity of Adoptive Immunotherapy F. Ito,[1]* J. Muhitch,[2] T. Vardam,[2] M. Appenheimer,[2] D. Fisher,[2] W. Wang,[2] J. Skitzki,[1] S. Gollnick,[2] S. Evans.[2] *1. Department of Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY; 2. Department of Immunology, Roswell Park Cancer Institute, Buffalo, NY.*

Background: Radiofrequency ablation (RFA) has emerged as a clinically effective treatment for variety of solid tumors. Unfortunately, in most cases an initial phase of tumor control is followed by local recurrence. We hypothesized that the local inflammfatory response generated as a consequence of RFA-induced catastrophic cell death provides a favorable environment for immune intervention in the sublethal region of tumor tissues proximal to the coagulation zone. Methods: Mice implanted subcutaneously with murine colon adenocarcinoma transfected with hemagglutinin cDNA (CT26-HA) or B16 melanoma expressing a surrogate tumor antigen, ovalbumin, (B16-OVA) were treated with RFA (90°C, 1 min). Tumor-antigen specific CD8 T cells were adoptively transferred 6 hours after RFA. Tumor growth and survival were assessed. Trafficking of T cells to tumor-draining lymph node (TdLN) or tumors was investigated by short-term homing assays and intravital microscopy 6 hours after RFA. Results: Strong upregulation of the trafficking molecule, ICAM-1, was observed in blood vessels in both TdLNs and tumor sites immediately after RFA. A corresponding increase in trafficking of naïve lymphocytes was detected in TdLNs, thereby overcoming the repression in homeostatic extravasation normally observed at this site. Improved homing was due to an increase in the proportion of lymphocytes undergoing firm arrest in HEVs of TdLN while rolling interactions were unaltered. RFA also elevated trafficking of activated tumor-specific CD8 T cells to tumor site which was linked to increased apoptotis of tumor cell targets. Significantly improved survival was observed with RFA and adoptive transfer compared to RFA or adoptive transfer alone ($P < 0.05$). This group further showed evidence for long term protection from tumor rechallenge. Tumor control by combined RFA and adoptive T cell transfer therapy was antigen-specific. Conclusion: RFA and adoptive immunotherapy have synergistic antitumor activity. These studies suggest that in addition to the role of RFA as a palliative therapeutic modality, RFA may have clinical potential as an adjuvant therapy to augment the efficacy of cancer immunotherapy.



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Demethylation Agents as Potential Therapeutics for Dedifferentiated Liposarcoma C.V. Angeles,* P. DeCarolis, S. Ugras, R. Gobble, R. O'Connor, S. Singer. *Surgery, MSKCC, New York, NY.*

Introduction: CEBPα is a key nuclear transcription factor necessary for adipocyte differentiation. We previously showed that expression of CEBPα is reduced in dedifferentiated liposarcoma (DDLS) tissue samples and cell lines and that CEBPα serves as a tumor suppressor in DDLS. In this study we sought to determine if the downregulation of CEBPα in DDLS results from promoter methylation and if demethylating agents would have anticancer effects in DDLS. Methods: Pyrosequencing of CpG islands in the CEBPα gene (CEBPA) was performed on DNA from 39 DDLS tissue samples and 4 DDLS cell lines. DDLS cells were treated with the demethylation agent decitabine (5-aza-2'-deoxycytidine) and the histone deacetylase inhibitor SAHA. Cell proliferation was analyzed by Cyquant, apoptosis by annexin V, and mRNA expression by qRT-PCR. SCID mice were xenografted with DDLS and treated with decitabine 4 mg/kg daily for 5 days with or without SAHA 50 mg/kg biweekly. Results: All 4 DDLS cell lines and 35% of DDLS tissue samples were found to have significant methylation of CpG-rich islands in CEBPA. The effects of treating DDLS cell lines with decitabine and with decitabine plus SAHA are shown in the Table. Both treatments resulted in a 40-50% decrease in CEBPA methylation and an increase in CEBPα mRNA levels. Proliferation was reduced 52% with decitabine treatment and 78% with decitabine plus SAHA, and apoptosis was increased 2- to 4-fold. In DDLS-xenografted mice, tumor growth was reduced by 50% with decitabine treatment and 70% with decitabine plus SAHA compared to untreated mice. Conclusions: Promoter methylation accounts for the suppression of CEBPα expression seen in 35% of DDLS patients. Treatment with a demethylation agent inhibits proliferation and induces CEBPα expression and apoptosis in vitro and reduces tumor growth in vivo. Demethylation agents may be promising targeted therapeutic agents for the subset of DDLS with methylated CEBPA.

Effects of decitabine in DDLS cells. All data are compared to untreated control.

	Decitabine		Decitabine plus SAHA	
	Fold change	p	Fold change	p
CEBPA methylation	0.60	0.005	0.67	0.001
CEBPα mRNA	3	<0.05	19	<0.05
Proliferation	0.48	<0.001	0.22	<0.001
Apoptosis	2	0.018	4	0.0015

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Chemokine CCL19 expressing poxvirus enhances safety and efficacy of oncolytic therapy through differential biodistribution and synergism with Cytokine-induced killer cell immunotherapy
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Background: Following promising results in preclinical models, oncolytic vaccinia viruses (vv) are currently in clinical trials. However, host immunity plays a major role in limiting viral efficacy. We investigated the use of CCL19-armed vv created on the backbone of a double-deleted virus (vvDD) currently in clinical trials, in order to enable synergism with immunotherapy and manipulate the tumor microenvironment to prolong viral presence. Methods: We constructed vvTk-Vgf-CCL19+ (vvCCL19). Safety, efficacy and biodistribution of these viruses were compared to its parental virus vvDD in MC38 (mouse colon cancer) tumor models. Cytokine induced killer (CIK) cell trafficking was studied using 6814p53 lymphoma tumor model in FVB mice. Results: First, expression of CCL19 was confirmed by ELISA using the supernatant of virus-infected MC38 cells. Chemotaxis assays of supernatant of virally infected MC38 cells showed significant attraction of naïve T cells, CD3/CD28-activated T cells, CIK and NK cells with vvCCL19, compared to vvDD. Pathogenicity studies in nude mice showed that vvCCL19 was safer than vvDD. Differential bio-distribution studies showed that vvCCL19 was cleared earlier from normal tissues than vvDD (2 days vs. 4 days, $p < 0.05$) while it persisted much longer in the tumor microenvironment than vvDD (12 days vs. 4 days, $p < 0.05$). There was greater reduction in tumor burden after treatment with vvCCL19 compared to vvDD (1767mm3 vs. 3080mm3; $p<0.03$). Immunohistochemical studies showed that vvCCL19 significantly recruited CD4+ and CD11c+ cells into the tumor microenvironment. CIK cell delivery in 6814p53 lymphoma tumor- bearing FVB mice following viral treatment showed significant reduction in tumor volume with vvCCL19 compared to vvDD (mean, 3600mm3 vs. 900mm3, $p < 0.05$). Conclusion: Arming oncolytic vaccinia virus with CCL19 may allow its prolonged presence in the tumor microenvironment but rapid clearance in other tissues and enabled synergistic immunotherapy with CIK cells. Such strategy may enable its use with a more virulent vaccinia virus in the future.

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Short interfering (si)RNAs silence VEGF and LIMK gene expression in melanoma: A novel strategy for therapy of metastases
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Introduction: Vascular endothelial growth factor (VEGF) and LIM kinase (LIMK) have been shown to be critical in the process of melanoma invasion and metastasis. A novel treatment that engages in RNA interference (RNAi) using small interfering RNAs (siRNAs, approximately 21 base-pair double stranded RNA) may provide a method of silencing gene expression of VEGF and LIMK in melanoma cells. Methods: We evaluated 46 human melanoma cell lines and found 38 expressed both VEGF and LIMK RNA and protein by quantitative PCR and western blots. Cell line M238 was chosen for VEGF and LIMK silencing studies. We designed our siRNA oligos based on the gene sequences from Genbank(http://www.ncbi.nlm.nih.gov/gene). M238 were plated at a density of 1 x 106 cells / 2 ml in 6 well plates and transfected (HiPerFect, Qiagen, Valencia, CA) according to the manufacture's protocol with the coding and non-coding siRNA oligos. At 48 hr, cells were harvested, RNA extracted and cDNA quantitated by qPCR (Applied Biosystems, Carlsbad, CA). Results: The housekeeping gene GAPDH was used to normalize RNA expression. Non-coding sequence siRNAs oligos had no effect on cell proliferation or expression of VEGF or LIMK. At a final concentration of 5 nm and 40 nm of coding siRNAs, VEGF gene expression was inhibited 51.9% and 40.3% and LIMK inhibited 69.6% and 72.6%. Conclusions: These data demonstrate the potential for RNA interference to produce post-transcriptional inhibition of VEGF and LIMK gene expression. SiRNAs may represent a novel approach for the treatment of melanoma.

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HIF-1α Regulates Lymphatic Vessel Regeneration Through Modulation of VEGF-A and VEGF-C
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Introduction: While VEGF-C is a key regulator of lymphangiogenesis, the mechanisms promoting VEGF-C expression are unknown. Studies of tumor metastases suggest that HIF-1α promotes peri-tumoral lymphangiogenesis through induction of VEGF-C. The goal of this study was to determine the role of HIF-1α in the regulation of VEGF-C and lymphatic vessel regeneration. Methods: We used a mouse tail model of lymphatic regeneration in which superficial and deep lymphatics are excised microsurgically. Following surgery, HIF-1α activity was blocked by small molecule inhibitors. Microlymphangiography, immunohistochemistry (IHC), and western blot were used to evaluate lymphatic regeneration. Finally, the role of hypoxia, lymphatic fluid stasis, and inflammation in HIF-1α stabilization was characterized. Results: Inhibition of Hif-1α delayed lymphangiogenesis, leading to increased edema (4-fold, $p<0.001$), dilated lymphatics (4-fold, $p<0.05$), reduced lymphatic vessel density ($p<0.05$), impaired lymphatic fluid flow, and downregulation of lymphatic differentiation markers (LYVE-1). Impaired lymphangiogenesis correlated with decreased VEGF-A and VEGF-C mRNA and protein expression (2-fold, $p<0.05$) as well as a reduced number of VEGF-C+ cells (2-fold, $p<0.001$) and LYVE-1+/VEGF-C+ cells (3-fold; $p<0.01$). HIF-1α expression correlated with gradients of tissue hypoxia in the early post-operative period. At later time periods (14-28 days), HIF-1α was stabilized in non-hypoxic, lymphedematous tissue, and expression localized to infiltrating inflammatory cells including lymphocytes. Finally, depletion of CD3+ cells reduced HIF-1α expression (2-fold), suggesting that T-cell mediated inflammation resulting from lymphedema may promote chronic HIF-1α stabilization. Conclusions: These results show that HIF-1α coordinates lymphatic regeneration by regulating VEGF-A and VEGF-C. Furthermore, HIF-1α stabilization is dependent on both hypoxia and inflammation, and chronic lymphedema promotes sustained HIF-1α stabilization. These findings provide insight into mechanisms regulating post-surgical lymphangiogenesis and suggest mechanisms by which tumor inflammation may promote lymphangiogenesis and metastasis.

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A Novel Genetically Modified Oncolytic Vaccinia Virus is Effective Against a Wide Range of Human Cancers and is Safe When Administered In Vivo
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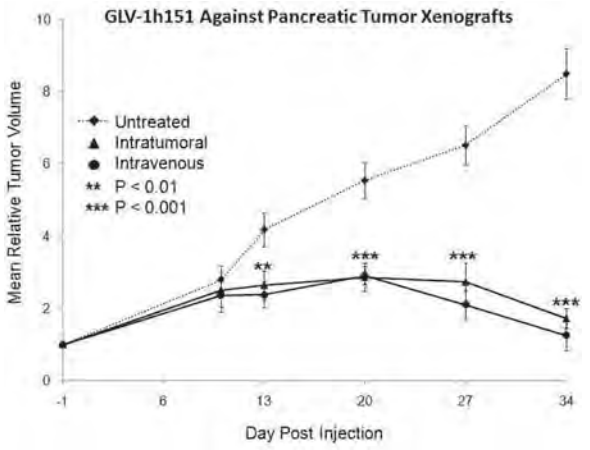
Introduction: Replication-competent oncolytic viruses have shown great promise as a potential cancer treatment. This study aims to determine if a novel vaccinia virus, GLV-1h151, with genetic modifications enhancing cancer specificity and enabling virus detection, is effective against a range of human cancers and is safe when administered in vivo. Methods: GLV-1h151 was modified with deletion of thymidine kinase enhancing specificity and insertion of the green fluorescent protein (GFP) gene. The virus was tested in several human cancer cell lines for cytotoxicity including breast, lung, pancreatic, and colorectal. Viral replication was assessed via visualization and flow cytometry of GFP expression and plaque assays. Finally, GLV-1h151 was administered systemically or intratumorally in mice with pancreatic cancer xenografts (Panc-1) to assess viral biodistribution, toxicity, and effect on tumor growth. Results: GLV-1h151 effectively infected, replicated in, and killed several cancer cell types. Detection and visualization of viral replication was successful via fluorescence imaging and flow cytometry of GFP expression, which was dose-dependent. When administered intravenously or intratumorally in vivo, GLV-1h151 regressed tumor growth ($p<0.001$), and displayed a good biosafety profile. GLV-1h151 infection and replication in tumors was successfully visualized via GFP and bioluminescence, with virus presence in tumors confirmed histologically. Conclusion: GLV-1h151 is effective as an oncolytic agent against a wide range of cancers in vitro and is effective against pancreatic human xenografts, displaying a good biosafety profile and ability to be detected via optical imaging. GLV-1h151 thus adds another potential medium for the killing of cancer and detection of virus in infected tissue.



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Intraductal Papillary Neoplasm of the Bile Duct (IPNB): A Biliary Equivalent to IPMN of the Pancreas? F.G. Rocha,* H. Lee, N. Katabi, R.P. DeMatteo, Y. Fong, M. D'Angelica, P.J. Allen, D.S. Klimstra, W.R. Jarnagin. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

Background: Intraductal papillary neoplasm of the bile duct (IPNB) is a type of cholangiocarcinoma characterized by intraductal growth, mucin production and a better outcome compared to the more common nodular-sclerosing type. IPNB may be analogous to IPMN of the pancreas and may be a precursor of invasive cholangiocarcinoma, but its pathogenesis and natural history are ill-defined. This study examines the incidence, clinicopathologic features and outcome of IPNB in a single center. Methods: A consecutive cohort of patients with bile duct cancer (hilar, intrahepatic or distal) was reviewed and those with papillary features identified. Histopathologic morphology and immunohistochemical staining for cytokeratin and mucin proteins were used to classify IPNB into subtypes. Survival data were analyzed and correlated with clinicopathological parameters. Results: Between 1993 and 2008, 40 IPNBs were identified in hilar (24/144), intrahepatic (4/86) and distal (12/113) bile duct cancer specimens (11.7%). Histopathologic examination revealed 27 pancreatobiliary, 4 gastric, 3 intestinal, and 6 oncocytic subtypes; cytokeratin and mucin staining was similar to that of IPMNs of the pancreas. Invasive carcinoma was seen in 29/40 IPNBs (72%). Overall median survival was 59 months and was not different between IPNB locations or subtypes. Factors associated with a worse median survival included depth of invasion (39 months for > 5mm, 128 months for < 5mm, and 144 months for none, $p < 0.05$), R1 vs R0 resection (36 months vs 82 months, $p < 0.05$), MUC1 expression (53 months for positive vs 144 months for negative, $p < 0.006$), and CEA expression (42 months for positive vs 128 for negative, $p < 0.02$). Expression of MUC2, MUC5A, MUC6, CDX2, mesothelin, p53, and Ki67 were not predictive of outcome. Conclusions: IPNBs are an uncommon variant of bile duct cancer representing approximately 10% of all cases, occur throughout the biliary tract and share histologic features with IPMNs of the pancreas. These lesions may represent an alternative carcinogenesis pathway. Given their significant invasive potential, they should be treated aggressively with margin-negative resection.

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Is Port Site Resection Necessary in the Surgical Management of Gallbladder Cancer? A.V. Maker,[1]* J. Oxenberg,[2] J. Butte,[2] D. Kuk,[2] M. Gonen,[2] Y. Fong,[2] R.P. DeMatteo,[2] M.I. D'Angelica,[2] P. Allen,[2] W.R. Jarnagin.[2] *1. University of Illlinois at Chicago, Chicago, IL; 2. Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: In selected patients with gallbladder carcinoma (GBCA) diagnosed after laparoscopic cholecystectomy (LC), definitive resection is warranted. Port site excision at the time of laparotomy and definitive resection remains a controversial aspect of management. **Methods:** Patients with a diagnosis of GBCA were identified through institutional and departmental databases. The subset of patients with incidental tumors identified after LC and submitted to definitive surgical therapy were selected. Those subjected to port site resection were compared with patients who underwent resection without port site removal based on GBCA T and N stage. The two groups were analyzed for differences in recurrence patterns and survival. **Results:** From 1992-2009, 112 patients with incidental GBCA presented for definitive resection after laparoscopic surgery; 69 patients had port site resection and 43 patients did not. In the resected port site group, depth of tumor invasion was T1b=6, T2=36, T3=27, and 13 (19%) had port site metastases. Five of 13 were also found to have peritoneal disease at the time of port site excision and four developed peritoneal disease subsequently (9/13, 69%). Port site disease was seen only in patients with T2 or T3 tumors and correlated with the development of peritoneal metastases ($p=0.03$). At a median follow-up of 24 months, 36/69 patients in the port site resection group were dead of disease, including 10/13 patients with port site metastases. Median survival of patients with T2/T3 tumors without port site metastases was 27 mo. compared to 17 mo. in patients with port site disease ($p=0.004$). When only R0 resected patients were compared, adjusted for T and N stage, port site resection had no impact on overall survival ($p=0.23$), death due to disease, time to recurrence, or recurrence free survival ($p=0.69$). **Conclusion:** In this study, port site metastases were associated with peritoneal disease and decreased survival. Port site resection was not associated with improved survival or disease recurrence and should not be considered mandatory during definitive surgical treatment. Long term follow-up and larger series are needed to validate these findings.

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Robotic-Assisted Pancreaticoduodenctomy at a High-Volume Pancreas Center A.H. Zureikat,* D.L. Bartlett, J.L. Steel, A.J. Moser, H.J. Zeh. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: Robotic-assisted pancreatic surgery is gaining momentum due to improved ergonomics, dexterity and visualization compared to standard laparoscopy. These technical advantages in combination with experience and improved robotic technology may reduce the significant morbidity associated with pancreaticoduodenectomy (PD). Methods: Retrospective analysis of consecutive robotic-assisted PD performed for all indications. Patientswith potentially-resectable tumors were selected for robotic PD on the basis of our EUS/CT predictive model.We evaluated perioperative events, final pathology, and complications occurring within the first 30 days on an intention to treat basis. Results: 42 robotic-assisted PD (22 women) were attemptedbetween October 2008 and June 2010. Mean age was 67 years (SD=16, range 27-85), with median BMI 26.5 (IQR=7.8). 52.4% of patients had an ASA score of III. Final pathology included pancreatic ductal adenocarcinoma (n=13), peri-ampullary adenocarcinoma (n=9), pancreatic neuroendocrine tumors (n=8), IPMN (n=5), cholangiocarcinoma (n=2), pseudo-papillary neoplasm (n=2), serous cystadenoma (n=1), mucinous cystic neoplasm (n=1), and duodenal adenoma (n=1). The first 34 patients underwent classic PD, and the final 8 patients had pylorus-preserving PD. Conversion to open was necessary in 8 patients (19%). Mean operative time was 576 min (SD=327, range 327-848 min) with 400mL median estimated blood loss (IQR=475). For malignancies, the R0 resection rate was 88% (4/34) with mean lymph node harvest of 17 (SD=7.3, range 8-37). Pancreatic fistula rate was 21% with ISGPF Grades B and Cleaks observed in 9.6%. 10 patients (23.8%) developed minor complications (Clavien grade 1/2), whereas 11 had major complications (26.2%). There was one late death (2.4%). Median length of stay was 10 days (IQR=5). Statistically significant reductions in estimated blood loss (643mL vs. 317mL, $p=0.003$) and conversion to open (7 vs. 1, $p=0.02$) were observed in the latter half of the series. Conclusions: Robotic assisted PD can be performed safely with postoperative and oncologic outcomes comparable to open surgery. The learning curve continues to evolve after 40 cases.

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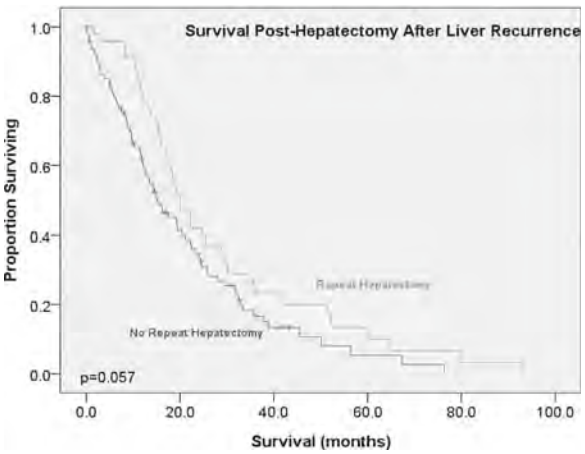
Repeat Hepatectomy for Metastatic Colorectal Cancer is Safe but Marginally Effective N.B. Jones,* M.E. McNally, L. Malhotra, S. Abdel-Misih, E.W. Martin, Jr., P.M. Bloomston, C.R. Schmidt. *Surgery, The Ohio State University, Columbus, OH.*

Background: In spite of survival of 40% or better, recurrence rates after hepatectomy for colorectal metastases approaches 70% with many occurring in the liver. We examined the utility of repeat hepatectomy to determine morbidity, mortality, recurrence patterns, and survival. Methods: We reviewed patients with metastatic colorectal cancer to the liver who underwent repeat

hepatectomy. Clinical and pathologic variables, perioperative complications, recurrence patterns and survival were assessed and compared to a group of patients during the same time period with liver recurrence that did not undergo resection using descriptive statistics, comparison of proportions (Chi-square) and Kaplan Meier curves with log rank. Results: Between 1988 and 2008, 405 patients underwent hepatectomy for metastatic colorectal cancer at our institution. 290 (72%) recurred at a median of 12.7 months. The liver was the most common site of recurrence (N=149, 41%) Repeat hepatectomy was undertaken in 50 (33.6% of liver recurrences) at a median time of 9.1 months after initial hepatectomy. Median length of stay was 9 days [range 4-34] and average estimated blood loss was 830 ml [range 50-5,000]. Major complications occurred in 12% after repeat hepatectomy resulting in one death (2%). Median overall survival after repeat hepatectomy was 20.1 months compared to 15.2 months (P=0.057, log rank, see Figure) in those who did not undergo repeat hepatectomy (N=99). Conclusion: Based on our experience, recurrence after hepatectomy for metastatic colon cancer is common and involves the liver in nearly half of patients. Repeat hepatectomy is often feasible in select patients with acceptable perioperative morbidity and mortality. Long-term survival after repeat hepatectomy is possible but uncommon. Given the efficacy of modern chemotherapy, repeat hepatectomy should be applied cautiously to realize a survival advantage over non-resectional therapies.



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Colorectal cancer liver metastasis T cell subset counts and ratios are independent predictors of outcome S.C. Katz,[1]* A. Maker,[2] V. Pillarisetty,[2] A. Yopp,[2] J. Shia,[2] C. Hedvat,[2] M. Gonen,[2] N.J. Espat,[1] W. Jarnagin,[2] Y. Fong,[2] M. D'Angelica,[2] R.P. DeMatteo.[2] *1. Surgery, Roger Williams Cancer Center, Providence, RI; 2. Memorial Sloan-Kettering Cancer Center, New York, NY.*

INTRODUCTION: Tumor infiltrating lymphocyte (TIL) status within colorectal cancer liver metastases (CRCLM) is a recently described predictor of outcome following resection. This study examines the correlation between various T cell subsets and outcome in CRCLM patients, in addition to determining the influence of disease burden on this relationship. METHODS: We studied patients who underwent CRCLM resection between 1995 and 2000, who had tissue sufficient for analysis. Immunohistochemistry was performed on tissue microarrays and correlation between TIL frequency and outcome was determined while controlling for established prognostic factors. Total T cells (CD3), helper T cells CD4), cytotoxic T cells (CD8), and regulatory T cells Treg, FoxP3) were analyzed. RESULTS: We analyzed the TIL status of 189 patients who underwent CRCLM resection, with a median follow-up time of 40 months for all patients and 96 months for survivors. Independent predictors of outcome included the clinical risk score, primary tumor lymph node metastases, liver metastasis size, and the presence of extrahepatic disease (EHD). The CD4 T cell count was an independent predictor of overall survival (OS) and recurrence-free survival (RFS, $p<0.05$). When analyzing only patients without EHD, the CD8 T cell count was an independent, significant predictor of OS ($p<0.05$). Patients with a high number of CD8 T cells relative to total T cells (CD8:CD3 ratio) had significantly longer OS times ($p=0.04$). High ratios of CD4:FoxP3 and CD8:FoxP3 were independent predictors of OS ($p<0.05$). While a high CD4 T cell count was an independent predictor of prolonged survival in patients without EHD, in those with EHD a high CD4 count actually proved to be an independent predictor of poor outcome ($p<0.05$). CONCLUSIONS: CRCLM T cell numbers and ratios predicted recurrence and survival. A relatively high number of Treg predicts poor outcome, while high CD4 and CD8 T cell infiltrates are favorable factors, depending on EHD status. Studies focused on enhancing the immune response to CRCLM are needed.

MULTIVARIATE OVERALL SURVIVAL ANALYSIS

	All Patients (n=189)	Without EHD (n=157)	With EHD (n=32)
CD3 HIGH	NS	NS	NS
CD4 HIGH	0.01, 1.85 (1.15-3.03)	<0.01, 3.21 (1.69-5.70)	0.01, 0.27 (0.10-0.75)
CD8 HIGH	NS	0.03, 1.8 (1.01-3.18)	NS
FoxP3 HIGH	NS	NS	NS
CD4:CD8 HIGH	NS	0.03, 1.58 (1.04-2.39)	NS
CD4:CD3 HIGH	NS	0.03, 1.68 (1.06-2.66)	NS
CD8:CD3 HIGH	0.04, 1.59 (1.03-2.50)	NS	NS
CD4:FoxP3HIGH	0.02, 1.59 (1.08-2.33)	0.01, 1.74 (1.12-2.71)	NS
CD8:FoxP3 HIGH	0.04, 1.47 (1.02-2.13)	0.05, 1.51 (1.0-2.29)	NS

Results presented in the following format: p value, relative risk (95% confidence interval). NS = not significant.

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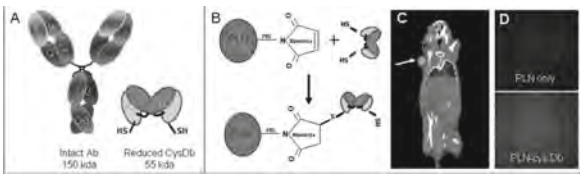
An Engineered Anti-CA19-9 Cys-Diabody for PET Imaging of Pancreas Cancer and Targeting of Nanoparticles M. Girgis,[1]* K. McCabe,[2] V. Kenanova,[2] T. Olafsen,[2] F. Bergara,[2] N. Federman,[3] C. Denny,[3] A. Wu,[2] J.S. Tomlinson.[1] *1. UCLA-VA Dept of Surgery, Los Angeles, CA; 2. UCLA - Dept of Molecular and Medical Pharmacology, Los Angeles, CA; 3. UCLA - Dept of Pediatrics, Los Angeles, CA.*

Background: Antibody based therapeutics is a rapidly growing field. Small engineered antibody fragments, such as the cys-diabody demonstrate similar antigen affinity compared to the parental antibody but have a shorter serum half-life (4hrs) and possess the ability to be conjugated to nanoparticles(Figure 1A). The goal of this study was to engineer an anti-CA19-9 cys-diabody fragment in hopes of imaging and targeting pancreatic cancer. Methods: The Anti-CA19-9 cys-diabody was created by cloning the variable region of the hybridoma, engineering a C-terminus cysteine, expressing in NS0 cells followed by protein purification utilizing HPLC. Maleimide chemistry was used to conjugate the cys-diabody to PLNs through the engineered cysteine residues(Figure 1B). Flow cytometry was used to evaluate targeting of cys-diabody and diabody conjugated PLNs to human pancreatic cancer cells. The cys-diabody was evaluated in a mouse xenograft model with CA19-9 positive(BxPC3) and negative(MiaPaca) tumors. The cys-diabody was radiolabeled with a positron emitter(I-124) and microPET/CT was performed at successive time intervals after tail vein injection. Percent of injected dose per gram(%ID/g) of radioactivity was measured in blood and tumor to provide objective confirmation of the microPET images. Results: Immunofluorescence and flow cytometry showed specific binding of the anti-CA19-9 cys-diabody. Tumor xenograft imaging of the anti-CA19-9 cys-diabody demonstrated an average tumor:blood (%ID/g) ratio of 3.3 and positive:negative tumor ratio of 7.4(Figure 1C). Successful conjugation of the cys-diabody to PLNs was indicated by immunofluorescence showing specific targeting of PLN-cys-diabody conjugate to human pancreatic cancer cells(Figure 1D) in vitro. Conclusions: Our results show that the anti-CA19.9 cys-diabody targets pancreatic cancer providing specific molecular imaging in tumor xenograft models. Furthermore, the PLN-cys-diabody conjugate targets human pancreatic cancer cells with the potential to deliver targeted treatment. Further studies evaluating the in vivo ability of the PLN-cys-diabody conjugate to target pancreatic cancer need to be performed.



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Recurrence Following Hepatectomy for Metastatic Colorectal Cancer: Development of a Model that Predicts Patterns of Recurrence and Survival C.R. St.Hill,[1]* R.B. Chapgar,[2] R.E. Brown,[1] G.G. Callender,[1] R.C. Martin II,[1] K.M. McMasters,[1] C.R. Scoggins.[1] *1. Surgery, Division of Surgical Oncology, Univeristy of Louisville, Louisville, KY; 2. M.D. Anderson, Houston, TX.*

Introduction: While several prognostic models have been developed to predict survival of patients who undergo hepatectomy for metastatic colorectal cancer (mCRC), few data exist to predict survival after recurrent cancer is diagnosed. Therefore, we sought to develop a model that predicts survival for patients who have developed recurrence following hepatectomy for mCRC. Methods: A retrospective analysis was performed on data from consecutive patients that underwent hepatectomy for mCRC. Clinicopathologic data, Fong score, recurrence patterns, and outcomes were analyzed. Kaplan-Meier survival analysis, univariate and multivariate analyses were performed. An integer-based model was created to predict the patterns of recurrence following hepatectomy. Results: This analysis included 280 patients with a median follow-up of 29.6 months. Fifty-three percent underwent major hepatectomy (>3 Couinaud segments) and 87% had negative margins. Sixty-three percent of patients developed recurrent disease. Following hepatectomy, common factors associated with short disease-free survival (DFS) and overall survival (OS) on univariate analysis included CEA > 200 ($p<0.0005$), >1 metastasis ($p<0.0005$), and a high Fong score ($p<0.0005$). Recurrence pattern post-hepatectomy was also found to be independently associated with OS, extrahepatic or combined liver and lung metastasis, portending a poorer prognosis than metastasis to only lung or liver (29.5 vs. 49.9 months, OR 2.2; 95%CI 1.42-3.43, $p<0.0005$). Independent predictors of this pattern of recurrence on multivariate analysis included CEA>200, tumor size>5cm, and >1 liver metastasis. Using the beta coefficients from this analysis, a predictive model consisting of a simple scoring system was developed that correlated with recurrence pattern ($p<0.0005$). Conclusions: After major hepatectomy, survival of patients with recurrent mCRC is strongly predicted by the patterns of recurrence, and the recurrence pattern can be predicted with a simple model.

Points in Recurrence Score	0	1	2	3	4
Probability of having only a liver or lung met	79.2%	72.2%	44.1%	25.0%	0%

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Outcome and Natural History of Patients with Stage IV Colorectal Cancer Receiving Chemotherapy without Primary Tumor Resection J. Nitzkorski,[1]* J.M. Farma,[1] R. Matteotti,[1] V. Siripurapu,[1] F. Zhu,[2] E.R. Sigurdson.[1] *1. Fox Chase Cancer Center, Surgical Oncology, Philadelphia, PA; 2. Fox Chase Cancer Center, Biostatistics, Philadelphia, PA.*

Introduction: Initial non-surgical management of patients with non-obstructing stage IV colorectal cancer (CRC) is used increasingly, although a subset will eventually undergo surgery. We examined the outcomes of patients with stage IV CRC who underwent immediate resection compared to those who underwent resection after chemotherapy. Methods: An IRB-approved database was retrospectively reviewed. All patients presenting with stage IV CRC from 2000-2008 were identified and analyzed. Results: 272 patients with stage IV CRC were identified. 153 (56%) were treated with chemotherapy alone, 85 (31%) underwent immediate resection, and 34 (13%) underwent resection after chemotherapy. Among patients who underwent immediate resection, the tumor was located in the right (42%), and left colon (38%), and rectum (16%) respectively. Among patients treated initially with chemotherapy, the tumor was located in the rectum (56%), left (26%), and right colon (18%), ($p<0.001$). Preoperative chemotherapy was oxaliplatin or irinotecan-based in 38%, and included bevaciumab in 26%. Sites of metastasis and number of sites did not differ between groups. Emergent operation was required after chemotherapy in four patients (12%). Obstruction occurred on the right (n=2), sigmoid (n=1), and rectum (n=1). The remaining 30 patients (88%) underwent elective primary tumor resection with synchronous or staged metastasectomy (n=7), RFA (n=4), chemoembolization (n=4), other (n=4). Median survival was 15 months for patients who did not undergo surgery, 32 months for patients who underwent immediate resection, and 39 months for patients who underwent primary tumor resection after chemotherapy. One patient with rectal cancer had a complete pathologic response. Conclusions: Among patients with metastatic CRC without an initial indication for surgery, chemotherapy can be given safely with a low risk of obstruction or perforation while on therapy (12%).

	Immediate resection n=85	Chemotherapy followed by surgery n=34	p
Demographics			
Male	30 (35%)	22 (65%)	0.003
Female	55 (65%)	12 (35%)	
Age, median (range)	59 (23-82)	56 (35-80)	NS
Tumor			
Right	36 (42%)	6 (18%)	
Left	32 (38%)	9 (26%)	<0.001
Rectal	14 (16%)	19 (56%)	
Operative data			
Operation for obstruction or perforation	32 (38%)	4 (12%)	0.001
Time from initiating chemotherapy to surgery (median days)		119 (16-348)	
Time from initiating chemotherapy to progression and emergency operation (median		80 (16-132)	
Chemotherapy data			
Oxaliplatin- or irinotecan-based therapy		38%	
Bevacizumab		26%	
Metastatic data			
Liver	65 (76%)	25 (74%)	
Lung	13 (15%)	5 (15%)	
Peritoneal	13 (15%)	6 (18%)	NS
Retroperitoneal or other	16 (19%)	11 (32%)	
1 site of disease	64 (75%)	23 (68%)	
>1 site of disease	21 (25%)	11 (32%)	
Local/Regional therapy			
Any local/regional therapy	40 (47%)	18 (53%)	
Resection (Liver or Lung)	23 (27%)	7 (21%)	
RFA	8 (9%)	4 (12%)	NS
Chemoembolization	2 (2%)	4 (12%)	
Sir-Spheres	7 (8%)	0 (0%)	
Other	9 (11%)	4 (12%)	

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A Phase I trial of thermal sensitization using induced oxidative stress in the context of HIPEC G.J. Tiesi, L. Harrison.* *UMDNJ-NJMS, Newark, NJ.*

Introduction: We have previously demonstrated that inducing oxidative stress under hyperthermic conditions significantly decreases tumor cell growth in a murine model of human colon cancer carcinomatosis. This Phase I study examines the safety and pharmacokinetics of induced oxidative stress by the addition of hydrogen peroxide (H2O2) to the perfusate in patients undergoing cytoreduction and HIPEC for advanced abdominal-only malignancies. Methods: Patients with advanced colon or appendiceal malignancies underwent maximal cytoreduction followed by HIPEC with mitomycin C (MMC). In addition, H2O2 was added to the perfusate at three concentrations (n=3/level, 0.075%, 0.05%, 0.1%). A control group consisted of patients perfused with MMC alone (n=3). Perfusate, serum MMC and H2O2 levels were measured, as well as tissue levels of MMC. Results: Twelve patients were enrolled in this trial. Tumor types included appendiceal adenocarcinoma (n=5), colon cancer (n=5) and diffuse peritoneal adenomucinosis (n=2). The median peritoneal carcinomatosis index was 13 (3-20) requiring a median OR time of 6.5 hrs (4-8) for cytoreduction and HIPEC. The median postoperative length of stay was 7 days (5–34 days), with six patients requiring re-admission within 30 days. The median follow-up time was 13 months (5–23). The addition of H2O2 to the perfusate significantly decreased systemic serum levels and maintained higher perfusate levels of MMC. Similar complications were observed at all three H2O2 levels, as well as in the control group. One patient required re-exploration for a colon perforation (control group) and three patients developed enterocutaneous fistulas (0.075% H2O2, 0.1% H2O2 and control group). There were no operative mortalities. Conclusions: We report that HIPEC with induced oxidative stress following maximal cytoreduction in patients with advanced colon or appendiceal malignancies is well tolerated. Encouraging toxicity profile and survival after cytoreduction and HIPEC with induced oxidative stress suggest that a Phase II trial to verify activity is indicated.

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Combined oxaliplatin and capecitabine is the most effective neo-adjuvant treatment for locally advanced rectal cancer R. Dudink,[1]* H. Rutten,[1] I. Martijnse,[1] G. Nieuwenhuijzen,[1] H. Martijn,[1] G. Creemers,[1] G. Brown,[2] D. Sebag-Montefiore,[3] R. Glynne-Jones,[4] P. Quirke.[5] *1. Catharina Hospital, Eindhoven, Netherlands; 2. Royal Marsden Hospital, Surrey, United Kingdom; 3. Leeds Cancer Center, Leeds, United Kingdom; 4. Mount Vernon Hospital, Middlesex, United Kingdom; 5. University of Leeds, Leeds, United Kingdom.*

INTRODUCTION: To achieve T-downstaging and better resectability in locally advanced rectal cancer, neo-adjuvant radiochemotherapy (RCT) has become the current standard of treatment. Different schemes have been used, but controversy exists whether to use one or more radiosensitizing agents. This study investigates which scheme had the best oncological outcome. METHODS: Our institution is a referral centre for locally advanced rectal cancer. Three different neo-adjuvant radiochemotherapy schemes have been used: (1) the Mayo/Bossett scheme (MB) consisting of 5-FU and leucovorin; (2) a combination of oxaliplatin and capecitabine (CORE); (3) Capecitabine monotherapy (CAP). Patient selection for the different schemes may be considered at random, because it followed the periodically updated guidelines. Data on all patients was collected prospectively. RESULTS: A total of 332 patients received RCT between 1999-2009. No significant difference was found in patient characteristics. The MB-scheme was used in 39 %, the CORE-scheme in 41 % and the CAP-scheme in 20 % of patients. T4-rates were 66, 58 and 72 %, respectively. Downstaging of at least one T-stage was achieved in 57, 73 and 58 % of patients, respectively. Circumferential margin involvement was significantly correlated to tumor downstaging. Surgical radicality was 88.3, 93.4 and 89.6 %, respectively, which was the strongest predictor of oncological outcome. When comparing the CORE-scheme to the MB- and CAP-schemes, all oncological outcome parameters where significantly better: 5-year overall survival was 75 vs. 57 %, 5-year cancer specific survival was 87 vs. 63 % (p=0.003), local recurrence rate was 6 vs. 15 % (p=0.034) and metastasis free survival was 78 vs. 61 % (p=0.007). CONCLUSION: Our analysis shows that a neo-adjuvant radiochemotherapy scheme combining oxaliplatin and capecitabine had the best oncological outcome. Furthermore, the CORE-scheme had the highest tumor downstaging rate, which was directly correlated to circumferential margin involvement and thus better outcome. Because this combination of agents seems to be very effective, we would recommend their combined use.

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Prognostic Impact of Postoperative Serum CA19-9 Levels in Patients with Resectable Pancreatic Cancer S. Hata,* Y. Sakamoto, Y. Yamamoto, S. Nara, M. Esaki, K. Shimada, T. Kosuge. *National Cancer Center Hospital, Tokyo, Bunkyo-ku, Tokyo, Japan.*

Introduction: Serum carbohydrate antigen 19-9 (CA19-9) level has been reported to be a useful prognostic marker in pancreatic cancer. The object of this study is to reveal the prognostic impact of postoperative serum CA19-9 levels in patients with pancreatic cancer. Methods: A total of 320 consecutive patients with pancreatic carcinoma who underwent macroscopically curative pancreatectomy between 2003 and 2009 were enrolled in this study. Pre- and post-operative (within 3 months after surgery) serum CA19-9 levels were available in 269 patients. Prognostic significance of clinicopathological factors including perioperative serum CA19-9 levels were evaluated using univariate and multivariate analyses. Results: Preoperative serum CA19-9 levels were more than normal range (> 37 U/ml, 38-4600 U/ml) in 218 patients (81%). After surgery, serum CA19-9 level remained more than normal range (> 37 U/ml) in 83 patients (31%) and within normal range (≤ 37 U/ml) in 186 patients (69%). Preoperative CA19-9 level was associated with microscopically positive surgical margin (R1) ($P = 0.013$) and nodal metastasis ($P = 0.001$), while postoperative CA19-9 level was associated with R1 ($P = 0.015$). In univariate and multivariate analyses, nodal metastasis ($P < 0.001$) and postoperative CA19-9 level ($P < 0.0001$) were independent predictors for survival. Conclusions: Postoperative CA19-9 within 3 months after surgery was associated with microscopically positive surgical margin, thereby would be a useful predictor for survival of patients with pancreatic cancer.

Univariate and multivariate analysis of prognostic factors in 269 patients with pancreatic cancer

Variables	No.	MST (yr)	Univariate analysis (*P*)	Multivariate analysis (*P*)
Total patients	269	1.4		
Gender			0.178	
Male	165	1.3		
Female	104	1.4		
Age (yr)			0.956	
< 65	130	1.3		
≥ 65	139	1.4		
Tumor location			0.175	
Head	186	1.2		
Body/Tail	83	1.6		
Type of resection			0.138	
PD	183	1.2		
DP/TP	86	1.5		
Intraoperative radiation therapy			0.481	
Yes	72	2.0		
No	197	1.3		
Residual tumor			0.016	0.287
Ro	173	1.5		
R1	96	1.2		
Histological differentiation			0.087	
Poor	28	1.0		
Well/Mod	241	1.4		
Tumor stage (UICC pT)			0.134	
pT1/T2	9	1.9		
pT3/T4	260	1.4		
Nodal stage (UICC pN)			<0.001	<0.001
pN0	65	1.9		
pN1	204	1.2		
Preoperative CA19-9 level			0.075	
≤ 37	51	1.4		
>37	218	1.4		
Postoperative CA19-9 level			<0.0001	<0.0001
≤ 37	186	1.6		
>37	83	1.0		

MSD, medain survival time; PD, pancreaticoduodenectomy; DP, distal pancreatectomuy; TP, total pancreatectomy.

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Toxicity, Quality of Life and Survival of Patients Treated with Interferon-Based Chemoradiation Following Pancreaticoduodenectomy: A Phase II Trial M.H. Katz,* R. Wolff, C. Crane, G. Varadhachary, D.B. Evans, J.E. Lee, J.B. Fleming, M. Javle, J. Abbruzzese, P.W. Pisters. *Surgery, UT MD Anderson Cancer Center, Houston, TX.*

Background: Adjuvant interferon-based chemoradiation is associated with favorable survival but substantial toxicity in patients with resected pancreatic adenocarcinoma. Methods: We initiated a phase II trial to characterize the toxicity, quality of life and survival rates associated with this regimen. 29 patients with resected pancreatic head adenocarcinoma were enrolled to receive interferon-alfa-2b (3 million units MWF), cisplatin (30 mg/m^2, 6 doses) and 5-FU (175 mg/m^2/day), concurrent with external-beam radiation (50.4 Gy) and followed by 2 courses of systemic 5-FU. The protocol was modified following the 11th patient to include a one week break in the middle of chemoradiation. Quality of life was assessed using validated instruments. Results: 28 patients were eligible for analysis. The operation of 15 (54%) patients was performed at another institution. All patients had an ECOG performance status of 0 (11, 39%) or 1 (17, 61%). All patients had T3 tumors, 22 (79%) had positive lymph nodes and 4 (14%) had positive (R1) margins. 24 (86%) patients completed therapy; 4 (14%) patients discontinued therapy due to toxicity (3) or metastasis (1). In all, 25 (89%) patients experienced grade 3 toxicity and 3 (11%) patients were hospitalized. The most common grade 3 events were leukopenia (15, 54%), neutropenia (12, 43%), fatigue, anorexia and stomatitis (each 8, 29%). No grade 4 toxicity occurred. Overall quality of life decreased during chemoradiation ($p < 0.01$) but returned to baseline prior to chemotherapy and was stable throughout surveillance. 19 patients have died; the median follow-up of the 9 survivors is 62 months. Cancer recurrence was documented in 20 patients: local (6), distant (13) and combined (1). The median OS duration of treated patients was 42.3 (95% CI, 30.5 – 54.2) months. Conclusion: Adjuvant interferon-based chemoradiation can be delivered safely and tolerably—though with substantial reversible toxicity—to patients of good performance status at an experienced cancer center. Therapy may be associated with an improvement in overall survival.

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Nipple Sparing Mastectomy: Long Term Follow up of 147 Procedures and Assessment of Oncologic Safety R.M. Silhy,* R. Venkat, E. Sbaity, M. Manahan, G. Rosson, A. Rad, C. Pesce, M. Camp, C. Balch, T.N. Tsangaris. *Breast Cancer Research Program, Johns Hopkins, Baltimore, MD.*

Background: Nipple-sparing mastectomy(NSM) has a good cosmetic outcome and high patient satisfaction. However, previous studies report that occult malignant involvement of the nipple-areolar complex (NAC) in women undergoing NSM ranges from 0% to as high as 58%. This has prompted re-evaluation of the oncologic safety of our series of NSM. Methods: We conducted a retrospective chart review of 95 self-selected patients, based on the absence of clinical and radiologic evidence of NAC tumor involvement. There were 147 NSM procedures between 2002 and 2010. The base of the NAC was routinely examined for tumor involvement by permanent histological section at the time of the mastectomy. Tumor involvement of the base of the nipple and local recurrence were evaluated. Tumor size, location, tumor to nipple distance (TND), axillary node status, and cosmetic outcome were additionally evaluated. Results: Of the 147 NSM, 59 (40.1%) were for prophylaxis, 60 (40.8%) for invasive cancer, and 28 (19.1%) for ductal carcinoma in situ (DCIS). Overall 96% of tumors were located peripherally in the breast. The average tumor size was 2.0 cm for DCIS and 2.2 cm for invasive cancer, with an average tumor nipple distance (TND) of 4.6 cm. 20 patients had positive axillary lymph nodes. Malignant involvement of the base of the nipple was found in 11 of 88 NSM (12.5%) done for cancer and in 1 NSM performed for unilateral prophylaxis. Eventually, only 2 nipples were later excised. On multivariate analysis, TND, positive axillary nodes or a central tumor location did not have significant associations with malignant NAC involvement. In addition, cancerous involvement of the base of the nipple was not associated with local recurrence. After a mean follow up of 29 months (range: 0.5 - 94 months), only 2 patients (2.1%) had local recurrence, neither of them involving the NAC. Conclusions: Preserving the nipple does not adversely affect local recurrence. However, careful patient selection and pathological evaluation of the sub-areolar breast tissue after mastectomy are essential for ensuring oncologic safety.

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Prospective Study to Evaluate Surgical Impact and Cost of Routine Preoperative Breast MRI in Women with Invasive Lobular Carcinoma S. Abdel-Rahman,[1] H. Le-Petross,[2] G.J. Whitman,[2] F. Meric-Bernstam,[1] G.V. Babiera,[1] K.K. Hunt,[1] R.F. Hwang,[1] A. Lucci,[1] B.W. Feig,[1] M.I. Ross,[1] E.A. Mittendorf,[1] H.M. Kuerer,[1] I. Bedrosian.[1]* *1. Dept of Surgical Oncology, University of Texas, MD Anderson Cancer Center, Houston, TX; 2. University of Texas, MD Anderson Cancer Center, Dept of Radiology, Houston, TX.*

Background: Breast magnetic resonance imaging (MRI) for preoperative staging of patients with invasive lobular carcinoma (ILC) has been reported to alter surgical management in 25-50% of women. Much of this data comes from retrospective reviews. The objective of this trial was to prospectively capture the change in surgical management and the downstream procedures and costs associated with use of preoperative MRI in women with ILC. Methods: Patients were eligible when ≥75% of the primary lesion on diagnostic biopsy was reported to be ILC. MRI was performed using a pre-defined protocol. Change in surgical management was captured prospectively by the surgeon and defined as conversion from lumpectomy to mastectomy or detection of contralateral carcinoma by MRI. Results: Thirty-nine evaluable women were enrolled between 2/2008 and 4/2010. All women underwent mammography and ultrasound of the index breast prior to MRI. Thirty-two patients (82%) had clinical T1/T2 disease, 34 patients (87%) were clinically node negative. Additional imaging/biopsy of the index breast was performed in 10 patients (26%) and resulted in conversion from lumpectomy to mastectomy in 5 patients (13%). This change was due to multifocality in 2 patients and multicentricity in 3 patients. Four of these 5 women were confirmed to have additional malignant disease at surgery (10% of the entire cohort). MRI resulted in additional imaging and biopsy of the contralateral breast in 6 cases (15%) and surgical biopsy in one case. Three of the 39 women (7.5%) chose to undergo contralateral prophylactic mastectomy due to anxiety resulting from MRI findings. No cases of contralateral cancer were identified. In this cohort, MRI generated additional downstream imaging/biopsy costs of $49,789. Conclusion: In this prospective trial of women with ILC, routine use of preoperative MRI altered surgical management in a much smaller proportion of patients than previously reported. Use of MRI was associated with significant downstream costs. In the absence of proven oncologic benefit, the practice of routine preoperative breast MRI in women with ILC is difficult to support.

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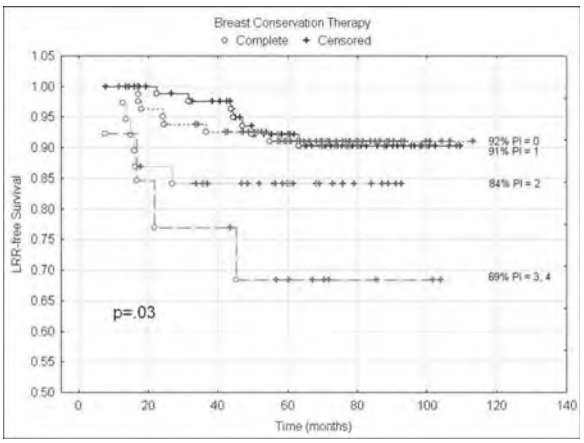
Validation of a Prognostic Index Score for Local-Regional Recurrence after Mastectomy or Breast Conservation Therapy in Patients Treated with Neoadjuvant Chemotherapy C. Akay,* F. Meric-Bernstam, L.G. Grubbs, K.E. Hoffman, G.V. Babiera, E.A. Strom, B.W. Feig, G.H. Perkins, I. Bedrosian, H.M. Kuerer, K.K. Hunt, T.A. Buchholz, E.A. Mittendorf. *The University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction Our group previously developed a prognostic index (PI) for assessing the risk of local-regional recurrence (LRR) in patients undergoing mastectomy or breast conservation therapy (BCT) after neoadjuvant chemotherapy. The PI is determined from a summed score of points assigned for each of the following variables: clinical N2/N3 disease, lymphovascular invasion, pathologic tumor size >2cm, and multifocal residual disease. The current study was undertaken to validate this PI. Methods We identified 551 patients treated with neoadjuvant chemotherapy, mastectomy or BCT, and radiation from 2001-2005 who were not part of the original cohort used to develop the PI. Clinicopathologic characteristics, treatment regimens and patient outcomes were assessed. Outcomes were stratified by PI score. Results For patients undergoing BCT, the 5-yr LRR-free survival rates were 92%, 91%, 84% and 69% when the PI score was 0 (n=91), 1 (n=82), 2 (n=38) or 3-4 (n=13), respectively (p=.03). [figure] In the BCT group, the risk of LRR was 4-fold higher for patients with PI scores of 3-4 compared to those whose score was 0 (HR=4.05, 95% CI 1.2–13.9). The 5-yr LRR-free survival rates were similar between patients undergoing mastectomy or BCT when the PI score was 0, 1 or 2 (p=NS for each), however, when the PI score was 3-4, the 5-yr LRR-free survival was significantly lower for patients treated with BCT compared with mastectomy (69% vs. 93%, p= .02). For patients with PI scores of 3-4, there was no difference in 5-yr disease-specific survival (DSS) between patients who underwent mastectomy compared to BCT (76% vs 78%, p=.65). Conclusion We found that the previously developed prognostic index for LRR in patients receiving neoadjuvant chemotherapy is validated in a contemporary independent patient cohort. BCT patients with a high PI score have significantly lower 5-yr LRR-free survival than mastectomy patients, however, this does not translate into a DSS advantage. These findings suggest that the PI score may be one factor to consider when planning surgery for patients receiving neoadjuvant chemotherapy.



LRR-free survival stratified by PI score for patients undergoing BCT after neoadjuvant chemotherapy.

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Morbidity of sentinel node biopsy: Relationship between number of excised lymph nodes and patient perceptions of lymphedema J.I. Goldberg,* E.R. Riedel, M. Morrow, K.J. Van Zee. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

Background: Sentinel lymph node biopsy (SLNB) for staging of the axilla has been associated with reduced morbidity, though lymphedema remains a

significant complication for patients. Previously, we found no relation between number of excised lymph nodes (LNs) and objectively measured lymphedema. The aim of this study was to examine the relationship between number of LNs excised during SLNB and patient-perceived lymphedema. Methods: 600 women undergoing SLNB for breast cancer were prospectively studied. Measured lymphedema was evaluated by circumferential bilateral upper extremity measurements taken preoperatively and at follow-up, 3 to 8 years after SLNB. Patient perceptions of lymphedema were evaluated by interviews at follow-up. The relationship between patient-perceived lymphedema and total number of LNs removed was assessed with Wilcoxon rank sum test and logistic regression; agreement between patient-perceived and measured lymphedema was tested using the kappa statistic. Results: At a median follow-up of 5 years, 18 (3%) patients reported perceived lymphedema. The mean (6.3 vs. 4.1) and median (5.5 vs. 3.0) number of LNs excised were greater for the patients with perceived lymphedema compared to those without (p=0.01). Risk factors associated with patient-perceived lymphedema were BMI and infection. After controlling for these factors individually, there remained a higher risk of perceived lymphedema with more LNs removed (OR 1.22-1.24, p<0.001). Agreement between perceived and measured lymphedema was very poor (kappa=0.22). Only a third (6/18) of women who reported perceived lymphedema had objectively measured lymphedema. None of the women with the most (≥10) LNs excised had measured lymphedema. Conclusion: Although there was a higher incidence of patient-perceived lymphedema with more LNs excised, there was no agreement with measured lymphedema, and only a minority of women with perceived lymphedema had measured lymphedema. These data suggest that other factors, such as sensory nerve injury resulting from retrieval of more LNs, may play a role in patient perception of lymphedema after SLNB.

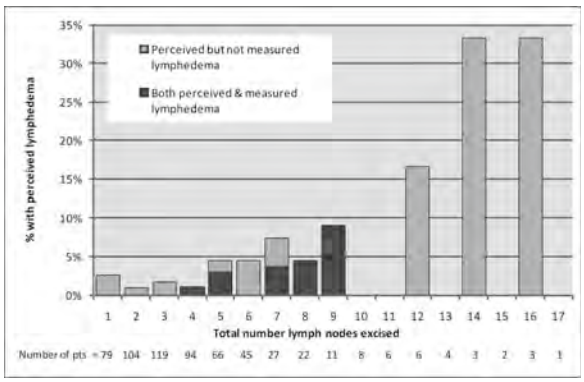

Figure 1: Histogram showing incidence of perceived lymphedema with or without measured lymphedema, by number of LN excised

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Is there a low grade precursor pathway in breast cancer?
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Studies of invasive and adjacent in-situ breast cancers suggest that molecular subtypes and patterns of genomic changes are preserved in the transition to invasive carcinoma and that these patterns can be separated according to tumor grade(high vs low). This has led to a model whereby lobular carcinoma in situ (LCIS) is a precursor lesion in a "low-grade pathway" and ductal carcinoma in situ (DCIS) may progress via either a high or low grade pathway. The purpose of this study was to determine whether this relationship is present in LCIS and DCIS cases and subsequent ipsilateral invasive breast cancers. Methods: We reviewed prospectively maintained databases of patients undergoing surveillance for LCIS (1994-2007) and patients in follow up after lumpectomy +/- radiation (BCT) for DCIS (1991-2004). Patients with subsequent ipsilateral invasive cancer and available tissue blocks (in-situ and invasive) were included. Those receiving tamoxifen were excluded. ER/PR/Her2 surrogates were used for molecular subtype. Results: Material was available for 27 pts with LCIS who developed ipsilateral invasive cancer (12 IDC, 14 ILC, 1 mixed) and 26 pts with DCIS (12 low gd, 14 high gd) who developed ipsilateral IDC after BCT. There was no difference in age at diagnosis of LCIS/DCIS or median time to invasive cancer between groups. All 27 LCIS lesions were ER+/Her2- (luminal A) and 23/27 (85%) subsequent invasive cancers had the same profile(Table). Among 26 DCIS cases, 19 (73%) were luminal A, 2(8%) luminal B, 1(4%) Her2 and 4 (15%) were basal-like. In 19/26 (73%) DCIS cases the subsequent IDC maintained the same subtype(Table). In contrast, 0/12 low grade DCIS developed low grade invasive cancer (3 grade 2; 9 grade 3), and only 1/12 LCIS pts that developed IDC, had low grade IDC. All 14 pts with high grade DCIS developed high grade invasive cancer. Conclusions: Our findings do not support a low grade precursor pathway characterized by LCIS and low grade DCIS. ER, PR, and HER2 status has a high rate of concordance between in situ and subsequent invasive lesions that develop over time. Additional studies of metachronous in-situ and invasive lesions are needed to better understand pathways of breast tumorigenesis.

	Subsequent Invasive Cancers			
	Luminal A ER+/Her2-	Luminal B ER+/Her2+	Her 2 ER-/Her2+	Basal-like ER-/Her2-
Original LCIS				
Luminal A (n=27)	**23**	2	2	
Original DCIS				
Luminal A (n=19)	**14**	1	1	3
Luminal B (n=2)	1	**1**		
Her 2 (n=1)			**1**	
Basal-like (n=4)			1	**3**

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Sentinel Node And Recurrent Breast cancer (SNARB): Results of an interim-analysis A. Maaskant-Braat,[1]* R. Roumen,[2] H. Pijpers,[1] G. Nieuwenhuijzen.[1] *1. Catharina Hospital, Eindhoven, Netherlands; 2. Maxima Medical Center, Veldhoven, Netherlands.*

Background Determining axillary lymph node status in patients with recurrent breast cancer can be important for locoregional control and prognosis. It is unclear whether sentinel node biopsy (SNB) or axillary lymph node dissection (ALND) should be the staging method of choice. SNB leads to less morbidity. Also, due to surgery and radiotherapy lymph drainage pathways could be altered and identification of these aberrant drainage pathways could lead to a more thorough staging and possible change in treatment strategy. To determine technical feasibility, validity and clinical consequences of performing SNB in patients with recurrent breast cancer we set up the Dutch SNARB study. Materials and methods Patients with recurrent breast cancer are being included in one of 36 participating hospitals. They undergo lymfoscintigraphy according to local protocol, the radioactive tracer is injected peritumoral or in the former scar after previous mastectomy. After this, SNB takes place and, in case of an intact axillary lymph node basin, ALND is performed in the same procedure. Results So far, the results of 88 patients are available for analysis. 31 patients underwent previous breast conserving therapy (BCT) with SNB, 44 patients underwent BCT with ALND and 13 patients underwent a mastectomy, of which 5 with SNB and 8 with ALND. In 58 patients a sentinel node was identified, in 25 patients after previous SNB and in 33 patients after previous ALND. In 48 patients the sentinel node was perioperatively removed. In 8 patients a (micro)metastasis was found on pathologic examination. In 13 out of 20 patients with a negative SNB and an intact axillary lymph node basin a confirming ALND took place. No additional axillary lymph node metastases were found. In 36 patients an aberrant drainage pathway was detected. The result of the SNB led to a change in treatment plans in 6 patients. Conclusion Based on this interim analysis of the SNARB study it seems technically feasible and valid to perform the sentinel node procedure in patients with recurrent breast cancer. In 41% of the patients the results of the SNB provided extra information based on which treatment plans were altered in 9% of patients.

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Axillary Reverse Mapping (ARM): Initial Results of Phase II Trial In Preventing Lymphedema after Lymphadenectomy C. Boneti,* B.D. Badgwell, Y. Robertson, S. Korourian, L.L. Adkins, V.S. Klimberg. *Surgery, UAMS, Little Rock, AR.*

Introduction: Axillary reverse mapping (ARM), blue dye mapping of and preserving the lymphatics draining the arm, is unproven in preventing lymphedema. The purpose of this study is to evaluate lymphedema rates with ARM

added to lymphadenectomy. Methods: 156 cases of SLNB± ALND from May 2007 to March 2010 were prospectively accrued to the study. After SLN localization with radioactive tracer alone, dye was used for mapping ARM lymphatics. Patients with an increase in arm volume greater than 20% over the contralateral side were considered to have lymphedema. Data was collected on identification and variations in lymphatic drainage, nodal status, ARM lymphatics preservation rate, regional recurrence, adjuvant treatment (XRT, chemo) and lymphedema rate. Results: 114 patients underwent SLNB only and 42 patients underwent ALND after SLNB, with a SLN identification rate of 100%. Median age was 58 (range 26-86) and BMI was 29 (range 19-55). Median follow-up was 12 months (range 6-36). 35% (54/156) of patients received radiation therapy. ARM lymphatics were seen within the SLN field in 45/114 (39%) of the SLNB cases and in 34/42 (81%) of the ALND. ARM nodes were preserved in 92.3% of the cases (144/156). A total of 12 ARM nodes were resected because of crossover or suspicious appearance. The 2 ARM nodes involved by malignancy were in heavily positive axilla (>5 positive nodes). Of those patients undergoing SLN alone 3.5% (4/114) had lymphedema by volume change. Another 1.7%(2/114) had arm symptoms but no volume change. Of patients undergoing SLN+ALND 7%(3/42) had lymphedema by volume change. An additional 4.6%(2/42) had arm symptoms without any volume change. 43%(3/7) of the patients with lymphedema by volume had known transection of at least some of their ARM lymphatics. No regional recurrences were seen. There was a steep learning curve in ability to find and preserve ARM lymphatics. Conclusion: Preserving the ARM nodes is safe and resulted in a low incidence of postoperative lymphedema after SLNB and ALND.

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Primary endocrine therapy for patients aged 75 years or older with operable breast cancer: a population-based study K. Woensdregt,[1]* K. Wink,[2] G. Nieuwenhuijzen,[3] S. Hutschemaekers,[2] J. Roukema,[4] M. Van der Sangen,[5] A. Voogd.[6] *1. Department of Surgery, Maastricht University Medical Centre, Maastricht, Limburg, Netherlands; 2. Faculty of Health Medicine and Life Sciences, Maastricht University, Maastricht, Limburg, Netherlands; 3. Department of Surgery, Catharina Hospital, Eindhoven, Brabant, Netherlands; 4. Department of Surgery, St.Elisabeth Hospital, Tilburg, Brabant, Netherlands; 5. Department of Radiotherapy, Catharina Hospital, Eindhoven, Brabant, Netherlands; 6. Department of Epidemiology, Faculty of Health Medicine and Life Sciences, GROW - School for Oncology and Developmental Biology, Maastricht University, Maastricht, Limburg, Netherlands.*

Introduction: Primary endocrine therapy (PET) in elderly breast cancer patients is much debated and seems to be on the rise. The aims of the study were to evaluate this increase, the indications for PET instead of surgery, time to response (TTR), time to progression (TTP) and overall survival following PET. Methods: For this retrospective observational study 223 patients aged ≥75 years, diagnosed with operable breast cancer between 2001 and 2008 and receiving PET, were selected from the Eindhoven Cancer Registry (ECR). Data of 184 patients were eligible and compared with data of all surgically treated patients aged ≥75 years in the ECR. Results: In 1989-1992, 21% of women ≥75 years with breast cancer received PET in the South of the Netherlands. This percentage decreased to 12% in 1997-2000, followed by an increase to 29% in 2005-2008. Our cohort (n=223) represents 43% of all patients treated with PET in the period 2001-2008. Median age at diagnosis was 84 years (range 75-89). Median length of follow-up was 2.6 years (range 0.1-8.5). 101 Patients were primarily treated with tamoxifen and 82 patients with an aromatase inhibitor (AI). For one patient type of PET was unknown. 107 patients (58%) showed initial response (mean TTR 7 months), 21 patients (12%) had stable disease. Eventually, 64 patients (37%) displayed progression, (mean TTP 20 months). No differences in TTR and TTP were observed between tamoxifen and AIs. 119 Patients (65%) had died by January 1, 2010. In 17 patients (14%) breast cancer was the cause of death. The 5-year overall survival after PET was 27% (95% CI 19.1-34.8%) versus 62.3% (95% CI 59.4-65.2%) for patients aged ≥75 years, treated with primary surgery in the same period (n=1504, p<0.001). The latter group however, was significantly younger (80 vs 84 years, p<0.001) and had significantly less comorbidity . Conclusions: Tumor progression was observed in a substantial proportion of our cohort, but only a small number of patients died of breast cancer. Further research is needed on the safety and effectiveness of PET for elderly women with breast cancer. Especially the role of AIs as monotherapy needs to be further assessed.

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Papillary breast lesions: should all of them be excised? M. Lowe,[1] M. Amin,[1] S.G. Gabram,[1] L. Pan,[2] L. Vasquez,[3] M.A. Cohen,[3] M. Mosunjac,[4] M. Rizzo.[1]* *1. Department of Surgery, Division Surgical Oncology, Atlanta, GA; 2. Biostatistics, Atlanta, GA; 3. Department of Radiology, Breast Imaging, Atlanta, GA; 4. Pathology and Laboratory Medicine, Atlanta, GA.*

Background: The clinical management of papillary breast lesions (PBL) diagnosed at percutaneous biopsy remains controversial. The objective of this study was to identify clinical and radiologic predictors of malignancy in a large cohort of PBL diagnosed on core needle biopsy (CNB) who underwent surgical excision within 6 months from the CNB. Methods: Retrospective Systematized Nomenclature in Medicine (SNOMED) search of the pathology database was performed to identify PBL from 2001 to 2009. We analyzed age, race, and clinical presentation (asymptomatic, nipple discharge, palpable breast mass). Radiologic features included location (central vs. peripheral), microcalcifications (pleomorphic, amorphous, cluster, linear and segmental), mass on mammogram. Upgrade was defined as a change in the surgical specimen to a lesion of greater clinical significance. One way ANOVA, logistic regression model and Fisher's exact test, and two tail sign test were applied to correlate upgrade with age, race, clinical and radiological characteristics. Results: From 2001 to 2009, we identified 276 patients (mean age=55.6; 22.8-88.0) with 303 PBL on CNB. Of these, 234 (84.7%) had PBL only and 42 had associated ADH or ALH on CNB. Minute PBL or incidental PBL associated with DCIS or IDC were excluded. The majority of the patients (n=173, 62.6%) had no breast symptoms. All patients had an abnormal mammogram and/ or ultrasound, BI-RADS (Breast Imaging reporting and Data System) 4 or 5, that prompted the CNB. PBL identified initially by breast MRI were excluded. 79 patients (28.6%) were upgraded to a lesion of greater clinical significance (p<0.0001); 16 (20.2%) presented with associated ADH on CNB. Age was predictive of upgrade as shown in Table 1. No radiologic or clinical presentation of PBL was predictive of upgrade. Conclusions: Since 28.6% of PBL identified by CNB were upgraded to ADH/ALH/LCIS, DCIS or IDC and no radiologic or clinical parameters were predictive of upgrade, we recommend surgical excision of all PBLs especially in older patients. These upgrades to ADH, ALH and LCIS affect the clinical treatment that has been shown to significantly lower the risk of subsequent invasive breast cancer.

Age correlation with histological findings at initial core needle biopsy and at surgical excision

TOTAL n=276	Downgrade or no change(%)	Upgrade to ADH/ALH/LCIS(%)	Upgrade to DCIS(%)	Upgrade to IDC(%)	p-value
PBL on CNB (n=234)	171(73%)	42(17.9%)	19(8.1%)	2(1%)	p<0.0001*
Age (mean)	52.6	58.4	60.8	65.2	p<0.001**
PBL+ADH on CNB (n=42)	26(61.9%)	n/a	14(33.3%)	2(4.8%)	p=0.16*
Age (mean)	59.2	n/a	64.5	73.0	p<0.05**

PBL=papillary breast lesions, CNB=core needle biopsy, ADH=atypical ductal hyperplasia, ALH=atypical lobular hyperplasia, DCIS=ductal carcinoma in situ, LCIS=lobular carcinoma in situ, IDC=infiltrating ductal carcinoma

*p-value for rate of upgrade calculated with two-tailed sign test

**p-value for age calculated with one way ANOVA

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Needle versus Excisional Biopsy for Noninvasive and Invasive Breast Cancer, Report from the National Cancer Database, 2003-2008 R.T. Williams,[1]* K. Yao,[2] A.K. Stewart,[3] D.J. Winchester,[2] M. Turk,[2] A. Gurchow,[2] N. Jaskowiak,[1] D.P. Winchester.[2] *1. University of Chicago Medical Center, Chicago, IL; 2. NorthShore University Health System, Evanston, IL; 3. Cancer Programs, American College of Surgeons, Chicago, IL.*

Background: There is an impetus to make needle biopsy rates in the diagnosis of breast cancer a quality measure for which hospitals are held accountable, but large multicenter studies looking at these rates are scant. The purpose of this study was to examine the utilization of needle versus excisional biopsy in a contemporary cohort of patients and to identify factors associated

with biopsy type. Methods: We selected women with non-metastatic, clinical Tis-T3 breast cancers diagnosed between 2003 and 2008 from the National Cancer Data Base (NCDB), which currently captures approximately 79% of breast cancers in the U.S. Patients whose cancer was diagnosed by needle biopsy (fine needle aspiration or core) were compared with patients diagnosed via excision, utilizing several patient, hospital, and tumor characteristics. A logistic regression model was used to identify important predictors of biopsy type. Results: 728,423 patients met selection criteria: 581,232 (79.8%) underwent needle biopsy while 147,191 (20.2%) had excisional biopsy to diagnose their cancer. The rate of needle biopsy increased from 73.4% to 85.5% ($p<0.001$) whereas the rate of excisional biopsy declined from 26.6% to 14.5% ($p<0.001$) over the study period. In 2008, patients were significantly more likely to undergo excisional biopsy if they had stage 0 disease (OR 4.60, 95% CI 4.00-5.28); were treated at a hospital located in the Atlantic census region (OR 2.27, 95% CI 2.05-2.52) or at a community hospital (OR 1.89, 95% CI 1.78-2.00); were at the extremes of age (<40 or ≥80 years) at diagnosis (OR 1.28, 95% CI 1.16-1.41); were less educated(OR 1.28, 95% CI 1.20-1.37); or were Asian/Pacific Islander (OR 1.25%, 95% CI 1.12-1.39). Income, insurance, and comorbidity index were not important determinants of biopsy type. Conclusion: The use of needle biopsy to diagnose noninvasive and invasive breast cancers is increasing. Tumor stage, hospital type, and hospital location were the most significant predictors of biopsy type. Further studies are needed to delineate an acceptable excisional biopsy rate if needle biopsy utilization is implemented as a quality indicator in breast cancer care.

Three most significant predictors of excisional versus needle biopsy in 2008

	Excisional Biopsy (n)	Excisional Biopsy (%)	Needle Biopsy (n)	Needle Biopsy (%)	P-value	OR*	95% CI (lower)	95% CI (upper)
Hospital Census Region								
Northeast	11,317	21.7	40,833	78.3	0.000	1.74	1.55	1.96
Atlantic	30,183	26.9	82,111	73.1	0.000	2.27	2.05	2.52
Southeast	32,584	21.0	122,705	79.0	0.000	1.52	1.37	1.68
Greatlakes	26,447	20.5	102,306	79.5	0.000	1.50	1.35	1.66
Midwest	9,313	18.2	41,817	81.8	0.000	1.38	1.23	1.55
West	9,845	17.9	45,139	82.1	0.361	1.06	0.94	1.20
Mountain	5,176	16.8	25,700	83.2	0.000	1.33	1.15	1.53
Pacific	16,022	15.9	84,685	84.1	0.181	1.08	0.97	1.21
South	5,482	14.0	33,753	86.0		1.00	reference	
Hospital Type								
Community	28,750	27.3	76,535	72.7	0.000	1.89	1.77	1.99
Comprehensive	73,605	18.7	319,027	81.3	0.000	1.20	1.14	1.26
Teaching/Research	43,205	19.3	180,283	80.7		1.00	reference	
AJCC Clinical Stage								
0	25,685	28.3	65,059	71.7	0.000	4.60	4.00	5.28
I	26,634	17.5	125,526	82.5	0.000	2.29	1.99	2.62
II	10,313	11.9	76,126	88.1	0.000	1.46	1.27	1.68
III	1,354	8.0	15,522	92.0		1.00	reference	

*OR 1.00 indicates reference group

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A Single Institution Review of Lymphedema Rates and Locoregional Recurrence in Patients Enrolled in NSABP B-32 M.C. Goodwin,[1]* T.S. Stull,[1] A.E. Collett,[1] M.R. Chernick,[2] A.V. Barrio,[1] T.G. Frazier.[1] *1. Comprehensive Breast Center, Bryn Mawr Hospital, Bryn Mawr, PA; 2. Lankenau Hospital, Wynnewood, PA.*

Introduction: National Surgical Adjuvant Breast and Bowel Project (NSABP) B-32 is a randomized, phase III clinical trial comparing sentinel node resection (SNR) to conventional axillary dissection (AND) in clinically node-negative breast cancer (BC) patients (pts). We performed a review of our pts enrolled in B-32 to evaluate differences in lymphedema (LE) and locoregional recurrence (LRR). Methods: An IRB approved retrospective chart review was conducted between September 1999 and September 2003. We enrolled 136 pts in B-32. Four pts were excluded from the study; 132 pts comprised our cohort. Group 1 consisted of 71 pts who had SNR followed by AND. Group 2 consisted of 61 pts who had SNR and AND only if the sentinel node was positive for metastatic carcinoma. LE was evaluated by standard volume displacement technique. Rates of LE, LRR, contralateral breast cancer (CBC), breast cancer specific survival (BCSS) and overall survival (OS) were compared between the 2 groups. Results: Median age was 57. Median follow-up was 8yrs. Of 71 pts in Group 1, 8 (11.3%) developed LE vs 0/61 pts (0%) in Group 2 (P=.007), with a median time to LE of 12 mo. Median number of lymph nodes (LN) removed was 15 in Group 1 vs 2 in Group 2. 71 (100%) pts had an AND in Group 1 compared to 8 (13.1%) in Group 2. There was no significant difference in ipsilateral breast tumor recurrence (IBTR) (5.6% vs 3.2%, P=.69) or regional recurrence (2.8% vs 1.6%, P=.71) between the two groups. Median time to IBTR and regional recurrence was 5.8 yrs and 1.4 yrs, respectively. There was no difference in CBC (2.8% vs 3.3%, P=.26) or distant recurrence (8.5% vs 13.1%, P=.27) between both groups. OS (90.1% vs 85.2%, P=.38) and BCSS (94.4% vs 90.2%, P=.51) were similar between Group 1 and Group 2. Conclusion: Routine AND is associated with a statistically significant increased risk of lymphedema compared to SNR followed by selective AND. SNR with selective AND results in equivalent local, regional and distant control compared with routine AND. Routine AND in BC pts with clinically negative axilla should be abandoned.

Table 1. Clinical Characteristics of Lymphedema Patients Stratified by Type of Axillary Surgery

	Group 1 (SNR+AND)	Group 2 (SNR+selective AND)
Total patients (N)	71	61
Patients with LE	8 (11.3%)	0 (0%)
Clinical LE[a]	6 (8.4%)	0 (0%)
Perceived LE[b]	2 (2.8%)	0 (0%)
Patients treated with AND	71 (100%)	8 (13.1%)
Median LN removed in AND Patients	15	20

SNR, sentinel node resection; AND, axillary node dissection; LE, lymphedema; LN, lymph nodes;
[a]A volume difference of 200 mL or more between the affected and contralateral arm with volume displacement technique was diagnostic of clinical lymphedema
[b]Perceived lymphedema was diagnosed if patient perceived arm swelling without a diagnostic increase in volume displacement

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Completeness of Dictated Operative Reports in Breast Cancer – The Case for Synoptic Surgical Reporting L. Donahoe,[1]* S. Bennett,[1] W. Temple,[2] A. Hilchie-Pye,[1] K. Dabbs,[3] E. MacIntosh,[4] G. Porter.[1] *1. Dalhousie University, Halifax, NS, Canada; 2. University of Calgary, Calgary, AB, Canada; 3. University of Alberta, Edmonton, AB, Canada; 4. University of Manitoba, Winnipeg, MB, Canada.*

Introduction: The quality of surgery in breast cancer is important, and the details of surgery are often important in subsequent treatment decisions. To date, the dictated operative report has formed the cornerstone of documenting such surgery. Synoptic electronic reporting using a standardized template has been proposed as a new model for breast cancer operative notes. The goal of this study was to determine the current completeness of dictated operative reports for breast cancer surgery. Methods: An iterative, consensus-based approach to determining required elements of a proposed synoptic surgical operative report identified critical preoperative evaluation and intraoperative technical elements. We then evaluated the dictated operative reports of 100 consecutive breast cancer patients for presence and completeness of such elements. Results: Among the 100 patients, one operative report was completely missing. As seen in the Table below, information regarding antibiotic and venous thromboembolism prophylaxis was rarely described (7%), and critical details regarding breast cancer presentation and diagnosis were frequently incomplete (84%). Among patients undergoing mastectomy, information regarding potential for breast conservation was never complete, and only partially described in 60%. There was variability in the frequency of specific intraoperative technical elements; 92% of patients had complete data about identification and preservation of nerves in axillary lymph node dissection and closure was at

least partially described in 98%. However, only 14% of reports contained complete information regarding sentinel lymph node biopsy and only 36% had data regarding intraoperative margin assessment. Among patients undergoing wire localization, this was accurately described in 75%. Conclusions: The dictated operative report for breast cancer surgery does not adequately capture important data. A synoptic reporting system, where clear documentation of important elements is required, would appear to be a potentially beneficial tool in breast cancer surgery.

Elements	Description	Not Described (%)	Partially described (%)	Fully described, (%)
Preoperative	Past history	98	2	0
	Presentation symptomatology, imaging and diagnosis	16	84	0
	Antibiotic and deep vein thrombosis prophylaxis	93	7	0
	Metastatic workup	98	0	2
	Choice of surgery (mastectomy patients)	40	60	0
Intraoperative technical	Use of needle localization with breast conservation	25	N/A	75
	Intraoperative margin assessment (presence and type)	45	19	36
	Level of deep resection with mastectomy	23	N/A	77
	Nerves identified and preserved during axillary node dissection	4	4	92
	Sentinel lymph node identification and assessment	0	86	14

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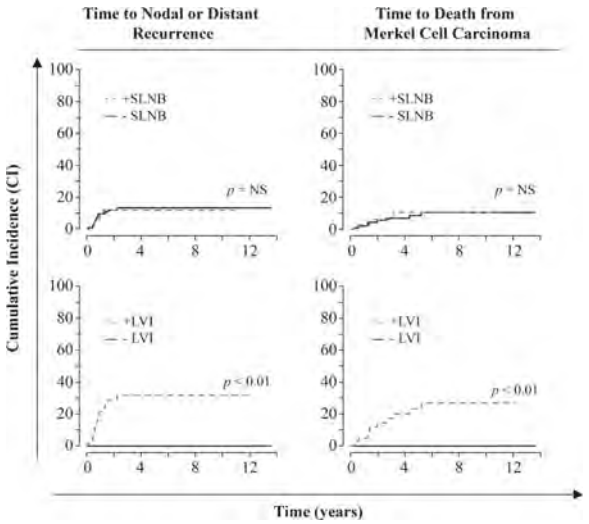
Recurrence and Survival in Patients Undergoing Sentinel Lymph Node Biopsy for Merkel Cell Carcinoma: Analysis of 153 Patients from a Single Institution R.C. Fields,[1]* K.J. Busam,[2] J.F. Chou,[4] K.F. Panageas,[4] M.P. Pulitzer,[2] D.H. Kraus,[3] M.S. Brady,[1] D.G. Coit.[1] *1. Gastric & Mixed Tumor Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; 2. Department of Pathology, Memorial Sloan-Kettering Cancer Center, New York, NY; 3. Head & Neck Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; 4. Department of Epidemiology & Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY.*

INTRODUCTION: Cutaneous neuroendocrine carcinoma, known as Merkel cell carcinoma (MCC), is a rare neoplasm with propensity for lymphatic spread. Detection of occult microscopic disease via sentinel lymph node biopsy (SLNB) is part of the AJCC staging for MCC. However, the rarity of MCC has precluded analysis of predictors of SLN positivity and associations with survival. METHODS: A retrospective review of a prospective MCC database was performed. Frequency and predictors of a +SLN were determined. Recurrence and death from MCC were analyzed using the cumulative incidence (CI) function, treating death from other causes (DOC) as a competing risk. RESULTS: Five hundred patients with MCC were identified in our database. From 1996-2010, 153 clinically node (-) patients underwent SLNB, of which 45 (29%) were positive. Predictors of +SLN were: clinical stage (25% stage I vs. 45% stage II; p=0.02) and presence of lymphovascular invasion (LVI) (55% +LVI vs 4% -LVI; p<0.01. +SLN patients were more likely to receive adjuvant radiation (RT) or chemotherapy (60% vs. 7%, p<0.01). Nodal RT was used in 23 (51%) of +SLN patients and 7 (7%) of -SLN patients, p<0.01. Median follow-up was 41 months. Among all 153 patients undergoing SLNB, there were 16 nodal or distant recurrences (10%), 11 deaths from MCC (7%), and 27 DOC's (18%). The 2-year CI of recurrence or death from MCC were 12% and 6%, respectively. There was no difference in recurrence or death from MCC between +SLN and -SLN patients (figure, top). All patients with recurrence had +LVI. The 2-year CI of recurrence or death from MCC for +LVI patients were 30% and 15%, respectively (figure, bottom). CONCLUSION: In patients with MCC presenting with clinically node negative disease, SLNB identifies occult nodal metastases in 29% of cases. Predictors of +SLN are primary tumor size and presence of LVI. +SLN patients receive adjuvant treatment more often than -SLN patients; however, SLN status is not associated with recurrence or survival. In contrast, LVI is a predictor of nodal or distant recurrence and survival.



TOP PANELS: There is no difference in recurrence (left) or death from MCC (right) between +SLN and -SLN patients. BOTTOM PANELS: All recurrences (left) and deaths from MCC (right) occurred in patients with +LVI, with a 2-year CI of recurrence or death in +LVI patients of 30% and 15%, respectively.

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Outcome following sentinel node biopsy versus wide local excision only for melanoma; analysis of a large single-institution experience A.P. Van der Ploeg,[1] L.E. Haydu,[2] A.J. Spillane,[1] M.J. Quinn,[1] R.P. Saw,[1] K.F. Shannon,[1] J.R. Stretch,[1] J.F. Thompson.[1]* *1. Melanoma Institute Australia, North Sydney, NSW, Australia; 2. Sydney Medical School, The University of Sydney, Sydney, NSW, Australia.*

Introduction: Worldwide, sentinel node (SN) biopsy (SNB) is now part of standard management for most patients with early stage melanoma. In a large retrospective single-institution study, we compared survival of patients who underwent SNB (n=2802, 50.3%) with patients in an observation (OBS) group (n=2765, 49.7%) who had only wide local excision (WLE). Methods: Patients treated from 1992-2008 were selected based on eligibility for SNB; tumours > 1mm or having ulceration or Clark level IV or V invasion. Median follow-up was 42 months. Results: Univariate analysis of melanoma-specific survival (MSS) demonstrated no difference when comparing all patients in the SNB and OBS groups. However, a stratified analysis of MSS for different Breslow thickness subgroups demonstrated a better prognosis for patients in the SNB group with melanomas > 1 mm (p=0.015) and in those with intermediate thickness melanomas (1.2-3.5 mm) (p=0.01). There were significant differences in the patient groups. The SNB group contained more young patients and tumours having nodular histology, while the OBS group contained more tumours <1mm thick and in head/neck sites. After adjusting for these differences in multivariate analysis of MSS, no significant therapeutic benefit for SNB patients was demonstrated. In both univariate and multivariate analyses, SNB patients showed improved disease free survival (DFS) (p<0.001) and regional lymph node control (p<0.001). In multivariate analysis of the SNB group, SN status was an independent prognostic factor for MSS (HR= 3.61; 95%CI: 2.79-4.67; p=0.0001). Conclusion: In this heterogeneous patient group, the overall outcome of patients having WLE alone was the same as for those having additional SNB. However, the results indicate that the prognosis for patients with intermediate thickness melanomas (1.2–3.5mm) may be improved if they have a SNB. We continue to recommend SNB as a staging procedure for patients with stage I-II melanoma, pending results of the randomized first Multicenter Selective Lymphadenectomy Trial, which should better define patient subgroups most likely to obtain a survival benefit from SNB.

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Preoperative ultrasound assessment of sentinel nodes in melanoma patients does not provide reliable staging: Results from a large multicenter trial J.F. Thompson,[1]* L.E. Haydu,[2] R.F. Uren,[3] A.J. Cochran,[4] D.R. Wen,[4] D.M. Morton.[5] *1. Melanoma Institute Australia, North Sydney, NSW, Australia; 2. Sydney Medical School, The University of Sydney, Sydney, NSW, Australia; 3. Nuclear Medicine and Diagnostic Ultrasound, RPAH Medical Centre, Camperdown, NSW, Australia; 4. University of California at Los Angeles, Los Angeles, CA; 5. John Wayne Cancer Institute, Santa Monica, CA.*

Introduction: It has been suggested that preoperative ultrasound (US) assessment of regional lymph nodes in patients with primary cutaneous melanoma provides staging that is sufficiently accurate to avoid the need for sentinel node (SN) removal. However, relative diagnostic accuracy of US and SN biopsy (SNB) is not well documented outside single institution studies. This study analyzed results of preoperative US assessment in a large multicenter trial. Methods: US data were extracted for all patients enrolled in the 2nd Multicenter Selective Lymphadenectomy Trial from 01/12/04 to 31/03/10. Patients treated at 29 sites worldwide had preoperative US assessment of SNs followed by SNB. Excised SNs were pathologically assessed and if negative, assessed with RT-PCR. Results: SNs were identified and removed from 2788 lymph node fields in 2481 patients. Positive SNs (containing metastatic disease by histopathologic or molecular evaluation) were identified in 578 (20.7%) lymph node fields in 554 patients. 96 (3.9%) patients had a positive (abnormal) US result in at least one lymph node field. US was true positive (TP) for SNs in 46 (1.6%) lymph node fields. Sensitivity of US in detection of positive SNs in all lymph node fields was 8% (95% CI 6%-10.5%) and the specificity 97.3% (95% CI 96.7%-97.9%). Tumor dimensions were measured for 384 histologically positive SNs. The median cross-sectional area (CSA) was 0.17mm2 (range 0.0001–182.29 mm2). SNs having TP US results (n = 19) had a median CSA of 6.11mm2; this was significantly greater than the median CSA of 0.16mm2 in measured SNs having false negative (FN) US results (n = 365) ($p<0.001$). Conclusions: With a sensitivity of only 8.0% in this large, multicenter clinical trial patient group, US is clearly not an effective substitute for SNB for the purpose of detecting positive SNs. The median detectable CSA for recognition by US is significantly greater than that for SLNs that are assessed using histopathology. Accurate staging to guide patient management and determine prognosis cannot be achieved by assessing SNs using US alone.

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Staging and prognosis of 634 melanoma patients with intralymphatic (IL) metastases C. Balch,[1]* S.J. Soong,[2] J.E. Gershenwald,[3] J.F. Thompson,[4] S. Ding,[2] D.G. Coit,[5] K.M. McMasters,[6] T. Johnson,[7] P.A. Gimotty,[8] S.P. Leong,[9] A.M. Eggermont,[10] V.K. Sondak.[11] *1. Johns Hopkins Medical Institutions, Baltimore, MD; 2. University of Alabama at Birmingham, Birmingham, AL; 3. University of Texas MD Anderson Cancer Center, Houston, TX; 4. Melanoma Institute of Australia, Sydney, NSW, Australia; 5. Memorial Sloan Kettering Cancer Institute, New York, NY; 6. University of Louisville, Louisville, KY; 7. University of Michigan, Ann Arbor, MI; 8. University of Pennsylvania, Philadelphia, PA; 9. Sutter Hospital, San Francisco, CA; 10. Erasmus University Medical Center, Rotterdam, Netherlands; 11. H. Lee Moffitt Cancer Center, Tampa, FL.*

In the updated AJCC melanoma database of over 34,000 prospectively followed patients,survival rates for IL disease (node- and node +)were analyzed to determine how they should be incorporated into staging. Materials and Methods: The 2008 AJCC Melanoma Staging Database contained new information on 399 patients with isolated intralymphatic metastases (N2c) and 235 with IL disease plus nodal metastases (N3) from 11 melanoma centers. This is the largest series of IL melanoma patients ever evaluated. Results: The 5/10 year survival rates for the 634 patients were 61/45%. A multivariate analysis (MV) showed the independent predictors of survival were: age > 70 (HR 2.2, $p<0.0001$), primary ulcer+ (HR 2.0, p=0.0003), primary thickness >6.0mm (HR 2.1, p= 0.0004), axial location (HR 1.7, p=0.0005) and nodal metastases (HR 1.6, p=0.0094). IL patients node-: (N2c), the 5/10 year survival rates were 69/52%. The independent prognostic factors were thickness > 6.0mm (HR 2.7, $p<0.0001$), axial location (HR 1.8, p= 0.03), and age > 70 (HR 1.6, p=0.0340). IL patients node+: There was a significant decrease in 5/10 year survival (46/33%)in IL patients with nodal metastases compared to node-patients ($p<0.0001$. Independent prognostic factors for IL node + patients were age > 70 (HR 2.5, p=0.0024), primary ulcer+ (HR 2.2, p=0.0127), and > 2 nodes+ (HR 1.8, p=0.0513). Stage grouping of IL patients: Ten-year survival for 399 IL node- patients (N2c) was somewhat better (52%) than for 576 N2a patients (46%) and 153 N2b patients (28%). When the IL node- patients were grouped, there was a slightly elevated 10-year survival when pooled with the entire cohort of 1391stage IIIB patients (38% without N2c, 43% with N2c patients). Adding the 235 IL node+ patients to the remaining 485 N3 patients only slightly increased the 10-year survival among stage IIIC patients (24% with IL node+, 22% without). Conclusions: Patients with IL node- (N2c) metastatic melanoma had a more favorable survival rate than previously reported. Classifying them as Stage IIIB was the closest fit for stage grouping. The addition of nodal metastases plus IL disease worsens prognosis significantly and causes upstaging to IIIC.

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Surgical Resection for Melanoma Metastatic to Distant Sites D.L. Morton,[1]* S. Stern,[1] R. Elashoff.[2] *1. John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, CA; 2. Biostatistics, UCLA, Los Angeles, CA.*

Introduction: Treatment of distant metastatic melanoma is inadequate; median survival is only 8-10 months, and there is no consensus on surgery versus systemic medical therapy (SMT). Resection has been reported in single-center studies for solitary metastases but usually not for multiple metastases. Except for a SWOG study we are aware of no multicenter series of surgery for distant metastatic melanoma. We examined the survival of patients receiving surgery vs SMT for stage IV recurrence in three international phase III trials. Methods: In MSLT-I, patients with primary melanoma were randomized to sentinel node biopsy+immediate lymphadenectomy or to nodal observation+delayed lymphadenectomy. MMAIT-III and MMAIT-IV randomized patients with nodal and distant metastases, respectively, to postsurgical BCG+placebo or BCG+melanoma cell vaccine. Treatment for distant recurrence was selected by multicenter investigator. We compared the number of patients in these three trials who developed distant recurrences, the initial therapy for recurrence, and survival. Results: Results from all three trials show that 42% of patients with metastatic melanoma were candidates for surgical resection (Table). The survival of patients receiving surgical therapy was superior to SMT: median 20.4 vs 9.5 months and 5-year 23.4% vs 8.4% ($p<0.0001$; HR 0.463). Conclusions: Forty-two percent of patients with distant metastatic melanoma are candidates for surgical resection and exhibit improved survival (HR 0.463). Selection bias as the explanation for more favorable prognostic factors in surgically treated patients cannot be excluded. We have begun a multicenter randomized trial comparing initial surgery versus initial medical therapy for distant metastatic melanoma. From the MSLT-I, MMAIT-III and MMAIT-IV Trial Groups. Funded with NCI support (PO1CA12582 and P01CA29605).

Survival From Distant Recurrence

Study	Total No.	No. with Distant Recurrence	Survival from Distant Recurrence						
			Initial Medical Therapy			Initial Surgical Therapy			P value
			N(%)	Median	5-Year	N(%)	Median	5-Year	Hazard ratio*
MSLT-I	2001	293	163 (56%)	8.7 mos	8.1%	130 (44%)	15.8 mos	22.0%	P≤.0001 HR=.517
MMAIT-III	1160	266	175 (66%)	9.2 mos	5.4%	91 (34%)	20.4 mos	25.2%	P≤.0001 HR=.363
MMAIT-IV	496	210	108 (51%)	12.0 mos	14.0%	102 (49%)	25.7 mos	23.4%	P≤.0003 HR=.536
Total	3657	769	446 (58%)	9.5 mos	8.4%	323 (42%)	20.4 mos	23.4%	P≤.0001 HR=.463

*Reference group = SMT

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Role of Sentinel Lymphadenectomy in Thin Cutaneous Melanomas with Positive Deep Margins on Initial Biopsy V.P. Koshenkov,* D. Shulkin, R. Bustami, A.H. Chevinsky, E.D. Whitman. *Atlantic Health, Morristown, NJ.*

INTRODUCTION: Breslow thickness (BRES) on initial melanoma biopsy (BX) primarily determines which patients undergo sentinel lymph node (SLN)

biopsy during definitive therapy. When the BX shows positive deep margins, many clinicians will treat these cases as potentially thicker melanomas and perform SLN biopsy, although without firm data to justify this clinical course. We hypothesized that otherwise thin (BRES <0.8 mm) melanomas with positive deep margins and thicker melanomas with BRES 0.8-2.0 mm have statistically equivalent risk of SLN metastasis. METHODS: A retrospective review was performed of adult patients undergoing wide excision plus SLN biopsy for melanoma from 01/2004 to 05/2010. Patients were classified based on BRES and BX deep margin status; Group 1: BRES < 0.8 mm and positive deep margins, and Group 2: BRES 0.8-2.0 mm, regardless of margin status. The primary outcome variable was the presence of metastatic disease in any SLN. A multivariate logistic regression model was constructed which also included the variables age, gender, Clark level, primary site, ulceration, residual disease (on wide excision) and vertical growth phase. RESULTS: A total of 260 patients were eligible, 73 (28%) in Group 1 and 187 (72%) in Group 2. Average age was 57 years, with 120 (46%) females. One or more SLNs were positive in 6/73 (8%) patients in Group 1 and 17/187 (9%) patients in Group 2 (p=0.82, Chi-square). The two groups remained statistically equivalent by multivariate regression analysis (p=0.66). In the multivariate model, female gender (OR =2.68, p=0.046) and Clark level IV-V (OR 3.54, p=0.024) were the only predictive factors for positive SLNs (See Table). Residual melanoma on wide excision approached statistical significance (OR 2.60, p=0.062). CONCLUSIONS: Positive deep margins on initial melanoma biopsy identify patients whose risk of SLN metastasis is statistically equivalent to patients with thicker melanomas. This data suggests these patients should be treated with both wide excision and SLN biopsy. Female gender and Clark level IV-V were significantly associated with positive SLN in the patients studied.

Multivariate Logistic Regression Model for the Risk of One or More Positive Sentinel Lymph Nodes. Total Number of Patients = 260, Number with One or More Positive Sentinel Lymph Nodes = 23 (9%)

Factor	Mean or %	OR	95% CI	p-value
Group 1 (vs Group 2)	28%	1.29	(0.42, 3.95)	0.66
Age (per 10 years)	57	-0.07	(-0.36, 0.22)	0.65
Gender (Female vs Male)	46%	2.68	(1.02, 7.09)	0.046
Clark level IV-V (vs I-III)	42%	3.54	(1.18, 10.59)	0.024
Primary site, Head/Neck (vs Extremities)	19%	0.68	(0.17, 2.77)	0.59
Primary site, Trunk (vs Extremities)	32%	0.73	(0.26, 2.09)	0.56
Ulceration (yes vs no)	6%	0.45	(0.05, 3.89)	0.47
Residual disease (yes vs no)	20%	2.60	(0.95, 7.11)	0.062
Vertical growth phase (yes vs no)	20%	1.60	(0.54, 4.72)	0.40

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Isolated limb perfusion with TNF-alpha en melphalan for the distal parts of the limb in soft tissue sarcomas patients J.P. Deroose,[1]* A.N. Van Geel,[1] J.W. Burger,[1] J.H. De Wilt,[2] A.M. Eggermont,[1] C. Verhoef.[1] *1. Surgical oncology, Erasmus MC - Daniel den Hoed, Rotterdam, Zuid Holland, Netherlands; 2. Radboud University Nijmegen Medical Center, Nijmegen, Netherlands.*

Introduction Fewer then 10% of all soft tissue sarcomas (STS) occur in the most distal parts of the extremity. Due to difficulty in achieving wide excision margins local recurrence (LR) after resection is up to 50%. Radiotherapy might improve this situation but is accompanied with serious co-morbidity. Since amputation does not improve survival rates, interest in regional treatment modalities increased, which has led to the successful introduction of isolated limb perfusion (ILP) with tumor necrosis factor-alpha (TNF) and melphalan. Herein we report on the results of ILP for locally advanced STS in the most distal parts of the limb Methods Between 1991 and 2009, 320 ILPs were performed for extremity STS of which 34 were in patients (n=28) with STS of the wrist, hand, ankle or foot. Trojani grade was I in 10 (29%), II in 13 (38%) and III in 11 patients (33%). Twenty patients (59%) were treated for unifocal whereas 14 patients (41%) had multifocal disease. ILP was executed in a mild hyperthermic fashion with a median dose TNF of 3 mg (1-4) and a median dose melphalan of 50 mg (25-90). Median clinical follow up was 23 months. Results Overall response rate was 62% (n=21) consisting of 11 (33%) complete responses and 10 (29%) partial responses whereas 13 patients (38%) had stable disease. Excision became possible after 14 ILPs in patients with unifocal disease (70%) resulting in a radical resection in 9 patients (45%). Adjuvant radiotherapy was administered in 6 patients (18%). LR rate was 32% after a median time of 53 months, LR in unifocal disease was 20% while multifocal disease showed 50% local recurrence (p=0.01). Amputation was unavoidable in 4 patients (14%) after a median time of 47 months. Five-year survival rate was 39% with a median survival of 47 months. Conclusion ILP made a radical resection possible in 45% of patients with unifocal STS of the most distal parts of the limb which has led to a LR rate of only 20% and a limb salvage rate of 86%. Therefore we believe TNF based ILP is a very effective treatment modality in patients with acral STS, a very difficult patient population.

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Genetic Basis of Sarcoma: Development of a Novel Mouse Model A. Gupta,* L. Kabaroff, C. Swallow, R. Gladdy. *Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, ON, Canada.*

Introduction: Existing mouse models of sarcomagenesis utilize knockout and transgenic mice but these fixed germline mutations do not recapitulate the stepwise development of sporadic human sarcoma. To mitigate these limitations, we have developed a genetically flexible mouse model of sarcomagenesis using a retroviral gene delivery system. Methods: p16/p19 null mice expressing the retroviral receptor, TVA, under the mesenchymal promoter nestin were used (p16/p19-/-xN-tva). DF1 cells, infected with retrovirus vectors (RCAS) carrying oncogenes (KrasG12D, c-Myc, IGF2) or GFP alone, were delivered by injection into the hindlegs of neonatal mice and tumor development was monitored. Results: GFP-positive cells were noted following in vitro infection of cultured p16/p19-/-xN-tva mouse skeletal muscle with RCAS-GFP. Similar results were seen in myoblasts cultured from mice injected with RCAS-GFP in vivo, suggesting successful cell infection and gene delivery into this lineage. To date we have identified 32 tumors in 97 p16/p19-/-xN-tva mice injected with oncogenic vectors. Tumors developed around the injection site in 22 mice, with a median onset of 22 weeks (range of 8-42 weeks). Ten mice developed spontaneous tumors at sites distant from the vector injection. No metastatic disease was observed. Gene-anchored PCR revealed retroviral vector DNA integration in 89% of tumors. Western blot analysis demonstrated increased Kras and c-Myc expression when compared to control tissues. Pathologic assessment of all tumors showed small, round cells with a high nuclear:cytoplasmic ratio. Anti-desmin and anti-smooth muscle actin immunohistochemistry showed heterogeneous staining in tumors from different mice, suggesting several subtypes of sarcoma were produced. Conclusions: We have generated a novel model of sarcomagenesis using the RCAS-tva system to deliver oncogenes into mouse hindlegs with a tumor formation rate of 23%. With further optimization of this model, somatic delivery of multiple oncogenes will facilitate closer recapitulation of human disease and will allow the validation of novel genes contributing to sarcoma development.

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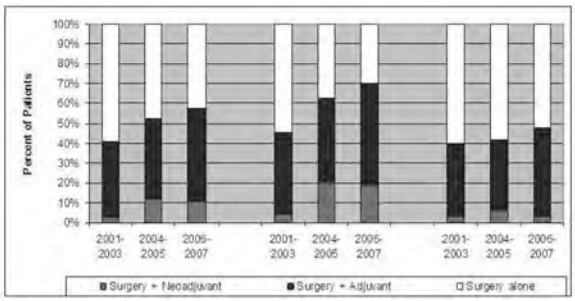
Evolution of Multimodality Management of Gastrointestinal Stromal Tumors of the Stomach K.Y. Bilimoria,[1]* R.P. Merkow,[2] J.D. Wayne,[2] D.E. Abbott,[1] J.N. Cormier,[1] B.W. Feig,[1] K.K. Hunt,[1] P.W. Pisters,[1] R. Pollock,[1] D.J. Bentrem.[2] *1. Surgical Oncology, MD Anderson Cancer Center, Houston, TX; 2. Northwestern University, Chicago, IL.*

BACKGROUND: Gastrointestinal stromal tumor (GIST) treatment has changed considerably with introduction of imatinib in 2001, initiation of ACOSOG adjuvant trial in 2002, and FDA adjuvant approval in 2008. However, little is known about how imatinib has been incorporated over time. Our objective was to examine the evolution of multimodality management of GISTs. METHODS: Patients coded specifically as gastric GISTs were identified (n=4,508; 443 hospitals) from the National Cancer Data Base (2001-2007). Changes over time were assessed with chi-squared test for trend. Separate mul-

tivariable regression models were developed to examine factors associated adjuvant and neoadjuvant practices. RESULTS: Gastric GISTs reported to NCDB steadily increased: 463 in 2001 to 831 in 2007. 3,289 underwent resection: 78% partial/wedge, 6% total/near-total, and 14% multivisceral. From 2001 to 2007, use of adjuvant therapy increased from 29% to 47% (P<0.001), although patients were less likely to get adjuvant therapy if older, tumors <3cm, low grade, negative margins, or treated at low-volume hospitals (P<0.01). Adjuvant systemic therapy for lesions <3 cm also increased (17% to 25%, P=0.001). For GISTs >6 cm, use of adjuvant therapy increased from 41% to 49% overall, with increases of 45% to 70% at high-volume centers and of 39% to 48% at low-volume centers (all P<0.001, figure). Neoadjuvant therapy increased from 0% to 15% (P<0.001) with patients more likely to receive neoadjuvant treatment if size >6 cm, treated at high-volume centers, or treated in 2006-2007 (P<0.001). Multivisceral resections decreased over time (19% to 12%, P<0.001). The proportion of patients treated at high-volume centers increased slightly over time (22.2% to 26.9%, P=0.006). CONCLUSIONS: Adjuvant systemic therapy use for GISTs was increasing and widespread prior to FDA approval of adjuvant imatinib, suggesting contemporaneous advances in advanced GIST management were being translated into the adjuvant setting more than expected. As relatively costly therapies are integrated into practice, more robust tracking systems are needed to follow and guide the incorporation of new treatments.



Use of systemic therapy in gastric GISTs >6cm.

Univariate analysis for variables associated with disease specific survival

Variable	Disease specific survival at 5 years	P-value
Neurofibromatosis-1 Yes No	45% 65%	0.025
Age (years) <45 ≥45	54% 65%	0.040
Tumor size (cm) <5 ≥5	85% 43%	0.001
Depth Deep to fascia Superficial to fascia	56% 81%	0.037
Grade High Low	44% 86%	<0.001
Tumor location Extremity Trunk Head & Neck	71% 38% 64%	0.041
Nodal Metastasis Positive Negative	22%* 61%	<0.001
Local Recurrence only Yes No	60% 60%	0.596
Distant Recurrence Yes No	74% 28%	0.001
Margins of Resection Negative (R0) Positive (R1/R2)	61% 36%	0.008
Adjuvant Chemotherapy Yes No	36% 59%	0.624
Adjuvant Radiation Yes No	63% 59%	0.265

* Extrapolated data to 5 years

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MPNST (Malignant Peripheral Nerve Sheath Tumors): The Mayo Clinic Experience C. Stucky,[1]* K.N. Johnson,[1] R.J. Gray,[1] B.A. Pockaj,[1] P.S. Rose,[2] N. Wasif.[1] *1. General Surgery, Mayo Clinic Arizona, Phoenix, AZ; 2. Mayo Clinic, Rochester, MN.*

Background: Malignant peripheral nerve sheath tumors (MPNST) are a rare form of soft-tissue sarcoma with few studies reporting on patient outcomes and prognostic variables. We report on our institutional experience with MPNST. Methods: A retrospective review of 175 patients diagnosed with MPNST from 1985-2010 was performed. Patient and tumor characteristics as well as information on surgical resection, chemotherapy and radiation treatment were evaluated to identify prognostic variables. Results: The median age of our study population was 44 years and 51% were female. Median tumor size was 6cm and 61% of patients had high grade tumors. Tumors were most commonly located on the extremities (45%), followed by trunk (34%) and head/neck regions (19%). The majority of patients underwent surgical resection (95%) and adjuvant treatment with chemotherapy (7%), radiation (40%) or both (23%). Margin status was as follows: R0 (69%), R1 (2%), R2 (9%) and unknown (20%). The 5- and 10-year disease specific survival (DSS) was 60% and 45% respectively, with a median follow-up of 74 months. On univariate analysis, no predictors for local recurrence were identified, whereas size >5cm and high tumor grade predicted distant recurrence. As outlined in the table below, age< 45 yrs, presence of neurofibromatosis syndrome-1, tumor size >5cm, location deep to the fascia, high tumor grade, tumor location, nodal metastasis and margins of resection were all associated with DSS on univariate analysis. Multivariate Cox regression analysis demonstrated high tumor grade (HR=3.4, 95% CI 1.3–9.3), size≥5cm (HR=3.6, 95% CI 1.3–9.9) and distant recurrence (HR=2.6, 95% CI 1.2–5.5) as poor prognostic indicators for DSS. Conclusions: Similar to other soft tissue sarcomas, high tumor grade and tumor size >5cm predict adverse DSS for MPNST. In the context of a multi-disciplinary treatment setting, however, outcomes at 5 and 10 years were better than previously reported for MPNST.

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Impact of Specialty and Clinical Experience on Treatment Sequencing in the Multi-modality Management of Soft Tissue Extremity Sarcoma N. Wasif,[1]* R.M. Tamurian,[2] S. Christensen,[2] L. Do,[2] S.R. Martinez,[2] S. Chen,[2] M.F. Brennan,[3] R.J. Canter.[2] *1. Surgery, Mayo Clinic, Phoenix, AZ; 2. University of California, Davis Medical Center, Sacramento, CA; 3. Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Multi-modality management of extremity soft tissue sarcoma (STS) is standard of care. However, variation in the pre or post-operative use of radiation and/or chemotherapy occurs clinically. Our goal was to identify some of the factors responsible. Methods: A questionnaire was emailed to active members of ASCO who specialize in the management of STS. Questions covered multi-modality treatment of STS. Survey responses were scored on a five point Likert scale (1-5). Results: The questionnaire was viewed by 490 potential respondents and completed by 320 (65%). Respondents self-identified by specialty, Medical Oncology (18%), Radiation Oncology (8%), Surgeons (67%), and Others (7%) as well as by percentage of clinical practice comprising STS care; >75% (12%), 25-75% (39%), and <25% (49%). As a whole, respondents were evenly split on the use of pre or post-operative radiation (mean 3.03 ± 0.06), a decision not influenced by specialty. However physicians with a >75% STS practice preferred pre-operative radiation as compared to those with <25% (2.58 ± 0.17 vs. 3.19 ± 0.08, p 0.003). Similarly physicians who had completed training <5 years ago preferred pre-operative radiation as compared to those who finished >15 years ago (2.79 ± 0.12 vs. 3.21 ± 0.09, p 0.025). Factors identified by respondents as being important in receipt of radiation include tumor size >10cm, high grade, positive margins and proximity to neurovascular bundles. As a group, respondents leaned towards pre-operative chemotherapy (mean 2.89 ± 0.06), with no significant difference among specialties or years in practice. Physicians with >75% STS practice preferred pre-operative chemotherapy as compared to those with <25% (2.51 ± 0.16 vs. 3.22 ± 0.07, p <0.001). Factors important for chemotherapy were tumor size >10cm, high grade, age

<50, and synovial sarcoma histology. Conclusions: Treatment sequencing in the management of STS is influenced by clinical volume and years in practice but not by physician specialty. This may be reflective of the recent trend towards regionalization of multi-modality STS care.

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Is the Current Staging System Applicable to Survivors of Retroperitoneal Sarcoma? A. Abbott,[1]* E.B. Habermann,[1] H.M. Parsons,[2] T.M. Tuttle,[1] W. Al-Refaie.[3] *1. Department of Surgery, University of Minnesota, Minneapolis, MN; 2. Department of Health Policy and Management, University of Minnesota, Minneapolis, MN; 3. Minneapolis Veteran Affairs Medical Center, Minneapolis, MN.*

Introduction: The ability of the current American Joint Committee on Cancer (AJCC) staging system to predict survival after the resection of retroperitoneal sarcomas (RPS) has been questioned. Whether it is also applicable to patients who have survived years after RPS resections remains unknown. We hypothesized that the current AJCC staging system has limited ability to predict conditional survival in patients surgically treated for RPS. Methods: Using the Surveillance Epidemiology and End Results database, we identified 1,176 patients who underwent resections of non-metastatic RPS or intra-abdominal sarcomas from 1988 to 2007. Conditional survival was defined as time-specific estimates conditioned on living 1, 3, and 5-years post-diagnosis and resection. Kaplan Meier methods were used to assess unadjusted conditional survival. Cox proportional hazards regression was used to assess the impact of the AJCC staging system variables and other relevant patient-, tumor-, and treatment-related factors on sarcoma-specific survival (SSS) while adjusting for covariates. Results: Older age, male gender, tumor size, histologic-subtype, and grade predicted poorer SSS at the time of diagnosis. The 1, 3, and 5-year survival estimates at baseline were 89%, 69%, and 57% respectively. Conditional survival analyses showed that older age, male gender, and tumor size were no longer significant predictors after one year of survival. A diagnosis of leiomyosarcoma predicted a worse SSS until three years after diagnosis. Only high grade tumors remained a significant predictor of poor prognosis even after five years of survival (Hazard ratio 2.3). Despite extensive multivariate modeling, the addition of adjuvant radiotherapy remained a non-significant predictor of SSS. (Table) Conclusion: This large population-based appraisal shows that the ability of the current AJCC staging system to predict conditional survival dampens after three years of survival. While limited by the absence of resection margin status, our results stimulate future investigations to re-assess the applicability of the AJCC staging system for RPS.

	Baseline HR N = 1175 D = 488	1-year HR N = 940 D = 361	3-year HR N = 558 D = 178	5-year HR N = 373 D = 85
Age				
18-35 yrs	Ref	Ref	Ref	Ref
36-50 yrs	1.11	1.29	1.11	0.85
51-64 yrs	1.38	1.49	1.13	0.76
65-80 yrs	2.04*	2.21*	1.99	1.09
81+ yrs	3.39*	2.67*	2.31	1.67
Tumor Size				
0-5 cm	0.70	0.71	0.52	0.24
5-10 cm	0.68*	0.64*	0.87	1.22
10-20 cm	0.91	0.78	0.68	0.94
20+ cm	Ref	Ref	Ref	Ref
Histology				
LPS	Ref	Ref	Ref	Ref
MFH	1.63*	1.38	0.90	0.73
LMS	1.58*	1.60*	1.53*	0.97
Other	1.74*	1.56*	1.19	0.94
High vs. low grade	2.33*	2.13*	1.64*	1.84*
Surgery + Adjuvant RT vs. Surgery alone	0.96	1.15	1.29	1.33

Abbreviations: N, sample size of each cohort; D, deaths; HR, hazard ratio; Ref, referent; RT, radiotherapy; LPS, liposarcoma; MFH, malignant fibrous histiocytoma; LMS, leiomyosarcoma.
* denotes p-value <0.05. We also adjusted for race, gender, and tumor registry location.

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Comparison of Clinicopathologic Factors in 113 Patients with Resected Pancreatic and Ileal Neuroendocrine Tumors from a Single Institution F.S. Dahdaleh,* D. Calva, T.M. O'Dorisio, J.C. Carr, J. Liao, J.J. Mezhir, J.R. Howe. *Surgery, University of Iowa, Iowa City, IA.*

Introduction: Recent population-based studies have demonstrated significant differences in outcome between patients with pancreatic and ileal neuroendocrine tumors. The objective of this study was to more closely examine the clinicopathologic differences between ileal and pancreatic neuroendocrine tumors following resection. **Methods:** A retrospective chart review of a prospectively collected database was reviewed for clinicopathologic variables, biochemical markers, and follow-up of patients with resected ileal (INETs) and pancreatic (PNETs) neuroendocrine tumors. **Results:** Between 1998 and 2010, 113 patients were explored (61 PNETs and 52 INETs). Ten separate clinicopathologic variables were analyzed and found to be significantly different between patients with PNETs and INETs **(Table)**. Notably, INETs were more often functional reflected by more clinical symptoms and elevation in serum levels of pancreastatin and serotonin. INETs more often had vascular invasion, nodal metastasis, and distant metastasis at presentation. At a median follow-up of 33 months (range 1 – 144 months), 10 (16%) patients with PNETs and 9 (17%) with INETs died. There was no significant difference in overall survival at 5-years between PNETs (81%) and INETs (75%; p=0.69) despite patients with INETs presenting at a later stage of disease. When analyzing patients with metastatic disease only, 5-year survival was not significantly different between PNETs and INETs (62% vs. 72%, respectively; p=0.23). **Conclusion:** In this series, patients with INETs presented with more advanced stages of disease compared to PNETs, with more functional tumors, higher biomarker levels, more symptoms, and a higher incidence of regional and metastatic disease. However, there were no detectable differences in overall survival between the groups. Translational studies are currently underway to elucidate the biologic differences between these tumor types.

Clinicopathologic variables of patients with resected neuroendocrine tumors of the ileum (INET) and pancreas (PNET)

Clinicopathologic Variable	INET	PNET	p-value*
Age (mean, years ± range)	58.4 ± 12.1	53.6 ±14.8	0.03
Flushing	23/52 (44%)	9/61 (15%)	0.001
Diarrhea	33/52 (63%)	11/61 (18%)	<0.001
Elevated Pancreastatin	45/50 (90%)	26/46 (57%)	<0.001
Elevated Serotonin	48/50 (96%)	24/43 (56%)	<0.001
Primary Tumor Size (mean, cm ± range)	2.4 ± 1.87	4.1 ± 2.50	<0.001
Vascular Invasion	42/44 (95%)	36/61 (59%)	<0.001
Nodal Metastases	40/47 (85%)	23/45 (51%)	<0.001
Distant Metastases	40/51 (78%)	24/61 (39%)	<0.001
Sandostatin Therapy	46/51 (90%)	27/61 (44%)	<0.001

*Student's t-test or Chi-square for continuous variables

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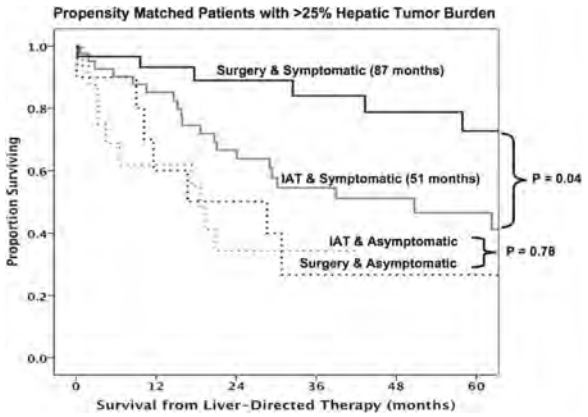
Surgery vs Intra-arterial Therapy for Neuroendocrine Liver Metastasis: a Multi-Center International Analysis S.C. Mayo,[1]* M.C. De Jong,[1] C. Pulitano,[2] B.M. Clary,[3] S.K. Reddy,[3] T.C. Gamblin,[4] S.A. Celinksi,[4] D.A. Kooby,[5] C.A. Staley,[5] J.B. Stokes,[7] C.K. Chu,[5] A. Ferrero,[8] D. Arrese,[9] R.D. Schulick,[1] M.A. Choti,[1] G. Mentha,[6] J. Strub,[6] T.W. Bauer,[7] R.B. Adams,[7] L. Aldrighetti,[2] L. Capussotti,[8] M. Bloomston,[9] T.M. Pawlik.[1] *1. Johns Hopkins University School of Medicine, Baltimore, MD; 2. Ospedale San Raffaele, Milan, Italy; 3. Duke Medical Center, Durham, NC; 4. University of Pittsburgh, Pittsburgh, PA; 5. Emory University School of Medicine, Atlanta, GA; 6. Hôpitaux Universitaires de Genève, Geneva, Switzerland; 7. University of Virginia, Charlottesville, VA; 8. Ospedale Mauriziano Umberto I, Turin, Italy; 9. Ohio State University, Columbus, OH.*

BACKGROUND: Management of patients (pts) with neuroendocrine tumor liver metastasis (NELM) remains controversial. Some clinicians advocate a surgical approach while others favor intra-arterial therapy (IAT). We sought to examine the relative efficacy of surgical management vs IAT for NELM and determine factors predictive of survival. METHODS: 753 pts who had surgery (n=339) or IAT (n=414) for NELM from 1985-2010 were identified from a

database of 9 hepatobiliary centers. Clinicopathologic data were assessed with multivariate Cox regression modeling and propensity score matching. RESULTS: Most pts had a pancreatic (32%) or a small bowel (27%) primary tumor; 39% had a hormonally active tumor. There were significant differences in baseline characteristics between surgery vs IAT groups (hormonally active tumors: 28% vs 48%; bilateral hepatic disease: 54% vs 84%; hepatic tumor burden >50%: 26% vs 65%)(all P<0.001). Among surgical pts, most underwent hepatic resection alone without ablation(78%). For pts who had IAT, the median number of IAT treatments was 1 (range, 1-4). Median and 5-yr survival of pts surgically managed was 123 mos and 74% vs 34 mos and 30% for pts treated with IAT(P<0.001). Pts managed with IAT had a higher risk of death compared with surgically managed pts(HR=2.7;P<0.001). Analysis of propensity score matched patients (surgery, n=52 vs IAT, n=66) revealed that surgical management remained associated with improved survival compared with IAT (median survival 84 vs 39 mos;P=0.04). In the propensity-adjusted multivariate Cox model, asymptomatic disease(HR=2.6) was strongly associated with worse outcome(P=0.001). While surgery provided a survival benefit over IAT among symptomatic patients with >25% hepatic tumor involvement, there was no difference in long-term outcome following surgery vs IAT among asymptomatic patients(Figure). CONCLUSIONS: Asymptomatic pts with a large burden of liver disease (>25%) benefited the least from surgical management and IAT may be a more appropriate treatment strategy. Surgery for hepatic NET metastasis should be reserved for pts with low volume disease or those with symptomatic, high volume disease.



Propensity matched patients with >25% hepatic tumor burden undergoing either intra-arterial therapy (IAT) or hepatic resection of neuroendocrine liver metastasis (NELM). Patients with high volume symptomatic disease benefitted the most from surgical management (median survival: surgery, 87 mos vs IAT, 51 mos;P=0.04).

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Transaxillary Gasless robotic thyroidectomy: A single surgeon's experience in North America M. Abdel Khalek,* G. Passot, P. Friedlander, E. Kandil. *Surgery, Tulane University, School of medicine, New Orleans, LA.*

Objective: To describe a robotic technique for transaxillary gasless thyroidectomy, with the addition of intraoperative peripheral nerve monitoring, in the surgical management of Thyroid disease. Design: Prospective study. Setting: Academic Institution. Patients: Sixty seven patients had robotic transaxillary thyroidectomy from September 2009 to September 2010. Main Outcome Measures: Feasibility of the robotic approach, patient and gland characteristics, operative time, and complications. Results: 53 females and 14 males were included with a mean age of 44.6 (range 13 – 76) years. There were 49 lobectomies and 18 Total (and subtotal) thyroidectomies. The mean nodule size (range) was 27.7 mm (10 - 83). The mean operative time (range) was 114 minutes (81 - 280) and mean docking time (range) was 38.6 minutes (10 - 90). Mean blood loss (range) 24 mL (10 - 100). Early detection of impending brachial plexus injury was noted intraoperatively in four patients. Prompt examination of patients' arms and repositioning to correct the compression was carried out. Arm repositioning in these cases corrected the problem, and no postoperative effects were found. There were no conversions to conventional open surgery. There were no perioperative or postoperative complications. In addition there was no evidence of vocal cord palsy or paresis on postoperative laryngoscopy. All patients were discharged home in 24 hours. Subjectively, the cosmetic results were considered excellent due to the hidden anatomic location of the incision site. Conclusions: We have demonstrated the technique to be feasible, safe and applicable for patients with thyroid disease. Intraoperative nerve monitoring would provide an adjunct to prevent brachial plexus palsy in patients undergoing this novel approach for thyroid surgery. We believe that the use of robotic technology for endoscopic thyroid surgeries could overcome the limitations of conventional endoscopic surgeries in the surgical management of thyroid disease.

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Regional recurrence after lymphadenectomy for clinically evident lymph node metastases from papillary thyroid cancer P.K. Shah,* K.K. Shah, G.C. Karakousis, C. Reinke, R. Kelz, D.L. Fraker. *Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia, PA.*

Introduction: The presence of lymph node (LN) metastases in papillary thyroid cancer (PTC) has limited prognostic utility for predicting disease-specific survival and characteristics of involved LNs (number, bulk, and extranodal extension) do not impact on staging of patients with PTC. Most patients however with PTC develop LN metastases that are microscopically involved; the natural history of those with clinically evident LN metastases and prognostic factors for recurrence in this group are understudied. Methods: Ninety-two consecutive patients were identified who underwent resection by a single surgeon for clinically evident LN metastases from PTC derived from a prospective database of 444 PTC patients (1999-2009). All patients were pre-operatively assessed by ultrasound. Surgical LN dissections were complete anatomic resections typically bilateral central and complete lateral dissections on the side of the involved LN. Univariate analyses were performed with the student's t-test and Fisher's exact test. A logistic regression model was developed to identify factors associated with recurrence. Results: With a median follow-up of 18 months after lymphadenectomy, there were no disease-related deaths. Twenty-seven patients (29%) developed recurrent disease all of which was in the regional cervical lymph nodes. Patients who recurred had a higher mean number of positive LN than those who did not recur (12 versus 6, p=0.03). Patients with and without recurrence were similar with respect to age, gender, histologic subtype, extrathyroidal extension, extranodal extension and total number of nodes sampled (Table 1). Number of positive LN remained significantly associated with the likelihood of recurrence (OR=1.15, CI(1.04-1.28)) in the logistic regression model. Conclusion: Patients with clinical evident LN metastases have an appreciable incidence of early regional cervical recurrence but not distant metastases. Among clinical and pathological factors evaluated, number of positive LNs appears to be associated with recurrence.

	RECURRENT	NON RECURRENT	ANALYSIS
N(%)	27(29)	65(71)	
GENDER MALE FEMALE	8 (30) 19(70)	22(66) 43(34)	P=0.81*
AGE (MEAN)	44	47	P=0.40**
PATHOLOGICAL TYPES FOLLICULAR CLASSIC TALL CELL WARTHIN SCLEROSING NOS PTC	4 (15) 7 (26) 10(37) 0 (0) 4 (15) 12(44)	8 (12) 12(18) 23(35) 2 (3) 4 (6) 26(40)	P=0.79*
PRESENTATION SYNCHRONOUS METACHRONOUS	17(63) 10(37)	28(43) 37(57)	P=0.11*
EXTRATHYROIDAL EXTENSION	13/17 (76)	18/27(66)	P=0.73*
CERVICAL LEVEL WITH DISEASE II III IV V VI	5 (18) 12(44) 16(59) 5 (18) 24(88)	12(18) 24(36) 43(66) 2 (3) 42(66)	...
MEAN NUMBER OF POSITIVE LN (RANGE)	12 (1-58)	6 (1-22)	P=0.03**
EXTRANODAL EXTENSION	13/16 (81)	24/39 (62)	P=0.42*
MEAN NUMBER OF SAMPLED LN (RANGE)	28 (1-92)	24 (1-68)	P=0.31
METHOD OF DETECTION OF LN CLINICAL EXAM U/S	8 (29) 19(71)	27(42) 38(58)	P=0.35*
ADJUVANT RAI	21(78)	37(57)	P=0.09*
XRT	5 (19)	6 (9)	P=0.29*

* - Fisher's exact test
** - Student's t-test

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BRAFV600E Mutation is Associated with Aggressive Papillary Thyroid Cancer in Elderly Patients G. Howell,* M.J. Armstrong, M.T. Stang, S.O. LeBeau, K.L. McCoy, S.E. Carty, Y.E. Nikiforov, L. Yip. *Surgery, University of Pittsburgh, Pittsburgh, PA.*

Introduction: BRAFV600E mutation is the most common genetic alteration in papillary thyroid cancer (PTC) and may be a marker for poor outcome. Advanced age is also associated with poor prognosis in PTC, but prior studies have not demonstrated a clear association with BRAF positive PTC and age. We hypothesize that aggressive PTC in this population is unrelated to BRAF mutation status and examine BRAF positive PTC in elderly patients. Methods: Under an IRB-approved protocol, we conducted a single center, retrospective review of elderly patients (age >65) with PTC who had their initial operation at our institution between 1/07 and 12/09. Persistent/recurrent disease was diagnosed after radioiodine ablation if 1) imaging demonstrated nodal or distant metastases, 2) thyroglobulin levels remained elevated, or 3) re-operation was required. BRAF mutation testing by real-time PCR and fluorescence melting curve analysis was performed as part of routine clinical care. Results: A total of 121 elderly patients had BRAF testing with mean follow-up of 15 months (range 0-43). The incidence of BRAF positive PTC was 38% (46/121). BRAF positive and BRAF negative patients were similar with respect to mean age, sex, and length of follow-up. BRAF positive PTC was less likely to be incidental (20 v. 40%, p=.02), and more likely tall cell variant (28 v. 3%, p<.001). Advanced TNM stage (III/IV) at presentation was more common in BRAF positive compared to BRAF negative patients (59 v. 21%, p<.001). However, BRAF positive patients with advanced TNM stage were not more likely to have persistent/recurrent disease than BRAF negative patients (37 v. 19%, p=.2). Conclusion: This study is the first to examine BRAFV600E positive PTC in elderly patients. We observed an association with aggressive histology and advanced TNM stage at presentation, but not an increased risk of persistent/recurrent disease in patients with advanced TNM stage. This suggests that another mechanism may be contributing to the well-known association between age and aggressive phenotype, which will become increasingly important to characterize as the population ages and the incidence of PTC continues to rise.

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Multiple Strategies to Ensure a Successful Minimally Invasive Parathyroidectomy C. Sommer,[1]* B.F. Calvo,[1] J.J. Yeh,[1] A.S. Caudle,[2] J. Frank,[1] D.W. Ollila.[1] *1. Division of Surgical Oncology, The University of North Carolina, Chapel Hill, NC; 2. The University of Texas M.D. Anderson Cancer Center, Houston, TX.*

INTRODUCTION: Reoperative parathyroidectomy for persistent or recurrent primary hyperparathyroidism (HPT) is associated with increased morbidity, high costs, and higher failure rates. Intraoperative strategies employed during minimally invasive parathyroidectomy (MIP) to improve accuracy include use of gamma probe localization, frozen section pathology, and PTH sampling (iPTH). The ideal intraoperative strategy would be inexpensive, widely available, timely, and accurate. We report the results of MIP performed using various intraoperative techniques. METHODS: This is a single-institution retrospective review of patients with primary hyperparathyroidism treated with MIP between October 1, 1998 and December 31, 2008. We previously reported our success rates using radio-guided MIP (Caudle AS Am Surg 2006). Since then our institution purchased iPTH technology. Adoption of this technology has been variable among our endocrine surgeons. We used bivariate and multivariate analysis to examine success rates and operative times using various intraoperative techniques. RESULTS: Two hundred and three patients with primary hyperparathyroidism were identified with a preoperative median calcium level of 11.3 (8.1-17) mg/dl and PTH level of 143 (19-5042) pg/mL. Median postoperative calcium level was 9.2 (7.4-11) mg/dL. In all cases preoperative sestamibi localization and intraoperative gamma probe were utilized. Frozen section was used in 101/203 (49.8%) of cases, no additional studies were used in 88/203 (43.4%), iPTH in 8/203 (3.9%), and both frozen and iPTH in 6/203 (3.0%). Compared to radio-guided alone, the addition of various tests increased operative time significantly (Table 1). Eleven patients (5.4%) required reoperation. Six patients had multigland disease, two developed secondary HPT, and two developed tertiary HPT. One patient required reoperation because the frozen section was misread. There was no statistical difference in the rate of reoperation across the different intraoperative test groups (p=0.57). CONCLUSIONS: A successful MIP can be accomplished regardless of which strategy is utilized. Each endocrine surgeon should document the success rate of his/her intraoperative strategy.

Table 1

INTRAOPERATIVE STUDY	NUMBER OF CASES(%)	MEAN OPERATIVE TIME IN MINS (RANGE) (N=195)*	REQUIRED REOPERATION(%)**
Gamma Probe (Radio-guided	88 (43.4%)	58.6 (19-129)	5 (5.7%)
Gamma & Frozen	101 (49.8%)	81.2 (23-232)	5 (5.0%)
Gamma & iPTH	8 (3.9%)	87.8 (62-139)	0
Gamma, Frozen & iPTH	6 (3.0%)	119.2 (65-158)	1 (16.7%)
Total	203	72.5 (19-232)	11 (5.4%)

* Difference in operative time statistically significant by one-way ANOVA (p<0.01)
** No significant difference in reoperation rate by Chi-squared test (p=0.57)

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Primary Hyperparathyroidism and Negative Tc99 Sestamibi Imaging: To Operate or Not? B.M. Dy,* M.L. Richards, G.B. Thompson, D.R. Farley, C.S. Grant. *General Surgery, Mayo Clinic, Rochester, MN.*

INTRODUCTION: The indications for surgery in 1HPT are the same for patients with and without localization on imaging. However, patients with negative imaging may not be referred for surgery or the surgeon may be reluctant to operate. This study compares outcomes in patients with negative imaging to those with localization to determine if surgery is appropriate or whether additional imaging should be obtained. METHODS: A

retrospective review of patients who had a primary operation for 1HPT with a preop Tc99 sestamibi-I123(MIBI) scan was conducted. Imaging, laboratory, operative findings, pathology and outcomes were used to compare patients with negative scans to those with localization (MIBI uptake). RESULTS: 2,681 had an operation for 1HPT with a preop MIBI (sensitivity 87%-PPV 92%). MIBI imaging was negative in 136(5%). Neck US was done in 56% with negative scans (sensitivity 37%,PPV 91%) and in 732(28%) with localizing scans (sensitivity 63%-PPV 91%).The negative MIBI group had a lower Ca (10.9 vs 11.0mg/mL p=0.02), Phos (2.9 vs 3.1mg/dL p<0.001) and urinary Ca (251 vs 287 mg/mL p=0.02).There was no difference in PTH, 25OH-vit D or bone loss (p>0.05). There was a greater incidence of renal lithiasis in the negative MIBI group (32% vs 27% p<0.01). IOPTH was used in 95% with negative MIBI (sensitivity 65%-specificity 96%-PPV 96%) and in 72% with localization (sensitivity 94%-specificity 74%-PPV 99%). Multiglandular resection (MGR) was higher with a negative scan (29% vs 13% p<0.001). A curative operation was performed in 90% with a negative MIBI compared to 96% with localization (p<0.001). Patients who underwent successful surgery despite a negative MIBI scan had lower Ca (10.8 vs 11.1mg/mL p=0.04) and PTH (98 vs 196 pg/mL p=0.03) than those not cured. Patients with both a negative US and negative MIBI had a cure rate of 89%. CONCLUSION: A curative operation is performed at an acceptable lower rate when MIBI imaging is negative and US is of minimal benefit. A decision to proceed with surgery with a negative MIBI should consider lower cure rates and symptom severity. Patients may benefit from high-volume surgeons due to an increased risk for MGR and lower IOPTH reliability.

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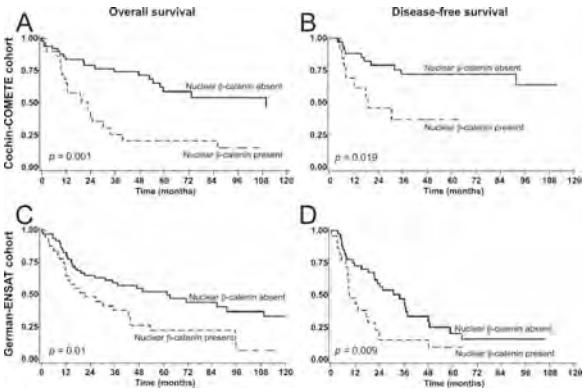
β-catenin activation is associated with specific clinical and pathological characteristics and a poor outcome in adrenocortical carcinoma S. Gaujoux,[1]* S. Grabar,[4] F. Fassnacht,[2] B. Ragazzon,[6] P. Launay,[6] R. Libé,[5] I. Chokri,[3] A. Audebourg,[3] B. Royer,[3] S. Sbiera,[2] M. Vacher-Lavenu,[3] B. Dousset,[1] X. Bertagna,[5] B. Allolio,[2] J. Bertherat,[5] F. Tissier.[3] *1. AP-HP - department of Surgery, Paris, France; 2. University of Wuerzburg, Wuerzburg, Germany; 3. AP-HP - department of pathology, Paris, France; 4. AP-HP - department of Statistic, Paris, France; 5. AP-HP - department of Endocrinology, Paris, France; 6. Inserm, U1016 - Institut Cochin, Paris, France.*

Introduction: Activation of the Wnt/β-catenin signaling pathway is frequent in adrenocortical carcinoma (ACC) and might be associated with a more aggressive phenotype. The objective of this study was to assess the prognostic value of β-catenin immunohistochemistry and CTNNB1 (β-catenin gene)/APC (Adenomatous Polyposis Coli gene) mutations in patients with resected primary ACC. Methods: In 79 patients with resected primary ACC from initial cohort, β-catenin expression was assessed on tumor specimen by immunohistochemistry. For patients with available DNA (n=49), CTNNB1 and APC, on its hotspot (Mutation Cluster Region), were sequenced. Association between these results and the clinicopathological characteristics of the ACC and overall and disease-free survival were studied. Results were confirmed on a tissue microarray from an independent multicentric cohort of 92 ACC from an other country. Results: In the initial cohort, the presence of a β-catenin nuclear staining was significantly associated with a higher ENSAT tumor stage (i.e. stage III and IV), higher Weiss score, more frequent necrosis, mitoses, and CTNNB1/APC mutations. β-catenin nuclear staining and presence of CTNNB1/APC mutations were both associated with decreased overall and disease-free survival, and were independent predictive factors of survival in multivariate analysis. Same results were observed in the validating cohort. Conclusions: Wnt/β-catenin activation, attested by the presence of β-catenin nuclear staining, is an independent prognostic factor of overall and disease-free survival in patients with resected primary ACC.



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Intercellullar Adhesion Molecule-1 (ICAM-1) is Upregulated in Aggressive Papillary Thyroid Carcinoma D. Buitrago,[1]* X.M. Keutgen,[1] M.J. Crowley,[1] H. Aildailami,[1] R. Hoda,[1] R. Hoda,[2] T. Scognamiglio,[2] M. Jin,[3] T.J. Fahey, III,[1] R. Zarnegar.[1] *1. New York Presbyterian Hospital - Weill Cornell Medical College, Department of Surgery, New York, NY; 2. New York Presbyterian Hospital - Weill Cornell Medical College, Department of Pathology, New York, NY; 3. Cornell University, Department of Biomedical Engineering, Ithaca, NY.*

Introduction: Intercellular adhesion molecule-1 (ICAM-1) is implicated in carcinogenesis. Our study examined the expression of ICAM-1 in papillary thyroid cancer (PTC). We hypothesized that ICAM-1 would correlate with indicators of tumor aggressiveness in PTC. Methods: Thirty-five primary and metastatic PTC, 5 follicular adenoma, 5 Hashimoto thyroiditis, 5 nodular hyperplasia, and 8 normal thyroid tissue samples were analyzed for ICAM-1 gene expression using quantitative RT-PCR. ICAM-1 gene expression was analyzed on a protein level by immunohistochemistry (IHC) using a semiquantitative score. Gene expression and intensity levels were correlated with markers of tumor aggressiveness including BRAF V600E mutation, tumor size, extrathyroidal extension (ETE), angiolymphatic invasion, and lymph node metastasis. Results: ICAM-1 gene expression was higher in PTC (p = 0.01) and lymph nodes metastases (p=0.03) compared to benign tumors and inflammatory disease. Further, papillary thyroid carcinomas exhibiting BRAF V600E mutation (p = 0.01), extrathyroidal extension (p<0.01) and lymph node metastasis (p=0.02) were associated with higher ICAM-1 levels compared to tumors without. Gene expression correlated with protein levels on IHC. Additionally, poorly differentiated thyroid carcinoma had a higher ICAM-1 intensity score compared to well-differentiated carcinoma (p=0.03). Conclusions: ICAM-1 expression is upregulated in papillary thyroid carcinoma. Furthermore, ICAM-1 upregulation is correlated with aggressive tumor features such as BRAFV600E mutation, extrathyroidal extension and lymph node metastasis, suggesting that ICAM-1 may play a role in thyroid cancer progression.

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Diagnostic Accuracy of Surgeon-Performed Ultrasound-Guided Fine-Needle Aspiration of Thyroid Nodules L. Bohacek,* Z. Alguraan, K. Milas, J. Mitchell, A. Siperstein, E. Berber. *Cleveland Clinic Foundation, Cleveland, OH.*

Background: There is scant data in the literature concerning surgeon performed fine needle aspiration (FNA), and controversy regarding its accuracy in thyroid nodules > 4 cm. The goal of this study was to specifically assess accuracy of ultrasound (US)-guided FNA by endocrine surgeons on a per-nodule basis, with a sub-analysis of nodule size. **Methods:** Data of 1000 surgeon-performed US-guided thyroid FNAs at a single institution from 2000 to 2010 were prospectively collected via a computerized database. Information extracted included nodule size on US, FNA results using the Bethesda System, surgical indications, pathology within and outside the nodule, and follow-up. **Results:** FNA results were reported as: cancer (7%), suspicious for cancer (2%), suspicious for follicular neoplasm (17%), atypia of unknown significance (AUS) (1%), benign (67%), and insufficient (6%). Of patients with FNA results of cancer, suspicious for cancer, suspicious for follicular neo-

plasm and AUS, 94% were operated on, with rates of malignancy in the nodule of 96%, 58%, 21%, and 12%, respectively. Of patients with benign FNA, 26% underwent surgery: 72% due to size or symptoms, 21% due to an additional nodule with concerning cytology, and 7% for other indications. 56% were followed, and 18% were lost to follow-up. Of patients with insufficient FNA, 46% had repeat FNA (yielding a diagnosis in 80%), 23% underwent surgery for other indications, 21% were followed as their lesions were felt to be hypocellular, and 9% were lost to follow-up. In size sub-analysis, rate of malignancy within nodules < 4 cm was 27%, while it was 29% in nodules > 4 cm *(NS)*. Cytologically benign nodules were found to contain cancer in 8% of nodules < 4cm, and 4% of nodules > 4 cm *(NS)*. There was no size cut-off that yielded significant results. **Conclusion:** To our knowledge, this is the largest series of surgeon-performed FNA. The Bethesda system appropriately stratified lesions as to risk of malignancy, and repeat FNA had high diagnostic yield in lesions with inadequate FNA. The results suggest no trend towards larger lesions harboring thyroid malignancy, nor increased likelihood of false negative benign FNA.

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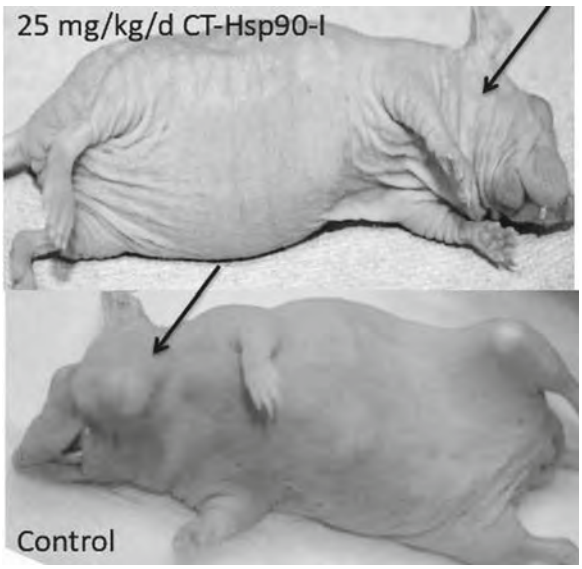
A Novel C-terminal Hsp90 Inhibitor for Head and Neck Squamous Cell Cancer (HNSCC) with in vivo efficacy and improved toxicity profiles compared to standard agents S.M. Cohen,* R. Mukerji, A. Samadi, M.S. Cohen. *Surgery, University of Kansas Medical Center, Kansas City, KS.*

Background: Current therapies for HNSCC, especially platinum agents, are limited by their toxicities and drug resistance. This study evaluates a novel C-terminal Hsp90 inhibitor(CT-Hsp90-I) for efficacy and toxicity in vitro and in vivo in an orthotopic HNSCC model. Our hypothesis is that C-terminal inhibitors have improved toxicity/efficacy profiles over standard therapies and may represent a novel group of anti-cancer agents. Methods: JMAR and MDA-1986 HNSCC cells were treated with doses of 17-AAG and CT-Hsp90-I and compared for anti proliferation by MTS and trypan blue exclusion and for apoptosis by flow cytometry, and PARP cleavage as well as caspase3 inactivation by Western analysis. In vivo studies in Nu/Nu mice involved injection of 10^7 MDA-1986 cells in the buccal mucosa followed by drug dosing i.p. for a 21 day period [mg/kg/dose: cisplatin=3.5,low dose CT-Hsp90-I=5,hi dose CT-Hsp90-I=25,17-AAG=175). Tumor size, weight and toxicity (body score) were measured 3x/week. Results: The IC_{50} levels for the CT-Hsp90-I=1.2-2μM in several cancer cell lines including JMAR and MDA-1986(IC_{90} <5μM).The CT-Hsp90-I induces apoptosis at 1μM with cleavage of PARP and inactivation of caspase 3 levels after 24 hours. Client proteins Akt and Raf-1 were also down-regulated at 1-3μM of drug. In vivo, 100% of controls had progressive disease (PD) while 100% of cisplatin animals showed some response (6 complete responses (CR), 2 partial response (PR)); all with significant systemic toxicity (weight loss and decreased body score). Hi dose CT-Hsp90-I showed 88% of animals responding(3 CR (37%),4 PR (50%),1 stable disease (SD)) and low dose CT-Hsp90-I)showed75% responding(1CR (12%),5 PR (63%),2 SD). CT-Hsp90-I animals showed significantly less toxicity ($p<0.01$) than cisplatin or 17-AAG (0 CRs, 5 PRs, 2 SD, 1 PD). Conclusion: This novel CT-Hsp90-I inhibitor has potent anti-cancer activity in HNSCC showing excellent in vivo efficacy and reduced toxicity compared to standard agents justifying future translational evaluation.



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Total Thyroidectomy for Multifocal Micropapillary Thyroid Cancer: Is it a safe and efficient approach? J.A. Ricci,[1]* A.E. Alfonso.[2] *1. SUNY Downstate Medical Center, Brooklyn, NY; 2. Long Island College Hospital, Brooklyn, NY.*

Introduction: While conservative resection diminishes the incidence of permanent hypocalcemia and recurrent laryngeal nerve injury, others have demonstrated decreased local recurrence and increased overall survival with total thyroidectomies applied to small well-differentiated papillary thyroid cancers (WDPTC). Methods: Clinical records of 516 consecutive surgically treated thyroid cancer patients were reviewed. A subset of 269 cases with WDPTC confined within the capsule of the involved single lobe subjected to total thyroidectomy was analyzed. The patients were stratified by age (< 45 years and ≥ 45 years), tumor size (< 1cm, 1 to 1.9 cm, 2 to 4 cm, and > 4 cm), evidence of ipsilateral multifocality, and presence or absence of contralateral non-palpable malignancy. Results: Overall contralateral histologic malignancy on routine serial sections was demonstrated in 46.4% (125/269) of patients and in 34% (30/88) of patients with sub-centimeter (< 1 cm) tumors. This significantly increased to 52% (95/181) in tumors ≥ 1cm ($p = 0.006$), and approached 76% (13/17) in those ≥ 45 years with sub-centimeter but multifocal tumors. Only one patient developed permanent hypocalcemia (0.4%) and there were no recurrent laryngeal nerve injuries. Conclusion: The incidence of bilateral histologic multicentricity was significant even in groups with small WDPTC. Patients ≥ 45 years of age that present with sub-centimeter multifocality are at a higher risk for bilateral disease. While total thyroidectomy is advocated for patients with WDPTC ≥ 1 cm in size, it should also be seriously considered in those over 45 years with multifocal micropapillary tumors, since it is a safe operation.

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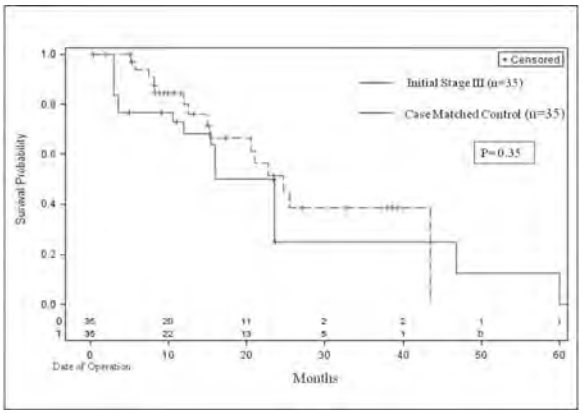
Down-staging in pancreatic cancer: A matched analysis of patients resected following systemic treatment of initially locally unresectable disease K.A. Bickenbach,* M. Gonen, M.F. Brennan, M.I. D'Angelica, R.P. DeMatteo, Y. Fong, W.R. Jarnagin, P.J. Allen. *Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

INTRODUCTION: Patients with locally unresectable pancreatic cancer (AJCC stage III) have a median survival of 10–14 months. Standard treatment for these patients is systemic therapy with or without radiation. The objective of this study was to evaluate outcome of patients who respond to this treatment and undergo resection. METHODS: Using a prospectively collected database (2000-2009), we identified patients who were initially deemed unresectable due to vascular invasion and had sufficient response to non-operative treatment to undergo resection (initial stage III). Overall survival (OS) was compared

between this group and a matched group of patients who were resected during the same time period without receiving preoperative treatment (stage I and II). Case-matching was performed using a previously validated pancreatic cancer nomogram. RESULTS: A total of 36 patients with initial stage III disease were identified who underwent resection after treatment with chemotherapy or radiation therapy. Initial unresectability was determined by operative exploration (n=15, 42%) or by cross sectional imaging (n=21, 58%). All patients received chemotherapy prior to resection and 58% of patients received radiation. Resection consisted of pancreaticoduodenectomy (n=31, 86%), distal pancreatectomy (n=4, 11%), and total pancreatectomy (n=1, 3%). Pathology revealed T3 lesions in 27 patients (73%), nodal positivity in 6 patients (16%), and a negative margin in 30 patients (83%). There were no operative mortalities. Median follow-up was 13 months (range 2 to 44 months). The median OS in this series was 25 months from resection and 30 months since treatment initiation. There was no difference in OS from time of resection between the initial stage III patients and matched patients who presented with resectable disease (p=0.35). (see figure) CONCLUSIONS: In this study, patients who were able to undergo resection following treatment of initial stage III pancreatic cancer experienced similar survival as those who presented with stage I and II disease. Resection is indicated in this highly select group of patients.



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Patterns of Recurrence and Survival after Complete Pathologic Response to Neoadjuvant Treatment for Gastric and Gastroesophageal Junction Adenocarcinoma R.C. Fields,[1]* V.E. Strong,[1] M. Gonen,[3] K.A. Goodman,[4] N.P. Rizk,[5] D.H. Ilson,[2] M.F. Brennan,[1] D.G. Coit,[1] M.A. Shah.[2] *1. Gastric & Mixed Tumor Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; 2. Gastrointestinal Oncology Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, NY; 3. Department of Epidemiology & Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY; 4. Department of Radiation Therapy, Memorial Sloan-Kettering Cancer Center, New York, NY; 5. Thoracic Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

BACKGROUND: Pathologic complete response (pCR) is rare following neoadjuvant chemotherapy ± radiation therapy (RT) for locally advanced gastric or gastroesophageal junction (GEJ) adenocarcinoma. Timing and patterns of recurrence and survival after pCR are not well characterized. METHODS: A retrospective review of a prospective database identified patients with pCR after neoadjuvant chemotherapy ± RT for gastric or GEJ adenocarcinoma. Timing and location of recurrence, overall survival (OS), recurrence free survival (RFS), and disease specific survival (DSS) were analyzed. RESULTS: From 1985 – 2010, 2,676 patients underwent resection for gastric and GEJ (Siewert II/III) adenocarcinoma. 714 patients (27%) received neoadjuvant treatment: 442 (62%) chemotherapy alone, 272 (38%) neoadjuvant chemoRT. There were 60 patients (8%) with a pCR: 47 (78%) GEJ and 13 (22%) gastric tumors. 51 patients (85%) received neoadjuvant chemoRT. With 46 month median follow-up, 14 patients (23%; 12 GEJ, 2 gastric) developed a recurrence. Sites of first recurrence were: 8 distant (5 CNS, 2 visceral, 1 skin), 4 local, and 2 regional nodal (table). 13 of 14 recurrences (93%) occurred within 2 years of follow-up with a median time to recurrence of 13.5 months. 5 patients (42%) recurred in the CNS. 12 of 14 patients (86%) received treatment for their recurrence (8 chemotherapy, 2 surgery, 2 whole brain RT). Median time to death after recurrence was 11.5 months. 5-year OS, RFS, and DSS were 56%, 70%, and 65%, respectively. There were no differences in 5-year OS, RFS, or DSS based on tumor location (gastric v. GEJ: 5-year DSS 66% v. 56%; p=0.94) or receipt of RT (yes v. no: 5-year DSS 62% v. 88%; p=0.51). CONCLUSION: pCR after neoadjuvant therapy for gastric or GEJ adenocarcinoma is associated with improved long-term survival. Despite pCR, there remains significant risk of recurrence and cancer-specific death, especially within the first 2 years. These patients demonstrate an atypical failure pattern with a predominance of CNS recurrences. Whole brain imaging during the first 2 years of follow-up should be considered.

Location and timing of first recurrence in 14 of 60 (23%) patients following a pathologic complete response (pCR) to neoadjuvant chemotherapy ± radiation for gastric* or gastroesophageal junction adenocarcinoma

Recurrence location	Time to recurrence (months)	Treatment	Status at last follow-up	Time from recurrence to death or last follow-up (months)
CNS	15	None	DOD	1
CNS*	5	Whole Brain RT	DOD	17
CNS	13	Surgery	DOD	26
CNS	6	Whole Brain RT	DOD	2
CNS, Liver*	24	None	DOD	2
Liver	5	Platinum/CPT11	DOD	12
Lung	54	Platinum/Taxol	AWD	38
Skin	4	FOLFIRI	DOD	16
Mediastinal LN	19	Platinum/Taxol	AWD	27
Mediastinal LN	11	Taxol	DOD	36
Local	20	Taxol	DOD	24
Local	14	Surgery	DOD	1
Local	6	Taxol/CPT11	DOD	11
Local	15	Taxol/CPT11	DOD	10

*Denotes gastric cancer primary

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Patterns of recurrence after pathological complete response (pCR) for rectal cancer treated with neoadjuvant chemoradiation and surgery P. Luna-Perez,* M. Ramirez-Ramirez, S. Rodriguez-Ramirez, M. Gutierrez de la Barrera. *Surgical Oncology, Hospital de Oncologia. CMN SXXI, Mexico City., Distrito Federal, Mexico.*

Background. Approximately 8-20% of rectal cancer patients undergoing neoadjuvant chemoradiation achieve pCR, which has been associated with low rate of local recurrence and long-term recurrence-free survival. Objective. To analyze the patterns of recurrence of those patients achieving pCR after neoadjuvant chemoradiation for rectal cancer and to identify the associated factors with recurrent disease. Materials and methods. Between 1996 and 2005, 840 patients with rectal adenocarcinoma were treated with neoadjuvant chemoradiation. All patients received neoadjuvant 5-FU-based chemotherapy and 50.4 Gy of external beam radiation (RT). Sixty-six (7.8%) achieved pCR. Multivariate analysis of associated factors with recurrence was performed. Results. There were 35 males and 31 females with a mean age of 56.2 years. Mean distance from distal tumor margin to the anal verge was 4.8 Cm. Endorectal ultrasound evaluation before neodjuvant chemoradiation was: uT3,N(-) = 25 and uT2-3, N(+)= 41. Median duration of RT was 5 weeks. Median time for surgery was 7 weeks. Surgery performed was: low anterior resection, 42; abdominoperineal resection, 12; trans-anal local excision, 10, and pelvic exenteration, 2. Median follow-up was 86 months. At median follow-up of 56 months, 13 patients developed recurrences and were: local and retroperitoneal and left supraclavicular lymph nodes (n = 1), spine (n = 3), retroperitoneal lymph nodes (n= 3), brain (n= 2), lung (n= 2), brain + lung (n= 1) and lung + liver (n= 1). Conclusion. Pathological complete response (pCR) for rectal cancer patients treated with neoadjuvant chemoradiation therapy and surgery

is associated with very low rate of local recurrence. However, atypical sites of distant recurrence were found. Associated factors with recurrence were: interval between RT/CT and surgery > 8 weeks, <11 harvested lymph nodes and local excision.

Multivariate analysis of disease-free survival

Covariate	OR	95% C.I.	p
Interval between RT/CT to surgery <8 weeks	2.8	1.18-4.2	0.01
Local excision	2.6	1.85-3.1	0.02
Harvested lymph nodes <11	3.1	1.03-5.4	0.001

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Short-course radiotherapy, neoadjuvant bevacizumab, capecitabine and oxaliplatin, and radical resection of primary tumor and metastases in primary stage IV rectal cancer. A phase II multicenter study of the Dutch Colorectal Cancer Group T.H. Van Dijk,[1]* G. Hospers,[1] J. Beukema,[1] H. Gelderblom,[4] G.L. Beets,[2] K.P. De Jong,[1] H.J. Rutten,[3] C.J. Van de Velde,[4] T. Wiggers,[1] K. Havenga.[1] *1. Groningen, University Medical Center Groningen, Groningen, Groningen, Netherlands; 2. University Hospital Maastricht, Maastricht, Limburg, Netherlands; 3. Catharina Hospital, Eindhoven, Noord Brabant, Netherlands; 4. Leiden University Medical Center, Leiden, Zuid Holland, Netherlands.*

Introduction Curative treatment of primary stage IV rectal cancer poses a logistical problem if long course radiation therapy is to be combined with optimal chemotherapy (CT) in a neoadjuvant setting.Short course radiation therapy (RT) has a biological effective dose comparable to long course schemes. We conducted a phase II study to test the efficacy of short course RT followed by capecitabine, oxaliplatin and bevacizumab followed by resection of the primary tumor and metastases. Methods Pts with primary rectal cancer and synchronous resectable metastases in 1 or 2 organs, ECOG PS 0-1 and limited comorbidity were eligible.Treatment started with 5x5 Gy RT to the pelvis. After 1 week bevacizumab (7.5mg/kg), capecitabine (2dd1000mg/m2) and oxaliplatin (130mg/m2) were administered in cycles of 3 weeks.Restaging was performed after 2 cycles. Unless progression was demonstrated, CT was continued with another 4 cycles. After completion pts were evaluated for surgery. Primary endpoint was radical resection and/or RFA of the primary tumor and all metastases.Secondary endpoints are two-year survival and recurrence rate. Results Since 2006 50 pts were enrolled in 7 centers: 42 presented with metastases in liver, 5 in lung and 3 in both lung/liver. Median time from RT to start CT was 11 days (3-44). 42 pts completed their 6 cycli CT. Total grade 3-4 toxicities during CT were: thrombosis (6), diarrhea (5), fatigue (2), pain (2), handfootsyndrome (1), cholecystitis (1) and obstipation (1). No progression was seen during CT. In 26 pts resection of rectal tumor and metastases was done simultaneously. No treatment related deaths occurred. The primary endpoint was achieved in 36 of the 50 pts (72%). In 4 pts rectal pathology demonstrated a R-1 resection. 23 of 36 pts presented with a recurrence after R0 resection (2 local). Median time to recurrence was 12 months (7-34). With a median follow-up of 24 months 12 pts died. Conclusion Short-course RT followed by systemic CT and surgery is a well-tolerated approach in stage IV rectal cancer.

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Long-Term Outcome Analysis of Patients with Complete Pathological Response after Neoadjuvant Chemoradiation for cT3 Rectal Cancer: Implications for Local Excision Surgical Strategies C. Belluco,* A. De Paoli, V. Canzonieri, R. Sigon, M. Cossaro, M. Fornasarig, A. Buonadonna, R. Talamini, F. De Marchi. *National Cancer Institute, CRO-IRCCS, Aviano, Italy.*

Introduction: Neoadjuvant chemoradiation therapy (CRT) followed by radical surgery including total mesorectal excision (TME) is standard treatment in patients with locally advanced rectal cancer. Emerging data indicate that patients with pathological complete response (pCR) after CRT have a favourable outcome, suggesting the possibility of less invasive surgical treatment. In this study we analyzed the long-term outcome of cT3 rectal cancer patients treated by neoadjuvant CRT in relation to pathological response and surgical treatment. Methods: Pre- and post-CRT staging was performed using endorectal US, CT scan, and MRI. Tumor regression grade (TRG) was assessed in the surgical specimen according to the Mandard method. Clinicopathological and outcome data were retrieved from our Institutional prospective rectal cancer database. Survival analysis was performed with Kaplan-Meier method, and hazard ratios calculated with Cox proportional model. Results: One hundred thirty-nine patients (93 men, 46 women; median age 62 yrs; range 25-87) with cT3 rectal adenocarcinoma were treated by CRT followed by surgery at our Institution between 1996 and 2008. Median distance of the tumor from the anal verge was 5 cm (range 1-12). TME was performed in 110 cases (18 APR and 92 LAR). Full thickness local excision was performed for different reasons in 29 cases. At re-staging after CRT primary tumor downstaging was observed in 96 (69.1%) patients. At pathology, pCR defined as TRG 1 (no residual cancer cells) was observed in 42 (30.2%) cases. During a median follow-up of 55.4 month, 21 (15.1%) patients developed local recurrence (LR), and 27 (19.4%) distant metastasis. Survival analysis demonstrated significant better outcome in patients with pCR compared to patients without pCR. In patients with pCR no significant difference in outcome was observed according to the type of surgery (TME vs. local excision). (Table) Conclusions: Our findings in cT3 rectal cancer patients with pCR after CRT confirm favourable long-term outcome, and warrant clinical trials exploring local excision surgical strategies.

Table. Outcome according to pathological response after CRT in 139 patients with cT3 rectal cancer, and according to surgical treatment in the sub-set of patients with pCR (N.=42).

	LRFS			MFS			DSS			OS		
	5-yr %	HR(95% CI)	p	5-yr %	HR(95% CI)	p	5-yr %	HR(95% CI)	p	5-yr %	HR(95% CI)	p
All patients												
pCR (N.= 42)	94.9	1		92.5	1		95.8	1		89.5		
No pCR (N.= 97)	79.6	4.7 (1.1-20.0)	0.04	73.9	3.6 (1.4-9.2)	<0.01	78.0	10.7 (1.4-79.7)	0.02	74.7	3.1 (1.1-8.9)	0.04
											1	
pCR patients												
Local excision (N.= 17)	92.9	1		87.4	1		100	1		92.3	1	
TME (N.= 25)	95.8	0.7 (0.0-10.7)	NS	96.0	1.0 (0.5-2.3)	NS	93.3	ND	-	87.8	0.6 (0.1-4.2)	NS

Abbreviations: LRFS: local recurrence free survival; MFS: metastasis free survival; DSS: disease specific survival; OS: overall survival; HR: hazard ratio; NS: not significant; ND: non detectable; CRT: chmoradiation therapy; pCR: pathological complete response; TME: total mesorectal excision

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Predicting Pathological Response to Neoadjuvant Chemotherapy in Locally Advanced Rectal Cancer Using FDG PET/CT S. Shanmugan,[1]* R. Arrangoiz,[2] J. Nitzkorski,[2] M. Yu,[3] T. Li,[4] A. Konski,[5] J. Farma,[2] E. Sigurdson.[2] *1. Department of Surgery, Temple University School of Medicine, Philadelphia, PA; 2. Department of Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 3. Department of Diagnostic Medicine, Fox Chase Cancer Center, Philadelphia, PA; 4. Department of Biostatistics, Fox Chase Cancer Center, Philadelphia, PA; 5. Department of Radiation Oncology, Wayne State University School of Medicine, Detroit, MI.*

INTRODUCTION: Pathologic complete response (pCR) after neoadjuvant chemoradiation has been observed in 15% to 30% of patients with rectal cancer. The utility of FDG PET/CT scans in the management of patients with rectal cancer is not well defined. The objective of this study is to determine if FDG PET/CT can be used to predict pCR and disease free survival in patients receiving neoadjuvant chemoradiation with locally advanced rectal cancer. METHODS: A retrospective chart review was conducted in patients with endorectal ultrasound-staged T3 to T4 rectal tumors who underwent preoperative and postoperative FGD PET/CT imaging. All patients were treated with neoadjuvant chemoradiotherapy (CRT). Maximum standardized uptake value (SUV) of each

tumor was recorded. Logistic regression was used to analyze the association of pre-CRT SUV, post-CRT SUV, % SUV change, and time between therapy and surgery in comparison to pathological complete response. Kaplan-Meier estimation was used to look for significant predictors of survival. RESULTS: Seventy patients (mean age 62; 42M:28F) with preoperative stage T3 (n=60) and T4 (n=10) underwent pre-CRT and post-CRT FDG PET/CT scans between November 2002 and March 2009. All patients underwent definitive surgery after therapy with standard pathologic evaluation. The pCR rate was 26%. Median pre-CRT SUV was 10.5 while the median post-CRT SUV was 4.05. Patients with pCR had a lower mean post-CRT SUV compared to those without pCR (2.7 vs. 4.5, P=0.02). Median SUV decrease was 61% (range 6% to 95%) and was significant in predicting pCR (P=0.004). Patients with a pCR had a greater time interval between neoadjuvant therapy and surgery (median 57 vs. 50 days) than those without (P=0.05). Patients with post-CRT SUV < 4 had a lower local recurrence rate compared to those with post-CRT SUV > 4 (P=0.03). Patients with SUV decrease > 61% (Figure 1) had improved overall survival at mean follow-up of 39 months than those without (P=0.01). CONCLUSIONS: PET/CT can predict response to neoadjuvant chemoradiation in patients with locally advanced rectal cancer. Pre-CRT SUV was the only predictor of disease free survival.

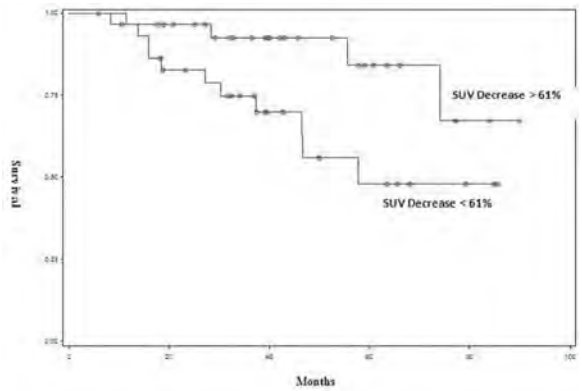

Figure 1. Improved Survival with SUV Decrease > 61%

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Isolated Hepatic Perfusion (IHP) for Patients with Unresectable Liver Metastases A.H. Zureikat,* D. Magee, H.J. Zeh, J. Steel, M.P. Holtzman, C.K. Brown, D.L. Bartlett, J.F. Pingpank. *Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: Isolated unresectable liver metastases portend a poor prognosis and are the main determinant of patient survival for several malignancies. Second and third line salvage chemotherapy has a poor response with median survival of less than a year. We hypothesize that intense regional therapy via IHP may prolong survival in select patients. Methods: A retrospective review of a prospectively collected database of patients undergoing IHP for unresectable liver metastasis from solid tumors. Perioperative events, toxicities, response, duration of response, progression free survival and overall survival were evaluated on an intention to treat basis. Results: Between Nov 2003 and Sep 2009, IHP was successfully completed in 49 out of 50 patients (M: F, 27:22). IHP employed Melphalan (1.5 mg/kg) (n=35), Oxaliplatin (n=8) or Oxaliplatin+5 FU (n=6). Mean age was 53.6 yrs (range 24-77). Primary solid tumor pathology was colorectal (CRC) (n=36, 73.4%), ocular or cutaneous melanoma (n=8, 16.3%), cholangiocarcinoma (n=3, 6.1%), other (n=2, 4.2%). Median percentage of liver replaced by tumor was 25% (IQR=20). For the CRC subgroup, 29 (81%) patients had prior chemotherapy with the majority (89.6%) receiving either FOLFOX or FOLFIRI. Hepatic arterial infusion pumps (FUdR) were placed in all CRC patients. Median operative time was 6.5 hrs (IQR=1.75). Median estimated blood loss was 500 ml (IQR=425). There were 3 perioperative deaths (6.1%). In 36 of 49 evaluable patients, the overall objective radiographic response rate by RECIST criteria was 47%. For the evaluable CRC subgroup (n=28), 14 pts (50%) had a response (13 PR, 1CR), 8 pts (29%) had SD/MR, and 6 pts (21%) experienced PD. Median duration of response for the CRC pts was 9.0 months (IQR=3) with median OS (from date of IHP) of 23.0 months (19.4-26.7, 95% CI), and hepatic PFS of 12.0 months (10.6-13.4, 95%CI). On multivariate analysis, the only factor found to be independently related to survival was CEA<35 ng/ml (P<0.039). Conclusion: IHP results in excellent response rates for patients with a variety of hepatic malignancies. Improved local control of hepatic disease may improve survival in selected patients.

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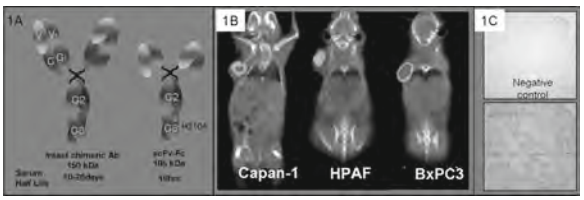
Targeting Pancreas Cancer Utilizing An Engineered Anti-CEA Antibody Fragment M. Girgis,[1]* V. Kenanova,[2] T. Olafsen,[2] K. McCabe,[2] A. Wu,[2] J.S. Tomlinson.[1] *1. UCLA-VA, Dept of Surgery, Los Angeles, CA; 2. UCLA, Dept of Molecular and Medical Pharmacology, Los Angeles, CA.*

Background: Targeting cancer with radiolabeled antibodies has both the potential for imaging and therapy. Intact antibodies are limited as imaging agents secondary to the prolonged serum half life (t1/2). Antibody fragments can be engineered to have a shorter t1/2 and thus increase contrast between tumor and background. Our aim was to quantitate the cell surface expression of CEA in pancreas cancer cell lines and to investigate our ability to image/target pancreas cancer in xenograft models with an Anti-CEA scFv-Fc antibody fragment (Fig 1A). Methods: Expression of CEA was quantified using flow cytometry on human pancreas cancer cells (BxPC3, HPAF, MiaPaca) using the DAKO Qifi-kit. A previously engineered Anti-CEA antibody fragment {Anti-CEA[scFv-Fc(H310A)]} with a mutated FcRN binding domain to decrease serum t1/2 was labeled with a positron emitting radionuclide (I-124) and injected into the tail vein of nude mice harboring an antigen positive (BxPC3, HPAF, CAPAN-1) and negative xenograft (MiaPaca). MicroPET/CT was then performed at successive time intervals after injection. Radioactivity was measured in tumor and blood. Immunolocalization was performed by injecting an unlabeled fragment and performing immunohistochemical staining for human Fc region to illustrate the microscopic pattern of tumor targeting. Results: Quantification of CEA expression revealed approximately 400,000 antigens per cell on BxPC3, HPAF, and CAPAN-1. MiaPaca cells were negative for CEA expression. MicroPET/CT imaging of pancreas cancer xenografts with the Anti-CEA [scFv-Fc (H310A)] antibody demonstrated average tumor:blood ratios of 5.2, 3.2, and 3.7, respectively (Fig 1B). Immunolocaliztion studies confirmed that the injected fragment penetrated the periphery of the tumor xenograft nodules (Fig 1C). Conclusions: Our results indicate that targeting CEA with the antibody fragment Anti-CEA [scFv-Fc(H310A)] shows great promise for molecular imaging/therapy of pancreas cancer.



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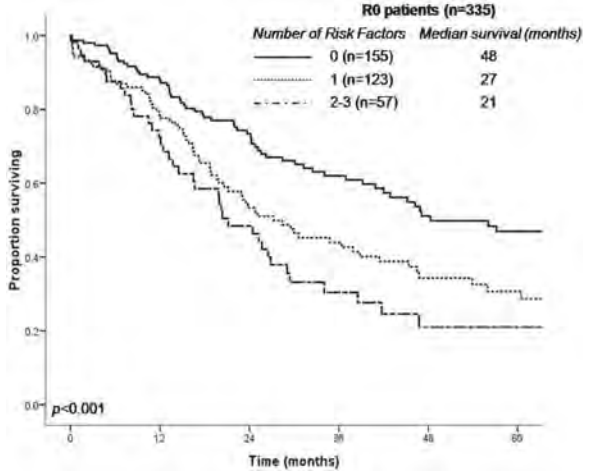
Intrahepatic Cholangiocarcinoma: An International, Multi-Institutional Analysis of Prognostic Factors and Lymph Node Assessment H. Nathan,[1] M. De Jong,[1] G. Sotiropoulos,[2] H. Marques,[4] C. Pulitano,[5] S. Alexandrescu,[3] E. Barroso,[4] L. Aldrighetti,[5] C. Ferrone,[6] A. Zhu,[6] T. Bauer,[7] D. Walters,[7] T. Gamblin,[8] K. Nguyen,[8] I. Popescu,[3] C. Hubert,[9] S. Hauss-Meyer,[10] J. Gigot,[9] G. Mentha,[10] R. Schulick,[1] M. Choti,[1] T.M. Pawlik.[1]* *1. Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD; 2. University Hospital Essen, Essen, Germany; 3. Institute for Digestive Diseases and Liver Transplantation, Fundeni Bucharest, Romania; 4. Curry Cabral Hospital, Lisbon, Portugal; 5. Ospedale San Raffaele, Milan, Italy; 6. Massachusettes General Hospital, Boston, MA; 7. University of Virginia, Charlottesville, VA; 8. University of Pittsburgh, Pittsburgh, PA; 9. Cliniques Universitaires Saint Luc, Brussels, Belgium; 10. Hopitaux Universitaires De Geneve, Geneva, Switzerland.*

Background: Intrahepatic cholangiocarcinoma (ICC) is a rare and poorly understood primary liver cancer. We sought to identify factors associated with outcome following surgical management of ICC and examine the impact of

lymph node (LN) assessment on survival. Methods: 411 patients who underwent curative intent surgery for ICC between 1973-2010 were identified from an international multi-institutional database. Clinical and pathologic data were evaluated using uni- and multivariate analyses. Results: Median tumor size was 6.5cm. Most patients had a solitary tumor (55%) and no evidence of vascular invasion (64%). Resection involved ≥hemi-hepatectomy (74%) and margin status was R0 (82%). Overall median survival was 28 months and 5-year survival was 32%. Factors associated with adverse prognosis included positive margin status (HR=3.11;p<0.001), multiple lesions (HR=2.16;p=0.007) and vascular invasion (HR=2.13;p=0.01). Tumor size was not a prognostic factor (HR=1.05;p=0.08). Lymphadenectomy was performed in 233 (57%) patients; 87 (37%) had LN metastasis. LN metastasis was associated with worse outcome (median survival: N0 39 months vs. N1 21 months;p=0.02). Preoperative factors such as tumor size, number, and morphologic sub-type did not predict presence of LN metastasis (all p>0.05), however vascular invasion did (OR=2.24;p=0.003). Among patients undergoing R0 resection, prognosis could be stratified based on the number of risk factors present (Figure). Conclusions: While tumor size provides no prognostic information, tumor number, vascular invasion, and LN metastasis were associated with survival. Presence of LN metastasis cannot be predicted using preoperative tumor features. Routine lymphadenectomy should be strongly considered as part of surgical resection for ICC as up to one-quarter of patients will have LN metastasis.



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Detection of aberrant drainage after sentinel lymph node mapping(SLNM) and its impact on staging and change of operation in colon cancer(CCa) S. Saha,[1]* A. Korant,[1] S. Nalluri,[2] M. Kanaan,[1] B. Ganatra,[2] S. Kaushal,[2] D. Desai,[2] S. Mannam,[2] D. Wiese.[2]
1. McLaren Regional Medical Center-Michigan State University, Flint, MI; 2. Mclaren Regional Medical Center, Flint, MI.

Background: SLNM in CCa upstages 15-20% of patients(Pts). Unlike in Breast Ca and Melanoma, aberrant drainage of SLNs in CCa is unknown. Hence, we aimed to study incidence and the impact of aberrant drainage after SLNM on staging and change of operation in CCa. **Methods**: Pts diagnosed with CCa were enrolled in our study and underwent SLNM plus standard oncological resection including regional LN resection. After initial years of experience since 2001, exact locations of the SLNs were mapped in relation to the primary tumor. Aberrant drainage was observed when a SLN was detected outside the standard LN basin. Our primary objective is to identify the frequency of detection of such aberrant drainage and the rates of positive aberrant SLNs leading to change of operation and staging. **Results**: Between 1996-2010, 359 pts were studied. The overall success rate of SLNM was 99.7%. The average(avg) number of resected LNs was 15.4. SLNM had a sensitivity, negative predictive value, accuracy and false negative rates of 85.3%, 91.7%, 94.4% and 14.6% respectively. Micrometastasis was detected in 15.1% of pts. Since 2001, 158 pts were evaluated for the presence of aberrant drainage and potential change of planned surgery. In 31 pts(19.6%), extended surgery was performed due to aberrant drainage. The nodal positivity in these 31 pts was ***58%***, compared to ***42.5%*** in 127pts who did not have any change of operation. The avg number of LNs in this group was 16 and the avg number of SLNs was 4.3. In 55.6% of pts with aberrant drainage, the most common location of the primary tumor was the right colon. In 13 pts (8.2%), change of operation led to the detection of positive SLNs leading to upstaging to stage IIIA/B diseases(Table). All 13 pts had T3 or T4 disease. All node positive pts underwent adjuvant chemotherapy. **Conclusions**: SLNM in CCa is highly successful, sensitive and overall accurate staging procedure. It leads to detection of SLNs outside the regional lymphatic basin and change of surgery in 19.6% of pts. This results in much higher nodal positivity and significant change of planned surgery in 8.2% of pts.

Table 1:Distribution of TNM stages with nodal positivity, sentinel lymph node involvement and change of operation in colon cancer patients with aberrant drainage.

TNM-Stages (Colon Cancer)	Number of Pts	Node +ve Pts	Node -ve Pts	Change of Operation	SLN Involve in Change of Opration
T1	23 (14.8%)	1 (4.3%)	22 (95.7%)	3 (13%)	0
T1	21 (11.5%)	2 (9.5%)	19 (90.5%)	5 (23.8%)	0
T3	103 (66.2%)	62 (60.2%)	41 (39.8%)	21 (20.4%)	12 (11.7%)
T4	11 (7.4%)	7 (63.6%)	4 (36.4%)	2 (18.2%)	1 (9.1%)
Total	158	***72 (45.6%)***	86 (54.4%)	***31 (19.6%)***	***13 (8.2%)***

+ve:positive, -ve:negative, pts:patients, SLN: Sentinel Lymph Node

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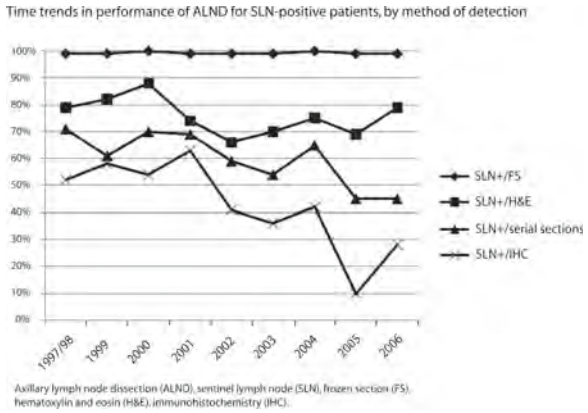
Sentinel Lymph Node Frozen Section and Axillary Dissection for Breast Cancer: Are These Procedures Becoming Obsolete? W.P. Weber,* M. Stempel, S. Patil, M. Morrow, H.S. Cody III. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

INTRODUCTION Standard practice for breast cancer patients with positive sentinel lymph nodes (SLN) has been to perform immediate axillary dissection (ALND) if the SLN is positive on frozen section (FS) and completion ALND if the SLN is positive on routine hematoxylin and eosin (H&E), serial sections, or immunohistochemistry (IHC). National trends and the recent results of the ACOSOG Z0010 and Z0011 Trials have called these practices into question. Here we present a 10 year trend analysis of the usage of SLN-FS and ALND in our practice. METHODS After IRB approval, we retrospectively reviewed our prospective SLN database (1997-2006, 7648 patients) for time trends and variation between surgeons in the usage of SLN-FS and ALND in patients with invasive breast cancer. RESULTS Usage of SLN-FS decreased from 100% to 62% ($p < 0.0001$), was associated with younger age, larger tumor, higher grade, and lymphatic invasion ($p < 0.0001$), and varied widely by surgeon (66% to 100%). Performance of ALND across all SLN-positive patients decreased modestly, from 84% to 78% ($n = 2500$, $p < 0.0001$). There were no significant downward trends in the performance of ALND for patients with SLN metastases detected by FS ($n = 1374$, 99% to 99%) or routine H&E ($n = 372$, 79% to 79%), but only for those detected by serial sections ($n = 445$, 71% to 45%, $p = 0.002$) or IHC ($n = 309$, 52% to 28%, $p < 0.0001$). These trends were associated with an increase in the proportion of completion versus immediate ALND (14% to 29%, $p = 0.0141$). CONCLUSIONS Over 10 years we have observed the gradual elimination of ALND for SLN-positive patients, a trend which has been limited to patients with low-volume SLN metastases. The adoption of the ACOSOG Z0011 data eliminating ALND in cN0 patients with H&E-detected metastases undergoing breast conservation represents a major change in practice. Our observation of trends toward fewer SLN-FS and more completion (versus immediate) ALND suggests that surgeons and patients are comfortable with a more nuanced approach to axillary management.



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Radioguided seed localization of nonpalpable invasive and in situ breast cancers: A prospective, randomized trial P.J. Lovrics,[1]* N. Hodgson,[1] G. Gohla,[1] C. Boylan,[1] C.H. Goldsmith,[1] D. McCready,[2] S.D. Cornacchi,[1] M. Reedijk.[2] *1. Surgery, McMaster University, Hamilton, ON, Canada; 2. Princess Margaret Hospital, Surgical Oncology, Toronto, ON, Canada.*

Introduction: Wire-guided localization (WL) is used to guide excision of nonpalpable breast tumours. Studies suggest radioguided seed localization (RSL) yields fewer positive margins. The goal of this study is to determine whether RSL is superior to WL. Methods: Women with confirmed invasive or ductal carcinoma in situ (DCIS) undergoing localization and breast conserving surgery (BCS) were enrolled in this prospective, multi-centre trial. Eligible patients were randomized to WL or RSL. Outcomes measured include positive margin and reoperation rates, specimen weight and volume, operative and localization times, and surgeon, patient and radiologist ranking of procedural difficulty. Results: Randomization was centralized, concealed and stratified by surgeon with 153 patient in the WL group and 152 in RSL group. Localizations were performed using either ultrasound (70%) or mammographic guidance (30%). Pathology was either DCIS (18%) or invasive carcinoma (82%). Procedures were performed at 3 sites, by 7 surgeons. No differences were found between groups for patient and tumor characteristics except for more multifocal disease in RSL group. Using intention-to-treat analysis, there were no differences in positive margins rates (malignant cells at inked margin) for RSL (10.5%) and WL (11.8%), (p=0.99) or for positive or close margins (< 1mm) (RSL 19% and WL 22%, p=0.61). Mean operative time (min) was shorter for RSL (RSL 19.4 vs WL 22.2, p<0.01). Specimen volume, weight and re-operation were similar for RSL and WL. Localization time (min) was the same for both groups (RSL 16.1 vs WL 15.8, p=0.91). Surgeon rankings of procedural difficulty showed that surgeons found the seed technique easier (p<0.01) while no difference in localization difficulty was reported by radiologists (p=0.39). Patient's pain rankings during localization were higher in wire group (p<0.05). Conclusion: In contrast to other trials positive margin and reoperation rates were similar for RSL and WL, but overall positive margin rates were low (11.2%). However, for RSL operative times were shorter, and the technique was preferred by surgeons, making it an acceptable alternative to WL.

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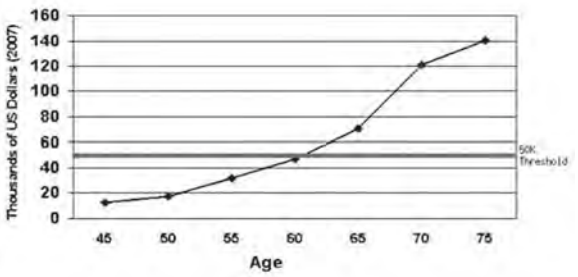
Cost-Effectiveness of Contralateral Prophylactic Mastectomy vs Routine Surveillance in Unilateral Breast Cancer Patients B. Zendejas,* J.P. Moriarty, J. O'Byrne, A.C. Degnim, D.R. Farley, J.C. Boughey. *Mayo Clinic, Rochester, MN.*

Purpose: Rates of contralateral prophylactic mastectomy (CPM) in women with unilateral breast cancer are increasing despite controversy regarding any survival advantage. Current scrutiny of the cost of health care led us to evaluate the cost-effectiveness of CPM versus routine surveillance as an alternative contralateral breast cancer risk management strategy Methods: Using a Markov model, we simulated breast cancer patients from breast cancer treatment (mastectomy) to death. All parameters of the model were gathered from published literature or publically available national databases. Base-case analysis included end of life costs and focused on patients with average-risk breast cancer with a starting age at treatment of 45 years. Costs are reported in 2007 US Dollars. Outcomes were valued in quality adjusted life years (QALY). Patients' age at treatment and risk level of breast cancer were varied to assess their impact on the overall results. Findings: Total mean costs for breast-cancer related treatment for women age 45 are comparable: $30,222 for the CPM strategy and $29,076 for the surveillance strategy. The CPM strategy provides 22.53 mean QALYs compared to 22.44 for the surveillance strategy, resulting in an incremental cost-effectiveness ratio of $12,733 per QALY gained for CPM when compared to surveillance. To prevent one contralateral breast cancer, five CPMs would be needed. CPM is no longer cost-effective for patients aged 65 (ICER $70,733/QALY) and over. For BRCA positive breast cancer patients, the CPM strategy is clearly cost-effective providing more QALYs while being less costly (dominant strategy) when compared to routine surveillance. Conclusion: CPM is cost-effective when compared to routine surveillance for breast cancer patients under the age of 65. Cost-effectiveness is greatest for high risk patients. For BRCA patients, CPM reduces cost expenditures of breast cancer-related health care.



Incremental cost-effectiveness ratio (ICER) by age for average risk breast cancer patients.

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Multiple Re-Excisions after Lumpectomy - is it Safe? S.B. Coopey,* B.L. Smith, S. Hanson, J. Buckley, K. Hughes, M. Gadd, M. Specht. *Massachusetts General Hospital, Boston, MA.*

Introduction: Approximately 33-62% of breast cancer patients who undergo lumpectomy have a close or positive margin. Multiple re-excisions may be attempted to obtain clear margins and avoid mastectomy. We sought to determine the local recurrence rate after breast conservation therapy (BCT) in patients who required two or more re-excisions and identify predictors of success in obtaining clear margins. Methods: Retrospective review of breast cancer patients who underwent BCT for invasive cancer or DCIS at a single institution from 1997 to 2007. Patients who underwent two or more re-excisions were identified. Pathological features of the primary tumor, surgical technique, and outcome of the procedure were evaluated by univariate analysis. Results: 3,737 patients underwent BCT over this 10 year period. 875 (23.4%) had close or positive margins requiring a second procedure; 797 (91.1%) had a re-excision and 78 (8.9%) went directly to mastectomy. 70 patients underwent multiple re-excisions; 66 patients had a total of 2 re-excisions, 3 patients had 3 re-excisions, and 1 patient had 4 re-excisions. 49/70 (70%) of multiple re-excision patients achieved clear margins (26 DCIS, 35 T1, 8 T2, and 1 T3 tumors). All 49 patients successfully treated with multiple re-excisions received post-operative radiation. At mean follow up of 54.6 months, 2 of 49 (4.1%) patients had an in-breast recurrence. 1 of 49 (2%) patients had a distant recurrence. Statistically significant risk factors for persistently involved margins after two re-excisions included multifocality and positive lymph node status (Table). Lymphovascular invasion, invasive lobular histology on re-excision, and more than 1 margin involved on re-excision did not reach statistical significance in this cohort. Conclusion: Multiple re-excisions to complete breast conservation therapy are a safe alternative to mastectomy in women with invasive breast cancer or DCIS. There is an acceptably low risk of local and systemic failure when negative margins are ultimately achieved. 70% of multiple re-excisions in our cohort were successful. Risk factors for failed multiple re-excisions include multifocality and positive lymph node status.

Analysis of Factors Predictive of Failed Second Re-Excisions

Risk Factor	OR	95% CI
Age ≤50 vs >51	1.04	0.38-2.83
Tumor DCIS vs IDC	0.85	0.29-2.49
Tumor ILC vs IDC	0.96	0.15-5.96
Pathologic T Stage T1b vs T1a	0.45	0.05-4.08
Pathologic T Stage T1c vs T1b	2.59	0.51-13.16
Grade 3 vs 1	0.75	0.16-3.40
EIC positive vs negative	0.61	0.22-1.70
LVI positive vs negative	2.26	0.51-10.01
Multifocal positive vs negative	51.19	9.95-263.30
Lymph Node Status positive vs negative	16.19	4.73-55.35
Pathology on Re-Excision DCIS vs Carcinoma	1.58	0.38-6.49
Pathology on Re-Excision ILC vs IDC	7	0.40-123.35
Margins on Re-Excision Positive vs Close	1.75	0.64-4.80
Number of Involved Re-Excision Margins ≥2 vs 1	2.27	0.79-6.49

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A Single Institution Review of Accelerated Partial Breast Irradiation in Patients Considered "Cautionary" by the American Society for Radiation Oncology T.S. Stull,[1]* M.C. Goodwin,[1] M.R. Chernick,[2] T.G. Frazier,[1] A.V. Barrio.[1] *1. Comprehensive Breast Center, Bryn Mawr Hospital, Bryn Mawr, PA; 2. Lankenau Hospital, Wynnewood, PA.*

Introduction: The American Society for Radiation Oncology (ASTRO) issued a consensus statement in 2009 regarding patient (pt) selection for accelerated partial breast irradiation (APBI) following breast conserving surgery (BCS) for breast cancer (BC). We reviewed our single institution experience with APBI in pts considered "cautionary" by ASTRO to determine patterns of recurrence. Methods: An IRB approved, retrospective chart review was conducted from January 2004 to July 2009. We identified 106 pts with 109 BC in the "cautionary" group. All pts were treated with BCS followed by APBI via balloon catheter brachytherapy. "Cautionary" criteria include pts 50-59, tumor size 2.1-3.0cm, close margins (<2mm), focal lymphovascular invasion, estrogen receptor (ER) negative tumors, invasive lobular carcinoma, or ductal carcinoma in situ (DCIS) ≤ 3cm. Rates of ipsilateral breast tumor recurrence (IBTR), regional recurrence, contralateral breast cancer (CBC) and distant metastasis were evaluated. Results: Of 109 "cautionary" cases, 65(59.6%) were in a single cautionary group, 37(33.9%) were in 2 groups and 7(6.4%) were in 3. Pts with DCIS or close margins comprised 58% of the "cautionary" cases. Median age at diagnosis was 68. Median follow-up was 3yrs. There were 3 IBTR (2.8%) at a median of 3.2yr. The 3yr actuarial IBTR rate was 2.85%. There were 2 regional recurrences (1.8%), 3 CBC (2.8%) and 1 distant metastasis (0.9%). All CBC occurred in pts with ER negative invasive BC at a median of 1yr. Of 9 total events, 6(66.7%) occurred in ER negative pts. On univariate analysis, the only variable associated with a significantly increased risk of recurrence was negative ER status (Odds Ratio=8.57, P=.01). Close margins were not associated with an increased risk of recurrence (P=.77). Conclusion: Pts considered "cautionary" for APBI based on ASTRO guidelines had low rates of IBTR and regional recurrence. Special consideration should be given to pts with ER negative invasive BC, as this factor was associated with a worse disease free survival.

Table 1. Breakdown of Study Cohort According to "Cautionary" Criteria

CRITERIA	N	%
Total[a]	160	100
Age 50-59	27	16.9
Tumor size 2.1-3.0cm	7	4.4
Close margins	47	29.4
Focal LVI	7	4.4
ER negative	17	10.6
ILC	9	5.6
DCIS	46	28.7

LVI=lymphovascular invasion, ER=estrogen receptor, ILC=invasive lobular carcinoma, DCIS=ductal carcinoma in situ
[a]=Some patients met more than one cautionary criteria

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Is Oncotype DX Recurrence Score of Prognostic Value Once HER2+ and Low-ER Expression Patients Are Removed? M. Milburn,* W.C. Mylander, M. Rosman, L. Tafra. *Anne Arundel Medical Center, Annapolis, MD.*

Background: Although commonly used, Oncotype DX has been criticized for not providing significantly more prognostic information than histopathological analysis. Oncotype was validated in cohorts that included poor prognostic factors (HER2+ & low-ER expression) raising the question: if patients with high recurrence rates are excluded, is the Recurrence Score (RS) still valid? Our purpose was to determine if RS can be predicted with readily available cost effective measures. Methods: 111 node-negative samples from 9/07 to 3/10 that underwent Oncotype testing were retrospectively analyzed. Data included RS, tumor type and grade, ER, PR, HER2 and Ki67 status by immunohistochemistry (IHC). IHC data was used to create linear regression models to predict the RS values. ER and PR scores obtained via Oncotype were also compared to IHC data. SAS Inc's JMP ver.7 was used for statistical analysis. Results: When comparing Oncotype and IHC derived ER and PR scores, there were 14 discordant samples in PR and 4 in ER; however, use of hormonal therapy would have been changed in only 5 instances. High RS values were associated with higher grade, low-ER, low-PR, and high-Ki67 expression. The best linear regression model created from all variables in the IHC data (ER, PR,& Ki67) had an adjusted R2 of 0.60 indicating a good model for predicting RS. Most (8/9) samples with low-ER also had a high-RS; one had a borderline-high RS. RS scores were then modeled without the low-ER and HER2+ samples. The adjusted R2 of 0.39 indicated a poor predictor of RS. Conclusion: As expected, Oncotype data in this cohort showed good concordance with IHC for ER and PR expression. Patients with low-ER expression had uniformly high RS scores. After removing low-ER and HER2+, an attempt to calculate RS from the remaining data showed a poor predictive model for RS (adj.R2 0.39). These data raise the question whether RS is prognostic in this group (who would most benefit from further clarification of recurrence risk) and is independent of IHC markers and pathology or is simply producing random RS values. Available databases can resolve this issue and thus determine the cost-effectiveness of Oncotype.

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Trends in Colon Cancer Lymph Node Examination A. Willis,* D. Nguyen, D. Nick, J. Gaughan, D. Dempsey. *Surgery, Temple University School of Medicine, Philadelphia, PA.*

INTRODUCTION: Examination (exam) of ≥12 lymph nodes (LN) in colon cancer (CC) is an accepted, but not mandated, quality indicator (QI). The aim of this study is to determine if this QI recommendation had a significant and enduring impact on LN exam. METHODS: CC patients from 2000-2008 were reviewed from an academic institution tumor registry for LN exam and frequency ≥12 LN exam. Yrs were grouped: 2000-02 (before ≥12 LN was QI), 2003-05 (≥12 LN published as QI), and 2006-08 (≥12 LN accepted as QI). RESULTS: 345 CC patients were reviewed (113 in 2000-02, 108 in 2003-05, 124 in 2006-08). Mean LN exam increased over time: 2000-02 (14.6 LN), 2003-05 (16.7 LN), 2006-08 (23.3 LN), P=0.0012. Exam ≥12 LN increased 2006-08 (82%) vs 2000-02 (53%) and 2003-05 (54%), P<0.0001. Cases <12 LN had extenuating clinical factors in 10/22 (45%) 2006-08 (3 stage IV, 4 in situ, 1 perforated, 2 carcinoid), 9/45 (20%) 2003-

05, and 11/49 (22%) 2000-02. Greater specimen length was associated with increased mean LN exam: <15cm=13.0, 15-30cm=15.4, 30-60cm=23.0, >60cm=34.3 (P<0.0001), and increased ≥12 LN exam: <15cm=50.1%, 15-30cm=68.4%, 30-60cm=87.3%, >60cm=83.3% (P<0.0001). There was no significant difference in the region-specific specimen length over time. Mean number LN and ≥12 LN exam did not vary between regions of colon. Finding at least one LN with metastasis was associated with increased exam ≥12 LN, P=0.0058. Frequency of lymph node metastasis did not vary over grouped yrs. Age, gender, ethnicity, insurance, surgeon, and pathologist were not significant predictors of ≥12 LN exam. The strongest predictors for achieving ≥12 LN on exam based on multivariate analysis were resection yrs 2006-08 (P=0.0014, OR=1.66), at least one LN metastasis (P=0.0015, OR=1.18), and specimen length >30cm (P=0.0011, OR=3.71). CONCLUSIONS: Increased exam of ≥12 LN in CC specimens is significantly associated with yrs 2006-08 (after ≥12 LN exam was published as a QI), the finding of at least one LN with metastasis, and specimen length >30cm. Although ≥12 LN exam increased significantly over time, length of specimen and frequency of LN metastasis did not change significantly across grouped yrs. Publication of QI can significantly impact LN exam practice.

Trends in Colon Cancer Lymph Node Examination

Characteristic	Years		
	2000-02	2003-05	2006-08
Number of cases (N)	113	108	124
Average number of lymph nodes examined	14.6	16.7	23.3 *
Frequency of ≥12 lymph nodes examined (%)	53.3%	54.2%	82.0% **
* P = 0.0012 ** P < 0.0001			

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Improving Nodal Harvest in Colorectal Cancer: So What?
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1. Dalhousie University/QEII Health Scince Centre, Halifax, NS, Canada; 2. University of Toronto, Toronto, ON, Canada.

Background: Adequate nodal harvest (≥ 12 lymph nodes) in colorectal cancer (CRC) has been shown to optimize staging and is widely used as a quality indicator of CRC care. We have previously demonstrated population-based improvements in nodal harvest over time, particularly with the use of an audit and feedback strategy. The goal of this current study was to evaluate the impact of improved adequate nodal harvest on clinical endpoints (node positivity rate, use of adjuvant chemotherapy, survival). **Methods:** This population-based study included all patients undergoing resection for primary stage I-III CRC in Nova Scotia, Canada, from 1/1/2001 to 31/12/2005. Linkage of the provincial cancer registry with other administrative databases (hospital discharge, physician billing, national census data and vital statistics) provided clinical, demographic, diagnostic, treatment, and survival data. The association between increased rates of adequate nodal harvest and clinically relevant endpoints was examined. **Results:** Among 2250 patients, the median nodal harvest was 8, and the overall node positive rate was 35.6%. The rate of adequate nodal harvest, node positivity rates, use of adjuvant chemotherapy and overall survival, by year, is shown in the Table below. Despite significant improvement in the proportion of patients undergoing adequate nodal harvest over time (p<0.0001), no significant change was noted in the node positivity rate (p=0.25), the proportion of patients undergoing adjuvant chemotherapy (p=0.49), or 3-year OS (p=0.19). In a subgroup analysis confined to patients where audit and feedback was used to improve nodal harvest rates, clinically relevant endpoints were not improved. **Conclusions:** Although improvements in the rate of adequate nodal harvest did occur over time, no corresponding meaningful improvement in clinical outcome was identified. Given that a quality indicator should be associated with clinically relevant outcomes *and* that these outcomes should improve as the indicator is optimized, this study questions the widespread use of a nodal harvest ≥ 12 lymph nodes as a quality indicator of CRC care.

Year	N (2250)	% with ≥ 12 lymph nodes	% node positive	% receiving adjuvant chemo	3-yr OS (%)
2001	460	21.7	35.0	28.3	73.0
2002	434	26.5	35.0	29.7	73.7
2003	443	31.4	34.3	29.1	80.1
2004	470	38.3	37.9	30.2	73.6
2005	443	41.8	35.9	28.7	73.6

chemo - chemotherapy; OS - overall survival

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Comparative Assessment of the Safety and Effectiveness of Radiofrequencby Ablation Among Elderly Medicare Beneficiaries with Hepatocellular Carcinoma N.N. Massarweh,* J.O. Park, R. Yeung, D.R. Flum. *Surgery, University of Washington, Seattle, WA.*

Introduction: Radiofrequency ablation (RFA) use among patients with hepatocellular carcinoma (HCC) has increased dramatically over the last decade. However, assessments of safety and effectiveness outside specialized centers are lacking. A population-based, comparative evaluation of RFA safety and effectiveness was conducted among a national cohort of HCC patients. Methods: A cohort study of HCC patients (diagnosed 2002-2005) was performed using linked Surveillance, Epidemiology, and End Results—Medicare data. Early (≤90-day) mortality and readmission as well as survival among patients undergoing RFA, resection, or no treatment were compared using multivariate and propensity score adjusted Poisson and Cox regression models. Results: Of 2,631 patients (mean age 76.1±6.1 years, 65.9% male), 16% received RFA (49.6%) or resection (50.4%). Early mortality (13.6 vs 18.7%, p=0.16) and readmission (34.5 vs 32.1%, p=0.60) rates as well as the risk of early death (IRR 1.18, 95% CI 0.99-1.40) and readmission (IRR 1.04, 95% CI 0.69-1.57) were not significantly different comparing patients who received RFA and resection. There was no difference in 1-year survival comparing RFA and resection (72.2 vs 79.7%, p=0.18), but beyond 3-years there was a survival benefit among patients undergoing resection (39.2 vs 58.0%, p<0.001). Patients receiving RFA as a sole therapeutic intervention at one year did not have a lower hazard of death compared to untreated patients (HR 0.88, 95% CI 0.59-1.31). Conclusions: In the general community, patients treated with RFA do not have a lower risk of early adverse events compared to those treated with resection with no clear long-term mortality benefit as compared to no treatment when RFA is used as a sole intervention. Although RFA has been described as a safe and effective primary treatment for HCC at specialized centers, this experience may not extrapolate to the general community and requires further evaluation.

Multivariate Cox Regression Analysis of Therapeutic Effectiveness

	All Patients	†FFS 6 months	‡FFS 6 months, additional RFA	†FFS 1 year	‡FFS 1 year, additional RFA
	Hazard Ratio for Death (95% CI)				
Untreated	1.0	1.0	1.0	1.0	1.0
RFA	*0.65 (0.50-0.85)	*0.70 (0.50-0.98)	*0.68 (0.49-0.93)	0.85 (0.53-1.36)	0.88 (0.59-1.31)
Resection	§0.35 (0.27-0.45)	§0.26 (0.19-0.36)	§0.26 (0.19-0.36)	§0.21 (0.13-0.36)	§0.21 (0.13-0.36)
^Resection vs RFA	§0.53 (0.42-0.67)	§0.37 (0.25-0.55)	§0.39 (0.26-0.56)	§0.25 (0.12-0.51)	§0.24 (0.13-0.47)

'FFS' indicates continuously fee-for service over that time period.
^RFA patients are the reference group.
†These subgroups did not undergo any other potentially therapeutic procedures within 6 months or 1 year of diagnosis, respectively. Similarly, untreated patients received no therapeutic interventions over this same time period.
‡These subgroups did not undergo any other potentially therapeutic procedures (except additional RFA sessions for those in the RFA group) within 6 months or 1 year of diagnosis, respectively. Similarly, untreated patients received no therapeutic interventions over this same time period.
*p<0.05, §p<0.001

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Adoption of Multimodal Esophageal Cancer Care in the United States R.P. Merkow,[1]* K.Y. Bilimoria,[3] M.D. McCarter,[4] A.K. Stewart,[2] W.B. Chow,[2] R. Williams,[2] C.Y. Ko,[2] D.J. Bentrem.[1] *1. Department of Surgery, Jesse Brown VAMC, Northwestern University Feinberg School of Medicine, Chicago, IL; 2. Division of Research and Optimal Patient Care, American College of Surgeons, Chicago, IL; 3. Department of Surgery, MD Anderson Cancer Center, Houston, TX; 4. Department of Surgery, University of Colorado Denver School of Medicine, Aurora, CO.*

BACKGROUND: Consensus guidelines recommend neoadjuvant therapy as the preferred treatment for locally advanced esophageal adenocarcinoma; however, it is unknown if this recommendation has been widely adopted in the U.S. Our objective was to examine use of neoadjuvant therapy for esophageal cancer and to assess the effect of neoadjuvant therapy on nodal status, margins, and perioperative mortality. METHODS: From the National Cancer Data Base, patients with middle third, lower third and GE junction (GEJ) clinical stage I-III adenocarcinomas that underwent surgical resection were identified. Multivariable logistic regression models were developed to identify predictors of neoadjuvant therapy utilization and associated outcomes. RESULTS: From 1998 to 2007, 8,051 patients underwent surgical resection for esophageal cancer: 16.3% stage I, 45.0% stage II and 38.7% stage III. For stage II/III tumors, neoadjuvant use increased (49.0% to 77.8%, P<0.001). On multivariable analysis, factors associated with underuse of neoadjuvant therapy in stage II/III patients were older age, Black or Hispanic ethnicity, more severe comorbidities, tumor location (GEJ and middle vs. lower third), tumor size ≥ 2cm, stage II (vs. III) and geographic region. Stage II/III patients not receiving neoadjuvant therapy had an over two fold increased risk of positive lymph nodes (OR 2.14. 95% CI 1.79 – 2.55, P<0.001). In addition, the positive surgical margin risk increased almost three fold (OR 2.80 95% CI 2.17-3.62, P<0.001). 30-day postoperative mortality risk was not significantly affected by neoadjuvant therapy (OR 1.50 95% CI 0.94-2.39; P=0.090). For stage I patients, neoadjuvant therapy use decreased over time (38.0% to 11.4%, P<0.001). The overuse of neoadjuvant therapy was associated with higher tumor grade, larger tumor size, and low surgical case volume (all P<0.05). CONCLUSION: The adoption of neoadjuvant therapy has increased in the past decade; however, opportunities exist to improve adherence with guideline recommendations. Cancer registry-based feedback to individual hospitals showing neoadjuvant therapy utilization rates could help institutions identify opportunities for improvement.

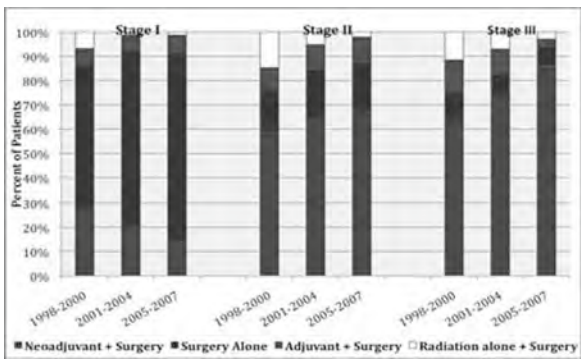

Figure. Multimodal therapy utilization by stage (I-III) and year of diagnosis for middle, lower third and GEJ esophageal adenocarcinoma patients undergoing surgical resection (n=8,051).

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Impact of Treatment Differences Upon Pancreatic Cancer Survival in Medically-Underserved Patients C.J. Wray,* E.C. Castro-Echeverry, L.S. Kao, T.C. Ko. *Surgery, University of Texas Medical School at Houston, Houston, TX.*

Introduction: Access to healthcare may impact survival among pancreatic cancer patients. Our hypothesis is that pancreatic cancer patients in a public, safety-net hospital system present with advanced stage at diagnosis, are less likely to receive therapeutic or palliative interventions, and have decreased survival compared to patients treated in a private hospital system. Methods: Retrospective review was performed of a prospectively collected pancreatic cancer database from a private and a publicly-funded hospital system in Texas from 1998-2010. Clinicopathologic parameters were recorded. Statistical analysis was performed using Student's t-test, chi square, Kaplan-Meier survival analysis, log-rank test, and linear regression models. Results: 1011 patients (N=505 male, N= 506 female) were identified, of whom 70% were treated in the private hospital system (N=773). Private hospital patients were more likely to be older, female, and Caucasian. There was no significant difference in stage at presentation. Private hospital patients were more likely to receive chemotherapy, radiation therapy, or palliative care. Only 8% of private patients underwent a Whipple procedure compared to 16% of public patients (p=0.05).Independent predictors of mortality included male gender, African-American race, advanced stage at diagnosis (III or IV), and increased age (see table). Surgery, chemotherapy, and chemoradiation (either alone or in combination) were associated with reduced mortality. After adjusting for all of these factors, treatment in the public hospital system was associated with improved overall survival. Conclusions: Despite equivalent stage at presentation, minority pancreatic cancer patients are less likely to undergo surgical resection in the private hospital system. Even though public hospital patients received less chemotherapy and radiation, unexplained factors contribute to improved survival. Further investigation is needed to understand the complex relationship between likelihood of treatment, socioeconomic status and survival.

	Private N (%) <b/>	Public N (%)<b/>	p value<b/>
Race <B/>			0.00
Caucasian	487(0.63)	46(0.19)	
African American	140(0.18)	83(0.35)	
Hispanic	79(0.10)	72(0.30)	
Asian/ Other	67(0.09)	37(0.16)	
Independent variable<b/>	Hazard Ratio <b/>	Confidence Interval <b/>	p value <b/>
Age	1.02	1.01-1.03	0.001
Male Gender	1.22	1.06-1.39	0.006
African American	1.21	1.01-1.44	0.04
Stage III at diagnosis	1.44	1.01-2.04	0.05
Stage IV at diagnosis	2.65	1.96-3.57	0.001
Surgery Alone	0.49	0.38-0.63	0.000
Chemotherapy alone	0.69	0.57-0.82	0.000
Surgery plus Chemotherapy	0.37	0.23-0.61	0.000
Surgery + Chemoradiation	0.42	0.29-0.61	0.000

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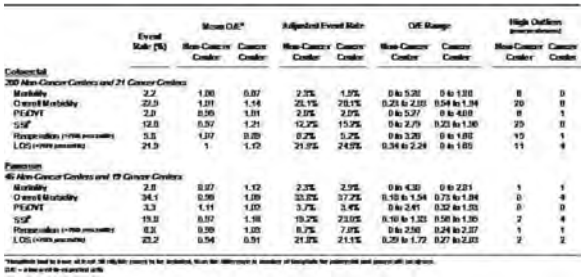
Do Cancer Centers Need to Assess Quality and Outcomes? Introducing A Customized ACS NSQIP for Oncology (Onc-NSQIP) K.Y. Bilimoria,[1]* X. Wang,[1] M.E. Cohen,[1] B.L. Hall,[1] K. Richards,[1] R.P. Merkow,[1] P.W. Pisters,[2] C.Y. Ko.[1] *1. American Collge of Surgeons, Chicago, IL; 2. Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

BACKGROUND: To identify quality improvement opportunities, hospitals can use ACS NSQIP to compare their risk-adjusted performance to other hospitals. However, Cancer Centers have few opportunities to compare their outcomes to similar hospitals for oncologic operations. Our objective was to develop an oncology-specific version of ACS NSQIP (Onc-NSQIP) and determine whether it could be useful for Cancer Centers. METHODS: From ACS-NSQIP (2006-2009), patients undergoing major colorectal (n=34,858; 221 hospitals) and pancreatic (n=7667; 65 hospitals) as well as esophageal, gastric, and soft tissue operations for malignancy were identified. Risk-adjusted postoperative outcomes were assessed with regression models adjusting for demographics, comorbidities, and operative procedure. Relative rankings of NCI-designated Comprehensive Cancer Centers in ACS NSQIP among the other

ACS NSQIP hospitals were compared. RESULTS: Cancer Center outcomes varied widely for colorectal and pancreas.* For overall colorectal morbidity, Cancer Centers were ranked in the top third (n=4), middle third (n=7), and bottom third (n=10). For colorectal 30-day mortality, Cancer Centers were ranked in the top (n=14), middle (n=3), and bottom third (n=4). For overall pancreatic morbidity, Cancer Centers were ranked in the top (n=5), middle (n=7), and bottom third (n=7). For pancreatic 30-day mortality, Cancer Centers were ranked in the top (n=5), middle (n=6), and bottom third (n=8). Similar results were observed for DVT/PE, SSI, reoperation, and length of stay.* Onc-NSQIP models were comparable to standard ACS NSQIP models. At least some Cancer Centers were statistical outliers for most outcomes (P<0.05).* Results were similar for other malignancies. CONCLUSION: Cancer Center outcomes varied as much as other ACS NSQIP hospitals, demonstrating need for quality assessment. Without standardized risk-adjusted outcomes comparisons, Cancer Centers cannot accurately assess their outcomes to identify quality improvement targets. ACS NSQIP's new platform allows customization so hospitals can compare surgical oncology-specific risk-adjusted processes and outcomes.



Comparison of Cancer Centers participating in ACS NSQIP vs. other ACS NSQIP hospitals. O/E = observed-to-expected ratio.

ABSTRACTS

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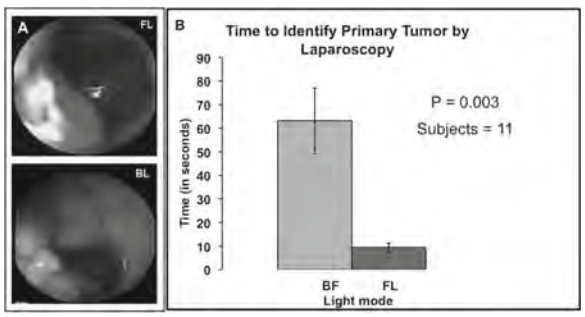
P1

Fluorophore-Conjugated Anti-CEA Antibody Improves Accuracy of Staging Laparoscopy in a Mouse Model of Pancreatic Cancer

H.S. Tran Cao,[1]* S. Kaushal,[1] C.A. Metildi,[1] C. Lee,[3] C.S. Snyder,[1] M.A. Talamini,[1] R.M. Hoffman,[2] M. Bouvet.[1] *1. University of California San Diego, San Diego, CA; 2. University of California San Diego and AntiCancer, Inc., San Diego, CA; 3. UVP LLP, Upland, CA.*

Introduction: Accurate staging of pancreatic cancer (PC) is vital in establishing the appropriate therapeutic strategy. Fluorophore-anti-CEA conjugates were used to label PC in clinically-relevant mouse models for fluorescence laparoscopy. Methods: Orthotopic and carcinomatosis mouse models of human PC were established with BxPC-3 human PC cells in nude mice. After 15 days, Alexa488-anti-CEA conjugates were injected by tail vein 24 hrs prior to laparoscopy. Up to five surgical residents examined each mouse under both brightfield (BL) and fluorescence (FL) laparoscopic modes. Outcomes measured included time to identification of the primary tumor for the orthotopic model, and number of metastases identified in 2 minutes for the carcinomatosis model. After laparoscopy, mice were sacrificed and their abdomens exposed. Images were obtained with the OV-100 Small Animal Imaging System with a GFP filter, serving as a positive control. All identified lesions were collected, when possible, for histological verification. Results: Fluorescence laparoscopy enabled more rapid and accurate identification and localization of both primary tumors and metastases than bright field laparoscopy. The average time to identification of primary tumor under FL was 9.45s + 1.81 vs. 63.1s + 13.94 under BL (P=0.003). In the carcinomatosis model, more metastatic lesions were detected and localized under FL compared to BL and with greater accuracy, with sensitivities of 95% vs. 30%, respectively, when compared to the positive control. BL yielded three times as many false positives as FL. FL was sufficiently sensitive to detect metastatic lesions <1 mm in size. There was no discrepancy of tissue histology between pathological review and OV-100 images, which correlated with the fluorescence laparoscopic images. Conclusions: The use of fluorescence laparoscopy and fluorophore-labeled anti-CEA permits rapid detection and accurate localization of primary and metastatic lesions of CEA-expressing PC. This technology will serve as a novel tool in the staging, and in the future, fluorescence-guided resection of pancreatic cancer.



In the orthotopic mouse model of pancreatic cancer, fluorescence laparoscopy permitted significantly quicker detection of primary tumors than brightfield laparoscopy (63.1s +/- 13.9 vs. 9.5s +/- 1.8, p = 0.003).

P2

New technologies in Sentinel Node Staging: what's the benefit? A study proposal A. Testori,* F. Verrecchia, J. Soteldo. *Melanoma and Sarcoma Division, European Institute of Oncology, Milan, Italy.*

Introduction. Melanoma biopsy is characterized by a concept of locoregional disease; from the primary lesion the diffusion to the regional nodes and then to the rest of the body. In particular, when the disease has involved the locoregional nodes, it not always spreads systemically. In this contest the proposal of sentinel lymph node biopsy (SNB) suggested to melanoma patients acquires a strong prognostic significance. Sentinel lymph node (SN) dissection is a minimally invasive procedure designed to identify and remove specific lymph nodes suspected of containing metastatic cancer cells. Clinical trials have demonstrated that excision and histologic inspection of the SN is highly predictive for the absence of metastatic disease in melanoma patients, if the SN is free of tumor cells. Since the standardization of SNB procedure with lymphoscintigraphy and radioguided surgery no major changes have been proposed. So far, any improvement in sentinel lymph node detection technique may have great potential benefit for patients and research. Materials. Sentinella102 is a surgical suite composed of a portable gamma camera with laser pointing system, a touch screen monitor, a software which allows to process the acquired images and to generate medical reports, traditional hand held gamma probe and an exclusive Gadolinium pointer. In our institution we performed 98 SNB using the Seninella102 suite during the last year with 100% node identification and excision rate. Endpoints. A trial to evaluate if the use of Seninella102 device will improve the accuracy in locating the sentinel node(s) is presented. The primary endpoint of this trial is to evaluate the number of sentinel nodes dissected with traditional gamma probe alone vs using the Sentinella102 equipment. The number of positive sentinel nodes identified using the intraoperative gamma camera, vs using only the traditional intraoperative probe will be evaluated and if this aspect may influence the false negative SN rate. Furthermore, cost-benefit analysis of this approach will be considered

P3

Use of a Nanoporous Biodegradable Miniature Device to Regulate Cytokine Release V. Grignol,* H. He, V.I. Karpa, C. Yen, K. LaPerle, X. Zhang, N.B. Jones, M.I. Liang, G.B. Lesinski, W. Ho, W.E. Carson, III, L.J. Lee. *Ohio State University, Columbus, OH.*

Background: Local injection of interferon-alpha (IFN) has been used for unresectable, locally recurrent malignant melanoma; however it is costly and inconvenient. We developed a capsule-like nanoporous miniature device (NMD) based on a biodegradable polymer [poly(polycaprolactone)], for controlling the local delivery of immunological agents to the tumor microenvironment. We hypothesized that the long-term, zero order, local release of high concentrations of immunotherapeutic agents from a NMD would improve their ability to exert an anti-tumor effect. Methods: The NMD consisted of a biodegradable drug reservoir packed with rhuIFN and bovine serum albumin powder (10:1) and a nanoporous release gate (average pore size = 20nM), both of which were coated with a protective layer. The morphology of the release gate pores was evaluated by electron microscopy. In vitro release of IFN was measured via ELISA. Biological activity of the released IFN was evaluated by flow cytometry of stimulated peripheral blood mononuclear cells (PBMCs) for phospho-STAT1. A human xenograft model of melanoma was used to evaluate IFN anti tumor effects in vivo. Results: Microscopy of the nanoporous gate showed excellent pore stability for > 2 mo. In vitro experiments demonstrated as gate area was decreased from 4.5 to 2.1 mm2 the constant release of IFN was improved from 15 to 23 days. To determine if the released IFN was biologically functional PBS or IFN-loaded NMDs were placed into chambers filled with PBS and supernatants were collected on day 5. Supernatants from NMDs loaded with IFN resulted in significant phosphorylation of STAT1 (a transcription factor activated by IFN) in PBMCs compared to PBS loaded NMDs. Tumor growth was significantly inhibited in mice receiving IFN-loaded NMDs as compared to those receiving PBS-loaded NMDs ($p < 0.01$). Tumors from IFN-treated mice had smaller areas of coagulation necrosis (17% vs. 22.67%) and fewer mean mitotic figures (7.33 vs. 11.67) than PBS-treated tumors. There was no inflammatory response to the NMD or encapsulation by fibrosis. Conclusion: Functional IFN was released from the NMD in vitro and in vivo. NMDs can be employed as a versatile drug delivery platform.

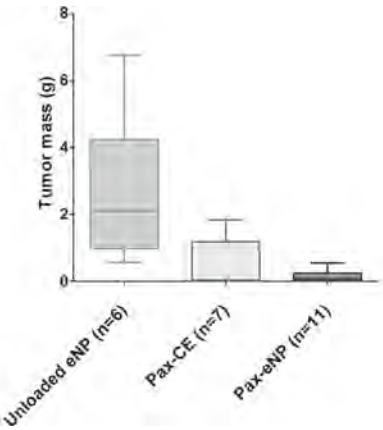
P4

Intraperitoneal Chemotherapy via Tumor-Localizing Polymeric Nanoparticles Following Surgical Debulking of Ovarian Carcinoma

M.D. Schulz,[1]* K.A. Zubris,[2] J.E. Wade,[1] R.F. Padera,[3] P.J. Catalano,[4] X. Xu,[5] M.W. Grinstaff,[2] Y.L. Colson.[1] *1. Division of Thoracic Surgery, Brigham and Women's Hospital, Boston, MA; 2. Departments of Chemistry and Biomedical Engineering, Boston University, Boston, MA; 3. Department of Pathology, Brigham and Women's Hospital, Boston, MA; 4. Department of Biostatistics and Computational Biology, Dana-Faber Cancer Institute, Boston, MA; 5. Department of Radiology, Brigham and Women's Hospital, Boston, MA.*

Introduction: Drug toxicity and catheter-related complications limit the clinical application of bolus intraperitoneal (IP) cisplatin and paclitaxel/ Cremophor®EL (Pax-CE) in the setting of surgically debulked ovarian carcinoma. In order to target drug delivery directly to sites of tumor and minimize toxicity, pH-triggered nanoparticles were designed for intracellular drug release and evaluated for tumor-specific localization and *in vivo* efficacy against human

xenografts in a mouse model of surgical debulking. **Methods:** Polymeric expansile particles containing paclitaxel (Pax-eNP) were synthesized resulting in 100 nm hydrophobic nanoparticles capable of pH-mediated expansion to a ~1μm hydrogel at endosomal pH (pH ≤ 5) with delayed release of the encapsulated chemotherapeutic agent. Four weeks after establishment of IP human ovarian (OVCAR-3) xenografts in female nude mice, laparotomy to debulk all evidence of gross disease was performed. Animals were treated with unloaded eNP or with 10 mg/kg IP paclitaxel delivered as bolus Pax-CE or Pax-eNP at fascial closure. All animals were sacrificed when controls developed tumor morbidity for equitable comparison of tumor burden. Rhodamine-labeled eNP (Rho-eNP), exhibiting endosomal uptake *in vitro*, were studied *in vivo* to evaluate local distribution of eNP in tumor bearing animals. **Results:** Surgical debulking of xenogeneic tumor implants was achieved with <3mm residual tumor in >95% of animals and <10% operative mortality. Extensive carcinomatosis was seen in the presence of unloaded eNP, whereas animals treated with Pax-eNP had minimal to no gross evidence of disease at sacrifice. IP treatment was well tolerated without development of adhesions and in vivo efficacy was equivalent to bolus dosing of Pax-CE. *In situ* localization of Rho-eNP following surgical debulking demonstrated exclusive eNP accumulation at the resection margins and known sites of residual tumor. **Conclusion:** These findings demonstrate that Pax-eNP are capable of localizing chemotherapy directly to sites of tumor *in vivo* and inhibiting locoregional tumor recurrence when administered at the time of debulking surgery.



Comparative tumor burden at sacrifice in mice treated with polymer vehicle control (unloaded eNP), paclitaxel/Cremophor®EL (Pax-CE), or paclitaxel-loaded expansile nanoparticles (Pax-eNP).

P5

Human Lymphedema is Characterized by CD4+ Infiltrate and Th2 Phenotype Inflammation S.D. Malliaris,[1]* J.C. Zampell,[1] T. Avraham,[1] A. Yan,[1] S.G. Rockson,[2] B.J. Mehrara.[1] *1. Sloan Kettering Institute, New York, NY; 2. Stanford University School of Medicine, Stanford, CA.*

Introduction: Lymphedema is a debilitating disorder associated with chronic mononuclear cell inflammation and tissue fibrosis. Although the histological features of lymphedema have been evaluated, the cellular composition of the inflammatory cell infiltrate and mechanisms that regulate fibrosis remain unknown. We have previously shown that lymphedema in a mouse model is associated with chronic T-cell inflammation with differentiation along Th2 cell lineage and that this response promotes tissue fibrosis secondary to expression of pro-fibrotic cytokines IL4 and IL13. The purpose of these studies was to determine if similar mechanisms contribute to chronic inflammation in clinical lymphedema. Methods: Matched 5mm skin punch biopsies were obtained from lymphedematous and normal upper extremities of patients (n=7) with secondary lymphedema and analyzed for Th2 cell markers (CD4, IL4 and IL13). In addition, systemic Th2 inflammatory response in lymphedema patients (n=16) was determined using ELISA to analyze serum levels of known Th2 markers CD30 and IgE before and after treatment. Results: Similar to our mouse model, matched human punch biopsies showed a 3-fold increase in the number of CD4+ cells and 2-fold increase in IL13+ cells in the lymphedematous tissues as compared to the contralateral normal limb ($p<0.05$). Furthermore, clinical lymphedema grade correlated with the extent of CD4+ infiltrate (Spearman $r=0.6332$, $p<0.016$). Similarly, serum analysis revealed that lymphedema treatment resulted in decreased in Th2 differentiation (CD30 decreased 13% ± 25%, $p<0.06$; IgE decreased 22% ± 29%, $p<0.01$). Conclusions: We have shown that similar to mouse models of lymphedema clinical lymphedema is associated with chronic T-helper cell infiltration with differentiation along the Th2 lineage. In addition, Th2 differentiation can be measured using serum markers, and lymphedema treatment can decrease Th2 differentiation markers. These findings provide a starting point for development of targeted anti-inflammatory treatments in patients with postoperative lymphedema which may be useful for flare-ups or as a way of breaking the progressive cycle of this debilitating complication.

P6

Serum Sphingosine -1-Phosphate Level in Breast Cancer Mouse Model and Patients M. Nagahashi,[1]* O.M. Rashid,[1] S. Ramachandran,[1] S. Milstien,[2] S. Spiegel,[2] K. Takabe.[1] *1. Surgical Oncology, Virginia Commonwealth University, Richmond, VA; 2. Department of Biochemistry and Molecular Biology and the Massey Cancer Center, Virginia Commonwealth University, Richmond, VA.*

INTRODUCTION: Sphingosine-1-phosphate (S1P), a pleiotropic bioactive lipid mediator and a ligand for specific receptors (S1P1-5) regulate cancer cell proliferation, migration and angiogenesis. S1P is generated by sphingosine kinases type 1 (SphK1), which is upregulated in breast cancer, associated with resistance to chemotherapy, and correlates with poor prognosis. We hypothesized that the serum level of S1P correlates with breast cancer progression and metastasis. The aim of this study is to reveal the hypothesis using in mouse model and patients. METHODS: Syngeneic metastatic breast cancer model with orthotopic implantation of 4T1-luc2 cells was used. Tumor burden was monitored live using IVIS 2000. Genome-wide gene microarray was used to profile S1P related genes, and qPCR was used for confirmation. Mass spectrometry (LC-ESI-MS/MS) was used to measure S1P level in mouse serum and serum from stage IIIa breast cancer patients and age/ethnicity-matched healthy volunteers. Student's t-test was used for analysis. RESULTS: In our model, lymph node metastasis was confirmed from Day 2-6 and lung metastasis confirmed from Day6-10 after 4T1 cell implantation. Microarray analysis and qPCR demonstrated that 4T1-luc2 cells highly overexpressed SphK1 both in vitro and vivo, whereas S1P1 were expressed higher in lung metastasis. S1P levels are significantly elevated both in tumor and axillary lymph nodes at Day 2 after implantation compared to naïve mouse breast. Interestingly, serum S1P level elevated from Day 2 to Day 10 in this model. Finally, serum S1P levels in stage IIIa breast cancer patients were significantly higher than age/ethnicity-matched volunteers. CONCLUSIONS: Our results support the notion that the serum S1P levels correlates with breast cancer progression and metastasis in vivo model and breast cancer patients. Serum level of S1P may be a good candidate as a biomarker for breast cancer progression. This work was supported by Sumitomo Life Social Welfare Services Foundation grant to MN, NIH-K12HD055881 and Susan G. Komen for the Cure (KG090510) to KT, and NCI (R01CA61774) to SS.

P7

Esophageal Carcinoma Contains a Radioresistant Subpopulation with Cancer Stem Cell Characteristics J.K. Smit,[1]* M. Niemantsverdriet,[2] R.P. Van Os,[3] H. Hollema,[4] J.T. Plukker,[1] R.P. Coppes.[2] *1. Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands; 2. University Medical Center Groningen - Radiation & Stress Cell Biology and Radiation Oncology, Groningen, Netherlands; 3. University Medical Center Groningen - Stem Cell Biology, Groningen, Netherlands; 4. University Medical Center Groningen - Pathology, Groningen, Netherlands.*

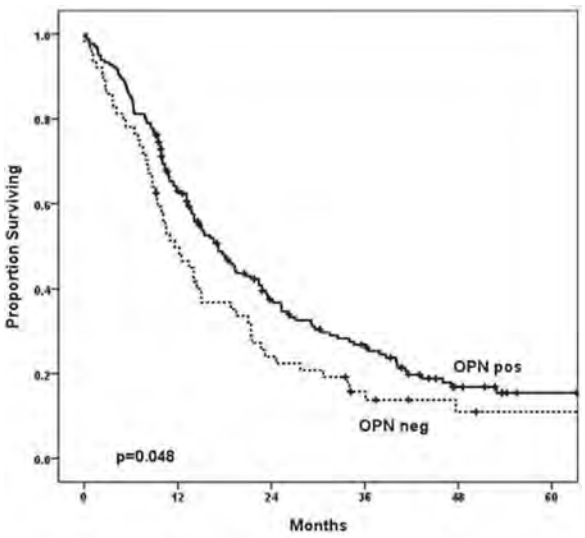
Introduction: Neo-adjuvant chemoradiation is considered as standard treatment in esophageal cancer (EC). However, a significant proportion of these tumors do not respond well to radiotherapy. Here, we investigated the presence of radioresistant cells in EC with cancer stem cell (CSC) characteristics. Methods: EC OE-33 adenotype and OE-21 squamous cell carcinoma cell-lines and fresh tumor material of EC patients were analyzed for common CSC-markers with Fluorecence Activated Cell Sorting (FACS) and immuno-histochemistry. Subpopulations were tested for clonogenic survival to determine radioresistance. Non-adherent 3D sphere-cultures was performed and xenograft tumors were generated in NOD/SCID mice to investigate stem cell properties. Results:

Both cell lines lacked expression of CD133 and CD90, whereas the expression of EpCam overlapped with CD44 in OE-33. In sub-confluent cultures the expression of CD44+/CD24- was 5.6% SD ± 2.3 and 35.1% SD ± 1.3 in OE-33 and OE-21, respectively. In a clonogenic survival assay the CD44+/CD24- cells showed up to a 2-fold lower radiosensitivity compared to CD44+/CD24+ cells in both the OE-33 (p=0.02) and the OE-21 cell line (p=0.01). The CD44+/CD24- subpopulation had a 2.2-fold higher sphere-forming capacity compared to the CD44+/CD24+ subset (p=0.01) in OE-33. Analysis of the spheres showed an enrichment in the CD44+/CD24- phenotype from 5.6% to 56.4% (p=0.01) after 4 days of culturing as measured by FACS, but differentiated to a higher percentage of CD44+/CD24+ in time. Furthermore, CD44+/CD24- cells exhibited a greater in vivo tumor initiating capacity, shorter latency time and faster growth speed compared with unsorted or CD44+/CD24+ cells. Importantly, a clear CD44+/CD24- population could be identified in fresh EC biopsies of patients. Conclusions: EC appear to contain a radioresistant CD44+/CD24- subpopulation. This phenotype displays some CSC characteristics in vitro and in vivo and is present in human EC tumors. This marker could be used in future trials to predict tumor response.

P8

Osteopontin is Associated with Improved Survival in Patients with Pancreatic Adenocarcinoma A. Collins,* J. Rock, L. Malhotra, W. Frankel, M. Bloomston. *The Ohio State University Medical Center, Columbus, OH.*

Introduction: Osteopontin (OPN) is a secreted protein of the extracellular matrix. It has been used as a marker for tumor aggressiveness and correlated with clinical outcomes in several solid tumors, such as liver, lung, and breast. We determined the osteopontin expression and its influence on survival in patients with resected pancreatic adenocarcinoma. Methods: Tissue microarrays were constructed from 246 resected pancreatic adenocarcinomas. Immunohistochemical staining for OPN was undertaken and compared to normal pancreas (n=12). OPN expression was then correlated with tumor size, grade, and node status using Fisher's exact test. Survival curves were created by the Kaplan-Meier method and compared by log rank analysis. Results: In total, 81 (33%) of pancreatic adenocarcinoma tissues expressed OPN compared to 7 (58%) of normal controls (p=0.11). Expression was seen predominantly in the cytoplasm of the tumor cells. OPN was more common in tumors less than 2cm in size (p=0.003) but did not correlate with tumor grade or nodal status. The median and 2-year overall survival was longer when OPN was expressed (17.1 months vs. 11.6 months, and 38% vs. 24%, respectively, p=0.04, Figure). Multivariate analysis showed OPN expression and tumor size to be independent predictors of overall survival, while other histopathologic factors such as tumor grade, T stage, and nodal status were not. Conclusions: These results suggest that the presence of osteopontin expression in pancreatic adenocarcinoma may have a protective effect independent of tumor stage. This emphasizes the importance of the interaction between pancreatic cancer cells and their stromal elements.



P9

sFRP1 Is a Prognostic Biomarker with Functional Significance in Gastric Cancer C.J. Moran,[1]* P. Ray,[1] S. Bagaria,[1] Y. Qu,[1] A. Fleisig,[1] M. Sim,[1] R. Turner,[2] X. Cui.[1] *1. surgical oncology, John Wayne Cancer Institute, Santa Moinca, CA; 2. St. John's Health Center, Santa Monica, CA.*

Introduction: Gastric adenocarcinoma (GA), a leading cause of cancer-related death world wide, lacks distinctive biomarkers and targeted therapies. Underexpression of the E-cadherin gene in GA is associated with an aggressive phenotype and a poor prognosis but the mechanisms of this observation are poorly understood. Identification of critical functional markers in GA may aid in developing targeted therapy for this disease. Methods: Unsupervised hierarchical clustering analysis of a publicly available 230-sample GA microarray dataset identified a prominent cluster (21.7%) associated with underexpression of E-cadherin and overexpression of a Wnt-family protein: secreted frizzled-related protein 1 (sFRP-1). Archival GA specimens were then assessed for the expression of sFRP-1 by immunohistochemistry. Prognostic significance was assessed using univariate and multivariate analyses. GA cell lines transfected with sFRP-1 were used to reveal sFRP-1's functional impact. Results: 85 patients with GA underwent surgery with curative intent; 39 stained positive for sFRP-1 (46%). In this positive group, sFRP-1 staining was focal; was commonly found on the leading edge of the infiltrating tumor mass; and was not restricted to one histopathologic group, grade, or clinical stage. On univariate analysis: T stage, nodal involvement, pathologic stage, nuclear grade, E-cadherin status and sFRP-1 status were predictive of overall survival. In a multivariate model, T stage ($p<0.001$), nuclear grade ($p<0.001$), E-cadherin status (p=0.031) and sFRP-1 status (p=0.0097) were predictive of overall poor survival. Overexpression of sFRP-1 in GA cell lines induced mesenchymal phenotype, enhanced growth and stem cell-like properties. sFRP-1 also attenuated Wnt signaling and E-cadherin expression, but potentiated Notch and Hedgehog signaling. These findings suggest a Wnt-independent mechanism mediated by sFRP-1. Conclusions: The aggressive biological subtype of GA may be linked to overexpression of sFRP-1. Our findings identify sFRP-1 as a functional prognostic biomarker for GA, which may serve as a potential therapeutic target.

P10

Electrochemotherapy with bleomycin: a local treatment with possible systemic implication A. Testori,* F. Verrecchia, P. Ferrucci. *Melanoma and Sarcoma Division, European Institute of Oncology, Milan, Italy.*

Introduction. A new, promising application of bleomycin was discovered and developed by Mir in 1991, combining the drug with electroporation. This new technique was called electrochemotherapy (ECT). The new treatment is based on the increased bleomycin delivery into tumor cells after cell membrane permeabilization by electric pulses administered locally at the site of superficial tumor localizations. Since 1991 more than 300 articles were published on the argument and experiences from many institutes in Europe seems to be very promising. Actually ECT is used for the treatment of cutaneous and subcutaneous tumoral lesions from different tumoral types. Favorable results in treating superficial metastatic lesions have been published with a complete response rate for treated nodules raging from 70% to 90%. Patients and methods. In our Institute 121 patients (75 evaluable) have been treated from 2006 to 2010 for superficial cancer lesions, especially metastatic melanomas (58 patients) and squamous or large basal cell carcinomas (15 patients). Results. The overall response rate (OR) was 90% with complete response rate (CR) of 72% in melanoma lesions and OR of 88% and CR of 65% in non melanoma lesions. Only 8/75 patients experienced relapse in the treatment field . The treatment is well tolerated either under general or local anesthesia with minimal side effects or discomfort for the patients. Conclusions. ECT is a safe and well tolerated procedure with quality of life improvement and can be used with meltiple aims: palliative (bleeding, pain, bulk control); palliative setting to get "chronic disease" progression (melanoma) and curative setting through a potential immunological involvment; curative (es. basal cell carcinoma). Furthermore we are currently evaluating development of immune responses elicited by ECT, by comparing serum levels of pro-inflammatory cytokines, and frequency and activation of T cell populations in peripheral blood of selected patients, before and after therapy

P11

Overexpression of miR-675 in AFP-secreting HCC modulates cell adhesion and proliferation pathways J.M. Hernandez,[1]* J. Wang,[1] A. Elahi,[1] G. Bloom,[1] B. Centeno,[1] L. Humphries,[1] C.W. Clark,[1] B. Fuchs,[2] K. Tanabe,[2] T. Yeatman,[1] D. Shibata.[1] *1. GI Oncology, Moffitt Cancer Center, Tampa, FL; 2. Massachusetts General Hospital, Boston, MA.*

INTRODUCTION: AFP-secreting (AFP+) HCC are generally associated with worse survival as compared to non-secreting (AFP-) tumors despite earlier diagnosis. Using gene expression profiling, we sought to identify potential novel therapeutic targets and biologic differences between AFP+ and - tumors. METHODS: From 2000-2009, we identified 27 patients having undergone resection for HCC and consented to our tissue banking protocol. Tumors (14 AFP+ and 13 AFP-) and cell lines were profiled using the Affymetrix 133 Plus 2.0 GeneChip. MetaCore gene ontology software was used to identify altered biologic pathways. Overexpressing transfections of miR-675 were carried out in the non-expressing HepG2 cell line, with phenotypic effects determined by MTT proliferation, matrigel invasion and soft agar growth assays. RESULTS: We identified 418 differentially regulated genes between AFP+ and AFP- tumors. H19, which encodes the precursor for miR-675, was found to be the most highly upregulated gene (+14 fold change) in AFP+ tumors. We validated the expression of miR-675 by quantitative RT-PCR in the clinical specimens, demonstrating an average fold-change of +12.5 in AFP+ tumors. In AFP+ HCC, we identified upregulated pathways involved in cell adhesion ($p<0.03$) and cell proliferation ($p<0.01$). Transfection of miR-675 into HepG2 resulted in a gene expression profile similar to that of patient samples; 6 upregulated pathways involved in cell adhesion ($p<0.01$) and 4 downregulated pathways involved in cell cycle regulation ($p<0.01$). Furthermore, overexpression of miR-675 resulted in a dramatic acquisition of colony formation in soft agar ($p<0.0001$) and a doubling of proliferation rates ($p<0.001$). Surprisingly, but in concordance with the alterations seen in cell adhesion pathways, we observed an abrogation of invasive potential ($p<0.01$). CONCLUSIONS: miR-675 appears to play a critical role in the development of AFP+ HCC through the deregulation of cell adhesion and cell cycle control pathways. Our results also suggest that proliferative and invasive processes may be regulated via divergent pathways. Further investigation of miR-675 as a potential therapeutic target is warranted.

P12

A Genetic and Proteomic Comparison of Primary and Metastatic Human Pancreatic Ductal Adenocarcinoma D.M. Walters,[1]* J.B. Stokes,[1] S.J. Adair,[1] S. Chowbina,[3] C.A. Borgman,[2] C.R. Cowan,[2] B. Lowrey,[1] J.A. Papin,[3] J.T. Parsons,[2] T.W. Bauer.[1] *1. University of Virginia, Department of Surgery, Charlottesville, VA; 2. University of Virginia, Department of Microbiology, Charlottesville, VA; 3. University of Virginia, Department of Biomedical Engineering, Charlottesville, VA.*

Introduction: Pancreatic ductal adenocarcinoma (PDAC) has a propensity for early metastasis. We sought to identify the genetic and proteomic differences between metastatic and primary human PDACs in order to identify rational targets for therapy. Methods: Resected human PDACs were implanted orthotopically in mice. Three metastatic and three primary pancreatic cancers were implanted, propagated, and analyzed. Gene expression profiling (GEP) (Affymetrix, Santa Clara, CA) was performed, along with human phosphoreceptor tyrosine kinase (pRTK) and cytokine arrays (R&D Systems, Minneapolis, MN) on tissue lysates from each tumor. GEP data was analyzed using Gene Set Enrichment Analysis (GSEA) to extract biological information regarding relevant cellular pathways using the Kyoto Encyclopedia of Genes and Genomes (KEGG). Cytokine and pRTK data was normalized using Z-score normalization and a Wilcoxon rank-sum test was used to determine significance. Results: GSEA revealed 11 KEGG pathways significantly enriched in metastatic tumors, including the Pancreatic Cancer, p53 Signaling, and Notch Signaling pathways, and 5 KEGG pathways decreasingly enriched in metastatic tumors, including Cell Adhesion Molecules and Extracellular Matrix Receptor Interaction pathways ($p<0.05$). Metastatic PDACs were associated with decreased activation of ErbB4, an EGFR-family RTK ($p<0.05$). Metastatic PDACs were associated with increased expression of the cytokines urokinase-type plasminogen activator (uPA) and IL-12, and decreased expression of ADAMTS-1, angiopoietin-1, MIP-1a, CXCL16, and IL-17E ($p<0.05$) when compared to primary tumors. Conclusions: This study demonstrates that there are significant genetic and proteomic differences between primary and metastatic PDACs. Further investigation into the relative importance of these pathways will lead to an understanding of which pathways are effective targets for therapy.

P13

Pancreatic cancer mediates upregulation and mobilization of MDSC J.B. Mitchem,* M.R. Porembka, S.P. Goedegebuure, D.C. Linehan. *Surgery, Washington University, St Louis, MO.*

Introduction:Myeloid derived suppressor cells (MDSC) are a heterogeneous group of immature cells which play an integral role in tumor induced immunosuppression, angiogenesis, and metastasis development. The role of MDSC is not well defined in pancreatic adenocarcinoma (PA). In this study we quantify MDSC in PA and show that depletion of MDSC in a mouse model improves antitumor response. Methods:Tumor tissue, marrow aspirate, and PBMC from patients with PA and cancer free controls (CFC) were analyzed by flow cytometry (FC) and immunohistochemistry (IHC) for markers of MDSC (CD11b, CD15, CD14, HLA-DR, CD33; values expressed as % of CD45+). To assess the role of MDSC in immune suppression and tumor growth, C57BL/6 mice were inoculated with Pan02 subcutaneously (SQ), a syngeneic murine PA cell line. Bone marrow, spleen, and tumor tissue was analyzed by FC for MDSC prevalence (CD11b, Ly6G, Ly6C) and suppression. For MDSC depletion experiments, mice were treated with placebo or zoledronic acid (ZA), a potent aminobisphosphonate. End-points included tumor growth, survival, MDSC prevalence and immune response. Results:PBMC and marrow from patients with PA were analyzed by FC and compared to CFC. MDSC were found to be upregulated in both compartments (Table 1). Tumor was shown by FC and IHC to avidly recruit MDSC. Similar to PA patients, mice bearing Pan02 tumors displayed an increased prevalence of MDSC in bone marrow and spleen; MDSC were also avidly recruited to the tumor microenvironment (60-90% of CD45+ infiltrating leukocytes). CD11b+ cells from the spleen and tumor of tumor-bearing mice were found to suppress CD8+ effector T cell responses. ZA effectively depleted intra-tumoral MDSC (placebo: 84.7% v ZA: 46.8% $p<0.0001$), resulting in an improved type I response demonstrated by increased IFN-γ ($p<0.05$) and decreased IL-10 ($p<0.05$), decreased tumor growth ($p<0.001$), and improved survival (59 v 73 days, $p<0.05$). Conclusion:MDSC play an important role in the growth and progression of PA. Treatment with ZA effectively diminishes MDSC accumulation in the tumor and improves survival. Therapeutic targeting of MDSC represents a novel treatment strategy for PA.

A

Compartment	Subset	Patients (% of total CD45+)	CFC (% of total CD45+)	p value
Marrow				
	$CD11b^{+}14^{+int}15^{hi}$	46.4±7.2	26.4±1.5	0.005
	$CD11b^{+}14^{hi}15^{+int}$	12.5±1.9	8.6±1.2	0.09
PBMC				
	$CD11b^{+}14^{+int}15^{hi}$	4.2±0.9	0.3±0.1	0.001
	$CD11b^{+}14^{hi}15^{+int}$	27.4±1.8	8.7±0.8	<0.001

B

Compartment	Subset	Tumor Bearing (% of total CD45+)	Non-Tumor Bearing (% of total CD45+)	p value
Marrow				
	$CD11b^{+}Ly6G^{-}Ly6C^{hi}$	20.2±0.8	12.4±0.5	p<0.001
	$CD11b^{+}Ly6G^{int}Ly6C^{+}$	66.1±1.2	49.9±1.4	p<0.001
Spleen				
	$CD11b^{+}Ly6G^{-}Ly6C^{hi}$	14.1±0.3	13.0±0.2	p=0.02
	$CD11b^{+}Ly6G^{int}Ly6C^{+}$	23.4±4.3	4.4±0.4	p<0.001

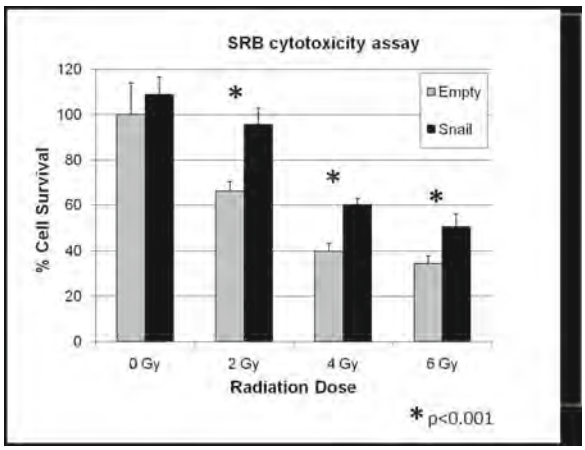
Table 1: Comparison of MDSC in human and murine studies. A) Comparison of MDSC in PA patients and cancer free controls, and B) comparison of MDSC in Pan02 tumor bearing and non-tumor bearing mice.

P14

Snail Expression Enhances Radiation Resistance in Colorectal Cancer E.R. Camp,* R.E. Moretz, S.G. Vaena, M.S. Ashenafi, D.T. Marshall, V.J. Findlay, D.K. Watson. *Surgery, Medical University of South Carolina, Charleston, SC.*

Introduction: Molecular factors mediating radiation sensitivity in colorectal cancer (CRC) are poorly understood. Loss of E-cadherin, the hallmark change in epithelial to mesenchymal transition (EMT), has been associated worse treatment outcomes in various malignancies and resistance to apoptosis. We hypothesize that expression of Snail, an E-cadherin transcriptional

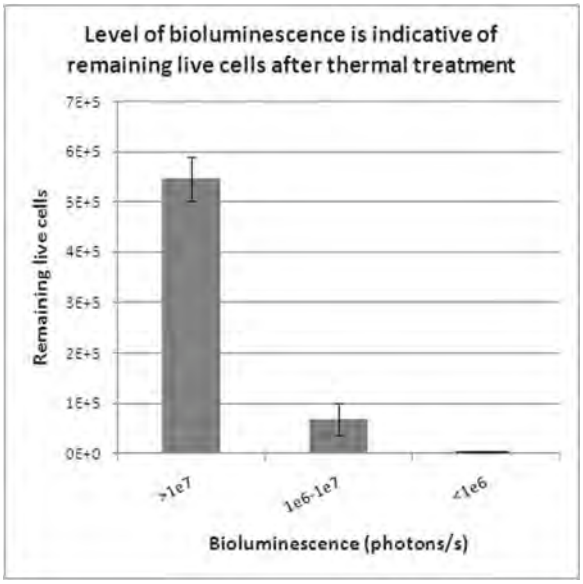
repressor, will decrease radiation sensitivity in CRC by inhibiting p53-mediated apoptosis. Methods: DLD-1 human colon cancer cells were stably transfected with pCMV-3Tag-1 vector expressing Snail cDNA (Snail DLD-1) or empty vector control (Empty DLD-1) based on antibiotic selection. Snail and E-cadherin expression was quantified by real time RT-PCR normalized to GAPDH. p53 expression was assessed by Western Blot analysis. Sulforhodamine B (SRB) assay was performed to assess cytotoxicity 96 hours following exposure to 0-6 Gray (Gy) radiation delivered by a Varian® Clinac 21EX linear accelerator. An in vitro clonogenic analysis was performed on cells in 6-well plates treated with 4Gy radiation and maintained for 2 weeks. Results: Snail DLD-1 cells exhibited features of enhanced EMT with altered morphology, demonstrating increased spindle shape and loss of cell-cell contact. Similarly, E-cadherin expression was reduced in the Snail DLD-1 cells by > 60% compared to Empty DLD-1 cells. Snail DLD-1 cells demonstrated reduced p53 protein levels. In response to radiation, Snail DLD-1 demonstrated 31to 33% enhanced cell survival at 2, 4, 6 Gy compared with Empty DLD-1 ($p<0.0001$, Figure). The in vitro clonogenic assay demonstrated significantly increased clone formation following radiation in the Snail DLD-1 cells confirming the SRB findings. Conclusions: Expression of Snail, a transcriptional mediator of EMT, leads to enhanced radiation resistance associated with inhibition of p53 in colon cancer cells. Therapeutic strategies targeting EMT may enhance conventional radiation treatment for CRC.



P15

Bioluminescent Imaging Serves As a Sensitive Dynamic Marker for Monitoring Thermal Treatment of Cancer J.T. Au,* C.H. Chen, L. Gonzalez, I. Serganova, Y. Fong. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

INTRODUCTION: Bioluminescence is a phenomenon where visible light is emitted by living organisms like the firefly. This light reaction has been harnessed in research for deep tissue imaging. Our study evaluates the potential of bioluminescent imaging for monitoring thermal treatment of cancer. METHODS: Mesothelioma cancer cells transfected with a firefly luciferase gene (MSTO-Td) were tested for bioluminescence and plated in serial dilutions to determine the lowest number of cells that can still be visualized by a bioluminescent signal. After establishing the presence and threshold of bioluminescence, MSTO-Td cells were subjected to thermal treatment in a heated chamber, and the bioluminescent signal was compared to the number of remaining live cancer cells. To test the utility of bioluminescent imaging in a living model, MSTO-Td cells were xenografted onto mice, and the flank tumors were imaged before and after electrocautery ablation. RESULTS: MSTO-Td cells emitted a bright bioluminescent signal that amplified with the number of cells plated ($P<0.001$). Conversely, the bioluminescent signal could be detected even when there were less than 10 cells. Upon thermal treatment, the bioluminescent signal decreased in a dose-dependant fashion as the temperature was increased from 37 to 70°C ($P<0.001$) and the duration of treatment from 1 to 20 minutes ($P<0.001$). This diminishing bioluminescent signal was significantly correlated to the falling number of remaining live MSTO-Td cells after thermal treatment (Pearson coefficient = 0.865; $P<0.001$). In mice, electrocautery ablation of MSTO-Td flank tumors was effectively monitored by bioluminescent imaging, with a thousand-fold drop in signal intensity upon killing of the cancer cells. DISCUSSION: Bioluminescent imaging is a sensitive and dynamic technique that provides quantifiable and immediate information on the thermal treatment of MSTO-Td cancer cells. This encourages research into bioluminescent markers for visualizing tumors and monitoring their treatment in real time.



P16

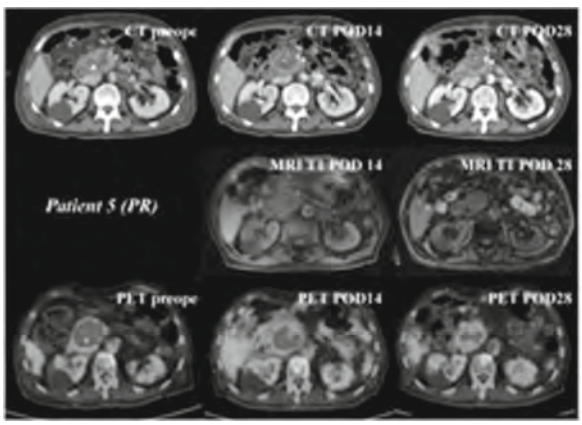
Synergistic Effect of Metformin and Polyamine Synthesis Inhibitor on Melanoma Growth E.C. Hsueh,* Y. Zhang, G. Peng. *Saint Louis University, St. Louis, MO.*

The mTOR and polyamine synthesis pathways are important metabolic pathways for tumor growth. Metformin exerts negative effect on mTOR regulatory pathway via MAP kinase activation. We hypothesized the inhibition of mTOR and polyamine synthesis with Metformin and ornithine decarboxylase (ODC) inhibitor would have synergism in melanoma growth inhibition. Five human melanoma cell line cells were evaluated. The cells were treated with or without various concentrations of DFMO (ODC inhibitor) or Metformin or combination at various concentrations then incubated up to 96 hours. Cell Proliferation Assay was performed at 24, 48, 72, and 96 hours using Cell Titer Blue cell proliferation Assay according to the manufacturer's protocol. Western blot were performed using polyclonal goat anti-ODC, phospho-p60, phospho-4E-BP1, nonphospho-4E-BP1, mTOR, and phospho-mTOR and rabbit mAB anti-GAPDH. For cell migration assay, 1x105 melanoma cells were seeded in each well of 24-well plate. An artificial homogenous wound was created onto the monolayer after overnight incubation. Migration of cells into the wound was measured at 0hr and 48hr with an inverted microscope. For comparison between groups, the student's t test was used and $p< 0.05$ was considered to be statically significant. Dose-dependent growth inhibition was observed with DFMO and Metformin treatment for all 5 human melanoma cell lines ($p<0.05$). Synergistic growth inhibition was noted in all 5 melanoma cell lines following addition of combination of DFMO and Metformin at various concentrations. Western blot analysis showed a significant down-regulation of phospho-4E-BP1 expression following the combination treatment. No significant change was observed with ODC or mTOR expression. Significant inhibition of tumor cell migration was also observed following combination treatment compared with either DFMO or Metformin treatment alone ($p<0.05$). Metformin administration and polyamine synthesis inhibition with DFMO have synergistic growth inhibitory effect on human melanoma. The combination also has negative effect on melanoma cell migration. The synergism may be correlated with the enhanced inhibitory effect on downstream effectors of mTOR.

P17

Biological therapeutics HF10 Oncolytic Virus Therapy H. Kasuya,[1]* A. Kanzaki,[1] T. Fujii,[1] H. Sugimoto,[1] S. Nomoto,[1] S. Takeda,[1] T. Sahin,[1] K. Yamamura,[1] S. Yamada,[1] T. Imai,[1] Y. Kodera,[1] Y. Nishiyama,[2] T. Sugae,[1] A. Nakao.[1] *1. Dept. of Surgery II, Nagoya University School of Medicine, Nagoya, AICHI, Japan; 2. Dept. of Virology, Nagoya University School of Medicine, Nagoya, AICHI, Japan.*

Oncolytic viruses are novel biological therapeutics for advanced cancer to have a wide spectrum of anticancer activity with minimal human toxicity. The genetic character of HF10 can be confirmed by detecting base pair deletions at positions 3832, 2295, and 6027 in both ends of the L region compared to the reference strain, HSV-1. In addition, UL43, 49.5, 55, 56, and LAT are functionally inactivated as previously described. At the lethal dose, the toxicity of HF10 in mice is 104 times lower than that of the wild-type virus, but the virus still exhibits active therapeutic effects in cancer cell lines. We have started clinical trial from early 2003 using HSV natural mutated virus, HF10. The replication capacity of HF10 is comparable or slightly higher than that of the wild type HSV-1 in most types of transformed cells. This strong oncolytic effect is one of differences from previous oncolytic HSV. Clinical trials of oncolytic virus therapy already have been performed over 2000 patients worldwide, however, in Japan clinical trials using oncolytic virus have been performed in only two facility. Nagoya University School of Medicine is one of them, including 3 patients of recurrent head and neck cancer, 6 patients of recurrent breast cancer, 6 patients of advanced pancreatic cancer (3 injections group) and 2 patients of advanced pancreatic cancer (6 injections group). Regarding 6 patients of advanced pancreatic cancer (3 injections group), we observed clinical efficacy in 4 of the 6 patients. The tumors were classified as SD or PR in 4 patients and PD in 2 patients. A patient showed significant tumor reduction over 60% PR on PET and CT. There were no adverse side effects. We found CD4 and CD8 massive invasion inside of tumor caused by injected virus. Surprisingly even if after over 318 days, still HF10 antigen remained inside of tumor. It has become clear that a major effecter of oncolytic herpes simplex virus efficacy is the host immune response. We also report most recent new date of advanced pancreatic cancer (6 injections group) using EUS (endoscopic ultrasound) too.



P18

Natural Enhancer of IRF-1 Suppresses Gastric Cancer Tumor Growth *in vivo* Y. Akmal,* Y. Wang, M. Senthil, Q. Xing, J. Yan, J. Gao, J. Yim. *General Oncologic Surgery, City Of Hope National Medical Center, Duarte, CA.*

Introduction Interferon Regulatory Factor-1 (IRF-1) is involved in mediating immunomodulatory and anti-proliferative effects. It has been shown to induce apoptosis *in vitro* in the gastric cell line AGS. Baicalein is a natural compound found in a botanical extract in traditional Chinese medicine. Baicalein induces IRF-1 protein and suppresses AGS cell *in vitro*. Genistein is an active component of soy, with the same molecular weight as baicalein, which has been felt to have anticancer potential. We compared the efficacy of baicalein to genistein in suppressing tumor growth *in vivo* in a mouse gastric cancer model. **Methods** Twenty SCID-Bg mice were implanted with $5x10^6$ AGS tumor cells with matrigel subcutaneously. Once tumors were about 70 mm^3 in volume the mice were randomized into 3 groups. Treatment was then initiated with intraperitoneal injection of control (DMSO in PBS), baicalein (20mg/kg) or genistein (20mg/kg). Treatment was given 5 times/week for 4 weeks and tumors measured weekly for 5 weeks. **Results** Nineteen of the twenty mice developed tumors ~5x5 mm in size and these were randomized: 7 mice in control group, 6 in baicalein group and 6 in genistein group. Tumor volumes increased in control group from 72.7 to 438 mm^3, from 76.8 to 446 mm^3 with genistein, and from 75.5 to 255 mm^3 with baicalein over the 5 weeks. There was significantly less tumor growth in the baicalein group (p=0.0063) versus control (Table 1). **Conclusion** We found that the natural compound baicalein significantly suppresses tumor growth in a xenogeneic gastric cancer model *in vivo*. Induction of IRF-1 is likely to play a significant role in this tumor suppression.

Tumor Growth *in vivo*

Group	Week 1	Week 2	Week 3	Week 4	Week 5
Carrier	72.74	115.7	137	232.7	437.6
Genistein	76.82	108.8	164.5	226.7	445.9
Baicalein	75.46	83.31	90.6	148	254.7

Tumor Volumes (mm^3)

P19

CD4+ T-cells Are Necessary for Fibrosis and Lymphatic Dysfunction in Chronic Lymphedema A. Yan,* J.C. Zampell, T. Avraham, S.D. Malliaris, S.Z. Aschen, B.J. Mehrara. *Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

INTRODUCTION: Chronic lymphedema results in soft tissue fibrosis and lymphatic dysfunction. However, the cellular mechanisms that regulate this response remain unknown. T-cells play an important role in fibrosis in a number of other fibroproliferative disorders. The purpose of these experiments was, therefore, to determine the role of various types of T-cells in the regulation of fibrosis and lymphatic dysfunction resulting from lymphatic fluid stasis. METHODS: Lymphedema was produced by circumferential skin excision and microsurgical ligation of the deep lymphatic system of adult female CD4 knockout (KO) and wild-type mouse tails. They were followed for 6 weeks and their lymphatic function was evaluated. Also, wild-type mice underwent tail excision and were selectively depleted of CD4 or CD8 cells beginning 2 weeks after surgery using monoclonal antibodies. Lymphatic function was evaluated 4 weeks later. RESULTS: CD4 KO mice had significantly decreased tail lymphedema (>50%), dermal thickness (>2x decrease), and fibrosis (2.5x decrease) as compared with wild-types ($p<0.05$ for all). These changes were associated with marked improvement in lymphatic function as assessed by microlymphangiography and lymphoscintigraphy (>100x increased uptake, $p<0.01$). Western blot analysis demonstrated markedly decreased expression of the profibrotic T-helper 2 (TH2) cytokines IL4 and IL13, and also decreased expression of the TH1 cytokine IFN-γ. Similarly, depletion of CD4+, but not CD8+ T-cells, decreased tail lymphedema and improved lymphatic function. This indicates that selective loss of CD4+ T-cells is necessary for fibrosis and lymphatic dysfunction resulting from lymphatic fluid stasis. CONCLUSION: We have shown that CD4+ T-cells are necessary for the development of fibrosis and lymphatic dysfunction in the setting of chronic lymphatic fluid stasis. This effect is due, at least in part, to decreased expression of the profibrotic TH2 cytokines IL4 and IL13. These findings are important since identification of the mechanisms regulating the pathologic responses to lymphedema may help identify targeted treatment or preventive measures for this debilitating and common disorder.

P20

IL-1 as a Mediator of Proliferation and Angiogenesis in Pancreatic Adenocarcinoma K. Turner,[1]* Z. Chen,[1] H.R. Alexander,[2] S. Varghese.[2] *1. Marlene and Stewart Greenebaum Cancer Center, Baltimore, MD; 2. Department of Surgery, Division of Surgical Oncology and The Greenebaum Cancer Center, University of Maryland Medical Center, Baltimore, MD.*

INTRODUCTION: Interleukin-1 (IL-1) is a pluripotent cytokine that mediates progression of solid organ cancers through multiple mechanisms including induction of cell proliferation and angiogenesis. We studied the role of IL-1β signaling through its receptor, IL-1RI, on pancreatic adenocarcinoma (Panc Ca) to test whether inhibition of IL-1 signaling suppresses

Panc Ca growth and angiogenesis. METHODS: We quantitated gene expression of IL-1α, IL-1β, and IL-1 receptor antagonist [IL-1Ra] in 5 Panc Ca cell lines by RT-PCR. IL-1RI levels were measured by Western blot. Three Panc Ca cell lines with either High (Hi, n=2) (>10^3 copies of IL-1 gene/10^5 β-actin) or low (Lo, n=1) expression of IL-1β were retrovirally transfected to constitutively over-express IL-1Ra. Cell proliferation (WST-1) and VEGF expression (RT-PCR) were measured in IL-1Ra transfected cell lines and compared with null transfected controls. RESULTS: Gene expression of IL-1β was high in 3 of 5 Panc Ca lines tested but IL-1Ra was very low in all. IL-1RI was detected in all cell lines and relative levels of IL-1RI appeared to correlate with IL-1β expression. Based on IL-1β expression, we categorized cell lines as high (Panc 08.13 and Panc 03.27) or low (MiaPaCa-2) expressors. All transfected cell lines produced high levels of IL-1Ra as confirmed by RT-PCR and Western blot. Cell proliferation was significantly decreased in IL-1Ra transfected Panc 08.13 and Panc 03.27 (P<.001) but not MiaPaCa-2 compared to null transfectants. VEGF gene expression (RT-PCR) was undetected in IL-1Ra transfected Panc 08.13 and Panc 03.27 but decreased in MiaPaCa-2 cells compared to null transfected controls. IL-1β treatment did not augment cell proliferation of wild type Panc Ca cell lines. CONCLUSION: IL-1 levels were elevated in 60% of Panc Ca cell lines tested and inhibition of IL-1 signaling in these cells markedly decreased cell proliferation and VEGF levels. These results signify that IL-1 inhibition may be a novel target in treatment of Panc Ca; however, further study is warranted.

P21

Serum metabolomic profiles acquired by gas chromatography-mass spectrometry (GC-MS) distinguish patients with pancreatic adenocarcinoma from those with other periampullary adenocarcinomas

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Introduction: Pancreatic adenocarcinoma has a substantially different prognosis from other periampullary adenocarcinomas (ampullary, duodenal, biliary), suggesting differences in tumor biology. Due to a lack of available techniques to accurately distinguish these two groups, unresectable periampullary tumors are often classified and treated as pancreatic adenocarcinoma in chemotherapy trials and practice. This study aims to identify differences in the metabolomic profile of serum between patients with pancreatic versus other periampullary adenocarcinomas. Methods: Fasting serum samples were collected on the day of surgery, as part of an institutional biorepository program (IRB#E20846), from patients who underwent resection of periampullary and pancreatic lesions. Accompanying clinical data were collected prospectively. Gas chromatography-mass spectrometry (GC-MS) spectra were acquired for aqueous metabolites and analyzed using multivariate methods (orthogonal partial least squares-discriminant analysis, OPLS-DA) using SIMCA-P+ (V12.0.1) software. Results: Seventy-one patients were included with definitive pathology of either pancreatic (n=52), ampullary (n=10), distal biliary (n=5), or duodenal (n=4) adenocarcinoma. Median patient age was 68 years, 34 were male, 14 were jaundiced, and 14 lesions were strictures whereas 57 were masses. The metabolomic profile of serum from patients with pancreatic adenocarcinoma was significantly different from that of patients with other periampullary adenocarcinomas on OPLS-DA (R2X=0.20, R2Y=0.69, Q2=0.41, p=6.3x10e-7, Figure 1). The differential metabolomic profile contained 123 metabolite peaks. The variables of patient gender, age, jaundice, and lesion type were not significant contributors to the model on regression analysis. Conclusion: The serum metabolomic profiles of resectable pancreatic adenocarcinoma and other periampullary adenocarcinomas differ significantly. Further analysis of these differences may yield a novel serum test to distinguish these tumors in clinical trials and practice.

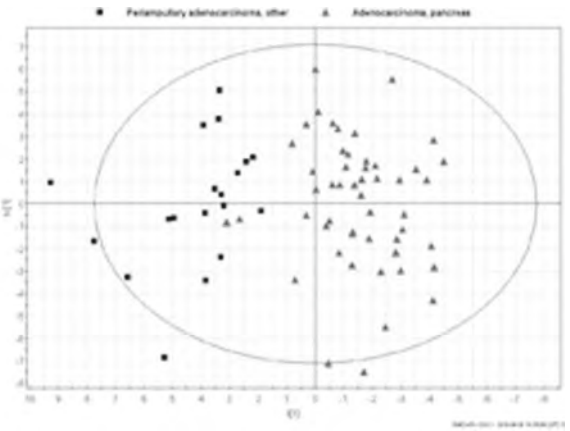

Figure 1. Serum metabolomic profiling distinguishes pancreatic adenocarcinoma from other periampullary adenocarcinomas (ampullary, duodenal, biliary) amongst patients with resectable lesions.

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Bone marrow-derived progenitor cells influence the metastatic behavior of murine breast cancer

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Introduction: Bone marrow-derived progenitor cells (BMPCs) have recently been recognized to play a major role in tumor progression and metastasis. To better understand this process and define genes implicated in breast cancer metastasis, we used the polyoma middle T (PyMT) spontaneous breast cancer mouse model to analyze changes in BMPCs along a previously defined tumor progression timeline (Lifsted et al. Int J Cancer. 1998 77:640–644). Methods: Three PyMT genetic backgrounds with different metastatic behaviors were analyzed: the low metastatic DBA1, the intermediate metastatic FVB, and the highly metastatic AKR. Primary tumor growth was observed at four time points: 6, 9, 12 and 14 weeks. Macroscopic analysis of lungs, and H&E staining were used to describe the pattern of metastasis. BMPCs were isolated using a lineage depletion kit and gene expression profile was analyzed by RNA microarrays. Results were then validated by quantitative PCR (qPCR) and flow cytometry. Controls in each group were mice from the same background lacking the middle T antigen. Results: Despite similar primary tumor growth curves and tumor size at sacrifice, there was a marked difference in metastatic burden between the three backgrounds. Microarray analysis of BMPCs in the FVB background revealed the mis-regulation of several signaling pathways controlling bone marrow stem cell proliferation, renewal and lineage commitment such as C/EBPs, Wnt, MAPK and several interleukins. Interestingly, we found the upregulation of extracellular matrix remodeling genes and stem cell mobilization factors such as MMP-9, MMP-13, osteopontin and several cathepsin genes, providing a mechanism for early homing of BMPCs to tumor and distant metastatic sites. Validation of this data by qPCR of BMPCs from all three backgrounds showed increased expression of some of these genes with tumor progression and more importantly, a higher level of expression in those backgrounds with greater metastasis. Conclusions: These findings support the hypothesis that BMPCs have a direct impact on metastasis in breast cancer. While the primary tumor influences BMPC behavior, these BMPCs then modulate metastatic propensity.

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Differential Methylation of DNA Exists between Triple Negative and Non-triple Negative Hormone Receptor Breast Cancer

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Introduction: DNA methylation has been shown to have strong regulatory roles in breast carcinogenesis. An association between breast tumor hormone receptor status and clinical outcomes has been demonstrated. However, the role

of DNA methylation in regulating hormone receptor expression has yet to be fully defined. We hypothesize that a strong association exists between DNA methylation of multiple genes and hormone receptor expression. Methods: DNA was extracted from formalin-fixed paraffin embedded breast cancer and normal reduction mammoplasty specimens. DNA was bisulfite converted and analyzed using a DNA methylation array. Over 800 genes were analyzed and mean methylation levels for each group compared. Clinical data from the corresponding patients was retrospectively collected. Luminal A was defined as estrogen receptor (ER) and/or progesterone receptor (PR) positive and her 2 neu (Her 2) negative. Luminal B was defined as ER and/or PR and Her 2 positive. Triple negative hormone receptor breast cancers were defined as ER/PR/Her 2 negative. Statistical analysis was performed in the R programming environment with significance considered at $p < 0.05$ after performing multiple comparisons correction. Results: 62 surgical breast cancer specimens and 10 normal reduction mammoplasty specimens were analyzed. Multiple genes were found to be significantly differentially methylated between cancer and normal specimens. Upon subgroup analysis of the cancer specimens, further differences were identified between patients with triple negative breast cancer, and those with either, luminal A or luminal B breast cancer. Conclusions: DNA methylation of multiple genes is strongly associated with hormone receptor expression. This data indicates that DNA methylation may play a role in the regulation of hormone receptor expression in breast cancer.

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Extract From Traditional Chinese Herb Scutellaria Baicalensis Suppresses Tumors and Inhibits p-Akt in Mice Y. Akmal,* M. Senthil, Q. Xing, J. Yan, Y. Wang, J. Yim. *General Oncologic Surgery, City Of Hope National Medical Center, Duarte, CA.*

Introduction: There is growing interest in use of herbal extracts as adjuncts to standard allopathic cancer therapy. The root of Scutellaria baicalensis used in Traditional Chinese Medicine for multiple maladies is also thought to have anti-cancer effects. However, the data regarding its efficacy and mechanism of action is limited. Phosphorylated-Akt (p-Akt) is the activated form of a serine/threonine kinase commonly overexpressed in breast cancer and thought to regulate tumor development and progression by promoting cellular survival and inhibiting apoptosis. We evaluated whether Scutellaria extract has any effect on tumor growth and/or p-Akt levels utilizing a murine breast cancer model. Methods: C3H/HeJ female mice bearing syngeneic established C3L5 breast cancer tumors were administered 200 μL of either water with 5% DMSO (control) or 100 mg/kg of the Scutellaria extract dissolved in 5% DMSO (treatment group). Mice received treatment by oral gavage 5 days/week for 3 weeks and were sacrificed 6 hours after last dose. Tumors were removed from mice and weighed. Western blot was performed on tumor samples and evaluated for beta-actin and p-Akt levels by densitometry. Results: The tumor weights in the Scutellaria group were significantly reduced ($p=0.036$) compared to controls. Western blot analysis demonstrated inhibition of p-AKT ($p<0.001$) but no significant effect on β-actin in the treatment group (Table 1). No toxicities were noted. Conclusions: We found that Scutellaria extract decreases tumor size and inhibits p-Akt in a murine breast cancer model. The findings suggest that Scutellaria extract is a potent p-AKT inhibitor and may be useful in combination with standard allopathic drugs in the treatment of breast cancer.

Tumor weights and Western Blot Densitometry Values

	Control Group (N=4)	Treatment Group (N=5)	p-values
p-AKT (INT/mm2)*	77295.7	10559.3	0.0000067
β-Actin (INT/mm2)*	80022.6	82591.5	0.26
Tumor Weights (mg)*	572.5	325.6	0.036

* Mean Values Provided

P25

Apricoxib, a novel COX-2 inhibitor, enhances the efficacy of standard therapy in human pancreatic cancer cell lines in vitro and in vivo A.R. Kirane,* J. Carbon, J. Toombs, K. Ostapoff, R. Schwarz, R. Brekken. *UTSW, Dallas, TX.*

Gemcitabine-erlotinib is standard of care (SOC) for pancreatic cancer, but this regimen can still be improved upon with regards to prolonging patient survival. Cyclo-oxygenase-2 (COX-2) is overexpressed in pancreatic cancer & implicated in pancreatic tumor progression. Inhibition of COX-2 decreases tumor growth, augments the activity of both gemcitabine and EGFR inhibition and may play a role in preventing or reversing EMT. This study characterized the effects of COX-2 inhibition on pancreatic cancer cell lines and determined if the addition of apricoxib enhances sensitivity to chemotherapy. Baseline EGFR and COX-2 expression were determined in 7 human pancreatic cancer cell lines & functional responses measured by changes in phospho-EGFR (p-EGFR) and prostaglandin E2 (PGE2) production by ELISA. Cytotoxicity was determined for gemcitabine, erlotinib & apricoxib independently and in combination by MTS assay. The effect of SOC therapy alone or in combination with 10 or 30mg/kg apricoxib PO on AsPC-1 & Colo357 tumors in vivo was determined in SCID mice bearing established orthotopic xenografts. Tissue was analyzed by IHC & VEGF levels were determined by ELISA. All lines expressed EGFR and COX-2, but expression was not predictive of p-EGFR level, PGE2 production or response to drug therapy. In vitro, AsPC-1 cells had negligible COX-2 activity, whereas Colo357 cells displayed high levels of COX-2 and PGE2 production. Cell growth and COX-2 activity decreased in all cell lines in the presence of apricoxib and addition of apricoxib improved response to chemotherapy. In vivo, addition of apricoxib to SOC significantly reduced primary tumor growth & almost eradicated metastases in mice bearing Colo357 but not AsPC-1 xenografts. Plasma VEGF levels were unaltered by apricoxib treatment in AsPC-1-bearing animals but were suppressed to undetectable levels in Colo357-bearing animals. Markers of EMT were significantly decreased in animals treated with apricoxib. Apricoxib enhances the efficacy of gemcitabine and erlotinib in vitro and in vivo & warrants clinical evaluation in patients with pancreatic cancer. A Phase 2 study is ongoing.

P26

Analysis of p53 Gene Polymorphisms in Familial Breast Cancer in a Colombian Population W. Sanchez M,* Y. Pinto, S. Ramirez, D. Gomez, D. Vanegas. *Military University Hospital and Universidad el Rosario, Bogota, Colombia.*

Background: The p53 tumor suppressor gene is frequently mutated in many forms of human carcinomas. Several studies have reported the association between breast cancer risk and genetic polymorphisms of p53 at exon 4 (codon 72), intron 3 (16bp duplication), intron 6 (MspI). However, the results are inconsistent. The purpose of the present case-control study was to analyze and correlate the genotype and allele frequencies at the three polymorphisms in p53 with the risk of familial breast cancer. Methods: We analyzed prospectively 186 familiar breast cancer patients and 186 controls. p53 genotype and allele frequencies were determined by RFLP analysis of peripheral blood DNA by direct counting. Odds ratios (OR) and 95% confidence intervals (CI) for breast cancer risk was done by logistic regression analysis using the SPSS 11.5 software. Results: Frequency of codon 72 genotype polymorphism was Arg/Arg (61,3% vs 44,2%;OR=2,19; CI:1,33-3,63, compared to Arg/Pro) Arg/Pro (32,3% vs 45,7%), Pro/Pro (6,5% vs 10,2%) between patients and controls respectively. Arg72 allele frequency was 77,4% and 67% ($p=0,001$) for patients and controls respectively. Frequency of intron 6 genotype polymorphism was W/W (75,3% vs 82,3%), W/M (24,2% vs 15,6%) M/M (0,5% vs 2,2%); while frequency of intron 3 genotype polymorphism was W/W (90,3% vs 98,9%), W/M (8,6% vs 0,5% OR=18;CI:2,25-141,84, compared to W/W) and M/M (1,1% vs 0,5%), between patients and controls. Conclusions: Our results support the important association between p53 codon 72 Arg/Arg and intron 3 W/W polymorphisms and risk of colombians familial breast cancer.

P27

Impact of CDK Inhibition Alone and in Combination with Chemotherapy on Breast Cancer Cell Proliferation E. Tarasewicz, A. Hardy, J. Straehla, A. Cooley, S. Zelivianski, J.S. Jeruss.* *Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL.*

Introduction: Our previous work showed that overexpression of cyclin D resulted in breast cancer cell cycle progression by mediating cdk4 phosphorylation and inhibition of Smad3 tumor suppression. Based on this finding, we hypothesized that treatment of cyclin overexpressing breast cancer cells with cdk inhibitors, alone and in combination with chemotherapy, would inhibit breast cancer cell proliferation. Methods: Immunoblotting was used to evaluate expression of study proteins in parental, vector control, and cyclin D overexpressing MCF7 and T47D cells and MDA-MB-231 cells, which express

cyclins D and E. T47D and MCF7 cells were treated with a cdk4 inhibitor alone or in combination with doxorubicin or paclitaxel. MDA-MB-231 cells were treated with cdk4, cdk4/6, or cdk2 inhibitors and chemotherapy. Cell proliferation was determined using an MTS assay. Results: Immunoblotting showed that study cells expressed cyclins D and E, cdk4, and Smad3 proteins. MTS assay proliferation results showed that treating T47D and MCF7 study cells with the cdk4 inhibitor had a dose-dependent effect on inhibiting cell proliferation and no effect on MDA-MB-231 cell proliferation. Treating all study cells with doxorubicin or paclitaxel had a dose-dependent effect on inhibiting cell proliferation. Combination therapy using a cdk4 inhibitor and doxorubicin or paclitaxel resulted in a further decrease in cell proliferation in MCF7 cells, while only the cdk4 inhibitor/paclitaxel combination treatment slowed T47D cell proliferation. MDA-MB-231 cells treated with the cdk4/6 or cdk2 inhibitor alone showed a slight decrease in cell proliferation. Combination therapy using both cdk4/6 and cdk2 inhibitor or paclitaxel and various cdk inhibitors resulted in a further decrease in cell proliferation in MDA-MB-231 cells. Conclusions: The results of our work indicated that cdk inhibitors have a growth inhibitory effect on cyclin overexpressing breast cancer cells alone or in combination with standard chemotherapeutic agents. Future studies will focus on the in vivo effects of these treatments in a murine cancer model.

P28

NVP-BEZ235, a novel dual PI3-kinase/mTOR inhibitor, enhances antitumor activities of gemcitabine and EMAP II in pancreatic cancer K. Ostapoff,* N. Awasthi, P.L. Yen, M.A. Schwarz, R.A. Brekken, R.E. Schwarz. *Surgery, UT Southwestern, Dallas, TX.*

Background: Gemcitabine (Gem, G) has limited benefits in pancreatic ductal adenocarcinoma (PDAC). The phosphatidylinositol-3-kinase (PI3K)/AKT and mammalian target of rapamycin (mTOR) signaling pathways are frequently dysregulated in diverse human cancers including PDAC. NVP-BEZ235 (BEZ, B) is a novel dual PI3K/mTOR inhibitor that has been shown to have antitumor activity in multiple tumor types. Endothelial monocyte activating polypeptide II (EMAP, E) is an antiendothelial and antiangiogenic agent that enhances Gem and docetaxel activity in PDAC. We tested the combination benefits of BEZ and Gem in addition to EMAP in experimental PDAC. Methods: In vitro cell proliferation and protein expression were analyzed by WST-1 assay and Western blotting. In vivo animal survival experiments were performed in NOD-SCID PDAC xenografts. Results: Cultured cells of PDAC (AsPC-1), endothelial (HUVECs) and fibroblast origin (WI-38) all expressed AKT and mTOR protein. BEZ inhibited in vitro cell proliferation of AsPC-1 and HUVECs cells, with some additive effects in combination with Gem or EMAP, after 72 hours of incubation. In AsPC-1, treatment of BEZ (100 nM), Gem (100 nM) and EMAP (1 μM) caused 34, -7, -16, 62, 51, 3 and 59 percent inhibition in proliferation in the B, G, E, B+G, B+E, G+E and B+G+E groups. In HUVECs, percent inhibition in proliferation was 35, 33, 15, 55, 35, 31 and 53 in the B, G, E, B+G, B+E, G+E and B+G+E groups, respectively. Compared to controls (median survival: 16 days), animal survival increased after BEZ and EMAP therapy alone (both 21 days) and Gem therapy alone (28 d). Further increases in survival occurred in combination therapy groups B+G (30 d, p=0.007), B+E (27 d, p=0.02), G+E (31 d, p=0.001) and B+G+E (33 d, p=0.004). Conclusions: Bez has experimental PDAC antitumor activity in vitro and in vivo that is further enhanced by combination of Gem and EMAP. These findings demonstrate advantages of combination therapy strategies targeting multiple pathways in pancreatic cancer treatment.

P29

Role of Dose and Schedule in Rapamycin-mediated Growth Inhibition in Breast Cancer P.F. McAuliffe,* A. Akcakanat, C. Sharma, F. Adkins, T. Sangai, G. Singh, A.M. Gonzalez-Angulo, F. Meric-Bernstam. *Surgical Oncology, M.D. Anderson Cancer Center, Houston, TX.*

INTRODUCTION: The mammalian target of rapamycin (mTOR) intracellular signaling pathway plays a key role in cell growth and metabolism and is being evaluated as a therapeutic target in breast cancer. While analogs of rapamycin (rapa) are effective anticancer agents in many preclinical models, objective response rates in clinical trials have been variable. This may be because the ideal dosing and schedule for rapa has not been determined. We hypothesize that intrinsic rapa resistance may be overcome with continuous dosing or with dose escalation. METHODS: MDA-MB-468 and MDA-MB-231, which are ER, PR and HER2 negative, were compared. After treatment with rapa or DMSO vehicle, cell proliferation was measured using sulforhodamine B (SRB) assay. Nu/nu mice with mammary fat pad tumors derived from either 468 or 231 cells were injected intraperitoneally with DMSO or 0.5mg/kg rapa daily (n=12/grp) for 2 wks, or with 1, 4 or 15 mg/kg rapa weekly for 3 wks (n=13/grp). Rapa levels were measured 24h after injection. Tumor volumes were compared using ANOVA. RESULTS: In 3 independent SRB assays, mean (±SEM) IC50 was 4±2nM for 468 (Fig,A) and >1000nM for 231 cells (Fig,B). Tumor volume after daily low-dose rapa was significantly decreased in 468 (0.15cm3 for DMSO vs 0.08cm3 for rapa, p<0.0001) but not in 231 xenografts (0.2 vs 0.18cm3, p=NS). In mice with 468 tumors, low (1, 4mg/kg) as well as high (15mg/kg) weekly doses of rapa decreased tumor volume (0.09, 0.11, 0.10cm3 respectively) compared to control (0.19cm3) (p<0.01). In contrast, only the highest dose of rapa (15mg/kg) significantly reduced 231 tumor volume (0.13cm3) compared to DMSO (0.24cm3) (p<0.03). Mean serum rapa levels were 21, 38, and 153ng/mL respectively for 1, 4, and 15 mg/kg (p<0.03). CONCLUSIONS: 468 cells are more sensitive to rapa than 231 cells, both in vitro and in vivo. In 231 cells, low-dose daily treatment could not overcome rapa resistance, whereas high-dose weekly rapa induced growth inhibition. Ongoing studies are focused on dose-dependent targets of rapa and strategies to enhance intra-tumoral drug delivery. The ideal dose and schedule of rapalogs required for growth suppression needs to be studied further.

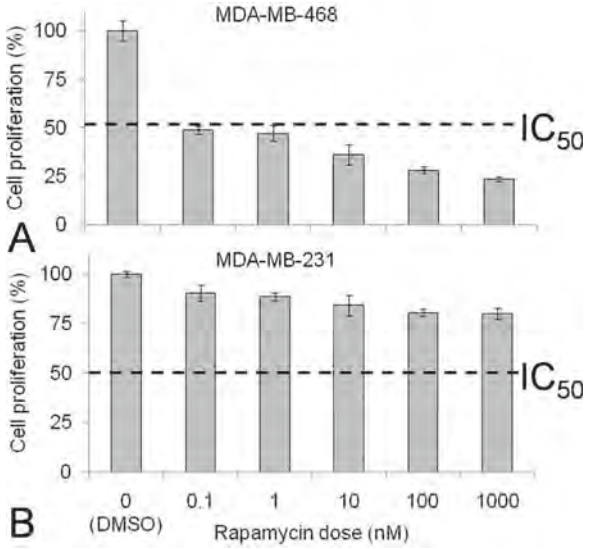

Figure 1. IC50 determined using SRB assay on 468 (A) or 231 (B) cell lines treated with increasing doses of rapamycin (0 - 1000 nM).

P30

A Mouse Model for Hepatocellular Carcinoma which Produces Murine Alpha-Fetoprotein, Measurable in the Plasma, with Tumor Progression V. Goz, Q. Wang, W. Luan, S.P. Hiotis.* *Surgery, Mount Sinai School of Medicine, New York, NY.*

Introduction: Several animals models for hepatocellular carcinoma (HCC) pose challenges in cost and feasibility to the mainstream laboratory. Models in unusual species such as the woodchuck are prohibitively expensive, with few available research materials such as monoclonal antibodies. Others based on spontaneous tumorigenesis in transgenic mice require maintenance of large colonies which often breed poorly and require months to over a year for tumorigenesis. Xenograft models are practical in some applications, but have no utility in studies involving immunity or immunotherapy. We describe here an immunocompetent and clinically relevant mouse model for HCC, in which tumor progression can be effectively followed via plasma alpha-Fetoprotein (AFP). Methods: C57L/J mice were challenged with intrahepatic Hepa 1-6 (iH16) at a cell dose of 1x10 6. Intrahepatic trypan blue (.25%) was used as vehicle in a control group. Plasma samples were assessed via western blot analysis over 4 weekly time points for murine AFP. Results: All iH16 animals developed liver tumors within 14 days of tumor challenge, assessable histologically as poorly differentiated HCC. Median survival of tumor-bearing mice

was 27 days, with 100% mortality by day 60. Progressive elevation in plasma AFP was measurable in test mice via western blot analysis with increasing tumor burden. No bands were observed in control mice. AFP was detectable in iH16 mice within 1 week, prior to the emergence of palpable tumor. AFP levels in mice with larger tumors were higher at all time points, indicating a strong correlation between tumor size and AFP levels. Conclusion: The iH16 model for HCC leads to reliable and rapid intrahepatic tumorigenesis, with predictable test animal mortality within 60 days of tumor challenge. This model is advantageous in its utility, providing a non-invasive means of following tumor progression with a clinically relevant plasma biomarker.

P31

PARP inhibition induces senescence in combination with ionizing radiation (IR) in human prostate cancer cells and tumors and improves the effect of IR J. Barreto-Andrade,* H.J. Mauceri, E.V. Efimova, M.A. Beckett, T.E. Darga, E.E. Vokes, S.J. Kron, R.R. Weichselbaum, M.C. Posner. *University of Chicago, Chicago, IL.*

INTRODUCTION: IR and surgery are current treatment options for localized prostate cancer; each has associated morbidity. PARP1 and 2 participate in DNA repair through several mechanisms. In addition to interaction with DNA damaging agents, PARP inhibitors have a potential role in cancer treatment as monotherapy in homologous recombination (HR)-deficient tumors, including PTEN-mutants, since PTEN is reported to mediate HR in some tumors. METHODS: Two human prostate cancer cell lines (PC-3 and DU-145) were treated in vitro and as tumor xenografts in nude mice with 6 Gy, alone or in combination with the PARP inhibitor ABT-888. Its effect on DNA damage was monitored by immunofluorescence (IF) staining of markers of DNA damage response. Cell proliferation and cycle phase were analyzed. RESULTS: Following treatment with IR and ABT-888, the combination treatment demonstrated increased cell killing and DNA damage in both cell lines compared to IR alone. Cell survival after 3 Gy was 48% vs 14% after combined treatment, $p = 0.003$. ABT-888 treatment alone was cytotoxic in the PTEN-deficient PC-3 cell line, decreasing cell survival by 23% compared to control, $p = 0.007$. Cell cycle analysis showed the majority of cells in permanent G2 cycle arrest; 67% vs 27% for control. At longer observation times, cells treated with IR and ABT-888 developed a senescent morphology, confirmed by positive SA-beta-Galactosidase staining and increased p21 expression (5-fold transcription expression compared to control). After combination treatment, both tumor models showed delayed growth compared to single treatment with IR, $p = 0.015$. PC-3 tumors treated with ABT-888 alone demonstrated significant growth delay compared to control tumors, $p = 0.017$. Histology sections of PC-3 tumors confirmed the presence of senescent cells. CONCLUSIONS: PARP inhibition significantly enhances the effect of IR in two prostate cancer cell lines in vitro and in vivo. PARP inhibition has a potential role as monotherapy in PTEN-deficient prostate tumors. Induction of senescence is a novel therapeutic approach that deserves further consideration in clinical studies.

P32

Effect of PARP inhibition in murine and human pancreatic cancer cell lines J. Barreto-Andrade,* E.V. Efimova, T.E. Darga, S.J. Kron, R.R. Weichselbaum, M.C. Posner. *University of Chicago, Chicago, IL.*

INTRODUCTION: Pancreatic cancer is a highly lethal tumor. Current therapy for unresectable disease is based on chemotherapy, sometimes combined with radiotherapy (IR), with marginal effectiveness. Poly(ADP)-ribose polymerase (PARP) inhibition has a potential role enhancing the antitumor effects of DNA damaging agents. We investigated PARP inhibition in combination with IR and gemcitabine in two pancreatic cancer cell lines. METHODS: Panc02, a syngeneic murine pancreatic cancer cell line, and MiaPaca2, a human pancreatic cancer cell line, were treated with gemcitabine and IR, alone or combined with the PARP inhibitor ABT-888. PARP activity was determined by measuring poly(ADP)-ribosylation of [32P]NAD. Cell survival was assessed, and DNA damage response was monitored using immunofluorescence (IF) staining of intracellular markers. In addition, panc02 cells were monitored using a green fluorescent protein construct with p53-binding protein 1 (GFP-53bp1). RESULTS: The addition of ABT-888 to either gemcitabine or IR enhanced their cytotoxic effects in both cell lines. Fluorescent imaging after treatment with ABT-888 and IR demonstrated an increased formation of DNA damage foci using immunostaining for gamma-H2AX, endogenous 53bp1 and ataxia-telangiectasia mutated (ATM) in both cell lines, and using the GFP-53bp1 construct in panc02 cells. ABT-888 combined with IR or gemcitabine induced significantly more cell death in vitro. After a 6 Gy dose of IR, mean cell survival was 49% vs. 16% with combination treatment, $p = 0.01$; after a 15 nM dose of gemcitabine, mean cell survival was 30% vs. 15% with the addition of ABT-888, $p = 0.01$. CONCLUSIONS: ABT-888 increased the cytotoxic effects of gemcitabine and IR in two different pancreatic cancer cell lines and increased the formation of foci of DNA damage. We are currently investigating these tumor cells in xenograft models.

P33

The Role of Screening Mammography in Detecting Breast Cancer: Who Should Be Screened? A.L. Kong,* K.A. Kelley, T.W. Yen. *Surgery, Medical College of Wisconsin, Milwaukee, WI.*

Introduction: Decreased mammography screening may result in fewer screen-detected cancers and more clinically apparent cancers, resulting in more advanced disease presentation. The purpose of this study is to evaluate methods of breast cancer detection by patient age and stage of presentation. We also evaluate potential cancers missed if the U.S. Preventative Services Task Force (USPSTF) guidelines, which recommend against routine annual mammography for women age 40-49 and age 75 and older, are followed. Methods: A retrospective chart review of a single institution's breast cancer tumor registry was conducted from 1999 to 2009. Exclusion criteria were males, LCIS, stage IV diagnosis or history of ipsilateral breast cancer. Clinicopathologic data was collected, including breast cancer presentation (palpable versus non-palpable). Results: A total of 2,350 women with breast cancer were identified; 46% had palpable tumors and 54% had non-palpable tumors. Approximately 50% of cancers in the 40-49 and >75 age groups were non-palpable. Of all screen-detected non-palpable cancers, 20% were in the 40-49 age group and 13% were in the >75 age group. Compared to palpable tumors, non-palpable tumors were more likely to occur in older women, be non-invasive, well-differentiated, hormone receptor positive, and present at a lower stage (Table 1). Women with non-palpable tumors were also more likely to be treated with lumpectomy and have fewer positive nodes. Of the 1,215 women with non-palpable tumors who underwent screening mammography, only 35 (3%) cancers would be missed using American Cancer Society screening recommendations while 398 (33%) cancers would be potentially missed following USPSTF recommendations. Of these 398 missed cancers, 62% were invasive and 37% were in situ. In addition, 44% of stage 3 and 37% of stage 2 presenting cancers would be potentially missed. Conclusions: Women with non-palpable breast cancers, compared to those presenting with palpable tumors, were more likely to have an earlier stage cancer with better prognostic features. Screening mammography remains important in the early diagnosis of breast cancer in women 40 years of age and older.

Clinicopathologic characteristics of palpable and non-palpable tumors

Variable	Palpable (N=1076)	Non-Palpable (N=1274)	P-Value
Age at Diagnosis	mean 55.4 (SD 14.23)	mean 59.2 (SD 12.02)	<0.0001
Histology			<0.0001
Invasive ductal carcinoma	761 (71%)	639 (50%)	
Invasive lobular carcinoma	122 (11%)	102 (8%)	
Ductal carcinoma in situ	99 (9%)	452 (35%)	
Other Carcinoma	72 (7%)	72 (6%)	
Unknown	22 (2%)	9 (1%)	
Grade/Differentiation			<0.0001
Well Differentiated	203 (19%)	332 (26%)	
ModeratelyDifferentiated	421 (39%)	460 (36%)	
Poorly Differentiated	319 (30%)	257 (20%)	
Not Determined	133 (12%)	225 (18%)	
ER/PR			<0.0001
Positive	704 (65%)	870 (68%)	
Negative	233 (22%)	154 (12%)	
Unknown	139 (13%)	250 (20%)	
Number of Positive Nodes *	mean 1.9 (SD 5.01)	mean 0.7 (SD 2.38)	<0.0001
Pathologic TNM Stage Group 6th Edition AJCC Staging			<0.0001
0	62 (6%)	313 (25%)	
I	351 (33%)	592 (47%)	
II	392 (36%)	221 (17%)	
III	154 (14%)	32 (2%)	
Unknown	117 (11%)	116 (9%)	
Surgery			<0.0001
Lumpectomy	650 (60%)	1007 (79%)	
Mastectomy	340 (32%)	245 (19%)	
None	79 (7%)	21 (2%)	
Unknown	7 (1%)	1 (0.1%)	

*includes patients with invasive disease only

P34

Is there a role for routine screening MRI in women with LCIS?

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Annual breast MRI is beneficial for women at increased risk due to BRCA mutations. Women with LCIS are also at elevated risk, yet the pathogenesis of cancer in women with LCIS differs from women with BRCA mutations, and the benefit of MRI screening is unclear. The purpose of this study was to examine the benefit of MRI screening in a large population of patients with LCIS. Methods:From a prospectively maintained database of 880 women with LCIS undergoing screening between 11/80-12/09 we identified 619 pts diagnosed with LCIS after 4/99(when we began using screening MRI). Patients with breast cancer and those taking chemoprevention were excluded. All pts were offered annual mammography and annual/biannual breast exam. MRI was performed at the discretion of the physician and patient. In Cox regression analysis, MRI was examined as a time-dependent variable. Results:MRI screening was performed in 351(57%) pts. Median time from LCIS diagnosis to first MRI was 8.3 mos., median number of MRIs/pt was 3(range 1-17). Patients having MRI were younger(49 vs 54yrs,p<.0001) more likely to have a 1st degree relative with breast cancer(27% vs 20%, p=0.02) and more likely to have ≥ 1 biopsy during surveillance(35% vs 14%,p<0.0001).There was no difference in BIRADS breast density or presence of concurrent atypia between groups. At a median follow-up of 41 mos(range 1-131),64(10%) patients were diagnosed with 67 screen detected cancers. The crude cancer detection rate was 10.8% and 10.7% in the MRI and no-MRI gp respectively. Adjusting for length of follow-up, MRI had an HR 1.6 (95%CI 0.98-2.70,p=0.06) for cancer detection. In the MRI gp, cancer was seen on MRI in 21/351(6%) pts and on standard imaging in 17(4.8%). There was no difference in stage distribution or tumor size by group or method of detection. Conclusion:Young age at LCIS diagnosis and family history of breast cancer were associated with MRI screening in our LCIS population. MRI screening resulted in significantly more biopsies during surveillance and a borderline increase in cancer detection (p=0.06), yet was not associated with earlier stage or smaller tumor size at diagnosis. A benefit for routine MRI screening in LCIS is not supported by this study.

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Usefulness of the Neutrophil to Lymphocyte Ratio in Predicting Short-and Long-Term Mortality in Breast Cancer Patients

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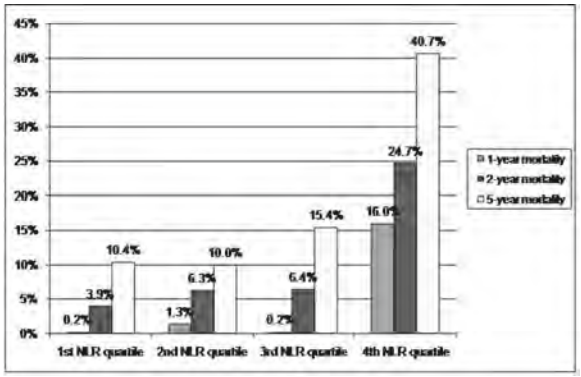
Background : The neutrophil to lymphocyte ratio (NLR) is a strong predictor of mortality in patients with colorectal, gastric, hepatocellular, pancreatic and lung cancer. To date, the utility of NLR to predict mortality in breast cancer patients has not been studied. Therefore, the aim of our study was to determine whether the NLR is predictive of short and long-term mortality in breast cancer patients. Methods: Our observational study used an unselected cohort of breast cancer patients treated between January 2004 and December 2006. A total of 316 patients had a differential leukocyte count recorded prior to chemotherapy. Survival status was retrieved from our cancer registry and social security death index. Survival analysis, stratified by NLR quartiles, was used to evaluate the predictive value of NLR. Results: Patients in the highest NLR quartile (NLR > 3.3) had higher 1-year (16% vs. 0%) and 5-year (44% vs. 13%) mortality rates compared to those in the lowest quartile (NLR < 1.8) (P<0.0001). Those in the highest NLR quartile were statistically significantly older and had more advanced stages of cancer. After adjusting for the factors affecting the mortality and/or NLR (using two multivariate models), NLR level >3.3 remained an independent significant predictor of mortality in both models (Hazard ratio 3.13, p=0.01) (Hazard ratio 4.09, p=0.002). Conclusion: NLR is an independent predictor of short- and long-term mortality in breast cancer patients with NLR>3.3. We suggest prospective studies to evaluate the NLR as a simple prognostic test for breast cancer.



The 1-, 2- and 5- year mortality rates according to NLR quartiles among breast cancer patients. NLR=Neutrophil to Lymphocyte Ratio, p<0.0001.

P36

Clinical Impact of Intraoperative Pathology Analysis for Patients Undergoing Breast Cancer Surgery

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Second surgeries in breast cancer, necessary in 30 to 60% of cases, are a significant detriment to the care of patients and increase the cost of therapy. We examined the impact of frozen section for margins and SLN on multiple facets of breast cancer surgery. Methods. We compared the 8 months prior to the establishment of a pathology lab, when intraoperative pathology consultaton was not available, to the 8 months subsequent, when it was performed routinely. Review of our IRB approved database was restricted to patients undergoing primary breast cancer surgery at our institution. Results. 271 patients were treated between 1/09 and 8/09 and 278 patients from 9/09 to 4/10. There were no significant differences in the age, presentation, histology or stage between these two groups. The average number of surgeries per patient dropped from 1.5 to 1.23; the fraction of patients requiring one surgery increased from 59% to 80%. Unplanned 2nd surgeries dropped from 31% to 11% and re-excision rates dropped from 26% to 9%. Among BCT-eligible patients, the BCT rate rose from 90% to 94%, and our BCT rate among patients undergoing neoadjuvant chemotherapy rose from 39% to 46%. Among 139 patients undergoing SLN biopsy with frozen section, there were 26 true positives, 0 false positives and 2 false negative, allowing 93% of node positive patients to avoid a 2nd operation for ALND. While the number of operations decreased, time spent operating increased between 13 and 35 minutes per case, depending on the operation. Overall, the incorporation of frozen section was time neutral, with minimal difference between the hours needed to complete therapy for 100 patients, ranging from a savings of 7 minutes per patient to an increase of 6 minutes per patient, depending on case distribution. Operative charges decreased between $540 and $998 per patient. Discussion. Incorporation of routine intraoperative margin and SLN assessment results in significant clinical benefit to the patient, dramatically reducing the number of 2nd surgeries. This did not significantly impact the time it required to treat patients but did substantially reduce the cost of therapy.

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Rural-Urban Disparities in the Use of Post-Mastectomy Radiation for Breast Cancer

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Background: Post-mastectomy radiation therapy (RT) is indicated for select breast cancer (BCa) patients. Patients with chronic illnesses living in rural areas are less likely to receive standard care than those living in urban areas. We hypothesized that candidates for post-mastectomy RT residing in rural areas would receive lower rates of RT than urban patients. Methods: We used the Surveillance, Epidemiology, and End Results database to identify patients diagnosed with BCa and treated with mastectomy in Sacramento County and its surrounding 13 counties between 2000 and 2006. All patients were without

distant metastases and had tumors > 5cm size, ≥ 4 metastatic lymph nodes, or both. According to a scale developed by the United States Department of Agriculture, a county was designated as rural if the population was less than 1 million. We used multivariate logistic regression models to predict use of RT; other than rural-urban status, covariates included patient age, race/ethnicity, tumor size, grade, hormone receptor status, and number of nodal metastases. Likelihood of undergoing RT was reported as odds ratios (OR) with 95% confidence intervals (CI); significance was set at $p \leq 0.05$. The number of radiation oncologists in rural and urban counties was determined using the American Medical Association database and evaluated in relation to the populations of these areas using census data. Results: Entry criteria were met by 1,507 patients. The majority of patients (56.5%) were from urban counties; only 61% received RT. A radiation oncologist was unavailable in 8/10 rural counties and 2/4 urban counties. Each radiation oncologist served 88,804 patients in rural counties compared with 68,624 patients in urban counties. On multivariate analysis, rural patients (OR 0.56, CI 0.44-0.72) and increasing age were the only factors predicting a decreased likelihood of receiving RT (OR 0.97, CI 0.96-0.98). Conclusions: Rural residents with advanced breast cancers are less likely to receive post-mastectomy RT according to current guidelines. The reasons for this disparity are unknown, but our data suggest that it may be due to limited RT access in rural areas.

P38

Ductal carcinoma in situ of the breast and subsequent distant metastases R.E. Roses,* B. Arun, S. Lari, E.A. Mittendorf, A. Lucci, H.M. Kuerer. *md anderson cancer center, Houston, TX.*

INTRODUCTION: The objective of the multidisciplinary treatment of ductal carcinoma in situ of the breast (DCIS) is to minimize the risk of progression to advanced breast cancer. Nonetheless, the rare patient diagnosed with DCIS can develop distant breast cancer metastases (DM). This study was performed to identify clinical and pathologic features that may contribute to such outcomes. METHODS: After IRB approval, the clinical and pathologic variables of 25 patients who presented with distant metastases after an initial diagnosis of pure DCIS from 1996 to 2008 were analyzed. RESULTS: The median age of patients at the time of diagnosis of DCIS was 48 years (range: 28-62 years); 48% of patients were post-menopausal. The median size of DCIS lesions at the time of initial surgery was 1.3 cm (range: 0.4-7.5 cm). Forty-four percent of patients had grade 3 disease; 64% of patients had ER negative disease. Definitive surgical therapy consisted of total mastectomy in 48% of cases. Seventy-seven percent of patients who underwent segmental mastectomy had radiotherapy. Median time from DCIS diagnosis to subsequent DM was 4.5 years (range: 1.0 – 11.2 years). Sixteen patients (66%) developed an invasive local-regional recurrence and synchronous or subsequent DM. Nine patients (34%) developed DM without local-regional recurrence. At last follow-up, 56% of patients had died of disease with a median time to death of 2.4 years. No dominant variables could be identified in the group of patients that developed DM without an intervening local regional recurrence. At a median follow-up of 4.7 years, the rate of development of DM was 0.14% among 2123 patients treated with surgery and/or radiation for pure DCIS at our institution. CONCLUSIONS: DM following initial treatment for pure DCIS is a rare event. While the majority of patients who develop DM after a diagnosis of pure DCIS have a preceding invasive local regional recurrence, some present with subsequent DM alone. Further study is required to identify clinical and pathologic features that predict this more rapid disease progression.

P39

Prediction of Oncotype DX Scores for Estrogen receptor (ER) positive and Lymph Node (LN) Positive Breast Tumors Based on Histopathological Characteristics: A Nomogram K.K. Turaga,[1]* G. Acs,[2] N.N. Esposito,[2] C. Laronga.[2] *1. Surgery, Medical College of Wisconsin, Milwaukee, WI; 2. Moffitt Cancer Center, Tampa, FL.*

Introduction: Oncotype DX (ODX) is a genomic assay validated to predict 10-yr distant recurrence in patients with ER positive LN negative breast tumors. Limited ODX data exists for prediction in LN positive disease. Our objective was to generate nomograms to predict the ODX score for LN negative and LN positive disease based on routine histopathological characteristics. Methods: We included patients with ER positive tumors who underwent ODX testing at our institution from 2006-2010. Nomograms for prediction of the ODX score were built for node negative patients in the original dataset and independently validated. The same model was then applied to patients with node positive disease in both datasets to estimate the receiver operating characteristics (ROC) curves Results: There were 153 patients (24 LN+, 129 LN-) in the training dataset and 195 (32 LN+, 163 LN-) in the validation dataset. For node negative patients, the area under the curve (AUC) in the validation dataset was 0.67 (0.61-0.74) for prediction of score 18 and 0.83 (0.68-0.98) for prediction of score ≥ 31. For node positive patients, the AUC was 0.89 (0.74-1.0) for RS≥18 and 0.78 (0.45-1.0) for RS≥31 in the original dataset, and 0.69(0.50-0.87) for RS≥18 and1.0 for RS≥31 in the validation dataset. Conclusions: The nomograms based on histopathological parameters can be used to predict the Oncotype DX recurrence score. Until more data exists with regards to LN positive disease, this nomogram may serve as a surrogate "marker" for Oncotype DX.

P40

Sentinel Lymph Node Biopsy Overused in Breast Conserving Surgery for DCIS N.B. Jones,* J. Wilson, J. Laubacher, W.B. Farrar, D.M. Agnese. *Surgery, The Ohio State University, Columbus, OH.*

Background: Current NCCN guidelines (V.2.2010) for management of ductal carcinoma in-situ (DCIS) recommend breast conservation therapy (BCT) and whole breast radiation without axillary lymph node sampling or total mastectomy with or without sentinel lymph node biopsy (SLNB). Despite these guidelines, SLNB is commonly performed in the setting of BCT for DCIS and omitted in mastectomy cases. We hypothesize SLNB is overused in BCT and is associated with complications such as 5-7% incidence of lymphedema. Methods: A prospectively maintained breast cancer database was retrospectively reviewed, identifying 555 cases of DCIS (548 patients) from 1998-2009 treated with BCT or mastectomy. Clinical pathologic characteristics of the tumor and patients with DCIS as well as follow-up were evaluated using Student's t test and Fisher's exact test. Results: Of the 354 patients who elected BCT, 104 patients had a SLNB performed. Contrastingly, in the mastectomy group of 201 patients, 75 patients did not have a SLNB. Table 1 summarizes patient characteristics. For BCT patients, high grade or multicentric DCIS, presence of comedo necrosis, and location of tumor in upper outer quadrant were statistically significant factors for performing SLNB. Surgeon preference may also be influential in decision to perform SLNB with BCT. 35 patients (4.5%) were upstaged from DCIS (stage 0) to T1 (stage 1) regardless of operation with no significant predictors identified. Eleven of these patients underwent BCT with SLNB at original operation, whereas 2 patients had mastectomy without SLNB. One of 35 patients (2.9%) had a positive node, which was discovered after pathology returned from lumpectomy and delayed SLNB was performed. Median follow-up (years) was statistically shorter for mastectomy with SLNB and lumpectomy with SLNB groups, correlating with an increasing trend over past 10 years in performing SLNB with either operation. Conclusion: SLNB is overused in the setting of BCT for DCIS in that no positive lymph nodes were identified for pathologic DCIS and nodal status was not affected by delayed SLNB for one upstaged patient. SLNB also subjects these low risk patients to unnecessary morbidity.

Table 1 - Patient Characteristics with DCIS

	Mastectomy without SLNB	Mastectomy with SLNB	Lumpectomy with SLNB	Lumpectomy without SLNB
Total number- DCIS (Stage 0)	75	124	104	250
Avg. age at diagnosis	56	54	58	58
Race (% Caucasian)	94.7%	88.7%	85.6%	90.0%
# upstaged to Stage 1(N=785)	2	13	11	8
# lymph nodes positive	0	0	0	0
Grade 2 or 3	83.6%	87.9%	94.2% *	77.1% *
Comedo type DCIS	37.3%	52.0%	61.5% *	34.4% *
Multicentric/widespread DCIS	56.0%	47.1%	9.6% *	2.4% *
Location in upper outer quadrant	42.0%	39.4%	63.6% *	48.6% *
Tamoxifen	38.7%	35.5%	56.7%	60.0%
Radiation	5.3%	2.4%	94.2%	82.4%
Alive with NED	92.0%	96.8%	100.0%	95.2%
Median follow-up (years)	7.8 *	2.6 *	3.4 *	6.6 *

* p<0.001 by Fisher's Exact or Student's t test

P41

MRI in Surgical Management of Women with Ductal Carcinoma In Situ N. Khakpour,* S. Willet, J. Kiluk, M.C. Lee, W. Sun, C. Laronga. *Women's Oncology, Moffitt, Tampa, FL.*

Background: The impact of breast magnetic resonance imaging (MRI) on surgical management for Ductal Carcinoma In Situ (DCIS) remains largely undefined. Our objective was to determine the effect of pre-operative MRI with mammography (MMG) versus MMG alone in the management of women with DCIS. Methods: A retrospective review of a prospective DCIS database identified 196 patients diagnosed with DCIS on core biopsy between December 1999 and November 2009. Of these, 104 consecutive patients who underwent both MRI and MMG and 92 with only MMG prior to surgery were evaluated. The groups were analyzed for patient demographics, clinicopathologic factors, imaging results, and surgical procedures. Chi-square and student t-test were used for statistical evaluation. Results: Median age was 57 years (range 28-85) for the MRI group and 60 (range 32-96) for the MMG group (p=0.002). Racial composition, menopausal status, prior cancer diagnosis, tumor grade, and the presence of necrosis were similar in both groups. A significant difference (p=0.007) was noted in the frequency of 1st degree relatives with breast/ovarian cancer in the MMG alone group (30.0% vs. 14.4%). MRI imaging revealed additional lesions in 36 patients (35%), leading to 18 (17%) additional biopsies. Six (5.8%) biopsies showed additional cancer and 12 (11.5%) were benign. Positive MRI biopsies did not alter these patients' surgical choice. Rates of mastectomy, breast conserving surgery, re-excision, and time to initial surgery were not statistically significant between the two groups. Additionally, there was no difference in use of adjuvant radiation and hormone therapy (p=0.47). The incidence of in-breast recurrence or contralateral cancers were similar in both groups (p=0.23). Median follow-up time was 34 months (2-100 months) for the MRI group and 38 months (1-113 months) for the MMG group (p=0.032). Conclusions: In this patient population, MRI use did not significantly alter surgical planning or outcomes. Routine pre-operative MRI use in patients with DCIS is of limited utility and warrants further prospective investigation.

P42

Follow-up axillary staging is important in neoadjuvant chemotherapy (neoCTX pts) presenting with node-pos (N+) breast CA T. Schwartz,* M. Sabel, R. Jagsi, A. Kolli, K. Kilbride, T. Breslin, K. Diehl, V. Cimmino, A. Chang, L. Newman. *University of Michigan, Ann Arbor, MI.*

Background:Pts presenting with N+ breast CA are often referred for neoCTX. Among pts undergoing primary surgery, routine axillary lymph node dissection (ALND) has been questioned in N+ disease identified by sentinel lymph node (SLN). The role of ALND following neoCTX in pts presenting with N+ disease is unclear. Our goal was to analyze local and distant recurrence (LR;DR) in neoCTX pts based upon pre-and-post-neoCTX nodal status. Methods:We reviewed 248 neoCTX pts (1998-2009)from a prospectively maintained single institution database. Axillary staging was documented pre-neoCTX by clinical (physical exam; ultrasound) and pathologic (fine needle aspiration; SLN) strategies. Pts with pre-neoCTX N-neg disease underwent breast surgery only after neoCTX; pts with pre-neoCTX N+ disease underwent ALND concomitantly with breast surgery after neoCTX; a subset of these pts had post-neoCTX SLN biopsy as well. Median follow up was 26.5 mos. Results: Median age-48; mean tumor size was 4 cm. 87% of total were staged histologically prior to treatment. 209 (84.3%) were N+. Of the 209 pre-neoCTX N+ cases, 39% were downstaged to N-neg according to post-neoCTX ALND. Trends (borderline statistically-significant) for higher DR were observed for pts that were persistently N+ pre- and post-neoCTX (20%) compared to downstaged pts (16%) and N-neg pts at presentation (5%) (p=0.055). LR was higher in persistently N+ cases (6.3%) vs downstaged (3.6%) and N-neg pts at presentation (5.1%). Of the 82 downstaged pts, 75 received XRT, which decreased LR from 33% to 1.3% in this subset (p=0.013). Among pts undergoing post-neoCTX SLN biopsy with ALND, the SLN was falsely negative in 13%. Conclusions: Pathologic staging of the axilla before and after neoCTX is important for treatment planning and prognostication. Pts with persistently N+ disease have increased risk of DR and should be considered candidates for high-risk systemic therapy protocols. Pts that are downstaged to N-neg face increased risk of LR compared to pts that present with N-neg disease, and they benefit from XRT. Accuracy of post-neoCTX SLN biopsy to identify downstaged patients warrants further study.

P43

Invasive lobular carcinoma predicts disseminated tumor cells in primary breast cancer patients A. Lodhi,[1] S. Krishnamurthy,[2] A. Bhattacharyya,[1] C. Hall,[1] A. Anderson,[1] B. Singh,[1] A. Lucci.[1]* *1. Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX; 2. University of Texas MD Anderson Cancer Center - Pathology, Houston, TX.*

Introduction: Invasive lobular cancers (ILC) represent 5-15% of breast cancer (BC) cases and are usually well-differentiated, estrogen receptor (ER) positive and may have delayed recurrences. Disseminated tumor cells (DTCs) in bone marrow (BM) predict worse outcomes in primary BC. The purpose of this study was to determine if DTCs were associated with ILC in stage I-III BC patients. Methods: Informed consent was obtained under IRB-approved study, wherein bilateral BM aspirates (5ml each) were collected during surgery for clinical stage I-III BC. Aspirates were examined for DTCs using an anti-CK antibody cocktail (AE1/AE3, CAM5.2, MNF116, CK8 and 18) following cytospin. One or more CK-positive cells meeting morphologic criteria for malignancy was considered a positive result. Statistics were performed using STATA IC11 employing Chi-square tests. Results: We prospectively evaluated 273 patients. Median follow-up was 25 months and mean age 53 (25-80) years. Thirty-nine patients (14%) had ILC and 232 (85%) had invasive ductal carcinoma (IDC). Seventy-nine (29%) patients received neoadjuvant chemotherapy (NACT) prior to BM collection. DTCs were identified in 89/273(33%) patients. DTCs were identified in a significantly higher percentage of ILC patients (19/39, 49%) vs. those with IDCs (70/234, 30%); {OR=2.2, 95% CI=1.05-4.68, P=0.02}. ER positivity rate was much higher in ILCs (35/39, 90%) vs. IDCs (157/234, 67%); {OR=4.3, 95% CI=1.29-17.45, P=0.004}. None of the nine ILC patients treated with NACT achieved pathologic complete response (0/9) vs. IDCs (27/98, 28%), {P=0.11}. Presence of DTCs in ILC patients did not correlate with tumor size, stage or administration of NACT. Conclusions: About a third of primary BC patients had DTCs. However, nearly half of ILC patients had DTCs. Larger studies are needed to see if DTCs in ILC are responsible for late recurrences.

P44

Surgery Does Not Improve Survival in Stage IV Breast Cancer J. Najita,[2] M. Hughes,[2] S. Javid,[6] Y. Wong,[4] K. Marcom,[5] B. Carter,[7] J. Niland,[8] S. Edge,[3] H. Burstein,[2] M. Golshan.[1]* *1. Brigham and women's Hospital, Boston, MA; 2. Dana Farber Cancer Institute, Boston, MA; 3. Roswell Park Cancer Institute, Buffalo, NY; 4. Fox Chase Cancer Center, Philadelphia, PA; 5. Duke University Medical Center, Durham, NC; 6. Fred Hutchison Cancer Center, Seattle, WA; 7. Moffitt Cancer Center, Tampa, FL; 8. City of Hope, Duarte, CA.*

Introduction: Standard treatment for stage IV breast cancer is systemic therapy without resection of the primary tumor. Registry-based studies suggest that resection of the primary tumor may improve survival in Stage IV cancer. These studies may be biased because of differences between those who do and do not have surgery. To reduce the chance of bias, we performed an analysis on patients with stage IV disease at the time of presentation who received surgery followed by systemic therapy compared to a matched group who received systemic therapy only (nonsurg). Methods: The National Comprehensive Cancer Network (NCCN) Breast Cancer Outcomes Database with data from 8 NCCN centers was searched for patients with distant metastatic breast cancer at initial presentation who either received surgery prior to any systemic therapy (surg) or received systemic therapy only. To identify nonsurg patients who were comparable to the surg group, patients in the nonsurg group were matched to those in the surg group by age at diagnosis, ER, HER2 status, and number of metastatic sites using a 5:1 matching ratio. Survival estimates were described using the Kaplan-Meier method. A stratified Cox model was used to account for the matching. Results: There were 1048 patients in the NCCN database diagnosed with Stage IV breast cancer from 1997 to 2007. 551 patients were eligible for the study and had data on all 4 factors used in the matching: 54 in the surg group and 497 in the nonsurg group, of whom 236 were matched to the surgery group. Characteristics and demographics of the two groups were similar (Table 1). In the stratified analysis, survival was similar between the groups after covariate adjustment (HR=0.94, CI=0.83-1.07, p=0.35) with a median survival of 3.4 years in the nonsurg group compared to 3.5 years in the surgery group. Conclusion: When matching for the variables associated with a survival benefit in previous studies, surgery was not shown to improve sur-

vival in the stage IV setting. Until the results of prospective studies become available, the survival benefit purported with surgery in the stage IV setting should be viewed with caution.

Table 1 CHARACTERISTICS AFTER MATCHING

Matching on age at metastatic diagnosis, ER, HER2, number of metastatic sites (5:1 matching)

Table 1: Patient characteristics AFTER matching

Variable	no surgery (n = 236)	surgery -> systemic rx (n = 59)	p-value
Age (years)			
<55	160 (68%)	35 (65%)	0.67
>=55	76 (32%)	19 (35%)	
ER status			
Positive	178 (75%)	39 (72%)	0.72
Negative	60 (25%)	15 (28%)	
HER2 status			
Positive	76 (32%)	19 (35%)	0.67
Negative	160 (68%)	35 (65%)	
No. metastases			
1	151 (64%)	37 (69%)	0.53
>=1	85 (36%)	17 (31%)	
Metastatic sites			
Liver	79 (33%)	14 (26%)	0.38
Lung	48 (20%)	17 (31%)	0.08
Bone	157 (67%)	34 (63%)	0.63
Brain	8 (3%)	2 (4%)	1.00*
Systemic therapy			
Any chemotherapy	199 (84%)	42 (78%)	0.28
Any hormonal therapy	158 (67%)	40 (74%)	0.31
Any trastuzumab	100 (42%)	19 (35%)	0.36
Any RT (primary or met)	22 (9%)	7 (13%)	0.42

*Based on a Fisher exact test. All other p-values are based on a Chi-square test

P45

Avoiding Mastectomy: Partial Breast Irradiation (PBI) in Breast Cancer Patients with Pacemakers and Automated Implantable Cardioverter-Defibrillators (AICD) R. Croshaw,* Y. Kim, E. Lappinen, T. Julian, M. Trombetta. *Human Oncology, Allegheny General Hospital, Pittsburgh, PA.*

Introduction: The objective of this report is to evaluate the safety, efficacy, toxicity, and planning concerns of PBI with either 3-D conformal radiotherapy (3-D CRT) or high dose rate balloon brachytherapy (HDR) for breast cancer patients with a pacemaker or AICD desiring breast conservation. Methods: An IRB approved review was performed of prospectively obtained data on early-stage breast cancer patients with an implanted pacemaker or AICD treated between April 2007 and July 2010. Patients were treated with either 3-D CRT or HDR based on the NSABP-B39 protocol. Treatment planning and simulation data, as well as treatment records were evaluated. Device interrogation was performed after the first and last radiation treatment with comparative cardiac monitoring performed prior to and following the first three treatments. Results: There were 8 patients treated by lumpectomy with a median of 7 months (range, 0 to 23 months) of follow-up. 3 patients received balloon brachytherapy with either a MammoSite® single-lumen balloon catheter (n=1), or a Contura® multi-lumen balloon catheter (n=2) delivering 34 Gy in 10 fractions. Mean lumpectomy cavity volume (LCV) was 53.4cc (range 49.3 to 59.8cc) with a planning target volume for evaluation (PTV_eval) coverage of 93.6% (range, 90.2 to 96.3%). The maximum dose of radiation delivered to the device was 103 cGy (range 39- 103 cGy) with a mean pacemaker distance to lumpectomy cavity (DLC) of 9.1cm (range 4.3- 23.2cm). 5 patients received 3-D CRT consisting of 38.5 Gy in 10 fractions. The mean LCV was 67.8cc (range 13.5-132.7cc). The mean PTV_eval coverage was 97.3% (range, 92.5-99.8%). The maximum dose delivered to the device was 168 cGy (range, 23-168 cGy) at a DLC of 9cm (range, 1.8-24.3cm)(fig. 1). No delays in treatment or local toxicities greater than grade I were identified. No adverse events were noted during or after treatment related to the pacemaker or AICD. Conclusions: The ability to safely deliver appropriate PBI therapy in patients with pacemakers or AICDs who desire breast preservation is supported by these data.

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Clinical significance of serum anti-p53 antibodies detection in breast cancer patients: Correlation with patient profiles and conventional tumor markers A. Takeda,* T. Ohara. *Digestive Surgery, International University of Health and Welfare Hospital, Tochigi, Japan.*

Background: Circulating anti-p53 antibodies can be found in sera of patients with various human malignancies, including breast cancer. No large-scale studies have examined the testing of serum anti-p53 antibodies (s-p53 abs) compared with the conventional markers of breast cancer, such as CEA, CA15-3 and NCC-ST439. The sensitivity of s-p53 abs was evaluated in breast cancer patients, and the relationship between the presence of s-p53 abs and patient profiles was investigated. Methods: Two hundred and fifty seven females who are diagnosed with primary breast cancer were enrolled. The titers of s-p53 abs were assessed preoperatively by the anti-p53 EIA kit (MESACUP anti-p53 TEST,MBL,JAPAN) which was domestically developed through a collaborative study. Results: The patients were divided into sero-positive and sero-negative groups. There was significant difference in nodal involvement (p=0.0001), however, no significant differences were observed in tumor size, histological type, TNM stage classification, presence of estrogen and progesterone receptors between two groups. The sensitivity of s-p53 abs was significantly higher than CEA (p=0.0007), CA15-5 (p=0.013). No obvious associations were evident between the status of s-p53 abs and values of the three tumor markers (p=0.792; CEA, 0.339; CA15-3, 0.182; NCC-ST439). The positive rate of the conventional three markers showed a significant increase with the progression of the stage from stage 1 to 3, however, sensitivity rate of s-p53 abs was no remarkable changes among three stages. The positive rates of the three conventional markers were extremely low at 4.8% (CEA), 2.9% (CA15-3) and 2.9% (NCC-ST439) in stage 1, which rate increased with the progression of the stages, showing 5.0%, 8.4%, 10.9% in stage 2 and 13.3%, 26.7%, 33.3% in stage 3. But s-p53 abs was 14.3% in stage 1, 15.1% in stage 2, 20.0% in stage 3, and showed a significant high positive rate in stage 1(p=0.0001) and 2(p=0.001) compared with the conventional markers. Conclusions: Measurement of s-p53 abs titers is expected to be effective as a biomarker in detecting early stage breast cancer.

P47

High TLK1B Overexpression in Breast Cancer Predicts Doxorubicin Resistance L.N. Davezac,[1]* M.A. Sicard,[1] Q.D. Chu, M.D.,[1] R.H. Kim, M.D.,[1] A. De Benedetti, Ph.D.,[2] B.D. Li, M.D..[1] *1. Surgery, Louisiana State University Health Sciences Center in Shreveport, Shreveport, LA; 2. Department of Biochemistry and Molecular Biology, Shreveport, LA.*

Introduction: TLK1B, whose upregulation is correlated with eIF4E overexpression, is a mammalian serine/threonine kinase that functions primarily in the nucleus. It phosphorylates histone H3 and Asf1, leading to chromatin remodeling concomitant with repair of double stranded DNA breaks (DSBs).

In vitro, this has been observed as resistance by cancer cells to chemotherapeutic agents that kill cells via generation of DSBs, such as doxorubicin. Methods: In this case control study, 16 patients rendered disease-free surgically and treated with doxorubicin (DSBs)-based chemotherapy was compared with 16 similarly matched patients treated with non-DSBs inducing adjuvant chemotherapy. TLK1B in cancer specimens was quantified using Western Blots. Study endpoint was cancer recurrence. Statistical analysis performed included Kaplan-Meier Survival Analysis and the log rank test. Results: DSBs inducing chemotherapy regimen (doxorubicin-based) patients were matched with non-DSBs treatment regimen patients based on age, stage, ER, PR, and HER2 status. They were grouped as high TLK1B overexpression (defined as >8-fold over benign) and low TLK1B overexpression (<3-fold). Patients with high TLK1B and treated with doxorubicin-based adjuvant chemotherapy had a statistically significant higher cancer recurrence rate than those with low TLK1B (Figure 1, log rank test, p = 0.02). This difference between high versus low TLK1B overexpression was lost if the adjuvant therapy used non-DBS inducing regimen (p = 0.83). Conclusion: High TLK1B overexpression predicts recurrence to doxorubicin-based adjuvant chemotherapy. In adjuvant regimen that uses non-DSB inducing agents, high TLK1B overexpression did not impact recurrence. This is consistent with in vitro observation that high TLK1B overexpression specifically predicts resistance in cancer treated with DSB-inducing agents, such as doxorubicin.

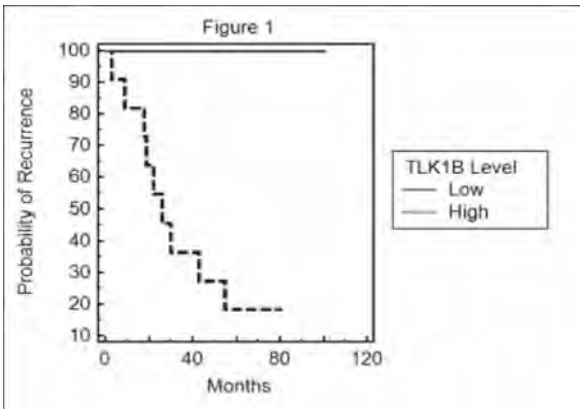

Figure 1. Kaplan-Meier Survival Analysis of patients that received doxorubicin-based chemotherapy. (log rank test, p = 0.02).

P48

The urokinase-type plasminogen activator is a direct JAG1-mediated Notch target in breast cancer M. Shimizu, B. Cohen, P. Goldvasser, H. Berman, C. Virtanen, M. Reedijk.* *Surgery, University of Toronto, Toronto, ON, Canada.*

Aberrant activation of the Notch signaling system and over-expression of the Notch ligand, JAG1 are associated with poor outcome in breast cancer. The plasminogen activator system, which includes urokinase-type plasminogen activator (uPA), has been validated as a marker of recurrence, high metastasis risk and death in breast malignancy. By using microarray profiling of breast cancer cell lines that had undergone siRNA-mediated abrogation of Notch signaling we uncovered a link between activated Notch and uPA expression. An association between elevated expression of the Notch ligand JAG1, uPA and the basal-like breast cancer subtype was confirmed in breast cancer cell lines. The association between JAG1 and uPA expression persisted in a survey of primary carcinomas of the breast. We found that Notch knockdown reduced transcription of uPA and phenocopied uPA knockdown in breast cancer cells. Through mutational analysis we identified a CBF-1 binding site in the uPA promoter that is required for direct transcriptional regulation by Notch. These data suggest that JAG1-induced Notch activation results in breast cancer progression through up-regulation of the plasminogen activator system and directly links these two poor prognosis pathways.

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Is age an independent predictor of survival and time to recurrence in breast cancer patients? S.C. Schiffman,[1]* K.M. McMasters,[1] A.B. Chagpar.[2] *1. University of Louisville, Louisville, KY; 2. Yale University, New Haven, CT.*

Introduction: While younger patients often present with larger tumors and lymph node-positive (LN+) disease, the impact of patient age at diagnosis (dx) on time to recurrence (TTR), overall- (OS) and disease-free survival (DFS) is unclear. We sought to determine if age at dx was independently associated with prognosis. Methods: Data from 1427 breast cancer patients diagnosed between 1996 and 2007 were reviewed. Median follow-up was 65 months. The impact of patient age on prognosis was evaluated using Cox Proportional Hazards models. Results: The median age of patients in this cohort was 54 (range; 21-89); median tumor size was 19 mm (range; 1-290). The cohort was divided into two age categories: <50 years (n=524; 36.5%) and ≥ 50 years (n=912; 63.5%). Younger age was significantly correlated with larger tumors (median 20 mm vs. 17 mm, p<0.001), of high grade (48.3% vs. 38.9%, p=0.004), that were ER-negative (22.3% vs. 15.5%, p=0.002), and LN+ (43.7% vs. 35.9%, p=0.002). On univariate analysis, older age predicted worse OS (p=0.001), as did larger tumor size (p<0.001), LN+ status (p<0.001), ER-negative status (p=0.037), and high tumor grade (p<0.001). On multivariate analysis, older age remained an independent predictor of worse OS (OR: 1.78, 95% CI: 1.33-2.38, p<0.001), as did larger tumor size (p<0.001), higher grade (p<0.001) and LN+ status (p<0.001). There was no significant difference in DFS between patients < 50 and those ≥ 50 (5-year actuarial DFS 78.0% vs. 79.9%, p=0.177). Of those who recurred, younger patients had a shorter median TTR (25 vs. 34 months, p=0.025). On multivariate analysis, controlling for tumor size, grade, ER and LN+ status, age was no longer an independent predictor of TTR (p=0.084). Conclusion: Despite presenting with larger, high grade, ER-negative tumors and LN+ disease, younger patients have better OS than their older counterparts. Age at dx does not independently predict worse TTR or DFS; younger patients' apparent shorter TTR is related to their poor clinicopathologic factors. Treatment decisions should be made based on these factors rather than age at dx alone.

Factor	Univariate	Multivariate		
	p-value	p-value	OR	95% CI
Older age	0.001	<0.001	1.78	1.33-2.38
Large tumors	<0.001	<0.001	1.01	1.00-1.01
LN+ status	<0.001	<0.001	0.38	0.29-0.51
ER-negative status	0.04	0.48	0.89	-0.11-0.16
High grade tumors	<0.001	<0.001	0.59	0.42-0.78

P50

Sentinel Lymph Node Interstitial Fluid Pressure in Breast Cancer D.S. Nathanson.* *Surgery, Henry Ford Health System, Detroit, MI.*

Elevated interstitial fluid pressure (IFP) in primary breast cancers results in flow through major lymphatic trunks to axillary sentinel lymph node(s)(SLNs). This flow can only occur when pressure in the SLN is lower. We hypothesized that intranodal IFP would increase as metastases filled the SLN; such elevated IFP might reach a threshold where lymphatic flow would be diverted to the next echelon nodes. METHODS: SLNs were 'hot' and 'blue' after injection of dilute methylene blue and filtered Tc99 sulfur colloid. IFP was measured in SLN and other axillary nodes by a needle connected through pressure tubing and a transducer to a recording device;116 breast cancer and 10 control patients (undergoing prophylactic mastectomy). Excised SLNs and other axillary nodes were examined pathologically by standard techniques and metastasis recorded and compared to IFP measurements for those nodes. RESULTS: IFP in control SLNs (n=10) ranged between 0 – 11 mmHg. IFP in tumor-replaced (>6mm) SLNs (n=14) was 29+14 mmHg (p<.05). IFP in SLNs and non-SLNs that were tumor free (n=140) was 9.6+5 mmHg and 10.1+6.6 in those SLNs with small metastases (n=16) (p=.53). In two patients IFP was measured in multiple nodes; tumor-laden SLNs (47 and 35 mmHg respectively) and two next echelon nodes tumor free (2mmHg each). In another patient two nodes, almost replaced with tumor, had IFPs of 36 and 42mmHg; in these cases blue dye was traced to the next node 'upstream' which was also 'hot.' CONCLUSIONS: Breast cancer metastasis in axillary LNs caused significantly higher IFP than tumor-free lymph nodes when metastases were greater than 6

mm. When the IFP levels were high in the 'true' SLN lymph flow direction changed; lymphophilic particles (blue dye and radio-colloid) were redirected to the next echelon of nodes where the pressures were much lower. Mechanical factors may increase the likelihood of metastasis to neighboring lymph nodes with lower IFP.

P51

Male Breast Cancer: An Institution's 25 year Experience J.S. Scow,* A.C. Degnim, J.W. Jakub, S.S. Shah, R.E. Jimenez, C.A. Reynolds, J.C. Boughey. *Mayo Clinic, Rochester, MN.*

Introduction: There are no prospective and few large retrospective studies of male breast cancer (MBC). This study's aim was to describe our institutional experience with MBC and evaluate the ability of the AJCC staging system to stratify survival. Methods: All MBC cases were identified from our institution's cancer registry from 1984-2008. Data collected included tumor characteristics, lymph node status, treatment, age, and survival. Results: During the study period 166 MBC cases were identified. Median age at diagnosis was 62 years (range 27-87). Most common presentation was a palpable breast mass (77%). Stage at diagnosis was stage 0 (6%), stage I (27%), stage II (36%), stage III (17%), stage IV (5%), and unknown (9%). Procedure performed was mastectomy in 148 patients (89%), lumpectomy in 10 patients (6%) and unknown in 8 patients (5%). Median tumor size was 2.0 cm (range 0.2-11.0 cm). Most common histology was invasive ductal carcinoma (91%). Estrogen and progesterone receptor status assessed at diagnosis was positive in 93% and 86% of cases tested respectively. Her2/neu status was positive in 6 of 47 cases tested (13%). Nodal staging was performed by axillary dissection (AD) (70%), sentinel node biopsy (SN) alone (11%), SN and AD (11%) and no axillary staging (8%); 43% were node positive, 47% node negative and 10% unknown. Adjuvant chemotherapy was given to 40 patients (24%), adjuvant hormonal therapy to 42 patients (25%) and adjuvant radiation therapy was used in 33 cases (20%). With a median follow-up of 5.5 years, 86 patients (52%) have died: 44 due to breast cancer, 23 due to causes unrelated to breast cancer, and in 19 the cause of death is unknown. Median overall survival was 9.3 years. Median cancer-specific survival was 16.0 years. For patients initially diagnosed at stage II, III, and IV median cancer-specific survival was 12.9, 7.2, and 0.8 years respectively. Median cancer-specific survival was significantly different for stages 2 vs. 3 (p=0.03) and 3 vs. 4 (p=0.0006) (figure). Conclusion: MBC most commonly presents as a palpable mass, is hormone responsive, and is most commonly treated with mastectomy. The TNM system appropriately stratifies men with MBC by duration of survival.

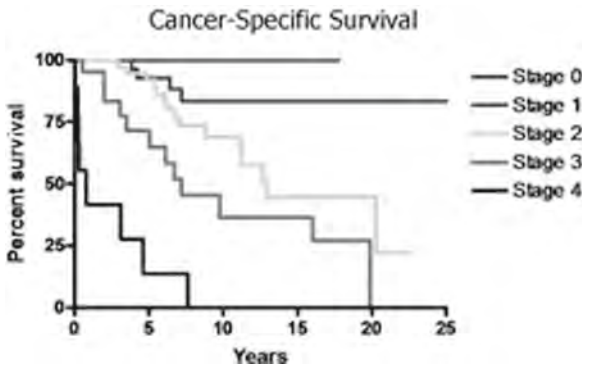

Figure: Kaplan-Meier estimate of time to death due to breast cancer according to stage at initial diagnosis. Median survival could not be calculated for patients initially diagnosed as stage 0 or 1. Patients with stage II, III, and IV disease had median cancer-specific survivals of 12.9, 7.2, and 0.8 years respectively. Median cancer-specific survival was significantly different for stages 2 vs. 3 (p=0.03) and 3 vs. 4 (p=0.0006).

P52

Breastfeeding, Baby Boomers and Breast Cancer R. Ellsworth,[1]* A.L. Valente,[2] J.L. Kane,[2] L.A. Field,[2] C.D. Shriver.[3] *1. Henry M. Jackson Foundation for the Advancement of Military Medicine, Windber, PA; 2. Windber Research Institute, Windber, PA; 3. Walter Reed Army Medical Center, Washington, DC.*

INTRODUCTION: Breastfeeding has been associated with an overall decreased risk of developing breast cancer and the protective effect of breastfeeding has been associated with decreased risk of triple negative and estrogen-responsive breast cancer. Although the mechanism by which breastfeeding provides a protective effect is not well-defined, physical changes in the mammary epithelium reflecting maximal differentiation, may be involved. METHODS: The database of the Clinical Breast Care Project was queried to identify all patients born between 1946 and 1964 with invasive breast cancer who had given birth to at least one living child. Clinicopathologic characteristics were compared between patients who breastfed (ever and at least 6 months) and those who never breast fed using chi-square and Fisher's exact tests. Gene expression data from microdissected tumors was generated using HG U133A 2.0 microarrays and analyzed using the Partek Genomics Suite. RESULTS: Of the 188 women who ever breastfed, 135 (72%) breastfed >6 months; an additional 120 parous women never breastfed. Age at diagnosis and menarche did not differ between groups; however, women who breastfed gave birth at a later age (25.2 vs. 22.3 years) and had more children (2.47 vs. 2.09). No differences were detected between patients who breastfed and those who did not for any tumor characteristics, including hormone and HER2 status, grade, size, lymph node status or mortality. At the molecular level, significant gene expression differences were not detected between tumors from patients who breastfed and those who did not, although when evaluated by tumor subtype, significantly more (P<0.009) patients who had never breastfed (50%) had basal-like breast tumors compared to those who had (14%). CONCLUSIONS: Although a molecular signature that effectively discriminated tumors from patients who breastfed from those who did not was not identified, never breastfeeding was associated with an increase in basal-like breast tumors. These data suggest that the beneficial effects of breastfeeding extend beyond decreased risk of developing breast cancer but provide a protective effect against aggressive breast disease as well.

P53

Contralateral Prophylactic Mastectomy: The Significance of Informed Decision, Personality Trait, Body Image and Reconstruction on Satisfaction J.C. Boughey,[1]* T.L. Hoskin,[2] L.C. Hartmann,[3] J.L. Johnson,[3] A.C. Degnim,[1] M.H. Frost.[3] *1. Surgery, Mayo Clinic, Rochester, MN; 2. Mayo Clinic - Biostatistics, Rochester, MN; 3. Mayo Clinic - Women's Cancer Program, Rochester, MN.*

Background: An understanding of the psychosocial consequences of contralateral prophylactic mastectomy (CPM) is important for counseling breast cancer patients. The aim of this study is to evaluate satisfaction with CPM, extent to which patients felt they made an informed decision and how various factors affect satisfaction. Methods: 523 unilateral breast cancer patients who underwent CPM between 1960 and 1993 were mailed a questionnaire evaluating QOL and satisfaction with CPM. Results: 284 (54%) patients returned the questionnaire with mean follow-up of 20.2 years. The majority of women felt they had made an informed choice (93%), were satisfied with CPM (89%) and would choose CPM again (92%). Although some satisfaction elements were adversely affected [body appearance (32%), feelings of femininity (25%) and sexual relationships (23%)], 61% of women reported CPM had no effect on their QOL and 32% reported a favorable effect. Satisfaction was moderately associated with lower decisional conflict (r=0.49), better body image (r=0.46) and higher level of current QOL (r=0.35), but only weakly associated by trait anxiety (r=0.26) and optimism (r=0.18). Of 284 respondents, 227 (80%) underwent reconstruction. Reconstruction patients were younger than those without reconstruction (mean 46 vs 50 yrs,p=0.004). Reconstruction was associated with lower overall satisfaction (p=0.02) and less favorable responses regarding choice of CPM again (p=0.03), but still only 9% (vs 2% in those without reconstruction) said they were dissatisfied and 4% (vs 0%) said they would not choose CPM again. Most (82%) would choose reconstruction again. Comparing those who did and did not undergo reconstruction, the percent that would change their respective choice was lower for those who had reconstruction than those who did not (10% vs 20%,p=0.04). Conclusions: Many years after surgery, women are highly satisfied with their decision to pursue CPM and

would elect to have CPM again. Reconstruction was associated with lower satisfaction. The associated long-term effects of CPM should be considered in decision-making.

P54

Feels Good, Looks Better: Proportion of Women Completing All Stages of Breast Reconstruction After Mastectomy for Breast Cancer Treatment or Prophylaxis N.M. Kawar,[1]* K. Tsai,[1] J. DiZoglio,[1] P. Michaud,[1] A. Doyle,[2] P. Liu,[2] J. Gass,[1] D.S. Dizon,[1] E.V. Tsiapali.[1] *1. Women & Infants Hospital/ Brown University, Providence, RI; 2. Roger Williams Medical Center, Providence, RI.*

INTRODUCTION: Breast reconstruction surgery (BRS) after mastectomy can be a lengthy process that involves multiple surgical procedures, concluding with nipple areolar complex reconstruction (NACR). The objective of this study was to examine reconstruction trends in our patient population and to determine the percentage and clinical characteristics of patients who completed BRS to NACR after mastectomy for breast cancer treatment or prophylaxis. METHODS: After obtaining IRB approval, a retrospective chart review of patients was performed of women who underwent mastectomy for breast cancer treatment, prophylaxis, or both, followed by immediate or delayed reconstruction, regardless of type. Demographic, clinical, pathologic, treatment, and BRS-related data were collected. RESULTS: Between 2000 and 2008, 326 patients underwent mastectomy at our institution. BRS information was available for 299 patients. One hundred twenty-four patients (41.5%) had BRS of any type. Of these, 61 (49.2%) began NACR, and only 24 (19.4%) completed both nipple reconstruction and tattooing. While no significant factors predicted completion of NACR, we found that those who did not proceed to NACR were more likely to be obese with BMI>30 (29.3% vs. 16.1%, p=0.09) and to have received chemotherapy (70.2% vs. 53.1%, p=0.07) or radiation therapy (42.3% vs. 25.5%, p=0.08). Women completing NACR underwent significantly more surgical procedures with four or more surgeries performed in 38.9% vs. 9.3% in those that did not undergo NACR (p=0.006). Median time from mastectomy to completion of NACR was 17 months (range 3-44 mos). CONCLUSIONS: Less than 20% of women undergoing BRS completed NACR. While no significant clinical factors were associated with the decision not to proceed with NACR, we found that those undergoing NACR underwent significantly more surgical procedures than those who did not. Understanding the reasons underlying the decision to proceed with NACR and ultimately the impact on body image and long-term quality of life warrants further examination.

P55

Localization of non palpable breast tumours using a 125-Iodine labelled titanium seed. Experience with 601 consecutive procedures Y.E. Van Riet,[1]* F.H. Janssen,[1] C.J. Van de Velde,[2] H.J. Rutten,[1] G.A. Nieuwenhuijzen.[1] *1. Surgery, Catharina Hospital, Eindhoven, Netherlands; 2. University Hospital, Leiden, Netherlands.*

Background: Resection guided by a radiologically placed hook wire is the most described surgical technique in breast conserving surgery in non-palpable breast cancer. This technique has several well described disadvantages like incidental migration, kinking or fracture of the wire and difficult logistics between the radiology, surgical and nuclear medicine departments. Furthermore, a high percentage of irradical margins has been described. Radioactive labelled 125I seed for localization of non-palpable breast tumours could potentially prevent these problems Methods: From October 2003 until June 2010, data on the use of 125I seed localization technique in 601 consecutive patients were collected prospectively. All patients with screen detected and histological proven invasive carcinoma as well as ductal carcinoma in situ (DCIS) were included. Patients with neo-adjuvant chemotherapy were excluded form this study. Results: The mean age of the women was 58.3 yrs (min: 32.1 – max: 82.5 SD: 11.9). Included were 479 patients with an invasive carcinoma and 122 patients with DCIS. Localization was ultrasound and stereotactically guided in 434 and 167 cases respectively. The 125I seed guided breast conserving surgery was performed after a mean time of 4 days (min: 1- max: 28, SD: 4.8). The mean operation time was 68.9 min (min: 35 – max: 160, SD: 21.2). Radicality was achieved in 569 cases (94,7%) (invasive carcinoma: 460/479 = 95,4 %, DCIS: 99/122 = 81,2 %). Conclusion: Localization of non-palpable breast cancer using a 125I seed is a safe procedure leading to a very high percentage of radical breast conserving surgery. Because it is possible to leave the 125I seed in situ for several days after localization, it leads to an independent planning in the radiology and surgical department.

P56

Characteristics of Multi-Focal and Multi-Centric Breast Cancers Detetected by Preoperative MRI B.K. Killelea,* M.M. Sowden, M. Rishi, B.J. Grube, A. Chagpar, L. Philpotts, D.R. Lannin. *Surgery, Yale University School of Medicine, Smilow Breast Center, New Haven, CT.*

Introduction: Many newly diagnosed breast cancer patients undergo preoperative MRI to define the extent of their disease, as well as to evaluate the contralateral breast. The purpose of this study was to determine the number of patients who were diagnosed with a second malignancy detected solely on MRI at our institution, to compare them to a control group of patients who had an MRI not leading to a diagnosis of cancer, and to compare tumor characteristics of the primary and secondary tumors. Methods: A breast center database was searched for all newly diagnosed breast cancer patients who underwent preoperative MRI from January 2005 to March 2010. Among those who were diagnosed with a biopsy-proven second malignancy based on suspicious MRI findings, pathology and imaging reports were reviewed and data regarding patients and tumors was collected. Results: Out of 624 patients with newly diagnosed breast cancer who had a preoperative MRI, 53 (8.5%) had a second tumor identified solely by MRI. Of these, 40 were ipsilateral, 12 were contralateral, and 1 bilateral. Thirty seven percent were multifocal and 56% were multicentric. Patients who had an MRI were younger than those who didn't, but there was no difference by age or race for those who had a second tumor found compared to those who didn't. Tumor size, nodal status, PR status, and Her2 status were significantly associated with the group who had a second tumor. Among the group with additional tumors found on MRI, histology, ER/PR status and grade were strongly correlated between the primary and the secondary lesion. Conclusions: Tumors that were larger, node positive, lobular histology, hormone receptor positive, or Her2 negative had a higher chance of having a second tumor on preoperative MRI.

	Second Cancer (n=53)	No Second Cancer (n=571)	p value
Mean age	53	53	ns
% lobular histology	19	12	.11
% multi-focal	37	11	
% multi-centric	56	3	
Size of first cancer (cm)	2.3	1.5	<.005
Size of second cancer (cm)	1.6	–	
% node positive	38	23	<.05
% ER positive	87	81	ns
% PR positive	85	70	<.05
% Her2 positive	5	17	<.05

P57

Which eligible breast conservation patients choose mastectomy in the setting of newly diagnosed breast cancer? C.D. Adkisson,* A. Parker, S. Bagaria, T. Gibson, C. Thomas, M. Heckman, S. McLaughlin. *General Surgery, Mayo Clinic Florida, Jacksonville, FL.*

Background: Breast conserving therapy (BCT) and mastectomy (Mx) offer equivalent survival for women with newly diagnosed, clinically localized breast cancer (BrCa). Despite this, many women eligible for BCT elect Mx. Herein, we identify factors associated with choosing ipsilateral Mx instead of BCT when Mx is not required. Methods: Between 7/2007 and 6/2010, 520 women with a new diagnosis of BrCa were treated by a single surgeon who prospectively documented patient eligibility for BCT. For those patients not requiring Mx (n=392), we evaluated associations between treatment choice and potential predictors using odds ratios (ORs) obtained from logistic regression models. P-values ≤ 0.0029 were considered significant after Bonferroni correction for multiple testing. Results: Of 392 women eligible for BCT, 106 (27%) chose Mx and 286 (73%) chose BCT. In univariable analysis the following factors were associated with electing Mx over BCT: personal history of Mx (OR 9.9, p<0.001), tumor detected by method other than mammogram (OR 2.0, p=0.0028), presence of multiple tumors (OR 2.6, p<0.001), absence of co-morbidities (OR 3.6, P<0.001), and abnormal MRI followed by multifocal biopsy positive for cancer (OR: 5.0, p<0.001). Also, we noted some evidence that

younger women were more likely to elect Mx (p=0.008). Compared to women with tumors <2cm, those with tumors >5cm were more likely to chose Mx (OR=1.54); but, this was not significant (p=0.3). In multivariable analysis, the associations with absence of co-morbidities (OR 5.4, p<0.001), personal history of Mx (OR 23.2, p<0.001), and abnormal MRI followed by a positive biopsy for cancer (OR: 4.3, p=0.0023) remained indicating that these factors are independently associated with selection of Mx over BCT. Conclusions: Approximately one in four eligible BCT patients chooses Mx. We observed factors associated with choosing Mx over BCT include tumor features such as findings on biopsy and other features such as personal history of Mx, absence of co-morbidities, and possibly younger age. If our data are confirmed, surgeons need to understand these reasons to appropriately counsel their patients.

P58

One and Done: No Re-operation for Sentinel Lymph Node Metastases? L.J. McGhan,* A.C. Dueck, R.J. Gray, N. Wasif, A.E. McCullough, B.A. Pockaj. *Mayo Clinic Arizona, Phoenix, AZ.*

Introduction: Many breast cancer patients who undergo completion axillary lymph node dissection (CALND) for sentinel lymph node (SLN) metastases have no further disease. This study's goal was to identify predictors of non-sentinel lymph node (NSLN) metastases in SLN+ patients. Methods: A retrospective review of all consecutive SLN+ breast cancer patients undergoing frozen section (FS) analysis at a single institution (2004-2010) was conducted. Chi-squared tests, t-tests and multivariate logistic regression were used to identify factors associated with incidence of NSLN metastases. Results: We identified 240 SLN+ patients. 155 patients (65%) were detected by FS and of these, 154 (99%) had same-day CALND. Permanent pathology identified an additional 85 SLN+ patients (35%) with 29 (34%) undergoing delayed CALND. SLN metastases identified on permanent pathology ranged from isolated tumor cells to macrometastases (>2mm). 57 patients (24%) had no CALND performed and did not develop any axillary recurrences (mean follow-up 31 months). NSLN metastases were present in 70 patients (45%) receiving same-day CALND compared to only 3 patients (10%) having delayed CALND (p<0.001). Univariate analysis revealed FS+, tumor size, ER- status, angiolymphatic invasion (ALI), high tumor grade and size of SLN metastases as significant predictors of NSLN+, whereas age, tumor histology, PR and HER2 status and number of positive SLNs were not. On multivariate analysis FS+, size of primary tumor and the presence of ALI were significant (all p<0.05). FS+, ALI and each additional cm increase in primary tumor size were associated with a 7.1 (CI: 2.0-24.9), 2.5 (CI: 1.3-4.8) and 1.3 (CI: 1.1-1.5) times greater likelihood of NSLN+. Using these variables we devised a risk score (0-5) for predicting NSLN metastases (Table). Points were allocated for FS+ (2), tumor size (2.0-3.9cm = 1; ≥4cm = 2) and ALI (1). Conclusions: A positive SLN biopsy on frozen section is a powerful surrogate marker for the presence of NSLN metastases and justifies immediate CALND. However the diagnosis of SLN+ on subsequent permanent pathology may obviate the need for CALND based on the low risk of NSLN metastases in our predictive model.

ALI	Size 2.0-3.9 cm	Size ≥ 4.0 cm	FS+	TOTAL SCORE	Incidence of NSLN+ (%)
				0	0
•				1	13
	•			1	
		•		2	31
			•	2	
•	•			2	
	•		•	3	39
•		•		3	
•			•	3	
		•	•	4	59
•	•		•	4	
•		•	•	5	74

TABLE – Prediction of NSLN Positivity Based on Frozen Section Positivity (FS+), Tumor Size (cm) and Presence of Angiolymphatic Invasion (ALI): Risk Score and Incidence of NSLN+

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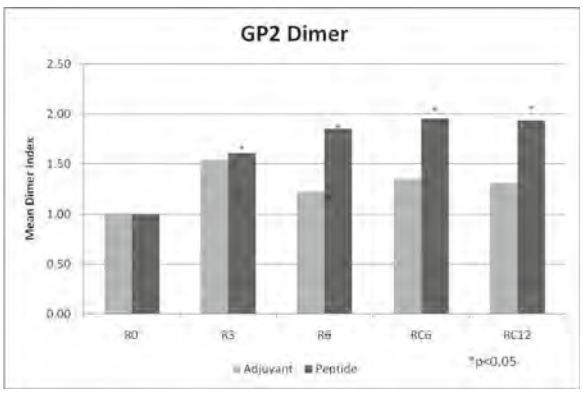
Vaccine-Specific Immunologic Responses to the HER-2/neu Peptide (GP2) Vaccine in a Prospective, Randomized Phase II Clinical Trial G.T. Clifton,[1] A.K. Sears,[1]* S.A. Perez,[2] K.S. Clive,[1] J.P. Holmes,[3] K. Georgakopoulou,[2] M. Papamichail,[2] S. Ponniah,[4] G.E. Peoples,[1] E.A. Mittendorf.[5] *1. Brooke Army Medical Center, San Antonio, TX; 2. Cancer Immunology and Immunotherapy Center Saint Savas Cancer Hospital, Athens, Greece; 3. Naval Medical Center San Diego, San Diego, CA; 4. Uniformed Services University of the Health Sciences, Bethesda, MD; 5. M.D. Anderson Cancer Center, Houston, TX.*

Introduction: GP2 is an HLA-A2-restricted immunogenic peptide from the HER-2/neu (HER2) protein (HER2: 654-662) capable of stimulating CD8+cytotoxic T-lymphocytes with the ability to recognize and lyse HER2-expressing tumor cells. We are currently conducting a prospective, randomized, single-blinded, phase II trial of GP2+GM-CSF(immunoadjuvant) vs GM-CSF alone administered in the adjuvant setting to prevent breast cancer recurrence. Here we present safety and immunologic data of this clinical trial. Methods: HLA-A2+ node positive or high-risk node negative HER2 -expressing (IHC 1+, 2+ or 3+) breast cancer patients who were clinically disease-free after completion of standard adjuvant therapy were enrolled. Patients were randomized to receive GP2+GM-CSF (VG) or GM-CSF alone (CG). Inoculations were given in six monthly intradermal inoculations. Ex vivo (HLA-A2:immunoglobulin dimer assay) and in vivo (delayed-type hypersensitivity (DTH)) responses were measured before (R0), mid-series (R3), upon completion (R6), and at six (RC6) and 12 (RC12) months after completion of the vaccine series. Results: To date, 88 patients (VG=38, CG=50) have enrolled. Systemic toxicities were ≤ grade 2 in 94% of vaccinated patients and 96% of control patients and all local toxicities were ≤ grade 2 in all patients. The population of circulating GP2-specific CD8+ T-cells measured by the dimer assay in the vaccinated group increased from R0 to all other measured timepoints (R0=1.00, R3=1.61, R6=1.85, RC6=1.95, RC12=1.93, p<0.05) while it did not significantly change in the CG (Figure 1). DTH responses increased in VG from pre- to post-vaccination (3.5cm vs 29.4cm, p<0.001) while they did not significantly change in the CG. Conclusions: In a prospective, randomized, single-blinded, phase II vaccine trial with a GM-CSF only control group, the novel HER2-derived GP2 vaccine appears safe and well-tolerated with minimal toxicity. GP2+GM-CSF is effective at generating HER2 -specific immunity as demonstrated by a significant increase in ex vivo and in vivo immune response in vaccinated patients.



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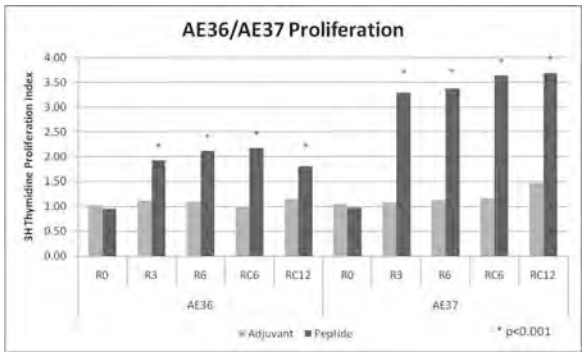
Vaccine-Specific Immunologic Responses to the Novel Ii-Key Hybrid HER-2/neu Peptide (AE37) Vaccine in a Phase II Clinical Trial A.K. Sears,[1]* G.T. Clifton,[1] S.A. Perez,[2] K.S. Clive,[1] J.P. Holmes,[3] K. Georgakopoulou,[2] M. Papamichail,[2] S. Ponniah,[4] G.E. Peoples,[1] E.A. Mittendorf.[5] *1. Brooke Army Medical Center, San Antonio, TX; 2. Cancer Immunology and Immunotherapy Center Saint Savas Cancer Hospital, Athens, Greece; 3. Naval Medical Center San Diego, San Diego, CA; 4. Uniformed Services University of the Health Sciences, Bethesda, MD; 5. M.D. Anderson Cancer Center, Houston, TX.*

Introduction AE37 is the Ii-Key hybrid of the HER-2/neu peptide AE36 (HER-2/neu: 776-790), and is capable of stimulating CD4+helper T-cells with

anti-tumor activity. We are currently conducting a prospective, randomized, single-blinded, phase II trial of AE37 + GM-CSF (immunoadjuvant) vs. GM-CSF alone for the prevention of breast cancer recurrence. Here we present safety and immunologic data for this clinical trial. Methods Node positive or high-risk node negative breast cancer patients with any level of HER-2/neu expression (IHC 1+, 2+ or 3+), disease-free after standard treatments were enrolled. Patients were randomized to receive either AE37 + GM-CSF (VG) or GM-CSF alone (CG). Vaccines were given in six monthly intradermal inoculations. Ex vivo (3H-thymidine proliferation assay) and in vivo (delayed-type hypersensitivity [DTH]) responses were measured before (R0), mid-series (R3), upon completion (R6), and at six (RC6) and 12 (RC12) months after completion of the vaccine series. Results We have enrolled 197 patients (VG=86, CG=111). Systemic toxicities were grade ≤ 2 in 96% of VG and 93% of CG; there were no grade 3-5 local toxicities. In the VG, proliferative responses to AE37 and AE36 increased from R0 to all other measured times (AE37: R0=0.98, R3=3.29, R6=3.38, RC6=3.64, RC12=3.68, p<0.001; AE36: R0=0.95, R3=1.92, R6=2.12, RC6=2.18, RC12=1.80; p<0.001) while they did not change in the CG (Figure 1). DTH responses increased in the VG from pre- to post-vaccination (AE37: 2.7 vs 30.2 mm, p<0.001; AE36: 2.2 vs 16.3 mm, p<0.001) while there was no change in the CG. Conclusions In a prospective, randomized, single-blinded, phase II vaccine trial with a GM-CSF only control group, the novel Ii-Key hybrid HER-2/neu AE37 vaccine appears safe and well-tolerated with minimal toxicity. AE37+GM-CSF is effective at generating HER-2/neu-specific immunity as demonstrated by a significant increase in ex vivo and in vivo immune response in vaccinated patients.



P61

Recurrence after mastectomy for DCIS T. Schwartz,* M. Sabel, R. Jagsi, T. Breslin, K. Diehl, V. Cimmino, A. Chang, L. Newman. *University of Michigan, Ann Arbor, MI.*

Background: Total mastectomy is frequently used in the surgical management of ductal carcinoma in situ (DCIS), and the role of post-mastectomy radiation (PMRT) is controversial in the setting of close mastectomy margins. Our goal was to analyze the frequency of local recurrence following mastectomy for cases of DCIS. Methods: 213 patients underwent total mastectomy for DCIS at our institution between the years 1998 and 2008. All patients with evidence of microinvasion were excluded. Pathologically close margins were defined as being < 3 mm. Median follow-up was 37.4 months. Results: Median age at presentation was 51 years and the median extent of DCIS was 16 mm (range 1-160 mm). Of the DCIS cases associated with mammographically-detected microcalcifications, the average span of calcifications was 26.75 mm. Negative margins were achieved by mastectomy in 180 cases (84%) and margins were close in 33 (16%). Of the 33 patients with close margins, 11 had a close superior margin, 11 had a close inferior margin, 10 had a close posterior margin and 1 had a positive lateral margin. Of the total sample, 5.6% received PMRT. Locoregional recurrences occurred in four cases (1.9%). All four recurrences were invasive ductal carcinoma. There were no statistically significant differences between the 4 cases with recurrence and the remainder of the sample. Of the 33 patients with close margins, 12 received PMRT and 21 did not receive PMRT. No local recurrences were observed in the cases of close margins that received PMRT and one occurred in a close margin case that did not receive PMRT. The remaining three cases of local recurrence occurred in patients with a margin-negative mastectomy (none of whom received PMRT). Conclusions: Locoregional recurrence following mastectomy for DCIS was uncommon in this retrospective series, and we did not identify close margins as a risk factor for local recurrence. However, only a small number of non-radiated patients with close margins were included, and some, possibly more concerning, cases with close margins received radiotherapy. The value of PMRT in this subset warrants further investigation.

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The Effect of Introducing Hematoma Ultrasound Guided (HUG) Lumpectomy in a Surgical Practice G. Larrieux,* J.A. Guidroz, J. Liao, C.E. Scott-Conner, R.J. Weigel. *Surgery, University of Iowa, Iowa City, IA.*

Introduction: Preoperative needle localization (NL) of breast lesions is the gold standard for lumpectomy of non-palpable cancer; however, NL has several disadvantages. The purpose of this study was to assess the use of intraoperative hematoma ultrasound guided (HUG) lumpectomy compared to NL in single surgical practice. Methods: Patients with non-palpable lesions who underwent lumpectomy from January 2007 to December 2009 with NL or HUG lumpectomy performed by the same surgeon were identified from a breast surgery database. Ease of scheduling, volume excised, re-excision rates, and operating room (OR) time were the main outcome variables. Univariate and multivariate analyses were performed to compare the two groups. Results: Lumpectomy was performed in 120 patients, 57 (48%) underwent HUG and 63 (52%) underwent NL. The likelihood of taking out an extra margin during operation was greater for HUG than with NL (p=0.017) but total amount of breast tissue removed was not statistically different (p=0.33). There was no difference in operative time comparing NL and HUG (p=0.12). The operative re-excision rates for NL vs. HUG were 16 (25.4%) vs. 10 (17.6%), which was not statistically different (P=0.297). The time from biopsy to surgery was shorter for HUG than for NL (9.06 Days, P=0.03) implying greater ease of scheduling for an average patient in this sample. Conclusions: HUG is equivalent to NL with regard to volume of tissue excised, need for operative re-excision and OR time. However, HUG had the advantage of not requiring mammographic localization and initial assessment indicates HUG to allow more timely and cost efficient care.

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Magnetic Resonance Imaging as compared to Mammogram in the evaluation of size, number of lesions and nodal positivity in breast cancer S. Saha,[1]* A. Korant,[1] M. Kanaan,[1] H. Nuthakki,[1] A. Bhakta,[3] L. Lawrence,[2] R. Hicks,[2] D. Strahle,[2] S. Nagpal,[2] D. Wiese.[2] *1. McLaren Regional Medical Center-Michigan State University, Flint, MI; 2. Mclaren Regional Medical Center, Flint, MI; 3. College of Osteopathic Medicine, Oklahoma State University, Tulsa, OK.*

Background: Magnetic Resonance Imaging (MRI) is thought to be more sensitive in detecting breast carcinoma (BrCa) than mammogram. Our study compares the lesion size and additional lesions between MRI and mammogram and the nodal positivity rate between the two groups. **Methods:** A retrospective analysis was performed on patients (pts) with BrCa who underwent both MRI and mammogram. Pts who had excisional biopsy prior to MRI or neoadjuvant chemotherapy were excluded. The number and size of lesions detected by mammogram and/or MRI were compared to pathology. Nodal Positivity of pts with additional malignant lesions detected by MRI only were compared to Nodal positivity of single lesions detected by both mammogram and MRI. **Results:** Between 2003 -2010, 318 pts were included. Of those 318 pts, 414 lesions were identified by MRI. Out of those 414 lesions, 210 lesions were detected by both MRI and mammogram and 204 were detected by MRI only. Out of those 210 lesions, MRI overestimated 56% of lesions by an average of 1.0 cm when compared to pathology; however mammogram underestimated the same lesions in 53% by an average of 0.6 cm. In 9 % of lesions MRI and mammogram detected same size compared to pathology. Out of 318 pts included in the study 67 pts (21%) had additional multiple lesions detected by MRI only which were not detected by mammogram, out of those 32 pts(10.1%) had invasive malignant lesions, 6 pts(1.8%) had DCIS and 29 pts(9.1%) had benign additional lesions. The nodal positivity of the pts with MRI detected additional malignant pts was 50% compared to the remaining 286 pts included in the study where the nodal positivity was 21.5%. (Table 1) **Conclusion:** MRI effectively evaluates the lesion size with a tendency toward overestimation when compared to mammogram. MRI can detect additional lesions when compared to mammo-

gram with higher nodal positivity. This finding suggests that MRI detected lesions are biologically significant and may predict more aggressive disease.

Table 1 A. Comparative analysis of the same 210 lesions detected by both MRI and Mammogram

Compared to Pathology	MRI (210 lesions)	Mammogram (210 lesions)	p-value
Overestimated	117(55.7%)	79(37.6%)	***0.035***
Underestimated	77(36.6%)	111(52.8%)	***0.021***
Sample size	19(9%)	20(9.5%)	0.84
Mean Overestimated	1.0cm	0.8cm	0.75
Mean underestimated	0.6cm	0.6cm	0.9

B. Comparative analysis of patients with MRI detected additional invasive malignant lesions and remaining patients with no additional malignant lesions detected by MRI

	Remaining patients with no additional malignant lesions detected by MRI	MRI detected additional invasive malignant lesions	p-value
Number of patients	286	32	***<0.0001***
Nodal positivity	21.5%	50%	

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Should Breast Density Influence Patient Selection for Breast Conserving Surgery (BCS)? N. Arora,[1]* A.E. Eaton,[2] T. King,[2] S.M. Patil,[2] M. Stempel,[2] E. Morris,[2] E. Brogi,[2] M. Morrow.[2] *1. Surgery, New York Presbyterian Hospital—Cornell, New York, NY; 2. Memorial Sloan Kettering Cancer Center, New York, NY.*

In a study of the relationship between breast density and cancer features, we observed a higher mastectomy rate in patients with extremely dense breasts. The purpose of this study was to examine possible explanations for this relationship. Methods:Data were obtained from a prospectively-maintained database of 1206 invasive breast cancer patients treated from 1/05-6/07. Mammographic density at diagnosis was evaluated using the BI-RADS classification. Margins were positive if tumor touched ink. Results:BCS was attempted in 904 patients(75%). Patients with extremely dense (BIRADS 4) breasts (n=118) were less likely to attempt BCS than those with less dense breasts(57%vs 77%; p<0.0001). After adjustment for patient, clinical, and tumor features the OR for mastectomy was 1.96(95% CI 1.21-3.96, p=0.006)in the BIRADS 4 density group. The positive margin rate after initial BCS was 55%. Extremely dense breasts were associated with positive margins in univariate analysis(OR 1.88; p=0.02), but after adjustment for age, histology, presentation, and methods of diagnosis and margin evaluation, density did not predict margin status. MRI was performed in 28% of BCS patients and was more common in the extremely dense group(49% vs 26%, p<0.0001). MRI did not decrease the overall rate of margin positivity(59% with MRI, 53% without, p=0.13), nor the rate of positive margins in those with extremely dense breasts(76% with MRI, 62% without, p=0.22). Thirty-five percent of patients with positive margins underwent conversion to mastectomy, and conversion was not predicted by breast density. In a multivariate model, age, method of diagnosis (needle vs surgical biopsy), extensive intraductal component, mutlicentricity/focality and tumor size significantly predicted conversion (p<0.01 for each). Conclusions:Density alone seems to influence the decision to proceed with mastectomy rather than attempt BCS. Breast density was not associated with positive margins or conversion to mastectomy when BCS was attempted. A benefit of MRI in decreasing positive margins was not observed in the subset of patients with dense breasts. These data do not support the use of breast density as a selection criteria for BCS.

P65

Chemoprevention among women with Lobular Carcinoma in Situ S. Oskar,* S. Muhsen, J. Sung, S. Patil, M. Morrogh, R. Sakr, M. Morrow, T.A. King. *Breast Surgical Oncology, Memorial Sloan-Kettering Cancer Center, New York, NY.*

Background: Lobular carcinoma in situ (LCIS), a benign high-risk lesion, increases a woman's risk of developing breast cancer by 10-20%. Chemopreventive agents such as tamoxifen and raloxifene reduce the risk of breast cancer in high-risk women; however, patients and physicians must weigh the potential risks and benefits. This study seeks to characterize and compare LCIS patients who have chosen chemoprevention with patients who have not. Methods: Data were obtained from a prospectively maintained database of 880 women with LCIS undergoing screening at our institution (11/80-12/09). Patient characteristics, clinical management factors, concurrent high-risk lesions, and long-term outcomes were compared between patients who took chemoprevention and those who did not. BIRADS breast density was reviewed and scored by a single radiologist. Results: Among 880 patients, 93(11%) had a history of chemoprevention use ≥ 5 months. The median duration of therapy was 56 mos (range6-144), 30(32%) pts have completed 5yrs of therapy and 37(40%) pts remained on therapy at last followup. Patients taking chemoprevention were older at the age of LCIS diagnosis (52 vs 50 yrs, p=.01) and more likely to be post-menopausal (53% vs. 37%, p=.01). There was no difference in family history of breast cancer, frequency of bilateral LCIS at diagnosis, concurrent presence of atypia, BIRADS breast density, or number of breast biopsies during surveillance between the 2 groups. At a median follow-up of 60 months (range 0-344), 2(2%) patients in the chemoprevention group have developed breast cancer as compared to 85(11%) patients who did not take chemoprevention (p=.002). Of 25 patients discontinuing therapy, 7 had reasons documented, none of which were traditional side effects of these agents. Conclusion: The majority of patients with LCIS at our institution chose to manage their LCIS diagnosis without chemoprevention. Paradoxically, chemoprevention uptake was less common in premenopausal women, the group with a more favorable safety profile for tamoxifen. The low rate of chemoprevention use suggests a need for further research to explore the acceptance of and compliance with chemoprevention in high-risk women.

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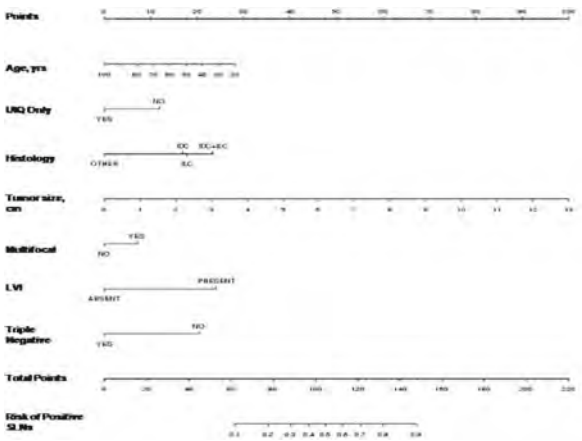
A Validated Risk Assessment of Sentinel Lymph Node Involvement In Breast Cancer Patients J. Veerapong,[1]* J. Boughey,[2] E. Mittendorf,[1] R. Harrell,[1] R. Bassett,[1] M. Ross,[1] M. Yi,[1] F. Meric-Bernstam,[1] G. Babiera,[1] H. Kuerer,[1] A. Lucci,[1] I. Bedrosian,[1] J. Brodt,[2] J. Jakub,[2] K. Hunt,[1] R. Hwang.[1] *1. The University of Texas M.D. Anderson Cancer Center, Houston, TX; 2. The Mayo Clinic, Rochester, MN.*

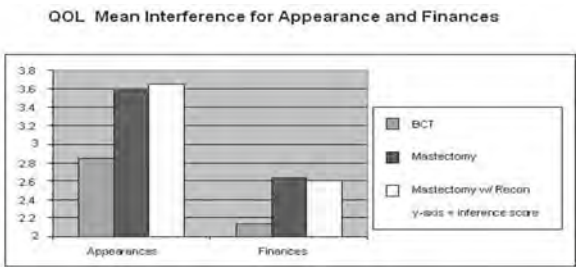
Introduction: Increasingly, the multidisciplinary treatment of breast cancer has become more individualized with the emergence of prognostic markers and predictive tools. In parallel with these trends, the use of aggressive axillary surgery has become more selective. How we approach the axilla may be influenced by understanding the risk of sentinel lymph node (SLN) involvement. In the current study, we developed and validated a nomogram to estimate the risk of SLN metastasis. Methods: We reviewed the records of all patients in our prospective database with invasive breast cancer who underwent SLN surgery without neoadjuvant therapy between 1994 and 2007. Clinicopathologic variables including age, tumor location, multifocality, nuclear grade, histology, tumor size, lymphovascular invasion, hormone receptor status, gender and type of breast surgery performed were analyzed. A nomogram to predict SLN metastasis was developed using multivariate logistic regression analysis and was validated using internal and external patient cohorts. Results: A total of 3582 patients underwent SLN surgery. Multivariate analysis revealed that young age, tumor histology, tumor size, multifocality, presence of lymphovascular invasion were independent positive predictors of SLN involvement whereas upper inner quadrant location and triple negative hormone receptor status were negative predictors. When the nomogram was applied to internal and external validation cohorts (271 and 318 patients respectively), the area under the receiver operating characteristic curve was accurate in both groups (74.6% and 73.9%). Patients with triple negative tumors had a significantly lower risk of having SLN metastasis (8%, OR 0.35, p<0.0001) whereas ER, PR and HER2/neu status individually were not significant predictors. Conclusions: The role of axillary surgery for patients with breast cancer has increasingly become more selective and understanding the risks of SLN metastasis in the preoperative setting can be valuable for multidisciplinary treatment planning. The nomogram described and validated here may be a useful tool in tailoring individual therapy decisions.



P67

Effects of Surgery on Quality of Life (QOL) in Premenopausal Breast Cancer Patients R.S. Bhati,[1]* E. Von Rottenthaler,[1] G. Quinn,[1] S. Karver,[1] R.R. Reich,[2] M.C. Lee.[1] *1. Surgical Oncology, Moffitt Cancer Center, Tampa, FL; 2. University of South Florida-College of Arts and Sciences, Sarasota-Manatee, FL.*

Introduction: Premenopausal women are a unique population of breast cancer patients and represent approximately 35% of all new breast cancer diagnoses. Psychological distress, alterations of self image, and aggressive lines of therapy lead to substantial disruption in QOL. Causative factors which may affect QOL remain largely speculative in this population. Methods: Premenopausal patients (ages 18-50) treated for nonmetastatic breast cancer between 2007-2009 were asked to participate by completing a mailed QOL questionnaire consisting of 67 items at a single institution. Self reported QOL measures were reviewed. In addition to discrete QOL measures, patient demographics, treatment, and recurrence data were collected. Cluster analysis and Crohnbach's alpha were used to measure the validity of the survey. ANOVA among responses was performed to measure outcomes. Lower interference scores conveyed a higher quality of life. Results: Over 300 patients were eligible; 144 responses were received (47.7% response rate). The overall Crohnbach's alpha for the questionnaire was 0.96. Information queried included relationships, appearance, sexuality, work/finances, family and social network. Immediate contralateral prophylactic mastectomy (CPM) carried the highest QOL interference score (mean 3.3148) with sexuality compared to women without CPM (mean 2.85) or with delayed CPM (mean 2.98), $F(2, 138) = 3.66$, $p = .03$. Patients undergoing breast conservation had the least interference with QOL measures in appearance, $F(2, 141) = 8.43$, $p < .01$, as well as with work and finances, $F(2, 138) = 3.99$, $p = .02$. Conversely, patients undergoing mastectomy or mastectomy with reconstruction carried a higher QOL interference score using the same indicators. Conclusions: Establishing causative factors for those patients at high risk of detrimental changes in QOL may improve preoperative counseling. Our results suggest that therapeutic mastectomy with or without reconstruction and immediate CPM adversely affect QOL. These findings demonstrate that the choice of surgical intervention and timing of reconstruction may significantly impact patient satisfaction and QOL.



P68

Neoadjuvant Chemotherapy is Associated with Improved Survival Compared with Adjuvant Chemotherapy in Patients with Triple Negative Breast Cancer Only After a Complete Pathologic Response C.S. Fisher,* F. Gao, R. Aft, W. Gillanders, T. Eberlein, J. Margenthaler. *Department of Endocrine and Oncologic Surgery, Washington University School of Medicine, St. Louis, MO.*

Introduction: Triple negative breast cancer (TNBC) is a unique subtype of breast cancer that has been shown to be generally chemosensitive initially. We sought to investigate the outcomes following neoadjuvant versus adjuvant chemotherapy in patients with TNBC and the characteristics associated with survival. Methods: We performed a retrospective chart review and identified 405 patients with Stage I-III TNBC who were treated between 1998-2008. Patients were divided according to receipt of neoadjuvant chemotherapy with a complete pathologic response (pCR), neoadjuvant chemotherapy without a pCR, and adjuvant chemotherapy. Data were compared using Chi-square, Fisher's exact test, and MANOVA. Kaplan-Meier curves were generated. Results: Of 405 patients, 154 (38%) received neoadjuvant chemotherapy and 251 (62%) received adjuvant chemotherapy. Twenty-six (17%) of those receiving neoadjuvant chemotherapy had a pCR. Patients undergoing neoadjuvant chemotherapy were younger ($p<0.05$) with larger tumor sizes and more advanced clinical stage than those undergoing adjuvant chemotherapy ($p<0.0001$). The groups did not differ with regards to patient race, tumor histology, or tumor grade ($p>0.05$). After controlling for covariates associated with survival in unadjusted tests, patients with neoadjuvant chemotherapy and a pCR had improved survival compared to patients receiving adjuvant therapy and those receiving neoadjuvant therapy without a pCR ($p=0.008$). The two neoadjuvant groups differed only in pathologic nodal status, whereby those in the pCR group had higher node negativity ($p=0.003$). Conclusions: Although previous clinical trials have not demonstrated a survival difference between patients receiving neoadjuvant versus adjuvant chemotherapy for breast cancer, our data indicate that this may not be true for patients with TNBC. However, only those patients experiencing a pCR following neoadjuvant chemotherapy had improved survival.

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The Influence of Margin Width on Local Recurrence Rates after Breast Conserving Surgery B.T. Miller,* A.M. Abbott, E. Gulbache, T.M. Tuttle. *University of Minnesota, Minneapolis, MN.*

Background: Surgical margin width for breast conserving surgery (BCS) remains controversial, with no clear consensus regarding adequate margins. The aim of this study was to determine the influence of margin width on tumor recurrence rates after BCS. Methods: We performed a retrospective review of patients who underwent BCS for treatment of breast cancer between 2002 and 2009. All patients underwent BCS for ductal carcinoma in situ (DCIS), stage I, or stage II invasive breast cancer. Exclusion criteria included previous breast cancer and positive margin status (ink on tumor). We collected information on patient and tumor characteristics, and performed chi-square testing to compare characteristics between margin width groups. Local recurrence was defined as the occurrence of either invasive breast cancer or DCIS in the ipsilateral breast. Results: Of the 231 patients who met inclusion criteria, 197 (85%) received radiation therapy. For the entire cohort, 29 (13%) patients had margins <1 mm, 44 (19%) patients had margins of 1-2 mm, and 158 (68%) had margins >2 mm. On univariate analysis, none of the patient and tumor characteristics evaluated was significantly associated with any margin width group (<1 mm v 1-2 mm v >2 mm). Seven (3%) patients developed a local recurrence (LR). No patients with margins <1 mm had LR (median follow-up 27 months), 2 (4.5%) patients with margins of 1-2 mm had LR (median follow-up 33 months), and 5 (3.2%) patients with margins >2 mm had LR (median follow-up 39 months). Of the 23 patients who did not receive radiation therapy, 1 patient (4%) had LR. Patients with LR had more high grade tumors than those without LR (57% v 36%), more ER negative tumors (43% v 19%), and more lymph node positive tumors (29% v 17%). Additionally, a higher percentage of patients with LR did not receive chemotherapy compared to patients with no LR (71% v 56%). Conclusions: We found that the early local recurrence rate for patients with close margins was quite low. Prospective studies with longer follow-up are needed to adequately assess tumor recurrences in patients with narrow margins.

P70

Effect of the Recency of Last Pregnancy on the Biologic Sub-Type of Breast Cancer M. Pilewskie,* P. Grodinsky, A. Fought, D. Scholtens, S.A. Khan. *Northwestern University, Chicago, IL.*

Introduction: Pregnancy associated breast cancers (PABC) display features associated with poor prognosis, including hormone receptor (HR) negativity, but other tumor markers have not yet been examined. Recently, it has been suggested that tumors that occur as long as 15 years following pregnancy share these features. We sought to define the tumor marker profile of PABC, including HER-2 and p53 expression, and examine the time interval over which this adverse tumor profile is observed relative to last pregnancy. Methods: A prospectively maintained database was reviewed to identify women with a breast cancer (BC) diagnosis between 1998 to present. Women with known date of last pregnancy ≤15 years prior to BC diagnosis were included. These were categorized based on the number of years between pregnancy and BC diagnosis; 0-2 years, >2-5 years, >5 to 10 years, and >10-15 years. Control subjects were age matched nulliparous women. When comparing cases and controls to covariates, t-tests or Kruskal-Wallis tests were used for continuous covariates and $\chi 2$ or Fisher's Exact Tests were used for categorical covariates. Results: A total of 141 parous women were identified, with 105 nulliparous controls. There was no difference seen between race, age at first birth, age at last birth, age at menarche, presence of any positive lymph nodes, and tumor size. Women who were 0-2 years from last parity at the time of BC diagnosis were the only group significantly more likely than controls to have grade 3 tumors ($p<0.01$), HR negative tumors ($p<0.01$), and triple negative tumors ($p<0.01$). These women were also the only group more likely to present with a self diagnosed mass rather than physician or screen detected tumor ($p<0.01$). There was no difference in HER-2 or p53 status. See Table 1. Conclusion: PABC is more likely to have poor prognosis tumor characteristics including high grade, negative HR status, and triple negativity. The time frame that these characteristics persist after pregnancy appears to be short, lasting only 2 years. More work is needed to delineate this time frame and to define PABC on a molecular level, so as to devise better prevention and therapy for this devastating problem.

Table 1

	Cases: Interval from Last Parity to Breast Cancer Diagnosis				Controls	
	0-2 years n=30	>2-5 years n=38	>5-10 years n=39	>10-15 years n=34	Nulliparous n=105	p value
	mean (SD)	mean (SD)	mean (SD)	mean (SD)	mean (SD)	
Age at Diagnosis	35 (4)	39 (5)	43 (5)	47 (4)	43 (7)	<0.01
Age at Last Birth	35 (4)	36(5)	35(5)	35(4)	-	0.47
	n (%)	n (%)	n (%)	n (%)	n (%)	
Self Presentation	25 (83)	22 (59)	19 (50)	12 (37)	52 (50)	<0.01
Grade 3 Tumor	21 (70)	18 (47)	18 (46)	14 (41)	38 (37)	0.03
Hormone Receptor Negative	14 (48)	4 (11)	8 (21)	5 (15)	13 (12)	<0.01
Triple Negative	10 (37)	4 (11)	6 (15)	3 (9)	10 (10)	0.01
Her-2 Negative *n=190	19 (79)	25 (83)	27 (84)	20 (77)	68 (87)	0.69
p53 Negative **n=138	15 (68)	15 (71)	17 (74)	14 (88)	43 (77)	0.71

P71

Receptor Changes in Metachronous Breast Cancer - Our 10 Year Experience J.S. Bhullar, A. Unawane,* G. Subhas, H. Poonawala, L. Dubay, L. Ferguson, Y. Goriel, M.J. Jacobs, R.B. Kolachalam, S. Silapaswan, V.K. Mittal. *Department of Surgery, Providence Hospital & Medical centers, Southfield, MI.*

Introduction: All women with breast cancer are at risk for synchronous and metachronous tumors. We analyzed the pattern of receptor expression and conversion in metachronous tumors specifically to facilitate better understanding of the receptor pattern and response to therapy. Methods: We reviewed charts of 108 women diagnosed and treated for primary and metachronous breast cancer over 10 years. The significant factors analyzed were age, grade, size, locations of the tumor, Her2 receptor, estrogen receptor (ER) and progesterone receptor (PR) status and treatment received. Patients with metastasis and regional recurrence were excluded. Results: Mean age at diagnosis was 59.4 years and subsequent metachronous tumor detection was within 2.2 years. Primary tumors of 35 patients were ER+/PR+; which was retained in 24 (69%) metachronous tumors. Of the 49 patients with ER-/PR- primary tumors, 41 (84%) retained the status in the metachronous tumor. From 22 patients with ER+/PR-, 16 (73%) retained the receptor status. Only 3 converted from ER- to ER+ and 4 converted from PR- to PR+. Unusually no primary or metachronous tumors were noted with ER-/PR+ profile. The highest concordance of 93% was seen with PR- primary tumors, which remained negative in 60 out of 65. Most Her2- tumors (22/31, 71%) remained Her2-, but 50% (8/16) of Her2+ Grade 3 primary tumors became negative. Adjuvant therapy - 36 did not receive either chemo or radiation, 28 received both, while the remaining received either. Except Herceptin in Her2+ group, no association of any particular therapy with receptor change was noted. Conclusion: Most metachronous tumors retained the ER/PR expression of the primary tumor irrespective of the primary tumor treatment, while half of primary tumor Her2 expression was lost in metachronous tumors with Herceptin treatment. Metachronous tumors were least likely to develop when primary tumors were ER-/PR+.

Receptor patterns in primary and metachronous breast tumors

ER/PR and Her2 receptor status	Number in Primary tumor	Number in metachronous tumor	Percentage (%)
ER+/PR+ to ER+/PR+	35	24	69%
ER-/PR- to ER-/PR-	49	41	84%
ER+/PR- to ER+/PR-	22	16	73%
ER+/PR+ to ER-/PR-	35	9	25%
ER-/PR+ to ER-/PR+	--	--	--
ER-/PR+ to ER+/PR+	--	--	--
Her2+ to Her2+	16	8	50%
Her2- to Her2-	31	22	71%

P72

Positive Margins Following Breast-Conserving Surgery: Technical Observations F. Al Mushawah, R.L. Aft, W.E. Gillanders, T.J. Eberlein, F. Gao, J.A. Margenthaler.* *Department of Surgery, Washington University School of Medicine, St. Louis, MO.*

Background: Margin status following breast-conserving therapy (BCT) is a risk factor for local recurrence, yet little agreement exists regarding the definition of an adequate margin and the best way to achieve it. We sought to describe the technical factors impacting margin status for non-palpable and palpable breast cancer. *Methods:* We identified 375 patients with Stage I-III breast cancer who were treated with BCT from 1999-2009. Data included patient/tumor characteristics, method of localization (needle vs palpation), and pathologic outcomes. Margin positivity was defined by the presence of *in situ* or invasive malignancy focally or extensively present at any margin. Descriptive statistics were utilized for data summary and data were compared using Chi-square. *Results:* Of 617 patients with Stage I-III breast cancer during the study period, 375 (61%) underwent BCT. Of these, 199 (53%) were non-palpable and had a needle localization, while 176 (47%) had a palpation-guided procedure. Patients undergoing palpation-guided procedures had larger tumors than those undergoing needle localization ($p<0.01$). Patient age, tumor grade, biomarker profile, and nodal status were not significantly different between the two groups ($p>0.05$). Overall, 137 (37%) patients had one or more positive margins; 85 of 199 (43%) who had a needle localization procedure and 52 of 176 (30%) who had a palpation-guided procedure ($p<0.05$). The number of margins affected did not differ significantly between those patients who had a needle localization vs those who had a palpation-guided procedure ($p>0.05$ for all): 38 (19%) vs 25 (14%) with one positive margin, 27 (14%) vs 14 (8%) with two positive margins, and 20 (10%) vs 13 (7%) with three or more positive margins, respectively. *Conclusion:* Although patients with palpable breast cancer have larger tumors than those with non-palpable breast cancer, the rate of positive margins was higher for those with non-palpable tumors who had needle localization. The number of affected margins, however, was not impacted by the method of localization. Newer methods of localization are needed to help reduce the rate of positive margins and need for re-excision.

P73

Association of HER2 status and ipsilateral breast tuomr recurrence after breast-conservation therapy for invasive breast carcinoma

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Background Ipsilateral breast tumor recurrence (IBTR) occurs in approximately 5% of patients with invasive breast cancer 5 years following breast–conservation surgery (BCS) with radiotherapy (RT). The impact of HER2 status on the local control of breast cancer is unclear. The purpose of this study was to examine the association of HER2 status and IBTR. Methods We reviewed 280 patients from a prospective breast cancer database diagnosed with invasive breast cancer between 1999 and 2005. In total 287 BCS (7 patients had bilateral primary breast cancer) were done. All had negative margins, adjuvant breast radiotherapy and known HER2, estrogen receptor (ER) and progesterone receptor (PR) status. Patients with histologically proven positive lymph nodes or high risk node negative disease were typically given third generation chemotherapy regimens. In patients with ER positive tumors, aromatase inhibitors were used if postmenopausal, otherwise adjuvant tamoxifen was given. IBTR rates were calculated using the Kaplan-Meier method. Cox proportional hazards models were fit to explore associations of HER2 status and IBTR after adjustment for patient and pathological characteristics. Results Twenty-eight (9.7%) of the cancers were HER2 positive, 234 (81.5%) ER positive, and 161 (56.1%) PR positive. Seventeen (60.7%) HER2 positive patients received Trastuzumab. After a median follow-up of 3.6 years (range 0.6-8.9 years), 10 (3.5%) patients had IBTR, five were HER2 positive. HER2 positive patients had a significantly higher 5-year IBTR rate compared to HER2 negative patients (19.1% versus 1.6%, respectively; p=0.0001). Three of the 5 HER2 positive patients with IBTR received trastuzumab. After adjusting for ER status, size of invasive tumor, grade, margin distance and age at surgery, HER2 receptor positive patients continued to have a higher risk of IBTR (hazard ratio [HR] 6.17; p= 0.013). Conclusion HER2 receptor positive breast cancer patients who underwent BCS with RT had a higher risk of IBTR compared to HER2 negative patients in our series. Trastuzumab did not appear to have a protective effect on IBTR.

P74

Preoperative Evaluation of Sentinel lymph node and Axillary reverse mapping by Computed tomography for breast cancer patients

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Background Sentinel lymph node (SN) biopsy can avoid unnecessary axillary lymph node dissection (ALND) in node negative patients, and minimize arm lymphedema. Several trials have shown lymphedema rates in approximately the 2-7% range with SN biopsy alone. Recently, axillary reverse mapping(ARM) technique has been developed to map and preserve lymphatic drainage pathway from arm. If the SN and ARM node was same node, it might be made arm lymphedema. Aim Aim of this study is to evaluate preoperative evaluation of SN and ARM by computed tomography in 67 consective patients and 69 breasts. Methods Preoperative lymphography by computed tomography (CTLG) of ARM was performed on the day before operation. Patients were underwent iopamidol injection subdemally into the upper inner arm along the medial intramuscular groove of the ipsilateral arm. And SN mapping was performed as the same way,the injection site was the subdermal of the nipple. SN mapping was performed using a subareolar injection of 40 MBq technetium-99 m nanocolloid 24 hours before surgery and blue-dye injection 5 minutes before surgery. Results The mean age was 60 (range 34-88). Lymphatic pathway of ARM was detected in 59 (85.5%) breasts, and mean number was 1. ARM node was detected in 56(81.2%) and mean number was 1.02. Lymphatic pathway of SN was detected in 66 (95.6%) breasts, and mean number was 1.09. SN node was detected in 66(95.6%) and mean number was 1.10 by CTLG.60 breasts (87.0%) could be detected both ARM node and SN. 5 nodes (8.3%) were same . 35 breasts (58.3%) were separated from ARM pathway and SN pathway, and 20 breasts (33.3%) had some relationship in ARM and SN. On the other hand, SN biopsy was succeccfully performed in all patients, and 9 breasts (13.0%) were lymph node positive. none of the patients had a diagnosis of lymphedema. Conclusion Detection of ARM and SN by CTLG was feasible and future prospective studies should evaluate whether performing ARM during SLNB reduces the risk of lymphedema.

P75

Axillary Sentinel Lymph Node (SLN) Micrometastatic Disease (N1mi): Completion Axillary Lymph Node Dissection (cALND) is Not Mandatory

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Introduction: ASCO guidelines recommend cALND for all positive SLNs. Recent ACOSOG Z0011 data suggest that those with N1mi SLNs achieve excellent disease control, even without subsequent cALND. We examined our N1mi SLN experience to identify which factors influenced decision to perform cALND and to assess outcomes. Methods: We obtained IRB-approval for retrospective chart review of patients with SLN for invasive breast cancer between 2003 and 2009. Data collected on N1mi SLN patients included age, menopause status, primary tumor and SLN pathology characteristics. If cALND occurred, pathologic results, main reason cited for cALND, adjuvant systemic treatment, and follow up status were determined. The Memorial Sloan Kettering Cancer Center Additional Nodal Metastasis Nomogram (MSKCCN) calculated risk of non-SLN disease for each N1mi patient. Results: Of 877 SLN patients, 48 (5.5%) had N1mi SLNs, with 26 (54%) undergoing cALND. Only 4 of 26 (15%) had non-SLN disease, but no upstaging to N2 occurred. Patients with cALND were on average younger, more likely premenopausal, had larger tumors, higher ALI rates, and higher ratios of positive/negative SLNs. The main indication for cALND was "to complete staging/aid adjuvant therapy decisions" (93%). Further staging was deemed "unnecessary" in 77% of the non-cALND group. cALND patients had higher average MSKCCN scores [18% (range 6-49) v. 9% (range 4-23)]. Average score among the 4 with non-SLN disease was only 17% (range 7-26). cALND patients more often received systemic chemotherapy than those without cALND (73% v. 59%). All patients undergoing cALND are disease free at available follow up. One non-cALND patient developed stage 4 bone disease without axillary recurrence. Conclusions: Despite guidelines recommending cALND, our data suggest dissection for N1mi SLNs must be individualized. Selection for cALND depends on multiple clinical factors, may be aided by the MSKCCN score, and should be considered if it will aid adjuvant treatment decisions. Overall, low rates of non-SLN disease and excellent axillary disease control without dissection argue against routine cALND for N1mi SLNs.

P76

WITHDRAWN

P77

Surgical margins after BCS: variation between hospitals in the Netherlands

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Obtaining clear resection margins is a parameter of adequate surgical treatment in breast conserving surgery (BCS). In the Netherlands, the National Health Care Inspectorate introduced a per institution cut-off value of 90% radicality for first BCS operations as a quality indicator (for both infiltrating and in situ carcinoma). The aim of this study is to describe the variation between hospitals in margin status after first BCS. In a retrospective population based study, data were collected regarding all newly diagnosed breast cancer patients (DCIS and invasive carcinoma(IC)), treated between July 2008 and July 2009 in 96 hospitals in the Netherlands. The classification of irradicality, as formulated in the most recent Dutch diagnostic and treatment guideline was adhered to: "any lumpectomy specimen containing more than focally positive margins". The institutional proportion of patients with "positive margins" following a first BCS was assessed for IC and DCIS. Results were displayed in a funnelplot demonstrating the confidence interval for the 10% criterion in relation to the hospital case-load. 7.327 patients were included, 895 (12%) of them had DCIS.

The average institutional proportion of patients with positive margins was 9,3% (95%BI: 8,7–10,1%) for IC, and 16,0% (95%BI: 13,7-18,5%) for DCIS. Figure 1 shows the variation in proportions of positive margins per hospital. While the average proporotion for IC was 9,3%, thirty-five of the hospitals scored higher than the predefined 10% quality parameter. Figure 1 shows that the outcome was significantly worse than the 10% criterion in four of the 96 hospitals. For DCIS, the range was very large(0-100%), the number of patients per hospital small (0-38), and due to these small numbers, estimations on hospital level were not reliable. When applying quality criteria to patterns of care, dictated hospital rates should be accompanied by confidence intervals that differ substantially in relation to hospital volume. The proportion of patients with "positive margins" after first BCS was lower than the defined cut-off value of 10% in almost half of the hospitals, but exceeded this rate significantly in only five percent of the hospitals.

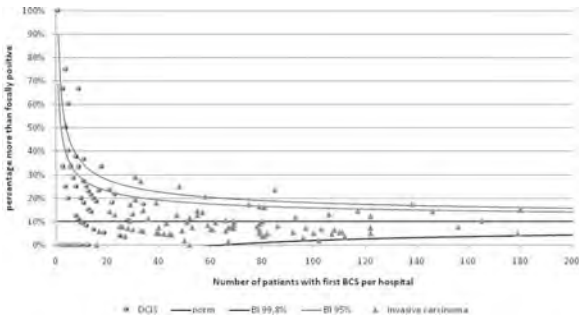

Figure 1 Funnelplot of the institutional proportions of "tumor-positive margins" after first BCS for patients with infiltrating carcinoma or DCIS.

P78

Routine Cavity Shave Margin Excision Reduces Total Volume of Tissue Removed in Partial Mastectomy for Breast Cancer

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Introduction: Breast conserving surgery (BCS) requires complete tumor excision with negative surrounding margins. Current comprehensive pathologic analysis closely evaluates all margins, with 30-50% re-excision rates reported. Cavity shave margin (CSM) removal is a simple surgical technique utilizing existing equipment that reduces re-excision rates. One criticism of this approach, however, has been the concern that negative margins are obtained primarily due to higher volumes of tissue being removed. This study evaluates the total volume of tissue removed in a group that underwent routine CSM versus one that underwent standard partial mastectomy (PM). Methods A single institution retrospective review identified 533 patients with a new diagnosis of breast cancer who underwent PM. A matched pair analysis of 59 patients that had undergone partial mastectomy with CSM versus 59 who had undergone standard PM was performed. Patients were matched for tumor size, presence of extensive intraductal component, and primary histology. Patients who underwent total mastectomy as their final treatment were excluded for the volume analysis. All additional margin volumes excised were added to the initial PM volume. Results The two groups were well matched for age, nuclear grade, associated lymphovascular invasion (LVI), receptor status, and multifocality. There was no statistically significant difference in final pathological tumor size between the two groups. Patients in the CSM group required fewer surgical interventions than the standard PM group and were less likely to undergo total mastectomy. Mean total volume of tissue excised in the CSM group was significantly lower than the standard PM group. Conclusions CSM at time of initial surgical intervention increases rates of successful BCT at the first operation. Total tissue volume excised is actually lower in patients who undergo CSM. This approach should be considered for all patients undergoing PM.

Table 1

	CSM	Standard PM	p-value
Total (n)	59	59	
Median tumor size (cm)	1.68	1.15	0.08
Median volume excised (cm^3)	75.31	114.8	0.025
Range of volume excised (cm^3)	14.53-932.4	21.15-670.3	
Need for re-excision	9	18	0.014
Total mastectomy performed as final treatment (n)	2	11	0.016

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Nipple Sparing Mastectomy: An Option for Cancer Treatment and Risk Reduction

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PURPOSE: The use of nipple sparing technique for mastectomy remains controversial due to concerns about complications and recurrence risk. Our objective was to report our experience in the setting of cancer treatment and risk reduction. METHODS: This is a retrospective review of all nipple sparing mastectomies (NSM) performed from 2007-2010. Minor complications included local skin necrosis, antibiotic treated infections, aspirated seromas, and partial loss of nipple areolar complex (NAC). Major complications included complete loss of NAC, flap necrosis, implant removal, and surgical drainage of seromas and hematomas. Statistical analysis included Chi-square, Fisher's exact, Mantel-Haenszel Wilcoxon two sample tests and multivariable regression analysis using SAS 9.2. RESULTS: Our cohort consisted of 113 patients having 214 mastectomies. 73 (65%) of the patients underwent NSM for risk reduction and 40 (35%) for cancer treatment. Of the patients with cancer, 13 were Stage 0, 13 were Stage I, 13 were Stage II, and 1 was Stage III. 12 (11%) patients underwent unilateral NSM and 102 (89%) underwent bilateral NSM. Clinical factors that were analyzed are listed in Table 1. 22 (19%) patients and 29 (13%) breasts had minor complications; 26 (23%) patients and 31 (14%) breasts had major complications. 17 (8%) of NAC were removed, 10 for positive tumor margins and 7 for necrosis. On univariate analysis, BMI, mastectomy weight, smoking history, and reconstruction type were ($p<0.05$) associated with minor complications. There were no associations seen for major complications. Multivariate analysis demonstrated mastectomy weight (O= 1.002, 95%CI: 1.0001-1.0039, p=0.0352) and smoking history (OR: 3.2131, 95% CI: 1.286-8.028, p=0.0125) to be significantly associated with minor complications. Median follow-up was 17 months (range 3-39). There have been no primary tumors or recurrences. CONCLUSION: Overall, nipple sparing mastectomy appears to be a safe and effective means for risk reduction and local control. Of the clinical factors investigated, only mastectomy weight and smoking history were significantly associated with minor complications.

Patient Factors	No (%)
Age	Mean 43 yo (24-74 yo)
Body Mass Index (BMI)	Mean 23 lb/in2 (range 15-40 lb/in2)
Smoking History	
Active or Past	27 (24%)
None	86 (76%)
Reason for NSM	
Cancer Treatment	40 (35%)
Risk Reduction	73 (65%)
Incision Location - Each Breast	
Inframammary	148 (69%)
Other - Radial, Inferolateral, Lateral, etc.	66 (31%)
Mastectomy Weight	Mean 355 grams (range 48-1050 grams)
Reconstruction Type	
Autologous-Tissue	11 (10%)
Tissue Expander Placement	28 (25%)
One-Stage Implant Placement	69 (61%)
Reverse One-Stage Implant Placement	5 (4%)

P80

The Modified Triple Test in Predicting Cancer in a Palpable Breast Mass C. Wai, G. Al-Mubarak, M. Homer, J. Rothschild, R.A. Graham.* *Tufts Medical Center, Boston, MA.*

The original triple test (TT) – exam, mammogram, and FNA biopsy – has long been used to evaluate palpable breast masses. We modified the original TT to include current imaging modalities (US) and biopsy techniques (core) to determine its role in evaluating palpable breast masses. Methods: A retrospective chart review of 320 female patients who underwent needle biopsy of a palpable breast mass from April 2000 to December 2006 was performed. We developed a modified TT score based on the following: physical exam (1-3), mammogram and/or US (1-3), and FNA and/or core biopsy (1-3). For the exam and imaging score, points were assigned by level of suspicion: low, moderate or high. The imaging score was based on the highest point total from the mammogram or US. The biopsy score was based on the higher score from the FNA or core and was listed as benign, atypical or malignant. Final outcome was determined by open biopsy or follow-up > 1 year. Results: Physical exam alone was 93% accurate (95% CI 0.89-0.96) at predicting whether a mass was benign or malignant. Imaging was 88% accurate (95% CI 0.84-0.92), and needle biopsy was 95% accurate (95% CI 0.92-0.98). For patients with a TT score of 3-4, 190 of 191 (99.5%) had a benign mass. The one patient with cancer had an incidental 2 mm focus of DCIS. For patients with a score of 5-7, 2 of 17 (11.8%), 8 of 14 (57.1%), and 32 of 34 (94%) had cancer, respectively. All 64 patients with a score of 8 or 9 had cancer. Each 1-point increment in the TT score was associated with an increased risk of cancer: odds ratio 9.73 (95% CI 5.16-18.3). Conclusion: For patients with a palpable breast mass and a modified TT score of 3-4, open biopsy or continued follow-up is not necessary. Patients with a TT score of 8-9 can proceed directly to definitive therapy. Patients with a score of 5-7, however, are at sufficient risk for cancer that open surgical biopsy is probably necessary. In reviewing data from the original Portland triple test, the addition of US and/or core biopsy added little to its accuracy or predictive value.

Modified TT Score and Outcome

TT Score	Benign n (%)	Cancer n (%)	Total n (%)
3	141 (99.3%)	1 (0.7%)	142
4	49 (100%)	0 0	49
5	15 (88.2%)	2 (11.8%)	17
6	6 (42.9%)	8 (57.1%)	14
7	2 (5.9%)	32 (94.1%)	34
8	0 0	21 (100%)	21
9	0 0	43 (100%)	43
Total	213	107	320

P81

Oncotype DX® Recurrence Score Correlation with Histologic Grade and Older Decision-Making Tools for Predicting Breast Cancer Recurrence Risk D. Gilman,[1]* G. Del Rosario,[2] T.D. Moore,[1] P.R. Renker,[1] B. Sickle-Santanello.[1] *1. Grant Medical Center, Columbus, OH; 2. Southbay Ob/Gyn, National City, CA.*

Introduction Oncotype DX® is a 21-gene assay that has recently been established as a reliable predictor of chemotherapy benefit and risk of 10-year distant recurrence in women with early stage breast cancer. The primary aim of this study was to establish if the Oncotype DX® Recurrence Score (RS) correlates with Adjuvant! Online in determining a patient's 10-year distant recurrence risk. A secondary aim was to compare those scores with histologic grade, tumor size, age, and race. Methods This is a retrospective study of breast cancer patients that underwent Oncotype DX® testing between May 2005 and May 2010. Oncotype DX® RS was compared with Adjuvant! Online, histologic grade, tumor size, age, and race using SPSS software. Results A total of 86 patients underwent Oncotype DX® testing during the study period. Of those patients, 15 had positive lymph node status and were excluded from the final analysis, for a total of 71 patients. Of the 71 remaining patients, 30 (42%) were categorized as low risk, 28 (39%) as intermediate risk, and 13 (18%) as high risk by Oncotype. We found a moderate correlation between the rate of 10-year distant recurrence as calculated by Oncotype DX® and by Adjuvant! Online ($r = 0.407$, $P = < .0001$). As expected, a higher tumor grade correlated with both the RS and the Adjuvant! Online score ($r = 0.481$, $P = < .0001$ and $r = 0.644$, $P = < .0001$, respectively). However, age, race and tumor size did not significantly correlate with Oncotype DX®. Interestingly, 10 of the 15 (67%) patients with positive lymph nodes were categorized as low risk by RS. Conclusions Oncotype DX® showed a moderate correlation with Adjuvant! Online, and a slightly stronger correlation with tumor grade. In the future, Oncotype may more accurately predict recurrence if age, race, and tumor size were included in the RS, as they did not correlate with the RS but are known predictors of recurrence.

P82

Institution of a Formal Breast Health Program Improves Care For African-American Women in A Community Teaching Hospital R. Orr,[2]* A. Lehn,[1] R. Hird,[2] C. Nguyen,[2] S. Corso.[2] *1. Medical Education, Spartanburg Regional Medical Center, Spartanburg, SC; 2. Gibbs Regional Cancer Center, Spartanburg, SC.*

Introduction: For a variety of reasons, fewer African-American women are treated with breast conservation, and many of those who save their breasts do not receive postoperative radiation therapy. Our hospital (a southeastern US community hospital with several residency teaching programs) lagged behind National norms for breast conserving therapy (BCT) in the mid-1990's. A breast health program was initiated to improve quality of care, targeting BCT in particular. Methods: Several interventions were achieved in 1998-9: 1) Institution of a breast health steering committee, 2) Hiring of a surgical oncologist with extensive BCT experience, 3) Educational offering targeted toward the hospital's general surgeons, 4) Hiring of a breast health navigator. During the following decade, additional improvements included 1) Hiring a minority recruiter for research and education, 2) Hiring an additional navigator, 3) Developing standards for individual physician participation in our NCCCP breast program, 4) Institution of a weekly multi-disciplinary breast conference, 5) Building a dedicated breast center. Results: More African-American women were treated for breast cancer following creation of the breast health program. From 1994-99, 72 African-American women were treated (14.4/yr) as compared to 415 women from 2000-8 (51.9/yr). BCT improved from 46.7% (1994-99 35/72) to 61.5% (255/415 2000-8), $p=0.002$. Similarly, more BCT women received postoperative radiation following the creation of the breast health program (48.6% vs. 74.1% $p<0.001$). From 2005-8, 78% of BCT patients received radiotherapy. Conclusions: Our breast health program has been successful in terms of improving breast cancer care to African-American women in our community. Despite our actions, however, over 20% of BCT women do not receive radiotherapy. It is hoped that our multi-disciplinary treatment conference will continue to improve in this area.

P83

Extent of Disease Breast MRI: Does it really help? R.L. Farkas,* C.H. Andrus, J.L. Peacock, J. Moalem, S. Mandeville, R. Ayer, A. O'connell, R. Iyer, L.M. Schiffhauer, K.A. Skinner. *surgery, university of rochester, Rochester, NY.*

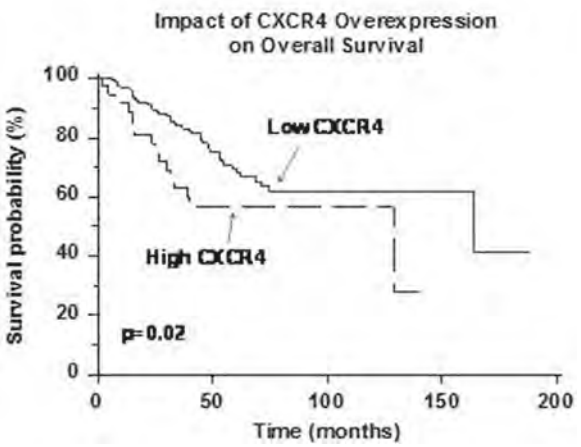
Introduction: MRI is increasingly used to delineate extent of disease (EOD) and to detect multicentric (MC) and contralateral (CL) disease in patients with breast cancer (BC). We compared information gained by EODMRI to conventional imaging and physical examination (standard workup (SW)), and to determine whether EODMRI impacted type of surgery. Methods: Records of 214 consecutive patients who underwent surgery for BC in 2009 were reviewed and MRI findings, workup, size based on SW, MRI, and pathology (PS), type and # of operations were noted. Overestimation was defined as >1.2 X PS, underestimation as <0.8 X PS. Results: 107 patients had SW and 107 underwent MRI. MRI identified additional lesions in 39.2%, leading to 28 biopsies in 24 patients (22.4%). Of 28 biopsies, 7 were positive (25%): 2 documented multifocal disease, 1 documented nodal disease that was also apparent on pre-MRI US, 2 documented MC disease (both 1 cm low grade DCIS), and 2 documented CL cancers (a low-grade DCIS, and a 1cm cancer). CL cancers that were MRI-occult were identified in 2 patients at risk reducing mastectomy. SW

size was larger than MRI size in 19% of patients, smaller in 46%, and similar in 32%. SW and MRI overestimated size in 17.7%, and 34%, underestimated in 41.7% and 38.1%, and were correct in 40.6% and 27.8% (p=0.02). MRI was more accurate than SW in estimating the size of the index lesion in 39% of patients. 37% of MRI patients underwent mastectomy, compared to 38% of SW patients. In contrast, 48.6% of patients with any additional lesion identified on MRI underwent mastectomy, although only 5% had a contraindication to breast conservation. Reexcision rates were similar in the 2 groups. Conclusions: MRI correctly predicted the size of the index lesion in only 27.8% of patients, but was more accurate than SW in 39%. MRI identified MC or CL cancers in 3.7%, but 75% of these were low grade in situ lesions. Only 1 CL invasive cancer was identified (0.9%), while at least 2 (1.8%) were missed. Having an MRI was not associated with higher mastectomy rates, but any finding on MRI was. MRI did not impact reexcision rate. Routine use of MRI to determine EOD does not appear to be warranted.

P84

The Chemokine Receptor CXCR4 as a Novel Independent Prognostic Marker for Node Positive Breast Cancer Patients C.C. Parker,[1]* L.W. Johnson,[2] L. Panu,[1] Q.D. Chu,[1] B.D. Li.[1] *1. Division of Surgical Oncology, LSU Health Sciences Center-Shreveport, Shreveport, LA; 2. LSUHSC - E. A. Conway Medical Center, Monroe, LA.*

Introduction: Node positive breast cancer patients are a high risk group. However, not all such patients will succumb to the disease. The molecular basis for this biologic heterogeneity is poorly understood. The chemokine receptor CXCR4 is a marker of metastatic disease. Its prognostic role in node-positive patients is unknown. We postulate that high CXCR4 overexpression in node positive breast cancer specimens predicts a poor outcome. Methods: 185 node positive breast cancer patients were evaluated. All had standardized treatment and surveillance protocols. CXCR4 levels were detected with Western blots. Results were quantified against 1 μg of HeLa cells. CXCR4 expression was defined as high (≥7.5-fold) or low (<7.5-fold). Primary endpoints were cancer recurrence and death. Statistical analyses were Kaplan-Meier curves, log-rank test, and Cox proportional hazard model, with a p value of ≤ 0.05 as significant. Results: The mean follow up time was 54 months; 148 patients (80%) had low CXCR4 and 37 patients (20%) had high CXCR4 level. The 5 year overall survival (OS) for the low and high CXCR4 group was 69% and 57%, respectively (p=0.02). The 5 year disease-free survival (DFS) for the low and high CXCR4 group was 62% and 53%, respectively (p=0.08). On multivariate analysis, T stage (p=0.001) and grade (p=0.04) were independent predictors of DFS, while T stage (p=0.005), grade (p=0.024), and CXCR4 level (p=0.01) were independent predictors of OS. Conclusion: High CXCR4 level in cancer specimens independently predicts a poor outcome for patients with node positive breast cancer.



P85

Phyllodes Tumors: Race Related Differences J.M. Pimiento,[1]* P. Gadgil,[2] A. Santillan,[2] M.C. Lee,[1] N.N. Esposito,[1] J.V. Kiluk,[1] N. Khakpour,[1] T.L. Hartley,[2] I.T. Yeh,[2] C. Laronga.[1] *1. Surgical Oncology, H Lee Moffitt Cancer Center, Tampa, FL; 2. University of Texas Health Science Center San Antonio, San Antonio, TX.*

Background: Phyllodes tumors (PT) are rare breast malignancies accounting from 0.5% to 1% of all breast tumors. PT have unpredictable behavior with recurrence rates as high as 40%. Due to the rarity of this disease, a dearth of information exists regarding racial differences, and is the objective of this study. Methods: Retrospective review of patients treated for PT at either Moffitt Cancer Center (MCC) or The University of Texas Health Science Center San Antonio (UTHSCSA) was performed from 1999 to 2010. Demographic, pathologic, treatment and outcome related data were recorded. The UTHSCSA sees a predominantly Hispanic population (81% of patients) thereby complementing the predominantly Caucasian MCC population (64%). Statistical analysis using Pearson chi-square, Mann-Whitney and log-rank test explored the racial differences among patients (pts). Results: Of the 128pts, 4 were referred for treatment of recurrent PT and excluded from further analysis. Of the remaining 124pts, 71 (57%) were treated at MCC and 53 (42%) at UTHSCSA. The mean age at diagnosis was 43.9years (range 15-70). 33 (29%) required mastectomy. Combined, 42% of the pts were Caucasian, 43% Hispanic, 12% Black and 3% corresponded to other races. The tumors were considered benign in 58pts (49%), borderline in 41 (34.75%), and malignant in 19 (16%), with a higher percentage of diagnosis of borderline and malignant tumors in Hispanic patients (p=0.0044). Furthermore, Hispanic patients tended to have larger tumors (p=0.035) and higher mitotic rates (p=0.013). At a mean follow-up time of 23 months, the recurrence rate was 8% and was associated with tumor size (p=0.0073), tumor grade (p=0.018), mitotic rate (p=0.006), and close margin status (<1cm) (p=0.041). However these findings did not translate into a survival difference by race. Conclusions: In this multi-institutional review of PT we found significant differences in tumor grade by race with higher-grade tumors present more often in Hispanic patients. These differences did not significantly affect outcome at short-term follow-up. Further investigation into additional biologic factors, geographic impact, and/or institutional biases is needed to more clearly delineate this finding.

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Tumor, Patient and Socio-economic Predictors of Contralateral Prophylactic Mastectomy in the United States N. Wasif,* C.C. Stucky, R.J. Gray, B.A. Pockaj. *Surgery, Mayo Clinic, Phoenix, AZ.*

Introduction: The incidence of contralateral prophylactic mastectomy (CPM) for breast cancer has increased steadily over the last decade, despite little evidence to suggest a survival benefit in most cases. Our goal was to identify tumor, patient and socio-economic variables associated with the decision to undergo CPM. Methods: The Surveillance, Epidemiology and End-Results Database (SEER) linked to the Area Resource File (ARF) was queried to identify 97,815 patients with unilateral invasive ductal carcinoma from 2004-2007. Patients undergoing CPM were compared to patients undergoing either segmental or unilateral mastectomy (USM). Logistic regression analysis was used to identify predictors of CPM. Results: The incidence of CPM increased from 2.5% in 2004 to 3.6% in 2007 (p <0.001). When compared with the USM group, patients in the CPM group were younger (median age 51 vs. 58 years, p <0.001) and more likely to be white (88% vs. 81%, p <0.001). On multivariate analysis, variables that predicted CPM were white race (OR 2.03, 95% CI 1.79-2.31), age < 55 years (OR 2.06, 95% CI 1.89-2.24), diagnosis in the year 2007 (OR 1.57, 95% CI 1.40-1.76), T3 stage (OR 2.17, 95% CI 1.68-2.80), ER negative tumors (OR 1.11, 95% CI 1.01-1.26), high tumor grade (OR 1.17, 95% CI 1.07-1.29) and clinically positive nodes (OR 1.39, 95% CI 1.26-1.53). Socio-economic factors predictive of CPM were high school completion rate >75th centile (OR 1.34, 95% CI 1.16-1.54) and unemployment <25th centile (OR1.21, 95% CI 1.04-1.41). Conclusions: The decision to undergo CPM for unilateral breast cancer is a complex interplay of tumor, patient and socio-economic variables.

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Clinical significance of p53-miR34a pathway in disseminated tumor cells in bone marrow of breast cancer patients Y. Kai,[3]* K. Mimori,[1] T. Yokobori,[1] Y. Kubota,[3] F. Tanaka,[1] K. Shibuta,[3] M. Mori,[2] H. Ueo.[3] *1. Division of Molecular and Surgical Oncology, medical institution of bioregulation,Kyushu university, Beppu, Japan; 2. Osaka university,graduate school of medicine,department of gastroenterological surgery, Osaka, Osaka, Japan; 3. Ueo breast cancer hospital, Oita, Oita, Japan.*

Backgrounds: MicroRNA(miR) in peripheral blood and bone marrow (BM) has been recently focused on as a new biomarker which forecasts the metastasis and recurrence of the breast cancer. We paid attention to miR34a expression induced from tumor suppressor gene, p53, and clarify clinical significance of miR34a expression and p53 in BM of breast cancer patients. Patients and Methods: 185 primary breast cancer patients who had curative operation (from 2000 to 2004) and were followed up for 4-89 months. Total RNA were extracted from BM of breast cancer patients, and we measured both expression levels of miR34a and wild-type p53 mRNA in BM by quantitative RT-PCR. Results: There were no significant difference in miR34a expression among breast cancer subtypes, and clinicopathologic variables. In disease free survival (DFS) rate in 5 year, patients of high miR34a expression showed significantly higher rate (80.5%) than those of low miR34a expression (55.8%) (HR1.50, 95%CI 1.14-2.00,$p<0.01$). In overall survival (OS) rate in 5years, patients of high miR34a expression indicated significantly higher rate (90.6%) than those of low miR34a expression (84.3%) (HR1.64,95%CI 1.04-2.76,$p<0.05$). A multivariate analysis indicated that miR-34a expression was an independent factor for relapse (HR=2.39; $p<0.05$). Expression levels of miR34a and p53mRNA had a positive correlation (correlation coefficient: 0.44). However, patients of higher miR34a showed higher DFS rate and OS rate than those of higher expression of p53 mRNA. Conclusion: We have identified miR-34a in BM as a novel prognostic marker in breast cancer patients. In case of relapse in breast cancer, the decreased p53-miR34a pathway in disseminated cancer cells in BM might be a definitive step to form metastasis in breast cancer.

P88

100 Women with DCIS Prospectively Evaluated by MRI: Radiologic/Pathologic Correlation K. Jaiswal,* C. Vallejo, J. Goldberg, S. Patil, E. Morris, K.J. Van Zee. *Department of Breast Surgery, Memorial Sloan Kettering, New York, NY.*

Background: Conventional imaging often underestimates microscopic extent of DCIS. Here, we compare MRI appearance to final histopathologic findings. Methods: 100 patients, <60 years old, presenting with core biopsy-proven DCIS ± microinvasion (MI), were enrolled and underwent MRI. Index lesion MRI characteristics were prospectively evaluated. Surgical specimens were serially sectioned and carefully mapped for extent of disease. The path-size of DCIS was calculated as the larger of (1) total number of slides spanned, multiplied by section thickness, or (2) the largest span of disease on a single slide. Results: Mean age was 48; 69% were premenopausal. 3 pts were excluded because slide review did not confirm the diagnosis of DCIS. Of 97 pts, 11 (11%) had no residual disease on final pathology, 51 (53%) had DCIS, 19 (20%) had invasive cancer, 16 (16%) had MI. MRI found a mass, focus, non-mass or no lesion in 19%, 2%, 52% and 28%, respectively. 14 (52%) of 27 with no MRI lesion had DCIS, 5 (19%) had invasion/ MI, and only 8 (30%) had no residual disease. Of 18 pts with mass on MRI, 6 (33%) had DCIS, and 11 (61%) had invasion/MI . Of the 50 pts with non-mass on MRI, 29 (58%) had DCIS, and 19 (38%) had invasion/MI. Sensitivity, specificity, PPV, NPV, and accuracy of MRI predicting any residual disease were 78%, 73%, 96%, 30%, and 77%; those statistics for MRI mass or focus predicting invasion were 31%, 85%, 55%, 69%, and 66%. In 44 pts, all disease was limited to a single resection specimen; in these an accurate path-size could be determined. Median lesion size by mammogram (1.0cm) or MRI (1.6cm) was significantly smaller than path-size (2.6cm) ($p=0.01, 0.03$, respectively). Path-size correlated better with MRI-size than mammogram size ($R2=0.61, 0.46$, respectively.) Conclusion: In the setting of biopsy-proven DCIS, a mass on MRI usually indicates invasive disease, while a non-mass is usually DCIS. However, even in the absence of an MRI lesion, most have residual DCIS or invasion. Although both mammogram and MRI generally underestimate the true extent of DCIS on surgical excision, MRI-size correlates better with path-size.

Correlation between MRI and pathologic findings, number of patients

	MRI Lesion				
Histologic Lesion	Mass	Focus	Non-mass	No Lesion	Total
Invasion	6	0	10	3	19
Microinvasion	5	0	9	2	16
DCIS	6	2	29	14	51
No Residual Disease	1	0	2	8	11
Total	18	2	50	27	97

P89

A simple risk score to predict the presence of NSN metastases in breast cancer patients with a positive sentinel node R.F. Van la Parra,[1]* P.G. Peer,[2] W.K. De Roos,[1] M.F. Ernst,[3] K. Bosscha.[3] *1. Surgery, Gelderse Vallei Hospital, Ede, Netherlands; 2. University Nijmegen Medical Center, Nijmegen, Netherlands; 3. Jeroen Bosch Hospital, 's Hertogenbosch, Netherlands.*

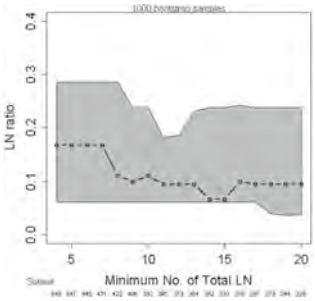
Background: Completion axillary lymph node dissection (ALND) remains the standard of care for patients with a positive sentinel lymph node (SLN). However, in 40-60% of patients the sentinel node is the only positive node. A risk score was developed to identify the patient's individual risk for non-SLN metastases. Materials and Methods: The risk score was developed based on data of 182 breast cancer patients who underwent successful SLN biopsy and completion axillary lymph node dissection for SLN metastases from one hospital. Based on the predictive factors of NSN metastases, identified in a previous meta analysis, a risk score was developed using pathological tumour size (≤ 20 mm / > 20 mm), lymphovascular invasion (yes/ no), extracapsular extension (yes/ no), size of the SLN metastases (≤ 2 mm/ > 2 mm) and number of positive SLNs (1/ > 1). The risk score was subsequently validated on an external population (n=180). A receiver operating characteristic (ROC) curve was drawn and the area under the curve was calculated to assess the discriminative ability of the nomogram. Results: The area under the ROC curve was 0.78 (range 0.71- 0.85) in the original population and 0.78 (range 0.70 - 0.85) in the validation population. Conclusion: The Dutch risk score integrates 5 clinicopathological variables to provide an individualized risk estimate of the likelihood of NSN metastases in breast cancer patients with a positive sentinel node. This risk score may assist in individual decision making regarding axillary lymph node dissection in sentinel node positive patients.

P90

In breast cancer the clinical significance of lymph node ratio is dependent on the total number of lymph nodes examined M. Huebner,[1]* C. Grant,[2] R. Qin,[1] A.C. Degnim,[2] J.C. Boughey,[2] J. Aakre,[1] J.W. Jakub.[2] *1. Health Sciences Research, Mayo Clinic, Rochester, MN; 2. Department of Surgery, Mayo Clinic, Rochester, MN.*

Introduction: Breast cancer survival is associated with the number of regional lymph nodes (LN) involved with metastasis. The variability of total number of LNs pathologically evaluated and its impact on LN ratio (LNR) categories is not known. The goal of this study is to identify LNR thresholds that are predict overall survival (OS) based on varying numbers of LN counts. Methods: The study group consists of 449 breast cancer patients with a positive axillary SLN who underwent axillary lymph dissection between 1997 and 2004. The LN count, the number of metastatic LNs, and LNR were used to stratify patients by their OS using a re-scaled logrank statistic, validated with resampling methods, and confidence intervals for LNR cutpoints were calculated. The prognostic value of the lymph node variables was assessed with Cox regression models. Results: The median number of LN examined was 20 (range 4-52). Cutoff values were identified that categorize patients with respect to OS (figure). LNR >0.17 indicated a worse prognosis for OS with an adjusted hazard ratio of 2.18 (95% CI: 1.4, 3.5). Five year OS for pN1 patients with LNR<0.17 (low LNR) was 92.2% while it was 78.5% for pN2 patients with LNR>0.16 (high LNR). Five year OS for pN1/high LNR and pN2/low LNR patients fell between these two groups. Nodal staging and LNR criterion together identified 18.4% (n=83) of patients at risk for death, while 8.2% (n=37) of those with mortality risk would have been missed using nodal staging alone. The threshold for LNR predicting a worse OS was 0.10 (95% CI: 0.06, 0.18) for patients with at least 11 LN examined. However, if patients with a lower LN count were included the threshold for LNR

predicting worse OS was increased to 0.17 (95% CI: 0.06, 0.29). Conclusion: Use of LNR in conjunction with nodal staging allows for more accurate prediction of breast cancer prognosis than nodal staging alone. The impact of LNR on outcome must be interpreted in the context of the total LN count. The value of LNR predicting OS is of significant value in patients with a low total number of LNs reported but is of limited value in patients with a high total LN count.



LNR cut-off values and 95% confidence intervals determined by specifying a minimum number of LN examined

P91

MRI vs Breast Specific Gamma Imaging (BSGI) in newly diagnosed ductal cell carcinoma in situ: A prospective head-to-head trial

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Introduction: Mammography remains the standard imaging technique for the diagnosis of ductal cell carcinoma in situ (DCIS). Functional breast imaging, including breast magnetic resonance imaging (MRI), has known limitations in evaluating DCIS. Breast Specific Gamma Imaging (BSGI) has emerged as an alternative functional imaging study. To date there is limited data on the utility of BSGI in DCIS. We sought to prospectively compare the sensitivity of BSGI to MRI in newly diagnosed DCIS patients. Methods: Patients with newly diagnosed DCIS from June 1, 2009 through May 31, 2010 were consented for an IRB approved protocol in which they underwent both breast MRI and BSGI. Each imaging study was read by a dedicated breast radiologist, with one radiologist reading all MRI, and another reading all BSGI studies. All subsequent biopsies were performed percutaneously, using image guidance. Patients were excluded if excisional biopsy was performed for diagnosis, or their MRI was performed at an outside facility. Patients with invasive carcinoma were also excluded. The sensitivity for each modality was calculated. Results: There were 18 patients enrolled in the study that had both MRI and BSGI for newly diagnosed DCIS. The sensitivity for MRI was 94% and for BSGI was 89% (Table 1) (p>0.5, ns). There was one index tumor not seen on either MRI or BSGI, and one index tumor seen on MRI but not visualized on BSGI. Discussion: While BSGI has previously been shown to be as sensitive as MRI for detecting known invasive breast carcinoma, this study shows that BSGI is equally as sensitive as MRI at detecting newly diagnosed DCIS. Due to the limited number of patients enrolled in the study, larger prospective studies need to be performed to determine the true sensitivity and specificity of BSGI.

Index cancer detected by imaging

	Detected	Not Detected
MRI	17	1
BSGI	16	2

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Near-Autonomous Breast Cancer Detection using Dynamic Contrast Enhanced-MRI and Computer-Aided Detection (CAD) with Three-Dimensional, Combined Kinetic and Morphological Analyses

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Introduction. This prospective study was conducted to determine the efficacy for pre-clinical use of near-autonomous (two clicks) computer-aided cancer detection (CAD) system by examining women of high risk referred for MRI of breast. Our goals were: 1) assess sensitivity/specificity of a near-autonomous CAD platform using DCE-MRI post-processing combining kinetic and morphological analyses, 2) assess concordance of CAD results, surgeon's estimation, and pathologist assay, for location within and size of malignancy in breast. Method. 1,976 patients with 2,149 abnormalities were scanned from 2007-1010, including women with dense breasts; BRCA1 or BRCA2 genes, family history of cancer, suspected recurrent cancer, anomalous mammogram/ultrasound, pain, or "clinical suspicion." All patients gave IRB and HIPAA compliant informed consent. 1051/1,638 (64.2%) of cases were bilateral DCE-MRI scans. Near-autonomous CAD detection employed both kinetic and morphological algorithms and was applied to entire breast(s) volume including chest wall. Virtually no operator intervention was required for detection (two mouse clicks) or results. No manually placed regions of interest (ROI) were used. Results. Of 1,976 women scanned consecutively, 361 (22.0%) underwent mastectomies, 17 (1.0%) were bilateral mastectomies, 488 (29.8.7%) received lumpectomies or excisional biopsies, while 623 (38.0%) received core or mammotome biopsies, with 166 (10.1%) receiving non-surgical approaches, i.e., radiation, chemotherapy, etc. Average tumor size resected was 2.956 cm; SD=2.856 cm, while CAD detected breast calculated size was 3.20 cm; SD=2.656 cm. Suspected tumor(s) was displayed visually, within interactive, translucent, 3D breast images. Conclusion. Near-automatic CAD applied to DCE-MRI of breast demonstrated high sensitivity, reasonable specificity, and accurate estimates of both location and volume for seven categories of breast cancer. 3D translucent display should aid surgeons in pre-surgical determination of location and volume of tumor, and provide better visual guidance in planning margin clearance.

Comparison of Autonomous CAD Findings to Pathology Results for Various Breast Cancer Types

Tumor Type	IDC	IDC+DCIS	DCIS	EIC	ILC	IDC+ILC	ILC+DCIS	Mamm.	FA
Number of Cases	254	355	66	60	65	40	9	23	21
Sensitivity	0.984	0.926	0.985	0.966	0.948	0.925	1	1	1
Specificity	0.833	0.825	0.571	0.50	0.600	0.750	0.625	0.5	0.52
PPV	0.996	0.994	0.956	0.982	0.958	0.925	0.8	0.952	0.142
NPV	0.556	0.359	0.8	0.333	0.545	0.750	1	1	1
Pos. Likelihood Ratio	5.903	7.41	2.298	1.931	2.37	3.698	2.67	2	
Neg. Likelihood Ratio	0.019	0.084	0.027	0.069	0.087	0.10	0	0	
Mean Tumor Size (cm)	2.614	2.883	3.236	2.603	4.192	3.296	3.646	2.167	2.5
SD Tumor Size	2.505	2.463	2.903	1.737	3.741	2.794	2.919	1.031	1.4
Mean CAD Tumor Size (cm)	3.168	3.207	3.445	3.452	3.665	3.206	3.188	3.258	2.119
SD CAD Tumor Size	2.508	2.568	2.934	2.65	3.248	2.542	2.563	4.173	1.999
Mean Nuclear Grade	2.396	2.361	2.406	2.267	1.546	2.25	2.0	2.1	
Mean Volume* (CC)	5.24	2.956	1.261	2.594	4.14	0.744	2.5	2.231	
SD Volume	9.168	5.626	2.452	4.02	2.927	1.201	2.304	0.271	
Mean Age	51.71	51.8	51.71	50.85	56.01	49.84	50.29	56	53.05
Min Age	89	82	80	76	82	75	74	70	36
Max Age	29	23	25	33	24	23	27	35	78

*Tumor volume reported is based on the relationship of malignant cells to characteristics of DCE-MRI volume averaging, specifically to a combination of the T/SI curves and morphological rules, and not on the surrounding volume of tissues that may comprise necrotic cells, fibrous cells, and/or parenchymal matrix.

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Pleomorphic LCIS: More Surgical Education is needed S. Blair,[1]* D. Emerson,[1] S. Hwang,[2] S. Kulkarni,[3] D. Ollila.[4] *1. University of California San Diego, La Jolla, CA; 2. University of California San Francisco, San Francisco, CA; 3. Roswell Park Cancer Institute, Buffalo, NY; 4. University of North Carolina, Chapel Hill, NC.*

Background: Most surgeons treat lobular carcinoma in situ (LCIS) as a high risk entity for future development of breast cancer. More recently, pathologists have described a variant called pleomorphic lobular carcinoma in situ (PLCIS) which has a more aggressive appearance and possibly a more aggressive clinical behavior. We under took this study to examine the variation of practice patterns among self-identified breast surgeons in treating PLCIS. Methods: We sent surveys to surgeons in surgical societies interested in the treatment of breast cancer. Chi-square analysis was used to determine whether the practice patterns of surgeons who had fellowship training differed from those who had not had fellowship training. Results: Three hundred and eighty one surgeons responded to this survey and 360 were used for the analysis (response rate 38%). Of these, 133 had fellowship training in surgical oncology/breast, while 227 did not have this training. Those with fellowship training were significantly more likely to be in university rather than community settings. Most surgeons reported that they did not re-excise the margin for patients with classic LCIS (83%). For PLCIS, overall 53% never re-excised patients 12% rarely, 11% sometimes and 24% always re-excised patients. Twenty eight percent of fellowship trained breast surgeons always re-excised as compared to 21% of non fellowship trained surgeons (p=NS). Similarly there was no difference in surgical treatment of LCIS and PLCIS by academic surgeons compared to community-based surgeons. Conclusion: There is little clinical outcome data concerning PLCIS; however, there is growing molecular data that PLCIS represents a separate entity from classic LCIS. A minority of surgeons treat PLCIS aggressively surgically. Aggressiveness of treatment was not associated with surgical fellowship training or practice setting. Our data supports the need for an increased awareness of the clinical significance of PLCIS within the breast surgery community.

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Triple Negative Status Does Not Affect Surgical Decision-Making C.L. Crutcher,[1]* L.B. Cornwell,[1] A.B. Chagpar.[2] *1. University of Louisville, Louisville, KY; 2. Yale University, New Haven, CT.*

BACKGROUND: Triple negative breast cancers have been associated with a poor prognosis. How tumor subtype affects surgical decision-making is not well-understood. We sought to determine whether patients with triple negative disease were more likely to choose mastectomy over lumpectomy. METHODS: From 2004 to 2010, 177 breast cancer patients participated in a prospective study of surgical decision-making. Immunohistochemical (IHC) profiles were evaluated in patients with invasive disease and correlated with choice of procedure. Non-parametric statistical analysis was used. RESULTS: The median patient age was 56 (range; 18-85); median tumor size was 1.6 cm (range; 0.1-15.0). Complete IHC data was available for 142 patients. Twenty-five (17.6%) were triple negative; the other 117 patients were divided between subtypes as follows: 95 ER/PR positive, her-2-neu negative, 13 triple positive, 9 ER/PR negative, her-2-neu positive. Comparing the triple negative population to those with other subtypes, patients with triple negative disease were more likely to be younger (median 50 vs. 58, p=0.009) and have a higher percentage of grade (III) tumors (77.3% vs. 40.2%, p=0.004) than those with other subtypes. Controlling for these factors, triple negative status did not significantly affect surgical decision-making (p=0.119). CONCLUSION: Triple negative status, while being associated with younger age and higher grade tumors, does not impact surgical treatment choice. Despite the fact that triple negative disease tend to be more aggressive, surgical decision-making likely rests on more traditional clinicopathologic variables and patient preference.

UNIVARIATE ANALYSIS			
Factor	Triple Negative	Other Subtypes	p-value
Median patient age	50	58	0.009
Median tumor size	2.0	1.7	0.363
African American race	3 (15.8%)	21 (20.0%)	1.000
Positive LN status	4 (16.0%)	35 (29.9%)	0.218
Invasive lobular subtype	1 (4.2%)	12 (11.8%)	0.463
Grade 3 tumor	17 (77.3%)	45 (40.2%)	0.004
Lymphovascular invasion	8 (36.4%)	38 (35.5%)	1.000
Lumpectomy	15 (60%)	54 (46.2%)	0.271
MULTIVARIATE ANALYSIS			
Factor	OR for partial mastectomy (95% CI)		p-value
Age	1.045 (1.010-1.082		0.011
Grade 3	0.841 (0.310-2.281)		0.734
Triple negative	2.289 (0.807-6.489)		0.119

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The Number of Distinct Preoperative Histopathological Changes in a B3 Breast Lesion is Associated with the Presence of Carcinoma A. Perhavec,* R. Petric, N. Besic, J. Zgajnar, M. Hocevar, M. Music, B. Gazic. *Department of surgical oncology, Institute of Oncology Ljubljana, Ljubljana, Slovenia.*

Introduction: The widespread implementation of screening mammography and core needle biopsy has resulted in an increased frequency of diagnosing lesions of uncertain malignant potential (B3 lesions). The aim of our retrospective chart review was to evaluate, whether the number of preoperative histopathological changes in B3 lesions is related to the presence of carcinoma in the surgical specimen. Patients and Methods: Altogether 327 B3 lesions were diagnosed mainly by vacuum-assisted core needle biopsy from 2006-2010. The object of this study were 120 surgically excised B3 lesions. The data on preoperative histopathological changes (papillary neoplasia, radial scar, atypical ductal hyperplasia, columnar metaplasia, columnar hyperplasia, planocellular atypia and LCIS) and histopathology of surgical specimen (DCIS and invasive carcinoma versus benign) were collected. For each patient the number of preoperative histopathological changes was counted. Mammographic and pathological factors were statistically correlated with histopathology of the surgical specimen using contingency tables. Results: Carcinoma was diagnosed in 25/120 (21%) lesions (3 invasive carcinomas and 22 DCIS). Mammographic BI-RADS 4 lesion were microcalcifications, spiculated tumor, nonspiculated tumor or disruption of breast architecture in 92 (77%), 12 (10%), 14 (12%) and 2 (2%) cases, respectively. The type of mammografic lesion did not correlate with histopathology of surgical specimen. Mammographic mean diameter of the benign lesion and carcinoma was 21 mm and 27 mm, respectively (p=0.12). The patients with three or more preoperative changes had a greater chance (p=0.045) of having carcinoma (38%) compared to those with less than three preoperative changes (17%). The preoperative change most often associated with carcinoma was planocellular atypia (31%), while papillary neoplasia had the smallest chance of carcinoma (18%). The difference was not statistically significant. Conlussion: B3 lesions with three or more distinct changes are associated with greater chance of harboring invasive carcinoma and/or DCIS than lesions with less than three distinct changes.

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National and Maine State Trends in Breast Reconstruction After Surgery for Breast Cancer A. Kieryn,* L. Rutstein, T. White. *Surgery, Maine Medical Center, Portland, ME.*

Introduction: Compare Maine State data to National benchmark for breast reconstruction after mastectomy. Methods: Retrospective observational review of surgical treatment after mastectomy of breast cancer patients in Maine between 2004-2006. Data: 37 community and academic hospitals in Maine (11 ACoS); all participate in the State Tumor Registry (Registry). Patients: Comprehensive review of female patients with breast cancer included in the Registry from 2004-2006. Patients who had mastectomies were selected for study inclusion. Interventions: Breast reconstruction after mastectomy. Patients were not chosen at random to receive reconstruction; surgical intervention after mas-

tectomy was selected by surgeon and/or patient. Results of reconstruction decisions were recorded in the Registry; hospital and patient Registry data are blinded to individual hospital, but not ACS-determined regions. Registry data were retrieved; analysis compared women post-mastectomy who did and did not have reconstructive surgery. Results were stratified by region. State and regional data were compared to national benchmarks. Conclusion: The national rate of breast reconstruction after mastectomy in 2006 was 75%. In Maine, 533 mastectomies were performed in 2006; 127 had reconstruction, giving the State of Maine a rate of 24%. Reconstruction rates differed significantly by region. Maine falls below the national average for breast reconstruction after mastectomy. We hypothesize this discrepancy is due to regional availability of immediate reconstruction and reluctance of community hospitals to transfer patients to tertiary centers. Further studies are needed to understand other factors affecting surgical decision making for breast cancer patients.

P97

Utility of preoperative magnetic resonance imaging in breast cancer M. Senthil,[1]* C. Behrendt,[2] L. Gonser,[2] J. Ellenhorn,[2] N. Kounalakis,[2] S. Mckenzie,[2] L. Vora,[2] J.H. Yim.[2] *1. Loma Linda University medical center, Loma linda, CA; 2. City Of Hope cancer center, Duarte, CA.*

Background and Objective: Utilization of Magnetic Resonance Imaging (MRI) as an adjunctive imaging tool in patients with breast cancer although controversial is on the rise. The purpose of our study is to evaluate the routine use of preoperative bilateral breast MRI and identify specific risk factors that are associated with MRI-only detected abnormalities and finally assess the benefit and risk incurred from preoperative MRI. Methods: We performed a retrospective chart review of women with the diagnosis of unilateral breast cancer that underwent bilateral breast MRI from during 2006-2008. Patient demographics and clinical data were manually retrieved by chart review. A preoperative MRI abnormality (PMA) was defined as a new lesion identified by MRI -only scored as BIRADS 0 or ≥4 or increase in the size of the index lesion by more than one centimeter. Results: A total of 344 patients were eligible with an age range of 24-90, mean 53.3(± 11.1 years). PMA was detected in 142 (41.3%) patients including 32 (9.3%) who had bilateral PMA. Most PMAs (145/174, 83.3%) were evaluable prior to surgery of which 85/145 (58.6%) represented a new or larger malignant lesion. In the index breast, detection of new in-situ or invasive cancer was 10.5% (36/344) and the index cancer was larger by greater than one centimeter in 10.8 % (37/344). New in-situ or invasive cancer was detected in 3.5% of contralateral breasts. On multivariate analysis the most important factor predictive of MRI –detected malignancy was age at diagnosis between 40-49years. MRI findings resulted in change in surgical plan in 88 patients (25.6% of all patients or 54.6% of those with PMAs). Conclusion: Our results show that MRI is capable of detecting additional lesions both in the ipsilateral and contralateral breast resulting in change in surgical plan in more than 25 % of the patients.

P98

Reasons for Choosing Contralateral Prophylactic Mastectomy in Women who Test negative for the BRCA mutation: A Retrospective Questionnaire M. Howard-McNatt,* S. Moore, E. Levine, G. Hurt. *Surgery, Wake Forest Baptist Medical Center, Winston-Salem, NC.*

Determination of BRCA1and 2 mutation carrier's status has become increasingly important. BRCA 1/2 carriers are offered bilateral mastectomy (BLM) and prophylactic oophorectomy. However, there is a cohort of women who still decide to have BLM at the time of their breast cancer diagnosis despite testing negative for the mutation. A questionnaire was sent to women who had prophylactic mastectomies to determine the reasons for their surgical choice. Methods: Women who received BRCA1 and 2 testing and tested negative but chose bilateral mastectomies between January 2005- May, 2010 were sent a questionnaire. For those who expressed an opinion, a two-sided Fisher exact test was used to compare responses. Results: A total of 35 surveys were mailed, and 29 were returned (82%). The mean patient age at diagnosis was 41.9 years. The majority of women were Caucasian and had some college to postgraduate education. Most women were married (72% vs 27% p=0.015) with children (p=0.0004). Although the majority had a relative with breast cancer, this fact did not influence their surgical decision (p=0.669). The man reason for having BLM was fear about breast cancer recurrence (p=0.0006) in comparison to being alive for a spouse or children. Most women had breast reconstruction (89.7%) Overall, 69% of the respondents were satisfied with their decision to have BLM. Conclusion: Increased rates of contralateral prophylactic mastectomies have been observed in women with negative BRCA results. In our study young, married, educated women with children were more likely to choose BLM. The main reason was fear of recurrence.

P99

Breast Cancer Surgery Impact on Quality of Life J. Bulatova MD,* M. Williams, N. Welling MD, N.Z. Carp MD, R.M. Ciocca DO, J.L. Sabol MD, R.D. Smink MD. *general surgery, LH, Wynnewood, PA.*

Introduction: Breast cancer surgery is known to influence aesthetic as well as functional aspects of patient's lives. Few studies have been performed to identify the magnitude of limitations in every day activities. The purpose of this study was to quantify the extent to which breast cancer surgery impacts quality of life. The publication is an adjunct to a prior study aimed at determining the incidence of lymphedema and factors associated with its development. Methods: We analyzed 504 patients following surgery for unilateral breast cancer. Patients completed a Quality of Life (QOL) questionnaire consisting of 37 questions. All related to activities of daily living including 1) symptoms (pain, tightness, paresthesias, swelling, weakness) 2) functional limitations (ability to lift, pull, push, carry) 3) subjective assessment of quality of life. Comparison was made between dominant and non-dominant extremities as well as operated and non-operated sides. Statistical analysis was conducted to correlate breast cancer surgery, limitations in every day activities as well as subjective grading of wellness. Results: The results of this study showed a direct correlation between lymphedema (delta arm displacement >200 cm3) and a lower Quality of Life Score(p=0.0053).Definition of lymphedema was based on the results of our prior study which is arm displacement > 200cm3, this correlated with patient's subjective identification of arm swelling(p=0.0060).QOL sub scores (with respect to symptoms, functional limitations) showed significant differences between patients with a delta of >200 cm3 and <200cm3(p=0.0008 and p=0.0022). Conclusions: Patients with arm displacements >200 cc had mild to minimal limitations in 10% of cases, 2% of patients have severe limitations. There is a direct correlation between lymphedema (delta arm displacement >200 cm3) and a lower Quality of Life Score (p=0.0053). Even with presence of clinical lymphedema, most of our patients were happy with results of their surgery and had minimal complaints 98%. Removal of 10 lymph nodes correlated with decline of QOL (p<.0001). This study could serve as a useful patient counselling tool.

P100

Excessive Rates of Nodal Staging in DCIS C. Truong,[1]* T. Owen,[3] A. Kurian,[2] I. Wapnir.[1] *1. Stanford University, Department of Surgery, Stanford, CA; 2. Stanford University, Department of Surgery, Stanford, CA; 3. Stanford University, Department of Health Research and Policy, Palo Alto, CA.*

Intro: Nodal staging(NS) of DCIS was abandoned in 1980s. DCIS is diagnosed commonly by core biopsy. Surgical decision is often based on size from imaging studies. Mastectomy (Mx) rates, including contralateral Mx and NS procedures are rising, counter to previous trends. We compare surgical patterns of full-time faculty (F) to community-based (C) physicians in the same academic center. Methods: The Tumor Registry of Stanford Hospital identified analytical DCIS cases from 2005-2009. Patients upstaged on surgery was excluded. The non-faculty or community group (C) consists of two subgroups. The main group C1 is a comparison group in all analyses; the C2 group comprises physicians from a contracted group who primarily use the hospital for Mx, and data were available for a sub-set of analyses (C2). Results: Of 376 DCIS cases in 5-years, 257, 68.4%, [95% CI 0.63 to 0.73] were performed by F and 119, 31.6% by C1 [0.27-0.37]. 59% of patients [0.50 -0.59] in both had lumpectomy(Lm). Sentinel node +/- axillary dissection (SN/ALND) was 46% [0.39-0.51] of DCIS cases in each group. NS was done in 16.4% [0.11-0.23] and 22.5% [0.14-0.34] of F and C1 Lm cases. In contrast, 88.6% [0.82-0.94] and 81.2% [0.68-0.90] of F and C1 Mx cases had SN/ALND respectively. The C2 group had additional 51 cases, with total of 204 Mx patients. 74% [0.65-0.82] of F Mx had immediate reconstruction compared to 77% [0.63-0.87] for C1 and 37.2% [0.25-0.51] for C2. Bilateral mastectomies (BMx) were performed in 55 /427 (12.8%) [0.10-0.16] patients. The proportion of BMx in the Mx cohorts was 22% [0.17-0.33] of F, 39% of C1 [0.27-0.54] and 21.5% of C2 groups [0.12-0.35]. In F, 60% [0.41-0.77] of BMx were associated with a family history compared to 32% in C1 [0.15-0.54] and 27% in C2 groups

[0.09-0.57]. Not biopsied findings in the other breast or patient choice was 24% of F [0.11-0.44], 37% of C1 [0.19-0.59] and 45% of C2 [0.21-0.72] of BM procedures. Contralateral breast cancer was 8% [0.01-0.26] of F, 21% of C1 [0.08-0.44] and 27% [0.09-0.57] of C2 BMx. Conclusion:. Nodal staging occurred in nearly half of DCIS cases and majority of Mx patients. The prevalence of BMx was higher among C1 and less likely to be associated with an inherited risk.

P101

Nipple sparing mastectomies, evaluation of complications and recurrence rates C. Moses,* T. Lillemoe, D. Dunn, T. Schaefer, D. Ruebeck, M. Migliori, C. Anderson, M. Bretzke. *Abbott NW Hospital, Minneapolis, MN.*

INTRODUCTION: The purpose of this study was to evaluate the complication rates and local recurrence/occurrence rates associated with nipple sparing mastectomies in patients undergoing treatment of breast cancer or risk reduction surgery. METHODS: We retrospectively analyzed 55 patients who underwent a total of 100 nipple sparing mastectomies (NSM) for breast cancer (n=35) or prophylactic risk reduction (n=20) between 9/07-9/10. Selection criteria for NSM in patients treated for breast cancer included an isolated tumor <3cm and .2cm from the nipple areolar complex, based on preoperative exam and imaging. Intraoperative frozen section analysis of nipple ducts within the nipple and at the mastectomy margin was performed prior to undergoing first stage breast reconstruction with tissue expanders. RESULTS: Among the patients treated for breast cancer, the pathological stage ranged from Stage 0 to Stage III (T1N2a). Five patients required axillary node dissection. Four patients (4%) were converted to conventional mastectomy due to nipple involvement (atypia, ADH, phylloides, LCIS) at the time of frozen section. At a median follow up of 19 months (range 0.5 to 36), the local recurrence/occurrence rate was 0%. Eighteen patients tested positive for the BRCA gene. Overall major complication rate was 9%. This included implant removal due to wound infection (n=4), implant removal due to breast deformity (n=1), nipple slough requiring reconstruction (n=4). CONCLUSIONS: NSM can be successfully performed in highly selected patients for prophylaxis with minimal complications and without compromising oncologic outcomes. Nipple involvement can be assessed adequately with preoperative imaging in addition to intraoperative frozen section analysis.

P102

Treatment of Ipsilateral Supraclavicular Metastasis in Breast Cancer Patients J.L. Wagner,[1]* M.I. Ross,[1] K.K. Hunt,[1] F. Meric-Bernstam,[1] E.A. Mittendorf,[1] E.A. Strom,[2] I. Berosian.[1] *1. M.D. Anderson Cancer Center Department of Surgical Oncology, Houston, TX; 2. M.D. Anderson Cancer Center Department of Radiation Oncology, Houston, TX.*

Background: The re-classification of ipsilateral supraclavicular (SCV) nodal metastasis as stage III disease in the 2002 AJCC staging system has renewed interest in examining the role of surgery in such patients (pts). The objective of this study was to examine the outcomes of women who underwent lymph node dissection as part of the multimodality treatment of ipsilateral SCV nodal metastasis. Methods: 90 pts with pathologically confirmed SCV nodal metastasis from 11/2000 to 12/2006 were identified. 75 (83.1%) pts had ipsilateral SCV metastasis at initial diagnosis of their primary breast cancer, 15 (16.7%) pts had isolated ipsilateral SCV recurrence. Time to local-regional recurrence (LRR), event-free survival (EFS) and overall survival (OS) from initial diagnosis of SCV disease was determined. Results: Of the 90 pts, 76 (84.4%) received chemotherapy (CTX) and radiotherapy (RT) for treatment of SCV metastasis while 10 (11.1%) underwent surgery in addition to CTX + RT. 4 (4.4%) pts had CTX (alone or with surgery) without RT. There were more patients in the surgery arm with recurrent SCV disease (p=0.01). 3/10 pts (30%) in the surgical group experienced LRR compared to 6/80 pts (7.5%) in the CTX-XRT group. On univariate analysis, triple negative subtype was associated with shorter time to LRR, reduced EFS and poorer OS (all p<0.01). Pts who presented with recurrent SCV metastasis had shorter time to LRR and decreased EFS (all p<0.01). On multivariate analysis, presentation with recurrent SCV metastasis and triple negative subtype remained significant predictors of reduced time to LRR and EFS (all p<0.05). Triple negative subtype was also associated with decreased OS (p<0.01). The use of surgery did not impact these outcomes. Conclusion: Triple negative subtype and presentation with recurrent SCV disease are independent predictors for poor outcomes in breast cancer pts with ipsilateral SCV metastasis. The use of surgery in patients with SCV metastasis did not improve outcomes however; it was confounded by the greater likelihood of recurrent presentation in this group. The role for surgical resection of SCV nodal metastasis from breast cancer requires further evaluation.

P103

Cinacalcet (Sensipar) provides no measurable clinical benefits for patients with primary hyperparathyroidism and may accelerate bone loss with prolonged use D. Politz, J. Norman.* *Norman Parathyroid Center, Wesley Chapel, FL.*

Introduction: Cinacalcet (Sensipar) has been shown to decrease calcium levels in patients with primary hyperparathyroidism (PHPT) in small trials, however few other endpoints have been studied and long-term effects are not known. Methods: At the discretion of a referring doctor 70 patients began Cinacalcet as an alternative to surgery for PHPT. Patients were followed as long as the drug was tolerated or until complications arose, at which time all were referred for parathyroidectomy. Results: Women comprised 73% while 27% were men. The average age was 62 (range 19-90). Prior to treatment, serum calcium levels averaged 11.7 (range 11.0 - 15.1) and PTH averaged 156 (range 88-815). Using a standard parathyroid-symptom questionnaire, 93% had 2 or more classic parathyroid symptoms (average 5.3, range 0-9). Cinacalcet had to be discontinued in 19 patients (26%) within 4 months because of nausea /vomiting. The remainder (n=51) were treated from 8 to 28 months. Calcium levels dropped in all patients but this was always intermittent. PTH levels dropped 5-15% in 80% of patients, however PTH always remained high. Only 3 (6%) had any symptom relief (p=0.3), while 11 (21.6%) said they felt worse (p<0.05). 23 patients had Cinacalcet for >1.5 years, 14 of which showed significant (>1 SD) decreases in bone density (p<0.05), none had an increase in bone density. All had curative parathyroid surgery as an outpatient with normalization of both calcium and PTH (both p<0.001) followed by partial or complete resolution of PHPT symptoms within 3 months in 88% (p< 0.001). Conclusion: Cinacalcet cannot be tolerated by a large percentage of patients. When tolerated, Cinacalcet reduces serum calcium in patients with PHPT, but provides symptom relief in almost none, making 22% feel worse. Prolonged use is associated continued bone loss which is often dramatic and may be due to persistent elevated PTH levels. Outpatient parathyroid tumor removal is clearly a better choice.

P104

Normal PTH Levels in Primary Hyperparathyroidism: Still the Same Disease? A.L. Amin,* T.S. Wang, T.W. Yen. *Department of Surgery, Medical College of Wisconsin, Milwaukee, WI.*

PURPOSE: Primary hyperparathyroidism (pHPT) can occur in patients with elevated calcium levels but normal PTH levels. It is unknown if these patients have a milder, less symptomatic form of pHPT. This study investigates the symptoms, laboratory values, imaging studies and outcomes of sporadic pHPT patients with normal PTH values. METHODS: A retrospective chart review of a prospectively-collected, single institution parathyroid database was performed of patients with sporadic pHPT who underwent parathyroidectomy by endocrine surgeons between December 1999 and June 2010. The cohort consisted of patients with only normal PTH levels for 6 months prior to surgery who were compared to a randomized control group of sporadic pHPT patients with elevated PTH levels, matched 1:2 for age and gender. RESULTS: Of the 861 patients, 58 (6.7%) had only normal PTH values within 6 months of surgery and represent the study cohort. The mean age of the cohort was 56 years (range 31-79) and 88% were female. 90% were symptomatic (19% nephrolithiasis, 7% fractures and 72% neurocognitive symptoms, including mood swings or fatigue); 70% had either osteopenia or osteoporosis. Most patients had single gland disease (SGD) and there was no difference in symptoms, bone health or preoperative calcium levels between the two groups (Table). However, compared to the control group, the study cohort was more likely to have higher preoperative vitamin D levels, smaller adenomas and require bilateral neck exploration. In addition, imaging studies, particularly Sestamibi, were less sensitive in the normal PTH cohort. CONCLUSION: Patients who have pHPT with either normal or elevated PTH levels present with similar symp-

toms and serum calcium levels. Although most patients with pHPT and normal PTH have single gland disease, the adenomas are significantly smaller and may explain why imaging studies are less sensitive and more patients require bilateral neck exploration. Patients with pHPT who have consistently normal PTH levels should be considered for parathyroidectomy but be counseled that they may be more likely to require a four-gland exploration.

Table

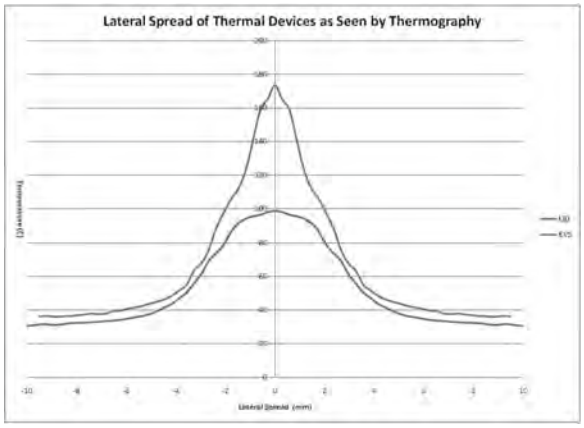
Variable		Cohort (n = 58)	Control (n = 116)	P value
Preoperative Calcium (mg/dL) [A]		10.7 (0.6)	10.9 (0.7)	0.073
Preoperative PTH (pg/mL) [A]		55.1 (12.0)	151.3 (91.5)	<0.001
Preoperative 25-OH Vitamin D (ng/mL) [A,B]		30.8 (13.7)	21.4 (11.2)	<0.001
Sestamibi	Sensitivity	40%	55%	0.086
	PPV	92%	98%	0.459
Ultrasound	Sensitivity	52%	63%	0.223
	PPV	88%	90%	0.986
Neck CT	Sensitivity	54%	67%	0.813
	PPV	100%	67%	0.656
Surgical approach				0.182
	MIP	16 (28%)	45 (39%)	
	Unilateral	9 (16%)	22 (19%)	
	Bilateral	33 (57%)	49 (42%)	
Pathology [C]				0.761
	SGD	51 (88%)	106 (91%)	
	MGD	6 (10%)	9 (8%)	
SGD Gland Weight (mg) [A]		405 (393)	978 (1202)	<0.001
Failed Surgery [D]		3 (5%)	2 (2%)	0.356

A: Expressed as mean (standard deviation)
B: Excludes 75 patients with missing data
C: Excludes 2 patients with missing data
D: Excludes 32 patients with follow up <6 months
Abbreviations: MGD, multiple gland disease; MIP, minimally invasive parathyroidectomy; PPV, positive predictive value; PTH, parathyroid hormone; SGD, single gland disease

P106

Comparison of Thermal Profiles of Vessel Sealing Technology Using Infrared Thermography C.T. Smith,* B. Zarebczan, A.Y. Alhefdhi, H. Chen. *The University of Wisconsin School of Medicine and Public Health, Department of Surgery, Madison, WI.*

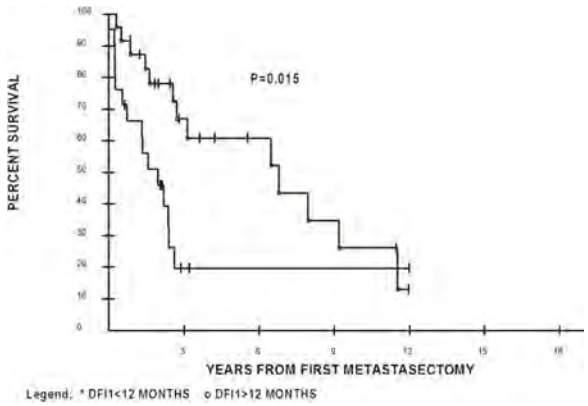
Introduction: The development of ultrasonic dissection (UD) and electronic vessel sealing (EVS) for hemostasis has had many potential benefits over conventional knot-tying technique. The use of the Harmonic FOCUS and Ligasure Precise has been investigated for use in a variety of operations including thyroidectomy, liver resection, pancreaticoduodenectomy, and hysterectomy. We sought to characterize the lateral thermal spread and temporal thermal profiles of each of these techniques on medium sized blood vessels in a porcine model. Method: The renal arteries of University of Wisconsin, Yorkshire female pigs were skeletonized and subjected to firings of each device. One side was utilized in each animal to prevent hemodynamic changes from altering renal flow. In each case the vessel was isolated and the thermal activity was recorded using infrared thermal imaging (SC660, Flir Systems Inc.) Multiple seals were performed with each instrument and the resulting thermal profiles were compared. Results: Thermal images were analyzed for temperature versus time as well as the lateral thermal heating profile at the time of maximum temperature. There were no significant differences in mean time above 39, 40, or 60 degrees Celsius between the UD and the EVS device (42.5 ± 6.8 vs. 45.7 ± 4.0, p = 0.69; 40.1 ± 7.4 vs. 41.1 ± 4.3, p = 0.74; 9.44 ± 0.59 vs. 8.64 ± 1.07 seconds, p = 0.53). UD reached a greater maximum temperature than EVS (173.8 ± 3.4 v 105.2 ± 3.1 degrees Celsius, p = <.001; see attached Figure). Lateral thermal spread was measured in millimeters from the seal center and was not statistically different for spread above 39, 40, or 60 degrees Celsius for UD or EVS (4.02 ± 0.44 vs. 4.28 ± 0.59 mm, p = 0.73; 3.91 ± 0.47 vs. 4.12 ± 0.56 mm, p = 0.77; 2.71 ± 0.24 vs. 2.71 ± 0.54 mm, p = 0.99). There was one seal failure with both EVS and with UD. Conclusion: The use of UD produced a higher maximum temperature during vessel sealing than EVS. This may translate into greater risk of thermal injury within the operative field with use of UD. However, the risk of lateral thermal spread injury during sealing appears similar between the two devices.



P107

Operative Management of Recurrent Adrenocortical Carcinoma – A Single Institution Experience N.M. Datrice,[1]* R. Langan,[1] R. Ripley,[1] C. Kemp,[1] U. Kammula,[1] U. Rudloff,[1] R. Royal,[2] S. Steinberg,[1] B. Wood,[1] D. Schrump,[1] S. Libutti,[3] T. Fojo,[1] I. Avital.[1] *1. National Cancer Institute, National Institutes of Health, Bethesda, MD; 2. MD Anderson Cancer Center, Houston, TX; 3. Montefiore Medical Center, Bronx, NY.*

Introduction: Adrenocortical carcinoma (ACC) is a rare tumor, contributing to 0.2% of cancer deaths in the United States. Despite complete resection of the primary tumor, local recurrence and distant metastases are frequently observed. Chemotherapy has limited efficacy, and surgical management for metastatic ACC remains controversial. Methods: A retrospective review was performed of all patients who underwent surgical intervention for metastatic ACC in a single tertiary center from 1977 to 2009. All available clinicopathologic data were analyzed to determine potential factors associated with response to treatment and survival. Results: Fifty-seven patients underwent 101 resections for recurrent or metastatic disease. 17/57 (29%) patients presented with stage IV disease. Fifteen resections were for local recurrence, twenty-three were for liver metastases, fifty were for pulmonary metastases and 13 were resections of metastases at other sites. Perioperative mortality was 1.7%. Eleven patients underwent radiofrequency ablation (RFA) as well as surgery, and three underwent RFA alone. The median and 5-year survivals from time of first metastasectomy was 2.5 (0.2-18) years, and 41%, respectively. Disease free interval (DFI) between primary resection and first recurrence, and right-sided primaries were found to be significant prognostic factors. The median survival of patients with DFI<12 months was 1.66 (0.2 to 12) years versus 6.56 (0.3 to 12) years for patients with DFI>12 months (p=0.015). Median survival for right versus left-sided primaries was 1.87 (0.3 to 12) years versus 3.82 years (0.2 to 18) years (p=0.034). Liver metastases were more common with right-sided primaries (67% versus 41%, p=0.05). Chemotherapy had no impact on survival. Conclusions: Surgery can be performed safely and may be beneficial in properly selected patients with recurrent and metastatic ACC. Our retrospective analysis suggests that surgery for metastatic ACC should be considered for patients with DFI longer than one year.



Kaplan-Meier curve of overall survival by disease-free interval

P108

Limited Adequacy of Thyroid Cancer Patient Follow-Up at a Canadian Tertiary Care Center E. Lam,* S. Strugnell, M. Robinson, C. Bajdik, S. Gill, D. Holmes, S. Wiseman. *University of British Columbia, Vancouver, BC, Canada.*

Introduction: The objective of this study was to evaluate the adequacy of follow-up of thyroid cancer patients that underwent surgery at a Canadian tertiary care center. Methods: This is a retrospective, cross-sectional study of thyroid cancer patients that underwent surgery from 2003 to 2007 at a tertiary care Canadian centre. A survey was mailed to their primary care physicians requesting information on disease status, laboratory, radiological, and physical examinations. The findings were analyzed relative to follow-up guidelines published by the American Thyroid Association (ATA). Statistical significance between early and late follow-up patterns were analyzed using the $\chi 2$ test. Results: 162 surveys were sent to primary care physicians. 91/162 (56.2%) surveys were responded to. All of these individuals had a diagnosis of papillary thyroid carcinoma. Range of postoperative follow-up was 1.24-7.13 years (mean 3.96 years). 87.9% of patients had a physical exam within the previous year. Only 37.4% and 14% of patients had a serum thyroglobulin measurement within 6 and 12 months prior to the survey, respectively. TSH levels were measured within the previous 6 months in 67% of patients and within the previous year in 13.2% of patients. TSH levels were suppressed <0.1mU/L in 24.2% of patients and between 0.1-2mU/L in 44% of patients. 17.6% of patients had TSH levels >2mU/L. Ultrasound was the most common imaging modality carried out followed by radioiodine scans, CT scans and MRIs. There was no statistically significant differences ($p<0.05$) between practice patterns in patients with earlier follow-up (≤2 years from surgery) and patients with later follow-up (>2 years from surgery). The most common barrier to follow-up cited by primary care physicians was a lack of knowledge of the surveillance guidelines. Conclusion: There is significant variation in follow-up patterns in postoperative thyroid cancer patients with considerable deviation from current ATA guidelines. These observations suggest that the follow-up of many thyroid cancer patients can be improved.

P109

Incidence and long term outcomes of thyroid cancer after total thyroidectomy for multinodular goiter without dominant nodules K.G. Lasithiotakis,* G. Zacharioudakis, N. Vrachassotakis, U. Zoras. *Department of General Surgery, University of Crete, Herakleion, Crete, Greece.*

Background: Exclusion of cancer is a main concern in patients with goiter. Herein, we determine the frequency, the natural history of thyroid cancer, as well as long term outcome in a large number of consecutive patients undergoing total thyroidectomy for multinodular goiter without dominant nodules. Methods: All patients undergoing total thyroidectomy for multinodular goiter without dominant nodules as evidenced from histology report, between January 1990 and October 2008 were included in the study. Demographics, clinical presentation, pathological characteristics and long term postoperative outcomes were retrospectively assessed and all patients underwent telephone interview with the use of structured form in the frame of the study. Results: There were 256 cases of thyroid cancer among 1191 patients included in the study (21.5%). Incidental cancer comprised 93.4% of total. Differentiated thyroid cancer accounted for most of the tumors (96%). There were 5 (2%) cases of myeloid cancer, 1 (0.4%) case of anaplastic cancer, and 2 (0.8%) cases of Hurtle cell carcinoma. Bilateral multicentric cancer was observed in 45.3% of patients. Approximately 70% of patients with differentiated thyroid cancer had papillary microcarcinomas. Transient and permanent postoperative complications ranged in approximately 25% and below 2%, respectively. After a median follow-up time of 78.5 months, overall recurrence rate was 6.7% and disease specific mortality 1.2%. Conclusion: Thyroid cancer is common among patients undergoing total thyroidectomy for multinodular goitre without dominant nodules. In these patients, favorable histology combined with radical surgery in experienced hands contribute to excellent surgical and oncological results.

P110

Predictive Factors of Carcinoma in 388 Patients with Follicular Neoplasm of the Thyroid Gland N. Besic,* A. Perhavec, M. Sesek, M. Hocevar, J. Zgajnar, R. Petric, A. Pogacnik, B. Gazic. *Surgical Oncology, Institute of Oncology, Ljubljana, Slovenia.*

Background and Objectives: Estimation of the risk of malignancy in a patient with follicular neoplasm is important for optimum extent of thyroid surgical treatment. The aim of this study was to find predictive factors of carcinoma in patients with follicular neoplasm. Methods: In this study we included 388 patients (314 females, 74 males; mean age 50 years, range 9–81 years) with follicular neoplasm who were surgically treated in the period 1990–2009. After retrospective chart review predictive factors for malignancy were identified by chi-squared test and logistic regression. Results: The histopatological diagnoses were carcinoma, benign goiter and adenoma in 123 (32%), 135 (35%) and 130 (33%) patients, respectively. The diameter of tumor on surgical biopsy specimen was 0.7–10 (mean 3.4) cm. The median and mean concentration of Tg in the patients with carcinoma was 407 and 1858 ng/ml, respectively. The median and mean concentration of Tg in the patients without carcinoma was 173 and 657 ng/ml, respectively. Predictive factors for carcinoma, shown by chi-square test, were: age of patients, solitary tumor, tumor size and Tg concentration. The independent predictors of malignancy as shown by multivariate logistic regression were solitary tumor, tumor size and Tg concentration. The relative risk of carcinoma in the patients with a solitary tumor was 1.48 in comparison to those with a tumor in multinodular goiter. The relative risk of carcinoma in the patients with a tumor larger than 4 cm was 1.62 in comparison to those with a smaller tumor. The relative risk of carcinoma in the patients with Tg over 300 ng/ml was 1.62 in comparison to those with a lower Tg concentration. Conclusions: The independent predictors of malignancy in follicular neoplasm were solitary tumor, tumor size and preoperative Tg concentration. We believe that the determination of Tg concentration may be useful in patients with follicular neoplasm before deciding about the extent of the thyroid surgical procedure in order to decrease the number of completion thyroidectomies.

P111

Pancreatic Neuroendocrine Tumors: Radiographic Calcifications Correlate with Grade and Metastasis G.A. Poultsides,* Y. Chen, B.C. Visser, R.K. Pai, W.G. Park, A.M. Chen, P.L. Kunz, G.A. Fisher, J.A. Norton. *Stanford University School of Medicine, Stanford, CA.*

INTRODUCTION: Studies to identify preoperative prognostic variables for Pancreatic Neuroendocrine Tumors (PNET) have been inconclusive. This study was undertaken to define the prognostic significance of calcifications detected on preoperative Computed Tomography (CT) for patients undergoing surgical resection of PNET. METHODS: From 1998 to 2009, 110 patients with well-differentiated PNET underwent surgical resection at a single institution. Synchronous liver metastases were present in 31 (28%) patents and were addressed with combined or staged liver resection and/or ablation with potentially curative intent. Patients with high-grade PNET were excluded. Data on preoperative CT imaging were available for 102 patients (93%). The presence of radiographic calcifications in the primary tumor was recorded and correlated with clinicopathologic variables and overall survival. RESULTS: Calcifications were present in 16% of patients and were more common in male patients with larger, functional tumors other than insulinomas (Table). In addition, calcified tumors were more commonly associated with lymph node or

synchronous liver metastasis, and intermediate tumor grade (Table). On multivariate analysis of factors available preoperatively, primary tumor calcifications (p = 0.015) and size (p = 0.006), but not gender or hormonal hypersecretion (other than insulin), were independently predictive of lymph node metastasis at the time of resection. Overall survival after resection was significantly worse in the presence of synchronous liver metastasis (5-year 64% vs. 86%, P = 0.04). However, among patients without synchronous liver metastasis, radiographic calcifications were not associated with overall survival after a median follow-up of 22 months (Table). CONCLUSIONS: This study shows for the first time that calcifications on preoperative CT correlate with higher grade and lymph node metastasis in well-differentiated PNET. This information is available preoperatively and supports the routine dissection of regional lymph nodes through formal pancreatectomy rather than enucleation in cases of calcified PNET.

	Calcifications on CT		P value
	Yes (n = 16)	No (n = 86)	
Age (yrs)*	53.2 (37-75)	54.0 (20-94)	0.881
Male Gender	81%	41%	0.005
Size (cm)*	4.5 (1.0-15.2)	2.3 (0.3-13.9)	0.040
Multifocal Tumors in Pancreas	12%	6%	0.302
Location in Head/Uncinate (vs. Body/Tail)	19%	42%	0.098
Non-functional vs. Insulinoma vs. Functional (other than Insulinoma)	62% vs. 0% vs. 38%	70% vs. 20% vs. 10%	0.007
Lymph Node Metastasis	73%	33%	0.012
Synchronous Liver Metastasis	62%	21%	0.001
Intermediate** (vs. Low) Grade	79%	31%	0.003
Positive Resection Margin	27%	20%	0.512
5-yr Overall Survival (Patients without Synchronous Liver Metastasis)	75%	87%	0.388

*, Median (range)
**, Intermediate grade was defined by the presence of at least one of the following: mitotic rate >= 2/10 HPF, Ki-67 >= 2%, necrosis, perineural or lymphovascular invasion on pathologic evaluation.

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Reoperative parathyroid procedures in the era of minimally invasive parathyroidectomy (MIP) K.K. Shah,* P.K. Shah, G.C. Karakousis, R. Kelz, D.L. Fraker. *Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia, PA.*

Introduction: MIP has been increasingly used to treat primary hyperparathyroidism (HPT), given the potential benefits of decreased OR time and morbidity associated with a more limited neck dissection. The tools employed for this technique however are variably used. We reviewed our experience of reoperative parathyroidectomies to identify causes for failure after MIP. Methods: Seventy-six consecutive patients underwent reoperative parathyroidectomy between 1999-2009 by a single surgeon for recurrent or persistent HPT. Eighteen patients were identified who were referred after undergoing MIP and for whom complete operative data and pathology were available. Descriptive statistics were performed. Results: Of the 18 patients who underwent MIP, 17 had an abnormal finding by sestamibi scan and 1 was localized by ultrasonography. Eleven (61%) underwent surgery with intra-operative parathyroid hormone (IOPTH) monitoring. In 10 cases where IOPTH was used, PTH levels dropped by > 50%. At initial surgery, 12 patients had a single abnormal gland found, 4 had multi-glandular disease (MGD), and the remainder 2 either had no or normal glands removed. Prior to reoperation, 7 patients had a positive sestamibi scan and an additional 3 were localized by ultrasound. Eight patients with no definitive pre-operative localization underwent jugular venous sampling (JVS). On reoperation, 11 patients (61%) were found to have a single abnormal gland and 9 patients had ectopically located glands, 6 of which were intra-thymic. In one patient, after extensive exploration no abnormal gland was identified. Among patients who underwent initial MIP without IOPTH monitoring, 6 were found to have single gland disease on re-exploration and 4 in an ectopic location (all intra-thymic). Conclusion: A significant proportion of patients who undergo reoperative parathyroidectomy after MIP for persistent or recurrent HPT did not have IOPTH used at initial surgery. In this group, a single abnormal gland is the most frequent finding on re-exploration, and an appreciable number of these patients will demonstrate an ectopic gland. IOPTH is critical when MIP is used to reduce the likelihood of operative failure.

P113

Preoperative or Postoperative Therapy for Resectable Gallbladder Cancer? A Retrospective analysis of patients treated at a single institution V. Siripurapu,* J.C. Watson, Y.S. Chun, A. Gumbs, J.P. Hoffman. *Fox Chase Cancer Center, Philadelphia, PA.*

Background Gallbladder cancer (GBC) is the commonest malignancy of the biliary tract. Less than 30% present at an early stage where surgical resection is curative. We examine a cohort of patients with GBC toward determining if preoperative and postoperative treatment of locally advanced GBC demonstrate any differing results in complications or survival. Methods A retrospective review of patients with GBC was performed. Demographics, clinical stage, surgical procedures, pathology stage AJCC 7th, details of neoadjuvant, adjuvant treatment & surgical complications were analyzed. Results Fifty-one patients with GBC were identified. Of these, 66% had their GBC found incidentally, 77% had Stage 2 or greater cancers, and 35 patients needed liver resection with portal lymphadenectomy. 13 patients had an extra-hepatic bile duct resection. 10 patients had extended resections including pancreatoduodenectomy (5) or colectomy (5), while 6 had cholecystectomy alone. 25% (N= 13) of the population had preoperative chemoradiation only30 %(n=15) had postoperative chemoradiation only, while 15% (n=8) received maintenance chemotherapy only. 10% (n=5) had preoperative and postoperative therapy, while twenty percent of the group (n=10) had surgery only. 49% had recurrences (n=25), with 48% percent of these being local-regional. Median survival was 30 months for the whole group, with 54.6 month median survival for the 41 patients without extended resection. No significant difference in survival was seen comparing preoperative therapy versus postoperative treatment(p=0.13). 5 year survival is 47% for those with minor hepatic resection compared to 25% for those with combined hepatic and colon or pancreatic resection. Conclusions We present a retrospective view of patients treated in our center, the majority of whom received either preoperative or postoperative adjuvant therapy, both of which had good median survival and acceptable morbidity and mortality. Given the poor survival and high recurrence rate for stage II and greater cancers, we suggest that preoperative or postoperative adjuvant therapy for these cases may be equally effective.

P114

Prediction of Malignancy Risk for Patients with Dominant Splenic Lesions K. Ostapoff, E. Kim, G. Balch, A. Yopp, R. Sharma, R.E. Schwarz, J.C. Mansour.* *Surgical Oncology, University of Texas Southwestern, Dallas, TX.*

Introduction: Radiologic imaging often identifies splenic lesions among patients who are either symptomatic or undergoing evaluation for other processes. The patient and radiologic characteristics associated with malignancy are poorly understood. We evaluated the preoperative work-up, pathology and outcomes for these patients in order to identify predictors of malignancy. Methods: We performed a retrospective review of all patients undergoing splenectomy from January 2000 to March 2010. Chi-square (Fisher's exact test) and simple logistic regression analyses (ANOVA) were performed to identify factors predictive of malignancy in the resected spleen. Results: We identified 910 patients undergoing splenectomy in the study period. Twenty patients underwent splenectomy for a mass lesion. Mean age was 52 years and 65% were women. Caucasian patients composed 85% of the study group. A history of cancer was reported for 9 (45%) of the patients. Symptoms were present in 11 (55%) patients and included abdominal pain, fevers, night sweats and early satiety. Preoperative CT scans were completed in 95% of the patients and MRI imaging in 45%. Only one patient had a preoperative biopsy. Laparoscopic splenectomy was attempted for 50% of patients with a 30% rate of conversion to open splenectomy. The median estimated blood loss was 200 ml (range: 20 – 4000 ml) and median length of stay was 5.5 days (range 2 - 11 days). Multiple lesions were present in half (10/20) of the patients. The mean size of the dominant mass was 5.3 cm (range 1 – 15 cm.) The final pathologic diagnosis was malignant for 9/20 (40%) of the patients. After a mean of 23

months of postoperative followup, 90% of patients were alive. Factors predicting malignancy are detailed on the attached figure. Conclusions: Patient symptoms and radiologic characteristics do not reliably predict the risk of malignancy among patients undergoing resection. A personal history of cancer and increasing patient age are associated with an increased risk of malignancy within these splenic lesions. Resection of the spleen can be performed safely and should be considered as the definitive diagnostic measure for patients with an unclear diagnosis.

Factors predicting malignancy

Factor (n)	Benign (%)	Malignant (%)	p-value
History of malignancy Yes (11) No (9)	4 (36) 8 (89)	7 (64) 1 (11)	0.01
Symptoms Yes (11) No (9)	8 (73) 3 (33)	3 (27) 6 (66)	0.18
Multiple lesions Yes (10) No (10)	6 (60) 5 (50)	4 (40) 5 (50)	1.00
Patient age, median, years (range)	45 (21-72)	61 (47-77)	<0.03
Median size of largest mass, cm (range)	5.3 (1-10)	3.7 (2-15)	0.99

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WITHDRAWN

P117

Preoperative Therapy Improves Lymph Node Ratio in Pancreatic Adenocarcinoma A.D. Yang,* M.H. Katz, H. Lin, X. Chopin-Laly, E.K. Abdalla, J.N. Vauthey, P.W. Pisters, G.R. Varadhachary, R.A. Wolff, C.H. Crane, J.E. Lee, J.B. Fleming. *The University of Texas MD Anderson Cancer Center, Houston, TX.*

INTRODUCTION: The ratio of the number of lymph nodes (LN) harboring metastatic cancer to the total number of lymph nodes examined (lymph node ratio [LNR]) is an independent prognostic factor in patients undergoing resection of pancreatic ductal adenocarcinoma (PDAC). The effect of preoperative therapy (PT) on LNR in PDAC is unknown; the aim of this study was to determine this effect. METHODS: 356 patients with PDAC who underwent resection between 1990-2008 were retrospectively identified from a prospective database under an IRB-approved protocol. Each patient underwent multidisciplinary evaluation, a standardized operative approach, and standardized pathologic evaluation of the surgical specimen. Patients with pancreatic body/tail tumors, multiple primary cancers, or those who received intraoperative radiation therapy were excluded. We examined the total number of LN retrieved in the surgical specimen, the number of positive LN identified, the LNR, and the pattern of postoperative recurrence. RESULTS: Of the 356 patients, 270 received PT (5 chemotherapy only, 111 chemoradiation only, 154 both) and 86 did not. While the mean number of LN retrieved did not differ between patients who did and did not receive PT (20.9 vs. 19.8 respectively, P=.33), patients who received PT had fewer positive LN than those who did not (3.2 vs. 5.0; P<.0001). LNR was therefore significantly decreased in patients who received PT (0.15 vs. 0.24; P<.00001). In multivariate analysis, preoperative chemoradiation was independently associated with a decreased number of positive LN (3.0 vs. 5.2; P<.0001) and LNR (0.15 vs. 0.24; P<.0001), while preoperative chemotherapy was not. Patients who received PT had a significantly decreased rate of local-regional recurrence relative to those who did not (15% vs. 24%; P=.048). CONCLUSIONS: In patients undergoing resection of PDAC, preoperative chemoradiation is associated with a reduced number of positive LN and a decreased LNR, while the total number of LN retrieved remains unchanged. This data suggests that PT may be a factor in reducing local-regional recurrence in patients with resected PDAC.

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Adverse Histopathological factors Predicting Local Recurrence in Rectal Cancer with Clear Circumferential Margins W.M. Gawad,[1]* I. Gouda,[2] M. Lotaef,[3] O. Mansour.[4] *1. National Cancer Institute-Surgical Oncology, Cairo, Egypt; 2. National Cancer Institute-Pathology, Cairo, Egypt; 3. National Cancer Institute-Radiation Therapy, Cairo, Egypt; 4. National Cancer Institute-Medical Oncology, Cairo, Egypt.*

Rationale :Involvement of Circumferential Resected Margins (CRM) is the main cause attributed to Local Recurrence (LR) in locally advanced rectal cancer. Nevertheless local recurrence could develop with clear circumferential margins raising the possibility of presence of other adverse pathological factors beside CRM contributing to the failure of local control of the disease. Aim:The aim of this study is to identify the adverse histopathological factors predicting the development of local recurrence in patients with clear circumferential margins. Methods:The study was conducted from1999-2009.One hundred sixty seven patients(167) with locally advanced rectal cancer were enrolled in this study, cases treated for local recurrence (n=55 patients) were matched to a control group (n=112) with no recurrence following rectal resection and were followed for at least 1.5 year. Both groups received the same neoadjuvant treatment. Different histopathological factors related to local recurrence were evaluated with focused analysis and review of the primary pathology. Results :The incidence of positive CRM was 24%.In patients with local recurrence, 28% had positive CRM .. Forty patients had positive CRM, out of this 37%developed local recurrence. Among patients with clear CRM(127), 31% developed LR. Logistic regression denoted predictive histopathological factors for local recurrence. Extramural venous invasion EMVI (OR 5.2,P≤0.001),Lymphovascular invasion LVI (OR 4.01,P≤0.002),positive CRM(O2.01,P≤0.021),serosal invasion (OR 5.6,P≤0.001) and poor tumour differentiation (OR 2.8,P≤0.01). Conclusion:Involvement of CRM is a detrimental element for local recurrence. EMVI, LVI,serosal invasion and poor tumour differentiation are also significant predictive factors for local recurrence. patients harboring such risk factors might benefit from adjuvant chemotherapy for better oncologic outcome.

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Laparoscopic versus Open Hepatic Resection for Hepatocellular Carcinoma: Improvement in Outcomes and Similar Cost C.R. St.Hill,[1]* R.E. Brown,[1] S.K. Maithel,[2] D. Kooby,[2] C. Staley,[2] C.S. Cho,[3] S. Weber,[3] E. Winslow,[3] C.R. Scoggins,[1] K.M. McMasters,[1] R.C. Martin II.[1] *1. Surgery, Division of Surgical Oncology, Univeristy of Louisville, Louisville, KY; 2. Emory University, Atlanta, GA; 3. University of Wisconsin, Madison, WI.*

Introduction: Laparoscopic hepatic resection (LHR) has become more prevalent with recent improvements in instrumentation and surgeon experience. Previous studies have shown equivalent perioperative and survival outcomes when benign and malignant histologies are reviewed. The aim of this study was to compare outcomes of laparoscopic versus open hepatic resection (OHR) exclusively for Hepatocellular carcinoma in terms of morbidity and cost. Methods: A review of multicenter, prospectively collected hepatobiliary databases from three institutions was performed from 12/1990 to 12/2009. Univariate and Cox regression analyses were used to identify statistically significant differences between the two surgical approaches and compare perioperative outcomes. Cost comparison was performed for one of the three institutions. Results: A total of 254 patients who had resections for Hepatocellular carcinoma were analyzed, in which 50 were performed laparoscopically. The two groups were similar in terms of demographics and preoperative comorbidities. Evaluation of operative outcomes showed significantly higher intraoperative estimated blood loss (EBL) in the OHR group (755 vs 336mL, p=0.02) although postoperative transfusion rates were similar and proportion of major resections in OHR vs. LHR group was higher (61 vs 32%, p=0.005). In the analysis of perioperative outcomes, rates of R0 resection and complications were similar. Cox regression analysis of disease free interval (OR=1.4, CI 0.31-6.3, p=0.66) and survival curves (OR=1.2, CI 0.59-2.5

p=0.6) for LHR vs OHR were not significantly different. Length of stay was significantly less in the laparoscopic group 6.2 vs 9.3 days (CI 1.3-4.8, p=0.001). Finally, higher operative charges were found for LHR ($51k vs $40k, p=0.006), however total hospital charges were not significantly different in LHR vs OHR ($75k vs $68k, p=0.6). Conclusion: Our study confirms previous literature showing that laparoscopic liver resection for HCC has comparable perioperative outcomes and recurrence rates. We further show comparable cost between the two with decreased length of stay for laparoscopic resection.

Table 1. Summary of Univariate Analyses

	Open	Laparoscopic	p-Value	95% Confidence Interval
Gender			0.3	
Female	33.5%	44%		
Male	66.5%	56%		
Diabetes	27.2%	28%	0.9	
Hepatitis B+	11.2%	12%	0.9	
Hepatitis C+	22.3%	28%	0.5	
Alcohol Abuse	18.9%	20%	0.9	
Cirrhosis	34%	40%	0.5	
Major Resection	61.2%	32%	0.005	
MELD (mean)	8.6	8.4	0.8	
Estimated Blood Loss (mean)	755mL	336mL	0.022	61.72-776.28
Length of Stay (mean)	9.28 days	6.2 days	0.001	1.347-4.816
Operating Room Charge (mean)	$40272.31	$51533.73	0.006	-$19191.80,-$3310.40
Total Hospital Charge (mean)	$68528.89	$75888.85	0.635	-$40941.80,-$26221.90

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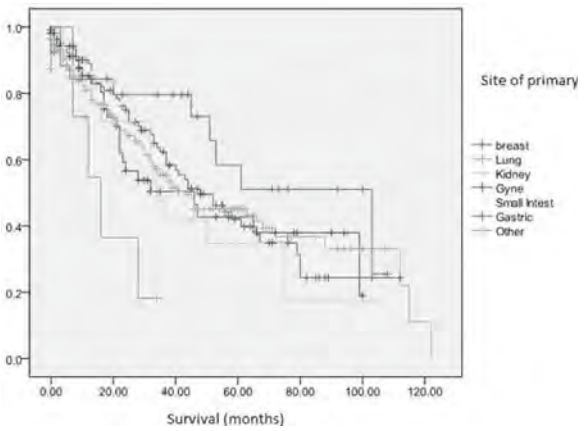
Hepatic Metastesectomy for Noncolorectal and Nonendocrine Cancer – A Multicenter Study I. Nachmany,[1]* S.K. Reddy,[2] E. Glazer,[3] M. De Jong,[4] D.A. Geller,[1] J.W. Marsh,[1] T.M. Pawlik,[4] B.M. Clary,[2] S.A. Curley,[3] T.C. Gamblin.[1] *1. Starzl Transplantation Institute, University of Pittsburgh Medical Center, Pittsburgh, PA; 2. Duke University Medical Center, Durham, NC; 3. MD Anderson Cancer Center, Houston, TX; 4. Johns Hopkins University, Baltimore, MD.*

Introduction: Although hepatic metastesectomy is well established for colon and endocrine cancer, the approach to hepatic metastases from other sites is not well defined. We sought to examine the management of noncolorectal and nonendocrine liver metastases. Methods: Multicenter retrospective study from four major US liver cancer centers. Demographics, operative outcome, recurrence, and survival were examined. Survival was assessed by Kaplan-Meier analysis. Multivariate Cox-regression identified factors predicting survival and recurrence. Results: There were 430 patients (311 females; 72.3%) with a mean age of 51.1±13.0 (median 55) years in the entire cohort (8/1990 - 9/2009). Median follow-up was 45±4.0 months (range: 0 – 150 months). R0 resection was achieved in 86.6% of cases, with a complication rate of 18.3% and 60-day mortality of 1.9%. Overall 1, 3, and 5 yr survival was 84.6%, 56.4% and 42.3%. Recurrence free 1, 3 and 5 yr survival was 58.6%, 31.5% and 25.0% respectively. The most common primary tumors were breast (118, 27.4%), sarcoma (105, 24.4%), and genitourinary (87, 20.2%). Median survivals for breast cancer, sarcoma, and GU patients were 48, 68 and 47 months, respectively. In patients with breast cancer, size of liver metastasis, lymphovascular (LV) invasion and extra-hepatic metastases were shown to have a negative influence on survival. Metastasis size and LV invasion were independent predictors of disease free survival (p<0.001). In sarcoma and genitourinary cancer, only R1/2 resection was associated with poor outcome (hazard ration of 2.1 and 2.6, respectively). Conclusion: Hepatic metastesectomy for noncolorectal and nonendocrine cancers is safe and feasible in selected patients. Survival compares favorably to survival of patients with metastatic colon cancer where metastesectomy is widely accepted.



P121

Pancreaticoduodenectomy in the elderly: Longevity, long term morbidity and quality of life G.J. Lahat,* F. Gerstenhaber, J. Grossman, N. Lubezky, E. Itzkowitz, I. Nachmany, S. Abu-abeid, R. Nakache, J.M. Klausner. *surgical oncology, Sourasky Medical Center, Tel Aviv, Israel.*

Introduction: Pancreaticoduodenectomy (PD) in the elderly is gaining acceptance and being performed in increasing numbers. Several reports demonstrate acceptable early postoperative and modest long term oncologic outcomes, yet data analysis of quality of life in this population is lacking. We evaluated long term morbidity, mortality, and residual quality of life after PD in the elderly. Methods: A prospectively accrued pancreatic surgery database was analyzed for postoperative complications and mortality (30 and 60 days), ICU, hospital and rehabilitation facility stay, and readmissions during the first year after surgery. Quality of life (QOL) was assessed by a validated questionnaire (EORTC QLQ-30), 3-6 and 12 months after surgery. Scores are reported as a percentile, with 100% being the highest possible score. Results: Overall, 172 patients aged ≥ 70 years had PD between 1995 and 2010, the majority for cancer (61%; n=105); most patients (72%; n=124) were categorized as ASA ≥ 3. There was no intra-operative death, 30- and 60-day postoperative mortality rates were 6.4% vs. 7.5%, respectively (p=0.23). Median ICU and general hospital stay were 2 days (range, 0-16) and 22 days (range, 8-63), respectively. Sixty-four patients (37.5%) were discharged to a rehabilitation facility where they stayed for a median length of 8 days (range, 4-45). Hospital readmission during the first year was documented in 54 patients (31%); of them, 75% were admitted once. Median follow-up length was 22 months (range, 1-187), 1- and 2-Y OS rates were 58% (SE: 3.1) and 36% (SE: 3.6), respectively. Overall QOL scores 3 and 12 months after surgery for the 51 responding PD patients were 68%, and 73%, respectively. These scores were comparable to those of 20 matched laparoscopic cholecystectomy patients. Conclusions: Most elderly cancer patients survive longer than one year after PD and approximately one third more than two years. These patients are likely to have an acceptable long term morbidity and overall good QOL, corresponding with their age. Our data justify surgery in select elderly patients, and should discourage the ongoing trend to avoid PD in this population.

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XRCC1 Single Nucleotide Polymorphism Predicts Pathologic Complete Response to Neoadjuvant Chemoradiation in Stage II/III Rectal Cancer M.N. Duldulao,* W. Li, J. Ho, Z. Chen, W. Lee, J. Kim, J. Garcia-Aguilar. *General Oncologic Surgery, City of Hope, Duarte, CA.*

Background: The X-ray repair cross-complementing protein 1 (XRCC1) gene plays an important role in DNA damage repair; and the R194W and R399Q single nucleotide polymorphisms (SNPs) are associated with attenuated DNA repair activity. Our objective was to determine whether XRCC1 SNPs were associated with response to neoadjuvant chemoradiation therapy (CRT) in rectal cancer patients. Methods: We conducted a prospective multicenter Phase II trial to investigate the effect of additional chemotherapy with

a longer CRT-to-surgery interval on treatment response in patients with rectal cancer. Paired normal and rectal cancer tissues were prospectively collected from enrolled patients (n=110). DNA was extracted from normal rectal mucosa and analyzed for XRCC1 R194W and R399Q by polymerase chain reaction and sequencing. Each SNP was compared to response to CRT. Response to CRT was determined by a central pathologist. Results: Of the 110 patients, 25% (n=27) achieved a pathologic complete response (pCR). We examined the XRCC1 R194W SNP and observed that the allelic frequency of patients with the R/R genotype was 84% (n=92), the R/W genotype was 14% (n=16), the W/W genotype was 1% (n=2). By Fisher's Exact test, patients harboring either the R/W or W/W genotype, had a significantly higher rate of pCR compared to patients with the R/R genotype (44% vs. 21%, respectively; p=0.04). We then examined the R399Q SNP and observed that the allelic frequency of patients with the R/R genotype was 34% (n=37), the R/Q genotype was 49% (n=54), and the Q/Q genotype was 17% (n=19). In contrast, the detection of XRCC1 R399Q SNPs was not associated with pCR. Conclusions: We demonstrate that XRCC1 R194W SNP is associated with increased rate of pCR in our prospective multi-center trial. Although the detection of XRCC1 R399Q SNP is not associated with pCR, the detection of XRCC1 SNPs that predict treatment response may help identify patients who are unlikely to respond to CRT and therefore may potentially avoid treatment-associated morbidities.

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Liver-Directed Therapy as Treatment of Hepatic Progression following Surgical Extirpation of Neuroendocrine Neoplasm Hepatic Metastasis A. Saxena,* T.C. Chua, D.L. Morris. *UNSW Department of Surgery, St George Hospital, Sydney, NSW, Australia.*

Background Surgery confers the best chance of long-term survival in patients with neuroendocrine neoplasm hepatic metastases (NENHM). Disease progression invariably occurs in the majority of patients. No previous study has addressed the outcomes after treatment of hepatic disease progression in patients who initially underwent surgical extirpation of NENHM. This was the principal aim of the current study. Methods Seventy-four patients with NENHM underwent surgery for NENHM between December 1992 and December 2009. Of these, 50 patients developed disease progression in the liver. These patients were then treated with specific liver-directed therapies according to consensus of a multidisciplinary team. The current study evaluates progression-free survival (PFS) and overall survival (OS) following treatment of hepatic disease progression with specific liver-directed therapies. Results No patient was lost to follow-up. The median follow-up after treatment of progression was 29 months (range = 2 to 137). The median PFS and OS after diagnosis of disease progression were 15 and 48 months, respectively. Specific liver-directed therapies included surgery in 10 patients, radioembolization in 15, cytotoxic chemotherapy in 14 and conservative therapy in 11. Four independent factors associated with PFS and OS were identified through a multivariate analysis. These were initial progression-free interval(OS p=0.012 PFS=0.006), extrahepatic disease (OS p<0.001 PFS=0.004), histological grade (PFS p=0.006) and type of secondary intervention (PFS p=0.024). Conclusion A multi-modality approach towards treatment of disease progression as shown in this study that includes repeat surgery or radioembolization have shown to achieve a superior outcome in the setting of disease progression/recurrence.

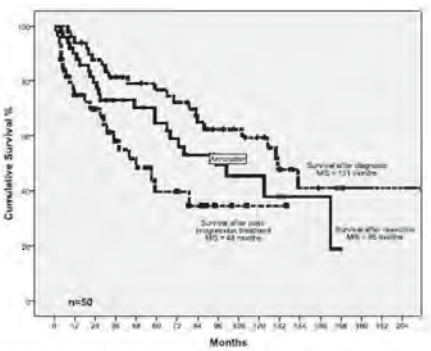

Figure 1. Overall survival after initial diagnosis of NET, hepatic resection of NETHM and treatment of disease progression following primary hepatic resection of NETHM (n = 50).

P125

Is survival better for patients with peritoneal carcinomatosis from gastrointestinal malignancies in the era of modern chemotherapy: Should we do more? K. Papalezova,[2] S. Zani,[1] S. Stinnett,[1] D. Hsu,[1] D.G. Blazer.[1]* *1. Surgery, Duke University, Durham, NC; 2. Montefiore Medical Center, Bronx, NY.*

INTRODUCTION: Peritoneal carcinomatosis (PC) from gastrointestinal (GI) malignancies has been historically associated with poor survival, ranging from 3 to 7 months. The majority of these reports predate the current era of more effective chemotherapeutics and targeted biologic agents. The use of irinotecan- and oxaliplatin-based chemotherapy regimens in combination with targeted agents has significantly improved survival in patients with metastatic colorectal carcinoma (CRC) outside the peritoneum. However, the efficacy of these regimens on patients with PC remains largely unknown. Our goal was to evaluate survival in patients with PC from GI malignancies treated with modern chemotherapeutics. METHODS: A retrospective chart review was performed to identify patients with PC from GI malignancies who presented for evaluation at our institution between 2003 and 2008. All patients with PC were identified by querying our institution's tumor registry. RESULTS: We identified 130 patients diagnosed with PC between 2003 and 2008. Seventy-four (56%) had synchronous and 58 (44%) had metachronous peritoneal disease. Primary tumors included: colon (n=73), gastric (n=40), rectum (n=9), appendix (n=8). Median follow up was 15 months from the time of diagnosis of PC. The median overall survival (OS) for all patients was 14 months. The median OS for patients with primary colon cancer was 16.3 months, gastric cancer 6.2 months, and rectal cancer 16.2 months. Median OS for patients with appendiceal cancer has not been reached. There was a statistically significant difference in survival outcomes between primary tumors (p<0.001). CONCLUSIONS: Survival in patients with PC from gastric cancer remains dismal and does not demonstrate improvement over previous reports. Patients with PC from CRC do appear to benefit from more modern systemic regimens but survival remains poor. Thus, despite progress with modern chemotherapy and targeted biologic agents, alternative management strategies such as surgical cytoreduction and hyperthermic intraperitoneal chemotherapy should continue to be investigated for these patients.

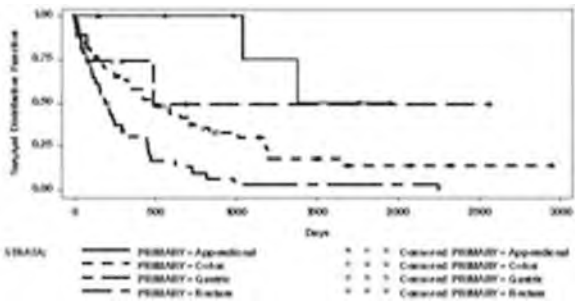

Figure 1

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Stage II Colorectal Cancer Patients with Perineural Invasion Benefit from Adjuvant Chemotherapy C.L. Marshall,[1]* S.T. Orcutt,[1] G.E. Ayala,[1] C.J. Balentine,[1] C.N. Robinson,[1] C.A. Liebig,[2] D.H. Berger,[1] D. Albo.[1] *1. Baylor College of Medicine, Houston, TX; 2. MD Anderson Cancer Center, Houston, TX.*

Introduction: Perineural invasion (PNI) is an independent predictor of poor outcomes for patients with colorectal cancer and is associated with increased risk of recurrence. Current guidelines recommend adjuvant therapy for Stage II colorectal cancer patients with high risk features; however, the relative benefit for Stage II patients with PNI who receive chemotherapy remains unclear. We hypothesize that Stage II colorectal cancer patients with PNI who receive adjuvant chemotherapy will have improved survival compared to those who do not receive adjuvant therapy. Methods: In a retrospective analysis containing 1394 patients with colorectal cancer, we identified 41 patients with Stage II colorectal disease and PNI, of which 44% received adjuvant chemotherapy. PNI

was defined as tumor cells within any layer of the nerve sheath or tumor in the perineural space that involved at least one-third of the nerve circumference. Data pertaining to demographics, pathology, oncologic therapies, and outcomes were reviewed. Survival analysis was carried out using Kaplan-Meier methods, with the logrank test for comparison. Results: Stage II patients with PNI who received adjuvant chemotherapy had improved overall and disease-free survival rates compared to patients who did not receive adjuvant therapy. Specifically, patients who did not receive adjuvant therapy had an overall five-year survival rate of 35%, compared to 74% for those patients who did receive it ($p<0.015$). Patients who did not receive adjuvant therapy had a five-year disease-free survival of 31% compared 75% for those who did ($p<0.008$). When Stage II patients were stratified according to PNI status and receipt of adjuvant therapy, patients with PNI who received adjuvant therapy had similar survival rates to those patients without PNI who received adjuvant therapy (Table 1). Conclusions: Patients with Stage II colorectal cancer and PNI may benefit from adjuvant therapy. Furthermore, the addition of adjuvant therapy may allow these patients to have similar survival rates to those patients without PNI who receive adjuvant therapy. Therefore, PNI should be considered in therapy stratification for Stage II disease.

	Five-Year Disease-Free Survival	Five-Year Overall Survival
No PNI, No Adjuvant Therapy	60%	63%
No PNI, Adjuvant Therapy Received	68%	74%
PNI Present, No Adjuvant Therapy	31.4%	35%
PNI Present, Adjuvant Therapy Received	75%	74%

Table 1. Stratification of patients by PNI status and receipt of adjuvant therapy.

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The Quality of Life trajectory of resected gastric cancer

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INTRODUCTION: The best treatment for gastric cancer involves the least toxicity, the least impact on QoL and the longest survival. The trajectory of disease recurrence and survival following resection for gastric cancer is well documented. However, relatively little is known about the effects of surgery on QoL or about the duration of benefit after recovery from surgery. Recently, the FACT-Ga was validated as a gastric cancer QoL instrument and is potentially useful in studying changes in QoL following gastrectomy. METHODS: Patients treated for gastric cancer were preoperatively enrolled and followed at defined intervals. QoL was measured using the FACT G, FACT Ga instruments and the Karnofsky performance status (KPS) was also followed longitudinally. Patients were followed to determine the effects of surgery on QoL and the duration of sustained QoL after recovery from surgery. RESULTS: QoL was evaluated in 43 patients who underwent gastrectomy for gastric adenocarcinoma, mean age was 65 yrs, with 28 patients (66%) undergoing total gastrectomy. Complications occurred in 12 patients (30%) and there was one death (2%). The 5yr overall survival was 40%, the median survival was 28 months and disease free survival was 18 months. At 3 months after surgery, the QoL and performance status was significantly reduced as determined by the FACT Ga ($p<0.0001$), FACT G ($p<0.0001$) and KPS ($p<0.001$). Patients who had a total gastrectomy had a significantly lower KPS at 3 months than patients who had a partial gastrectomy ($p<0.0001$). The QoL as determined by the FACT G and FACT Ga was not affected by the type of surgery. QoL and performance status returned to baseline at 6 months. Following that, QoL and performance status remained stable for a median of 10 months (2- 10 months). Typically a clinical significant reduction in QoL and performance status preceded death by median interval of 3.2 months (0 – 16 months). CONCLUSIONS: Gastrectomy has a significant impact on QoL, which takes up to 6 months to normalize. QoL and performance status closely parallel disease course. The QoL costs and benefits of gastrectomy for gastric cancer represent important outcomes.

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Reduction of nodal micrometastases in patients with histological node negative esophageal cancer after neoadjuvant treatment

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Background: Neoadjuvant chemoradiation (CRT) is important in the treatment of esophageal cancer. Rationales are tumor-downstaging and elimination of micrometastases improving resectability and curability rate. In this study we evaluated the effect of neo-adjuvant CRT on nodal micrometastases (NMM) in pN0 esophageal cancer patients. Methods: From a prospective database, we selected a matched group of patients on cT-stage, histological type and treatment without (group 1) or with neo-adjuvant CRT (group 2). Patients were staged by EUS, PET-scan, CT-scan and EUS guided cytology. CRT was given in a randomized clinical trial and consisted of paclitaxel 50 mg/m2 and carboplatin AUC = 2 for 5 weeks and concurrent radiotherapy (41.4 Gy/23frs). All patients (n=19) underwent a curative intended transthoracic esophagectomy with extended 2-field nodal dissection. After reviewing routine pathological examination all tumors were confirmed as stage pN0. Four sections of every examined lymph node (n= 261) were made at different levels according to a sentinel node protocol and further analyzed immunohistochemically with anti-CK8/18 (CAM 5.2) to detect NMM. Results: Patients characteristics were equally distributed. All patients had a microscopically radical (R0) resection. In group-2 (n=9) the response rate was 55% which was complete (CR) in 33%. The median number of resected nodes was comparable: 15 ± 6.5 and 15 ± 5.6 in both groups. Thirteen of the 261 (5%) pN0 nodes in these 19 pts contained NMM. In Group-1 (n=10); 12 of the 136 (9%) examined pN0 lymph nodes were positive and in group-2 only one of the 125 (0.8%) examined pN0 nodes was positive ($p=0.003$). NMM were found in 7 pts (70%) in group-1 and in only one patient (11%) in group-2 ($p=0.02$). Interestingly, this last patient had responded well to CRT. Conclusions: Neo-adjuvant CRT seems to have a significant impact on the numbers of NMMs in esophageal cancer. Based on the presence of NMM even in patients with good responses, we still advocate a curatively intended nodal dissection.

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Direct Xenografts: An In-Vivo Assay To Predict Pancreatic Cancer Aggressiveness and Cancer Related Outcomes After Resection

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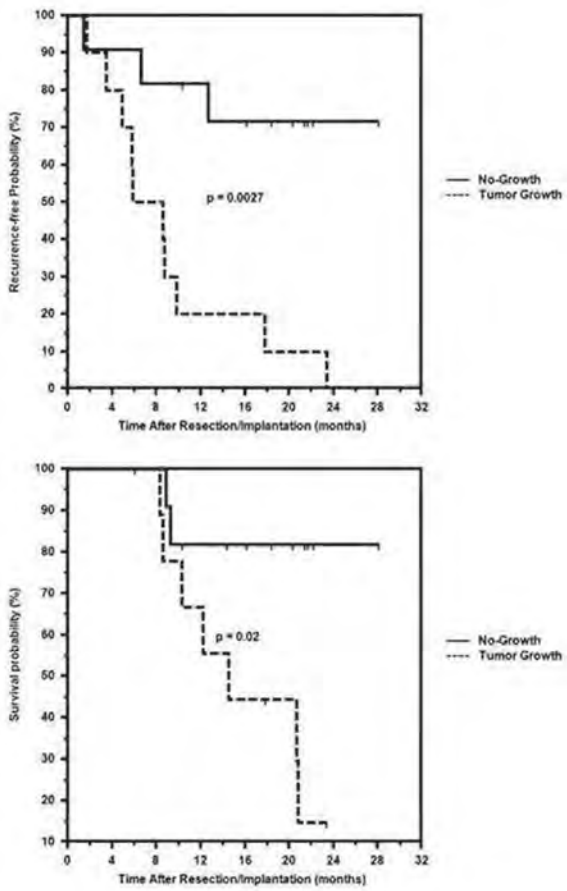
Introduction: Direct xenograft models of pancreatic cancer (PDAC) offer significant advantages over other described methods. These tumor-grafts retain their original genetic traits and tumor characteristics unique to the cancers from which the grafts are derived. As clinical outcome is determined by these features, we hypothesized that successful growth of direct xenografts reflects biologic aggressiveness of the source PDAC and can predict patient outcome. Methods: Using established methods as part of a prospective study (Nat Protoc. 2009;4(11):1670-80), human PDAC tumors obtained at surgery were implanted in NOD/SCID mice. Patients were offered pre/postoperative chemo/radiotherapy. Patient/tumor factors and clinical endpoints were measured. The ability of human PDAC tumors to grow in mice and postoperative patient outcomes were primary endpoints. Statistical relationship between tumor engraftment and clinical outcome was determined using Kaplan-Meier methods. Chi-square and Fisher's exact tests were used for other variables. Results: Establishment of tumor-grafts was attempted from 21 PDAC's obtained at surgery. The overall tumor establishment rate was 74%. Successful xenograft growth was highly predictive of metastatic recurrence ($p = 0.0027$) and survival ($p = 0.02$), in contrast to those tumors that failed to engraft (Figure). The median time to recurrence/survival in patients whose tumors engrafted was 8.6/14.5 months respectively. The median time to recurrence/survival in patients whose tumors did not engraft was not met. There were no significant differences in pre/postoperative therapy to account for xenograft growth or recurrence and survival. Other clinical/pathologic variables were not found to be predictive of tumor growth. Conclusions: This data demonstrates that the engraftment of direct PDAC xenografts obtained at surgery forms the basis of a novel in-vivo assay that reflects the biologic aggressiveness of the original tumor and predicts recurrence/survival in individual patients independent of other factors. Such personalized assays may allow for tailored treatment that is dependent on the status of tumor engraftment.



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Long Gastrojejunostomy Following Pancreaticoduodenectomy is Associated with Decreased Incidence of Delayed Gastric Emptying D.M. Walters,* D.J. LaPar, A.L. Shada, R.B. Adams, T.W. Bauer. *University of Virginia, Department of Surgery, Charlottesville, VA.*

Introduction: Delayed gastric emptying (DGE) is a common problem after pancreaticoduodenectomy, occurring in 30-45% of patients, and is associated with increased length of hospital stay, increased healthcare costs, patient discomfort, and other morbidity. We compared the rates of DGE among different methods of gastric anastomoses following pancreaticoduodenectomy. Methods: We performed a retrospective review of prospectively collected data on patients who underwent pancreaticoduodenectomy at our institution between August, 2000 and July, 2010. All patients underwent standard pancreaticoduodenectomy (SP), pyloric-preserving pancreaticoduodenectomy (PP), or a long gastrojejunostomy pancreaticoduodenectomy (LP) with an 8-9 cm-long anastomosis. Primary outcomes included presence and grade of DGE and length of hospital stay. The International Study Group of Pancreatic Surgery (ISGPS) definition was used to define and grade DGE. Patient characteristics, operative features, and outcomes were compared by univariate analyses. Results: A total of 28 patients underwent SP, while 82 patients underwent PP, and 84 received a LP. The rates of DGE were 46.4%, 37.8%, and 16.7%, respectively among the groups (p=0.001). Patients who underwent LP had significantly lower rates of grade B and C DGE (2.4%) compared to patients who underwent SP (10.7%) and PP (17.5%) (p=0.004). Post-operative complications, including pancreatic leak, abdominal abscess, and fluid collections were similar among the groups. Overall, patients who had DGE had significantly longer hospital stays (16.0±8.0 vs. 7.2±2.1 days, p<0.001) and required more days in the ICU (1.8±4.8 vs. 0.4±0.9 days, p =0.001). Conclusions: Long gastrojejunostomy after pancreaticoduodenectomy is associated with a significantly decreased rate of delayed gastric emptying compared to standard and pylorus-preserving methods. This technique warrants further exploration as a means to improve care for patients who undergo this operation.

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The Impact of Metabolic Syndrome and Components on Outcomes and Response to Neoadjuvant Chemoradiation in Rectal Cancer Patients D.R. Mansker,* H. Sweeney, A. Wahlquist, D. Marshall, D. Cole, B. Hill, N. Esnaola, R. Camp. *Surgery, Medical University of South Carolina, Charleston, SC.*

Introduction: Neoadjuvant chemoradiation (CMT) is standard of care in locally advanced rectal cancer (LARC) patients. The triad of obesity, diabetes (DM), and hypertension (HTN) representing metabolic syndrome (MetS) has been associated with an increased incidence of cancer as well as resistance to apoptosis. We hypothesize that LARC patients with MetS will demonstrate poor response to CMT and have increased treatment-related complications. Methods: A retrospective review was performed of 86 patients with LARC treated with CMT. Patients underwent initial TNM staging based on endoscopic US (EUS), CT, and/or MRI. Surgical pathology determined the post-treatment tumor stage. Tumor response was characterized as a pathologic complete response (CR, no residual tumor), partial response (PR, tumor downstaging 2 T stages or an N stage), or no response (NR, no change from EUS). Chi-square tests and logistic regression models were used to analyze the data. Results: Of 86 patients treated with neoadjuvant CMT, CR was observed in 14 patients (16%), PR in 24 patients (28%), and pathologic tumor downstaging (CR + PR) in 38 patients (44%).NR was identified in 48 patients (56%). Patients with either HTN (p=0.001) or DM (p=0.02) demonstrated significantly less tumor downstaging with neoadjuvant CMT. The odds of tumor response (CR+PR) CR was 11 fold greater for patients without DM compared to those with DM (p=0.02). Similarly, patients with two criteria for MetS had a 7-fold increase in risk of surgical complications compared to patients without any MetS criteria (p=0.036) adjusted for age, race, and gender. DM alone was not found to have a significant effect on complication rate. Conclusions: LARC patients with MetS criteria such as DM and/or HTN demonstrate decreased tumor response to neoadjuvant CMT and experience more treatment-associated complications. Strategies targeting MetS should be investigated to enhance response to CMT and to improve post-operative recovery.

Tumor Response to Neoadjuvant Chemoradiation in Patients with Characteristics of Metabolic Syndrome

		COMPLETE RESPONSE		PARTIAL RESPONSE		NO RESPONSE		
		n	%	n	%	n	%	p-value
HYPERTENSION	Yes: n=41	3	7.32	18	43.90	20	48.78	0.0014
	No: n=44	11	25.00	5	11.36	28	63.64	
DIABETES	Yes: n=12	0	0.00	1	8.33	11	91.67	0.0199
	No: n=69	13	18.84	22	31.88	34	49.28	

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Multimodal Approach to 18F-FDG-Directed Surgery: A Single-Institution Cumulative Experience D.A. Murrey, Jr,* S.P. Povoski, N.C. Hall, J.R. Gaglani, A.Z. Chow, E.E. Bahnson, C.M. Mojzisik, M.P. Kuhrt, C.L. Hitchcock, M.V. Knopp, E.W. Martin, Jr. *The Ohio State University Medical Center, Arthur G. James Cancer Hospital, and Richard J. Solove Research Institute, Columbus, OH.*

Background: 18F-FDG PET/CT imaging is widely utilized in the clinical management of cancer patients. The aim was to describe our cumulative expe-

rience with a multimodal approach to 18F-FDG-directed surgery. Methods: From June 2005 to June 2010, 145 patients were intravenously injected with 18F-FDG in anticipation for proceeding to the operating room on that same day for surgical exploration, biopsy, and possible resection of known or suspected malignancy. Each patient underwent one or more of the following modalities (Figure 1): (1) same-day preoperative patient PET/CT (pPET/CT); (2) intraoperative gamma probe assessment; (3) clinical PET/CT (cPET/CT) and/or micro PET/CT (mPET/CT) of whole surgically resected specimens (WSRS), research designated tissue (RDT), and/or sectioned research designated tissue (SRDT); and (4) same-day postoperative pPET/CT. Results were expressed as mean(±SD). Results: 18F-FDG injection dose was 15.1(±3.5) mCi. 55 same-day preoperative pPET/CT were performed. Of the 145 patients, 142 were taken to surgery. 3 same-day preoperative pPET/CT led to cancellation of the surgical procedure. 141 cases utilized intraoperative gamma probe assessment. 62 postoperative pPET/CT were performed. 14 tumor types were represented among surgically resected specimens. WSRS, RDT, and SRDT were scanned by cPET/CT and mPET/CT in 109 and 32 cases, 33 and 22 cases, and 49 and 26 cases, respectively. Time from 18F-FDG injection to preoperative pPET/CT, to intraoperative gamma probe assessment, and to postoperative pPET/CT were 77(±16), 286(±93), and 516(±134) minutes, respectively. Time from 18F-FDG injection to scanning of WSRS, RDT, and SRDT by cPET/CT and mPET/CT were 389(±148) and 458(±97) minutes, 619(±119) and 661(±117) minutes, and 674(±186) and 752(±127) minutes, respectively. We were able to identify 8 18F-FDG-avid lesions not surgically excised at the time of 18F-FDG-directed surgery on postoperative pPET/CT at 544(±122) minutes after 18F-FDG injection. Conclusions: Our multimodal approach to 18F-FDG-directed surgery is technically feasible and allows for real-time intraoperative staging and surgical planning.

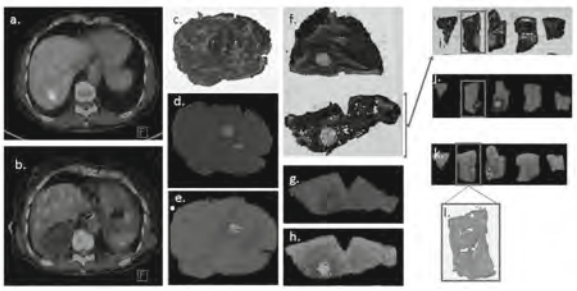

Figure 1: (a) Preop pPET/CT showing 18F-FDG-avid lesion in the liver. (b) Postop pPET/CT showing complete removal of 18F-FDG-avid lesion. (c) Photo of whole surgically resected specimen (WSRS) showing 2 discrete tumors (2 red arrows). (d) Clinical and (e) micro PET/CT of WSRS showing 2 discrete 18F-FDG-avid lesions. (f) Photo depicting first phase of pathologic processing, producing research designated tissue (RDT), consisting of a single 0.5 cm slice through 1 of 2 tumors (shown in red bracket). (g) Clinical and (h) micro PET/CT of RDT showing 18F-FDG-avid lesion corresponding to visible tumor. (i) Photo after sectioning of RDT into 5 pieces, designated as sectioned research designated tissue (SRDT), with 2 pieces containing visible tumor. (j) Clinical and (k) micro PET/CT of SRDT showing 18F-FDG avidity in 2 pieces corresponding to visible tumor. (l) Low mag H&E image of SRDT piece (in red box), demonstrating confirmation of presence and corresponding location of tumor in this SRDT piece.

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Expression of the nuclear receptor, FXR, predicts benefit from chemotherapy in St. II colon cancer L.L. Lai,* X.Y. Liu, E.E. Thomson, S. Desilva, D. Smith, P.G. Chu. *General and Oncologic Surgery, City of Hope, Duarte, CA.*

Background: There remains no definitive biomarker predictive of benefit to adjuvant chemotherapy (C) in St. II colon cancer (CC). We tested whether a nuclear receptor, farnesoid X receptor (FXR), in primary CC predicts clinical outcome with chemotherapy. Methods: St. II CC patients treated from 1990 – 2000, with a median follow of 79 mos., were identified from an integrated clinical database and tissue repository. Immunohistochemistry using an antibody directed against the human FXR protein was completed on 116 FFPE specimens. FXR expression was graded by investigators blinded to patient characteristics and clinical outcome. Cancer survival endpoints were calculated using Kaplan Meier survival method and significance was determined using log-rank tests. Multivariate analysis was completed to determine variables predictive of survival. Results: The 10–yr overall survival (OS) of the entire cohort (n = 116) was 55%. There was no difference in OS between those who received (n = 45) and those who did not receive C (n = 72); between patients with FXR expressing (n = 98) and FXR non-expressing cancers (n = 18). However, in the group that did receive adjuvant C, patients with FXR expressing cancers had an increase in OS when compared to patients whose cancers do not express FXR (log rank p = 0.0015). In the patients whose cancers expressed FXR (n = 98), C was associated with an improved OS (log-rank p = 0.009) while in the patients whose cancers did not express FXR (n = 18), C was associated with a decrease in OS (log rank p = 0.04). Multivariate analysis confirmed that C was predictive of improved OS in patients with FXR expressing cancers (p = 0.01) while of worse OS in the patients with FXR non-expressing cancers (p = 0.08). Mismatch repair protein deficiency and other clinical factors such as gender and age were not predictive of survival. Conclusions: Although adjuvant C does not confer a survival benefit to all St. II CC patients, C is predictive of OS when patients are stratified based on cancer expression of FXR. Further studies are needed to validate the utility of FXR as a novel predictive biomarker of survival benefit from C.

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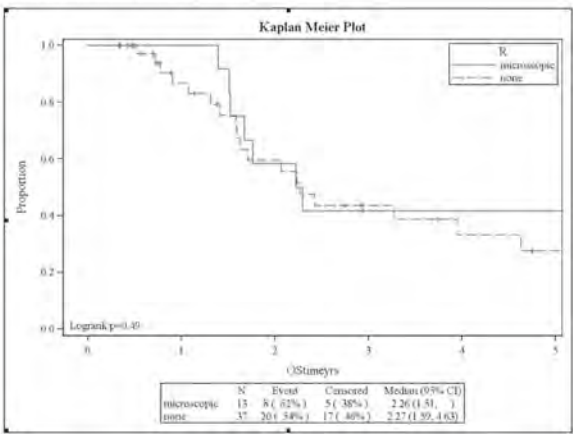
Oncologic outcomes following radical resection with intraoperative electron radiation therapy in patients with locally advanced recurrent rectal cancer O.H. Llaguna,[1]* M.O. Meyers,[1] M.B. Smith,[1] K.B. Stitzenberg,[1] A.M. Deal,[4] S.A. Bernard,[2] B.H. O'Neal,[2] R.M. Goldberg,[2] A.Z. Wang,[3] J.E. Tepper,[3] B.F. Calvo.[1] *1. University of North Carolina School of Medicine, Division of Surgical Oncology & Endocrine Surgery, Chapel Hill, NC; 2. University of North Carolina School of Medicine, Division of Hematology & Oncology, Chapel Hill, NC; 3. University of North Carolina School of Medicine, Department of Radiation Oncology, Chapel Hill, NC; 4. Lineberger Cancer Center Biostatistics Core, Chapel Hill, NC.*

Introduction: Of the 40,000 rectal cancer patients treated annually, as many as 15% will experience a local recurrence (LR). Resection alone for LR is historically fraught with a 30–60% positive margin rate in which case the addition of intra-operative electron radiation therapy (IOERT) may prove beneficial. This study evaluated the oncologic outcomes of patients treated for a locally advanced recurrent rectal cancer (LA-RRC) with radical resection and IOERT. Methods: Under IRB approval a prospective database of patients with LA-RRC undergoing resection and IOERT from April 2001 to January 2010 was analyzed. Demographic, clinical, and pathologic variables were collected. The Kaplan-Meier method estimated 5-year overall survival (OS) and Fisher's Exact test's explored associations with developing a LR. Results: 50 patients (32 male, mean age 58±11) underwent resection and IOERT (median dose 1500 cGy). Primary procedures included pelvic exenteration (n=17), APR (n=10), LAR (n=7), isolated pelvic tumor (n=7), para-aortic lymphadenectomy (n=7), and partial colectomy (n=2). 56% (n=28) required multi-visceral resections including partial/total cystectomy (n=14), small bowel resection (n=10), vaginectomy (n=6), hysterectomy (n=3), oophorectomy (n=3), nephrectomy (n=2), and other (n=4). 34 pelvic sidewall resections and 12 partial sacrectomies were required. Margins were R0 in 37 (74%) and R1 in 13 (26%). Median LOS was 10 days and there were no peri-operative deaths. 5 year OS was 32% with a 19-month follow-up of survivors. 32% (n=16) developed a LR, of which 2 were isolated and 14 were in the setting of distant metastasis. No difference was noted in OS (p=0.5) or development of LR (p=0.3) in patients with R0 vs. R1 resections. Initial T (p=0.1), N (p=0.2), and stage (p=0.7) were not associated with LR. Conclusions: This study reveals that radical resection combined with IOERT provides good local control and reasonable long-term survival in patients with LA-RRC. Similar OS and LR for R0 and R1 resections could be interpreted as a measure of the beneficial effect of IOERT on microscopic disease.

Figure 1: 5-year overall survival R0 versus R1 resection status



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Resection of Liver Metastases from Breast Cancer: Timing of Surgery and Estrogen Receptor Status Define Outcome D. Abbott, A. Brouquet, F. Meric-Bernstam, V. Valero, M.C. Green, H.M. Kuerer, S.A. Curley, E.K. Abdalla, K.K. Hunt, J. Vauthey.* *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

INTRODUCTION: The oncologic benefit of resecting liver metastases (LM) in breast cancer patients is unclear. Identifying predictors of improved outcome would be useful in selecting appropriate candidates for surgery. METHODS: Charts of 86 breast cancer patients who underwent LM resection from 1997 to 2010 were reviewed. RECIST criteria were used to define the best response to chemotherapy as the optimal response at any time during the course of metastatic disease and the preoperative response to chemotherapy as the response immediately before LM resection. Univariate and multivariate analyses were used to identify predictors of survival. RESULTS: Sixty-four patients (74%) had primary tumors that were either estrogen receptor (ER) or progesterone receptor (PR) positive. Fifty-three patients (62%) had solitary LM, and 73 patients (85%) had LM smaller than 5 cm. Sixty-five patients (76%) received preoperative chemotherapy, and 10 patients (12%) received 2 or more chemotherapy regimens before LM resection. Only 2 patients (3%) had progressive disease (PD) as a best response to chemotherapy, whereas 19 patients (29%) had PD as preoperative response to chemotherapy ($p < 0.001$). No perioperative mortality was observed. At a median follow-up of 62 months, the median durations of overall and disease-free survival were 57 and 14 months. Five year overall survival was 44%. Univariate analysis revealed that ER and PR primary tumor status, best response to chemotherapy, and preoperative response to chemotherapy were associated with overall survival after LM resection. On multivariate analysis, an ER-negative primary tumor (p=.009, hazard ratio [HR] = 3.3, 95% confidence interval [CI] =1.4-8.2) and preoperative disease progression (p=.003, HR = 3.8, 95% CI = 1.6-9.2) were independently associated with worse survival after LM resection. CONCLUSIONS: Resection of liver metastases in breast cancer patients with ER positive disease that is responsive to chemotherapy is associated with prolonged survival. Timing of surgery is critical and resection before progression is associated with better outcome.

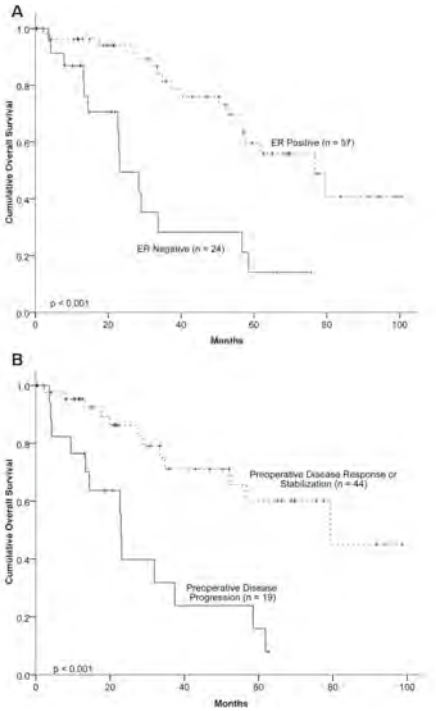

Figure 1. Cumulative survival of patients undergoing hepatic resection for breast cancer metastases based on (A) primary tumor ER status and(B) pre-operative RECIST criteria.

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Margin Status, Recurrence Pattern, and Prognosis after Resection for Pancreatic Adenocarcinoma T. Sugiura,[1]* K. Uesaka,[1] K. Sasaki,[2] H. Kanemoto,[1] T. Mizuno.[1] *1. Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center, Shizuoka, Japan; 2. Division of Pathology, Shizuoka Cancer Center, Shizuoka, Japan.*

Introduction: The impact of resection margin status on pattern of recurrence and prognosis after resection for pancreatic adenocarcinoma is still controversial. Methods: Between 2002 and 2009, 168 patients underwent surgical resection with curative intent for pancreatic adenocarcinoma. After excluding 10 patients who had positive peritoneal cytology, 158 patients were enrolled in this study. All patients met our resection criteria by preoperative computed tomography. Surgical procedure included 131 pancreaticoduodenectomy and 27 distal pancreatectomy. Positive resection margin was defined as microscopic tumor at the surgical specimen according to the UICC Classification. Recurrence patterns and survival rates were calculated and predictors of R1 resection were identified. Results: The resection margin was negative (R0) in 133 patients (85.4%) and positive (R1) in 25 patients (14.6%). No patients had macroscopically positive margins. Residual cancer was detected at the transection margin of the pancreas in 3, dissection margin in 21, and both in 1. Multivariate analysis revealed that only tumor size more than 3 cm was independent predictor of an R1 resection. Recurrence was identified in 95 of 133 (71.4%) with R0 and in 19 of 25 (76.0%) with R1 (p=0.640). Forty-five patients developed recurrence at more than 1 site. Resection margin status did not influence the pattern of recurrence except for local recurrence. Local recurrence occurred more frequently in patients with R1 resection; 17 of 133 (12.8%) with R0 and 9 of 25 (36.0%) with R1, respectively (p=0.008). The overall 3- and 5-year survival and median survival time (MST) were 37.8%, 27.6%, and 26 months in patients with R0 and 46.2%, 27.7%, and 27 months in patients with R1, respectively (p=0.911). The disease-free 3- and 5-year survival rates and MST were 26.8%, 22.1%, and 14 months in patients with R0 and 24.4%, 12.2%, and 12 months in patients with R1, respectively (p=0.679). Conclusion: Although R1 resection affected the incidence of local recurrence, there was

no significant difference in overall and disease-free survival according to the resection margin status.

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The clinical values of methylation status of P16 and APC genes in bile in diagnosis of malignant obstructive jaundice X. Yin,[1]* G. Yan,[2] J. Peng,[1] L. Liang.[1] *1. Department of Hepatobiliary Surgery, The First Affiliated Hospital,Sun Yat-Sen University, Guangzhou, Guangdong, China; 2. The First Affiliated Hospital,Guangdong Pharmaceutical College, Guangzhou, Guangdong, China.*

BACKGROUND: Preoperative definitive diagnosis of malignant obstructive jaundice caused by biliary and pancreatic carcinomas still remains a major challenge. Hypermethylation of tumor suppressor genes have been implied in carcinogenesis of biliary and pancreatic malignancies. The diagnostic values of methylation status of tumor suppressor genes in bile in malignant obstructive jaundice have not been well-documented. AIMS: The present study aimed at evaluating the diagnostic values of methylation status of P16 and APC genes in bile in malignant obstructive jaundice. METHODS: Bile was prospectively collected from 70 patients with obstructive jaundice treated at our hospital between November,2008 and Sepetember,2009. Forty-eight of them were proved to be malignant obstructive jaundice (biliary carcinoma in 36, pancreatic carcinoma in 8 and duodenal carcinoma in 4) by pathological examination, and 22 were benign obstructive jaundice caused by cholelithiasis. DNA was extracted from bile and modified by sodium bisulfite. Methylation-specific PCR was run to detect methylation status of P16 and APC gene promoters. Their diagnostic values in malignant obstructive jaundice were assessed. RESULTS: Hypermethylation of P16 promoter was presented in 72.9% (35/48) malignant obstructive jaundice, and 9% (2/22) bengin obstructive jaundice ($p<0.05$). Hypermethylation of APC promoter was presented in 56.2% (27/48) malignant obstructive jaundice, and 9% (2/22) bengin obstructive jaundice ($p<0.05$). With respect to their diagnostic values in malignant obstructive jaundice, sensitivity, specificity, positive predictivity and negative predictivity were 72.9%, 90.9%, 94.6% and 60.6%, respectively, for P16 gene; 56.2%, 90.9%, 93.1%, 48.8%, respectively, for APC gene. CONCLUSIONS: Methylation status of P16 and APC gene promoters in bile was valuable in diagnosis of malignant obstructive jaundice, with an excellent specificity. P16 gene had a higher sensitivity than APC gene.

Figure 1 The methylation status of P16 gene promoter CpG island in some patients with malignant (T1-T9) and benign (N1-N7) obstructive jaundice. M stands for methylated status, and U stands for unmethylated status. (* lane is DNA ladder).

P138

Use of perioperative therapy in Gastric cancer; A retrospective comparision of ECF and Chemoradiation V. Siripurapu,* F. Zhu, C. Watson, J. Hoffman. *Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Gastric Cancer (GC) remains a major cause of cancer related morbidity and mortality in Western Countries with five year survival rates between 30-40%. Preoperative therapy has been championed by groups extrapolating data from the Intergroup 0116 and the MAGIC trials, with a view to enhancing completion of therapy and improving survival in locally advanced tumors. Methods: Patients with preoperative treatment of GC were reviewed from our tumor registry. Stages were assigned by AJCC 7th edition. A comparison between the ECF regimen and non-ECF chemoradiation regimens was performed to view patterns of pathologic complete response (pCR), recurrence, toxicity and overall survival. Results: Forty two patients were identified and stratified into two groups; Group1 ECF treatment arm (n=16) compared to group 2 non-ECF chemo-radiation arm (n=26). No statistical difference was noted in age, ethnicity or stage stratification. All of Group 1 received their chemotherapy regimen after 2005. In contrast, 60% of Group 2 patients received their treatment pre-2005. Only 56% the ECF group completed their treatment course(19% received other postoperative therapy). Seventy percent of group 2 received adjuvant chemotherapy. A grade 2 or higher toxicity was noted in 16% of Group 1 compared to 60% in Group 2 (p=0.035). Seven complications were noted in the group 1 compared to 10 in group 2 (p=NS). The differentiation of tumor between groups was not significant (p=0.97). Length of stay was significant (Group 1:9 days, Group 2:12 days,p=0.02). More nodes were retrieved from group 1 versus group 2 (20.2 versus 15.2 p=0.03). Group 1 had 3 recurrences (19%) while Group 2 had 11 recurrences (42%),(p=0.94). In both groups 80% of recurrences were distant. Group 1 had a 19% pCR versus 23% in group 2 (P=0.79). Two-year survival was 70% in both groups, with a median survival of 51 months for group 2. Median survival was not reached for group 1. Conclusion: No difference was noted in pCR, recurrences, or survival between these two regimens. If this can be confirmed in larger, prospective, randomized trials, use of radiation and its potential morbidity may be avoided.

P139

Presence of pancreatic intraepithelial neoplasia in the permanent transection margin does not influence outcome in patients with R0 resected pancreatic cancer H. Matthaei,[1]* S.M. Hong,[1] M. Dal Molin,[1] M. Goggins,[2] B.H. Edil,[3] C.L. Wolfgang,[3] J.L. Cameron,[3] R.D. Schulick,[3] A. Maitra,[1] R.H. Hruban.[1] *1. Johns Hopkins University School of Medicine - Department of Pathology, Baltimore, MD; 2. Johns Hopkins University School of Medicine - Department of Oncology, Baltimore, MD; 3. Johns Hopkins University School of Medicine - Department of Surgery, Baltimore, MD.*

Introduction: Numerous studies have proved the importance of negative resection margins (R0 resection) in the treatment of pancreatic ductal adenocarcinoma (PDAC). However, the significance of pancreatic intraepithelial neoplasia (PanIN) at surgical margins after the resection of an invasive carcinoma has not been established. In particular, the clinical impact of PanIN-3 lesions is unclear. Methods: Two hundred eleven surgically resected PDAC patients with R0 resection were retrospectively selected from 2004 to 2008. Frozen sectioned slides containing final resection margins of the pancreas were evaluated for presence or absence, number and grade of PanINs. Data were compared to clinicopathologic factors, including survival of the patients. Results: PanIN lesions were present on the resection margins in 109 of 211 patients (51.7%). Median number of PanINs per resection margin was 1 (range, 1 – 11). Of the 211 patients, 73 had PanIN-1 (34.6%), 44 PanIN-2 (20.9%), and 16 PanIN-3 (7.6%) at their pancreatic resection margins. Presence of any degree of PanIN and each grade of PanINs did not correlate significantly with clinicopathological characteristics (including, age, gender, T and N stage, and microscopic vascular and perineural invasion). No significant survival difference was present regarding presence of different degrees of PanINs (PanIN-1, PanIN-2, and PanIN-3) nor any degree of PanINs. Conclusion: Presence of PanINs on resection margins does not affect survival in patients who underwent complete resection (R0) for PDAC. Therefore, no additional resection seems to be indicated whenever intraoperative frozen sections reveal even high grade PanIN (PanIN-3) when the resection is being performed for an invasive carcinoma.

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Pancreatic failure following resection for cancer: Incidence and coincidence of exocrine and endocrine insufficiency M.A. White,[1]* S.C. Agle,[1] J.H. Mehaffey,[2] T.L. Fitzgerald,[1] S.T. Ryan,[2] E.E. Zervos.[1] *1. East Carolina University/Pitt County Memorial Hospital, Greenville, NC; 2. East Carolina Universtiy, Brody School of Medicine, Greenville, NC.*

Introduction: Endocrine insufficiency following pancreatectomy is commonly thought to correlate with extent of resection while the cause of exocrine insufficiency may be multifactorial. The purpose of this study was to determine the incidence and mitigating factors of complete (endocrine and exocrine insufficiency) and partial pancreatic failure following resection for cancer. Methods: A prospective tumor registry was reviewed to identify all patients undergoing pancreatic resection for cancer at a large, rural university hospital between 1996 and 2010. The incidence of post-operative endocrine and exocrine insufficiency was established. Records were reviewed to determine: operation performed, extent of resection, and major complications. Fisher's exact test was used to determine whether the incidence of either type of insufficiency predicted complete failure. Results: 101 patients were identified to have undergone Whipple (80) or distal pancreatectomy and splenectomy (DPS, 21). 10% of patients developed total pancreatic failure while 39% developed exocrine failure only and 9% developed solely endocrine failure (new onset or worsened glycemic control). Pre-existing endocrine failure worsened in 19% (8/42) but improved in 33% (14/42). 20% (10/49) of exocrine failure patients developed new onset diabetes or worsened glycemic control while 53% (10/19) of endocrine failure patients developed exocrine insufficiency. Of patients with major complications (35/101), 57% had exocrine insufficiency and 29% had endocrine failure, equivalent to those without complications. Patients requiring Whipple were significantly more likely to develop exocrine insufficiency (56%), compared to 23% of those with DPS ($p = 0.0078$, Fisher's exact test), but endocrine insufficiency occurred with equal frequency in both. Conclusions: Total pancreatic failure occurs commonly following pancreatic resection and can be predicted by extent of surgery and complications. Exocrine insufficiency does not predict endocrine insufficiency and half of patients with worsened endocrine function developed exocrine failure. Exocrine insufficiency is less likely to occur with DPS.

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Histologic subtypes of neuroendocrine tumors of the appendix have varying malignant potential C. Hsu,[1]* A. Rashid,[2] Y. Xing,[1] Y. Chiang,[1] G.J. Chang,[1] Y.N. You,[1] B.W. Feig,[1] J.N. Cormier.[1] *1. Surgical Oncology, M. D. Anderson Cancer Center, Houston, TX; 2. M. D. Anderson Cancer Center - Pathology, Houston, TX.*

Background Neuroendocrine tumors of the appendix are rare malignancies often diagnosed incidentally. Several histologic subtypes have been described including malignant carcinoid tumors (MCT), goblet cell carcinoid (GCT, adenocarcinoid), and composite goblet cell carcinoid-adenocarcinoma (CGCC-A). The objective of this study was to assess the characteristics of patients with appendiceal neuroendocrine tumors and compare survival outcomes. Methods Patients coded to have appendiceal tumors were identified from the National Cancer Data Base (1998-2007). Neuroendocrine tumors were selected and cohorts were stratified according to histologic subtype. Descriptive statistics were used to compare the cohorts and survival was calculated using the methods of Kaplan-Meier. Results A total of 9,520 patients were identified with appendiceal tumors, of which 2,770 (29.1%) were neuroendocrine tumors. The most common histologic subtype was GCT (60.7%), followed by MCT (32.3%) and CGCC-A (7.0%). CGCC-A had a significantly higher incidence of lymph node (35.6%) and distant (23.7%) metastases at presentation ($p =<0.001$) (Table). Survival data was available for 1059 patients. With a median follow-up of 5.3 years, the 5-year overall survival by histology was 87.6% [95% CI:82.8-91.1] for MCT, 78.2% [95% CI: 74.5-81.4] for GCT, and 56.3% [95% CI: 42.1-68.4] for CGCC-A (log-rank $p<0.001$). Among the 769 patients who underwent colectomy, the 5-year overall survival by histology was 89.6% [95% CI: 83.5-93.6] for MCT, 80.0% [95% CI: 76.1-83.4] for GCT, and 58.2% [95% CI: 42.4-71.1] for CGCC-A (log-rank $p<0.001$). Conclusions Neuroendocrine tumors account for a minority of tumors occurring in the appendix. The various histologic subtypes of appendiceal neuroendocrine tumors represent a spectrum of disease with varying malignant potential: MCT (low), GCT (intermediate), and CGCC-A (high). GCTs represent the most common subtype while CGCC-As are at highest risk for regional and distant metastases and have the worst prognosis.

	MCT (n=894)	GCT (n=1682)	CGCC-A (n=194)	p value
Median Age (yrs)	41	52	53.5	<0.001
Males (%)	37.0	51.0	46.4	<0.001
Surgical Treatment with Colectomy	57.5	78.7	82.8	
Tumor Stage (%)				<0.001
T1	19.1	12.4	5.7	
T2	18.5	15.2	10.6	
T3	55.5	55.4	47.2	
T4	6.9	17.0	36.6	
≥ 1 Lymph Node Examined (%)	40.4	59.6	79.4	<0.001
≥ 1 Positive Node (%)	18.0	11.8	35.6	<0.001
Metastatic Disease at Presentation (%)	1.9	3.6	23.7	<0.001

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Computed Tomographic Assessment of Resectability after Neoadjuvant Therapy in Pancreatic Cancer P. Papavasiliou,* R. Arrangoiz, B.N. Milestone, J.P. Hoffman, Y.S. Chun. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Neoadjuvant treatment for borderline resectable pancreatic cancer poses a challenge for surgeons in determining extent of disease with computed tomography (CT). The objective of this study was to determine the accuracy of surgeons reading CT scans before and after neoadjuvant therapy for pancreatic cancer. **Methods:** Twenty-eight consecutive patients who underwent resection of borderline resectable pancreatic cancer after neoadjuvant chemoradiation with available pre- and post-treatment CT scans were reviewed. The portal-superior mesenteric vein (PV-SMV), hepatic artery, superior mesenteric artery (SMA), and celiac artery were assessed using the National Comprehensive Cancer Network (NCCN) guidelines by three surgical oncologists blinded to operative and pathology reports. κ Statistics were used to determine interobserver agreement. **Results:** Agreement among the three readers was highest for pre-treatment involvement of the celiac artery (κ=1), followed by SMA (κ=0.67), hepatic artery (κ=0.54), and lowest for PV-SMV (κ=0.47). Agreement was inferior for post-treatment assessment of the celiac artery (κ=0.77), hepatic artery (κ=0.46), and PV-SMV (κ=0.28). Fifteen of 28 patients underwent PV-SMV resection and/or had a positive vein margin, while five had a positive SMA margin. Two patients required hepatic artery resection. On consensus review by the three readers, sensitivity for assessing vascular invasion was highest for the celiac and hepatic arteries and lowest for the SMA (Table). Specificity was highest for the celiac artery and lowest for the PV-SMV. None of the patients had radiographic progression in PV-SMV, celiac, or hepatic artery involvement after preoperative therapy. Two patients developed radiographic SMA abutment after preoperative therapy; both had positive SMA margins in their pathologic specimens. **Conclusion:** Neoadjuvant therapy was associated with inferior interobserver agreement of vascular invasion on preoperative CT but did not affect diagnostic accuracy. In this study, CT assessment by NCCN guidelines overestimated PV-SMV and underestimated SMA involvement.

Table. Accuracy of assessing vascular involvement pre- and post-neoadjuvant therapy

	Sensitiviy		Specificity	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
PV-SMV	14/15 (93%)	13/15 (87%)	1/13 (8%)	2/13 (15%)
Hepatic Artery	2/2 (100%)	2/2 (100%)	21/26 (81%)	23/26 (88%)
SMA	5/9 (56%)	5/9 (56%)	16/19 (84%)	15/19 (79%)
Celiac Artery	1/1 (100%)	1/1 (100%)	27/27 (100%)	27/27 (100%)

P145

Neoadjuvant Chemoradiotherapy for esophageal cancer : It works A.S. Khithani, K.M. Lowe, D.J. Christian, J. Jay, D. Jeyarajah.* *Methodist Dallas Medical Center, Dallas, TX.*

Introduction: Neoadjuvant therapy can provide sufficient tumor downstaging such that more patients are able to undergo R0 resection. The aim of this study was to assess the role of neoadjuvant therapy and esophagectomy in patients with esophageal cancer. Methods: All esophagectomies cooperatively performed by two surgeons between September 2005 and August 2010 were reviewed. The response to neoadjuvant therapy, post resection for esophageal cancer was evaluated by comparing the preoperative EUS staging and final histopathological staging. Results: Eighty four patients underwent esophagectomy for malignancy over a five year period. Forty seven patients who received neoadjuvant therapy underwent preoperative EUS as part of the preoperative staging. This was our study group. Fifty five percent (55%) patients were shown to have a pathologic response to chemotherapy on final histopathology (PR). A complete pathologic response (cPR) on final histopathology was achieved in 36% of the patients. Postoperative stage remained the same as preoperative stage in 28% patients while 17% patients were seen to have been upstaged on final histopathology. Eighty one (81%) percent patients who received neoadjuvant therapy had adenocarcinoma and 19% had squamous carcinoma. Of the adenocarcinoma 53% patients had a PR and 34% had a cPR on final histopathology. Of the squamous carcinomas 67% showed PR and 44% patients had a cPR to neoadjuvant therapy. Conclusions: Neoadjuvant therapy can be successfully used prior to esophagectomy to achieve a complete response. In our experience squamous carcinomas showed a better response to neoadjuvant therapy as compared to adenocarcinomas.

Table showing pathologic response to neoadjuvant therapy for esophageal cancer

	No of pts(n)	PR	Same	Upstaged	CR
Overall	47	26(55%)	13(28%)	8(17%)	17(36%)
Adenocarcinoma	38	20(53%)	11(29%)	7(18%)	13(34%)
Squamous carcinoma	9	6(67%)	2(22%)	1(11%)	4(44%)

P146

Clinical significance of DNMTs expression in hilar cholangiocarcinoma X. Yin,* J. Peng, K. Zhang, L. Liang. *Department of Hepatobiliary Surgery, The First Affiliated Hospital,Sun Yat-Sen University, Guangzhou, Guangdong, China.*

Background: DNA hypermethylation is a key factor in development of malignancies. A growing body of literature showed that DNA hypermethylation is commonly present in hilar cholangiocarcinoma. DNA methyltransferases (DNMTs), including DNMT1, DNMT3a and DNMT3b, are the key enzymes responsible for DNA methylation. The significance of DNMTs expression in hilar cholangiocarcinoma has not been well-documented. The present study aimed at evaluating clinical significance of DNMTs expression in hilar cholangiocarcinoma. Methods: Tissue samples of 111 hilar cholangiocarcinoma and 39 choledochocele, treated between April,1997 and May,2007 in our hospital, were retrospectively collected and tissue chip was prepared. Expression of DNMT1, DNMT3a and DNMT3b was evaluated using immunohistochemical staining. Correlation between its expression and clinicopathological features and survival was analyzed. Results: DNMT1, DNMT3a and DNMT3b were strongly expressed in hilar cholangiocarcinoma in 76.7%, 46.8% and 76.7%, respectively, in choledochocele in 53.8%,33.3% and 53.8%, respectively. Expression of DNMT1 and DNMT3b was significantly elevated in hilar cholangiocarcinoma compared with choledochocele ($p<0.05$). DNMT1 expression in hilar cholangiocarcinoma was related to Bismuth-Corlette classification and TNM staging (both $p<0.05$), and DNMT3b expression was related to Bismuth-Corlette classification ($p<0.05$), but not TNM staging ($p>0.05$). DNMT3a expression had no relation to either Bismuth-Corlette classification or TNM staging. Survival analysis showed that patients with weak expression of DNMT1 had markedly longer overall survival than those with strong expression of DNMT1, with a median overall survival time of 24 months vs 11 months ($p<0.05$). Neither DNMT3a nor DNMT3b had correlation with overall survival. Conclusion: DNMT1 and DNMT3b might play an important role in development of hilar cholangiocarcinoma, and DNMT1 represented as an independent prognostic factors.

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Thrombocytosis in patients with gastric cancer – does it correlates with advanced disease? R. Lavy,* A. Achildiev, B. Chikman, A. Kapiev, A. Halevy. *Assaf Harofeh Medical center, Tel Aviv, Israel.*

Background Most studies addressed the possible association of thrombocytosis and prognosis showed an inverse relationship between a prognosis and excessively high number of platelets in blood. Such correlation was reported in patients with lung, colon cancer, renal cell carcinomas, gynecological malignancies and gastric cancer. However, the effect of thrombocytosis on patients' prognosis is scarce and the data variable. Material s and methods This retrospective study is based on 178 patients with gastric cancer. A data base was created by analysis of medical charts, and pathological reports. The cutoff point in order to define thrombocytosis was selected at 350,000/μl and above. Statistical tests were performed against 2-sided alternatives using SPSS-15.0 computer program. The disparities in number of patients in the different subgroups

are the result of missing data. Results: 111 males and 67 females (ratio – 1:1.65), constituted the study group. The mean pre-treatment PLT count for all patients was 264.533+91.521 (range, 59.000 to 631.000). The number of patients with PLT < 350.000 was 156 (87.6%), and 22 patients (12.4%) were with thrombocytosis (350.000 and more platelets count). Thrombocytosis was found in 12/48 patients with proximal localization (25.0%) versus only 6/78 in patients with distal location (7.7%), (p=0.009). Signet ring cell type of cancer was not different from non-signet ring cell gastric cancer. Vascular invasion also was not associated with thrombocytosis (p=0.395). Association of thrombocytosis with lymph node metastases, primary tumor extension are presented in table. Metastatic disease at presentation was associated with thrombocytosis in 13/59 pts (22.0%) versus 9/119 pts (7.6%) patients without evidence of metastatic disease at presentation (p<0.001). Conclusion: 1) Thrombocytosis is quite rare condition associated with gastric cancer 2) Thrombocytosis is associated with direct extension of tumor or disseminated disease at presentation 3) Proximal localization of gastric cancer is more frequently associated with thrombocytosis

Pathological characteristics and disease extension - association with

Pathological characteristics and disease extension	PLT < 350.000	PLT > 350.000	P
Vascular invasion			
Yes	42/45 93.3%	3/45 6.7%	0.395
No	93/106 87.7%	13/106 12.3%	
T stage			
T1+T2	48/50 96.0%	2/50 4.0%	0.035
T3+T4	86/103 83.5%	17/103 16.5%	
N stage			
N0	48/53 90.6%	5/53 9.4%	0.781
N1-3	72/82 87.8%	10/82 12.2%	
Distant metastases at presentation			
YES	46/59 78.0%	13/59 22.0%	<0.001
NO	110/119 92.4%	9/119 7.6%	
Pathological type			
Signet ring cell	51/57 89.5%	6/57 10.5%	0.808
Non-signet ring	105/121 86.8%	16/121 13.2%	

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Emerging Role of Robotic Surgery in Hepatobiliary Malignancies K. Kitisin,[1]* V. Packiam,[1] S. Celinski,[1] S. Chalikonda,[2] J. Pingpank,[1] H. Zeh,[1] D. Bartlett,[1] A. Tsung.[1] *1. Surgical Oncology, University of Pittsburgh Medical Center, Pittsuburgh, PA; 2. Cleveland Clinic, Cleveland, OH.*

Introduction: Minimally invasive techniques are increasingly used for liver surgery due to recent advancements in technology and increasing understanding of hepatic anatomy. Robotic-assisted surgery is emerging as an important option for hepatobiliary surgery due to the inherent limitations of laparoscopic surgery. The purpose of this study was to assess the feasibility and outcomes of robotic-assisted surgery in hepatobiliary malignancies. Methods: 29 robotic-assisted surgeries were performed for hepatobiliary malignancies at our tertiary referral center from January 2008 to September 2010. We conducted a retrospective analysis to review pre-operative, pathologic, and post-operative data. Results: 28 patients, 67% male, underwent robotic-assisted hepatobiliary surgery with a median age of 62(39-84) years. The indications for surgery included primary liver cancers in 9 patients (6 hepatocellular carcinoma, 3 cholangiocarcinoma), liver metastases from colorectal cancers in 15 patients, and liver metastases from melanoma, parotid, gastric, or esophageal cancer in 4 patients. A total of 25 liver resections were performed, with 24% being major hepatectomies involving more than 3 segments, 16% anatomical left lateral segmentectomies, and 60% non-anatomical liver resections. The mean tumor size was 3.9±2.2 cm and negative margins were achieved in 96% of patients. 3 patients (11%) were found to have cancer recurrence within 12 months. In addition, 6 patients (21%) received robotic-assisted placement of hepatic arterial infusion pumps. Overall, 4 cases (14%) required conversion to an open operation. The mean operative time was 306±104 min, median blood loss was 200(30-3600) ml, and mean post-operative length of stay was 5.9±3.1 days. Major morbidity occurred in 1 patient (3%) with no 30-days mortality. Conclusion: Robotic-assisted surgery for hepatobiliary malignancies is feasible without sacrificing oncologic principles in terms of margins, morbidity/mortality, and 1 year recurrence. While it is too early to draw conclusions about long-term cancer recurrence, future prospective randomized trials can compare these outcomes of robotic-assisted surgery to laparoscopic and open procedures.

P149

Genetic Variations Predict Toxicity Associated with Neoadjuvant Chemoradiation for AJCC Stage II/III Rectal Cancer J. Ho,* W. Li, M.P. Duldulao, Z. Chen, J. Kim, J. Garcia-Aguilar. *City of Hope National Medical Center, Duarte, CA.*

Introduction Genetic polymorphisms have been associated with toxicity from chemotherapeutic agents for colon cancer, but none has been identified for rectal cancer. We examined the association between polymorphisms in genes for DNA repair, cell cycle progression, angiogenesis, and drug metabolism with toxicity from neoadjuvant chemoradiation treatment (CRT) for rectal cancer. Methods Patients with AJCC stage II/III rectal adenocarcinoma were enrolled in a Phase II multicenter trial examining timing of rectal cancer response to neoadjuvant CRT. There were two treatment arms: (I) radiation (XRT) and 5-FU followed by surgery and (II) XRT/5-FU and FOLFOX followed by surgery. Treatment toxicity, classified by the NCI Common Terminology Criteria guidelines as Grade 3 and above, was recorded. DNA was extracted from normal rectal mucosa and analyzed for 22 polymorphisms in 17 genes. Results We evaluated 110 patients (Group I, n=52; Group II, n=58). A total of 19 patients experienced Grade 3+ adverse events (AE) [Group I, n=10 (19%); Group II, n=9 (16%)]. Gastrointestinal symptoms were the most common AE [Group I, n=5 (10%); Group II, n=4 (7%)]. The detection of lys allele (lys/lys or lys/gln genotypes) at codon 751 of the Xeroderma pigmentosum group D (XPD) gene was associated with increased toxicity in Group II (p=0.03), whereas homozygosity for the arg allele (i.e. arg/arg genotype) at codon 399 of the X-ray cross-complementing protein 1 (XRCC1) gene was associated with a significant increase in toxicity in both treatment groups (p=0.009). Conclusion Genetic polymorphisms in DNA damage repair genes XPD and XRCC1 are associated with toxicity in rectal cancer patients receiving CRT. The identification of gene polymorphisms that predict adverse events may help to optimize patient therapy while minimizing morbidities.

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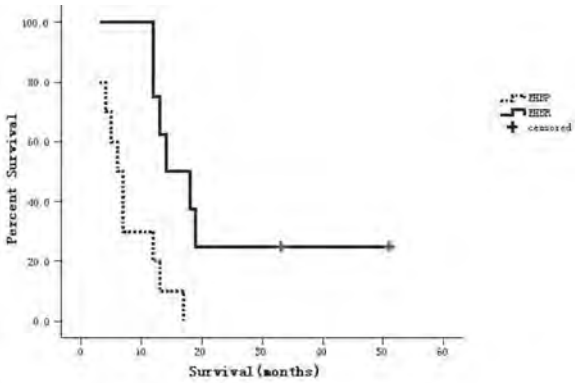
Extrahepatic Bile Duct Resection in the Treatment of T3 and T4 Gallbladder Carcinoma Y. Zheng,* M. Zhong, H. Hu, H. Zhang, Z. Zhuang, A. Lu, B. Chen. *Surgery, Shanghai East Hospital, Shanghai, China.*

Objective To evaluate the clinical outcome of extrahepatic bile duct resection (EBDR) in the treatment of T3 and T4 gallbladder carcinoma. Methods A total of 18 patients with T3 or T4 gallbladder carcinoma were randomly assigned

to undergo either radical/extended radical resection with extrahepatic bile duct preservation (EBDP, n=10) or radical/extended radical resection with extrahepatic bile duct resection (EBDR, n=8). Clinicopathologic factors, postoperative complications, and survival in the two groups were compared. Results There were no significant differences in terms of age, sex, and postoperative complications. One-year survival rates after surgery were 22% in the EBDP group and 62.5% in the EBDR group; 2-year survival rates were 0% and 25%, respectively. The postoperative median survival period of patients was 6 and 14 months in the two groups, respectively. The median survival after surgery was significantly longer in the EBDR group than in the EBDP group (p=0.0023). Conclusion EBDR might be necessary to improve the survival of patients with T3 and T4 gallbladder carcinoma when performing radical or extended radical resection.



Group	Median Survival (Months)
EHBP	6
EHBR	14**

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The extent of lymphadenectomy and overall survival depend on the timing of radiotherapy for rectal cancer M. Le,* B.A. Mailey, W. Lee, M.P. Duldulao, J. Garcia-Aguilar, J. Kim. *City of Hope, Duarte, CA.*

Background: Accurate pathologic staging and local disease control depend on the extent of lymphadenectomy (LAD) in rectal cancer. Previous studies suggest that lymph node (LN) number may vary with neoadjuvant therapies. Our objectives were to measure the impact of timing of radiotherapy on extent of LN retrieval and to determine the prognostic role of LN number in rectal cancer. Methods: Patients undergoing curative-intent surgery for rectal adenocarcinoma (1988-2006) in Los Angeles County were identified from the Cancer Surveillance Program. Patients were grouped according to radiotherapy timing (neoadjuvant, adjuvant, or none). To determine prognostic significance, an optimal LN cutoff number was assessed for patients with N0 disease by dichotomizing LN numbers from 3-7. Results: Query of the registry identified 6358 patients. Of these, 20% (n=1280) and 25% (n=1573) received neoadjuvant and adjuvant radiotherapy, respectively; and 55% (n=3545) received no radiotherapy. There was no difference in LN number between patients with and without radiotherapy (7 vs. 8 LNs, p=NS). However, within the radiotherapy cohort, there was significantly lower LNs in the neoadjuvant group (5 vs. 9 LNs, respectively; p<0.001). Survival differences for dichotomization numbers favored the groups with higher LN number. The optimal LN cutoff with no survival difference was 7 for patients receiving adjuvant radiotherapy; there was no optimal cutoff for neoadjuvant therapy patients. Conclusions: From our population-based cohort, we observed that patients receiving neoadjuvant radiotherapy had decreased LN retrieval and that LN number was non-prognostic. In contrast, the extent of LAD is a prognostic factor for overall survival in patients receiving adjuvant radiotherapy.

Characteristics of radiotherapy cohort

Clinical factor	Radiation Therapy		
	Neoadjuvant (n=1280) n (%)	Adjuvant (n=1573) n (%)	p-value
Tumor size (cm)			0.005
</= 5	552 (68)	864 (62)	
> 5	262 (32)	532 (38)	
Tumor grade			<0.001
Well	70 (6)	79 (5)	
Moderate	881 (76)	1042 (69)	
Poor	203 (18)	386 (25)	
Undifferentiated	4 (0)	10 (1)	
LN status			<0.001
Negative	703 (64)	496 (40)	
Positive	402 (36)	741 (60)	
LN number			<0.001
Median	5	9	
Extent of disease			<0.001
Local	438 (36)	239 (15)	
Regional	639 (53)	1188 (76)	
Distant	136 (11)	133 (9)	
Surgery			<0.001
LAR	785 (67)	813 (55)	
APR	385 (33)	663 (45)	

P152

Surgery is Associated With Prolonged Survival in Stage IV Pancreatic Neuroendocrine Tumors J.M. Pimiento,* J. Strosberg, A. Chema, L. Kvols, P. Hodul. *Moffitt Cancer Center, Tampa, FL.*

Background: Surgery plays an important role in the treatment of pancreatic neuroendocrine tumors (PNETs). Whenever complete surgical resection is not feasible, debulking surgery is considered with reported improved survival. However, many patients have been excluded from this therapy due to an inability to eradicate >90% of the disease. Here we investigate whether surgical debulking impacts survival in stage IV disease and whether complete debulking is necessary to achieve improved survival. Methods: A retrospective review of patients treated for PNETs at Moffitt Cancer Center between 1999-2010 was performed. All patients were staged according to the new AJCC classification. Overall survival for each stage was determined using the log-rank test. Stage IV patients treated with non-operative therapies were compared to those treated operatively. Results: 425 patients with histologically proven PNETs were identified. The 5-year survival rates for Stages I-IV were 92%, 84%, 81%, and 57% respectively. 275 patients had Stage IV disease at presentation. Non-operative management occurred in 182 patients and 93 patients underwent surgical intervention. Of the 93 patients, 11% underwent cytoreduction of metastasis with unresectable primary, 21% had resection of the primary without surgical treatment of metastasis, and 68% had both the primary resected and the metastasis debulked. Overall 5-year survival was higher in the surgical group vs. the non-operative group (78.4% vs. 44.6%, p=0.001). The 5-year survival amongst surgical treatments was not statistically different (p=0.5). Furthermore, no statistical difference in survival was noted for stage II or stage III disease and patients with stage IV treated with surgical intervention, p=0.113 and p=0.756 . Conclusions: Surgical intervention in patients with stage IV PNETs was associated with prolonged survival. This survival is not statistically different from patients initially

presenting with stage II or III disease. These findings suggest that cytoreductive surgery, even limited, in selected individuals with metastatic PNET can be beneficial.

P153

Epidermal Growth Factor Receptor Overexpression in Resected Pancreatic Cancer A. Mahipal,* M.J. McDonald, A. Witkiewicz, B. Carr. *Hematology/Oncology, Thomas jefferson university, Philadelphia, PA.*

Background. The effect of overexpression of epidermal growth factor receptor (EGFR) in pancreatic carcinoma is uncertain. In this study, we examine the association between EGFR overexpression (membrane and cytoplasmic) and histopathologic features and clinical outcomes in patients post resection. Methods. Seventy three patients underwent curative resection for pancreatic cancer from 4/08 to 4/10. Tumor EGFR expression was determined immunohistochemically using EGFR pharmDxTM kit. Cytoplasmic overexpression was considered positive if EGFR expression was seen in the cytoplasm in ≥10% of cells. Cell membrane staining scores were assigned: 0 (no membrane staining), 1+ (incomplete membrane staining in ≥ 10% of cells, 2+ (complete weak/moderate membrane staining in ≥ 10% of cells) and 3+ (complete heavy staining in ≥ 10% of cells). A score of 2+ and 3+ were considered as membrane overexpression. Comparisons between EGFR overexpression and clinicopathologic features were assessed by chi-square test with p-value < 0.05 as statistically significant. Proportional hazard regression was used to estimate PFS and OS. Results. Out of 73 patients, 43 (59%) and 50 (68%) patients had membrane and cytoplasmic EGFR overexpression respectively. AJCC stages were: stage I: 8, stage II: 63, stage III: 1 and stage IV: 1 patient. There was statistically significant correlation between cell membrane EGFR overexpression and lymph node positivity (p=0.04). Membrane EGFR overexpression was not significantly associated with local invasion, margin positivity, vascular invasion, perineural invasion, histologic grade or stage (see table). Cytoplasmic EFGR overexpression was significantly associated with margin positivity (p=0.01) only. The hazard ratios (95% CI) for PFS and OS in patients with membrane EGFR overexpression was 1.37 (0.72-2.60) and 1.27 (0.62-2.61) respectively. The corresponding values for patients with cytoplasmic overexpression were 1.65 (0.80-3.37) and 1.25 (0.58-2.71) respectively. Conclusions. Membrane EGFR overexpression was associated with lymph node status and cytoplasmic EFGR overexpression with margin positivity. There was no association of EFGR expression and clinical outcomes.

EFGR overexpression and histopathologic features

	Membrane EGFR overexpression			Cytoplasmic EFFR overexpression		
	yes	no	P-value	yes	no	P-value
Local invasion						
yes	36	22	0.28	39	19	0.65
no	7	8		11	4	
Grade III						
yes	15	10	0.89	18	7	0.64
no	28	20		32	16	
Margin positive						
yes	13	4	0.09	16	1	0.01
no	30	26		34	22	
Vascular invasion						
yes	25	17	0.90	27	15	0.38
no	18	13		23	8	
Perineural invasion						
yes	36	27	0.44	45	18	0.17
no	7	3		5	5	
Lymph node positive						
yes	35	18	0.04	33	20	0.06
no	8	12		17	3	
Stage IIb or higher						
yes	35	19	0.08	34	20	0.08
no	8	11		16	3	

P154

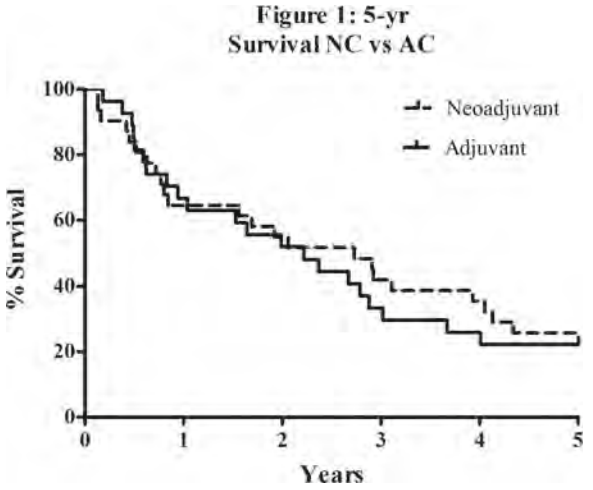
Patients with high-grade appendix cancer and extensive disease do benefit from Cytoreduction and heated intraperitoneal chemotherapy if complete cytoreduction can be achieved H.M. El Halabi,* V. Gushchin, R. Macdonald, J. Francis, A. Sardi. *Institute for cancer care Mercy Medical center, Baltimore, MD.*

Background: Patients with peritoneal mucinous carcinomatosis (PMCA) of appendiceal origin and extensive disease are commonly advised against cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC). We hypothesize that CRS and HIPEC is an effective treatment for this high recurrence risk group. Methods: A retrospective analysis of PMCA patients was performed from the prospectively collected database. Extent of disease was assessed by peritoneal cancer index (PCI). PCI was studied in relation to the following variables, completeness of cytoreduction (CC), lymph node (LN) status and prior surgery score (PSS). We estimated overall survival (OS) by plotting Kaplan-Meier survival curves and test differences using the logrank test. Results: From 134 patients with appendix cancer that underwent CRS and HIPEC 77 had high-grade disease (PMCA). The mean follow up was 22 months, range (3-90 months). The OS was 91%, 74%, and 70% for 1, 3, and 5-years, respectively. Fifty-one patients had PCI ≥ 20 (66%). In patients with PCI ≥ 20, 24 out of 51 had LN metastasis; while in PCI < 20 group 7 out of 26 patients had LN metastasis. Thirty-seven out of 50 (74%) and 16 out of 26 (62%) patients had PSS of 2 or 3 in PCI ≥ 20 and PCI < 20 groups respectively. Complete cytoreduction was achieved in 75 % of all cases; 65 % in PCI ≥ 20 group and 96 % in PCI < 20 group (P=0.002). In patients with complete cytoreduction the 5-year OS were 43 % in PCI ≥20 group and 66 % in PCI < 20 (P=0.109). Nineteen patients had incomplete cytoreduction. Eighteen out of 19 had PCI ≥ 20, their 3-year OS was 27 %, and none was alive at 5 years. On multivariate analysis using Cox regression with PCI score and complete cytoreduction hazard ratios were 2.8 (95% CI 0.8-10.2) and 3.6 (95% CI 1.5-8.8), respectively. Conclusion: Meaningful long-term survival could be achieved in patients with PMCA even with extensive peritoneal disease. PCI ≥ 20 should not be used as an exclusion criterion when selecting these patients for CRS and HIPEC and every effort should be made to achieve complete cytoreduction.

P155

Locally Advanced Esophageal Cancer: Actual 5-year Survival Comparing Neoadjuvant and Adjuvant Chemoradiation C.S. Davis,[1]* J.R. Johns,[1] G.J. Abood,[2] T.A. Baker,[1] D.C. Zank,[3] S. Nagda,[1] G.V. Aranha,[1] C.V. Godellas,[1] M. Shoup.[1] *1. Surgery, Loyola University Medical Center, Maywood, IL; 2. University of Pittsburgh Medical Center, Pittsburgh, PA; 3. University of California, San Diego, La Jolla, CA.*

Background: Patients undergoing esophagectomy for locally advanced esophageal cancer are often candidates for chemoradiotherapy (CRT). It is unclear if there is a survival advantage for CRT when administered in the neoadjuvant (NCRT) versus the adjuvant (ACRT) setting. We report a single institution experience with actual long-term follow-up of patients with resected esophageal cancer treated with NCRT or ACRT. Methods: Following IRB approval, a retrospective review of 123 patients undergoing Ivor-Lewis esophagectomy between January 1, 1990 through December 31, 2001 was conducted. Clinicopathologic variables were analyzed, and survival was determined from hospital records, the Social Security Death Index, and direct patient follow-up. All patients were followed for at least five years, and survival was assessed by Kaplan-Meier analysis. Results: Of the 123 patients, 65 had surgery alone for early esophageal cancer and were excluded from the analysis. Of the remaining 58, 31 received NCRT and 27 received ACRT. There was no difference between groups for length of operation, blood loss, or complication rate. With all patients having at least 5 years of follow-up, the overall 1-year survival was 65% and 67% (p=0.866), 3-year survival was 42% and 33% (p=0.508), and 5-year survival was 26% and 22% (p=0.755) for the NCRT and ACRT groups, respectively (Figure 1). Among those in the NCRT group, patients with a complete or partial response (n=20) had an improved 1-year survival as compared to those with no response at all (n=11; p=0.025). However, this difference did not persist at 3 and 5-years (p=0.224 and p=0.896, respectively). Conclusions: In this study, all patients with locally advanced esophageal carcinoma who underwent Ivor-Lewis esophagectomy with either NCRT or ACRT were followed for at least 5 years. Not only was there no difference in perioperative morbidity or mortality, but the overall 5-year survival was almost identical between groups. Therefore, as NCRT may be better tolerated and more easily administered, we advocate its use over ACRT in those with locally advanced esophageal cancer.



P156

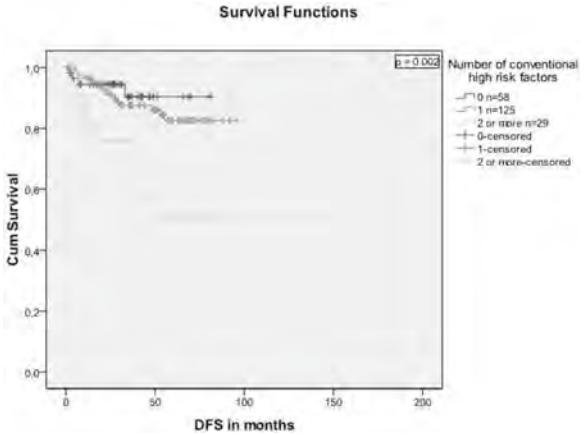
Palliative Oophorectomy in Patients with Metastatic Colorectal Cancer to the Ovaries B. George,[2] Y.N. You,[1] C. Viswanathan,[1] S. Wen,[1] V. Baladandayuthanpani,[1] M.J. Overman,[1] B.K. Kee,[1] S. Kopetz,[1] C. Eng,[1] C.R. Garrett.[1]* *1. GI Medical Oncology, MD Anderson, Houston, TX; 2. Medical College of Wisconsin, Wisconsin, TX.*

Background: The ovaries are an uncommon site for secondary spread from metastatic colorectal cancer (CRC). We hypothesize that palliative oophorectomy improves survival among patients (pts) with metastatic colorectal cancer to the ovaries (mCRC-O). Method: We undertook a single institution IRB-approved (DR-09-623) retrospective evaluation of women with mCRC-O from 2001 -2008; 110 pts with ovarian metastases and follow-up information for survival analysis were identified out of 3,776 female pts with CRC (2.9%). Survival data was calculated from the date of diagnosis of ovarian metastases (by pathology or radiology) to date of death. Results: Median age of pts was 49 years (range 19-82); median duration of follow-up was 49 months. Twenty pts were identified from 1,758 female patients with CRC seen at our institution from 2001-2004 (1.1%) and ninety pts identified from 2,018 female CRC patients from 2005-2008 (4.5%). Sixteen evaluable pts who received systemic chemotherapy with mCRC-O and other sites of metastatic disease were identified; five (31%) had a mixed radiographic response (progression in the ovarian metastases with disease response in other sites of metastases). Seventy-one (64.5%) patients had metastatic disease at the time of initial presentation; 39 (35.5%) had completely resected stage II or III CRC with mCRC-O occurring at a later date. 86 (78.2%) underwent unilateral or bilateral oophorectomy for treatment of their disease. Pts who had metastatic disease at presentation and underwent oophorectomy had a median survival of 39.4 months versus 18.2 months for those with ovarian metastases left in situ ($p < 0.0001$); pts who developed ovarian relapse after prior colectomy and subsequently underwent oophorectomy had a median survival of 50 months versus 12 months for those pts who did not ($p = 0.001$). Pts with mCRC-O and peritoneal metastases had a significantly worse survival ($p = 0.003$). Conclusion: This single institution retrospective data analysis suggests that women with colorectal cancer metastatic to the ovaries may derive a survival benefit from palliative oophorectomy.

P157

The number of high risk factors in stage II colonic cancer patients is related to outcome K. Bosscha,* D. Lips, J. Pruijt, J. Van der Linden, M. Ernst, K. Bosscha. *surgery, Jeroen Bosch Hospital, 's Hertogenbosch, Netherlands.*

Introduction. A subgroup of stage II colonic cancer patients are considered to be at high risk for recurrent disease and/or metastases based on 1) tumor obstruction or perforation at presentation 2) less than 10 lymph nodes found in the surgical specimen by the pathologist 3) T4 lesions and 4) lymph angioinvasion at pathological examination. These patients are regarded as comparable to stage III colonic cancer and should therefore receive adjuvant chemotherapy. We determined i) the prognostic significance of the above-mentioned conventional high risk factors ii) analyzed whether the number of high-risk factors is related to outcome in stage II colonic cancer patients. Methods. We retrospectively analysed 212 stage II colonic cancer patients for high risk factors undergoing surgery alone between January 2002-December 2008. No adjuvant chemotherapy was given. Univariate & multivariate analyses were performed using the Cox regression analysis. Results. 154/212 patients were considered high risk patients. In the entire patient group, 58 patients did not meet any high risk factor, 125 patients met 1 and 29 patients met 2 or more high risk factors. The following 6 significant factors for recurrent/metastatic disease were identified in the univariate analysis: age, length of hospital stay, emergency surgery, obstruction, perforation of the tumour and lymphangio-invasion. Multivariate analysis identified 4 independent risk factors for recurrent/metastatic disease: age, obstruction, perforation of the tumour and lymphangio-invasion. The 3-year DFS-rates for the low risk group, the high risk group with 1 high-risk factor and the high risk group with ≥ 2 high-risk criteria are 90.4%, 87.6% and 75.9% respectively. Patients meeting >2 high risk criteria had a significantly worse 3-year disease free disease survival ($p < 0.001$). Conclusions. Four independent high risk factors were identified. The number of high risk factors in the individual patient does significantly influence outcome. Therefore, patients meeting > 2 high risk factors should, if possible, receive chemotherapy without any hesitation.

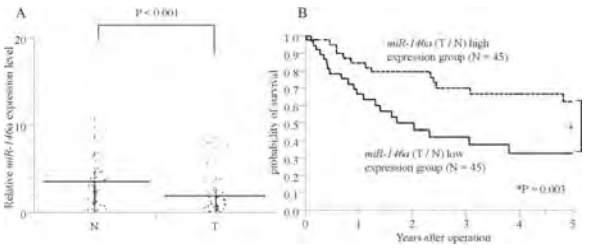


P158

Significance of miR-146a expression and SNP in the seed sequence in gastric cancer cases R. Kogo,[1]* K. Mimori,[1] F. Tanaka,[1] K. Shibata,[1] S. Komune,[2] M. Mori.[3] *1. Department of Surgery, Medical Institute of Bioregulation, Kyushu University, Beppu, Japan; 2. Department of Otorhinolaryngology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan; 3. Department of Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Osaka, Japan.*

Introduction Gastric cancer is the most popular tumor in Japan and advanced gastric cancer with lymph node metastasis is still poor prognostic disease. microRNAs regulate multiple genes and involve cancer progression. We focused on miR-146a targeting EGFR and analyzed the significance of miR-146a in gastric cancer cases. Methods (1)We investigated miR-146a level by qRT-PCR in 90 gastric cancer cases and evaluated the association between miR-146a and clinicopathologic factors. (2)We established miR-146a transfected gastric cancer cell, MKN45 for further analysis. We generated EGFR 3'UTR luciferase construct and corroborated miR-146a-EGFR 3'UTR binding. (3)We investigated the single nucleotide polymorphism of pre-miR-146a seed sequence using direct sequence and analyzed the association between the genotype and mature miR-146a level. Results miR-146a expression in the cancer tissues were significantly lower than in the corresponding noncancerous tissues ($P<0.001$). As for clinicopathologic significance of miR-146a levels, miR-146a low expression group (n=45) showed more progressive tumor depth, lymph node metastasis and venous invasion than high expression group (n=45) ($P<0.05$). Additionally, miR-146a low expression group (n=45) had a significantly poorer prognosis than high expression group (n=45; $P=0.003$). Multivariate analysis

showed that miR-146a is an independent prognostic factor (RR:1.53, CI:1.06-2.26, P=0.022). miR-146a transfected MKN45 cells significantly reduced capabilities of migration and invasion (P<0.05), and EGFR expression (P<0.05). Luciferase assay showed EGFR is a direct target of miR-146a. Moreover, genotypes of pre-miR-146a seed sequence showed CC: 34 cases (44.7%), GC: 34 cases (44.7%) and GG: 8 cases (10.5%). Intriguingly, the patients with GG genotypes indicated lower miR-146a level than those with CC genotype in both cancer tissue and noncancerous tissue (P=0.009, P=0.023). Conclusions In gastric cancer cases, impaired miR-146a expression acts a novel prognostic marker, and the functional polymorphism in much more number of cases might indicate its expression level, and predict diagnosis by using of genomic DNA from peripheral blood.



P160

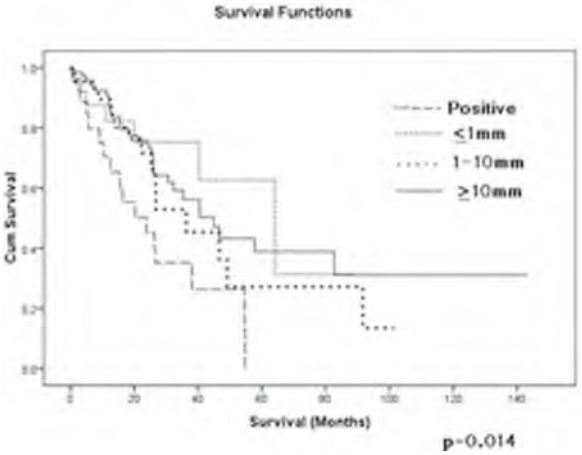
Short- and long-term outcomes of laparoscopic complete mesocolic excision for sigmoid colon and rectosigmoid cancers T. Akasu,* S. Yamamoto, M. Takawa, K. Sato, S. Fujita, H. Motohashi. *Colorectal Surgery Division, National Cancer Center Hospital, Tokyo, Japan.*

Background: The short- and long-term safety of conventional or limited laparoscopic dissection for colon cancer is well established. Complete mesocolic excision (CME) is a new surgical concept entailing high ligation of the vascular pedicles and complete resection of the mesocolon from the retroperitoneum. To retrospectively evaluate the short- and long-term outcomes of laparoscopic CME for sigmoid colon and rectosigmoid cancers as compared to limited laparoscopic lymph node dissection. Methods: All patients undergoing laparoscopic colectomy for sigmoid colon or rectosigmoid cancers between 2003 and 2008 were assessed using a prospectively maintained database. Results: Of the 232 patients identified, 89 with clinical stage II–III tumors underwent laparoscopic CME while 143 with clinical stage 0–I tumors received conventional limited laparoscopic dissection. There was no conversion, blood transfusion, or mortality in either group. Patients undergoing CME had significantly more pathologic stage II–III tumors (81% vs. 22%; P < 0.001), longer operating time (median, 224 vs. 200 min; P = 0.01), and more lymph nodes harvested (median, 24 vs. 17; P < 0.001) as compared to conventional dissection. Intra- and post-operative complication rates and postoperative recovery were comparable between the two groups. For CME, 3-year overall survival rate was 99% with a median follow-up of 3.1 years. There were 10 patients with distant recurrence and one with peritoneal recurrence. But there were no patients with local recurrence and only one with regional recurrence. Conclusion: This study confirmed feasibility and short-term safety of laparoscopic CME for sigmoid colon and rectosigmoid cancers. Furthermore, laparoscopic CME may be associated with improved survival through harvesting more lymph nodes and avoiding any breaching of the visceral fascia.

P161

Impact of Hepatectomy Margin on Survival following Resection for Colorectal Metastasis M. Bower,* R. Brown, C. Scoggins, K. McMasters, R. Martin. *Surgical Oncology, University of Louisville, Louisville, KY.*

Introduction The optimal margin width for hepatic resection for colorectal cancer (CRC) metastasis has been debated. The aim of the current study is to evaluate the influence of width of surgical margin upon disease free survival (DFS) and overall survival (OS). Methods All patients undergoing hepatectomy for colorectal metastasis from 1997 to 2008 were identified from a prospectively maintained, IRB approved, hepatobillary database. Patients who had concurrent or prior ablative procedures were excluded. Patients were divided into four subgroups based on the parenchymal margin: positive, ≤1 mm, 1mm to 10mm, and ≥ 10mm. Survival estimates were calculated using the Kaplan–Meier method and compared using the log-rank test. Multivariate analysis was conducted using Cox regression. Results A total of 173 patients were included with a median follow-up of 16 months (range 1-103 months) and a median OS of 45 months. All margin groups were similar in terms of age, gender, size of largest tumor, and location of the primary tumor. The resection margin was positive in 26 patients. Twenty-eight patients had a resection margin <1mm; 42 patients had margin of 1mm to 10mm, and 77 patients had a margin ≥10mm. Patients with positive margins had the shortest DFS, median 16 months (p=.35). The DFS was similar among the margin negative groups (≤1mm: 21 months, 1mm-10mm: 22 months, ≥10mm: 25 months, p=.13). Margin positive patients had the lowest median OS, 24 months (p=.014). Patients with negative margins of ≤1mm, 1mm to 10mm, and ≥10mm had median survivals of 64 months, 36 months, and 44 months respectively (p=.72). Of the variables tested (age, primary location, metastasis number, and size of largest metastasis) only positive hepatectomy margin was significantly related to OS. On multivariate analysis, lesion number was the only significant predictor of local recurrence (p=<.001). Conclusion Patients who are likely to have close but negative surgical margins should undergo hepatic resection for CRC metastasis as the margin width does not impact survival or recurrence. A positive surgical margin is a marker of worse outcome in patients undergoing hepatectomy for CRC metastasis.



P162

Safety and Advantages of Combined Resection and Microwave Ablation in Patients with Bilobar Hepatic Malignancies S.C. Schiffman,* T. Metzger, S. Ellis, C.R. Scoggins, K.M. McMasters, R.C. Martin. *Department of Surgical Oncology, University of louisville, Louisville, KY.*

Introduction: Microwave ablation (MWA) has recently gained favor in the treatment of primary and metastatic unresectable hepatic lesions due to increased efficiency and improved efficacy. Combination resection and MWA has not been reported in the treatment of bilobar disease. We sought to determine if the perioperative complication rate for combination therapy is similar to that of ablation alone. Method: A review of our 1745 patient prospective hepatobiliary database identified consecutive patients who underwent MWA from 5/2004 to 9/2010. Patients treated with MWA and hepatic resection were compared to patients treated with MWA alone using chi-square, logistic regression and t-test. Results: Ninety seven patients underwent MWA for a primary or metastatic hepatic lesion. The most common were metastatic colorectal cancer (48.5%), carcinoid (14.4%) and hepatocellular carcinoma(12.3%). The median follow up time was 17.6 months. Thirty eight patients (39.2%) underwent MWA and hepatic resection, whereas 59 patients (60.8%) underwent MWA only. Of the patients undergoing resection, ten (10.3%) underwent right hepatectomy, 23 (23.7%) had left hepatectomy and five (5%) underwent caudate resection. There was a higher complication rate in the ablation and resection patients as compared to ablation only patients (57.9% vs. 35.6%; p=0.038). There was no difference in age (p=0.42), diagnosis (p=0.27), size of largest tumor (p=0.25), operative time (p=0.25), LOS (p=0.44), and surgical approach

(p=0,5) in the patients who were ablated compared to those who received bimodality therapy. The ablated patients had fewer liver lesions (1 vs. 3.5 lesions; p=0.004). The ablated patients had lower EBL (p=0.08) and received fewer transfusions (p=0.03) than the ablation and resection group. Conclusion: The use of MWA in combination with hepatic resection is safe and feasible in the management of patients with bilobar disease. There was a higher complication rate in patients undergoing hepatic resection following MWA, but similar LOS. This technique can be considered in the appropriate patients, in which the biology of the disease is well understood.

	Ablation Only	Ablation and Resection	p-value
Age	63.2 years	58.2 years	0.42
Tumor Size	3 cm	3.5 cm	0.25
Number of Tumors	1	3.5	0.004
Operative Time	120 mins	140 mins	0.25
LOS	4 days	5 days	0.44
EBL	100 cc	250 cc	0.08
Blood Transfusion	15.2%	28.9%	0.03
Surgical Approach (Laproscopic/Open)	54.2% Open	60.6% Open	0.5
Complications	35.6%	57.9%	0.03

P163

Does Neo-adjuvant Chemotherapy Improve Outcomes for Patients with Gastric Adenocarcinoma? S. Misra,* N. Solomon, E. Gennis, P. DiPasco, D. Franceschi, A.S. Livingstone, L.G. Koniaris. *University of Miami, Sylvester Comprehensive Cancer Center, Miami, FL.*

Background: The benefit of neoadjuvant chemotherapy (NAC) for patients with gastric adenocarcinoma remains undefined. We examined our experience of patients treated with surgical extirpation for gastric cancer with the addition of neoadjuvant, adjuvant or no additional therapies. Methods: A single institution, retrospective evaluation of a prospective database of resected gastric cancer patients treated in the USA from 2000-2008. Results: Overall, 178 patients with gastric adenocarcinoma who underwent surgical extirpation were identified. Mean age for the group was 67 years with 55% males. By stage, 43.2 % were early (defined as in situ and Stage 1a and 1b) and 56.8% were more advanced stage (stage 2 and above) gastric cancer. Thirty-day survival was 90.4%. Median survival for patients from first therapy treated with NAC (n=49), adjuvant chemotherapy (n=39) or surgery only (n=90) were 22.4, 35.4 and 43.4 months respectively. Complete pathologic response (CPR) was seen in 9% of NAC patients and this group had a median survival of 60 months. Down-staging was noted in 42% of patients who received NAC but no significant improvement in survival was noted with partial responses. By univariate and multivariate analysis, factors associated with improved survival were female gender, Hispanic ethnicity, distal gastric tumors, addition of radiation, surgery only for early stage tumors, node negativity, mucinous adenocarcinoma histology and CPR. Conversely, NAC overall, stage IIb and above, positive node status, poorly differentiated or signet histology portend a worse prognosis ($p< 0.05$). Conclusions: Although a CPR following NAC is associated with a dramatic improvement in survival for advanced gastric carcinoma, this is achieved only in a small patient subgroup. Partial down-staging or failure to induce tumor shrinkage does not appear to provide any added survival benefit and may, in fact, be detrimental. Prognosis for patients undergoing NAC may be optimized by immediate surgical extirpation if neoadjuvant therapies are not resulting in a dramatic clinical response. In the setting of advanced disease, adjuvant chemoradiation appears to provide a clear survival benefit.

P164

Survival comparison of stage III rectal adenocarcinoma down staged by preoperative chemo-radiation with a matched stage II cohort V. Siripurapu,* K. Ruth, J.R. Nitzkorski, E.R. Sigurdson, J.M. Farma. *Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Patients with stage III rectal carcinoma (RC) have a worse overall survival than those presenting with stage II RC. We aim to determine if down staging patients with clinical stage III RC using neoadjuvant CRT results in similar recurrence and overall survival compared to a stage II cohort. Methods: Patients with stage II & III RC were identified from a prospective database from 2000 to 2008. Clinicopathologic data was evaluated including: preoperative staging method, neoadjuvant regimens, tumor location, operative procedures, pathologic variables, morbidity, recurrence and overall survival. Results: 74 patients were identified; 34 had clinical stage II disease (group A), 40 had clinical stage III cancer (group B). Clinical tumor (T) stage and neoadjuvant and adjuvant regimen used were not significantly different between groups. All pts had N0 disease on final pathology. 25 pts (34%) had complete pathologic response (cPR), 13 in group A and 12 in group B (p=0.6). 38 pts (51%) had a partial pathologic response (pPR), with 10 patients in group A and 28 patients in group B. Tumor location was designated 0-4cm, 5-8cm and 9 - 12cm from anal verge; no difference was noted between groups (p=0.94). No survival difference is noted with tumor length stratified from 1-2cm, 3-5cm or >5 cm (p=0.29). Mean follow-up was 48 months versus 43 months (p=0.41). Recurrences were noted in 11 cases; 8 versus 3, with a recurrence free survival for group A of 64% versus 93% for group B(p=0.02). 5 year overall survival is 61% versus 74% respectively (p=0.22). No survival difference is noted from 2000-2004 or from 2004-2008 (p=0.89). Those with a cPR had improved 5 year survival (p=0.04). Conclusion: This study suggests that there is no difference in survival in patients with stage III rectal cancer successfully downstaged compared to a stage II rectal cohort. The patterns of failure depends on the extent of tumor response related to tumor biology, with complete responders having improved survival over partial responders in both groups. Further investigation is warranted to determine factors that may predict downstaging.

Comparison of stage II and Stage III rectal cancer cohorts

	Group A (Clinical stage II) (N, %)	Group B (Clinical stage III) (N, %)	P value
Patients	34	40	
PATHOLOGY			
Complete pathologic response	13 (38.2%)	12 (30%)	
Partial pathologic response	10 (29.4%)	28 (70%)	0.001
No pathologic response	11 (32.3%)	0 (0%)	
SURGERY			
Low anterior resection	16 (47%)	20 (50%)	
Abdominoperineal resection	18 (52.9%)	17 (42.5%)	0.306
TUMOR CHARACTERISTICS			
Tumor location < 10cm (n)	30 (88.2%)	35 (87.5%)	0.944
Median Tumor length (cm)	3	4	0.004
Adjuvant therapy	23 (67.6%)	33 (82.5%)	0.177

P165

Long-term survival after Radiofrequency Ablation for Cirrhotics with Unresectable Hepatocellular Carcinoma M. Raoof,[1]* E.S. Glazer,[1] S. Curley,[1] V. Albino,[2] R. Palaia,[2] M. Piccirilio,[2] R. Giacomo,[2] F. Izzo.[2] *1. The University of Texas M. D. Anderson Cancer Center, Houston, TX; 2. The G. Pascale National Cancer Institute, Fondazione G. Pascale, Naples, Italy.*

BACKGROUND: Hepatocellular carcinoma (HCC) is the fifth most common cancer and the third leading cause of cancer related death worldwide. At the time of diagnosis, only 10-20% patients are amenable to transplantation or curative resection. For patients with disease confined to the liver, radiofrequency ablation (RFA) is rapidly evolving as an important modality of treatment. In this study we report long-term survival, recurrence, morbidity and mortality rates after RFA for unresectable HCC in cirrhotic patients. METHODS: All patients with unresectable HCC that were treated with RFA between January 1, 1995, and December 31, 2008, were prospectively evaluated at two tertiary care referral centers. Patients were treated with RFA by using a percutaneous or an open intraoperative approach with ultrasound guidance and were evaluated at regular intervals thereafter to determine disease recurrence and survival. Patients undergoing any other intervention (including resection) in addition to RFA were excluded. RESULTS: Entry criteria were met by 1168 patients, 662 (56.7%) men and 506 (43.3%) women. All surviving patients were followed for at least 18 months. Median age was 58 years (range 18-85 years). 63% of patients in the cohort had advanced cirrhosis (Child's class B or C). A total of 2116 tumors were ablated (median, 3 lesions per patient). Percutaneous and open approach was used in 733 (62.8%) and 435 (37.2%) patients, respectively, with a tumor size ranging from 1 cm to 8 cm (median,

2.7 cm). Overall morbidity and mortality rates were 5.5% and 1.5%, respectively. After a median follow-up of 5 years, the total cancer recurrence rate was 49% while local recurrence at an RFA site was 11%. 1-, 3- and 5-year overall actuarial survival rates were 88.7%, 67.3% and 44.5% for percutaneous approach and 88.5%, 55.3% and 47% for open approach. CONCLUSION: This is a large cohort of cirrhotic patients undergoing RFA for HCC followed prospectively. RFA offers significant long-term survival rates with reasonable morbidity and mortality rates. RFA is well suited as a first line treatment for HCC patients with cirrhosis not amenable to other surgical treatments.

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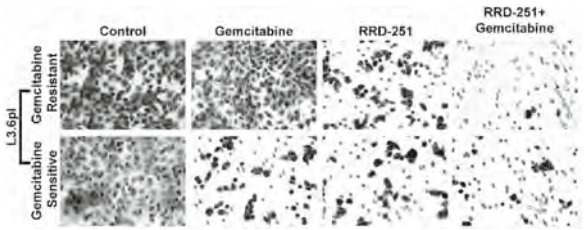
Disruption of the Rb-Raf-1 Kinase is a Potential Therapeutic Target for Pancreatic Adenocarcinoma J.G. Trevino,* S.S. Kunigal, S.P. Chellappan. *Tumor Biology, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL.*

Retinoblastoma tumor suppressor binding protein, Rb, is often implicated in cell cycle progression in human cancers through phosphorylation by Raf-1 kinase, a proto-oncogene involved in cell division cycle, apoptosis, cell differentiation and migration. We have demonstrated that increased binding of Raf-1 to Rb have contributed to tumor progression and inhibition of this interaction might be a suitable strategy to inhibiting kinase function for cancer therapies. Therefore, we hypothesize that disruption of the Rb-Raf-1 interaction with small molecule inhibitor RRD-251 (Rb-Raf-1 Disruptor 251) will be a viable strategy in pancreatic cancer. To test our hypothesis, we initially probed a panel of primary pancreatic cancer cell lines (PANC-1, Mia-PaCa-2, CD18/HPAF, L3.6pl) and demonstrated disruption of Rb-Raf-1 kinase interaction by immunopreciptation western blot analysis in the presence of RRD-251 (50 μM). To fully define the anti-tumor effects of RRD-251, cell cycle analyses, proliferation/cell viability (MTT), cell migration (wound healing assay), and invasion (Boyden chamber assay) experiments were performed. RRD-251 significantly reduced proliferation by 3-fold and significantly reduced the ability of metastatic variant, L3.6pl, and other pancreatic cancer cell lines to migrate with a 5-fold decrease in invasion ($p<0.05$). Prolonged exposure of RRD-251 (48 hours) demonstrated that disruption of the Rb-Raf-1 interaction would induce apoptosis defined by cleavage of PARP protein, decreased anti-apoptotic proteins Mcl-1 and Bcl-2, and an increase in pro-apoptotic protein Bax demonstrated by western blot analysis. Additionally, combination of RRD-251 with gemcitabine (125ng/ml) induced a synergistic effect on induction of apoptosis, proliferation/cell viability (7.5 fold decrease from control), migration, and almost complete loss of the invasive capacity of pancreatic cancer cells ($p<0.05$). In this study, we demonstrate a disruption of the Rb-Raf-1 kinase interaction with RRD-251 significantly affects the malignant properties of pancreatic cancer cells with synergism with gemcitabine. Further studies with RRD-251 in an invivo mouse model are currently underway.



P167

Lymph node ratio as predictor of survival in gastric carcinoma H. Medina-Franco,* Y. Suarez-Bobadilla, F. Cabrera-Mendoza, S. Almaguer-Rosales, F. Guillen-Perez. *Surgery, National Institute of Medical Sciences and Nutrition, Mexico City, Mexico.*

Background: According to 2002 AJCC classification, the number of metastatic lymph nodes is the main prognostic factor in gastric cancer. The ratio of metastatic lymph nodes (Lymph Node Ratio - LNR) has been proposed as better prognostic factor. Methods: We retrospectively analyzed patients who underwent resection for gastric cancer in a tertiary referral center in Mexico City between 1985 and 2010. Demographic, clinical, pathological and surgical data were obtained. The number of metastatic nodes was reported according to the AJCC 2002 (N0; N1:1-6; N2: 7-15 and N3 >15 metastatic nodes) and the LNR was determined as follows: LNR0:0%, LNR1:1-10%, LNR2:11-25% and LNR3> 25%. Survival was calculated with the Kaplan-Meier method, and the Long-rank test was used to determine associated factors with overall survival. $p<0.05$ was considered significant. Results: Two-hundred patients were included. There was an even gender distribution. Median patient age was 61.5 years (range 27-91). Median number of retrieved nodes were 18 (0-129) and the median number of metastatic nodes were 2.5 (0-58). In patients 62% of patients a dissection of > 15 nodes was performed. With a median follow-up time of 13 months (0-252), median survival of the entire cohort was 44 months. According to AJCC, median survival for N0 have not been reached and for N1, N2 and N3 patients were 68, 14 and 12 months, respectively ($p=0.001$) but there was no significant difference between N2 and N3 ($p=0.3$). According to LNR, median survival for LNR 0,1,2,3 were 117, 68, 44 and 14 months, respectively ($p<0.001$). In subgroup analysis of patients with less than 15 nodes removed, AJCC classification was not predictor of survival ($p=0.09$), but LNR was ($p=0.04$). Conclusions: LNR is better predictor of survival than the actual number of metastatic lymph nodes, particularly in the group of patients with suboptimal node dissection according to AJCC recommendation.

P168

Surgical Outcome after Curative Resection for Ampulla of Carcinoma of Vater T. Sugiura,[1]* A. Yasuda,[1] H. Kanemoto,[1] T. Mizuno,[1] K. Sasaki,[2] K. Uesaka.[1] *1. Division of Hepato-Biliary-Pancreatic Surgery, Shizuoka Cancer Center, Shizuoka, Japan; 2. Division of Pathology, Shizuoka Cancer Center, Shizuoka, Japan.*

Introduction: Because of the relative low incidence in Japan, there were a few reports regarding carcinoma of ampulla of Vater (CAV). The aim of this study was to clarify the clinicopathologic factors associated with survival and pattern of recurrence after resection for CAV. Methods: Between 2002 and 2009, a total of 34 patients underwent surgical resection (33: pancreaticoduodenectomy, 1: ampullectomy) for CAV. The patients comprised of 24 men and 10 women with median age of 67 years. Clinicopathologic findings were reviewed and multivariate analyses were conducted to determine the predictor of survival. Results: Pathologic examination revealed lymph node (LN) metastasis in 18 (53%), pancreatic invasion in 5 (15%), biliary invasion in 21 (62%), duodenal invasion in 20 (59%), ulcer formation in 20 (59%), lymphatic infiltration in 22 (65%), venous infiltration in 10 (29%). The 3- and 5-year overall survival rates after resection were 62.2% and 49.0%. Multivariate analysis revealed lymph node metastasis (OR: 10.3, $p=0.015$) and pancreatic invasion (OR: 5.3, $p=0.030$) as the independent risk factors significantly associated with survival. The 3- and 5-year overall survival rates after resection were 88.9% and 88.9% in node negative patient, and 39.3% and 13.1% in node positive patients. The overall 3- and 5-year survival rates were 76.9% and 60.6% in patients without pancreatic invasion and 20.0% and 0% in patients with pancreatic invasion. Sixteen patients (47.1%) developed tumor recurrence. Locoregional recurrence alone was recognized in only three patients, and the remaining 13 patients had distant metastases. The most common site of recurrence was the liver: 9 of 16 patients (56.2%). By multivariate analysis, LN metastasis (OR: 22.7, $p<0.001$) and pancreatic invasion (OR: 4.8, $p=0.021$) were the independent risk factors significantly correlated with the recurrence. Conclusion: LN metastasis and pancreatic invasion were powerful risk factors for the survival and recurrence after resection of CAV. Establishment of new therapeutic strategy, such as development of effective adjuvant chemotherapy, is an awaiting solution.

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Pelvic Malignancies Undergoing Exenteration R.J. Chokshi,* D. Arrese, M.P. Kuhrt, M.M. Routt, E. Kocak, E.W. Martin. *Surgical Oncology, The Ohio State University - The James Cancer Hospital and Solove Reseach Institute, Columbus, OH.*

Background: Pelvic exenteration is reserved for patients with locally invasive and recurrent pelvic malignancies. The literature demonstrates a high morbidity and mortality associated with this operation. At our institution, a high volume of pelvic exenterations are undertaken and their outcomes have been studied. Methods: The medical records of fifty-three patients with varying pelvic pathologies who underwent pelvic exenteration between 2004 and 2010 were reviewed. Demographics, histologies, periprocedural events, and outcomes were analyzed. Results: Patients were divided into a colorectal (n=37) and non-colorectal (n=16) group for analysis based on histology. The two groups

were similar in demographics, perioperative events, and length of stay. Resection status, chemotherapy use, and intraoperative radiation therapy showed no statistical difference. Complications showed a difference in perineal abscesses in the colorectal group. The colorectal group showed a survival difference when comparing R0 resection versus R1/R2, however no difference was seen in primary versus recurrent tumors. The median survival was 20.3 months in the colorectal group and 4.8 months in the non-colorectal group. Conclusions: Patients undergoing exenteration for colorectal histology have improved survival when compared to pelvic malignancies of other origins. The greatest effect on long term survival is seen in the colorectal group undergoing a R0 resection. Despite pelvic exenterations carrying a high morbidity and mortality, careful patient selection can optimize outcomes.

Variables	Colorectal N=37	Non-Colorectal N=16	P Value
Mean Age (Range)	57.8 (40-80)	55.9 (38-79)	0.57
Gender M:F	16:21	5:11	0.54
Comorbidities	30	13	1.00
Mean (±SD) Length of Stay (Days)	15.6 ± 9.8	20 ± 11.6	0.16
Operative Time (Minutes) *	603 ± 214	508 ± 151	0.37
Estimated Blood Loss (Liters)	1.9 ± 1.1	2.0 ± 2.2	0.15
Primary:Recurrent	10:27	4:12	1.00
Complications	31 (84%)	13 (81%)	1.00
Wound Infections	17	6	0.76
Wound Dehiscence	8	3	1.00
Pelvic Abscess	20	5	0.14
Perineal Abscess	10	0	0.02
Enteric Fistula	11	3	0.51
Sepsis	16	5	0.54
Bleeding	10	1	0.14
Respiratory Failure	10	2	0.30
DVT	7	1	0.40
30 Day Morbidity	29	11	0.49
30 Day Mortality	0	0	1.0
Median Survival (months)	20.3	4.8	0.007

* Analysis performed on available data

P170

New biomarker candidates of HOPX and its therapeutic potential in human gastrointestinal cancer K. Yamashita,* H. Katoh, A. Ooki, M. Waraya, M. Watanabe. *Surgery, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan.*

(Background) DNA promoter hypermethylation is a landmark of cancer cells having potentiality as a biomarker in human cancer. We previously developed a screening method to identify novel methylation genes specific to cancer (Yamashita K, Cancer Cell, 2002). Among the numerous candidates, we are focusing HOPX (homeobox only protein) in human gastrointestinal cancers. (Materials and Methods) Tumor as well as the corresponding normal tissues were examined for methylation level by Q-MSP. Clinicopathological significances were revealed in 170 gastric cancer and 269 colorectal cancer (CRC). We also transfected HOPX gene into cancer cells not constitutively expressing HOPX and examined phenotypic changes and the mechanistic insight. (Results) (1) Cancer specific methylation of HOPX was demonstrated in both gastric (AUC: 0.85, optimal cut-off value 3.60) and CRC tissues (AUC: 0.85, optimal cut-off value 2.89). Methylation status was consistent with HOPX protein expression by immunohistochemistry in human tissues. (2) HOPX hypermethylation (cut-off value 11.28) can predict poor prognosis in 65 advanced gastric cancer (AGC), and this result could be validated in an independent 90 AGC. Multivariate analysis revealed that HOPX hypermethylation was an independent prognostic factor in AGC. (3) HOPX hypermethylation (cut-off value 2.89) can predict poor prognosis in 170 stage III CRC. Multivariate analysis revealed that HOPX hypermethylation was an independent prognostic factor in stage III CRC. (4) HOPX transfection suppressed cell proliferation, Matrigel invasion, tumorigenesis, resistance to apoptosis, and angiogenesis in cancer cells. (4) HOPX transfection induced well established tumor suppressor genes such as PTEN, TRAIL, and Syk in CRC cell lines (DLD1 and HCT116). (Conclusion) HOPX hypermethylation is a tumor suppressor gene which is silenced by promoter DNA hypermethylation in human gastrointestinal cancers. HOPX can cause suppression of metastatic phenotype of human cancer cell lines, and this is at least partially explained by induction of well-known tumor suppressor genes.

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Transitioning Pancreatic Surgery from a SSO Fellowship to a Community Teaching Hospital and Cancer Center M.G. Mount,* R.B. Hird, R.K. Orr, C.L. Nguyen. *Spartanburg Regional Healthcare System, Spartanburg, SC.*

Introduction: Regionalization of pancreatectomy to high volume centers has resulted in improved morbidity and mortality. Carefully selected smaller hospitals have also shown excellent results. Although SSO-approved fellowships provide appropriate training in pancreatectomy, there are no data regarding the transference of this skill set. The purpose of this study is to evaluate the feasibility and safety of transitioning contemporary pancreatic surgery from a SSO fellowship program to a community teaching hospital. Methods: A prospective database was maintained from July 2006 through July 2010 for all pancreatectomies performed by a single surgeon following completion of a SSO approved fellowship. Data on diagnosis, procedure, length of stay, morbidity and mortality were collected and analyzed. Results: During the study period 44 cases were performed; 27 pancreaticoduodenectomies (PD), 16 distal or subtotal pancreatectomies (D/SP) and 1 total pancreatectomy. Of these, 34 were performed for suspected cancer with the remainder performed for complications of pancreatitis. The rate of pancreatic fistula as defined by ISGPF criteria was 40%, and occurred in 10/27 (37%) patients after PD and 6/15 (40%) patients after D/SP. For those undergoing PD, delayed gastric emptying occurred in 8/27 (29%). Portal vein resection with PD occurred in 1/27 (3.7%). Of the 34 cases performed for suspected cancer, 20/34 (58.8%) demonstrated adenocarcinoma on final pathology. Positive nodal metastases were noted in 10/20 (50%) of patients. A R0 resection was performed in 29/34 (85%) patients and 5/34 (15%) received a R1 resection. There were no R2 resections and no operative deaths. The 30-day mortality rate was 2/44 (4.5%) and was unrelated to pancreatic fistula. Conclusions: A SSO fellowship-trained surgeon was able to transport his skill set into a community hospital setting lacking pancreas protocols or significant high-level experience. By adherence to the standards taught in fellowship, acceptable outcomes are reported. Completion of a SSO approved fellowship appears to allow achievement of acceptable outcomes for pancreatectomy when transitioned to a community setting.

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Minor liver resection for liver metastases and Pringle Maneuver: is it still necessary? P.L. Pilati, E. Mammano,* C. Smaniotto, E. Tessari, D. Nitti. *clinica chirurgica 2, Padova, Italy.*

Introduction The portal triad clamping (Pringle maneuver) is worldwide used to decrease blood loss and the need of blood transfusion during hepatic surgery: intraoperatively blood loss has been shown to impact negatively on perioperative morbidity and mortality. The major concern of the Pringle maneuver is hepatic ischemia-reperfusion injury subsequent to the clamping: this process itself may cause liver and systemic injury mediated by cytokine and reactive oxygen radicals. Methods 47 consecutive minor hepatectomy (< = 3 segments) for colorectal liver metastases from March 2004 to June 2010 were performed: the first 23 were conduced with Pringle Maneuver (group A), the latest 24 without any inflow and outflow clamping (group B). All the patients underwent preoperative chemotherapy and had no liver cirrhosis. Intraoperative blood loss, number of blood transfusions, operating time, peri-operative mortality and morbidity, post-operative ICU and hospital stay were analyzed. Result In group A were performed no trisegmentectomy, 4 bisegmentectomy, 8 segmentectomy, 11 atypical resection. In group B were performed 2 trisegmentectomy, 1 bisegmentectomy, 1 segmentectomy, 15 atypical resection. Mean intraoperative blood loss was 661 ml in group A and 932 ml in group B. Mean number of blood transfusions was 4.3 in group A and 2.8 in group B. Mean operating time was 230 min in group A and 257 min in group B. There was no peri-operative mortality in the 2 groups. The morbidity rate was 47.8% in group A and 70.8% in group B. The post-operative ICU was 1.3 days in group A and 0.5 in group B; the hospital stay was 9 days in group A and 14 days in group B. None of this parameters is statistically different between the 2 groups. Discussion In liver metastases from colorectal cancer Pringle maneuver didn't add any advantage in the intra-operative and post-operative parameters that we analyzed. Moreover the increasing use of more effective liver dissectors and the

use of intra-operative ultrasound to perform an anatomical resection allow to lower the intraoperative blood loss and the operating time.

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Quality of Life in Rectal Cancer Patients Subjected to Low Anterior Resection (LAR)is Worse Compared to Subjects Operated on by Means of Abdominosacral Ampitation of the Rectum (ASAR)

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Introduction The importance of postoperative quality of life assessment has increased recently along with improvement in survivals of patients treated surgically for rectal cancer. The aim of this study was to verify this hypothesis by comparing postoperative quality of life in rectal cancer patients subjected to sphincter-saving LAR and low-rectal cancer cases operated on by means of ASAR with subsequent permanent colostomy formation. Patients and Methods This study included 141 rectal cancer patients treated surgically at the Regional Comprehensive Cancer Center in Wroclaw (Poland) between 2008 and 2009, among them 89 cases subjected to LAR and 52 operated on by ASAR. Quality of life was assessed preoperatively three and 12 months following surgery with an aid of EORTC QLQ-C30 and QLQ-CR38 questionnaires. Results In both groups studied, surgical treatment was reflected in improvement in the overall quality of life with significant changes observed one year following surgery. Three months after surgery, patients subjected to LAR did not differ from those operated on by ASAR in terms of overall quality of life, but 12 months following surgery their quality of life was significantly lower compared to the ASAR group. The most frequent problem that significantly diminished quality of life in patients subjected to LAR was fecal soiling and urgency, and difficulties in distinguishing between fecal urgency and intestinal gases. In the group subjected to ASAR, the only factor that affected the quality of life was the necessity of stoma acceptance during the period of a few months after its formation. Conclusions From a long-term perspective, quality of life in patients subjected to LAR is significantly lower compared to subjects operated on by means of ASAR. Colostomy does not decrease a patient's quality of life since it is easier to manage and is not associated with "low anterior resection syndrome", a frequent side effect of sphincter-saving procedures.

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Tumor-Infiltrating Lymphocytes Derived from Pancreatic Adenocarcinoma Exhibit an Activated, Pro-Inflammatory Phenotype

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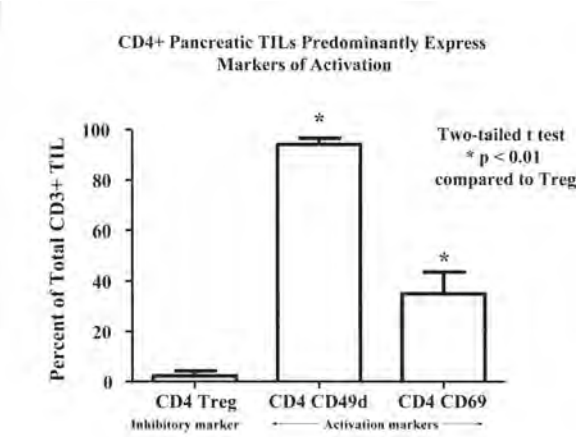
INTRODUCTION: Current dogma maintains that pancreatic adenocarcinoma (PA) is infiltrated by predominantly inhibitory, regulatory CD4+ T cells (Treg). Our objective is to demonstrate the feasibility of growing activated tumor-infiltrating lymphocytes (TILs) from PA that could be used for adoptive cell therapy. METHODS: Patients with primary or metastatic PA undergoing resection were prospectively consented for tissue procurement. Fragments were grown in high-dose interleukin-2, and resulting TILs were expanded with α-CD3. TILs were assessed for both activated and inhibitory T cell phenotype as a percent of total CD3+ cells by flow cytometry. TILs were then stimulated with phorbol myristate acetate/ionomycin. The proinflammatory function of CD4+ TILs was assessed by interferon-γ (IFNγ) production and expression of the cytolytic marker CD107a. RESULTS: TILs were expanded in 4 of 5 tumors. Pancreatic TILs were predominantly CD4+ (mean frequency 95%, range 92-97%). TILs were assessed for the inhibitory Treg phenotype by CD4, CD25 and FoxP3 expression as a percent of total CD3+ TILs. Tregs were found to comprise the minority of TILs (mean=2.3%, range=0.54-4.5%). We assessed TIL expression of known markers of T cell activation, CD69 and CD49d. Strikingly, a relatively high percent of CD4+ TILs expressed CD69 (mean=35%, range=26-46%) and CD49d (mean=94%, range=91-97%). The mean percent of CD69 and CD49d expression was significantly higher than the mean percent of Treg (Figure, $p<0.01$). To confirm pro-inflammatory function, TILs were stimulated in vitro, and expression of the pro-inflammatory cytokine IFNγ and the cytolytic marker CD107a was assessed by flow cytometry. CD4+ TILs demonstrated a relatively high level of expression of IFNγ (mean=34%, range=22-44%) and CD107a (mean=23%, range=10-26%), confirming a pro-inflammatory function. CONCLUSIONS: This is the first report demonstrating that CD4+ TILs derived from PA have a predominantly activated, pro-inflammatory phenotype. Further work involving TIL reactivity to autologous tumor targets is required to support a phase I clinical trial involving adoptive TIL therapy for PA.



Four TIL lines derived from PA were analyzed for activated and inhibitory phenotype by flow cytometry. Means were calculated as a percent of total CD3+ TILs. Error bars indicate standard deviations. Statistical comparisons of two different activated phenotypic panels to the inhibitory Treg phenotype (CD4+ CD25+ FoxP3+) were made using the paired, two-tailed t test.

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Efficacy of Repeat Cytoreductive Surgery (CRS) with Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in the Treatment of Peritoneal Surface Malignancy

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Background: Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) has dramatically improved the survival of patients with peritoneal surface malignancy. Upon progression or recurrence a repeat CRS-HIPEC is a treatment option. Methods: A retrospective analysis of a prospectively collected database of 868 CRS-HIPEC procedures was performed. Type of malignancy, ECOG graded functional status, R status of resection, hospital and ICU stay, morbidity, mortality and median survival were reviewed. Results: Sixty two patients (7.7%) underwent a second CRS-HIPEC including thirty three patients with appendiceal primaries, eight ovarian, seven mesotheliomas, four colon cancers and ten patients with various malignancies. Four patients had a third procedure that was excluded from the analysis. Median follow up was 60.8 months. ECOG status was graded as 0/1 for 74% of the patients at the time of the second CRS-HIPEC. Median ICU and hospital stay was one and 7.5 days respectively. The median time elapsed between the two procedures was 85.3 months for appendiceal cancer, 52.9 for mesothelioma, 60.1 for ovarian and 137.4 months for colon cancer. R1 resection was achieved in 43.5% (27/62) of the patients both after the first and second CRS-HIPEC procedure. Median survival after the second CRS-HIPEC based on type of malignancy was 52.1 months for appendiceal cancer, 21.8 for mesothelioma, 53.9 for ovarian and 55.7 for colon cancer. The median survival based on R status of resection was 55.7 months for R1 resection and 20.3 months for R2a resection. The thirty day combined major and minor morbidity after the second CRS-HIPEC was 48.38% and mortality was 3.2%. On multivariate analysis the R status of the second CRS-HIPEC ($p=0.013$) and the interval between the two procedures ($p=0.009$) were significant in predicting improved survival. Conclusion: In tertiary centers with experience in the treatment of peritoneal surface malignancy and for selected patients, a repeat CRS-HIPEC procedure is associated with prolonged median survival and acceptable morbidity and mortality.

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The Use of Molecular Analysis in the Management Intraductal Papillary Mucinous Neoplasms of the Pancreas R.S. Bhati,[1]* R.M. Nair,[1] J.M. Weber,[1] C.V. Oliveri,[2] D. Coppola,[2] B.A. Centeno,[2] M.P. Malafa.[1] *1. Moffitt Cancer Center-Department of Gastrointestinal Oncology, Tampa, FL; 2. Moffitt Cancer Center-Department of Pathology, Tampa, FL.*

Background: Molecular profiling of pancreatic cyst fluid obtained from intraductal papillary mucinous neoplasms (IPMN) of the pancreas has been proposed as a way to predict histologic grade and thereby guide clinical management. However, data regarding the outcomes of these tests have been rarely reported. In this study, we report our experience with a commercially available DNA molecular test in the management of IPMNs of the pancreas. Methods: All consecutive patients at a single-institution during a two year period who had analysis of pancreatic cyst fluid obtained by endoscopic ultrasound-guided fine needle aspiration were included. Patients who met clinical criteria for resection underwent surgery based on international guidelines. The pathology, gastroenterology, and surgical records of these patients were queried and concordance between the predicted neoplastic grade of the IPMN and final pathology was determined. All cases that were discordant were resubmitted for analysis and reviewed. Results: A total of 72 patients with cystic lesions of the pancreas had their cyst fluid analyzed by the molecular assay. Twenty-seven patients underwent resection or open biopsy and thus had histologic correlation performed. Lesions with invasive cancer or carcinoma in situ were correctly predicted by the molecular test in 8 of 13 cases (62% sensitivity) while, lesions with low grade or moderate dysplasia were correctly predicted in 13 of 14 cases (93% specificity). The assay had a positive predictive value of 89% and a negative predictive value of 72%. The tissues from 5/6 cases that were resubmitted for analysis remained discordant after reanalysis. Conclusions: Our initial experience of a commercially available DNA molecular test to predict the grade of IPMNs of the pancreas may underestimate high grade lesions. Therefore, routine use of these tests should be approached with caution. These results suggest that knowledge of the molecular mechanisms involved in neoplastic progression of IPMNs of the pancreas remains incomplete.

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Is a Quantitative Measure of Visceral Adiposity Superior to BMI in Predicting Rectal Cancer Outcomes? C. Parsons,* C.W. Clark, J. Weber, S. Thareja, J.M. Hernandez, E.M. Siegel, J. Choi, D. Shibata. *Moffitt Cancer Center, Tampa, FL.*

Background: Obesity is a major health problem in the U.S. and there is a growing interest in studying its impact on cancer risk and outcomes. While Body Mass Index (BMI) is the traditional measure of obesity, studies have been inconsistent with respect to its effect on cancer outcomes. We hypothesize that a quantitative measurement of visceral adiposity is a more useful predictor of outcomes in rectal cancer patients. Methods: From 1999-2009, we identified 101 rectal cancer patients with digitized pre-treatment CT scans treated by neoadjuvant chemoradiation (NCR)/radical surgery. Visceral and subcutaneous fat were quantitated by CT at L4-L5 and reported as a ratio (V/S). Clinicopathologic variables were analyzed according to BMI (non-obese < 30, obese ≥ 30) and V/S (non-obese < 0.4, obese ≥ 0.4) using Fisher's exact test and t-tests as appropriate. Survival was analyzed using the Kaplan-Meier method and the log-rank test. Results: Our population consisted of 58 men and 43 women with a median follow up of 27 months (range 0-92). By BMI, 38.6% were obese vs 61.4% by V/S. High V/S (but not BMI) was associated with hypertension (p=0.02), dyslipidemia (p=0.04) and diabetes (p=0.09). High V/S patients were less likely to be downstaged by NCR (55% vs 80%; p=0.02) and had an increased length of stay (LOS; 8.3 vs 6.8 days; p=0.04). There were no differences in stage, grade, margin status, sphincter preservation, or complications between obese and non-obese patients in either analysis. Patients with visceral obesity showed a trend towards decreased 5-yr disease-free (DFS; 45.8% vs 89.6%, p=0.07) and overall survival (OS; 47.8% vs 96.9%, p=0.09) as compared to non-obese patients. Patients with high BMI showed only a trend towards worse DFS (40.4% vs 72.3%, p=0.06). Conclusions: In rectal cancer patients, a high V/S correlates more strongly with co-morbidities, decreased response to NCR, and increased LOS than does high BMI. Moreover, patients with an elevated V/S showed a trend towards worse OS and DFS. Quantitative measures of visceral adiposity should be included in studies looking at the effects of obesity on cancer outcomes.

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Pattern of In Vitro Chemotherapy Response In Pancreatic Cancer And Its Clinical Implication J. Franko,[1]* M.M. Bilimoria,[2] S. Chalikonda,[3] D.A. Iannitti,[4] C. Tian.[5] *1. Mercy Medical Center, Des Moines, IA; 2. Northwestern Community Hospital, Arlington Heights, IL; 3. Cleveland Clinic, Cleveland, OH; 4. Carolinas Medical Center, Charlotte, NC; 5. Precision Therapeutics, Inc, Pittsburgh, PA.*

BACKGROUND: Gemcitabine and 5-fluorouracil (5-FU) with or without oxaliplatin are used to manage advanced or recurrent pancreatic cancer. Options are limited for patients who do not respond to these agents. This study determined the pattern of response to alternative agents using an in vitro chemotherapy assessment. METHODS: From August 2006 to January 2010, 113 tumor specimens from pancreatic cancer patients were tested for response to gemcitabine, 5-FU, oxaliplatin, docetaxel, or irinotecan using an in vitro chemosensitivity assay (ChemoFx, Precision Therapeutics, Inc., Pittsburgh PA). Tumors were classified as sensitive or resistant based on in vitro dose response curves. RESULTS: Thirty-five percent of tumors exhibited in vitro chemosensitivity to irinotecan, 23% to gemcitabine, 19% to 5-FU, 9% to oxaliplatin, and 8% to docetaxel. For tumors resistant to gemcitabine, 23% were sensitive to irinotecan, 6% (4/72) to 5-FU, 3% (2/68) to oxaliplatin, and 2% (1/64) to docetaxel (Table). Of the 68 tumors resistant to both gemcitabine and 5-FU, 11/59 (19%) were sensitive to irinotecan, 2/61 (3%) to oxaliplatin, and 0/57 (0%) to docetaxel. Forty-nine tumors were resistant to all tested agents. CONCLUSIONS: ChemoFx analysis of pancreatic cancer patient specimens indicates a high resistance rate to gemcitabine and 5-FU. The sensitivity of 19% of the gemcitabine/5-FU resistant specimens to irinotecan suggests that some patients who do not respond to standard therapy may respond to irinotecan. The potential of ChemoFx to identify the potentially most effective therapy in pancreatic cancer patients will be examined in future studies.

In vitro chemosensitivity profile of pancreatic cancer

	Individual Chemosensitivity All tumors (n=113)		Chemosensitivity of gemcitabine resistant tumors (n=79)	
Drug	No. tumors tested	No. sensitive (%)	No. tumors tested	No. sensitive (%)
Irinotecan	85	30 (35%)	64	15 (23%)
Gemcitabine	103	24 (23%)	–	–
5-FU	102	19 (19%)	72	4 (6%)
Oxaliplatin	93	8 (9%)	68	2 (3%)
Docetaxel	92	7 (8%)	64	1 (2%)

NOTE: Not all tumors were tested for all drugs

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Survival Benefit of Adjuvant Radiation therapy for Gastric Cancer Following Gastrectomy and Extended Lymphadenectomy R.A. Snyder,[1]* E.T. Castaldo,[1] C.E. Bailey,[1] S.E. Phillips,[2] A.B. Chakravarthy,[3] N.B. Merchant.[1] *1. Vanderbilt University, Department of Surgery, Nashville, TN; 2. Vanderbilt University, Department of Biostatistics, Nashville, TN; 3. Vanderbilt University, Department of Radiation Oncology, Nashville, TN.*

Introduction: Although adjuvant chemoradiation therapy (XRT) is widely used in the United States following surgery for gastric adenocarcinoma, its use remains controversial. The benefit of adjuvant XRT is less clear in patients who undergo an extended lymphadenectomy. The purpose of this study was to determine if a survival benefit exists in patients who undergo postoperative radiation following an extended lymphadenectomy. Methods: Using the Surveillance, Epidemiology, and End Results (SEER) registry, all records of patients with resected gastric adenocarcinoma from 1988-2007 were queried. Patients with metastatic disease, multiple primary malignancies, or pre-operative XRT were excluded. Clinical and pathologic data included patient demographics, tumor characteristics, number of lymph nodes (LN) resected, and the use of adjuvant

XRT. Multivariable Cox regression models were used to assess independent prognostic factors affecting overall (OS) and disease free survival (DFS) with age, race, sex, grade, stage, adjuvant XRT, and number of LN resected as covariates. Results: A total of 16,997 patients were identified of which 3,457 (20%) received adjuvant XRT. Patients of younger age (≤ 60), male sex, and higher stage tumors were more likely to receive adjuvant XRT. Adjuvant XRT was independently associated with improved overall survival (HR 0.67, CI 0.64-0.71) and disease free survival (HR 0.69, CI 0.65-0.73) in patients with resected gastric cancer. This OS and DFS benefit persisted regardless of the extent of lymphadenectomy (< 15 LN, 15-25 LN, or > 25 LN resected). In this model, a more extensive lymphadenectomy (> 25 LN) was associated with improved overall and disease free survival when compared to a less extensive lymph node resection (< 15 LN (OS HR 0.65, CI 0.60-0.69; DFS HR 0.62, CI 0.57-0.67) or 15-25 LN (OS HR 0.84, CI 0.78-0.91; DFS HR 0.81, CI 0.75-0.88)). Conclusion: This observational study of a large database shows the overall and disease free survival benefit of adjuvant radiation after gastrectomy for non metastatic gastric cancer. This benefit persists even in patients who have undergone extensive lymphadenectomy.

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Selection of the appropriate neoadjuvant treatment and extralevatoric resection during abdominoperineal resection for rectal cancer result in a high number of complete resections I. Martijnse,[1]* R. Dudink,[1] G. Nieuwenhuijzen,[1] P. Quirke,[2] H. Rutten.[1] *1. Surgery, Catharina Hospital, Eindhoven, Netherlands; 2. University of Leeds, Leeds, United Kingdom.*

Introduction: Patients undergoing abdomino-perineal (APR) resection for low rectal cancer are reported to have a high rate of irradical resections, which results in a poor oncological outcome. This study reports the results of selective neoadjuvant radio-chemotherapy (RCT) and extralevatoric resection. Methods: A total of 262 patients underwent APR resection between 2000 and 2010. 42 patients with a wide (>2mm) margin between the tumour and the mesorectal fascia on MRI were treated with 5x5 short course preoperative radiotherapy. All patients with threatened (<2mm) or involved margins received a long course of neoadjuvant RCT. All patients were operated in supine position with their legs in movable stirrups. Since 2005, the perineal approach first was implemented as a didactical principle to avoid coning in during the abdominal phase. Results: Overall the irradical resection rate was 9%. After short course 5x5 Gray preoperative radiotherapy and immediate surgery 5%, after long course radiotherapy with or without bolus 5FU and delayed surgery 16% and after long course RCT with daily capecitabine 6%. Negative circumferential resection margin (CRM) is directly related to an improved oncological outcome. In this group, the patients with a negative CRM had a five year local recurrence of 6%, metastasis free survival 78 %, relapse free survival 77%, cancer specific survival of 82% and overall survival of 69%, which is significantly better for all parameters compared to a positive CRM. Interestingly, in the group with perineal approach first the number of radical resections are much higher. Despite the relative short follow up a significant reduction in LR rate was noticed. In multivariate analysis perineal approach first was a stronger predictor to obtain negative CRM than the type of neoadjuvant treatment, preoperative T stage or use of adjuvant CT. In conclusion, with the correct choice of neoadjuvant treatment and appropriate surgical technique, even in patients with locally advanced rectal cancer more than 90% radical resection can be achieved.

Oncological results APR 2000-2010: 5 year results

	Local Recurrence Rate	Metastasis Free Survival	Relapse Free Survival	Cancer Specific Survival	Overall Survival
Negative CRM	6%	78%	77%	82%	69%
Postive CRM	25%	48%	51%	44%	28%
	p=0.022	p=0.004	p=0.001	p<0.001	p<0.001

CRM Circumferential Resection Margin

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Optimal Timing of Systemic Therapy in Resectable Colorectal Liver Metastases C.U. Ihemelandu,[1]* E. Levine,[1] M. Aklilu,[2] T. McCoy,[3] R. Howerton,[1] G. Yacoub,[2] P. Shen.[1] *1. General Surgery, Section of Surgical Oncology, Wake Forest University Health Sciences, Winston-Salem, NC; 2. Section of Hematology and Oncology, Wake Forest University Health Sciences, Winston-Salem, NC; 3. Department of Biostatistical Sciences Wake Forest University Health Sciences, Winston-Salem, NC.*

Introduction: Perioperative chemotherapy has been shown to improve disease free survival compared to surgery alone for resectable colorectal liver metastases (CLM). We examined our experience with systemic chemotherapy in this clinical setting Methods: A prospectively collected liver surgery database identified 220 patients treated for resectable CLM from 1996-2010. Results were correlated to four treatment groups (adjuvant only, neoadjuvant only, perioperative, surgery only). Results: Sixty-two (28.2%) patients received only adjuvant treatment following resection, 45(20.5%) received only neoadjuvant treatment, 46(20.9%) received perioperative (neoadjuvant and adjuvant) treatment, while 67(30.5%) received surgery alone. Neoadjuvant and adjuvant systemic therapy regimens were as follows: 45(48.9%) and 19 (17.6%) received a 5FU/Leucovorin based regimen, 42(45.7%) and 59(54.6%) received a FOLFOX or FOLFIRI based regimen, 5(5.4%) and 30(27.8%) received some other combination. Biologic agents such as avastin and erbitux were given in 49.6% of patients. Treatment groups showed no difference in: gender, mean tumor size, number of tumors, margin status, or postoperative complications with the only difference being higher median age in the surgery only group (p=0.04) and higher incidence of metachronous tumors in the neoadjuvant only and perioperative groups (p=0.004). Median follow up and overall survival was 24 and 40 months, respectively. The adjuvant, neoadjuvant, perioperative, and surgery only groups had a median survival time of 51, 29, 42, and 26 months, respectively (log-rank p=0.006). Chemotherapy was an independent predictor of survival outcome. Compared to the adjuvant only group, the neoadjuvant only (HR=2.6, 95% CI 1.2-5.5, p=0.008), and surgery only groups (HR=2.7, 95% CI 1.4-5.2, p=0.003) were more likely to have a shorter life expectancy while there was no difference in life expectancy with the perioperative treatment group (HR=1.5, 95% CI 1.7-3.0, p=0.24). Conclusion: - Perioperative and adjuvant only systemic therapy were associated with an improved survival in resectable CLM. Prospective randomized trials are needed to confirm these findings.

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Skip Metastasis after Sentinel Lymph Node Mapping in Gastrointestinal Malignancies and its Biological Impact S. Saha,[1]* M. Mozayen,[3] S. Sirop,[2] M. Kanaan,[3] A. Korant,[3] S. Nalluri,[3] O. Machek,[3] M. Manyam,[3] S. Nagpal,[3] D. Wiese.[3] *1. McLaren Regional Medical Center-Michigan State University, Flint, MI; 2. Mayo Clinic Foundation, Rochester, MN; 3. McLaren Regional Medical Center, Flint, MI.*

Introduction: Over the last decade, sentinel lymph node (SLN) mapping has been used in gastrointestinal (GI) cancers for accurate nodal staging. However, due to variable incidence of skip metastasis between different parts of the GI tract, its usefulness has been questioned for the proper staging. Hence, we aimed to evaluate the rates of skip mets, its mechanism, and its impact in GI cancers if any. **Methods**: A search of the English literature was performed incorporating MEDLINE and Cochrane library databases using the following terms: skip metastasis, sentinel node, colorectal, gastric, and esophageal cancer. The following were excluded: comments, case reports, reviews, series with less than 40 patients. **Results**: A total of 27 studies between 2000-2009 with a total of 3589 patients were included. One hundred and twenty-two had esophageal, 1185 had gastric, 2113 had colon and 169 had rectal cancer. The overall success rate of SLN mapping was 95% (96.6% in esophageal, 94% in gastric, 94.3% in colon, and 95.6% in rectal cancer). Nodal positivity (positive SLNs and/or non-SLNs) was 34% in esophageal, 36.6% in gastric, 48.1% in colon, and 41% in rectal cancers. Rates of skip mets were 18%, 14%, 20% and 15% in esophageal, gastric, colon and rectal cancers respectively. In patients with skip mets, T3/T4 disease was found in 65%, 44%, and 82.5% of patients with esophageal, gastric and colon cancer retrospectively. The average tumor size ranged between 3 cm in gastric to 4.4 cm in colon cancer. The most common site for skip mets was the right side (50%) in colon cancer, and LN basin 7, 8, 9 in gastric cancer. All node positive (true and false negative) patients were staged as stage III and were treated with adjuvant chemotherapy.(Table

1) **Conclusion**: Skip mets are more common in T3/T4 disease, and in larger tumors suggesting difficulty injecting the dye circumferentially. All node positive patients (true positive and false negative) are treated with chemotherapy. Hence, unlike in melanoma and breast cancer patients with skip mets are neither understaged nor undertreated; hence has very little clinical relevance.

Table 1: results of skip metastasis(*) in esophageal, gastric, colorectal cancer

Organ site	Esophagus (4centers)	Stomach (4centers)	Colon (17centers)	Rectum (3centers)	Total
Number of patients	122	1185	2113	169	3589
Average age(year)	62	63	68.6	67	65.15
Success rate(**)	96.6%	94%	94.3%	95.6	95%
SLN per patient	2.7	2.9	1.97	3.23	2.7
Average no. of nodes per pt	28	27.5	15	12	20.5
Nodal positivity(‡)	34.25%	36.6%	48.1%	41%	39.98%
Rate of Skip metastasis (†)	18%	14.17%	19.9%	15%	16.76%
No. of pts with skip mets	9	44	183	12	248
Average size of the tumor	N/A	3 cm	4.4cm	3.5cm	3.6cm
T1+T2	35%	56%	17.6%	19%	27%
T3+T4	65%	44%	82.4%	81%	73%
False negative SLNs totally replaced by the tumor	yes	N/A	yes(45%)	N/A	N/A
All node positive pts received chemotherapy	yes	yes	yes	yes	yes

* Skip metastasis=failure to identify cancer cells in the SLN when they are subsequently identified in the non SLN.
** Success rate=percentage of patients whom SLN mapping was successful to identify sentinel node.
‡ Nodal positivity=no of pts with positive nodes /no of patients with advanced disease
† Rate of skip metastasis=false negative/ [false negative+ true positive]

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A Phase I trial of thermal sensitization using induced oxidative stress in the context of HIPEC G. Tiesi,* L.E. Harrison. *UMDNJ-New Jersey Medical School, Newark, NJ.*

Introduction: We have previously demonstrated that inducing oxidative stress under hyperthermic conditions significantly decreases tumor cell growth in a murine model of human colon cancer carcinomatosis. This Phase I study examines the safety and pharmacokinetics of induced oxidative stress by the addition of hydrogen peroxide (H2O2) to the perfusate in patients undergoing cytoreduction and HIPEC for advanced abdominal-only malignancies. Methods: Patients with advanced colon or appendiceal malignancies underwent maximal cytoreduction followed by HIPEC with mitomycin C (MMC). In addition, H2O2 was added to the perfusate at three concentrations (n=3/level, 0.075%, 0.05%, 0.1%). A control group consisted of patients perfused with MMC alone (n=3). Perfusate, serum MMC and H2O2 levels were measured, as well as tissue levels of MMC. Results: Twelve patients were enrolled in this trial. Tumor types included appendiceal adenocarcinoma (n=5), colon cancer (n=5) and diffuse peritoneal adenomucinosis (n=2). The median peritoneal carcinomatosis index was 13 (3-20) requiring a median OR time of 6.5 hrs (4-8) for cytoreduction and HIPEC. The median postoperative length of stay was 7 days (5–34 days), with six patients requiring re-admission within 30 days. The median follow-up time was 13 months (5–23). The addition of H2O2 to the perfusate significantly decreased systemic serum levels and maintained higher perfusate levels of MMC. Similar complications were observed at all three H2O2 levels, as well as in the control group. One patient required re-exploration for a colon perforation (control group) and three patients developed enterocutaneous fistulas (0.075% H2O2, 0.1% H2O2 and control group). There were no operative mortalities. Conclusions: We report that HIPEC with induced oxidative stress following maximal cytoreduction in patients with advanced colon or appendiceal malignancies is well tolerated. Encouraging toxicity profile and survival after cytoreduction and HIPEC with induced oxidative stress suggest that a Phase II trial to verify activity is indicated.

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Effects of centralization on morbidity and mortality after surgical treatment of esophageal cancer D. Faraj,[1]* B. Langenhoff,[2] F. Van Workum,[3] H. Bonenkamp,[3] H. De Wilt,[3] C. Rosman.[1] *1. Surgery, Canisius-Wilhelmina Hospital, Nijmegen, Netherlands; 2. Rijnstate Hospital, Arnhem, Netherlands; 3. Radboud University Nijmegen Medical Center, Nijmegen, Netherlands.*

Aim: To evaluate the effects of centralization of esophagectomy on morbidity and mortality in the Eastern part of the Netherlands. Methods: A retrospective comparison of 174 patients operated on for esophageal cancer in five hospitals between January 2000 and June 2005 (group 1, pre-centralization) and 61 patients operated on between March 2008 and May 2009 in two dedicated esophageal cancer hospitals (group 2, post-centralization), after implementation of centralization in the Eastern part of The Netherlands. Results: The mean duration of follow-up was 25 months (0.1-83.7) for group 1 and 12.8 months (0.9-22.5) for group 2. The mean number of operated patients per hospital increased from 7 to 25 patients per year. The use of neoadjuvant chemoradiotherapy increased from 8.5% to 52.5% of the patients (P<0.001). Median blood loss decreased significantly from 1250 to 575 mL (p<0.001). The median number of harvested lymph nodes increased from 8 to 11 per patient (p<0.001), and R0-resection rate increased from 75% to 84% of patients (p=0.155). The incidence of postoperative pneumonia decreased from 35% to 23% (p=0.031). Median ICU- and hospital stay decreased from 3 to 2 days (p=0.018) and from 16 to 10 days (p<0.001) respectively and in-hospital mortality rate decreased from 5.7% to 1.6% (p=0.30). One year survival increased from 70% to 84% (p=0.035). Conclusion: Centralization of esophagectomy was successfully implemented in the Eastern part of the Netherlands with a significantly positive effect on postoperative morbidity and survival.

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Differential Expression of Small Ubiquitin-Like Modifier Family of Proteins in Patients with Colorectal Adenocarcinoma R. Wiatrek,* M.P. Duldulao, Z. Chen, W. Li, J. Kim, Y.J. Li, Y. Chen, J. Garica-Aguilar. *City of Hope National Medical Center, Duarte, CA.*

Introduction: The cytotoxic effects of radiation and chemotherapy are mediated in part by DNA damage. The Small Ubiquitin-like Modifier (SUMO) family of proteins regulates DNA repair pathways by activating factors involved in homologous recombination (HR) or non-homologous end joining (NHEJ). Our objective was to determine the potential role of SUMO proteins in patients with colorectal cancer. Methods: We first assessed two established colorectal cancer cell lines (HCT116 and HT29) and two normal colonic mucosa cell populations utilizing ultra high-throughput expression analysis (Solexa) to examine differential expression of genes involved in SUMOylation (SAE1, SAE2, PIAS-1, and DNAPKcs). To verify the clinical relevance of SUMOylation in colorectal cancer, we obtained archived specimens from patients with colorectal cancer (n=51) and examined the expression of these proteins in both benign and malignant tissue by immunohistochemistry (IHC). Results: Ultra high-throughput expression analysis of cancer and normal cells revealed a 10 to 15-fold upregulation of SAE2 (heterodimer of the E1 activation enzyme in SUMOylation), a 10 to 11-fold upregulation of DNAPKcs (catalytic subunit in NHEJ repair pathway), and a 6-fold upregulation of SAE1 in cancer cells. In contrast, PIAS-1 showed similar expression levels between cancer and normal colonic cells. By IHC, SAE1 and SAE2 were highly expressed in 65% and 53% of tumor specimens, respectively (see Figure 1); but only in 7% and 0% of normal tissues, respectively. DNAPKcs was also highly expressed in tumor tissues (63%) with corresponding low expression (0%) in normal tissues. Corroborating the cell line results, PIAS-1 was infrequently expressed in both tumor (10%) and normal tissues (0%). Conclusions: We are the first to demonstrate the differential expression of SUMO proteins in colorectal cancer cell lines and in clinical specimens. SUMO proteins have a role in DNA repair and their expression in colorectal cancer may modify tumor response to chemoradiotherapy.

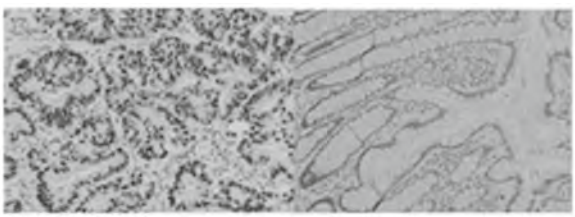

Figure 1. Representative immunohistochemistry showing overexpression of SAE2 in colon cancer (left panel) in comparison to matched normal mucosa (right panel).

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Cytopathologic Evaluation of the In-Situ Margin in Patients Undergoing Hepatectomy N.B. Jones,* P.E. Wakely, Jr., D.L. Klemanski, O. Al-Saif, G. Young, W.L. Frankel, E.W. Martin, Jr., P.M. Bloomston. *Surgery, The Ohio State University, Columbus, OH.*

Background: Margin status is a persistent predictor of outcome for liver malignancies, although what constitutes a negative margin is still debatable. Traditionally we estimate completeness of resection by evaluating the resected margin on the specimen, whereas the in situ margin is potentially more important. The true margin is often altered by parenchymal transection techniques. We evaluated the feasibility of assessing margins by using cytopathologic techniques. Methods: 84 consecutive patients with primary or metastatic liver tumors undergoing resection were enrolled in this IRB-approved prospective study. We assessed the in situ margin using a "touch prep" cytologic technique and compared it with traditional specimen tissue margin. Patients were then followed for a minimum of one year to assess for local recurrence. Results: Follow-up data was complete for 58 patients for median of 24.6 months (range, 12-56 months). 26 patients were excluded due to peri-operative death (N=4, 4.8%) or follow-up less than 12 months. Seven patients (12.2%) had positive tissue specimen margins, but only one was positive by cytology (1.8%). However, no in situ positive margins were identified along the cut edge of the liver remnant. Overall recurrence in the liver or extrahepatic sites was 56.7%, whereas local recurrence was 1.8%. The one patient with local recurrence also demonstrated simultaneous extrahepatic recurrence. Conclusion: We have shown for the first time that in situ margins can be assessed using cytopathologic methods. This method is quick (<2 minutes) and can be universally applied using standard techniques. Given the difficulty of accurately assessing resection margins after hepatectomy, cytopathologic evaluation may be more reflective of the true margin.

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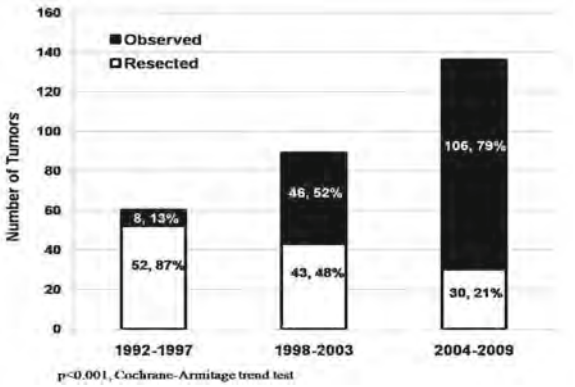
Selective Management of Benign Liver Tumors: A Safe and Effective Strategy J.J. Mezhir,[1]* L.T. Fourman,[2] R.K. Do,[2] M. Gonen,[2] B. Denton,[2] P.J. Allen,[2] M.I. D'Angelica,[2] R.P. DeMatteo,[2] Y. Fong,[2] W.R. Jarnagin.[2] *1. Surgery, University of Iowa, Iowa City, IA; 2. Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Benign liver tumors (BLTs) are encountered frequently and management is controversial. With the advent of laparoscopic liver surgery, some advocate a liberal policy of resection. The objective of this study was to demonstrate the safety of a selective management approach. **Methods:** Patients were identified from a review of a prospective hepatopancreaticobiliary operative database and an institutional ICD-9 search. Patients were only included if BLT was the primary diagnosis. Patients with no follow-up or with an incidental BLT in the setting of concomitant, active malignancy were excluded. **Results:** From 1/1992 to 8/2009, 285 patients were evaluated with hemangioma (53%), focal nodular hyperplasia (24%), adenoma (10%), or indeterminate/other (13%). Evaluation was most commonly with CT (82%), MRI (75%), and/or ultrasound (46%). Forty percent of patients (N=115) underwent immediate resection, most commonly for inability to exclude adenoma or malignancy (N=55, 48%) or symptoms (N=35, 30%). There were 170 patients (60%) followed with serial imaging with a median follow-up of 30 months. During the period of observation, 10 patients (6%) underwent resection for tumor growth or symptoms; however no BLT underwent malignant transformation. During the study period, there was a significant increase in the number of BLTs seen and a similar marked increase in the proportion of patients observed: 1992-2002 (N=129, 36% observed) vs. 2003-2009 (N=156, 72% observed), p<0.001 (**Figure**). Diagnostic uncertainty led to resection in 30% of patients during the early time period vs. 13% over the last 7 years. Patients selected for observation had no change in median tumor size during serial imaging: median tumor size during initial imaging was 2.7cm vs. final imaging 2.6cm, p=NS. **Conclusions:** Asymptomatic BLTs, without concern for malignancy or adenoma based on high quality cross-sectional imaging, can be safely observed with minimal risk of misdiagnosis. Patients selected for observation rarely require resection or develop tumor-related complications.



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Age Influences Likelihood of Treatment, But Not Overall Survival in Exocrine Pancreatic Cancer A.A. Wheeler, P.S. Dale, M.B. Nicholl.* *Surgery, University of Missouri, Columbia, MO.*

Background: Pancreatic cancer is a disease primarily diagnosed in elderly patients; however a significant number of young patients will also be affected. We hypothesized young patients with pancreatic cancer would be treated more aggressively and therefore have better prognosis. Methods: A retrospective review of a prospectively maintained cancer database was queried for all patients treated for pancreatic cancer at our institution. Age 50 years was selected to stratify patients as young or old. Results: Of 309 pancreatic cancer patients identified from the database, 54 (17%) were ≤ 50 years old. Exocrine cancer was the most common histology (89%). Young patients were significantly more likely to have an endocrine cancer (22%vs. 7%, p<0.001). For all tumor histologies, there was no difference between young and old patients regarding stage, grade, or likelihood curative intent surgery; however, young patients were more likely to receive chemotherapy (67% vs. 41%, p=0.003) and radiation therapy (36% vs. 17%, p=0.004). There was a trend toward improved overall survival in young patients (24.1 months vs. 14.1 months, p=0.08). When only exocrine pancreatic cancers were considered, there was no difference between young and old patients regarding stage, grade, location, or likelihood of undergoing surgical treatment. In this group, young patients were again more likely to receive chemotherapy (65% vs. 40%, p=0.002) and radiation therapy (35% vs. 16%, p=0.003). There was no difference in overall survival between young and old patients with exocrine pancreatic cancer (9.8 vs 11.8 months, p=ns). Conclusions: A considerable number of patients treated for pancreatic cancer are ≤ 50 years old. Exocrine cancers are the most common pancreatic neoplasm regardless of age; however endocrine tumors are more common in young patients. Despite more frequent use of adjuvant treatment in exocrine pancreatic cancer patients ≤ 50 years old, there is no improvement in overall survival. Significant improvements in pancreatic cancer survival are not dependent on aggressive use of adjuvant therapies, but await the development of new treatment strategies.

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Total Laparoscopic Mesorectal Resection for Rectal Cancer (TLRC) in Overweight Patients with Locally Advanced Disease K. Ryan,* N.J. Espat, S. Katz, P. Somasundar. *Roger Williams Medical Center, Providence, RI.*

INTRODUCTION: Prior reports have shown that laparoscopic proctectomy is equivalent to open proctectomy, with regard to patient safety and oncologic staging adequacy. However, TLRC outcomes for overweight patients with advanced disease have not been well defined. METHODS: Consecutive patients who underwent TLRC from July 2008 to March 2010 were identified, using a prospectively collected colorectal database. Demographics, body mass index (BMI), neoadjuvant chemoradiation (NCR), EBL, pathology, and MM data were analyzed under IRB approval. *Technique:* The left colon was mobilized laparoscopically without hand assistance. Mesorectal dissection was carried distally to achieve a 2cm margin. The bowel was divided laparoscopically and then removed through a 4-cm incision, followed by fascial closure and intracorporal stapled anastomosis. RESULTS: Twenty-seven patients (16M, 11F), median age 66 (range 46-86), underwent TLRC during the study period. Fifty-six percent of patients were over age 65 and had ≥2 comorbidities. The mean

BMI was 28.6; 74% were overweight (BMI≥25), and 26% were obese (BMI≥30). Six patients had very low tumors (VLT), <5cm from the anal verge, and 5 patients received NCR. Mean lymph node retrieval was 18.4. Three patients had fewer than 12 nodes removed, all of whom received NCR. The mean distal margin was 2.3cm, and the mesorectum was intact in 26 specimens (96.3%). Most tumors (26 of 27) were T3 or T4, and 66.7% had lymphatic metastases. Mean EBL was 255ml, but over the last 9 months of the study, mean EBL decreased to 129ml. Six patients (22.2%) had major complications: 1 fatal PE; 1 cardiopulmonary arrest caused by MI; 2 pelvic abscesses (IR drainage); 1 anastomotic leak (reoperation); 1 bleed (negative laparoscopy). CONCLUSION: TLRC achieves adequate surgical margins, does not compromise nodal staging, and has acceptable MM rates in overweight patients and in those with locally advanced disease. The role for TLRC with VLT needs to be further defined by randomized trials.

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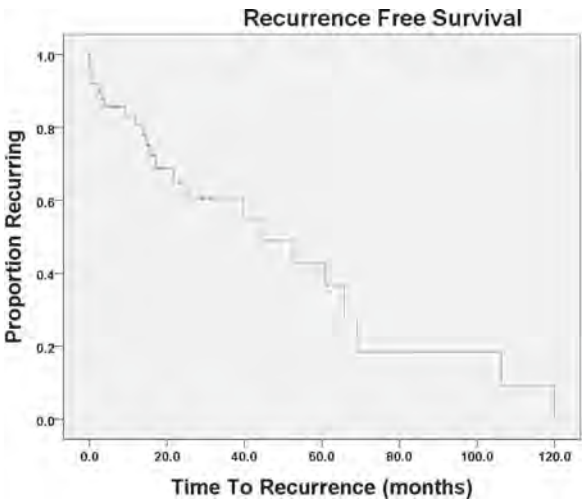
Even in the Best Patients, Recurrence Rates are High after Hepatectomy for Metastatic Colon Cancer M.E. McNally,* N.B. Jones, L. Malhotra, S. Abdel-Misih, E.W. Martin, P.M. Bloomston, C.R. Schmidt. *General Surgery, The Ohio State University- The James Cancer Hospital and Solove Research Institute, Columbus, OH.*

Introduction Half of patients with colorectal cancer will develop metastatic disease in the liver. While hepatectomy is associated with prolonged survival in select patients, recurrence rates remain high and long-term cure rates low. Factors associated with improved survival after hepatectomy for metastatic colorectal cancer (mCRC) include node-negative primary disease and metachronous development of metastases.We examined our outcomes after hepatectomy for mCRC in patients with those favorable factors. Methods We reviewed our experience of all persons undergoing hepatectomy for mCRC over the past 12 years. Demographic information and outcome data were collected. Metachronous disease was defined as development of liver metastases at least six months after resection of the primary tumor. The Kaplan Meier method and Chi-square analysis were used to determine survival and significance between groups. Results A total of 438 patients underwent hepatectomy for mCRC between 1988 and 2009. There were 105 patients with a node-negative primary tumor, and 60 (57.1%) of these presented with metachronous hepatic mCRC. In this group, the median age at hepatectomy was 63.0 (31.1-82.4) years and 17 (28.3%) were female. Twenty-two (36.7%) patients underwent a major hepatectomy. The median survival after hepatectomy was 33.5 (18.2-48.7) months with an estimated 5-year survival of 25%. In those patients undergoing hepatectomy with curative intent (N=51 with no extrahepatic disease), the median time to recurrence after hepatectomy was 23.1 months with an estimated 3-year recurrence-free survival of 36% (Figure). Conclusion Even patients with favorable tumor biology experience high rates of recurrence after hepatectomy. Recurrences may occur many months to years after hepatectomy. Despite recent advances in systemic chemotherapy and improved perioperative outcomes after hepatectomy, novel liver-directed therapies will be critical to improving the rate of cure for hepatic metastatic colorectal cancer.



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Serum ghrelin levels and weight loss do not recover after total gastrectomy for gastric cancer M. Koizumi,[1]* Y. Hosoya,[1] K. Dezaki,[1] T. Yada,[1] H. Hosoda,[2] K. Kangawa,[2] H. Nagai,[3] N. Sata,[1] Y. Yasuda.[1]
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[Introduction] Weight loss after total gastrectomy significantly affects patient quality of life. Ghrelin increases weight by stimulating appetite and is produced in the stomach and up-regulated via specific ghrelin receptors located on the vagal and other central neurons. This prospective study was undertaken to investigate an association between weight loss, appetite, serum ghrelin levels and clinicopathological findings in patients with gastric cancer following total gastrectomy. [Methods] Forty-one patients underwent total gastrectomy including 33 males and 8 females. The average age was 66.0 years (range 45-79). Measurements of serum ghrelin, weight, serum albumin and an appetite questionnaire were performed preoperatively and postoperatively at 1, 3, 6 and 12 months. [Results] Preoperative mean concentration of serum total ghrelin was 51.6 ± 31.9 (fmol/ml ± SD), and at 1, 3, 6, 12 months after surgery were 16.9 ± 9.0, 21.2 ± 16.0, 28.0 ± 19.1 and 29.6 ± 20.6 (fmol/ml ± SD) respectively. There was a significant reduction ($p<.05$) comparing the preoperative levels with those at one month postoperatively. There were no significant differences in ghrelin levels when stratified by pathological stage, adjuvant therapy, or tumor recurrence. Body mass index decreased significantly ($p<.05$) after surgery, by 2.7±1.4, 3.1±1.5, 3.6±1.7, and 3.9±2.0 at 1, 3, 6, and 12 months, respectively. Serum albumin levels were significantly ($p<.05$) increased, at 3.77±0.45, 3.89±0.33, 3.95±0.35, 4.04±0.41 and 4.07±0.46 mg/dl measured preoperatively and at 1, 3, 6, and 12 months after surgery, respectively The appetite questionnaire showed an average score of 2.02 ± 1.09 at 1 month postoperatively, and increased significantly to 2.61 ± 1.00 at 12 months. [Conclusions] Serum ghrelin levels were significantly decreased postoperatively and remained decreased at 12 months. This decrease was not associated with tumor stage, adjuvant therapy or recurrence. Body mass index decreased at one month and continued to decrease at 12 months postoperatively. These results suggest that the use of exogenous recombinant ghrelin following gastrectomy may be beneficial and deserves further study.

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Microwave Ablation of Larger and Perivascular Hepatic Tumors J.A. Kuhn,[1]* T. Fisher,[1] K. Kuhn.[2] *1. Department of Surgery, Baylor University Medical Center, Dallas, TX; 2. Department of Surgery, Medical City of Dallas, Dallas, TX.*

Background: Microwave ablation of unresectable hepatic tumors, remains relatively unstudied, but offers a potential innovative approach to ablate larger tumors and tumors near vascular structures. Methods: A retrospective study of microwave ablation of hepatic tumors by the same surgeon over a two year period. Data related to safety, efficacy, and technique are presented. Results: Seventeen patients (9 female), with an average age of 66 years (range 40-92) received microwave ablation to one or more liver tumors (28 total), an average of 27 months (range 0.5-96) after initial diagnosis of their primary cancer. Tumor types included colorectal (n=8), primary hepatic (n=2), breast (n=2), ovarian (n=2), and one each of small bowel, gallbladder, and primary cholangiocarcinomic. On average, two tumors (range 1-4) were ablated per patient, median size of 4cm (range 1-9.5cm). Each lesion was ablated using a standard protocol which depended on the size and number of lesions. Ablation "zones" were crafted using multiple microwave probes and multiple probe placements. The average duration of ablation was 10 minutes per placement. Proximity to major venous structures was noted in 13/25 lesions. There were no cases of postoperative abscess or hemorrhaging. Average length of stay was 5 days (range 1-21, n=8). After an average follow-up of 8 months (range 1-18), 14 (82%) patients showed successful ablation of lesions. Only three of the twenty-five lesions had recurred in the remaining 3 patients (18%). In the 13 lesions with venous proximity, tumor recurrence was seen in 2/13 (15%). In tumors over 5cm, tumor recurrence was seen in 0/5 (0%), which was not significantly higher than tumors under 5cm. Conclusions: The flexibility of multiple probes and multiple probe placements with microwave ablation provides a safe and effective way to treat a wide range of nonresectable liver tumors including those that are near major vessels and tumors larger than 5 cm.

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Perioperative Outcomes of Esophagectomy following Neoadjuvant Therapy S. Nurkin,[1]* V.R. Kakarla,[2] A. Nguyen,[2] S.A. Paul,[2] N. Wilkinson.[1] *1. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY; 2. New York Hospital Queens, Flushing, NY.*

Background:Although still investigational,preoperative chemoradiation followed by surgery has become the most common approach to resectable esophageal cancer.Two meta-analyses have shown that this therapy decreased local recurrences rates, down-staged tumors and increased 3-year overall survival.However, a recent phase III trial(FFCD 9901)showed that neoadjuvant therapy increased postoperative 30-day mortality.As neoadjuvant therapy is becoming the more common approach for resectable esophageal cancer, it is important to make sure that this modality is safe in the short-term. Methods: Using the American College of Surgeons-National Surgical Quality Improvement Project(ACS-NSQIP) participant-use file, patients were identified who underwent esophagectomy for cancer at the 211 participating hospitals in 2005 - 2008.Demographic, clinical, intra-operative variables and 30-day morbidity and mortality were collected.Logistic regression analysis was performed to determine factors that increased risk of poor outcomes following resection. Results:We identified a total of 582 patients that underwent esophagectomy.Patients were subdivided into 2 groups: Surgery alone (n-400) versus neoadjuvant and surgery (n-182). There were no differences in age, sex, comorbidities or ASA class between the two groups.There were no differences noted in intra-operative outcomes including operative time or transfusion requirements. When comparing surgery alone to neoadjuvant and surgery, there were no differences in post-operative length of stay(17.6 days vs. 16.0 days, p=0.31), serious morbidity(34% vs. 34.6%, p=0.4), wound complications(19.5% vs. 22.5%, p=0.4) or 30-day mortality(3.3% vs. 4.4%, p=0.48). Using logistic regression analysis, patients that had PVD and previous cardiac surgery were at an increased risk of mortality and morbidity within 30 days, respectively. Conclusion:In an NSQIP analysis of 582 patients that underwent esophagectomy, there was no difference in post-operative morbidity or mortality if they had neoadjuvant therapy prior to surgery.As multimodality therapy is becoming the standard for resectable, locally advanced esophageal cancer, it appears to be as safe as surgery alone in the short-term.

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Impact of Neoadjuvant Systemic Chemotherapy on Cytoreductive Surgery combined with Heated Intraperitoneal Chemotherapy for Carcinomatosis from Appendix Cancer L. Bijelic,* A.S. Kumar, O.A. Stuart, P.H. Sugarbaker. *Surgery, Washington Hospital Center, Washington, DC.*

Systemic chemotherapy administered prior to cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) for carcinomatosis of appendiceal origin (PMCA) is associated with a significant rate of histologic response. The impact of preoperative systemic chemotherapy on intraperitoneal tumor burden, completeness of cytoreduction and perioperative complications is not known. We performed an analysis of prospectively collected data from our institutional HIPEC database.Thirty–four patients with proven PMCA were prospectively recruited and treated with systemic chemotherapy prior to CRS and HIPEC using an oxaliplatin containing regimen. Perioperative variables in this group of patients were compared to 24 patients with PMCA who did not receive systemic chemotherapy prior to CRS and HIPEC. Student t-test and chi square analysis were used. Ten of 34 patients receiving preoperative systemic chemotherapy had a complete or near complete histologic response.Patients receiving preoperative systemic chemotherapy had a lower peritoneal carcinomatosis index and required fewer peritonectomies and visceral resections compared to patients not receiving preoperative chemotherapy. The rate of complete cytoreduction was not significantly different between the two groups. The incidence of perioperative complications was not increased in patients who received neoadjuvant chemotherapy. (Table 1) Preoperative systemic chemotherapy in PMCA from appendix cancer is associated with a significant rate of histologic complete or near-complete response which may reduce the tumor burden and facilitate less aggressive surgical cytoreduction. The incidence of perioperative complications is not increased with the use of preoperative chemotherapy.

Variable	Neoadjuvant Chemotherapy prior to CRS and HIPEC	CRS and HIPEC	p Value
Number of patients	34	24	
Gender			NS
Male	17	10	
Female	17	14	
Completeness of Cytoreduction			NS
CCR 0/ CCR 1	22	12	
CCR 2	7	5	
CCR 3	5	5	
Peritoneal Cancer Index (mean)	19	28	0.001
Number of peritoneactomies (mean)	2.35	3.66	0.003
Number of visceral resections (mean)	2.73	4.37	<0.001
Complications of any grade	24	21	NS

CCR 0=no visible tumor, CCR 1=residual tumor < 2.5mm, CCR 2=residual tumor >2.5mm, <2.5 cm, CCR 3=residual tumor >2.5cm

P196

Validation of Consensus Panel Guidelines for the Management of Pancreatic Cystic Neoplasms R. Hoffman,* J. Gates, N. Ahmad, G. Ginsberg, M. Kochman, J. Drebin. *University of Pennsylvania School of Medicine, Philadelphia, PA.*

Introduction: Pancreatic cystic neoplasms (PCN) are identified with increasing frequency. To address the management of PCN, an international panel presented recommendations in 2006 (Tanaka, et al, Pancreatology 6:17-32). However, these recommendations remain controversial. The aim of this study was to characterize pathologic findings and surgical outcomes in a large series of patients with resected PCNs, in which the Tanaka criteria were followed in surgical decision making. Methods: A retrospective chart review was conducted on 117 consecutive patients who underwent pancreatectomy by a single surgeon for presumed PCN between June 2004 and October 2009. Preoperative, intraoperative and postoperative findings were evaluated. Results: Demographics, surgical procedures and pathologic findings are shown in Table 1. Median length of hospital stay was 8 days, 21% of patients required a perioperative transfusion, and there was one perioperative mortality. 66% of resected mucinous PCN demonstrated moderate dysplasia or malignancy. Elevated cyst fluid CEA was seen in 97% of mucinous lesions evaluated by endoscopic ultrasound guided aspiration. There was no correlation between serum CEA and cyst fluid CEA. On multivariate analysis, neither cyst CEA, serum CEA or serum CA 19-9 were useful in distinguishing benign from malignant PCN. PCN size greater than 3 cm was shown to be an independent predictor of malignancy. All lesions containing carcinoma in asymptomatic patients were greater than 3cm in size. Conclusions: The surgical resection of PCN can be performed with low mortality and acceptable morbidity. Applying the consensus panel criteria to surgical decision making results in the resection of frank cancer or disease with malignant potential in the majority of patients. Our findings support the conclusion that asymptomatic lesions smaller than 3 cm are unlikely to harbor carcinoma. The use of EUS/FNA is helpful in discriminating mucinous from serous cysts. Serum tumor markers were not useful in predicting malignancy or differentiating cyst type. This study supports the use of the Tanaka consensus panel criteria in surgical decision making for patients with PCN.

Patient Data

Demographics	Median Age	62 years
	Female	54%
	Male	46%
Co-Morbid Medical Conditions	Hypertension	63%
	Diabetes	21%
	COPD	8%
	CAD	7%
	Renal Failure	2%
Surgical Procedures	Distal Pancreatectomy	62
	Pancreaticoduodenectomy	51
	Central Pancreatectomy	3
	Total Pancreatectomy	1
Pathology	IPMN- Carcinoma or CIS	16
	IPMN- Moderate Dysplasia	29
	IPMN- Low/No Dysplasia	10
	MCN- Carcinoma or CIS	5
	MCN- Moderate Dysplasia	13
	MCN- Low/No Dysplasia	15
	Serous Cystadenoma	16
	Pseudocyst	6
	Cystic Neuroendocrine Tumor	3
	Lymphoepithelial Cyst	1

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Modified Appleby Resection for Locally Advanced Pancreatic Adenocarcinoma Following Neoadjuvant Therapy J.M. Baumgartner,* M. Dauoadi, A. Zureikat, W. Marsh, K. Lee, A.M. Moser, H. Zeh. *UPMC, Pittsburgh, PA.*

Background: A recent study demonstrated that 28% of patients who present with locally advanced pancreatic cancer will not develop systemic metastases and succumb to local progression alone. Encasement of the celiac trunk by tumors of the pancreatic body frequently precludes surgical resection for adenocarcinomas of the pancreatic. We hypothesized that selected patients may derive prolonged survival benefit from aggressive surgical resection following neoadjuvant treatment. Methods: We analyzed the outcomes of modified Appleby procedures for pancreatic adenocarcinoma at the University of Pittsburgh Medical Center between 2002 and 2010. Results: Eleven patients underwent a modified Appleby procedure for adenocarcinoma of the body of the pancreas. All patients received at least three months of gemcitabine-based neoadjuvant chemoradiation therapy. Median operative time was eight hours and median estimated blood loss was 1200 ml. There was no clinically significant hepatic or gastric ischemia postoperatively. Median length of stay was nine days. Four patients (35%) had pancreatic leaks; all but one were ISGPF grade A. There were no perioperative deaths in the first 30 days; one patient died on day 54. Ten patients achieved R0 status (91%). Median pathologic tumor size was 4.0 cm, and the median lymph node harvest was 13. Six patients recurred; four systemic and two locoregional (median follow up nine months). Three patients have died; two with no evidence of disease at the time of death. Two patients are alive for greater than 36 months (18%). Conclusions: Resection of pancreatic body adenocarcinoma with en bloc celiac axis resection is technically feasible with acceptable perioperative morbidity and mortality. Aggressive surgical resection can provide long term survival in select patients. Future studies will focus on understanding genetic and proteomic features that predict long term survival.

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Role of Laparoscopic Radiofrequency Ablation in the Management of Colorectal Liver Metastases T. Kennedy,[1]* M.A. Cassera,[2] T. Diwan,[2] C. Hammill,[2] P.D. Hansen.[2] *1. Montefiore Medical Center, New York, NY; 2. Providence Medical Center, Portland, OR.*

Radiofrequency ablation (RFA) is being increasing utilized for the treatment of liver tumors. This study analyzes our experience with laparoscopic RFA in management of patients with colorectal liver metastases (CRLM). From January 2000 to July 2010, 130 patients underwent laparoscopic RFA for management of CRLM. A retrospective analysis of patient medical records was performed. Local recurrence was defined as radiographic evidence of recurrent disease within 1cm of prior ablation zone. Kaplan-Meier survival was used to assess survival. Cox proportional hazards regression modeling was performed for multivariate analysis. In this cohort, mean age was 65 years, 66% were male, mean BMI 28.2, mean ASA 2.8, mean clinical risk score 1.8 and average time from primary colon resection was 18.4 months. The mean number of tumors per patient was 2.0 and the mean maximum tumor diameter was 2.9cm. Median follow up time was 28.6 months with a median survival of 40 months and a 5 year survival of 30%. Mean time to recurrence was 14.8 months - 8% of patients had local recurrence, 28% liver-only recurrence and 34% with distant metastatic disease. On multivariate analysis, factors predictive of death were ASA classification ($p=0.01$), lack of preoperative chemotherapy ($p=0.02$), bi-lobar disease ($p=0.03$) and maximum tumor diameter ($p<0.01$). The only factor predictive of local recurrence was maximum tumor diameter ($p=0.03$); 9 of the 11 local recurrences had a tumor diameter > 3cm. The indications for RFA were technically unresectable disease in 24%, significant medical comorbidities in 40%, and patient decision in 36%. Median survival for patients who were considered either unresectable or high risk was 34 months while median survival for those patients who selected RFA was 50 months ($p=0.07$). The role of RFA in the management of patients with CRLM is unclear. Our data demonstrates that laparoscopic RFA can achieve a median survival of 40 months, 5 year survival of 30% and a local recurrence rate of 8%. Patients with tumors > 3cm are at higher risk for local recurrence. Patients who are liver resection candidates have higher median survival than patients who are not.

P199

Reproducibility of colon tumor grade and relationship to recurrence in the context of clinical, pathologic, and genomic tumor features in 504 stage II colon cancer (CC) patients treated with surgery alone I. Lavery,[1] F. Baehner,[2] M. Lopatin,[2] G. Iezza,[3] C. Millward,[2] K. Clark-Langone,[2] M. Lee.[2]* *1. Cleveland Clinic, Cleveland, OH; 2. Genomic Health, Inc, Redwood City, CA; 3. University of California, San Francisco, CA.*

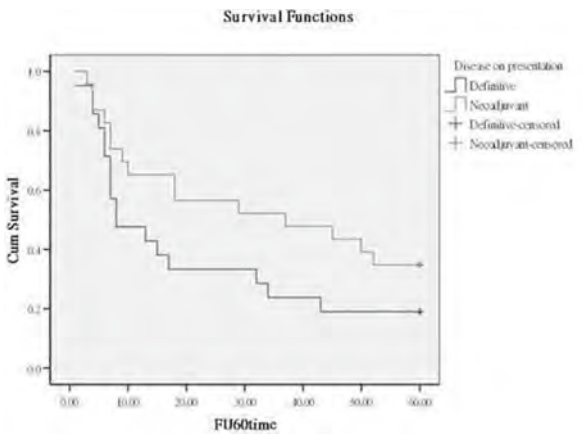
Background: High tumor grade is included in practice guidelines as a marker of higher recurrence risk in stage II CC. Multiple systems for tumor grading exist, w/out a standardized approach. We characterize agreement of 2 methods for tumor grading and association with recurrence in the context of clinical, pathologic, and genomic tumor features including mismatch repair(MMR) and the 12-gene Recurrence Score(RS). Methods: Colon tumors were graded independently by 2 academic GI pathologists(P1, P2). Grade was defined by %tumor with gland-like structures: well (>95%), moderately (50-95%) and poorly (<50%) differentiated, P1 used this 3-tier system. P2 used a 2-tier scheme with well and moderately differentiated tumors defined as low grade and poorly differentiated as high grade. All mucinous tumors were high grade by P2 but not P1. Relationship to recurrence-free interval(RFI) was assessed by Cox regression. Results: Primary tumors from 504 stage II CC pts treated with surgery alone were included. 18%(P1) and 31%(P2) were high grade. High grade tumors were more likely right-sided (≥60%) and MMR Deficient (≥35%) for P1 and P2 (all $p<0.001$). Proportion of mucinous tumors was similar for high and low grade by P1(25% v 21%,$p=0.39$). P2 high grade trended to lower recurrence ($HR=0.63$, $p=0.10$) while P1 grade was not associated w/ RFI($p=0.46$). In multivariate analyses including grade and RS, P2 high grade was associated w/ lower recurrence($p=0.007$) but P1 grade was not associated w/ RFI($p=0.30$). Neither grade was associated w/RFI($p>0.30$) after controlling for RS, MMR, tumor location and mucinous histology. Using the two-tier scheme, agreement b/w P1 and P2 was low (kappa=0.30,95%CI 0.21-0.39) in all pts and moderate if mucinous tumors were excluded(kappa=0.52,95%CI 0.40-0.64). Conclusions: High tumor grade was not found to be a marker of higher recurrence risk in stage II CC. Other

markers validated in stage II CC, such as MMR and Recurrence Score, should be considered. Inter-pathologist agreement on colon tumor grade is modest, even w/ central expert review.

P200

Neoadjuvant against definitive chemoradiotherapy for treatment of squamous esophageal cancer P.W. Chiu,* A.Y. Teoh, S.Y. Liu, M.Y. Yung, C.C. Lam, B. Tsung, S.K. Wong, E.K. Ng. *Surgery, Institute of Digestive Disease, The Chinese University of Hong Kong, Hong Kong, China.*

Introduction Squamous esophageal cancer carried grave prognosis. From results of meta-analysis, neoadjuvant chemoradiotherapy may potentially offer an improvement in survival. From our prospective randomized study comparing definitive chemoradiotherapy (CRT) against esophagectomy for treatment of squamous esophageal cancer, we found that early survival was similar between the two groups. This study aimed to compare neoadjuvant against definitive chemoradiotherapy for treatment of squamous esophageal cancer in retrospective case-controlled manner. Method The data of consecutive patients who had squamous esophageal cancer were prospectively collected since 1993. Patients who received either neoadjuvant CRT (NCRT) or definitive CRT (DCRT) would be recruited. Patient who received neoadjuvant CRT would be scheduled for esophagectomy within 4 weeks after CRT, while patients treated by definitive CRT would receive salvage esophagectomy if there was residue disease or recurrence. The baseline characteristics, tumor staging and clinical outcomes were reviewed and compared between these two groups. Results Patients with squamous esophageal cancer were treated by different strategies. From 1998 to 2000, 21 patients received neoadjuvant CRT while from 2000 to 2004, 23 patients underwent definitive CRT. There was no difference in the mean age (58.4 vs 64.1) and gender distribution (male 95.7% vs 90.6%) between the two groups. Majority of these patients suffered from grade 2 dysphagia in the two groups. 4 patients who were treated by Definitive CRT received salvage esophagectomy because of residual disease. There was no difference in the post-treatment tumor volume between the two groups (NCRT = 18.8 +/-15.0; DCRT 17.4 +/- 15.6; p = 0.61). At 5 years, 34.8% of patients who were treated with neoadjuvant CRT survived as compared to 19% of those who received definitive CRT (Log rank test p = 0.052). Conclusions Neoadjuvant CRT achieved a better 5 year survival when compared to definitive CRT for treatment of squamous esophageal carcinoma. Further prospective randomized study is necessary to confirm this finding.



P201

Sorafenib in Combination with Doxorubicin-Loaded Beads is Safe and Effective as a Combination Treatment Option for Hepatocellular Cancer R.W. Farmer,[1]* K. Robbins,[2] T. Metzger,[1] R. Padr,[3] J. Urbano,[4] D. Enguix,[4] G. Narayanan,[5] R.C. Martin.[1] *1. University of Louisville, Louisville, KY; 2. Baptist Heath, Little Rock, AR; 3. FN Motol, Prague, Czech Republic; 4. La Fe Hospital, Valencia, Spain; 5. University of Miami, Miami, FL.*

BACKGROUND: Sorafenib, an oral VEGF inhibitor has established its efficacy in advanced HCC patients. Doxorubicin-loaded drug eluting Beads (DEBDOX) have recently demonstrated an improved safety profile and efficacy when compared to conventional chemoembolization in intermediate-stage HCC and may offer benefit to patients with more advanced disease. Recent data has suggested that a more aggressive HCC biology maybe predicted by radiologic features, elevated alpha-feto protein levels, and presence of portal vein thrombosis. The aim of this study was to assess the safety and efficacy of combining sorafenib with doxorubicin-loaded Beads in HCC. METHODS: Analysis of a 742 patient prospective, multi-center, multi-national Bead registry database from 6/2007-9/2010 identified 269 HCC patients treated with Beads, 47 of which also received concurrent Sorafenib. We analyzed the clinicopathologic factors of patients receiving sorafenib and Beads versus Beads alone using Chi-Square, ANOVA, and Kaplan-Meier analyses. Primary endpoints were safety, tolerance, and tumour response. RESULTS: In comparison to the 47 patients who underwent combination Sorafenib and Bead therapy, there was no difference in Child class, Okuda stage, number of target lesions, AFP level, disease location, or % liver involvement. Combination patients were more likely to have IVC thrombosis (8.9% vs. 1.5%, p = .007). The combination patients underwent a median of 2 Bead treatments (range 1-7) compared to median of 1 (range 1-10) in the Bead alone group. In the combination group, 15 patients sustained 33 complications with a median grade 2 (1-4), compared to 55 patients sustaining 84 complications with a median grade 2 (range 1-5)(p=.310). After a median follow up of 12 months the combination group's median overall survival was 14 months, compared to 12 months in the bead only group. CONCLUSIONS: Combining sorafenib and doxorubicin drug eluting beads safe and effective in intermediate and advanced staged HCC. Initial improvements in overall survival are demonstrated and should be evaluated with larger prospective randomized control trials.

Comparison of Treatment Groups

Group	N	Child B	Okuda >1	Number of Target Lesions (mean/median)	Right Lobe Involvement	< 25% liver involvement	Adverse Event	Adverse Event Grade ≥3	Liver AE	OS(months)
DEBDOX Bead	222	39%	33.3%	1.74	41.3%	61.5%	34%	24.6%	10.1%	12
Sorafenib & DEBDOX Bead	47	32.6%	26.3%	1.80	40.0%	46.2%	30%	24.2%	15.2%	14
P-value		0.942	0.729	0.816	0.627	0.126	0.2	.193	0.897	.326

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Accuracy of Preoperative Computed Tomography Findings and its Role as a Surrogate Marker of Operative Complications and Outcomes after Cytoreductive Surgery and Perioperative Intraperitoneal Chemotherapy for Pseudomyxoma Peritonei T.C. Chua,* D.L. Morris, D. Glenn, A. Saxena. *UNSW Department of Surgery, St George Hospital, Sydney, NSW, Australia.*

Background Pseudomyxoma peritonei is characterised on computed tomography (CT) imaging as low-attenuation ascitic material within the peritoneal space. This study seeks to evaluate the accuracy of CT scoring of the peritoneal cancer index (PCI) and to examine its role as a surrogate marker of surgical morbidity and outcomes. Patients and Method Forty-seven patients with mucinous appendiceal neoplasm with pseudomyxoma peritonei had preoperative evaluation of CT scans and were subsequently treated with cytoreductive surgery and perioperative intraperitoneal chemotherapy. Their radiological PCI and intraoperative PCI were scored for determination of accuracy and for correlation with morbidity and outcomes. Results Accuracy in detecting peritoneal lesions regardless of sizes ranged from 51% to 85% in the abdominopelvic regions and 21% to 25% in the small bowel regions. The sensitivity of CT detection of peritoneal implants ranged from 67% to 84% in the abdominopelvic regions and from 56% to 57% in the small intestinal regions. The specificity of CT detection of peritoneal lesions was 100% in all regions. Preoperative CT identification of larger peritoneal lesions in the right upper quadrant (p=0.016), epigastrium (p=0.003), left upper quadrant (p=0.019), proximal jejunum (p=0.022), distal jejunum (p=0.022) and proximal ileum (p=0.022) predicted for development of severe complications. Similarly, larger peritoneal lesions in the right upper quadrant (p=0.039), epigastrium (p=0.024), right flank (p=0.005), right lower quadrant (p=0.034) was negatively associated with disease-free survival, and the right upper quadrant (p=0.037) was negatively associated with overall survival. Conclusion Preliminary data suggests that preoperative CT scan depicting extensive upper abdominal and small bowel dis-

ease predicts for severe complications post cytoreduction. Extensive disease in the right upper quadrant appears to be associated with a poorer survival outcome.

P203

Lymph node metastasis predicts survival in patients with high-grade appendix cancer H.M. El Halabi,* V. Gushchin, R. Macdonald, J. Francis, N. Athas, A. Sardi. *Institute for cancer care Mercy Medical center, Baltimore, MD.*

Background: In treating patients with high-grade appendix cancer, appropriate patient selection for cytoreductive surgery (CRS) and heated intraperitoneal chemotherapy (HIPEC) is essential. The effect of lymph node (LN) status on survival is not clear from previous studies. We hypothesize that LN metastases negatively affect long-term survival. Methods: A retrospective analysis of peritoneal mucinous carcinomatosis (PMCA) patients from a prospectively managed database was conducted. LN status was compared to completeness of cytoreduction (CC) and peritoneal cancer index (PCI). Their effect on survival by using Kaplan-Meier survival curves and Cox proportional hazards ratio analysis was studied. Results: From 134 patients with appendix cancer that underwent CRS and HIPEC 77 had high-grade disease (PMCA). The mean follow up was 22 months, range (3-90 months). The OS was 91%, 74%, and 70% for 1, 3, and 5-years respectively. Thirty-one patients (40%) had LN metastasis. Mean PCI score was 29.8 (SD 11.7) and 23.1 (SD 14.4) in patients with positive and negative LN respectively. Complete cytoreduction was achieved in 58 out of 77 Patients (75%), while it was 65% in patients with positive LN and 82% if LN were negative. The 5-year OS for patients with LN metastasis was 14 % compared to 64 % when LN metastasis was absent (p=0.002). Among patients with complete cytoreduction, the 5-year OS for LN metastasis present vs. absent was 21% and 73% respectively (p=0.002). On multivariate regression analysis including LN status, CC score and PCI, the following hazard ratios and confidence intervals were obtained 2.5 (95% CI 0.9-6.3), 3.0 (95% CI 1.2-7.8), and 2.3 (95% CI 0.6-8.5), respectively. Conclusion: CRS and HIPEC are effective in treating high-grade appendix cancer with LN metastasis if complete cytoreduction can be achieved. However, LN status was a significant predictor of survival and that should be strongly considered in patient selection.

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Safety of Pancreaticoduodenectomy in Patients Older than 80 Years: Risk vs. Benefits M. Melis,[1]* F. Marcon,[2] U. Sarpel,[2] G. Miller,[2] H. Moore,[2] S. Cohen,[2] R. Berman,[2] H.L. Pachter,[2] E. Newman.[2] *1. NYHHS VAMC and NYU School of Medicine, New York, NY; 2. New York University School of Medicine, New York, NY.*

Introduction: Surgery offers the only chance for cure in patients with pancreatic cancer. Currently, pancreaticoduodenectomy can be performed with a mortality of under 5% and a morbidity of 40-50%. Little, however, is known about outcomes of pancreaticoduodenectomy (PD) in octogenarians. This manuscript details outcomes after PD for adenocarcinoma in patients 80 years and older. Methods: From our comprehensive pancreatic adenocarcinoma database of 248 patients, we identified 200 patients who underwent PD (1990-2009). We categorized patients into two groups, according to age at time of surgery: Group I (≥ 80 year-old) and Group II (< 80 year-old). The study end-points were length of post-operative stay (LOS), overall morbidity, 30-day mortality, overall survival (OS). Differences between groups were evaluated using t-test or chi-squared test. Survival was compared using Kaplan–Meier analysis and log-rank test. Results: There were 25 patients in group I (mean age 83.1) and 175 patients in Group II (mean age 64.4). Octogenarians had worse ECOG performance status (PS ≥ 1 in 90% vs. 50.8%, $p < 0.01$) and ASA score (ASA 3-4 in 70.8% vs. 47.4%, $p < 0.01$). The two groups were similar in regard to underlying co-morbidities (including coronary artery disease, COPD, diabetes, chronic renal failure), operative time, rates of portal vein resection, intraoperative complications, blood loss, pathologic AJCC stage, status of resection margins. Octogenarians had longer LOS (20 vs. 13.7 days, p=0.01) and higher overall morbidity (68% vs. 44%, p=0.03). There was a single death in each group (p=0.23). At median follow-up of 13 months older patients had a median OS of 17.3 months compared to 13.1 months in younger patients (p=0.06). Conclusions: Surgical morbidity and LOS are significantly increased in octogenarians. However 30-day mortality was not significantly increased and OS was superior (but not statistically significant) when compared to younger patients. The decision for PD should be individualized and offered to carefully selected octogenarians.

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Emergent GI surgery in patients who have undergone radiotherapy has increased complications and mortality: A review of 536 patients M.C. Sullivan,[1]* F. Li,[2] S. Yu,[2] S.A. Roman,[1] J.A. Sosa.[1] *1. Yale University School of Medicine, New Haven, CT; 2. Yale Center for Analytical Sciences, New Haven, CT.*

Background: There is a paucity of data for patients undergoing emergent GI surgery following radiation therapy (RT). This study examines morbidity and mortality of patients having emergent GI surgery ≤90 days after RT. Methods: We identified patients ≥18 yrs who had RT ≤90 days before emergency surgery in ACS-NSQIP 2005-8. Patients having concomitant chemotherapy were excluded. Subjects were compared to a control group who did not have preop RT but underwent similar emergent procedures (matched 1:1 on age and procedure/CPT code). Demographic and clinical characteristics, including patient comorbidities, functional status, and preop lab values, were assessed. Primary outcomes included 30-day postop morbidity and mortality. Log-transformed data, bivariate and multivariate linear and logistic regression were used. Results: 536 patients were selected: 268 per group. Patient demographics and preop comorbidities were similar between groups. The most common procedures were partial colectomy, exploratory laparotomy, and small bowel resection. The RT group had greater mortality (23.9% vs. 11.6%, p<.001; OR:2.4), more major complications (45.1% vs. 34.7%, p= .014; OR:1.55), and a greater likelihood of ≥1 complication (48.1% vs. 38.1%, p =.019; OR:1.51). Average number of complications per patient also was greater in the RT group (p=.042). Days from admission to operation, operative time, number requiring re-operation, days from operation to death, and total LOS were not statistically different. Multivariate analysis identified 5 variables predictive of death: disseminated cancer, preop impaired functional status, low albumin, hypernatremia and intraop transfusion. Three variables were associated with postop complications, and 5 with major complications: COPD, high preop BUN, prior operation within 30 days, intraop transfusion, and >1 intraop procedure. RT was not an independent predictor of death or postop complication. Conclusions: Patients needing emergent GI surgery within 90 days of RT have higher morbidity and mortality. Pre-op lab abnormalities and intra-op events are modifiable factors which may improve RT patient outcomes.

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Detection and Prognostic Impact of Micrometastasis in Colorectal Cancer S. Saha,[1]* M. Kanaan,[1] S. Sirop,[2] A. Korant,[1] D. Wiese,[1] D. Eilender,[1] S. Nagpal,[1] M. Arora,[1] T. Singh.[1] *1. McLaren Regional Medical Center-Michigan State University, Flint, MI; 2. Mayo Clinic Foundation, Rochester, MN.*

Introduction: The prognostic impact of micrometastasis(Mmets) in colorectal carcinoma(CRC) is still somewhat controversial. In order to determine the prognosis of Mmets in CRC, a review of literature was performed on studies that had survival data including disease-free survival(DFS), overall survival(OS) and/or recurrence rate. The results of those studies were compared with our pilot series of sentinel lymph node mapping(SLNM) regarding the prognostic impact of Mmets in colon cancer patients(pts) after receiving chemotherapy. **Methods:**A search of the English literature from 1993-2010 was done from MEDLINE and Cochrane library databases using the following terms:Mmets, prognosis, CRC. Among 16 studies included, 13 used immunohistochemical(IHC) staining and 3 used reverse transcriptase-polymerase chain reaction(RT-PCR). In our trial, a retrospective review of 109 consecutive pts with colon cancer was undertaken. Minimum follow up was 5 years. All pts underwent SLNM at surgery. SLNs were examined by multilevel sections and CK-IHC for detection of Mmets while non-SLNs with conventional H&E. The 5-year DFS was compared among pts with Mmets, macrometastasis and node negative disease(NND). **Results:**A total of 1221 pts from 16 studies with colon(875 pts) and rectal(346 pts) cancers were included. Mmets was detected in 27%(323/1221) pts. The detection rate increased from 25 % in IHC group to 37 % in RT-PCR group. For IHC group, 6 out of 13 studies revealed that Mmets was associated with poorer prognosis compared to NND, one found correlation with poor prognostic factors, and the others revealed no influence on prognosis. In all 3 RT-PCR studies Mmets was associated with poor prognosis when compared to NND. In our trial of 109 pts,

13% had Mmets, 30% had macrometastasis and 57% had NND. Pts with Mmets were upstaged to stage III, and treated with chemotherapy. The 5-year DFS was 100%, 75% and 96% in pts with Mmets, Macrometastasis and NND respectively.(Table 1) **Conclusion:**Most analysis revealed that Mmets carries a poorer prognosis when compared to NND. Our pilot study showed improved prognosis of Mmets after being upstaged and treated with chemotherapy when compared with NND.

Table 1: A)Summary of 16 studies included in review. B) Our pilot study distribution and 5-year disease disease free survival in patients with Micrometastasis/Macrometastasis/Node Negative Disease in patients with colon cancer

A: Summary of 16 studies included in the review

	Number of studies	Total sample size	Colon cancer patients	Rectal cancer patients	Percentage of micrometastasis (number of pts with micrometastasis /total number of pts included in the study)	Results
IHC studies	13	1003	735	318	25%	6 out of 13 studies revealed that Micrometastasis was associated with poorer prognosis compared to Node negative disease, one revealed correlation with poor prognostic factors, and the others revealed no influence on prognosis.
RT-PCR studies	3	175	118	57	37%	Micrometastasis was associated with poor prognosis when compared to Node negative disease in all 3 studies
Total	16	1221	875	346	27%	10 studies revealed that micrometastasis was associated with poor prognosis when compared to node negative diseas

B: Our pilot study distribution and 5-year disease free survival in patients with micrometastasis/macrometastasis/node negative disease in colon cancer

		Node negative disease	Micrometastasis	Macrometastasis
Total number of patients		62	14	33
Stage	I	32 (51.6%)	0	0
	II	30 (48.4%)	0	0
	III A	0	4(28.6%)	3(9.1%)
	III B	0	10(71.4%)	16 (48.5%)
	III C	0	0(0.0%)	14(42.4%)
Average tumor size(cm)		4.1	3.7	4.4
5 year disease free survival		96%	100%	75%

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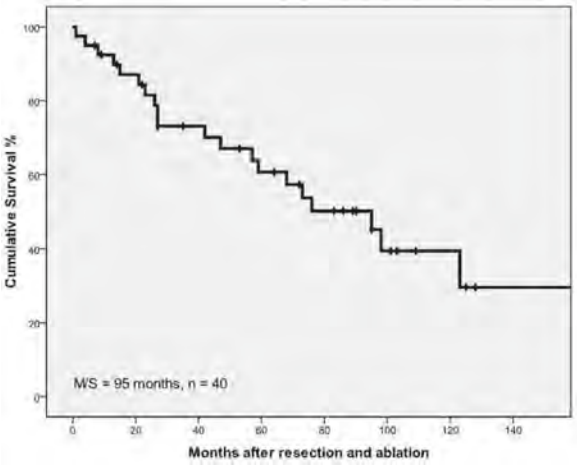
Optimizing the Surgical Effort in Patients with Advanced Neuroendocrine Tumor Hepatic Metastases by Combining Hepatic Resection with Ablation: A Critical Analysis of 40 Patients A. Saxena,* T.C. Chua, J. Zhao, D.L. Morris. *UNSW Department of Surgery, St George Hospital, Sydney, NSW, Australia.*

Background The liver is the most common site of metastasis from neuroendocrine tumors (NET). Surgical extirpation of NET hepatic metastases (NETHM) provides the best opportunity of long term survival but is not feasible in the majority of patients given the widespread presentation of the disease. Combining resection with local ablation can potentially expand the resection criteria and thereby improve survival. The current study, the first of its kind, critically evaluates the progression-free survival (PFS) and overall survival (OS) of patients with NETHM who underwent concomitant hepatic resection and ablation. Methods Forty patients with NETHM underwent concomitant hepatic resection and ablation between December 1992 and June 2010. Patients were assessed radiologically and serologically at monthly intervals for the first three months and then at six monthly intervals after treatment. PFS and OS was determined; clinopathological and treatment-related factors associated with PFS and OS were evaluated through univariate and multivariate analyses. Results No patient was lost to follow-up. The median follow-up for the patients who were alive was 61 months (range 1 to 162). The median PFS and OS after hepatic resection was 22 and 95 months, respectively. Five-year and 10-year overall survival rate was 61% and 40%, respectively. One independent factor was associated with OS: histological grade (p=0.001). One independent factor was associated with PFS: extra-hepatic disease (p=0.003) Conclusion Concomitant hepatic resection and ablation is associated with excellent survival outcomes in selected patients. This treatment modality can expand the role of surgery in the management of NETLM and thereby improve patient outcomes.



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Molecular Factors Associated with Recurrence and Survival in Patients with Intrahepatic Cholangiocarcinoma: A Guide to Adjuvant Clinical Trials S.C. Schiffman,* C.R. Scoggins, K.M. McMasters, R.C. Martin. *University of Louisville, Louisville, KY.*

BACKGROUND: The prognosis for intrahepatic cholangiocarcinoma (ICC) remains variable and the specific factors influencing survival are unclear. This study sought to determine the clinical and molecular factors related to recurrence and survival in patients with ICC status post hepatectomy. METHODS: A review of prospectively-collected hepatobiliary database from 1997 to 2009 identified 185 consecutive patients with ICC. Molecular markers (Ki-67, P-53, B catenin) and standard pathological evaluations were performed. Predictors of recurrence and survival were determined. RESULTS: Thirty four patients with ICC status post hepatectomy were identified. The median age was 64 years (36-81). The most common surgical resections were right hepatectomy (n=11), extended right hepatectomy (n=8), and left hepatectomy (n=7). The 90 day mortality was 11.8%. The median tumor size was 7.8 cm (2.2-16 cm) and nine patients (26.5%) had positive lymph nodes. Nine patients (26.5%) received adjuvant therapy. After a median follow up of 33.5 months, the median disease free interval was 6 months (1.3-83 mos) and the median overall survival was 37.9 months. In an evaluation of recurrence, univariate predictors were tumor size (p=0.02) and differentiation (p=0.05). On multivariate analysis, differentiation (p=0.03; OR=0.38; 95%CI: 0.17-0.89) remained significant. In an evaluation of survival, univariate predictors were tumor size (p=0.02), lymphovascular invasion (p=0.02), satellite nodules (p=0.006), B-catenin expression (p=0.008), and recurrence (p=0.026). On multivariate analyses, satellite lesions (p=0.05, OR=3.15, 95% CI: 0.96-10.4) and B-catenin (p=0.04, OR=3.23; 95% CI: 1.1-9.7) remained significant and differentiation (p=0.045; OR=0.42; 95% CI: 0.18-0.98) was identified as an additional predictor of survival. CONCLUSION: Certain molecular markers and pathologic factors influence recurrence and survival for patients with ICC status post hepatectomy. Future clinical trials should include these predictors of outcome in order to determine the necessity and type of adjuvant therapy that should be offered.

Predictors of survival and recurrence

PREDICTORS	RECURRENCE		SURVIVAL	
	UNIVARIATE	MULTIVARIATE	UNIVARIATE	MULTIVARIATE
SIZE	0.02		0.02	
NODAL STATUS	0.42	0.03 (OR=0.38; CI:0.79-0.9)	0.11	
DIFFERENTIATION	0.05		0.09	0.045 (OR=0.4; CI:0.18-0.9)
LVI	0.12		0.02	
SATELLITE NODULES	0.13		0.006	0.05 (OR=3.2; CI:1-10)
KI-67	0.98		0.44	
P53	0.16		0.08	
B-CATENIN	0.18		0.008	0.04 (OR=3.2; CI:1-9.7)
MARGIN STATUS	0.42		0.75	

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Evaluation of the Incidence and Pattern of local Recurrence Following Sphincter Saving Resection for Low Rectal Cancer

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Rationale:Abdomino-perineal resection has been the standard treatment for rectal tumours within 5cm from the anal verge. Sphincter saving resection has become a valid surgical option.Aim: Evaluation of the incidence and pattern of local recurrence in patients with T1-2 &T3 rectal cancer, who underwent Intersphincteric Resection (ISR) without radiation therapy .Study Design:Between the year 2004-2009, 55 patients with T1-3 rectal cancer located within 5cm from the anal verge (median 2.3 cm) were included in the study.21 patients were T1-2 &34 were T3. Primary rectal resection (ISR) with Total Meso Rectal excision(TME) was performed for all patients. Partial ISR was done for 35 patients while complete ISR& external sphincter resection was performed for 20 patients. Lateral node dissection was carried out in all T3 patients.Patients were followed for a median of 1.5 years (Range 1-4.6 years).Results:The surgical morbidity occurred in 14 patients (25%) with one mortality from pelvic sepsis.15 patients were managed conservatively and 3 patients were re-operated upon. The 3 years cumulative overall recurrence rate was (10%), local recurrence rate was 5.4% (3 patients) & overall survival was 89% . The estimated local recurrence rate in T1-2 was 0% when compared to T3 10%,($p \leq 0.001$). In T3 patients all local recurrences(3 patients) occurred in this group, the pattern of recurrence in the 3 patients were,one patient with sacral recurrence and two patients with lateral nodal recurrence (obturator group & internal iliac one).All the three patients had positive(CRM). The 2 years rate of local recurrence in negative and positive (CRM) were 5% & 33% respectively (P=0.0003).The estimated 3 years cumulative distant metastasis occurred in T1-2& T3 was 5% &18% respectively..Conclusion:Intersphincteric resection with total mesorectal resection does not affect the local recurrence or overall survival rate. In early rectal cancer T1-2, there is no need for radiation therapy with meticulous dissection and stump irrigation. In T3 lesions neoadjuvant radiation therapy is to be considered for better local control of the disease.

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Treatment of rectal cancer is safe among octogenarians: analysis of a single institution's short-term operative risk using advanced techniques E. Flanagan,* D. Schnipper, K. Kolli, L. Smith, A. Kumar.
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Purpose: The prevalence of rectal cancer increases with life expectancy. In octogenarians, optimal surgical planning, local excision vs. standard resection, necessitates consideration of long-term survival. This study compares transanal endoscopic microsurgery(TEM) to local excision in octogenarians, relating results to epidemiologic rectal cancer long-term survival data using SEER7 Database. Methods: From a single institution database of 300 local excisions of rectal neoplasms performed over a 10 year period, we compared local excision and TEM. STATA10 was used to compare perioperative outcomes among patients >80 (N=35), and <80 (N=265). Comparison of 5 year relative survival rates of rectal cancer patients <80 years (N=12,675) and >80 (N=2,794) via the actuarial method (CI 95%) was performed using the NCI SEER7 Database 1999-2002. Results: TEM was utilized in 24 octogenarians(69%); 5 with advanced tumors for palliation, while 19 patients underwent curative resection by TEM, 8 for cancer. Blood loss was <30 ml in 78%. Average length of stay was 0.53 days (range 0-7) with 60% of patients discharged from the PACU. Octogenarians were more likely to require admission than their counterparts (p=0.03). Postoperative urinary retention was statistically significant in TEM patients >80 compared to <80 years(p=0.003). Despite severe comorbidities (MI, CVA, CHF and COPD), there were no perioperative mortalities. 68% of patients treated with curative intent were followed for an average of 40 months(range 5-133), of which recurrence occurred in 5%, death in 3%. SEER7 data reports the national rectal cancer 5 year survival rate in patients <80 years as 66.5% vs. 55% for those >80. Stage specific 5 year survival of patients <80 is 90.6% (Stage I), 72.8% (Stage II), 62.9% (Stage III), and 9.2% (Stage IV) vs. patients >80: 74.1% (Stage I), 59.5% (Stage II), 41.3% (Stage III), and 3.0% (Stage IV). Conclusions: Advanced techniques for local excision of rectal neoplasms are safe and feasible in octogenarians. Minimally invasive techniques will play an increasingly important role in the aging population.

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Local recurrence rate of liver tumors after radiofrequency ablation (RFA) M. Lutke Holzik,* A. Schepen, J. Van der Palen, J.M. Klaase.
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Objective:Local recurrence rates of 5-46% after RFA have been mentioned in literature. The aim of this study is to evaluate success of RFA in our non-academic clinic by measuring the local recurrence rate and to compare this rate with data from literature. Patients and methods: RFA-treated patients were selected from a database containing all patient data of 176 liver operations in 156 patients performed between 1995 and 2010 in our hospital. It involved 41 patients, 32 (78%) patients were treated with RFA for colorectal liver metastases (CRLM), 5 (12%) for HCC and 4 (10%) for metastases from another primary tumor. The local recurrence rate was calculated over the total number of tumors treated with RFA. Results: 58 tumors (in 41 patients) were treated by RFA, the median follow-up was 15 (0-74) months. 9 (22%) patients were treated by RFA because of a poor physical condition, 6 (15%) patients because of an expected remaining liver volume of less than 30% after resection, 4 (10%) patients because of the central location of the liver tumor, 15 (37%) patients due to diffuse spread of metastases and 7 (17%) patients had another indication. 23 (56%) patients were treated with RFA by laparotomy, 2 (5%) patients with percutaneous RFA and 16 (39%) patients by RFA combined with liver resection. The local recurrence rate was 13 (22%). Patients treated with RFA by laparotomy had a local recurrence rate of 21%, patients treated with RFA and resection 32%. Patients treated with percutaneous RFA had no local recurrences. There proved to be no relationship between the the presence of local recurrences and the overall diameter of RFA treated liver tumors ($p = 0.59$) and the number of liver tumors ($p = 0.48$). Conclusion: A local recurrence rate of 22% following RFA is high but fits within the range mentioned in literature. A stronger indication for RFA (smaller tumors and more accurate placement of RFA needles), should decline the amount of local recurrences.literature. A stronger indication for RFA (smaller tumors and more accurate placement of RFA needles), should decline the amount of local recurrences

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Impact of Body Mass Index on Outcomes of Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy K. Fournier,* R. Royal, S. Rafeeq, C. Eng, M. Overman, M. Taggart, T. Sagebiel, A. Matamoros, P. Mansfield. *University of Texas, MD Anderson Cancer Center, Houston, TX.*

Background: Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) can be associated with substantial morbidity and mortality. Obesity is increasingly common in these patients. We sought to evaluate the impact of Body Mass Index (BMI-kg/m2) on outcomes in patients with appendiceal adenocarcinoma undergoing CRS/HIPEC. Methods: All patients with a pathologic diagnosis of appendiceal cancer who underwent

CRS/HIPEC at a single institution between September 1993 and July 2009 were retrospectively reviewed to identify patients with a BMI greater than 30. This study was performed comparing the incidence of surgical complications and outcomes among obese patients (BMI≥30) versus a control group (BMI<30) matched for age, gender, year of diagnosis and extent of disease. Patient demographics, Peritoneal Carcinomatosis Index (PCI), operative details, complications, pathology, recurrence, overall (OS) and disease free survival (DFS) were analyzed. Results: 167 patients underwent CRS/HIPEC. Of those, 52 (31%) were obese. Comparison with 52 control subjects demonstrated no differences in patient demographics or PCI 15.2 v 15.5 (p=0.9) except for BMI-24.8 (19.9-29.2) v. 33.7 (30.02-42.65) in normal v. obese (p=0.0001). There were no deaths in either group. There were no statistically significant differences between groups in regards to operative blood loss or operative time. The incidence of complications and length of hospital stay were also similar between the 2 groups (table). The 3 year DFS was 67% v. 68% in non-obese v. obese (p=NS). There was a trend towards decreased 3 year overall survival 78% v. 85% in obese v. non-obese (p=0.09) patients. Conclusions: Obesity does not appear to increase the risks for postoperative morbidity in patients undergoing CRS/HIPEC. A high BMI should not be considered a contraindication to using CRS/HIPEC for the operative management of disseminated appendiceal cancer.

Perioperative Outcomes According to BMI

	BMI<30	BMI≥30	
	Median	Median	p-Value
BMI	24.8	33.7	0.0001
PCI	15.5	15.2	0.9
Operative Time (minutes)	562	596	0.4
Blood Loss (cc)	720	901	0.2
Complicatioins (per patient)	1.7	1.6	0.8
Lenght of stay (days)	25.2	29	0.2

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Impact of synchronous digestive surgery on the outcome of two-stage hepatectomy M. Stella,* A. Dupre, S. Chabaud, T. Gargi, P. Meeus, M. Rivoire. *Léon Bérard Cancer Center, Lyon, France.*

Aim: To compare feasibility, outcomes and long-term results of two-stage hepatectomy with or without synchronous surgery of the digestive tract. Methods: We analyzed a prospective database of 63 patients with unresectable bilobar colorectal liver metastases undergoing two-stage hepatectomy between July 1995 and November 2009. Patients undergoing a digestive resection in association with the first and/or the second hepatectomy (group I) were compared to patients without associated digestive surgery (group II). Results: Seven patients undergoing only portal vein embolization without liver resection during the first procedure were excluded from the study. Of the remaining 56 patients, 35 were in group I and 21 in group II. Seven patients (3 in group I, 4 in group II) did not undergo second hepatectomy because of tumor progression. All but two patients (group I) received preoperative chemotherapy. All but 4 patients in group II ($P < 0.05$) presented synchronous liver metastases (median number 7). The type and extension of hepatectomy as well as the rate of portal vein embolization (62.5%) did not differ in the two groups. The mean interval between hepatic procedures was similar in the two groups: 2.8 and 3.3 months for groups I and II respectively. One patient died of postoperative liver failure (group I) after the second hepatectomy. Postoperative morbidity rates following first and second hepatectomy were comparable : 37.1% (group I) vs 28.6% (group II) and 46.9% (group I) vs 52.9% (group II) respectively. The mean hospital stay after the first hepatectomy was longer (15.2 days) in group I than in group II (12 days) ($P < 0.01$). After the second hepatectomy, it was similar in the two groups (14.2 days). With a median follow up of 59 months, the 3-year overall survival and 1-year progression-free survival rates were 39% vs 58% ($P = 0.023$) and 71% vs 81% ($P = 0.31$) in groups I and II respectively (intent-to-treat analysis). Conclusions: For patients presenting with synchronous primary colorectal tumor associated with bilobar unresectable liver metastases, digestive tract resection associated with two-stage hepatectomy is safe and does not increase postoperative mortality or morbidity.

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Risk Prediction in Hepato-Pancreato-Biliary Surgical Oncology T.M. Pawlik,[1]* K. Bilimoria,[2] J. Smiley,[3] M. Cohen,[3] C. Ko,[4] H. Pitt.[5] *1. Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD; 2. M.D. Anderson Cancer Center, Houston, TX; 3. American College of Surgeons, Division of Research, Chicago, IL; 4. UCLA, Los Angeles, CA; 5. Indiana University, Indianapolis, IN.*

Introduction: Hepatic, pancreatic and complex biliary (HPB) oncologic surgery can be associated with major morbidity and significant mortality. For the past five years, the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) has gathered robust data on patients undergoing HPB surgery. We sought to use the ACS-NSQIP data to determine which preoperative variables were predictive of adverse outcomes in patients undergoing HPB oncologic surgery. Methods: Data collected from ACS-NSQIP on patients undergoing hepatic, pancreatic, or complex biliary surgery between 2005-2009 were analyzed (n=13,558). Diagnoses and surgical procedures were categorized into 10 and 8 groups, respectively. Seventeen preoperative clinical variables were assessed for prediction of postoperative morbidity and mortality. Multivariate logistic regression was utilized to develop a risk model. Results: Of the 13,558 patients who underwent an HPB procedure, 7321 (54%) had pancreatic, 4881 (36%) hepatic, and 1356 (10%) complex biliary surgery. Overall, 70.3% of patients had a cancer diagnosis. Post-operative complications occurred in 3850 patients for an overall morbidity of 28.4%. Serious complications occurred in 2522 (18.6%) patients; 366 patients died for an overall peri-operative mortality of 2.7%. Peri-operative outcome was associated with diagnosis and type of procedure (Table). Specifically, hepatic trisectionectomy (5.8%) and total pancreatectomy (5.4%) had the highest 30-day mortality. Of the 17 preoperative variables examined, 6 significantly predicted morbidity and mortality: age > 74, dyspnea with moderate exertion, steroid use, prior cardiac procedure, ascites, and pre-operative sepsis (all $P<0.05$). Conclusions: While overall morbidity and mortality for HPB oncologic surgery is low, peri-operative outcomes are heterogeneous and depend on diagnosis, procedure type, and key clinical factors. By combining these factors, an ACS-NSQIP "HPB Risk Calculator" may be able to better risk-stratify patients being considered for complex HPB surgery.

Morbidity and Mortality Stratified by Diagnosis and Procedure

Diagnosis/Procedure	Overall Morbidity	Serious Morbidity	30-Day Mortality
All Patients	28.4	18.9	2.74
Hepatic Malignancy	21.0	13.2	2.41
Pancreatic Malignancy	30.8	19.9	3.53*
Biliary Malignancy	38.6*	26.9*	2.56
Trisectionectomy	32.8*	22.5†	5.82*
Total Pancreatectomy	31.9	23.5*	5.42*

*p<0.01, †p<0.05 vs All Patients

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Preliminary evaluation of accuracy of diffusion-weighted magnetic resonance imaging in preoperative nodal staging of rectal cancer K. Sato,[1]* T. Akasu,[2] M. Miyake,[2] H. Motohashi,[2] M. Takawa,[2] Y. Arai,[2] G. Iinuma.[2] *1. Surgery, Ome Municipal General Hospital, Tokyo, Japan; 2. National Cancer Center Hospital, Tokyo, Japan.*

Background: We previously reported accuracy of high-resolution (HR) magnetic resonance imaging (MRI) in preoperative staging of rectal cancer (Ann Surg Oncol 2009). Especially, accurate nodal staging is essential for deciding treatment. The aim of this study was to evaluate whether an addition of diffusion-weighted (DW) MRI improve an accuracy of preoperative nodal staging for rectal cancer. Methods: Between April and December 2007, 40 patients with primary rectal cancer were examined with HRMRI and DWMRI using a 1.5-T or 3-T scanner and underwent radical surgery. Lymph node metastasis was assessed prospectively and classified according to the TNM system by pathologists blind to clinical information. A clinical fellow with 1-year experience of diagnostic radiology retrospectively reviewed HRMRI images and measured the short-axis diameters of the pelvic lymph nodes, and then HRMRI plus DWMRI images were evaluated. Patient-by-patient, receiver operating characteristic curve analyses were performed. Results: Of the 18 patients with lymph node metastasis, 17 had mesorectal and 5 had lateral pelvic node involvement (3, right; 2, left). Area under the receiver operating characteristic curves

(AUCs) of HRMRI for mesorectal, right lateral pelvic, and left lateral pelvic nodes were 0.54 (95% confidence interval, 0.34–0.74), 0.49 (0.19–0.79), and 0.53 (0.19–0.88), respectively. AUCs of HRMRI plus DWMRI for mesorectal, right lateral pelvic, and left lateral pelvic nodes were 0.62 (0.44–0.81), 0.89 (0.76–1.0), and 0.96 (0.90–1.0), respectively. Conclusions: This study suggests that an addition of DWMRI to conventional HRMRI may improve diagnositic accuracy of staging for both mesorectal and lateral pelvic lymph node metastasis from rectal cancer.

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In-vitro Sensitivity to 5-FU and Gemcitabine in Pancreatic Cancer

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BACKGROUND: Gemcitabine and 5-fluorouracil (5-FU) represent the mainstay of chemotherapeutic options for pancreatic cancer. Currently, approximately 40% of patients with pancreatic cancer receive chemotherapy. Relapse is common after resection and adjuvant therapy, and response rates are low in patients with advanced/metastatic disease. The purpose of this study was to describe the prevalence of in vitro drug sensitivity or resistance to these agents in pancreatic cancer and explore the clinical implication of in vitro assessment. METHODS: From August 2006 to January 2010, 74 specimens from patients with primary/metastatic pancreatic cancer were tested for response to gemcitabine, 5-FU, and their combination using an in vitro chemosensitivity assay (ChemoFx, Precision Therapeutics, Pittsburgh, PA). Tumors were classified as sensitive or resistant based on in vitro dose response curves. RESULTS: Thirty-four of the 74 tumor specimens (46%) exhibited in vitro chemosensitivity to gemcitabine, 5-FU, or their combination. Fourteen tumors (19%) were sensitive to gemcitabine, and 12 (16%) to 5-FU. Of the 60 patient specimens resistant to gemcitabine, 4 (7%) were sensitive to 5-FU. Conversely, of the 62 specimens resistant to 5-FU, 6 (10%) were sensitive to gemcitabine. Eight of the 74 specimens (11%) were sensitive to both gemcitabine and 5-FU and 56 (76%) were resistant to both agents. Of these 56 specimens, 16 (29%) showed sensitivity to the gemcitabine/5-FU combination. CONCLUSIONS: The ChemoFx data indicates a high (76%) in vitro resistance rate to traditional chemotherapy. In vitro chemosensitivity to gemcitabine only partially overlaps with that of 5-FU and the gemcitabine/5-FU combination. Thus, tumors resistant to one drug, were not necessarily resistant to the other and vice versa. Further correlation with clinical outcomes is needed to determine the clinical efficacy of the ChemoFx assay.

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Colorectal cancer in patients with inflammatory bowel disease

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Introduction: One of the most feared complications of chronic inflammatory bowel disease (IBD) is the development of colorectal neoplasia. Severity, frequency and chronicity of disease are associated with increased risk of developing colorectal cancer. We reviewed the clinical features of our patients with ulcerative colitis or Crohn's colitis who developed colorectal cancer. to see if there were any differences from non IBD colorectal cancer patients. Methods: We performed a retrospective chart review of patients referred to our practice with ulcerative colitis or Crohn's colitis from 2001 to 2010. Patient demographics, type of inflammatory bowel disease, presence and location of neoplasm were recorded. Time interval between the diagnosis of IBD and development of neoplasm, tumor stage and tumor differentiation were also noted. Results: A total of 269 patients presented with inflammatory bowel disease with colonic involvement, of which 125 (46.5%) had Crohn's colitis and 144 (53.5%) had ulcerative colitis. Of the 18 (6.7%) patients who developed colorectal cancer, 14 (78%) had ulcerative colitis and 4 (22%) had Crohn's colitis. The median age of diagnosis with IBD was 30 years (range: 7-39 yrs), and the median age of diagnosis with cancer was 53 years (range: 38-71 years). The median time between IBD diagnosis and cancer diagnosis was 26years (range: 9-43 years). Of the 15 patients who had surgery the pathologic stages revealed 1 (7%) patient with stage 4 cancer, 4 (27%) with stage 3, 6 (40%) with stage 2, and 4 (27%) stage 1 patients. Only 7 (39%) patients with colorectal cancer had evidence of preexisting polyp. Eight of the 18 patients had anorectal cancer. Eight (53%) patients had moderately differentiated tumors, and 4 (27%) had poorly differentiated tumors. Conclusion: There is a long interval period between diagnosis of IBD and development of colorectal cancer. Patients with ulcerative colitis are more likely to develop cancer. The median age of colorectal cancer development in patients with chronic IBD is much younger than that of the general population. This underscores the necessity for aggressive screening and surveillance strategies for these patients.

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Postoperative mortality following liver resection for metastatic disease in the elderly

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INTRODUCTION: Postoperative mortality following liver resection for metastatic disease has not been well characterized in the elderly. Our aim was to examine the risk and predictors of mortality following liver resection in elderly patients with liver metastasis. We hypothesized that mortality in well-selected patients is low and comparable to that seen in younger patients. METHODS: Patients undergoing liver resection for liver metastasis were identified from the National Inpatient Sample Database (2005-2008) using a validated diagnostic algorithm. Patients were categorized into young (<65 y), old (65-74y), and oldest (≥75y) age groups. Clinical, surgical, and outcome data were recorded. Univariate and multivariate analyses were performed. RESULTS: 4,026 patients with liver resection were identified. Elderly patients (old + oldest) comprised 37% (n=1,475) of the population. Increasing age was associated with a higher comorbidity index (CI); 41.8% in the oldest group had a CI ≥3 compared to 39.5% and 36.5% for the old and young groups, respectively ($p<0.001$). Overall mortality rate was 1.8%; mortality was higher but still low in the oldest compared to the old and younger groups (3.3% vs. 2.2% vs. 1.2%, $p=0.005$). On multivariate analysis, age ≥75y (OR 2.5 [1.4-4.6]), CI ≥3 (OR 1.8 [1-3.1]), and major resection (lobectomy) (OR 1.7 [1.1-2.8]) were identified as independent predictors of postoperative mortality. CONCLUSIONS: Well-selected elderly patients experience higher –yet acceptable- rates of postoperative mortality following hepatectomy for liver metastasis. Advanced age alone should not be considered a contraindication to liver resection; other predictors such as comorbidities and the required extent of surgery should be examined to help select elderly patients most likely to benefit from liver resection.

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Total number of lymph nodes retrieved is prognostic of survival in St. III colon cancer patients treated with adjuvant chemotherapy

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Introduction: Total number of lymph nodes (LN) retrieved has been well documented to improve survival for St. II colon cancer (CC) patients. Since adjuvant chemotherapy is given to node positive patients, the survival benefit of total LN retrieval in St. III CC remains undefined. Methods: St. III CC patients treated with adjuvant chemotherapy (n = 178) from 2000 – 2009 were identified from a prospectively maintained clinical database. Median follow up was 38 mos. Total number of LNs, number of positive LNs, and ratio of positive/total number of LNs were evaluated for each patient. Kaplan Meier method was used for survival analyses. Significance was determined using the log-rank test. Cox proportional hazard models were used to determine clinical and treatment factors predictive of survival and of LN retrieval. Results: The 5-yr overall survival (OS) in the entire cohort was 69.3%. 69.1% of the patients had >12 LNs retrieved in their surgical specimens. The total number of LNs retrieved per patient ranged from 1 to 56 (median=16); 111 had N1 and 67 had N2 disease; the median ratio of positive/total LNs was 0.18 (mean ratio=0.26). The cohort was separated into quintiles based on total number of LNs retrieved. OS was improved in the patients who had >23 LNs retrieved (Quintile 5) when compared with those who had fewer (Quintiles 1 – 4) (log-rank $p=0.03$). Total number of LNs ($p=0.002$), positive LNs ($p=0.002$) and cancer differentiation ($p=0.011$) were factors prognostic of OS on multivariate analysis. Age, gender, time period treated, time to chemotherapy, type of procedure (laparoscopic v. open), and t-stage did not affect survival. Younger age ($p=0.09$) and positive LNs ($p=0.0095$) were factors associated with increased total number of LNs retrieved. Conclusion: The identification of positive LNs in CC improves cancer outcomes by directing adjuvant treatment. However, even in node positive patients treated with adjuvant chemotherapy, the total number of LNs retrieved is associated with an improvement in overall survival.

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Motor and Sensory branching of the Recurrent Laryngeal Nerve
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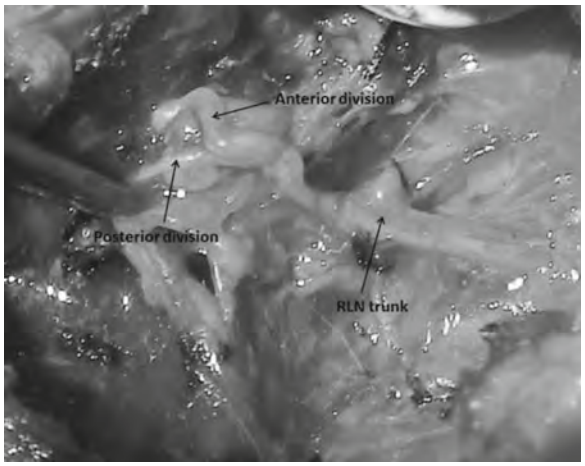
OBJECTIVE: This study aimed to establish the frequency of extralaryngeal bifurcation of the recurrent laryngeal nerve (RLN) and to demonstrate the location of the motor fibers from the sensory fibers within the branches of the RLN. BACKGROUND: Recognition of extralaryngeal branching of the RLN is crucial, as inadvertent division of a branch may lead to significant postoperative complications despite the surgeon believing the nerve was preserved. METHODS: Two years of prospectively collected data from a single surgeon on branching of the RLN. Data were collected in 99 patients undergoing thyroidectomy. Nerve monitoring was utilized to document the position of the motor fibers in the RLNs in all patients. RESULTS: Data on 267 RLNs in the 189 patients were collected (136 nerves were located on the right side and 131 nerves on the left). 117 of these RLNs (43.8%) were bifid, with a distribution of 59 (50.4%) bifurcations on the right, and 58 (49.6%) on the left. Of the 78 Patients dissected bilaterally, bilateral bifurcation occurred in 27 (34.6%) of them. The mean branching distance from the cricothyroid membrane on the right was 5.72 +\- 2.25mm, and on the left was 6.19 +\- 2.29mm. In all 117 cases of bifid RLNs, motor fibers of the vocal cords were located exclusively in the anterior branches of RLN, and none in the posterior branches. CONCLUSION: Extralaryngeal bifurcation of RLN is a common anatomical variant (43.8%). The motor fibers of RLN are located in the anterior branch while the posterior branch is only sensory in function. Great caution is therefore required following the presumed identification of the RLN to ensure there is no unidentified anterior branch to decrease postoperative risk of nerve injury.



Bifurcation of the Recurrent laryngeal nerve trunk into anterior and posterior branches.

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Survival after Reirradiation Therapy Combined with Chemotherapy for Recurrent Head and Neck Squamous Cell Carcinoma
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Introduction: Patients with head and neck squamous cell carcinoma (HNSCC)previously treated with radiation and not suitable for surgery have few curative treatment options. The purpose of this study is to report our ongoing experience with reirradiation and concurrent chemotherapy at a tertiary referral cancer center. Methods: Retrospective cohort study of 56 patients with recurrent HNSCC treated with reirradiation and chemotherapy on protocol. Survival from the initiation of reirradiation was estimated using the Kaplan-Meier method. The Cox proportional hazard model was used for the multivariable analysis (MVA). Results: Twenty-two patients had recurrences in the oral cavity(40%), 11 in the oropharynx(20%), 4 in the hypopharynx(7%), 10 in the larynx(18%), and 7 in the nasopharynx(14%). Median patient age was 61 years(26-88 years). There were 40 males (71%). Fifteen patients (27%) received chemotherapy as part of the initial HNSCC treatment. Fifty-three (95%) patients received cisplatin and paclitaxel with reirradiation. Median first dose of radiation was 60 Gy (15-74 Gy). Median reirradiation dose was 30 Gy (15-60 Gy). Median survival of 10 patients (18%) who did not complete reirradiation was two months. Median survival for the group was 8 months (0.3-138 months). However, 14 patients (25%) survived at least 2 years, and 9 (16%) survived 55 months or more. Prior chemotherapy, oral cavity site and younger age were associated with diminished survival on univariable analysis. On the MVA, patients with oral cavity malignancies were five times more likely to die compared with those with pharyngeal cancers (HR=5; p=0.005, 95%CI: 1.6-16.4). Prior chemotherapy increased the risk of death 9 fold (HR=9; p=0.0001; 95% CI: 3.1-25.4). There was a marginal association between younger age (age < 60) and worse survival (HR=1.8; p=0.09; 95% CI .9-3.83). Conclusion: Although survival remains poor, a subset of patients with head and neck cancer previously treated with radiation are cured with concurrent chemotherapy and reirradiation. Oral cavity malignancies, prior chemotherapy, and age 60 or less were associated with decreased survival.

Multivariable Analysis from The Cox Proportional Hazard Model

Parameter	Class of Variable	Hazard Ratio (HR)	HR Lower CI	HR Upper CI	p Value
Site Group	Larynx vs.Pharynx	1.24	0.43	3.59	0.690
Site Group	Oral Cavity vs.Pharynx	5.17	1.63	16.36	**0.005**
Gender	M vs. F	2.09	0.86	5.13	0.11
Prior Chemotherapy	Y vs. N	8.89	3.11	25.43	**<0.0001**
Age	< 60 vs. >/ = 60	1.87	0.91	3.83	**0.09**
Time Period from First Treatment to Reirradiation (Months)	>30 vs.< / = 30	1.31	0.67	2.54	0.43
Grade 3 to 4 Toxicity	Y vs N	1.64	0.84	3.23	0.15
First Dose of Radiation (Gy)	>60 vs. < / = 60	1.67	0.57	4.91	0.35

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Malignant Melanoma in the Elderly: Different Regional Disease and Poorer Prognosis
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Introduction: Age has been shown to be a poor prognostic factor in melanoma patients. Elderly melanoma patients have been reported to have a different presentation and clinical course than their younger counterparts. Our goal was to evaluate the impact of age ≥70 years (yrs) on the diagnosis and natural history of melanoma in patients who present with poor prognosis melanoma. Methods: Retrospective review of 610 patients with malignant melanoma entered into a prospective sentinel lymph node (SLN) database, treated from June 1997 to June 2010. Disease characteristics and clinical outcomes were compared between patients ≥70 yrs vs. <70 yrs of age using chi-squared tests and t-tests. Mean follow up was 3.8 yrs. Results: 237 patients (39%) were ≥70 yrs. Elderly patients had a higher proportion of head and neck melanomas (34% vs. 20%, p<0.001), and a greater mean tumor thickness (2.4mm vs. 1.8mm, p<0.001). 42% of elderly patients had a T3 or T4 melanoma compared to 23% in the non-elderly (p<0.001). The presence of ulceration was more common in the ≥70 group but was not significant: 29% vs. 23% (p = 0.14). The elderly had a greater mean number of mitotic figures: 3.6/mm2 vs. 2.7/mm2 (p=0.005) including a greater preponderance of lesions with a high mitotic rate (>5mm2, p=0.01). Despite greater mean thickness of melanoma, incidence of SLN metastases was less in the ≥70 yrs group, though not significant (11% vs. 15%, p=0.20) but was dramatically different among T3/T4 melanomas (Table). The elderly had a higher rate of local and in-transit recurrences, 14.5% vs. 3.4% at 5 yrs (p<0.001). 5 yr disease-specific mortality and overall mortality was worse for those ≥70 yrs: 16% vs. 8% (p=0.004), and 30% vs. 12% (p<0.001), respectively. Conclusions: Elderly (≥70 yrs) melanoma patients present with thicker melanomas and a higher mitotic rate but have fewer SLN metastases. A higher incidence of local/in-transit metastases is seen among the elderly, which has implications for further investigations and clinical trials. Five- year disease-specific mortality and overall mor-

tality are both worse for the elderly, reflecting both worse melanoma biology and competing co-morbidities.

Tumor Depth	SLN+ < 70 years	SLN+ >70 years	P-value
T1/T2	9.2%	6.1%	0.28
T3/T4	33.3%	18.2%	0.02

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Recurrence and post-recurrence survival after radical lymph node dissection (RLND) for melanoma S. Pasquali,[1] A.J. Spillane,[1] L.E. Haydu,[2] K.F. Shannon,[1] R.P. Saw,[1] M.J. Quinn,[1] J.R. Stretch,[1] J.F. Thompson.[1]* *1. Melanoma Institute Australia, North Sydney, NSW, Australia; 2. Discipline of Surgery, Sydney Medical School, The University of Sydney, Sydney, NSW, Australia.*

Introduction Recurrence after RLND represents an adverse event for melanoma patients. This study investigated the incidence and pattern of first relapse after RLND, prognostic factors for recurrence after RLND, and post-recurrence survival (PRS). Methods The following variables for 1705 melanoma patients submitted to RLND at a single institution (1992-2010) were considered: age (≤50 vs >50 years), sex, tumor site, regional node field, tumor thickness (<4mm vs ≥4mm), mitotic rate, ulceration, number of retrieved nodes, nodal disease as per TNM stage grouping at the time of RLND (IIIA, IIIB, IIIC), and lymph node ratio (LNR), defined as number of involved nodes/total number of nodes removed at RLND: A ≤10%, B 11-25%, and C >25%. Survival was calculated from time of primary tumor diagnosis (DFS) and time of first relapse (PRS). Since collinearity existed between LNR and TNM stage, each of these parameters was evaluated in 2 separate survival multivariate models. Results Local, in-transit, nodal and distant metastases as a first event after RLND were observed in 65 (3.8%), 126 (7.3%), 125 (7.3%) and 502 (29.4%) patients, respectively. LNR (B vs A, HR 1.37; P=.002; C vs A, HR 2.07; P<.0001) and TNM staging system (IIIB vs IIIA, HR 1.68; P<.0001; IIIC vs IIIA, HR 2.84; P=.001) were independent predictors of recurrence as well as age >50, male sex, head and neck site, tumor thickness >4mm and ulceration (only in the model including LNR). Median PRS for patients that recurred following RLND was 9 months (95% CI 7-10 months). LNR C (HR 1.89; P<.0001) and IIIC stage TNM (HR 2.17; P<.0001) independently predicted PRS in 2 different models as did distant metastasis as first site of relapse after RLND, age >50 (for TNM stage model only) and male sex (for LNR model only). Conclusions Melanoma recurrence was observed in nearly half the patients after RLND. LNR as well as TNM staging independently predicted recurrences after RLND and PRS. Patients who had any recurrence after RLND had a poor prognosis, with a median survival of 9 months.

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S-100B Concentrations Predict Disease Specific Survival in AJCC Stage III Melanoma Patients S. Kruijff,[1]* E. Bastiaannet,[2] M.J. Speijers,[1] I.P. Kema,[1] R.J. Van Ginkel,[1] H.J. Hoekstra.[1] *1. University medical hospital Groningen, groningen, Netherlands; 2. LUMC, Leiden, Netherlands.*

Introduction Serum S-100B is used as a tumor marker in melanoma patients but its role in AJCC stage III melanoma patients is still undefined. The role of S-100B was evaluated as a pre-operative tumor marker in FDG-PET and/or CT staged stage III melanoma patients undergoing a therapeutic lymph node dissection. Methods All patients with melanoma Stage III between January 2004 and August 2010 were included. S-100B was measured one day pre-operatively and recorded as elevated when S-100B was ≥0.15 μg/l. Univariate and multivariable Cox Proportional Hazard Models were used to assess the association of S-100B with Disease Free Period (DFP) and Disease Specific Survival (DSS). Results Overall, 100 patients were included. There were 52 males and 48 females with a median age at time of primary diagnosis of 54.7 (21.8-90.6). Median follow up was 18 (2-76) months. S-100B was elevated in 50% of the patients. Patients with a normal S-100B level had a 5-year DFP of 40.6% (23.0-57.5) versus 15.3% (5.6-29.4) in patients with an elevated S-100B (Hazard Ratio (HR) 2.3 (95%CI 1.4-4.0); p=0.002). Adjusted for potential confounders in multivariable analyses, S-100B was an independent prognostic factor: (HR 2.6 with p-value of 0.002). Patients with a normal S-100B had a 5-year DSS of 46.2% (27.1-63.3) while patients with an elevated S-100B had a 5-year DSS of 28.1% (14.9-42.9); HR 2.4 (95%CI 1.3-4.3; p=0.003). In multivariable analysis, S-100B was an independent prognostic factor (HR 2.2 (95%CI 1.2-4.0); p=0.01). Conclusion Preoperatively elevated levels of S-100B in stage III melanoma patients are strongly correlated with a reduced survival. S100-B should be used as a prognostic marker in stratifying patients for adjuvant systematic treatment trails and should be considered for addition to the AJCC melanoma staging system.

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Local Immune Response and Ulceration Predict Disease-Specific Mortality (DSM) in Patients with T4 (>4.00 mm thick) Melanomas G. Karakousis,[1]* R. Hammond,[2] D.E. Elder,[4] R. Elenitsas,[4] X. Xu,[4] M.E. Ming,[3] D. Guerry,[5] L.A. Fecher,[6] D.L. Fraker,[1] B.J. Czerniecki,[1] P.A. Gimotty.[2] *1. Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia, PA; 2. Department of Biostatistics and Epidemiology, Univeristy of Pennsylvania School of Medicine, Philadelphia, PA; 3. Department of Dermatology, University of Pennsylvania School of Medicine, Philadelphia, PA; 4. Department of Pathology, University of Pennsylvania School of Medicine, Philadelphia, PA; 5. Department of Medicine (emeritus), University of Pennsylvania School of Medicine, Philadelphia, PA; 6. Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA.*

Introduction: Tumor infiltrating lymphocytes (TIL) in the primary tumor and histological regression are generally considered indicators of the local immune response to melanoma but their roles as prognostic factors has been variably reported. Previous studies have suggested that the variable association of TIL with prognosis may be explained by an interaction with tumor thickness, with TIL carrying more prognostic significance in thicker lesions. We examined the predictive role of both variables in patients with thick (T4) primary melanomas. Methods: 183 patients were identified from our prospectively collected database between 1971-2004 with melanomas thicker than 4 mm and with complete histopathologic data. Univariate and multivariate Cox regression models were done to identify clinical and histopathologic predictors of DSM, and recursive partitioning using survival curves was used to define profiles associated with differential survival. Results: With a median follow-up of 6.8 years among surviving patients, axial anatomic location, age >60 years, presence of ulceration, absence of TIL, and presence of regression were the factors associated with DSM by univariate analysis. In the final multivariate model, ulceration (hazard ratio (HR) 2.98), p<0.001), absence of TIL (HR 3.17, p<0.001) and regression (HR 1.74, p=0.03) remained significantly associated with DSM. In the recursive partition analysis, for patients whose lesions had TIL, disease-specific survival was significantly worse (p<0.0001) when regression was also present compared to patients whose lesions had no concomitant regression. There was no difference in the disease-specific survival curves based on regression in patients whose lesions had no TIL (p= 0.62), Figure 1. Conclusion: In addition to ulceration, absence of TIL and regression were found to be independently associated with DSM in patients with T4 melanomas. Presence of TIL with regression in T4 melanomas is associated with a significantly poorer prognosis and may reflect an ineffective local host immune response whose further characterization can be used in the development of immunomodulating therapies.

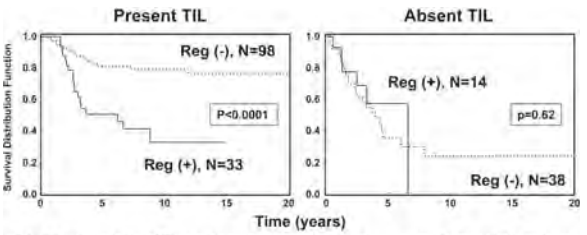

FIGURE 1. Association of TIL and histologic regression with disease-specific mortality in patients with T4 melanomas. Abbreviation: TIL, tumor infiltrating lymphocytes; Reg, regression

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Merkel Cell Carcinoma from an Unknown Primary J.S. Zager,* S.S. Marzban, R.J. Gonzalez, B.M. Walls, C.W. Cruse, J.L. Messina, V.K. Sondak. *Cutaneous Oncology, Moffitt Cancer Center, Tampa, FL.*

Introduction: Merkel cell carcinoma (MCC) is a rare neuroendocrine tumor of the skin. MCC from an unknown primary source (MCCUP) is not frequently reported on and can present a diagnostic challenge since other small round cell tumors are in the differential. We herein describe our single institutional experience with the diagnosis and management of MCCUP. Methods: After IRB approval, our institutional MCC database spanning 1988-2010 was queried for patients (pts) who presented with MCCUP. Demographics, clinicopathological variables and outcomes were assessed. Results: From a database of 321 pts with MCC, 39 (12%) were identified as having MCCUP. Median age was 69 (range,42-86) and 82% were male. CK20 staining was positive in 29/30 (97%) tumors tested; the remaining pt was positive for broad spectrum keratin with perinuclear dots and negative for CK20, chromogranin and CK7. All tumors tested were TTF-1 negative. One pt presented with stage IV disease in the retroperitoneum and lungs and was not further analyzed. The remainder presented as stage III disease involving cervical (22/38, 58%), axillary or epitrochlear (7, 18%) or inguinal nodes (9, 24%). 4 pts were seen as second opinions without treatment or outcome data available. 29 pts treated at our institution underwent completion node dissection (CLND), the remaining 5 pts received XRT as definitive treatment. Adjuvant XRT was used in 26/29 (90%) and adjuvant chemotherapy in 49%. 93% of CLNDs demonstrated extracapsular extension, all but one received adjuvant XRT. Median follow was 24 months (range,2-163), 32% of pts recurred, and 24% died. Conclusions: MCCUP appears to present more frequently than generally recognized and almost always with extensive disease in the regional nodal basin. Possible explanations of the high incidence of MCCUP can be that it is indeed under recognized; there has been ablation without biopsy of skin lesions; or regression of primary tumors akin to that seen in melanoma. However, although an aggressive malignancy, stage III MCCUP appears to be treatable via an aggressive multidisciplinary approach with recurrences seen in approximately 1/3 of pts and intermediate to long term survival being possible in the majority.

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A Multi-institutional Experience of Repeat Limb Regional Perfusion Therapies C.Y. Chai,[3]* G.M. Beasley,[1] S.S. Marzban,[3] Y.A. Chen,[3] B. Rawal,[3] J.L. Deneve,[3] S.R. Grobmyer,[2] S.N. Hochwald,[2] D.S. Tyler,[1] J.S. Zager.[3] *1. Duke University, Durham, NC; 2. University of Florida, Gainesville, FL; 3. Moffitt Cancer Center, Tampa, FL.*

Introduction: Isolated limb infusion (ILI) is a well tolerated therapy for extremity intransit melanoma. It is less invasive and technically easier to perform compared to isolated limb perfusion (HILP). However, the role and efficacy of which salvage procedure is better (ILI or HILP) after failed initial regional therapy remains unclear. The aim of study was to evaluate the regional toxicities, length of stay (LOS) and response rates (RR) for repeat isolated limb therapies. Methods: Data from patients (pts) who underwent repeat ILI or HILP from 3 institutions from 2002 to 2010 was retrospectively reviewed. Limb toxicity using the Wieberdink (WBD) scale, serologic toxicity using serum creatine phosphokinase (CPK, u/L), and LOS after each procedure were compared. RR was assessed at 3 months post procedure. Results: A total of 38 pts who underwent repeat regional procedures were identified: M= 44%, F=55%. The median age was 67y (range, 29-85). The median follow up for pts was 46 mo (range, 10-208). The following groups were identified: A) ILI-ILI (n=25); B) ILI-HILP (n=10); C) HILP-ILI (n=8); D) HILP-HILP (n=3). LOS, WBD and CPK toxicity and RR are listed in the table and were compared within groups and between groups after the 2nd procedure. Regardless of type of 2nd procedure, there were no significant differences in WBD toxicity, peak CPK or LOS and similar RR. While ORR were similar, CR in those pts undergoing HILP as a salvage procedure were higher than those with ILI; 50% and 66% [group B and D] vs. 25% and 25% [group A and C]. When looking at differences between the 1st and 2nd procedures within the same group A or B, no significant differences were noted with respect to LOS, WBD, CPK and RR. However, there appears to be a trend towards an increase in WBD and a better CR when HILP is used to salvage ILI. Conclusions: All pts in our series tolerated repeat regional therapy without increased toxicity or LOS regardless of sequence of procedures. It appears from this small series, that HILP may be a better salvage procedure after ILI failures due to recurrence or progression of disease.

Comparison of Repeat Regional Limb Therapies

	ILI-ILI		ILI-HILP		HILP-ILI		HILP-HILP	
N	25		10		8		3	
	Initial	Repeat	Initial	Repeat	Initial	Repeat	Initial	Repeat
Median LOS (days)	7	6	6.5	6	n/a	6	6	6
Overall Response (ORR)%	42	42	30	70	n/a	25	100	100
Partial Response (PR)%	25	17	10	20	n/a	0	33	33
Complete Response (CR)%	17	25	20	50	n/a	25	66	66
Median WBD scale	2	2	2	3	n/a	2.5	3	3
Median Peak CPK u/L(range)	214 (39-4830)	201 (37-4548)	197 (42-8705)	457 (3945-9129)	n/a	180 (60-8609)	n/a	1122 (399-1191)
Median Peak CPK post op day	7	7	3.5	1	n/a	2	n/a	n/a

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Prospective Assessment of Lymphedema Following Lymph Node Surgery for Melanoma J.R. Hyngstrom,* M.I. Ross, Y. Xing, Y. Chiang, K.S. Mungovan, S. Taylor, N.D. Bagde, J.E. Lee, J.E. Gershenwald, R.E. Royal, A. Lucci, P.F. Mansfield, J.N. Cormier. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Background: Lymphedema after lymph node dissection is a chronic, progressive, and debilitating condition associated with physical and psychosocial morbidity. The objective of this prospective study was to assess changes in limb volume and associated symptoms of lymphedema in patients undergoing sentinel lymph node biopsy (SLNB) or therapeutic lymph node dissection (TLND) for melanoma. Methods: To estimate the incidence of lymphedema, objective limb volume measurements were collected preoperatively and 10-12 months postoperatively using an infrared optoelectronic device (perometer, JUZO 1000M). Limb volume differences and percent limb volume change (LVC) were calculated by subtracting preoperative baseline measurements from 12 month postoperative limb volume measurements and adjusting for changes in weight by correcting for LVC noted in the non-affected limb (McLaughlin, SA et al., JCO, 2008). Lymphedema, as represented by LVC, was categorized as <5%, 5-10% and >10%. A validated 19-item lymphedema symptom assessment questionnaire was also administered with scores reflecting the number of affirmative responses. Results: Of 186 melanoma patients enrolled, 125 had measurements at 12 months. A summary of LVC according to treatment are summarized below (Table). The mean (+/- standard deviation) symptom scores for upper extremity patients with 5-10% and >10% LVC were 4.22 (4.7) and 4.14 (3.97), respectively, which was higher than in those patients with <5% LVC (1.96 (2.77)) (p= 0.035). For lower extremity patients, the mean symptom scores were 3.04 (3.44), 5.30 (4.47) and 6.77 (4.28) for those with <5%, 5-10% and >10% LVC, respectively (p=0.022). Conclusion: Using a prospective approach and strict objective criteria, LVC was relatively common following both SLNB and TLND for melanoma; LVC as low as 5% is associated with clinical symptoms. Informed consent for melanoma patients undergoing lymph node surgery should include a discussion of the risks of lymphedema. Early recognition through objective limb volume measurement and symptom assessment with referral for early treatment may reduce the incidence of severe lymphedema.

Limb Volume Change Following Lymph Node Surgery at 12 Months

	<5% LVC		5-10% LVC		>10% LVC	
	n	%	n	%	n	%
Upper Extremity						
SLNB(n=53)	37	69.8	5	9.4	11	20.8
TLND(n=20)	12	60.0	4	20.0	4	20.0
Lower Extremity						
SLNB (n=35)	20	57.1	7	20.0	8	22.9
TLND(n=17)	9	52.9	3	17.7	5	29.4

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Outcomes for Deep Melanoma (> 4 mm): An analysis of 1731 cases M. Cukier,* N.G. Coburn, C.H. Law, F.C. Wright. *Surgery, University of Toronto, Toronto, ON, Canada.*

Background: Outcomes and optimal surgical treatment for patients with deep melanoma (>4 mm) have not been well studied. The purpose of our study is to describe the clinicopathological features of this population and analyze the predictive factors for survival. Methods: We performed an analysis of the Surveillance, Epidemiology, and End Results (SEER) database, selecting patients age 18-80, diagnosed 2004-2007, who had truncal or limb melanoma, with a Breslow depth of > 4.0 mm. Overall survival (OS) was calculated with Kaplan-Meier methodology and prognostic factors were adjusted using a Cox proportional hazards regression model. Results: We identified 1731 patients with deep melanoma of whom 63% were male with a median age of 61. At presentation, 90% had no evidence of metastatic (M0) disease (N=1560). Among the M0 patients, 11% had clinically positive lymph nodes (LN) and of those with clinically negative LN (1348), 34% had pathologically positive LN disease. Of all patients, 24% did not undergo any type of lymph node biopsy. Ulceration was present in 58% of the patients. The Breslow thickness was reported 4.01-5.99 mm in 786 patients (45.4%), 6.00-7.99 mm in 410 patients (23.7%), 8.00-9.88 mm in 239 patients (13.8%) and ≥ 9.89 mm in 296 patients (17.1%). The 3-year OS was 60.2%. Multivariate Cox analysis demonstrated that improved survival was associated with age < 60 years [HR 0.599, 95% CI 0.318-0.677; p < 0.001], no ulceration [HR 0.656, 95% CI 0.521-0.826; p 0.0003], clinically negative LN [HR 0.339, 95% CI 0.260-0.442; p < 0.0001] and Breslow 4-8 mm (compared to > 8 mm) [HR 0.667, 95% CI 0.539-0.825; p 0.0002]. Conclusions: This study demonstrated that ulceration, nodal status, metastases, and melanoma depth negatively predict survival; however, thickness was the least influential. Overall, we found that patients with deep melanomas have encouraging outcomes. We advocate that in the absence of metastatic disease, these patients should be offered the same surgical treatment as those with intermediate thickness melanomas.

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Age and its interaction with the prognostic value of tumor mitotic rate in melanoma patients M.J. Speijers,[1]* E. Bastiaannet,[1] M. De Vries,[1] A.H. Brouwers,[2] A.J. Suurmeijer,[3] R.J. Van Ginkel,[1] H.J. Hoekstra.[1] *1. Division of Surgical Oncology, University Medical Center Groningen, Groningen, Netherlands; 2. Department of Nuclear Medicine, University Medical Center Groningen, Groningen, Netherlands; 3. Department of Pathology, University Medical Center Groningen, Groningen, Netherlands.*

Introduction Tumor mitotic rate (TMR) is established as prognostic value for survival and is related to a tumor-positive sentinel lymph node biopsy (SLNB) in melanoma patients. However, it remains unclear if this is true for patients of all ages. The aim of this study was to investigate if TMR maintains its prognostic qualities for patients in different age groups. Patients&Methods All patients who underwent SLNB for clinically localized melanoma in the period May 1995-September 2010 were included. TMR was recorded as number of mitoses/mm2 and divided in low (0-1) and high (≥2) values. All analyses were stratified for age; group 1 (≤45 years), group 2 (46-64 years) and group 3 (65 years). To assess factors associated with a tumor-positive SLNB, a multivariable logistic model was used. Univariate and multivariable Cox Proportional Hazard Models were used to analyze factors associated with Disease Free Survival (DFS) and Disease Specific Survival (DSS). All variables with p≤0.05 in univariate analysis were entered into the multivariable analysis. Results Overall 479 patients (244 females (51%), 235 males (49%)) with a median age of 53.8 (range 11.5-88.9) years, were analyzed. After stratification for age, group 1 contained 31% of patients, group 2 47% and group 3 22%. The median follow-up duration for all patients was 58.8 (range 1-173) months. A tumor-positive SLNB was found in 31% of patients (median Breslow 2.4 (0.90-20) mm). For group 1 high TMR was associated with a tumor-positive SLNB in multivariable analyses (Odds Ratio (OR) 2.1; p=0.03). This association was not found for groups 2 and 3 (p=0.2 and p=0.5, respectively). For DFS and DSS TMR was associated with survival for younger patients (group 1) but not for middle-aged and elderly patients (groups 2 and 3). In multivariable analyses younger patients with a high TMR had decreased DFS (HR 2.1; p=0.02) and decreased DSS (HR 2.3; p=0.04). In the middle-aged (p=0.4 DFS, p=0.4 DSS) and the elderly (p=0.2 DFS, p=0.2 DSS) TMR was not associated with survival. Conclusion High TMR is only associated with tumor-positive SLNB and decreased survival in patients aged ≤45 years. These new findings need further researching.

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Neoadjuvant therapy in stage III melanoma patients undergoing regional lymph node dissection N. Kounalakis,* D. Gao, J. Poust, R. Gonzalez, M. Becker, K. Lewis, N. Pearlman, W. Robinson, M. McCarter. *Surgery, University of Colorado, Aurora, CO.*

Completion lymph node dissection and adjuvant therapy is recommended for node positive melanoma patients; yet the type and the timing of systemic therapy remain unclear. At our institution, biochemotherapy is offered for stage III melanoma patients prior to and then following completion lymph node dissection. The aim of this study was to analyze the safety and efficacy of this treatment algorithm, and report its influence on surgical outcomes.Clinical and pathological information was extracted from a retrospective database on stage III melanoma patients treated from 1998-present. Eligible patients had tissue confirmation of stage III disease and administration of 2 cycles of biochemotherapy prior to and then following completion lymph node dissection. Toxicities, delays in treatment, surgical complications and survival were recorded. Statistical analysis was performed by Fisher's exact test, Student's t test and Kaplan-Meyer estimates.There were 153 patients available for analysis. The mean age was 44, BMI 27, and 26% of patients had a significant medical comorbidity. Average depth of tumor was 2.5mm. Mean positive node count and total nodal count following lymph node dissections were 1.5 and 20. Surgical complications occurred in 23% of patients. Mean time between initiation of neoadjuvant biochemotherapy to lymph node dissection was 48 days and between lymph node dissection to the resumption of biochemotherapy was 31 days. Median follow up was 3yrs. A significant toxicity or delay in treatment occurred in 79 patients (51%). When compared to those who did not experience a delay, toxicity or change in treatment, no difference in comorbidities, positive or total nodes harvested and overall survival was noted. In the major toxicity group, disease free survival was significantly worse, 71% vs 88% at 5yrs (p=0.01).Our data suggests that aggressive systemic treatment prior to lymph node dissection does not appear to significantly impact surgical outcomes or overall survival. Despite potential toxicities and delays, neoadjuvant therapy can be delivered with acceptable results.

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Cutaneous Adnexal Malignancies: A Treatment Controversy C. Puleo,* V.K. Sondak, J.S. Zager, C.W. Cruse, S. Marzban, R. Rossi, D.A. Almendares, H. Prince, J.L. Messina. *Cutaneous Oncology, H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.*

Introduction: Adnexal carcinomas of the skin are a diverse group of tumors with widely varied clinical behavior. Because of their relative rarity, there is little data on clinical outcomes, and no definitive treatment guidelines exist with respect to regional nodal metastases. We reviewed our institutional experience focusing on local recurrence and regional nodal involvement. Methods: A single institution, retrospective analysis of patients (pts) from 1994-2010 with a diagnosis of adenexal carcinoma was conducted, examining the incidence of local, regional and distant metastasis, with an attempt to generate a classification of these tumors by biologic potential. Results: 65 pts with adnexal malignancy were identified (see table). 62/65 pts (95%) were treated with wide excision. Sentinel lymph node (SLN) biopsy was performed in 14 pts and positive in 6 (43%): 5 porocarcinomas and 1 microcystic adnexal carcinoma (MAC). 4 pts presented with regional nodal disease, 2 apocrine adenocarcinoma and 2 porocarcinoma, and underwent nodal dissection. In all 10

pts (15%) were noted to have regional nodal metastasis either at presentation, SLN biopsy, or upon recurrence with a median follow-up of 8 months (range 1-159). 11 pts (16%) demonstrated recurrence of all types: 9 local, 1 regional and 1 distant (spine). Local recurrence developed in 4/23 pts with porocarcinoma, 2/16 with MAC, 1/1 with chondroid carcinoma, 1/11 with sebaceous carcinoma, and 1/7 with eccrine adenocarcinoma. The only regional recurrence occurred in a porocarcinoma pt with a positive SLN who declined node dissection. The distant spine metastasis occurred in a pt with apocrine adenocarcinoma. Conclusions: In this small series, despite limited follow-up, our data suggest porocarcinomas have a particularly high risk of regional node metastasis, as well as a substantial risk of local recurrence, and should be treated aggressively. Tumors of sebaceous and pilar origin demonstrated lower grade behavior and may be managed by wide excision alone. At present, we continue to consider patients with eccrine tumors as good candidates for sentinel node biopsy, as we try to accumulate larger numbers and longer follow-up.

Table 1

Category	iagnosis	Patients	+LN at Presentation	+ SLN pts/total SLN pts	Local Recurrence/pts	Regional Recurrenc	Distant Recurrence
Follicular	Pilomatrix (pilar) Carcinoma	2	0	0/0	0/2	0	0
Apocrine	Apocrine Adenocarcinoma	5	2	0/0	0/5	0	1
Sebaceous	Sebaceous Carcinoma	11	0	0/1	1/11	0	0
Eccrine (A)	Porocarcinoma	23	2	5/10	4/23	1	0
Eccrine (B)	Eccrine Non-porocarcinoma Agressive digital papillary carcinoma 2 Papillary adenocarcinoma 1 Chondroid carcinoma 1 Adenoid cystic carcinoma 1 Eccrine ductal carcinoma 3 Microsystic adnexal carcinoma 16	24	0	(MAC) 1/1 Adenoid cystic 0/1 Digital papillary 0/1	MAC 2/16 Chondroid carcinoma 1/1 Eccrine ductal carcinoma 1/1	0	0

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Clinical Impact of Biopsy Technique in Melanoma R. Vassell,[2]* T. James,[1] T. Ashikaga,[1] A. Gray.[1] *1. University of Vermont, Burlington, VT; 2. Danbury Hospital, Danbury, CT.*

Introduction: There has been concern that partial biopsy impairs accuracy of depth of invasion in melanoma. We sought to evaluate the accuracy of partial versus excision biopsy and determine if various biopsy techniques lead to differences in Breslow thickness which would alter surgical management. Methods: A retrospective secondary analysis from 2003-2008 was performed comparing Breslow thickness after initial diagnostic biopsy to Breslow thickness following definitive excision. Cases were then reviewed to identify instances where initial and final Breslow thickness differed significantly enough to alter clinical decision making regarding surgical margins and sentinel lymph node biopsy. Guidelines for recommended surgical margins were based on the 2010 National Comprehensive Cancer Network guidelines. Indications for sentinel node biopsy were based on the inclusion criteria for the Multicenter Selective Lymphadenectomy clinical trial; which included intermediate thickness melanoma (1.2 -3.5 mm). Results: In 247 cases; shave biopsy was performed in 44%, punch biopsy in 24%, and excisional biopsy 32%. Mean initial Breslow thickness for all biopsy techniques was 0.97 mm. Mean Breslow thickness after WLE was 1.16 mm. Breslow thickness was underestimated in 15.6% shave, 30% punch, and 7.7% excisional biopsies (two-tailed p=0.002, one-tailed p=0.007). Differences in Breslow thickness between initial biopsy and final pathology would have altered recommendations for surgical margin width in 6.4% shave, 8.3% punch, and 2.5% excisional biopsies (two-tailed p=0.236, one-tailed p=0.125). Upstaging between initial and final Breslow thickness was substantial enough to warrant SLNB in 2.75% shave, 5.0% punch, and 0 excision biopsy cases (two-tailed p=0.176, one-tailed p=0.099). Conclusions: Upstaging of Breslow thickness between initial biopsy and final pathology altered recommended surgical margins and indications for SLNB more frequently with partial compared to excisional biopsies. This difference did not reach statistical significance. Further study is needed to determine the clinical impact of partial biopsies in the diagnosis of cutaneous melanoma.

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Is a Level III Axillary Dissection Necessary for a Positive Sentinel Lymph Node (SLN) in Melanoma? J. Namm, A.E. Chang, V.M. Cimmino, R.S. Rees, T.M. Johnson, M.S. Sabel.* *Surgical Oncology, University of Michigan, Ann Arbor, MI.*

SLN biopsy has become standard of care for the surgical staging of melanoma. For a positive SLN in the axilla, a level I-III dissection is often recommended, but the need for level III is debated. We have primarily utilized a level I/II ALND in this situation. Methods: Utilizing our IRB-approved prospective melanoma database, we identified all patients, 18 years and over, who underwent an ALND for a positive SLN from 1998 to 2008 to investigate morbidity, locoregional and distant recurrence and survival. Results: We identified 270 melanoma patients who underwent a level I/II ALND for a +SLN. Median Breslow thickness was 2.2mm, with ulceration in 36%, angiolymphatic invasion in 14%, and a median mitotic rate of 3 mitoses/mm2. 51 patients (19%) had drainage to more than one basin, with 15 of the patients having B/L ALND. Average number of SLN removed was 2.8, and the average number of involved SLN was 1.8. ALND yielded an average of 18.7 nodes in the specimen. Involved non-sentinel lymph nodes were found in 37 dissections (13%). Post-operative complications occurred in 31 patients (11%); infectious (8%), seroma (2%) and hematoma (1%). Median f/u for this group was 44 months. 6 patients (2%) suffered a local recurrence at the site of the primary melanoma and 19 patients (7%) developed in-transit disease. There were 57 patients (22%) who ultimately developed distant disease. Regional recurrence occurred in 14 patients (5%); 10 of these patients had distant recurrences, 6 synchronous and 4 subsequent to regional recurrence. At last follow-up, 191 (71%) were alive, 180 (67%) without disease, 9 (3%) with disease and 2 (1%) with an unknown disease status. Seventy-nine patients (29%) had died, 52 (19%) of metastatic melanoma, 19 (7%) without melanoma and 8 died of unknown reasons. Discussion: In the largest series of ALND following a positive SLN, both the complication rate and regional recurrence rate was lower than or on par with other series, despite being limited to a level I/II dissection. Routine level III dissection does not appear necessary when performing ALND for a positive SLN.

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Long-term Follow-Up of All Isolated Limb Perfusions for In-transit Metastasis of Malignant Melanoma in Sweden During 25 Years R. Olofsson,* J. Mattsson, P. Lindnér. *Sahlgrenska University Hospital, Göteborg, Sweden.*

Objective: The aim of this study is to describe our single centre experience with isolated limb perfusion (ILP) for in-transit metastasis of malignant melanoma. Methods: A retrospective chart review of all patients treated with ILP for in-transit metastasis of malignant melanoma in Sweden during 25 years (1984-2008). Outcome, morbidity and survival were analyzed after the first-time ILP. Results: 163 consecutive patients with a median age of 70 years (23-92) were treated. 64% of the patients were females and 6% had general metastasis at the time of ILP. 56% were iliacal perfusions, 35% femoral perfusions and 9% upper limb perfusions. 91% received melphalan only and 9% received melphalan and TNF-alpha. At 3 months follow-up 65% had complete response (CR), 21% partial response (PR), 12% stable disease (SD) and 2% progressive disease (PD), which gives a total response rate of 86%. Median time to local recurrence/progress and general metastases was 12 months and 25 months respectively. There was a significant difference in time to recurrence/progression and general metastasis dependent on response. Time to local recurrence/progress was 20 months for CR compared to 5 months for PR, and time to general metastasis was 33 months for CR compared to 14 months for PR. This difference was also significantly reflected in the overall survival where patients with CR had a survival of 45 months compared to 24 months for

patients with PR. Median survival for the whole group was 31 months. Conclusion: ILP results in excellent response rates in patients with in-transit metastasis of malignant melanoma. The response after ILP predicts survival as well as time to local and systemic progress. This most probably reflects the aggressiveness of the tumour but yet unknown positive systemic effects of ILP may also be an explanation.

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Suppression of GSTP1 Expression Induces Apoptosis and Senescence in Human Melanoma Cells R.S. Turley,* J. Liu, D.S. Tyler, F. Ali-Osman. *Surgery, Duke University, Durham, NC.*

The Glutathione S-transferase P1 (GSTP1) protein, highly expressed in melanoma and other human cancers, functions both in Phase II metabolism and in the regulation of cell signaling. In this study, we investigated GSTP1 as a regulator of cell signaling, cell survival/apoptosis and drug resistance in human melanoma cells. Methods: A375 human melanoma cells were infected with a lentiviral vector carrying short hairpin RNA (shRNA) targeting GSTP1 or eGFP (control). A heterogeneous stable population was isolated by puromycin selection and confirmed as GSTP1 negative by PCR and western blotting. Population growth kinetics of the GSTP1 negative and control cells was monitored in real time over 72 hrs by electronic cell sensing and the results used to compute growth rates and doubling times. Apoptosis (level of caspase 3/7 activation) was determined as the cleavage of the caspase substrate, Ac-DEVD-AFC. MAP kinase (JNK) signaling was analyzed by immunoprecipitation and western blotting for phosphorylated JNK and c-jun. Results: GSTP1 shRNA-lentiviral infection effectively suppressed GSTP1 expression in melanoma cells, relative to uninfected and eGFP infected cells. GSTP1 suppression significantly increased basal levels of apoptosis and decreased overall growth. The growth rate of the GSTP1-ve cell population (0.0013 Hr-1) decreased by ~6-9 fold, compared to GSTP1+ve controls (0.0115 Hr-1 for eGFP and 0.0085 Hr-1 for uninfected cells) and the doubling time increased by 2.3-fold from 14.3 hrs (controls) to 34.1 hrs (GSTP1-ve cells). We observed a significant increase in activated JNK1/2 and c-jun in the GSTP1-ve, compared to controls. GSTP1 suppression resulted in a ~ 4-fold sensitization to cisplatin (IC50 decreased from 72.6±6.0 to 18.5±1.2 after 12 hr cisplatin exposure) and a more than 5-fold increase in drug-induced apoptosis. Conclusions: Based on the results we conclude that: 1) GSTP1 is an obligate requirement for growth and survival of GSTP1-expressing melanoma cells; 2) GSTP1 suppression activates the JNK signaling pathway and increases basal apoptosis in melanoma cells; 3) targeted inhibition of GSTP1 may represent a clinically efficacious strategy in melanoma.

GSTP1 slows melanoma cell growth and sensitizes cells to cytotoxic therapy.

	A375	A375 - shRNA eGFP	A375- shRNA GSTP1
Doubling Time (hrs)	17.3±1.02	14.0±0.63	32.3±3.30
Growth Rate (Hr-1)	0.0085±.0001	0.0115±0.0002	0.0013±0.0001
IC50 Cisplatin (μM)	62.4±2.9	72.6±6.0	18.5±1.2
Normalized Caspase 3/7 Activity*			
-Baseline	1.00±0.05	1.29±0.05	5.31±0.06
-12.5 μM Cisplatin	1.00±0.04	1.26±0.04	6.00±0.06
-25 μM Cisplatin	1.00±0.05	1.13±0.04	5.92±6.77

*Apoptosis (Caspase 3/7 activity) is normalized for each treatment group to the untreated parental cells.

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Comparison of SPECT/CT to Planar Lymphoscintigraphy for Sentinel Lymph Node Biopsy of Melanomas Draining to the Head and Neck A.D. Yang,* H.A. Macapinlac, J. Gardner, J.N. Cormier, A. Lucci, P.F. Mansfield, R.E. Royal, J.N. Myers, R.S. Weber, J.E. Gershenwald, M.I. Ross, J.E. Lee. *The University of Texas MD Anderson Cancer Center, Houston, TX.*

INTRODUCTION: For patients with a primary melanoma that drains to head or neck nodal basins (HNM), sentinel lymph node biopsy (SNB) can be difficult given the anatomic complexity and potential for multiple drainage patterns. Planar lymphoscintigraphy (PL) is used to aid preoperative planning for HNM SNB, but can be anatomically nonspecific. Single photon emission computed tomography/computed tomography lymphoscintigraphy (SPECT/CTL) is a fused imaging modality that potentially provides more accurate anatomic localization of SNs. We compared PL to SPECT/CTL in a cohort of HNM patients who underwent both modalities prior to SNB. METHODS: 57 consecutive patients with HNM who underwent both PL and SPECT/CTL from 2007-2009 were retrospectively identified from a prospectively maintained database. An expert nuclear physician (HAM) blinded to SNB results reviewed all images and identified anatomic correlates of focal radiotracer uptake. Results of PL and SPECT/CTL were correlated with findings at SNB and to SN histopathology. RESULTS: SPECT/CTL identified at least one SN in all patients while PL failed to identify any SNs in 5 patients (failure rate 0% vs. 9% respectively; P=.028). Based on operative findings, SPECT/CTL identified the correct SN basin(s) 77% of the time, compared to 40% with PL (P<.0001). SPECT/CTL and PL correctly identified basin(s) containing the positive SN in 12/14 and 6/14 patients respectively (86% vs. 43%; P=.023). SPECT/CTL and PL correctly identified SNs located outside of a lateral cervical LN basin (levels II-V) in 12/18 patients and 1/18 patients respectively (67% vs. 6%; P=.0001). CONCLUSIONS: SPECT/CTL provides more accurate localization than PL, including in patients with occult SN metastases. The superior anatomic information provided by SPECT/CTL improves preoperative planning in HNM patients undergoing SNB, and it may be especially helpful when the SNs are located outside of the lateral neck. Nonetheless, our data emphasize that intraoperative use of the gamma probe by the surgeon is essential to confirm lymphoscintigraphic findings and to identify additional SNs not visualized by either imaging modality.

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Src family kinase inhibition as a novel strategy to augment melphalan based regional chemotherapy of advanced extremity melanoma Y. Tokuhisa,[2]* C.K. Augustine,[2] H. Toshimitsu,[2] R. Turley,[1] G.M. Beasley,[1] K. Sharma,[1] D.S. Tyler.[1] *1. Surgery, Duke University Medical Center, Durham, NC; 2. Durham VA Medical Center, Durham, NC.*

Introduction: Src kinase inhibition has been shown to augment the effectiveness of chemotherapeutics. Dasatinib, a dual Src/Abl kinase inhibitor, is under investigation as a single agent for tumors such as melanoma. The goal of this study was to determine if Src kinase inhibition using dasatinib could augment the effectiveness of regionally administered melphalan in melanoma. Methods: Mutational status of c-Kit, BRAF and NRAS as well as patterns of gene expression predictive of dysregulated Src kinase signaling were evaluated in a panel of 28 melanoma cell lines. The effectiveness of dasatinib was measured by quantifying protein expression and activation of Src kinase, focal adhesion kinase (FAK) and Crk-associated substrate (p130CAS) in conjunction with in vitro cell viability across 6 melanoma cell lines. Using an animal model of regional chemotherapy, we evaluated the clinical effectiveness of systemic administration of dasatinib in conjunction with regional melphalan against one cell line (DM443) grown as a xenograft. Result: High c-Kit expression was observed in 4 out of 28 cell lines however no cell lines harbored c-Kit mutation. BRAF and NRAS mutation were observed in 60.7% and, 19.2% respectively. In Western blot analysis dasatinib (10nM) blocked activation of FAK and p130CAS. In vitro response to dasatinib alone was observed in 4 of 6 cell lines (See Table). No correlation was observed between c-Kit expression or Src dysregulation and sensitivity to dasatinib. Dasatinib in combination with melphalan inhibited cell proliferation compared to melphalan treatment alone in 5 of the 6 cell lines tested (See Table). In the animal model of, tumor doubling time with systemic dasatinib in combination with regional melphalan (44.8days) was significantly longer (p=0.007) than either dasatinib alone (21.3days) or melphalan alone (24.7days). No increased toxicity was observed with dasatinib. Conclusion: Systemic dasatinib in combination with melphalan markedly improves the efficacy of this regionally administered alkylating agent. Validation of this concept should be considered in the context of a regional therapy clinical trial.

	% inhibition of cell proliferation with Dasatinib alone			
	10nM	100nM	1000nM	3000nM
DM366	9.4	21.9	24.1	25.6
DM443	-5.4	-0.35	1.0	13.0
DM738	-0.71	8.4	14.9	17.7
PRMel	28.1	38.5	46.3	45.3
DM6	-2.6	-4.8	-6.2	-10.3
DM440	-0.16	-2.0	0.66	-0.20
	% increase in response to melphalan with Dasatinib			
	10nM	100nM	1000nM	3000nM
DM366	15.9	22.7	24.0	20.2
DM443	1.89	2.38	5.64	32.2
DM738	-1.96	10.1	7.80	15.9
PRMel	35.6	50.6	51.8	48.6
DM6	1.48	2.51	-11.1	-3.14
DM440	0.63	8.34	9.13	24.3

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Comparison of melanoma in a pediatric vs. young adult population

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Introduction: Despite increased awareness, the incidence of pediatric melanoma continues to rise in the United States. As this trend continues, pediatricians and pathologists will need a better understanding of presentation and histologic features to ensure prompt diagnosis and treatment. It remains unclear whether pediatric melanoma represents a unique entity or simply an earlier presentation of the adult disease. Methods: A retrospective review of our IRB approved melanoma database was undertaken to identify all patients since 1998 under 18 years of age. Patient characteristics including age, sex, and location of lesion were collected. Histologic features of the primary lesion and sentinel node were gathered. Patients were matched by Breslow depth and ulceration to melanoma patients aged 19-30 for comparison using chi-squared analysis. Results: Seventy-one pediatric patients were identified with a median age of 14 years (3-18 years). The average Breslow depth was 2.44mm (0.25-19mm) with 10% ulceration rate. The location of the primary was trunk in 38 (54%) compared to 23 (32%) in young adults (p=.018). The median mitotic rate was 1.5 vs. 1.0 in pediatric vs. young adults, respectively (p=NS). There was no difference in angiolymphatic invasion identified. Satellitosis was more common in pediatric patients (13% vs. 0% (p=0.006)). Sentinel nodes were histologically positive in 44% vs. 25% of pediatric and young adult patients, respectively (p=.045). The rates of non-sentinel node positivity was similar at 13% and 22%, respectively (p=0.7). With a mean follow-up was 2 years there was no difference in disease specific mortality (7% vs. 13%, p=0.4) Conclusions: Because of its rarity, little is known about the disease progression of pediatric melanoma and how it differs from the adult disease. Pediatric patients presented with more aggressive primary lesions and a higher positive sentinel node rate. This did not, however, translate into higher disease specific mortality.

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Acral Lentiginous Melanoma. Epidemiology and Prognostic Factors

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Introduction: The ALM is the most frequent type of Melanoma in Latin-America with special characteristics and different evolution. We report the mean epidemiologic features from a Mexican database from thirty years. Methods: A retrospective review was carried out and includes 1,614 patients with histologically confirmed malignant melanoma from January 1980 to December 2009. We analyze the presence of ulceration, Sentinel Node status, clinically positive nodes and distant metastases, Breslow Thickness, growth pattern, gender and age. Concomitantly we revised the impact of each variable in our population. Results: There were 331 ALM patients with enough information to be analyzed. The male-female ratio were 1:1.25 (F 55.6%, M:44.4%). Mean age were 62.59 years and 53% were older than 60 years. The most frequent localization was sole of the foot (50.17%), subungueal melanoma (33.8%) and the palm (7.7%). 28% of all patients had positive nodes and 7% distant metastases at diagnosis. A sentinel node staging was done in 161 patients with a 35.4% positive rate. There were no differences between ALM and other types of melanoma in age and gender, but has a deeper Breslow Thickness, positive node rate, ulceration, positive sentinel node rate and worst prognosis. Conclusion: The majority of patients with ALM had thicker and ulcerated lesions, with higher rate of positive nodes and worst prognosis

	ALM (n=331)	Nodular (n=125)	Superficial Spreading (n=54)	Lentigo Maligno (n=33)	p
Age (mean)	62.5	54	53.2	66.5	0.53
Female (%)	55.6	57.4	63.6	61.6	0.60
Male (%)	44.4	42.6	36.4	38.4	
Breslow (mm)	6.09 (0.02 - 75)	4.3 (0.2-22)	2.6 (0.1-19)	1.8 (0.1-10)	<0.0001
N + (%)	34	25.6	13	9.4	0.0005
Ulceration (%)	67.1	46.3	13.7	16.1	<0.0001
SN +	35.4	26.2	12.9	7.7	0.0105

P244

Preoperative Positron Emission Tomography/Computed Tomography Changes Management in Patients with Merkel Cell Carcinoma

P. Papavasiliou,* R. Arrangoiz, A. Turaka, M. Lango, J.Q. Yu, J. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: The aggressive nature of Merkel cell carcinoma suggests that more extensive initial workup prior to surgical intervention may alter the definitive treatment plan. The objective of this study was to determine the utility of positron emission tomography/computed tomography(PET/CT) in identifying patients with regional or metastatic disease prior to operation leading to a change in management. **Methods:** A retrospective chart review of patients who were referred for treatment of Merkel cell carcinoma was conducted. Patients who underwent preoperative PET/CT were included in this study. Data collected included PET/CT results, clinicopathologic variables and the definitive treatment for each patient. **Results:** Twenty-eight patients underwent PET/CT imaging prior to surgical treatment, (M: 17, F: 11) with a mean age of 69 years. The primary site of disease was detected on PET/CT in only 5 patients (17.9%). Five patients presented with an unknown primary, and PET/CT did not detect the primary in any of these patients. The sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) for detecting regional nodal disease was 70.5%, 100%, 100%, and 68.75% respectively. Metastatic disease was identified in 6 patients (21.4%). The SN, SP, PPV and NPV for detecting metastasis was 100%, 76%, 66%, and 100% respectively. Incidental cancers were identified in 2 patients (thyroid cancer and bronchial carcinoid). Overall, preoperative use of PET/CT altered the management in 13 patients (46%). **Conclusion:** This study suggests that PET/CT will alter the treatment plan in a significant number of patients with Merkel cell carcinoma and should be included in the preoperative evaluation.

Demographics and PET/CT Findings

Patients	28
Age, mean (range)	69 (38-86)
Gender	M:17, F:11
Size of Primary, mean	1.9 cm
Stage	
I	7 (25%)
II	2 (7.1%)
III	13 (46.4%)
IV	6 (21.4%)
Location of Primary	
Unknown	5 (17.8%)
Head and Neck	10 (35.7%)
Extremity	12 (42.9%)
Trunk	1 (3.6%)
PET/CT Findings	
Regional Nodal Disease	7 (25%)
Metastasis	6 (21.4%)
Incidental Cancer	2 (7.1%)

P245

Desmoplastic Melanoma: Is Sentinel Lymph Node Biopsy Necessary? H. Beitollahi,* W. Chandler, N. Woll, H. Sun, M. Shabahang, J. Blansfield. *General Surgery, Geisinger Medical Center, Danville, PA.*

Introduction: Desmoplastic melanoma (DM) is a distinct subtype of malignant melanoma that may be sub-classified as pure (PDM) or mixed (MDM). There is no clear consensus regarding the role of sentinel lymph node biopsy (SLNB) in DM. Our goal is to assess recurrence and survival in patients with PDM and MDM and determine the necessity of SLNB. Methods: This is a single institution based retrospective study of 41 patients with DM out of approximately 2500 patients with melanoma treated at our institution. The study period spanned January 1, 1988 to August 1, 2010. Clinical and histopathologic characteristics, recurrence, and survival were analyzed. Results: Demographic and clinical characteristics are included in Table 1. Forty-one patients with DM were identified, 20 patients with PDM and 21 patients with MDM. Tumors were treated with wide local excision (WLE) or Mohs surgery. Twenty patients had a SLNB (49%), 10 patients with PDM and 10 with MDM. The median number of lymph nodes sampled was 2 (range 1-3). Three patients had a positive sentinel lymph node (15%), 1 patient with PDM and 2 with MDM. One patient had a negative SLNB which was a false negative (5%). Two patients had distant disease at presentation, 1 patient with PDM and 1 with MDM, and both died of disease. Seven patients in our study cohort experienced recurrence and 4 died of disease. Three patients with PDM experienced recurrence and all died of disease. In the MDM group 4 patients recurred and 1 died of disease. Three patients with MDM had locoregional recurrence, underwent re-excision and now have no evidence of disease. Conclusion: Although our study is limited due to small sample size, the data suggests SLNB is necessary and has a role in the staging workup of DM. DM has potential for both local recurrence and distant metastasis, regardless of sub-classification as PDM or MDM. Further studies are necessary to continue to assess the clinical significance of SLNB in DM.

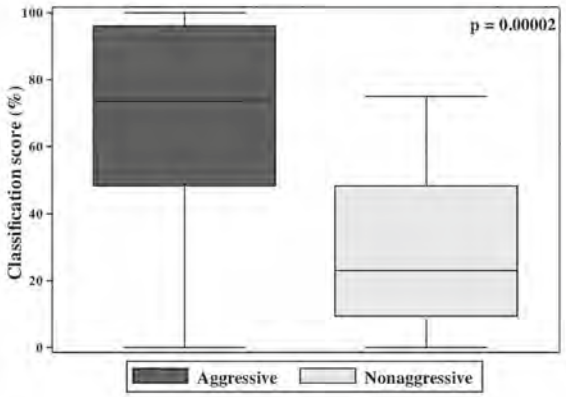
Table 1: Demographic and Clinical Characteristics

Variable	n	%
Sex		
Male	24	59
Female	17	41
Age		
Median	66	
Range	31-89	
Site		
Head and Neck	19	46
Trunk	10	24
Extremity	12	29
Procedure		
WLE	35	85
Mohs	6	15
Pathologic Subtype		
PDM	20	49
MDM	21	51
Median Breslow Thickness (mm)		
Total	2	
PDM	3	
MDM	1.5	

P246

Karyometry of Cutaneous Squamous Cell Carcinoma Discriminates between Aggressive and Nonaggressive Phenotypes E.S. Glazer,[1]* P.H. Bartels,[3] M. Yozwiak,[3] A.R. Prasad,[2] H.G. Bartels,[3] J. Einspahr,[3] D.S. Alberts,[3] R.S. Krouse.[2] *1. Surgery, The University of Arizona, Tucson, AZ; 2. Southern Arizona Veterans Affairs Health Care System, Tucson, AZ; 3. The Arizona Cancer Center, Tucson, AZ.*

Introduction: Analysis of malignant nuclei –karyometry- yields information not readily seen on pathology. Six nuclear features (out of 95) discriminate between normal skin, pre-cancerous actinic keratosis, and cutaneous squamous cell carcinoma (SCC). We hypothesized that karyometry could discriminate between aggressive and nonaggressive SCC. Methods: Cutaneous SCC from 46 male patients were retrospectively identified. 23 patients had evidence of aggressive behavior (local/regional recurrence or second primary SCC) and 23 patients were controls who were age and site-matched based on diagnoses of SCC without evidence of aggressive behavior. Non-supervised karyometric analysis was performed on H&E stained SCCs to investigate nuclear variations. Nuclear features (significance $p < 0.0001$, Kurskal Wallis test) formulated an aggressiveness classification score (range 0% – 100%). Comparisons were made with Fisher's exact and Student's t-test. Uncertainties represent standard deviations. Results: Six of the 46 patient samples were not of sufficient quality to analyze. The average age was 79 ± 7 years for aggressive SCC (n = 22) and 80 ± 9 years for nonaggressive SCC (n = 18, p = 0.66) with a mean follow up of 5.5 years. 96 ± 8 nuclei were analyzed per patient in the aggressive cohort while 96 ± 9 nuclei were analyzed in the nonaggressive cohort (p = 0.53). Karyometry discriminated between nuclei from these cohorts with an accuracy of 89.3% ($p < 0.0001$). The classification score (percent aggressive) for aggressive lesions was significantly higher than nonaggressive lesions (Figure, 69 ± 28 vs. 28 ± 23, p = 0.00002). The classification score accurately categorized 79% of patients (p = 0.0004, sensitivity = 86%, specificity = 72% with a threshold score = 37). Conclusions: Karyometry successfully discriminated between patients with aggressive and nonaggressive cutaneous SCC. The utility of the classification scores is that it provides relative percent aggressiveness for each lesion. This information can be utilized for risk stratification and risk/benefit analyses at the individual patient level. Future studies will investigate its clinical prognostic utility.



Although aggressive squamous cell carcinoma classification scores span the spectrum, the vast majority of scores are greater than a DF score of 37 while a majority of nonaggressive cSCC classification scores are less than 37. However, the aggressive cohort does have a few low DF score outliers.

P247

Number of excised lymph nodes as a measure of quality after axillary and groin radical lymph node dissection in melanoma patients: results from a small volume melanoma centre S. Pasquali,[1]* S. Mocellin,[1] A. Vecchiato,[2] P.L. Pilati,[1] A. Di Maggio,[2] M.C. Montesco,[3] D. Nitti,[1] C.R. Rossi.[2] *1. Dpt. of Oncological & Surgical Sciences, University of Padova, Padova, Italy; 2. Venetian Oncological Institute, Padova, Italy; 3. Dpt. of Pathology, University of Padova, Padova, Italy.*

Introduction Radical lymph node dissection (RLND) is the treatment of choice for regional lymph node metastasis from cutaneous melanoma. There is a lack of agreement on quality assurance standards for RLND, in particular for the number of lymph node removed, which is already adopted in many solid tumors. Here the experience of a small referral melanoma centre has been reviewed to investigate on the number of excised lymph nodes after axillary and groin RLND. Methods Data from melanoma patients submitted to full-three levels axillary and ilio-inguinal RLND were extracted from a prospectively collected database (1992-2008). Mean, median value of retrieved nodes and 90th percentile were compared with the proposed standards. Survival of patients having a nodal count < 90th percentile was compared with patients having a nodal count =/> 90th percentile. Results There were 87 patients submitted to a full three-level axillary RLND. The mean and the median number of excised nodes were 23 (95% confidence interval [CI] 21-25), and 20 (range, 8-54); 90% of patients have more than 14 nodes excised. There were 146 patients submitted to an ilio-inguinal RLND. The mean and the median number of excised nodes were 20 (95%CI 18-21), and 18 (range, 6-44); 90% of patients have more than 11 nodes excised. Prognosis of patients with nodal count < 90th percentile (N=21) was not statistically different from those who had a node count ≥90th percentile (log rank test, not significant). Conclusions In the present series, 90% of patients have more than 14 and 11 retrieved nodes after axillary and groin RLND, respectively. These lymph node counts are greater than those previously proposed for axillary (10 and 8 nodes) and groin dissection (7 and 6 nodes) on the basis of the Melanoma Institute Australia experience and SEER database, respectively. More evidence is needed to define the optimum quality assurances standards for RLND according to the number of retrieved lymph nodes, particularly in regard of the impact of this measure on patients' prognosis.

P248

Routine Restaging PET/CT and Detection of Recurrence in Sentinel Lymph Node Positive Stage III Melanoma J.J. Baker,* M.O. Meyers, J.J. Yeh, J. Frank, K.D. Amos, K.B. Stitzenberg, P. Long, D.W. Ollila. *Surgery, University of North Carolina, Chapel Hill, NC.*

Introduction: The follow-up (f/u) of patients with stage III melanoma is controversial. In addition to history and physical exam, cross-sectional imaging is often utilized. We sought to evaluate the impact of routine PET/CT scans on the detection of recurrence in sentinel lymph node (SLN) positive stage III melanoma. Methods: We analyzed a prospective, IRB-approved, database of all cutaneous melanoma patients treated at our institution from 2003-2009 to identify SLN positive stage III patients with at least one year of f/u. Our routine f/u recommendation has included history and physical exam every 3 months for the first three years along with annual LDH and PET/CT scan. Results: 83 patients with SLN positive stage III melanoma were identified. 28(34%) developed a recurrence within 1 year and 17 were lost to f/u. 38 had disease-free survival(DFS) of > 1 year and at least one routine re-staging PET/CT scan. Demographics: Male=20/Female=18; Median age 48.5 yrs; Mean Breslow depth 2.37 ± 1.59 mm; 13/38(34%) ulcerated; 30/38(79%) with only 1 positive node (range 1-6). Median f/u 27.5 months. 108 PET scans were performed in 38 patients. 7(18%) developed a recurrence(3 distant/4 regional); median time to recurrence was 25 months. Recurrence was detected as follows: 3 patient detected; 1 physician exam; 1 elevated LDH; 1 PET scan; 1 brain MRI. Breslow depth(p=0.02) was associated with recurrence, but SLN tumor burden(p=0.35) and ulceration(p=0.22) were not. There were 10(9%) false-positive scans which required additional imaging(n=6) or percutaneous/surgical biopsy(n=4). In total 2/38(5%) patients had an asymptomatic metastasis detected by routine imaging. Conclusions: The utility of routine PET/CT scans in identifying unsuspected recurrence in patients with SLN positive stage III melanoma with greater than 1 year DFS appears minimal. Modest f/u and small patient number limit absolute interpretation. If confirmed in a larger data set with longer f/u, this routine PET/CT may not be useful for these patients. With many patients(34%) having early recurrence, it may make sense to have earlier f/u restaging if a high risk group could be identified.

P249

Augmenting Regional Therapy with Targeted Agents: A Phase I Multi-Institutional Study of Systemic Sorafenib in Conjunction with Regional Melphalan for In-Transit Melanoma of the Extremity A.P. Coleman,[1]* G.M. Beasley,[1] N. McMahon,[1] A. Raymond,[1] G. Sanders,[1] M.S. Brady,[2] M.A. Davies,[3] C.K. Augustine,[4] D.S. Tyler.[1] *1. Duke University Medical Center, Department of Surgery, Durham, NC; 2. Memorial Sloan Kettering Cancer Center, Department of Surgery, New York, NY; 3. MD Anderson Cancer Center, Department of Melanoma Medical Oncology, Houston, TX; 4. VA Medical Center, Durham, NC.*

INTRODUCTION: Isolated limb infusion with melphalan (ILI-M) corrected for ideal body weight (IBW) is a well-tolerated treatment for patients with in-transit extremity melanoma with an approximate 31% complete response (CR) rate. Sorafenib, a multi-kinase inhibitor, has been shown to augment tumor response to chemotherapy in pre-clinical studies. METHODS: A multi-institutional, dose-escalation, phase I study was performed to evaluate the safety and antitumor activity of sorafenib in combination with ILI-M. Patients with AJCC stage IIIB/IIIC/IV were treated with sorafenib starting at 400 mg PO daily for seven days before and seven days after ILI-M corrected for IBW. Drug pharmacokinetics and Braf/Nras mutational status were measured and correlated with response. RESULTS: Twenty patients were enrolled over 22 months at 2 institutions. A maximally administered dose of sorafenib (600 mg) was defined by 4 dose-limiting toxicities (DLTs), which included soft tissue ulcerations and compartment syndrome. One patient developed squamous cell carcinoma in the treated extremity. There were 3 CRs (16%) and 4 partial responses (PRs, 21%). Response was not associated with Braf or Nras mutational status. Short-term sorafenib treatment did not appear to inhibit MAP kinase signaling as measured by RPPA but it did cause dose-dependent changes in a number of other proteins including the pro-apoptotic protein Bim, the cyclin dependent kinase inhibitor p21, VEGFR2, CRaf, and c-kit (figure). Sorafenib did not alter melphalan pharmacokinetics. CONCLUSIONS: This trial defined the MTD of systemically-administered sorafenib in combination with ILI-M. Although some clinical responses were seen, the addition of sorafenib to ILI-M did not appear to augment melphalan's efficacy but did increase loco-regional toxicity. Sorafenib did not alter melphalan pharmacokinetics or MAP kinase signaling, suggesting that the increase in local-regional toxicity may have been mediated by one of the other proteins found to change in response to short-term sorafenib treatment.

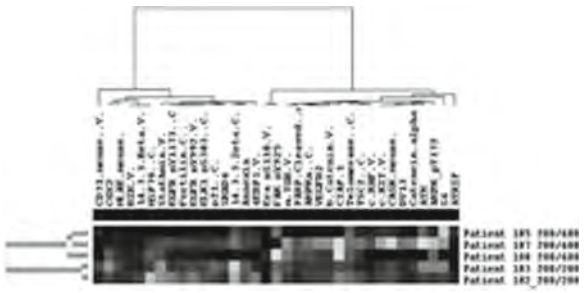


FIGURE: Dose-dependent changes in protein expression. Unsupervised hierarchical clustering was performed on linear load-corrected measurements of protein expression and a heatmap generated where relative protein expression is color-coded such that red indicates higher expression and green indicates lower expression. Rows represent patients and columns represent the ratio of post-treatment to pre-treatment expression for each protein. Patients 102 and 103 received a lower dose (400 mg) of sorafenib while patients 105, 107, 108 received a higher dose (600 mg) of sorafenib. Expression ratios are shown for the 35 proteins with $p < 0.10$ in an unpaired t-test comparing low dose to high dose patients.

P250

The Value of Preoperative Positron Emission Tomography/ Computed Tomography (PET/CT) in Patients with High-Risk Melanomas T.J. Miner,* M. Barsky, L. Cherkassky, M. Vezeridis. *Surgery, Brown University, Providence, RI.*

Introduction: PET/CT scanning is increasingly used for preoperative staging of patients with high-risk malignant melanoma. The role of preoperative PET/CT as a routine staging procedure in asymptomatic patients with negative physical examinations is not established. **Methods:** Records of all patients receiving an operation for a high-risk melanoma (lesion ≥1mm) from June 2005 to June 2010 were examined. Results of preoperative PET/CT scans were evaluated in asymptomatic patients with documented negative physical examinations. **Results:** A PET/CT scan was performed in 71 patients with high-risk melanomas. This represents 13% (71/530) of all melanoma patients at our institution and 58% (71/123) of PET/CT performed. Positive scans were identified in 34% (24/71) patients. Increased FDG uptake was found in 8 local, 6 regional, and 12 distant sites. An invasive procedure to further aid in diagnosis was performed in 54% (13), yet only 3 (12.5%) patients were diagnosed with metastatic cancer. Each of these patients had regional disease subsequently diagnosed by a sentinel lymph node biopsy that corresponded to the suspicious PET/CT finding. Malignancy was excluded with additional imaging studies in 5 patients while 6 PET/CT positive outcomes were attributed to biopsy site changes at the primary site. Although PET/CT scans changed treatment approach in 75% of patients, mostly with invasive procedures, 88% of the findings on the PET/CT scan were false positives. No distant metastatic disease was identified at initial evaluation, and metastatic disease was confined to regional locations. Two distant positive PET/CT scans identified unrelated disease (recurrent prostate adenocarcinoma, and sarcoma). At one year, 3 patients (6.4%) with negative PET/CT scans had melanoma recurrence. **Conclusions:** Preoperative PET/CT in asymptomatic patients with high-risk melanomas is of limited benefit. The test was associated with a high false-positive rate and many invasive and unnecessary procedures. Metastatic melanoma was not identified in any patient and no additional regional disease distinct from the sentinel lymph node was identified.

P251

Preoperative F-18 Fluorodeoxy-D-Glucose-Positron Emission Tomography is an Important Tool in the Management of Patients with Thick (T4) Melanoma R. Arrangoiz,[1]* P. Papavasiliou,[1] C. Housock,[2] A.C. Berger,[2] J.C. Kairys,[2] M.J. Mastrangelo,[2] M. Zook,[1] J.Q. Yu,[2] E.R. Sigurdson,[1] J. Farma.[1] *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Thomas Jefferson University, Philadelphia, PA.*

Background: The diagnostic yield of preoperative PET for regional and distant metastases for thin and intermediate thickness melanoma is low. Our previously published work did not support the use of PET for intermediate thickness melanoma. The objective of our study was to determine if preoperative PET performed for T4 melanomas helped guide management and alter the treatment plan. Methods: A retrospective chart review identified 216 patients with T4 melanomas treated at two tertiary institutions between 2003-2009. Fifty-six patients met our inclusion criteria of having a T4 lesion with a preoperative PET and no clinical evidence of regional or distant metastatic disease. The patient's age, gender, pathology, surgery and PET findings were reviewed. Results: Of the 56 patients (M: 32, F: 24, mean age 67 years) the median tumor thickness was 6 mm. Tumor ulceration was identified in 61% (n=34) and satellitosis in 25% (n=25) of the cases. Preoperative PET identified seven (13%) patients with regional and four (7%) patients with metastatic disease. The melanoma related-treatment plan was altered in 11% (n=6) of the cases based on PET findings. PET was negative 60% (n=33) of the time and in 35% (n=20) of the cases it identified incidental findings that required further evaluation (mediastinal lymphadenopathy, lung, colon, and thyroid lesions). Twenty-three patients (48%) had a positive sentinel lymph node biopsy. Conclusion: In patients with T4 lesions preoperative PET changed the treatment plan for the melanoma in 11% of our cases with an additional 20 pts with incidental findings. In this subset of patients we feel there is a benefit to preoperative PET; further studies should be performed to validate our findings.

Demographics and Results

Characteristics	Number of Patients and Percentages
Total Number of Patients	216
Fox Chase Cancer Center Patients	116 (53%)
Thomas Jefferson UniversityPatients	100 (46%)
Number of Patients that Met Inclusion Criteria	56 (30%)
Gender Male Female	 32 24
Age Mean Age Median Age	 67 70
Tumors with Satellitosis	14 (25%)
Tumors with Ulceration	34 (61%)
Lesions on the Trunk	16 (29%)
Lesions on the Extremities	28 (50%)
Lesions in the Head and Neck	12 (21%)
Positive SLNB	23 (48%)
PET Results Negative Changed Melanoma Plan Incidental Findings	 33 (60%) 6 (11%) 20 (35%)
PET Identified Regional Metastasis Distant Metastasis	 7 (13%) 4 (7%)

P253

Short-Term Outcomes after Combined Colon and Liver Resection: A Population Study A. Abbott,[1]* H.M. Parsons,[2] T.M. Tuttle,[1] E.H. Jensen.[1] *1. Surgery, University of Minnesota, Minneapolis, MN; 2. Department of Health Policy and Management, University of Minnesota, Minneapolis, MN.*

Introduction Single and multi-institution studies have demonstrated the safety of combined colon and liver resection (CCLR) for metastatic colon cancer. The aim of our study was to compare the short-term outcomes of patients after CCLR with those who underwent colon resection (CR) or liver resection alone (LR) using a population database. Methods We used the National Inpatient Sample to select patients between 2002 to 2006 who underwent surgical resection for colon cancer. Chi-square tests were used in our unadjusted analyses to compare patients undergoing CCLR versus CR or LR. Logistic regression was used to identify predictors of peri-operative morbidity, mortality, and length of stay (LOS). Results We identified 361,096 patients during our study period (CCLR 1.0%; CR 89.3%; LR 9.7%). Patients undergoing CCLR were younger than those undergoing CR (67 years vs 71 years), and older than those

undergoing LR (67 years vs 61 years). The most common complications overall were hematologic (37%) and gastrointestinal (35%). On multivariate analysis, age >70 years, male gender, African American race, non-private health insurance, non-teaching hospital status, geographic location, and Elixhauser score >1 were predictive of increased risk of peri-operative morbidity. CCLR was not associated with increased risk of complications compared to CR alone (OR 1.12, 95% CI 0.94 to 1.33, p=0.21) (Table). Prolonged LOS was associated with age >70, male gender, African American race, non-private insurance, urban hospital setting, non-teaching hospital status, geographic location, and Elixhauser score >1. CCLR was not associated with prolonged LOS compared to CR alone (OR 1.19, 95% CI 0.99 to 1.4, p = 0.06). Mortality was associated with age >61, male gender, Hispanic race, non-private insurance, geographic location, and Elixhauser score >1. In- hospital mortality was not significantly higher after CCLR compared to CR (OR 1.17, 95% CI 0.79 to 1.74, p=0.43). Conclusion In this population based study, CCLR has similar in-hospital morbidity and mortality compared to CR and LR. The low proportion of patients who had CCLR in our cohort (1.0%) indicates that this procedure may be under-utilized.

Predictors of Peri-operative Complications after Combined Colon and Liver Surgery, Colon Surgery, or Liver Surgery for Metastatic Colon Cancer

Predictor	Odds Ratio	95% Confidence Interval	p-value
Age			
<50	Ref	Ref	Ref
51-60*	0.91	0.85, 0.97	0.005
61-70	1.03	0.96, 1.10	0.42
>70*	1.67	1.55, 1.80	<0.0001
Sex			
Female	Ref	Ref	Ref
Male*	1.19	1.15, 1.22	<0.0001
Race			
White	Ref	Ref	Ref
Black*	1.11	1.04, 1.18	0.002
Hispanic	0.93	0.85, 1.02	0.1
Other	0.89	0.81, 1.00	0.05
Procedure			
Colon	Ref	Ref	Ref
Liver*	0.89	0.82, 0.98	0.01
Combined Colon/Liver	1.12	0.94, 1.33	0.21
Primary Payer			
Private Insurance	Ref	Ref	Ref
Medicare*	1.15	1.10, 1.22	<0.0001
Medicaid*	1.26	1.15, 1.39	<0.0001
Self-pay*	1.27	1.16, 1.39	<0.0001
Hospital Location			
Urban	Ref	Ref	Ref
Rural	0.96	0.89, 1.03	0.25
Teaching Status			
Teaching	Ref	Ref	Ref
Non-teaching*	1.08	1.02, 1.15	0.008
Geographic Region			
Midwest	Ref	Ref	Ref
Northeast	0.99	0.91, 1.08	0.85
South*	1.09	1.01, 1.17	0.03
West	1.07	0.98, 1.16	0.13
Elixhauser Score			
0	Ref	Ref	Ref
1*	1.43	1.35, 1.53	<0.0001
2*	2.11	1.98, 2.25	<0.0001
3*	2.89	2.70, 3.10	<0.0001
>4*	4.66	4.31, 5.02	<0.0001

Abbreviations: Ref, referent
* denotes p-value <0.05

P254

The adverse effects of smoking on postoperative outcomes following major cancer surgery in the VA population C. Gajdos,[1]* E. Campagna,[1] W. Henderson,[1] J. Singh,[2] R. Merkow,[1] T.K. Houston,[3] M.T. Hawn.[1] *1. Surgery, University of Colorado at Denver, Aurora, CO; 2. University of Alabama at Birmingham, Birmingham, AL; 3. University of Massachusetts, Worcester, MA.*

There is evidence in the general surgery literature that smokers have higher rates of postoperative complications compared to non-smokers. The possible negative effects of smoking on postoperative outcomes have not been well-studied in cancer patients. We used the VA National Surgical Quality Improvement Program assessing outcomes for patients undergoing major cancer surgery within the VA system during years 2002-2008. Multilevel multivariable logistic regression analysis was performed with a random effect for hospital to examine the relationship between smoking status and post-operative complications, adjusting for age, race/ethnicity, work RVU, ASA class, surgeon specialty, and year of operation. Gastointestinal (GI) oncology patients and urologic oncology (UO) patients were more likely to be never smokers (NS), compared to the majority of patients being current (CS) or prior (PS) smokers in the thoracic surgery (TS) and CNS malignancy (CNS) groups (P<0.05). Compared to NS, PS and CS with GI malignancies were significantly more likely to have surgical site infection (SSI); combined pulmonary complications (CPC: pneumonia, failure to wean from ventilator and reintubation). Both PS's and CS's had a significantly higher mortality at 30 days and one year. TS patients with a current smoking status were more likely to develop CPC compared to NS, but SSI rates were not affected by smoking status in TS patients. CS's in the TS population also had significantly higher mortality rates at one year. PS status did not affect the same postoperative complications in TS patients. CS's undergoing surgery for CNS tumors had increased odds of CPC compared to both never and PS's. UO patients had the least adverse events related to smoking status. PS and CS status is a significant risk factor for major postoperative complications and mortality following GI tumor operations in veterans. CS status is associated with worse postoperative outcomes in thoracic and CNS cancer surgery patients compared to never smoking. Smoking cessation should be encouraged prior to all major cancer surgery with the most short-term benefits likely seen following TS and CNS operations.

Cancer site	Smoking status	SSI	Compositepulmonary outcome	Death (30 days)	Death (1 year)
GI (N=12803)	Prior	1.26 (1.10, 1.44)*	1.60 (1.38, 1.86)*	1.46 (1.16, 1.83)*	1.21 (1.07, 1.36)*
	Current	1.19 (1.04, 1.37)*	2.01 (1.73, 2.34)*	1.44 (1.12, 1.86)*	1.60 (1.42, 1.82)*
Thoracic (N=5661)	Prior	0.87 (0.49, 1.54)	1.19 (0.92, 1.53)	1.38 (0.89, 2.12)	1.19 (0.95, 1.50)
	Current	1.08 (0.64, 1.83)	1.90 (1.50, 2.40)*	1.35 (0.88, 2.07)	1.47 (1.18, 1.83)*
CNS (N=1775)	Prior	1.37 (0.69, 2.74)	1.38 (0.87, 2.18)	NA	0.94 (0.65, 1.36)
	Current	1.79 (0.99, 3.22)	2.48 (1.62, 3.78)*	NA	1.22 (0.86, 1.72)
Urology (N=3713)	Prior	1.12 (0.69, 1.82)	1.25 (0.87, 1.80)	1.00 (0.55, 1.80)	1.02 (0.77, 1.35)
	Current	1.17 (0.77, 1.77)	1.60 (1.14, 2.24)*	0.96 (0.53, 1.73)	1.19 (0.92, 1.55)

All cells have odds ratios and 95% confidence intervals compared to never smokers with an odds ratio of 1.
* statistically significant
NA: There was not enough 30-day mortality in the CNS group to run an adjusted model

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The Efficacy of Graduated Compression Stockings for Prevention of Lymphedema after Inguinal Lymph Node Dissection M.M. Stuiver,[1]* J.D. De Rooij,[2] C. Lucas,[3] O.E. Nieweg,[4] N.K. Aaronson.[5] *1. Department of Physical Therapy, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; 2. Department of Rehabilitation Medicine and Physical Therapy, Erasmus University Medical Centre - Daniel den Hoed, Rotterdam, Netherlands; 3. Department of Clinical Epidemiology, Biostatistics and Bioinformatics, Faculty of Medicine, University of Amsterdam, Amsterdam, Netherlands; 4. Division of Psychosocial Research and Epidemiology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; 5. Department of Surgical Oncology, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands.*

Introduction: Graduated compression stockings have been advocated for prevention of lymphedema after inguinal lymph node dissection (ILND). Scientific evidence of their efficacy is lacking, they are bothersome to put on and take off, and their use may have side-effects. The primary objective of this study was to assess the efficacy of class II compression stockings for the prevention of lymphedema in cancer patients following ILND. Secondary objectives were to investigate the influence of using stockings on the incidence of wound com-

plications and genital edema and on health-related quality of life (HRQoL) and body image. Methods: Eighty patients who underwent inguinal lymph node dissection at one of two specialized cancer centers were randomly allocated to compression stocking use for six months or a control group. Lymphedema in the leg and the genital area was assessed at baseline, at two-month intervals during the first six post-operative months and at 12 months. Wound complications were recorded. HRQoL was assessed at baseline, 6 months and 12 months. Body image perception was assessed at 6 and 12 months follow up. Time-to-event analysis was used to compare the risk of developing lymphedema in each group. Results: Forty-five patients with melanoma and 35 patients with a urogenital tumor were included. At 6 months, 14 patients in the experimental and 16 patients in the control group had lymphedema (adjusted hazard ratio 0.69, 95%CI 0.38-1.26, p=0.23). At twelve months, twenty-eight patients in each group had lymphedema (adjusted hazard ratio 0.71, 95%CI 0.40-1.24, p=0.22). Lymphedema in the genital area developed in 27% of patients in the experimental and 31% in the control group. No significant differences were observed between groups in the frequency of wound complications, HRQoL or body image. Conclusion: This study was unable to demonstrate the efficacy of prophylactic use of graduated compression stockings for prevention of lymphedema after inguinal node dissection. Based on these results, routine prescription of graduated compression stockings for the prevention of lymphedema should be questioned.

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Treatment trends for gastroesophageal junction carcinoma, 1998-2007 D.D. Cox,[1]* S. Fedewa,[2] A. Chen,[2] K. Virgo,[2] E. Ward.[2] *1. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY; 2. American Cancer Society, Atlanta, NY.*

INTRODUCTION: The incidence of distal esophageal (EC) and gastroesophageal carcinoma (GEC) has steadily increased throughout the Western world. Treatment regimens including surgery and/or chemoradiation (adjuvant vs. neoadjuvant) have varied depending on the subsite location, histology, and classification of these tumors. Previous studies have demonstrated benefit of neoadjuvant regimens on survival and highlighted clear differences in tumor location and histology according to race/ethnicity. We examined if the treatment of EC/GEC has changed over time and if treatment rates varied by race/ethnicity. METHODS: We used the National Cancer Data Base (NCDB), a national hospital-based cancer of registry to study 53,545 adults diagnosed with locoregional EC/GEC over a ten year period (1998-2007). Demographic, insurance clinicopathological, and treatment variables were obtained from the NCDB. Logistic regression and multivariate model analysis was performed to predict odds ratios (OR) and 95% confidence intervals (CI) of receiving surgery alone (S), surgery plus adjuvant therapy (SA), surgery plus neoadjuvant therapy (NAS), and systemic therapy (ST) alone. RESULTS: The trend of NAS has gradually increased over the time period with 15.74% patients receiving NAS in 1998 to 22.73% in 2007. African American (OR=0.50, 95% CI 0.38-0.66) and Hispanic (OR=0.57, 95%CI 0.43-0.76) patients were less likely to receive NAS versus S. Uninsured, Medicaid and older patients were less likely to NAS. CONCLUSIONS: Overall,an increase in neoadjuvant therapy plus surgery has been observed. Despite this trend,African American,Hispanic,uninsured, and lderly patients were less likely to receive NAS. Treatment disparities such as these may lead to poorer survival.

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WITHDRAWN

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Long-Term Survival After Pneumonectomy for Non-Small Cell Lung Cancer: Prognostic Implications for the 5-year Survivor J. D'Cunha, N.M. Rueth,* M.A. Maddaus, E.B. Habermann. *Department of Surgery, University of Minnesota, Minneapolis, MN.*

Introduction: The long-term impact of undergoing pneumonectomy for non-small cell lung cancer (NSCLC) is not well understood beyond the initial years after surgery. Our aim was to evaluate the long-term survival rates and factors associated with mortality for pneumonectomy survivors. Methods: Using the Surveillance Epidemiology and End Results (SEER) Database 2007 submission, we identified patients who underwent lobectomy or pneumonectomy for NSCLC from 1988-2002. To assess the impact of pneumonectomy vs. lobectomy (control group) on long-term (10-year) overall survival (OS), cancer-specific survival (CSS), and non-cancer-specific survival (NCSS), we performed unadjusted survival analyses using the Kaplan Meier method for all patients at time of diagnosis, and then only for those who survived 5 years after resection. For 5-year pneumonectomy survivors, we constructed a logistic regression model to determine clinicopathologic characteristics associated with long-term survival (α=0.05). Results: 15,102 patients met inclusion criteria (pneumonectomy 651, lobectomy 14,451). For those who survived 5 years beyond surgical resection (pneumonectomy 296, lobectomy 6,826), there were no significant differences in 10-year OS, CSS, or NCSS (see table), despite anticipated significant differences in OS and CSS from the time of diagnosis (p<0.001). For 5-year pneumonectomy survivors, long-term OS, CSS, and NCSS were not predicted by gender, race, laterality (right vs. left), stage, tumor histology, or SEER registry. Age >70 was associated with significantly poorer OS (HR=2.3; 95% CI=1.2-4.2) and NCSS (HR=5.5; 95% CI=1.6-19.1), but not CSS. Interestingly, mortality from NSCLC remained high in 5-year survivors (pneumonectomy=36.4%, lobectomy=34.6%). Conclusions: Among NSCLC pneumonectomy patients that survived 5 years, long-term outcome was equivalent to those who underwent lobectomy, suggesting that clinicopathologic characteristics associated with undergoing a pneumonectomy were significant only in the early period. Importantly, cancer death remained a considerable source of mortality beyond 5 years.

10-YEAR SURVIVAL RATES FOR PATIENTS WHO UNDERWENT PNEUMONECTOMY VS. LOBECTOMY

SURVIVAL FROM TIME OF DIAGNOSIS:	PNEUMONECTOMY	LOBECTOMY	p-value
OS	22.8%	27.9%	<0.001
CSS	33.1%	39.7%	<0.001
NCSS	69.2%	70.5%	0.38
5-YEAR SURVIVORS:	PNEUMONECTOMY	LOBECTOMY	p-value
OS	50.2%	52.7%	0.47
CSS	63.6%	65.4%	0.64
NCSS	79.1%	80.8%	0.56

OS: OVERALL SURVIVAL; CSS: CANCER-SPECIFIC SURVIVAL; NCSS: NON-CANCER-SPECIFIC

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Current Outcomes of Pelvic Exenteration among Female Patients: Analysis of Nationwide Inpatient Sample 2002-2008 H. Dao,* J.H. Lee, C.V. Strom, P.E. Miller, M.J. Lopez. *St. Elizabeth's Medical Center. Tufts University School of Medicine, Boston, MA.*

Introduction: Pelvic exenteration remains an established operation for treatment of selected patients with favorable tumor biology. This intervention has been associated with high rates of complications and postoperative mortality. The objective of this paper is to characterize this subset of the population undergoing surgery and describe current outcomes at a national level. Methods: Analysis of the Nationwide Inpatient Sample from the Healthcare Cost and Utilization Project for the years 2002 through 2008 was performed. This is an administrative database incorporating 100% of discharges from a 20% stratified sample of U.S hospitals. ICD-9 codes were used to identify diagnoses and procedures. Patient demographics, payer, in-hospital mortality, and complications were included as variables. Results: A total of 11,243 patients were identified with a mean age ± SD of 63.02 ± 13.25 years. 79% of the patients were white and 85% of the population was insured privately or by medicare. Mean LOS was 14.28 ± 13.00 days. In-hospital mortality was 2%. No difference in mortality could be accounted for based on insurance status or race. The most common complication encountered was postoperative ileus (19.7%), followed by acute renal failure (ARF) (9.8%), respiratory failure (3.4%), deep vein thrombosis (1.0%), severe sepsis (1.0 %) and postoperative bowel obstruction (0.8%). Univariate analysis revealed that development of the following conditions was associated with increased in-hospital mortality: ARF (p<0.0001, OR 2.71, 95% CI 1.94-3.78), severe sepsis (p<0.0001, OR 45.12, 95% CI 30.10-67.62), congestive heart failure (p=0.02, OR 1.94, 95% CI 1.27-2.96), and acute respiratory failure (p<0.0001, OR 8.80, 95% CI 6.28-12.33). Performance of the surgery in teaching centers was associated with decreased in-hospital mortality (p< 0.05). Conclusions: Despite the fact that total pelvic exenteration continues to carry significant postoperative morbidity, in-hospital mortality has seen a reduction

from the rates reported historically among this subset of patients. The best results seem to be obtained when the operation is performed in large teaching centers.

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The impact of ethnic group background on presentation and outcomes for patients with gastroesophageal adenocarcinoma

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Introduction: Among patients with gastric and esophageal adenocarcinoma, race has been associated with decreased survival. Often the reported differences are heavily weighted by the improved outcomes for Asian gastric cancer patients. We examined the association between ethnicity, cancer stage, and outcomes in a largely Hispanic and Black population. Methods: We reviewed tumor registry data at two hospitals between 1999 and 2009. Patients with gastric or esophageal adenocarcinoma were included. Interval to treatment was defined as time from diagnosis to first therapy. Continuous variables were assessed with ANOVA. X2 was used for categorical variables. Median overall survival was estimated with Kaplan-Meier method and log-rank comparison and Cox regression to control for covariates. Results: For 515 patients meeting inclusion criteria, 254 (50%) identified themselves as Hispanic or Black. Ethnic group distribution, demographic and staging information, treatment variables, and overall and stage-specific survival are included in the attached table. Hispanic and Black patients more often presented with gastric or GE junction cancer and metastatic disease than the remainder of the study population. Interval to treatment and percentage of patients receiving chemotherapy did not differ between ethnic groups. Age and gender were not associated with survival differences. Median survival was reduced within the Hispanic and Black groups compared to the remainder of the study population (8.8 v 14 months, $p<0.01$). Multivariate analysis identified both advanced cancer stage ($p<0.001$, HR 1.90, 95% CI 1.68–2.15) and Hispanic or Black ethnic group ($p<0.04$, HR 1.10, 95% CI 1.004–1.202) as independent predictors of decreased survival. Conclusion: Hispanic and Black patients with gastric and esophageal adenocarcinoma present with later stage disease at a younger age. Overall survival is decreased for Hispanic and Black patients when adjusting for cancer stage. Difference in outcome is not associated with differences in either time to treatment or systemic chemotherapy use. Differences may be due to tumor biology, healthcare access, or patient-related factors.

Presentation and outcomes for patients with gastroesophageal adenocarcinoma by ethnic group

	White, non-Hispanic	Hispanic	Black	Black or Hispanic	Other/Unknown	p-value
Patients (% of total)	232 (45)	133 (26)	121 (24)	254 (50)	29 (6)	
Age in years, median (range)	63 (28-92)	54 (21-92)	61 (29-95)	57 (21 -95)	60 (26 - 77)	< 0.001
% Male	82	59	55	57	66	<0.001
% Gastric or GE junction cancer	48	86	90	88	83	<0.001
Cancer Stage Stage I Stage II Stage III Stage IV	37 (19) 34 (18) 38 (20) 84 (44)	9 (8) 12 (10) 21 (18) 76 (64)	18 (16) 7 (6) 19 (17) 67 (60)	27 (12) 19 (8) 40 (18) 143 (62)	2 (8) 4 (15) 7 (27) 13 (50)	<0.01
Interval to treatment in days, median (std. dev.)	28 (48)	22 (33)	26 (34)	25 (33)	28(85)	0.26
% Received chemotherapy All stages Stage IV	125 (54) 50 (60)	73 (55) 40 (53)	49 (41) 27 (40)	122 (48) 67 (47)	16 (62) 7 (53)	0.98 0.71
Median survival, months (95% C.I.) Stage I Stage II Stage III Stage IV Stage I-IV	47 (22-73) 17 (12-22) 14 (8 - 21) 7 (5-9) 14 (10-18)	59(0-123) 71 (---)* 13 (9-17) 6 (2-9) 10 (8-12)	NR NR 16 (8-23) 3 (2-4) 6 (3-9)	59 (46-72) 71 (---)* 14 (9-18) 4 (3-5) 9 (7-11)	26 (---)* (---)* 30 (0-79) 11 (2-20) 29 (22-38)	0.37 0.15 0.61 0.01 0.05

*not calculable

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Body Mass Index is Associated with Morbidity after Pancreatic Resection: Results from the ACS-NSQIP D.Y. Greenblatt,* Y. Wan, E.R. Winslow, C.S. Cho, S.M. Weber. *Department of Surgery, University of Wisconsin, Madison, WI.*

Introduction: There is a worldwide pandemic of obesity, and obesity is a risk factor for pancreas cancer and other malignancies. Previous studies on the impact of body mass index (BMI) on outcomes after major cancer surgery have yielded conflicting results. In this study we utilized a multi-institutional database to study the association between BMI and early outcomes after pancreatic resection (PR). **Methods:** Patients who underwent pancreaticoduodenectomy, distal pancreatectomy, and total pancreatectomy from 2005-2008 were identified from the American College of Surgeons National Surgical Quality Improvement Program database. For each patient, BMI was calculated and classified according to World Health Organization definitions. Associations between BMI and outcomes after PR were determined. Odds ratios for morbidity were calculated after controlling for more than 30 potential confounders, including demographics, comorbid conditions, laboratory values, and operative factors. **Results:** Of 6774 patients who underwent PR, 2457 (36%) were normal weight, 220 (3%) underweight, 2379 (35%) overweight, and 1718 (26%) obese. The rate of 30-day morbidity in obese patients was 36.3%, compared to 30.0% in normal weight individuals ($p<0.001$). Obesity was associated with increased rates of wound infection, abscess, venous thromboembolism (VTE), and renal failure (Table). Underweight correlated with increased respiratory complications, VTE, and length of stay. After adjusting for potential confounders, the association between BMI class and morbidity remained significant. The adjusted odds ratio for morbidity in patients with class III obesity (BMI ≥40 kg/m^2) was 1.61 (95% CI 1.26-2.09) relative to normal weight controls. In obese patients, loss of ≥10% of body weight prior to surgery decreased the odds of morbidity (adjusted OR 0.62; 95% CI 0.45-0.87). Weight loss was not protective for patients in other BMI classes. **Conclusion:** Both obesity and underweight are associated with increased morbidity after PR. Preoperative weight loss in obese patients, and optimizing nutritional status in underweight patients, may improve outcomes in patients undergoing pancreatectomy.

Table. Frequency of 30-day outcomes after pancreatic resection, stratified by World Health Organization body mass index class. BMI denotes body mass index in kg/m^2; VTE, venous thromboembolism; LOS, length of hospital stay; SD, standard deviation.

Outcome	Underweight (BMI <18.5) n=220	Normal Weight (BMI 18.5-24.9) n=2457	Obese (BMI ≥30) n=1718	p-value
Any complication, %	30.0	30.0	36.3	<0.001
Wound infection, %	10.0	10.5	14.6	<0.001
Abscess, %	9.6	9.9	13.8	<0.001
Respiratory, %	14.6	8.0	10.1	0.001
VTE, %	4.5	2.3	4.2	0.004
Renal failure, %	0.5	1.1	2.2	0.030
LOS, days, mean (SD)	15.3 (17.5)	12.0 (9.9)	12.4 (12.8)	<0.001

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Decreasing disparities in access to Partial Breast Radiation in a Large Inner City Public Hospital M. Amin,[1]* S. Gabram,[1] H. Bumpers,[2] J. Landry,[3] A. Jani,[3] R. Diaz,[3] M. Rizzo.[1] *1. Department of Surgery, Divison of Surgical Oncology, Emory University, Atlanta, GA; 2. Morehouse School Of Medicine, Atlanta, GA; 3. Department of Radiation Oncology, Emory University, Atlanta, GA.*

INTRODUCTION: Adjuvant radiotherapy with Breast Conservation Surgery (BCS) has revolutionized medicine by allowing women to avoid a mastectomy. Whole Breast Irradiation (WBI) has a compliance rate for enrollment and completion of 75-95%. Partial Breast Irradiation (PBI) has emerged as a valid alternative that requires a shorter time commitment with possible advantages for women with financial constraints and/or transportation issues. We are the first to report experience with PBI at a large public hospital that serves low income and potentially noncompliant patients. METHODS: A retrospective chart review was conducted of female patients who underwent BCS for Stage 0-IIa breast cancer from August 2007 to August 2010 treated with PBI with a MammoSite brachytherapy catheter. RESULTS: 24 patients (83%

AA, 4%Caucasian, 12% other) were considered for PBI. Average age was 61years (range 46-80). Four patients could not undergo PBI, 2 for inadequate skin distance from the balloon and 2 due to asymmetry of the balloon identified after planning and completed WBI over a 5-week period. Median follow-up was 15 months (2-35). 7 patients had DCIS with an average size of 0.4 cm (0.2-1.3) and 13 patients had invasive ductal carcinoma with an average size of 1.1 cm (0.8-2.5). All patients had negative margins: average 5.9mm. The MammoSite average balloon size was 53ml (30-70) and the skin distance 1.02cm (0.6-2.4). The treatment consisted of 34 GY delivered at 3.4 GY per fraction twice a day for 10 treatments. There were no major complications, 1 patient(5%) developed mild radiation dermatitis. 1 patient(5%) with DCIS was found to have in breast recurrence 1 year after surgery and managed with completion mastectomy. Thus, all 24 patients (100%) initially identified for PBI successfully completed adjuvant radiation therapy. CONCLUSION: Patient compliance with postoperative radiation is key to minimize local recurrence after BCS for breast cancer. This is the first report to describe success with the MammoSite catheter in underserved women at a public hospital setting with comparable outcomes of compliance, complications and recurrence rate to nationally published results.

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Surveillance Strategies Following Treatment with Curative Intent for Breast Cancer R. Parmeshwar,[1]* E. Allam,[1] L. Chen,[2] K.S. Virgo,[3] J.A. Margenthaler,[2] F.E. Johnson.[1] *1. Department of Surgery, St. Louis University School of Medicine, St. Louis, MO; 2. Washington University, Saint Louis, MO; 3. American Cancer Society, Atlanta, GA.*

Introduction: Primary therapy for potentially curable breast cancer is standardized and large well-designed, clinical trials of post-treatment surveillance strategies have been published. American Society of Clinical Oncology (ASCO) guidelines recommend only office visits and mammograms. We evaluated how post-treatment patient surveillance is carried out by radiation oncologists (RO), medical oncologists (MO), and surgeons (SO) after initial treatment for breast carcinoma. Methods: A survey instrument with 4 idealized vignettes describing generally healthy women with breast carcinoma of differing prognoses (TNM stages 0 - III) was emailed to the 3245 ASCO members who identified themselves as having breast cancer as a major focus of their practice. They were asked how often they would recommend 12 specific surveillance modalities for these 4 idealized patients during post-treatment years 1–5. Responses were grouped for all 4 vignettes; mean, standard deviation, median and range of frequency of use for each modality were calculated. We compared surveillance practices across specialties (RO vs. MO vs. SO) by ANOVA. Results: There were 1012 total responses; 846 were evaluable. 5% were RO, 70% were MO, 10% were SO and 15% did not specify. Statistically significant variation in surveillance intensity among the 3 groups of experts was observed ($p<0.05$). For example, RO recommended 3.1 ± 1.4 (mean ± SD) office visits; MO recommended 3.5 ± 1.6; SO recommended 3.0 ± 1.7 in post-treatment year 1. The range of recommended office visits in year 1 was 0-12 for all 3 groups. For the other 10 surveillance modalities, similar variation was noted. In post-treatment year 1, there were significant differences among the groups of experts for office visit, complete blood count, liver function test and serum CA 15-3 ($p<0.05$). Conclusions: Many surveillance tests not recommended in ASCO guidelines are routinely utilized by RO, MO, and SO. There are significant differences in surveillance practice among specialties (RO, MO, SO).

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Surgeon knowledge is associated with clinical and oncologic outcomes in patients with rectal cancer D.P. Richardson,* G.A. Porter, P.M. Johnson. *Dalhousie University, Halifax, NS, Canada.*

Introduction: Much of the variation in rectal cancer outcomes has been attributed to surgeon factors. It is unknown how surgeon knowledge of rectal cancer care may impact patient outcomes. The purpose of this study was to analyze the relationship between surgeon knowledge of rectal cancer care and quality of care, as measured by sphincter-preservation (SP) rate, use of total mesorectal excision (TME), lymph node harvest, local recurrence (LR) and overall survival (OS). Methods: A mail survey with 11 questions pertaining to staging, surgical decision-making in low rectal cancer, surgical margins, lymph node harvest and surveillance was sent to all general and subspecialty surgeons in Nova Scotia, Canada. Each surgeon received a score based on the number of correct responses (max score=11). Surgeons were dichotomized into high and low score groups based on the median score. The provincial cancer registry was used to identify new rectal cancer patients from 7/1/2002-6/30/2006 in Nova Scotia. A comprehensive review of inpatient, outpatient and cancer center medical records was used to assemble this population-based cohort. Results: Of 521 patients who underwent treatment with curative intent, 377 (72%) were treated by 25 surgeons who responded to the survey (median survey score 8, range 4-11). The median follow-up after surgery was 4.2 years. On multivariate logistic regression analysis, controlling for patient and tumor factors, patients treated by surgeons with a high survey score were more likely to receive SP surgery (OR 2.28 95%CI 1.26-4.13), a TME (OR 2.52, 95%CI 1.59-4.00) and have an adequate lymph node harvest (2.31 95%CI 1.45-3.67). On multivariate Cox proportional hazards regression, patients treated by surgeons with a high survey score had a 33% improvement in OS (HR 0.67, 95%CI 0.46-0.98) and were 46% less likely to develop LR (HR 0.54, 95%CI 0.30-0.96) compared to patients treated by surgeons with a low survey score. Conclusion: There was a clear association between surgeon knowledge, quality of care and outcome in rectal cancer. These results suggest that rectal cancer may be well-suited to knowledge-based quality initiatives.

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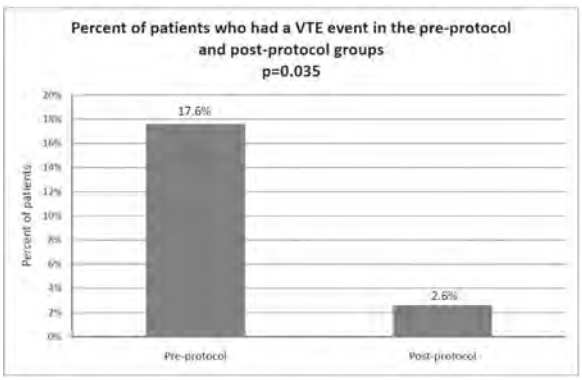
Timing of Pre-operative Pharmacoprophylaxis for Pancreatic Surgery Patients: A Venous Thromboembolism Reduction Initiative C. Reinke,* J. Drebin, S. Kreider, C. Kean, A. Resnick, S. Raper, R. Kelz. *Hospital of the University of Pennsylvania, Philadelphia, PA.*

Introduction: Venous thromboembolism (VTE), a potentially fatal complication, remains a clinical problem in surgical oncology. General anesthesia results in venous stasis and has been implicated in the cause of post-operative VTE. Current literature fails to confirm the importance of the pre-operative use of pharmacoprophylaxis (PP). We report the impact of a single dose of pre-operative subcutaneous heparin (SQH) on VTE events following pancreatic surgery. Methods: A retrospective cohort study of patients undergoing pancreatic surgery by a single surgeon and enrolled in the ACS NSQIP database (FY09/10) was performed. In FY10, a protocol was developed to encourage the routine use of pre-operative PP for high risk patients. We compared patient characteristics before and after the implementation of the new protocol. Our primary outcome was percent of VTE within 30 days of surgery and secondary outcomes were bleeding events and 30-day mortality. Outcomes were compared using the student's t-test and the Fischer's exact test. Results: A total of 73 patients were studied. Thirty-four patients underwent surgery prior to and 39 had surgery following the implementation of the new protocol. All patients received pre-operative intermittent compression boots (ICB) and post-operative PP. Patients in the two groups were statistically equivalent with respect to age, BMI, length of procedure, and overall VTE risk factors. The percentage of patients with a VTE significantly decreased from 17.6% to 2.6% (FY09 vs FY10, p=0.035.) The number of red blood cells transfused in the OR was not statistically different between the two groups (mean number of units transfused 0.44 vs 0.72, p=0.43.) One patient returned to the operating room for bleeding after the implementation of the protocol. There were no deaths. Conclusions: Pre-operative ICBs alone are inadequate for VTE prophylaxis for high risk patients. The use of a preoperative dose of SQH in high-risk surgical patients resulted in a dramatic reduction of VTE events following pancreatic surgery.



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Complete versus selective peritonectomy does not increase the risk of complications after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Analysis of 406 combined procedures

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Management of peritoneal carcinomatosis by cytoreductive surgery involving peritonectomy procedures and organ resections, combined with hyperthermic intraperitoneal chemotherapy (HIPEC) is associated with improved survival and substantial morbidity. Risk-factors for operative complications are still not well defined. Our analysis mainly focused on technical factors affecting operative outcome, aiming at improving the safety of the procedure. METHODS A prospective database of 406 combined procedures was reviewed. The main characteristic of our institution's approach consists of performing either selective or routine complete parietal peritonectomy of both macroscopically involved and uninvolved surfaces, according to the different dissemination patterns of the disease entities being treated. Multivariate analysis tested potential predictors of moderate/severe morbidity (NCICT-CAE): 5 peritonectomies (greater and lesser omentectomy, pelvic, left and right upper quadrant peritonectomy), 12 organ resections, 9 other operative factors and 11 clinical control variables. RESULTS Mortality and morbidity were 2.2% and 25.6%. Bowel perforation/anastomotic dehiscence occurred in 10.3% of procedures, renal and hematologic toxicity in 5.7% and 6.2%, respectively. Complete versus selective peritonectomy correlated to complications at univariate but not multivariate analysis (P=0.733). The most powerful risk-factor for complications was the extent of peritoneal involvement, expressed as peritoneal cancer index ranging from 1 to 39. Each single point increase on this score increased the risk of complications by 5%. Additional independent predictors of major morbidity were poor performance status, number of organ resections, HIPEC with cisplatin and doxorubicin, cisplatin dose >240mg. (see table) CONCLUSIONS Acceptable morbidity and low mortality can be achieved in high-volume centres. Operative complications are associated with tumor, patient and HIPEC-related factors, but not with complete versus selective peritonectomy. This information may help in optimizing operative techniques.

Univariate and multivariate analysis of factors affecting operative complications

Independent variables	Univariate Odds ratio (95%CI) P value		Multivariate Odds ratio (95%CI) P value	
ECOG performance score (0 vs.1-2)	2.43(1.41-4.20)	0.002	1.89 (1.03-3.50)	0.041
PCI (continuous variable, 1-39)			1.05 (1.01-1.08)	0.007
Visceral resections (continous variable, 0-9)			1.41 (1.09-1.84)	0.009
HIPEC (cisplatin and doxorubicin vs. cisplatin and mitomycin-C)	2.09 (1.33-3.30)	0.002	2.16 (1.27-3.66)	0.004
Cisplatin dose (>240 mg vs. ≤240 mg)	2. 76 (1. 53-5.01)	0.001	3.42 (1.72-6.81)	0.001
Peritonectomy (complete vs. selective)	1.90 (1.38-3.54)	0.002		0.733

CI: confidence interval; ECOG: Eastern Cooperative Oncology Group; PCI: peritoneal cancer index; HIPEC: hyperthermic intraperitoneal chemotherapy.

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Concordance with NCCN Practice Guidelines as a Measure of Quality of Care: A Review of Practice and Identification of Quality Gaps

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Background: Assessing concordance with practice guidelines is an attractive method for evaluating quality of cancer care. Guideline concordance alone may not be sufficient for quality tracking because care may be non-concordant (NC) with guidelines for acceptable reasons (physician recommendation, patient choice), thus limiting the value of using NC for accountability. This study examines the extent of NC with adjuvant systemic therapy (AST) breast cancer guidelines of the National Comprehensive Cancer Network (NCCN) at Roswell Park Cancer Institute (RPCI). Methods: Data on all breast cancer patients treated at RPCI are entered into the NCCN Breast Cancer Outcomes Database. Medical records were reviewed from all women with Stage I-III breast cancer with NC care for AST from 2000 – 2008 to identify circumstances for guideline NC care, defined as physician recommendation, patient choice, system failure (loss to follow-up), or an error in the database with truly concordant care. Results: There were 1602 patients of whom 580 (36%) received guideline NC AST. In patients with microinvasion, or Stage I with favorable histology (n=276), 66% were non-concordant, all for receiving endocrine therapy not recommended in the guidelines. The remainder of the results are summarized in the following table. There were database entry errors in 9% of cases. Overall, system failure with no reason for omission of AST occurred in 2.4% of cases. Conclusions: Measuring concordance with guidelines is a useful tool for quality assurance. In a Comprehensive Cancer Care Center, most NC was for clearly documented and appropriate reasons. The finding of cases lost to follow-up, or lack of referral to medical oncology supports establishing patient tracking systems to minimize system failure.

Group	Total (n)	Non-Concordant n (%)	Database Error, Concordant Care (n)	Physician Recommended (n)	Patient Choice (n)	System Failure (n)
Stage I,II Node Neg, ER/PR +	573	224 (39%)	12	151	56	5
Stage I, II Node Neg ER/PR -	173	30 (17%)	4	13	13	0
Stage II Node Pos ER/PR +	341	102 (30%)	23	42	31	7
Stage II Node Pos ER/PR -	109	7 (6%)	2	3	2	0
Stage III	130	36 (28%)	11	20	3	2
TOTAL			52	229	105	14

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The Reality of Pancreas Cancer Care from Access to Delivery

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Introduction: Prior literature has identified significant demographic differences in surgically treated patients with pancreas cancer (PC). Therefore, we hypothesized that disparities in socio-demographics exist in critical parameters throughout the continuum of PC care. **Methods:** We compiled a retrospective cohort of AJCC Stage I- IV PC from the California Cancer Registry. We used logistic regression to study socio-demographics as predictors of: 1) resectability at diagnosis or treatment (defined as absence of pre- or post-operative features of advanced or metastatic disease), 2) undergoing pancreatectomy, and 3) receipt of adjuvant chemotherapy (with/without radiotherapy) after surgery, while adjusting for confounders. **Results:** Of 20,312 patients with PC (1994-2008), 37% presented with resectable disease. Of those, only 40% received pancreatectomy. At multivariate analysis, race did not predict resectability, yet independently predicted undergoing pancreatectomy and receiving adjuvant therapies. Whites were 1.5 times as likely as blacks to undergo pancreatectomy and, following surgery, were more likely to receive chemotherapy with or without radiotherapy (for all, $p < 0.01$). Blacks were more likely to carry Medicaid than whites (10% vs. 5%, $p<0.01$). Compared to those with other insurances, Medicaid recipients showed lower odds of undergoing pancreatectomy (Table). **Conclusions:** Our results suggest that race and insurance continue to influence the continuum of optimal PC care. Going forward, further policies and research should identify effective strategies to neutralize disparities in PC care.

Socio-demographics and PC Care			
	OR	95% CI	P-Value
Predictors of Resectability*			
Whites v. Blacks	1.0	0.9-1.1	0.859
Managed Care/ Other Insurance v. Medicaid	1.1	1.0-1.3	0.045
Predictors of Pancreatectomy*			
Whites v. Blacks	1.5	1.2-1.9	<0.001
Managed/Other Insurance v. Medicaid	1.7	1.4-2.2	<0.001
Medicare v. Medicaid	1.8	1.4-2.4	<0.001
Predictors of Chemotherapy Receipt**			
Whites v. Blacks	1.3	1.0-1.7	0.037
No Insurance v. Medicaid	0.6	0.3-1.0	0.046
Predictors of Chemoradiation Therapy**			
Whites v. Blacks	1.4	1.0-1.9	0.023
No Insurance v. Medicaid	0.5	0.3-1.0	0.044

After adjusting for *patient- and tumor-related factors **and type of surgery

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Association of race and socioeconomic status and outcomes with patients with rectal cancer J. Nitzkorski,[1]* A.I. Willis,[2] J.M. Farma,[1] S.J. Cohen,[3] F. Zhu,[4] D.M. Nick,[5] E.R. Sigurdson.[1] *1. Fox Chase Cancer Center, Surgical Oncology, Philadelphia, PA; 2. Temple University School of Medicine, Department of Surgery, Philadelphia, PA; 3. Fox Chase Cancer Center, Medical Oncology, Philadelphia, PA; 4. Fox Chase Cancer Center, Biostatistics, Philadelphia, PA; 5. Temple University School of Medicine, Department of Health Information, Philadelphia, PA.*

Introduction: Few studies have evaluated disparities of race and socioeconomic status (SES) with outcomes in rectal cancer (RC) patients. We hypothesize that disparities exist in treatment and outcomes of RC. Methods: Medical records were retrospectively reviewed of RC patients treated from 2000-2009 at an NCI cancer center and an urban academic center. SES was estimated using census data. Quartiles of income and education based on zip codes were calculated. Lowest vs. other quartiles were compared. Clinicopathologic variables included: initial stage, chemotherapy refusal, sphincter preservation, and overall survival (OS). Results: 748 patients were included (581 white, 135 black, 6 other, 26 unknown). Patients with Medicaid were more likely to present with advanced disease (Table 1). Initial stage did not differ by race, income, or education. Non-white (NW) patients and those with low education were more likely to refuse chemotherapy. Only 7 patients refused radiation, limiting analysis. After excluding stage IV patients, sphincter preservation was higher among those with higher income. Median OS for all stages was worse for NW patients (31 months vs. 50 months, p<0.001), and among those with low income and education. Survival differences were greatest among NW patients with advanced disease (Table 1). Insurance was not associated with survival difference. Advanced age, stage, and NW race (HR 1.49, 95% CI 1.10-2.02, p=0.01) were independent predictors of survival. Conclusions: Disparity exists in treatment acceptance and outcomes in patients with RC. NW race and lower SES is associated with advanced disease, lower rates of sphincter preservation, chemotherapy refusal, and worse OS in patients with RC.

(N)	Advanced Disease	Chemotherapy Refusal	Sphincter Non-preservation
Race			
Non-white (141) vs. white (581)	NS	OR 4.82 CI 1.22-19.09, p=0.025	NS
Income			
Lowest (190) vs. others (545)	NS	NS	OR 4.10 CI 1.44-11.65, p=0.008
Education			
Lowest (191) vs. others (544)	NS	OR 10.68 CI 1.69-67.26, p=0.012	NS
Insurance			
Medicaid (202) vs. private (283)	OR 2.63 CI 1.51-4.57, p=0.005	NS	NS
Overall Survival	**Stage (N) ≤II / III / IV**	**Median OS Stage III**	**Median OS Stage IV**
White	187 / 122 / 161	75	25
Non-white	68 / 20 / 27	30	7
		p=0.006	p<0.001

NS: non-significant; OS: overall survival

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Healthcare Disparities Exist in Laparoscopic Colectomy for Colon Cancer C.N. Robinson,[1]* S. Sansgiry,[3] C.J. Balentine,[1] C.L. Marshall,[1] S. Tewani,[1] D.A. Anaya,[2] A. Artinyan,[2] D. Albo,[2] D.H. Berger.[2] *1. Baylor College of Medicine, Michael E. DeBakey Department of Surgery, Houston, TX; 2. Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX; 3. Houston VA Health Services Research and Development Center of Excellence, Michael E. DeBakey VA Medical Center, Houston, TX.*

Background: Minimally invasive (MIS) colon resection improves short-term outcomes in patients with colon cancer. However, it is unknown if the adoption of MIS is equally distributed amongst racial and socioeconomic groups. Therefore, we hypothesize that healthcare disparities exist in the utilization of laparoscopy for colon cancer. Methods: The National Inpatient Sample database was used to retrospectively review minimally invasive colon resections for cancer from 2005 through 2007. ICD-9 codes were used to identify laparoscopic colon cancer resections. Categorical variables were compared using chi square tests. Continuous variables were analyzed by dependent t-tests. Results: From 2005 to 2007, data from 240,446 open and MIS resections for colon neoplasms were available for review in the NIS database. Overall, only 13,564 (5.7%) minimally invasive resections were performed. Patients with private insurance were significantly more likely to undergo laparoscopic colectomy (7.1%) than were patients with Medicare (5.0%) or Medicaid (4.3%). Additionally, patients within the highest income quartile were more likely to have a MIS approach for their colon cancer (p< 0.001). Lastly, the utilization of MIS for colon neoplasms in African American patients was comparable to Caucasian patients (Table 1). Conclusion: Although minimally invasive surgery for colon cancer offers superior short-term outcomes compared to open surgery, there are significant economic disparities that exist in its use. Future studies should be aimed at identifying access barriers to laparoscopy in the treatment of colon cancer patients.

Characteristics	Laraposcopic	P value
Race		
Caucasian	8259 (5.9%)	0.293
African American	781 (4.7%)	
Primary Payer		
Private/ Self pay	5253 (7.1%)	<0.001
Medicare	7684 (5.0%)	
Medicaid	361 (4.3%)	
Median household income		
I: $1 - $38,999	2221 (3.9%)	<0.001
II: $39,000 - $47,999	2902 (4.7%)	
III $48,000 - $62,999	3424 (5.8%)	
IV: ≥ $63,000	4749 (8.3%)	

Table 1. Race, insurance status, and income of laparoscopic colon adenocarcinoma resections from 2005-2007.

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Does chemotherapy prior to emergency surgery affect patient outcomes: Examination of 1,912 patients M.C. Sullivan,[1]* F. Li,[2] S. Yu,[2] S.A. Roman,[1] J.A. Sosa.[1] *1. Yale University School of Medicine, New Haven, CT; 2. Yale Center for Analytical Sciences, New Haven, CT.*

Background: Data regarding preop chemotherapy as a risk to surgical outcomes is limited. This study examines morbidity and mortality of patients necessitating emergent surgical procedures ≤30 days after chemotherapy. Methods: We identified patients ≥18 yrs who had chemotherapy ≤30 days before emergency surgery (chemo) in ACS-NSQIP, 2005-8. Subjects were compared to a control group who did not have preop chemotherapy but underwent similar emergent procedures (matched 1:1 on age and procedure/CPT code). Demographic and clinical characteristics, including patient comorbidities, functional status, and preop lab values, were assessed. Primary outcomes included 30-day postop morbidity and mortality. Log-transformed data, bivariate and multivariate linear and logistic regression were used. Results: 1,912 patients were identified (956/group). Patient demographics were similar. The chemo group had lower BMI (26.3 vs. 28.3, p<.001) and more frequent preop lab abnormalities (lower hematocrit, WBC, platelets). After surgery, chemo patients had more major complications (44.0% vs. 39.2%, p=.033; OR:1.2), a greater risk of having ≥1 complication (45.0% vs. 40.5%, p= .047; OR:1.2), and higher mortality (22.4% vs. 10.3%, p<.001; OR 2.53). Average number of intraop transfusions (p<.001), and percentage receiving transfusion (26.8 vs. 18.7, p<.001; OR:1.59) were greater in the chemo group. Number of days from admission to operation was greater (3.6 vs. 2.6, p<.001) and total LOS was longer (p=.001) in the chemo group. Total operative time and number of days from operation to death were not different between groups. Multivariate analysis identified 6 variables predictive of mortality (preop functional status, dyspnea, low albumin, elevated SGOT/bilirubin, and intraop transfusion), and 9 associated with a major complication. Chemotherapy was not an independent predictor of postop morbidity or death. Conclusions: Patients having emergent surgery after chemotherapy have more comorbidities and severe disease, which are associated with higher complication rates and mortality. Identifying correctable parameters in chemo patients prior to surgery may improve postop outcomes.

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Outcomes for Patients with Synchronous or Metachronous Breast and Colon Cancer C.S. Fisher,[1] M.S. Wachtel,[2] J.A. Margenthaler.[1]* *1. Department of Surgery, Washington University School of Medicine, St. Louis, MO; 2. Texas Tech University Health Sciences Center, Lubbock, TX.*

Introduction: Breast and colorectal cancer diagnoses in the same patient, either synchronously or metachronously, is not uncommon and is likely to increase as the population ages and treatment modalities improve. The overall survival outcomes for patients who are diagnosed with both cancers have not been previously reported. *Methods:* Using the 1988-2007 Surveillance, Epidemiology, and End Results data, we conducted a retrospective, population-based cohort study of women diagnosed with both breast and colorectal cancer. Kaplan-Meier survival curves were created for disease-specific survival. Wald chi square tests evaluated differences between survival estimates; boot strap standard errors were estimated from 3,000 replicates. *Results:* We identified 4,835 women who were diagnosed with both breast and colorectal cancer. Of these, 2,844 (58.8%) were diagnosed with breast cancer first and 1,807 (37.4%) were diagnosed with colorectal cancer first; 184 (3.8%) had synchronous cancers. Overall, at five years following the second cancer diagnosis, 316 (6.5%) died of breast cancer and 779 (16.1%) died of colorectal cancer (p<0.05). Patients with an initial diagnosis of breast cancer followed by colorectal cancer were more likely to die from the colorectal cancer (p<0.05). In contrast, patients with an initial diagnosis of colorectal cancer followed by breast cancer were equally likely to die from either cancer (p>0.05). For patients with synchronous diagnoses, there was a trend toward higher colorectal cancer mortality, but this did not reach statistical significance (p>0.05). These findings persisted regardless of patient age, stage at diagnosis, or breast tumor histology. *Conclusion:* Patients who are diagnosed with both breast and colorectal cancer are nearly three times as likely to die from colorectal cancer compared to breast cancer. Disease-specific survival is variable depending on the order of cancer diagnosis. Colorectal cancer-specific mortality increases with time, while breast cancer-specific mortality decreases with time. Consideration should be given to these findings when discussing prognosis and making treatment decisions.

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The Surgical Treatment of Appendiceal Cancer in the Modern Era J.S. Hill,[1]* J.K. Smith,[2] S.C. Ng,[2] L.A. Lambert,[2] P.F. Mansfield,[1] K.F. Fournier,[1] R.E. Royal,[1] J.N. Cormier,[1] J.F. Tseng.[2] *1. Surgical Oncology, MD Anderson, Houston, TX; 2. University of Massachusetts, Worcester, TX.*

Background: Non-carcinoid appendiceal neoplasms (NCAN) include a wide spectrum of histologic subtypes with varying biologic behavior and frequent peritoneal dissemination. Consequently there are a heterogeneity of surgical procedures employed. There has been no national investigation into the surgery performed or outcomes following surgery for patients with NCANs. Methods: The Nationwide Inpatient Sample revealed 4,261 patients with NCAN (diagnosis code 153.5) who underwent surgery. Patients were classified based on procedural ICD-9 codes into 5 groups: (1) appendectomy, (2) appendectomy with other abdominal procedures, (3) colectomy, (4) colectomy with other procedures, and (5) other procedures without appendectomy or colectomy. Descriptive statistics were performed to examine the differences in patient demographics, Charlson Comorbidity Index, and hospital characteristics. Outcome measures included complication rates and in-hospital mortality. Results: Mean age equaled 56.6 years; 51.9% were female and 59.9% were white. The majority of patients (40.2%) had colectomy; whereas 23.7% had only an appendectomy, 23.0% had colectomy plus another procedure, 9.3% had an appendectomy plus another procedure, and 3.7 % had other procedures only. Overall inpatient mortality was 1.6% and unrelated to extent of surgery. However, 11.9% of patients had at least one complication which was influenced by the extent of surgical procedure (7.3 – 17.0%, P<0.001). For all patients, the average length of stay (LOS) = 8.1 days. Factors influencing LOS were extent of surgery, age group, and comorbidities. Multivariable analysis revealed factors significantly associated with mortality included age ≥70 vs. <55 (OR 7.2, 95% CI: 3.3, 15.6), increasing number of comorbidites (Charlson score of 4+ compared to 0-1) (OR 2.9, 95% CI: 1.3, 6.4). Adjusted for other factors, the type of surgical procedure (Group assignment) was not predictive of mortality p=0.32. Discussion: Factors predictive of increased in-hospital mortality include advanced patient age and multiple comorbidities. In this cohort, extent of surgical procedure did not impact operative mortality but did increase the risk of complications and length of stay.

Group	N	% Mortality	% Complications	% LOS > average
1 (Appy only)	1011	0.8%	7.3%	12.9%
2 (Appy + Other)	400	1.8%	11.0%	25.3%
3 (Colon only)	1712	1.8%	12.0%	28.9%
4 (Colon + Other)	981	1.8%	17.0%	48.7%
5 (Other)	157	1.9%	14.6%	47.8%

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Adequate Lymph Node Dissections in Melanoma Patients with a Positive Sentinel Node: Are the standards to low? S.D. Trocha,[1]* A. Gleason,[2] M. Merritt,[3] H. Bruch,[4] C. Schammel.[1] *1. Dept of Surgery, Greenville Hospital System University Medical Center, Greenville, SC; 2. Medical University of South Carolina, Charleston, SC; 3. Furman University, Greenville, SC; 4. Clemson University, Clemson, SC.*

BACKGROUND: Staging and prognosis in melanoma are related to an adequate regional lymph node dissection. Recently, guidelines have been put forth for the number of lymph nodes to be resected from each of the three major basins. The purpose of our study was to evaluate if our lymph node dissection performed within these proposed guidelines. METHODS: From 1/1/99 through 12/31/99, 619 patients with melanoma were treated at our institution. A total of 60 pts had stage III disease. Clinico-pathologic data, SLNB status, patterns of recurrence and date of last follow-up were collected. Patients were excluded if they did not undergo completion nodal dissection. RESULTS: Of 60 pts with stage III disease, 43 had completion regional nodal dissections. The average number of lymph nodes dissected from cervical, axillary, and inguinal regions was 30.8, 20.8, and 14 nodes, respectively. These numbers were double the recommended numbers for node

dissections of 15, 8, and 6 for cervical, axillary, and inguinal basins, respectively. Local-regional failure occurred in 0/4 cervical, 6/19 (32%) axillary, and 11/24 (46%) of inguinal dissections. CONCLUSION: As in colorectal and gastric cancer, where a minimum number of lymph nodes should be dissected to assure quality of surgery, accurate staging and potential impact on survival, so too have standards been suggested for melanoma regional node dissections. We demonstrate that these numbers can be easily attained but surprisingly, even though having more than double the number of nodes we still had significant local-regional failure in axillary and inguinal dissections raising the question of how many are enough and is an absolute number an important bench mark.

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Outcome Of Unclassified Sarcoma In Children A.A. Hayes-Jordan,* L. Xiao, A. Lazar, W. Huh. *Surgical Oncology and Pediatrics, MD Anderson Cancer Center, Houston, TX.*

Background: Unclassified sarcomas (USTS) (or sarcoma "not otherwise specified", NOS) are an underappreciated class of soft tissue sarcoma (STS) seen in the pediatric population that have not been carefully studied. Because there has been no standardized approach to these pediatric patients, multiple approaches to treatment have been applied. Optimal therapeutic approach and efficacy of chemotherapy or radiation therapy are unknown in these patients. We conducted a single institutional review of pediatric USTS patients in a STS referral institution. Methods: A retrospective review was completed of pediatric STS patients between 1990 and 2006. Demographics, tumor characteristics, chemotherapy, radiation therapy and surgical treatment were recorded. Results: Of 61 pediatric non rhabdomyosarcoma STS patients 22 were USTS (diagnosed by a sarcoma pathologist). Five year overall survival (OS) for stage AJCC stage 1 and 2 patients was 88.9% and for stage 3 and 4 patients was 30.3%. On univariate analysis, size of the tumor (maximum dimension) predicted OS. (p= 0.0047) On multivariate analysis, stage (p=0.008) and local recurrence (p=0.009) were significant prognostic factors in OS. Gender, race, margins of resection, chemotherapy or radiation therapy were not significant. For disease free survival (DFS), stage and chemotherapy were statistically significant predictors. (p<0.001, p=0.012 respectively) Patients who received salvage chemotherapy after recurrence fared more poorly than those who received either adjuvant chemotherapy, neoadjuvant chemotherapy or radiation therapy and surgery alone. There was no difference in DFS in patients who received no chemotherapy (radiation and surgery alone) and either adjuvant or neoadjuvant chemotherapy. Conclusions: This is the largest review of USTS identified in the English literature. Besides stage, local recurrence may be the most important predictor of outcome in pediatric USTS patients. While this may be a surrogate of underlying aggressive biology, the initial surgical extirpation with perhaps the addition of radiation, may well be critical in determining outcome. The use of chemotherapy in USTS may not improve outcome.

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MET receptor: a potential therapeutic target for malignant peripheral nerve sheath tumors K.E. Torres,* K. Bill, G. Lahat, J. Liu, J. Liu, M. Ghadimi, B. Belousov, E. Young, G. Lopez, A. Lazar, R. Pollock, D. Lev. *University of Texas, MD Anderson Cancer Center, Houston, TX.*

INTRODUCTION: Malignant peripheral nerve sheath tumors (MPNST) harbor a dismal prognosis due to their chemoresistant nature and enhanced metastatic propensity. The main goal of the current study was to evaluate the role of the MET receptor as a novel therapeutic target for MPNST. METHODS: Expression level of MET, its ligand HGF and phosphorylated MET (activated-MET) was determined immunohistochemically in a tissue microarray of human MPNSTs (n = 96) and benign neurofibromas (n = 31). Results were analyzed using univariable and multivariable statistical analysis. To evaluate the impact of MET activation (by HGF) and inhibition (using anti MET specific shRNA), we conducted multiple experiments to determine effects on cell proliferation, survival, migration, invasion and angiogenesis using a panel of MPNST cell lines and a xenograft MPNST mouse model. RESULTS: MET receptor, HGF and activated MET were found to be over-expressed in MPNST as compared to their pre-malignant precursors (neurofibroma; p<0.05). Univariable and multivariable analyses identified a statistically significant correlation between activated-MET expression and poor patient outcome (HR=2.32, p=0.012 and HR=1.48, p<0.001, respectively). Furthermore, constitutive autocrine MET activation was found in MPNST cells but not in normal human Schwann cells. MET activation resulted in significantly increased MPNST cell motility and invasion in vitro. Additionally, MET activation enhanced the pro-angiogenic effects of MPNST in vivo. MET knockdown (via shRNA) abrogated the HGF-induced downstream signaling and MPNST cell migration/invasion. Furthermore, blockade of MET significantly abrogated MPNST local and metastatic growth in vivo. CONCLUSIONS: MPNST tumors and cell lines express the MET receptor which, upon activation, results in increased MPNST migration, invasion, and angiogenesis. Inhibition of MET-mediated signaling impairs MPNST metastatic capacity. MET receptor merits further consideration as a potential MPNST therapeutic target.

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Clinical prognostic factors in patients submitted to hindquarter amputations for bone and soft tissue tumors R.S. Batista, S. Aguiar,* J.H. Fregnani, T.B. Santana, T.S. Bezerra, A. Lopes. *Pelvic Surgery, AC Camargo Cancer Hospital, Sao Paulo, Brazil.*

Introduction: Nowadays, hindquarter amputations are rarely indicated for the treatment of bone or soft tissue sarcomas. Its indications are usually controversies, especially because of the mutilating consequences and the uncertain prognosis. As a rare operation, the identification of factors that influence the survival can be performed only in historical series from reference centers. Objective: to identify clinical prognostic factors in a historical series of hindquarter amputations. Methods: we retrospectively studied a series of 119 patients submitted to hindquarter amputation for bone or soft tissue tumors between 1954 and 2007. The variables analyzed were age; gender; origin (bone or soft tissue); status at the time of amputation (recurrent or primary); neoadjuvant treatment; intention of surgery (curative or palliative); and pattern of resection (R0 or R1 / R2). The primary endpoints were local recurrence; distant recurrence; death by any cause. Survival was estimated by Kaplan-Meyer method and the curves were compared by log rank. Results: 60 (50.4%) amputations were performed for bone sarcomas and 59 (49.6%), for soft tissue sarcomas. After a mean follow-up time of 54.6 months, we observed rates of 5-year local recurrence free-survival, distant metastases-free and overall survival of 63.3%, 47.4%, and 49.5%, respectively. In univariate analysis, the variables significantly associated with local failure were: age less than 40 years; and R1 / R2 resections. The only variable significantly associated with distant failure was the palliative intention. The variables associated with poor overall survival, in univariate analysis, were age less than 40 years; R1 / R2 resections; and palliative intention. In multivariate analysis, the factors that remained significantly associated with de risk of death were R1 / R2 resections (HR=3.3; 95%CI=1.4 – 7.8) and palliative intent of surgery (HR=2.1; 95%CI=1.2-3.7). Conclusions: acceptable rates of disease-free and overall survival can be achieved in highly selected patients with locally advanced bone or soft tissue sarcomas that require a hindquarter amputation, since negative margins can be obtained.

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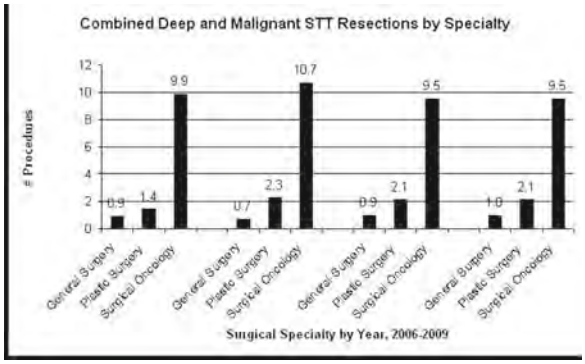
Soft Tissue Tumor Surgery by Surgical Specialty: Should there be Benchmarks for Number of Cases Performed per Year? R.J. Canter,* C.A. Smith, D.H. Wisner, S.R. Martinez. *Surgery/Surgical Oncology, University of California at Davis, Sacramento, CA.*

Introduction: Resection of soft tissue tumors (STT) requires careful preoperative assessment since unplanned and incomplete resection of malignant STT may adversely impact both surgical morbidity and longterm outcome. We sought to characterize the extent of STT resections performed among surgical specialties. We hypothesized that substantial variation exists in site and number of STT resections performed by specialty. Methods: We queried the UHC-AAMC Faculty Practice Solutions Center database for coding data from 85 institutions for fiscal years 2006-2009. We abstracted data on total number of musculoskeletal (MSK) procedures (CPT codes 20000-29999), subcutaneous (SQ) STT resections, deep STT resections, and malignant STT resections. Data were analyzed by anatomic site and surgical specialty [general (G), plastics (P), and oncology (Onc)]. Results: On average, G performed 19.2 MSK procedures per year, P 179.6, and Onc 32.4. SQ STT resections per year were similar among specialties (1.6 G, 2.6 P, and 2.2 Onc), while deep and malignant resections were more likely performed by Onc (combined deep and malignant: 0.9 G, 2.0 P, and 9.9 Onc). Although deep and malignant STT resections only represented 4.5% and 1.1% of all MSK procedures performed for G and P respectively, they represented 22.5% of all deep and malignant STT resections performed. G were more likely to resect proximal STT (shoulder

and hip), while P were more likely to resect distal STT (forearm and lower leg). STT resections by Onc were more evenly distributed by site. Conclusion: Although 22.5% of deep and malignant STT resections are collectively performed by G and P, each practitioner on average only performs 0.9 and 2.0 procedures per year, respectively. This has significant implications for quality of care in soft tissue tumor surgery.



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Comparison Between Isolated Limb Perfusion Protocols (Melphalan, Melphalan-TNF and High Dose Regional Ifosfamide) in the treatment of Locally Advanced Soft Tissue Sarcoma of the Extremities H. Martinez-Said,[1]* A. Tavares,[2] L. Dominguez-Parra,[3] R. Padilla-Longoria,[4] R. García-Matus,[5] M. Cuellar,[1] A. Padilla-Rosciano,[1] A. Mohar-Betancourt.[1] *1. Instituto Nacional de Cancerología, Mexico City, Mexico; 2. Hospital Regional Alta Especialidad Bajio, Leon, Guanajuato, Mexico; 3. Hospital Regional Alta Especialidad Peninsula, Merida, Yucatan, Mexico; 4. Centro Médico ABC, Mexico City, Mexico; 5. Hospital Regional Alta Especialidad Oaxaca, Oaxaca, Oaxaca, Mexico.*

Introduction: The management of Locally Advanced Soft Tissue Sarcoma is complex. The most active neo-adjuvant treatment for STS is chemo-radiation and isolated limb perfusion for limb sparing protocols. We report our experience with three different approaches with ILP. Methods: A retrospective review of two prospective protocols and one pilot study of isolated limb perfusion was carried out and includes 36 patients with histologically confirmed locally advanced soft tissue sarcoma of extremities. The drugs used in each protocol were: Group A (n=11) Ifosfamide (78 gr/m2 of perfunded limb area), Group B (n=14) 10-13 mg/L Melphalan alone, and Group C (n=11) 10-13 mg/l Melphalan with 1-2 mgs of TNF (Beromun®). All protocols were done with mild hyperthermia (39-40C). We compare clinical (WHO) and pathologic response rate, toxicity and limb salvage rate. The clinical response rate was assessed with MRI. Results: The limb sparing surgery was observed in 54%, 64% and 100% of groups A, B and C respectively. Complete pathologic responses (no viable tumor in residual resected specimen) were only seen in 4 patients, all of group C. A major pathologic response (50% or less of viable tumor) was more frequent in TNF based protocol (45% vs 64% vs 91% p=0.003). Regional toxicity was recorded according to Wieberdink scale; all the patients develop erithema and mild edema of the extremities (Wieberdink II). No late toxicity was recorded and similar between groups. Systemic toxicity was seen in one patient of Group C. Conclusion: The addition of TNF to ILP protocol offers a better response rate and a frequent limb sparing surgery.

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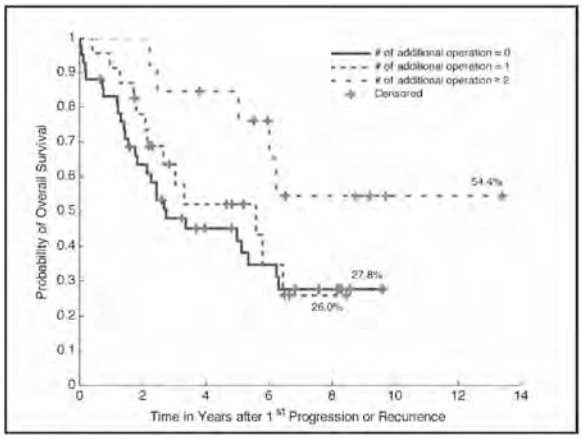
A selective surgical approach to advanced gastrointestinal stromal tumors is associated with improved overall survival C. Parsons,* J. Kim, A. Martin, J.S. Zager, T. Yeatman, R. Karl, M. Malafa, J. Strosberg, V. Sondak, D. Letson, R.J. Gonzalez. *Moffitt Cancer Center, Tampa, FL.*

Background: Gastrointestinal stromal tumors (GIST) are rare sarcomas of the GI tract. Margin negative resection remains the only chance for cure. While tyrosine kinase inhibitors (TKI) have improved survival, many patients recur on therapy. We hypothesize that resection of advanced GIST, and possibly multiple resections, improves overall survival. Methods: We identified 193 pts with GIST from 1999-2009. 168 (87%) tumors were resected, and 78 (46.4%) recurred. The records of these 78 pts were reviewed. Overall survival (OS) was estimated from the time of disease recurrence or progression using the Kaplan-Meier method. Results: Of the 78 pts, 66 (85%) were referred to our center after initial resection. Final margins of resection were R0/R1 in 60 (77%) and R2 in 18 (23%) pts. 38 (49%) pts received a TKI for a median of 12 mos (1-52). The 5-yr OS for all pts was 52% with a median follow-up of 38 mos (0.3-61). 45 (58%) pts were managed nonoperatively (TKI therapy alone), 20 (26%) pts underwent one reoperation, and 13 (17%) pts underwent ≥2 reoperations [median OS was 33 mos vs 67 mos vs not reached; (p=0.016); Figure]. Final resection margins for initial reoperations were R0/R1 in 26 (79%) and R2 in 7(21%) pts with a 5-yr OS of 71% vs 19% (p=.02), respectively. Median time to first recurrence was 21 vs 27 mos in those with ≤1 vs ≥2 reoperations (p=.22). Patients who underwent ≥2 operations were younger (p=.04), developed low volume sarcomatosis without liver metastases (p=.01), and had not been treated with TKI therapy prior to first recurrence (p=.02). A significant survival advantage was noted with maintenance TKI therapy compared to reoperation resulting in an R2 resection (46% vs 19%, p=.02). Conclusions: Reoperative surgery for recurrent GIST can be associated with improved overall survival in highly selected patients. However, continuing TKI therapy may be preferable to an incomplete resection for recurrent disease. Careful patient selection with a multidisciplinary team focusing on patients with GIST is crucial to optimizing outcomes.



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True Myomatous Tumors of the Gastrointestinal Tract M. Raoof,* S. Curley, R. Pollock. *The University of Texas M. D. Anderson Cancer Center, Houston, TX.*

BACKGROUND: Gastrointestinal (GI) mesenchymal tumors have similar histological appearances, leading to a classification dilemma. Recent understanding of molecular pathways and advancement in immunophenotyping techniques has led to a more accurate distinction of gastrointestinal stromal tumors (GIST) from true myomatous tumors. Using recent data from National Cancer Institute's (NCI) Surveillance, Epidemiology and End Results (SEER) we studied the demographics, survival and prognosis of true leiomyosarcomas of the GI tract. METHODS: All patients diagnosed with primary GI tract tumors between January 1, 2001 and December 31, 2007, with ICD-O-3 codes corresponding to myomatous neoplasms (8890/3 – 8896/3), were identified from NCI's SEER database. Patients lacking histological evaluation and autopsy-only cases were excluded. Demographics, extent of disease and survival data were recorded. Survival analysis was performed using the Kaplan-Meier method and Cox-proportional hazard model. RESULTS: Entry criteria were met by 277 patients, 136 (49.1%) male and 141 (50.9%) female. Median age was 62 years (IQR: 50-74 years). Small intestine (25.6%) and stomach (25.3%) were the most common sites. 24.5%, 10.8%, 11.9% and 4.3% tumors were anaplastic, poorly, moderately or well differentiated, respectively. At the time of diagnosis, most tumors were localized (38%) while 28.2% and 20.9% tumors had regional or distant metastases, respectively. Surgery

was performed in 207 (74.7%) patients and 24 (8%) patients received radiation alone or as an adjunct to surgery. Median follow-up was 16.5 months. 1-, 3- and 5-year overall survival rates were found to be 70.4%, 51.6% and 45.2%, respectively. Overall median survival was 40 months. Patients who underwent surgery had significantly better survival (median survival 74 vs. 9 months, p <0.0001). Grade, stage, and radiation treatment were not associated with improved survival. CONCLUSION: Leiomyosarcoma is pathologically and clinically a distinct entity. While patients with GIST have improved outcomes secondary to targeted drug therapy, treatment options for GI leiomyosarcomas are limited. Surgical resection offers survival advantage and is the mainstay of therapy.

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Worse survival in elderly extremity soft tissue sarcoma patients

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Background. Nearly half of the diagnosed soft tissue sarcoma (STS) patients are over 65 years of age and these elderly patients have often been reported to be undertreated. The aim of this study was to assess the impact of age on survival in extremity STS (ESTS) patients and gain insight in treatment differences between young and elderly ESTS patients. Methods. Patients 18 years and older, diagnosed with ESTS between 1990-2004, were selected from the regional cancer registry of the Comprehensive Cancer Center North East (CCCNE). Survival rates and treatment characteristics were analyzed for patients in all age categories. Factors associated with survival were evaluated to see whether they were different between young and elderly patients. Results. Overall, 355 patients were included in this study; 179 (50.4%) male and 176 (49.6%) female. Tumor morphology was different between young and elderly patients (p<0.001). Elderly patients were relatively more often diagnosed with Pleomorphic Undifferentiated Sarcomas (PUS) and less often with liposarcomas and synovial sarcomas. However, compared to younger patients, elderly were not diagnosed with a higher stage of disease (p=0.81). Elderly did receive less chemotherapy (p=0.01) however not less surgery (p=0.5) or radiotherapy (p=0.5). Age was significantly associated with relative survival: relative 2-year survival was 87.3% for patients < 65 years, 79.0% for patients 65-74 years and 70.4% for patients ≥ 75 years (p=0.04). Adjusted for treatment differences, age still remained a significant prognostic factor for relative survival (p=0.001). The survival of ESTS did not improve over time, as relative 5-year survival rates were stable between 1990-2004 for both the younger and the elderly patients. Conclusions. There is a difference in tumor morphology and treatment between younger and elderly ESTS patients, but not in tumor stage. Survival rates of ESTS did not improve during the last twenty years. Elderly age is still a significant prognostic factor for relative survival of ESTS.

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Intra-abdominal metastatic soft tissue sarcoma (STS): Who may benefit from debulking surgery?

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Introduction: Unlike the conventional targeted therapy for metastatic gastrointestinal stromal tumors (GIST), there is no effective treatment for intra-abdominal metastatic STS (IMS). Moreover, in contrast to surgery for STS pulmonary metastases, an aggressive loco-regional approach towards IMS is still controversial. We evaluated outcomes of a relatively large and homogenous cohort of patients who had surgery for IMS in a single institution. METHODS: A retrospective retroperitoneal STS database was reviewed; patients who had surgery for intra-abdominal metastatic STS between 1995 and 2007 were identified and are included in the study cohort. RESULTS: Thirty- four patients had 48 operations for IMS; 22 patients had one operation, 10 patients had two, and three patients underwent three consecutive resections. Median age was 58 years (range, 31-81). Most patients (n=26; 76.5%) were treated for recurrent IMS; 50% (n=17) of primary tumors originated in the retroperitoneum, high grade liposarcoma was the most frequent histological subtype (n=20; 58.8%). Complete macroscopic resection was documented in 37 cases (77.1%); 9 patients were additionally treated with hyperthermic intra-peritoneal chemotherapy (HIPEC). There was no intra- or peri-operative mortality; morbidity rate was 24%. After a median follow-up length of 75 months (range, 2-297), intra-abdominal disease progression occurred in 15 patients (44.1%), pulmonary metastasis in 5 (14.7%), and both in 10 patients (29.4%). Median overall survival (OS) for the entire cohort was 34.2 months (2-132); 13 patients (38.2%) were alive at 16-132 months. In multivariable analysis completeness of resection was the only independent prognosticator of survival; R0 vs. R1 and R2 (HR: 2.3, CI 95% 1.23-5.82). In the present series disease free interval did not emerge as an independent predictor of survival. CONCLUSIONS: Overall, results of aggressive surgical treatment for intra-abdominal metastatic STS appear to prolong life in comparison to systemic therapy. Completeness of resection is the only favorable predictor of outcome and therefore should be the surgical goal.

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ANATOMICAL PRESENTATION OF RETROPERITONEAL SARCOMA: WHEN MULTIVISCERAL RESECTION IS MORE APPROPRIATE?

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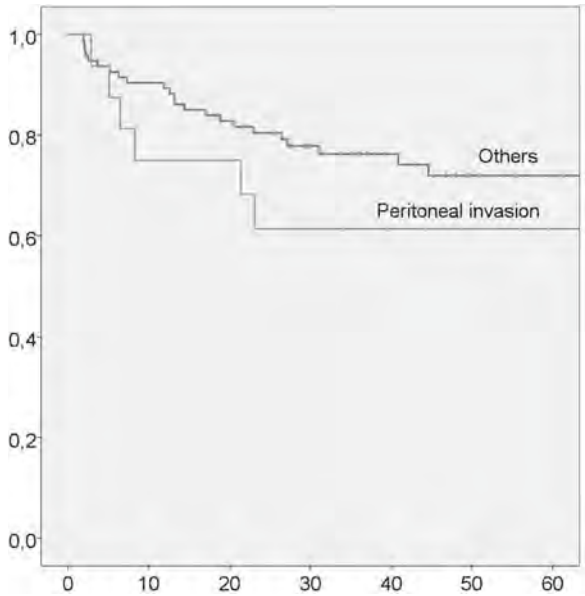
Objective: Frontline aggressive surgery with multivisceral resection has been proposed as a standard treatment for retroperitoneal sarcoma (RPS). However, heterogeneous anatomical presentation within the retroperitoneum may have surgical and prognostic implications. Methods: Patients affected by primary RPS treated at a referral institution between 2002 and 2008 with systematic frontline aggressive surgery were reviewed. Anatomical presentation was classified based on preoperative CT scan as follows: 1 - Exclusively Suprarenal (contact with the surface of suprarenal organs, such as liver, duodenum, head of pancreas on the right, and body and tail of pancreas, spleen, diaphragm on the left); 2 - Exclusively Infrarenal (close to the renal hilum and/or within the psoas muscle or on its surface); 3 - Perirenal (involvement of the renal capsule and kidney with or without Suprarenal and/or Infrarenal extension as described above); 4 - Peritoneal invasion (prominent mesenteric involvement and/or intraperitoneal extension into the small bowel and/or widely close to the stomach or the hepatic hilum); 5 - Pelvic (mainly pelvic localization and/or extension to the ileo-inguinal region or into the sciatic notch); 6 - Unclassified (none of the above). Local recurrence-free survival (LRFS) was estimated by Kaplan-Meier. Results: 111 of 137 consecutive patients were evaluated for anatomical presentation. Most frequent anatomical presentation was Perirenal (45%), followed by Infrarenal (14%), Peritoneal invasion (14%), Pelvic (14%), Unclassified (5%) and Suprarenal (4%). Overall 5-year LRFS was 71% (SE 4%). According to anatomical presentation, no significant difference in LRFS was found. A trend towards worse outcome was documented for the subgroup of Peritoneal invasion (5-year LRFS = 61%). Conclusion: Though extremely variable, different anatomical presentation of primary RPS based on preoperative CT scan doesn't seem to affect the quality of local control after frontline multivisceral resection. Preoperative evidence of peritoneal invasion should be considered in surgical decision-making, when extended organ resection would be associated with high morbidity.



Local recurrence-free survival according to anatomical presentation.

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Postradiation angiosarcoma after breast cancer has a high recurrence rate and poor survival despite optimal surgical intervention J. Seinen,* V. Verstappen, A.J. Suurmeijer, E. Pras, R.J. Van Ginkel, H.J. Hoekstra. *University Medical Centre Groningen, Groningen, Netherlands.*

Background. Breast irradiation is a part of breast conserving treatment (BCT) for breast cancer. Postradiation angiosarcoma of the breast is a rare and severe long-term complication to BCT. Patients often have localized, but multifocal disease confined to the breast at presentation. Surgery, with or without plastic surgical reconstruction, is the only potential curative treatment and no other adjunctive treatment is currently available. We characterized a population based cohort of postradiation angiosarcomas in order to get insight in this disease and define the surgical treatment and outcome. Methods. A total of 19 patients, median age 67 (range 50-90) years, with a history of radiation for breast cancer and a histologically proven angiosarcoma were identified since 1984. Of these 19 patients, 16 underwent surgery (84%) and were included in this study. Overall survival (OS) and disease-free survival (DFS) were calculated according to the Kaplan-Meier method. Results. The total radiation dose to the breast/thoracic wall ranged from 45-70 Gy. The median time for the development of angiosarcoma of the breast was 7 (range 4-25) years. In 14 cases an ablation was performed and in 2 cases a local resection because of previous mastectomy and adjuvant radiation. In 12 out of 16 cases complete excision could be obtained after the 1st operation (R0=75%), and in another 3 cases after the 2nd operation (overall R0=94%). Of these 15 patients with R0 resection, 9 patients developed, after a median follow-up of 6 (3-42) months, a local recurrence (60%), 2 patients developed a distant recurrence after local recurrence and 3 only a distant recurrence (overall distant recurrence 33%). The median follow-up for these 15 patients was 31 (range 4-70) months, and the median DFS and OS were 10 (range 0-51) and 38 (range 4-70) months respectively. Conclusion. Our data show that despite a nearly 100% overall R0 resection rate, 60% of the patients developed a local recurrence, followed by dismal prognosis and median overall survival of three years. More insight in the tumorbiology of this rare sarcoma is required for the development of new target therapies.

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The Effect of Preoperative Chemotherapy Prior to Complete Resection or Stereotactic Body Radiotherapy (SBRT) of Pulmonary Metastasis from Sarcoma R.M. Baskin,* J. Urbanic, G. Russell, E. Levine. *Wake Forest University, Winston-Salem, NC.*

Introduction: Complete resection of pulmonary metastasis from sarcoma is known to improve overall survival; however, the utility of preoperative chemotherapy prior to resection is unclear. Further, the efficacy of radiation as an alternative to resection is uncertain. This study aimed to determine the effect of preoperative chemotherapy as well as the use of SBRT for this population. Methods: Between March 1997 and July 2010, 28 patients (13 men and 15 women; median age 46 yrs. [range 23-78 yrs.]) underwent complete resection for pulmonary metastasis from sarcoma, including those with (12) and without (16) preoperative chemotherapy. A retrospective review of these subgroups compared end points including disease-free and overall survival. These endpoints were also used to compare those who had complete resection to a series of 8 patients who had SBRT instead of resection. Results: The median disease-free survival for all 28 patients who underwent complete resection was 1.8 yrs., while median overall survival was 3.4 yrs. The median disease-free survival for patients who did not receive preoperative chemotherapy was 1.8 yrs. versus pre-operative chemotherapy patients where it was 1.4 yrs (p=0.27). The median overall survival for the non-chemotherapeutic group was >5 yrs. (not yet reached) compared to that for the chemotherapeutic population which was 3.4 yrs. (p=0.26). The presenting stage, grade and DFI of the tumors were similar between groups. The median disease-free survival for patients who underwent SBRT was 1.1 yrs. and median overall survival was >3 yrs. (not yet reached). Disease-free survival (p=0.40) and overall survival (p=0.72) were similar between SBRT patients and all surgical patients. Conclusions: This analysis indicates that preoperative chemotherapy for resection of pulmonary metastasis from sarcoma does not influence disease-free or overall survival. With limited follow-up, SBRT has similar recurrence and survival rates to complete resection and should be considered for poor surgical candidates.

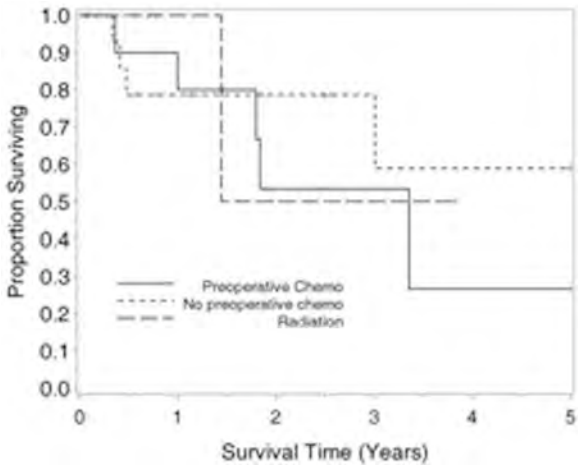

Figure 1: Overall survival among patients in the chemotherapeutic, non-chemotherapeutic, and SBRT populations.

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Retroperitoneal fat content: An independent adverse prognosticator in retroperitoneal soft tissue sarcoma (STS) M. Papoulas, A. Mahamid, R. Weizer, G. Rosen, N. Lubezky, I. Nachmany, R. Nakache, J.M. Klausner, G.J. Lahat.* *surgical oncology, Sourasky Medical Center, Tel Aviv, Israel.*

Introduction: Reported data demonstrate that obesity is an adverse prognosticator in various cancers, yet little is known about its significance in soft tissue sarcoma (STS). We evaluated the association of retroperitoneal and circumferential fat contents with STS local recurrence and survival. Methods: CT Imaging studies were reviewed by a senior radiologist who was blinded to the clinical data; retroperitoneal and circumferential fat contents were measured as previously described. Correlations between imaging findings, clinical, pathological, treatment, and outcome characteristics were analyzed. Results: One hundred and ten STS patients who had complete macroscopic resection at our institution between 2002 and 2010 were identified and included in the study cohort. Sixty STS tumors (54.5%) were retroperitoneal; of them, 65.1% were high grade, median size was 15cm (range, 3-49), and the most common histological subtype was high grade liposarcoma (23.8%). Median follow-up length for the entire cohort was 45 months (range, 6-159). Retroperi-

toneal fat diameter (RFD) > 15mm vs. ≤ 15mm was identified as a risk factor for adverse outcomes. Retroperitoneal STS patients with RFD > 15mm vs. ≤ 15mm had a higher rate of local recurrence; 65.1% vs. 26.7%, respectively (p=0.04). Median overall survival (OS) length of patients with RFD > 15mm vs. ≤ 15mm was 31 months (range, 2-144) vs. not reached, respectively (p=0.007). Multivariable analysis identified RFD > 15mm as an independent risk factor for local recurrence (HR: 4.08, CI 95% 1.03-11.36) and decreased OS (HR: 4.2, CI 95% 1.07-16.67). In contrast, circumferential fat content did not correlate with retroperitoneal STS patient outcome; moreover, there was no correlation between RFD and extremity STS patient outcomes. Conclusions: Retroperitoneal fat content is an adverse prognosticator of retroperitoneal STS local recurrence and survival. It is possible that co-localization of both tumor and adipose cells plays a role in fat- induced STS tumorigenesis; however, further clinical and molecular research is needed to establish this premise.

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Adult Extra-osseous Ewing's Sarcoma: Outcomes of Multimodality Therapy at a Specialized Center A.E. Gillis,* R. Gladdy, B. Dickson, C. Swallow. *Mount Sinai Hospital, Toronto, ON, Canada.*

Introduction Extra-osseous Ewing's (EES) is a rare sarcoma in adults, and outcome data are limited. While resection has been recommended as part of multimodality treatment, its role after complete clinical response (cCR) to chemotherapy (CT) and/or radiotherapy (RT) is unclear. The objectives of this study were to determine the management and outcomes of patients with EES treated at a specialized sarcoma center over a 20 year period. Methods We performed a retrospective review of all adult patients with a confirmed pathologic diagnosis of EES managed at our center from 01/89 through 03/10. Kaplan-Meier survival curves were constructed and univariate and multivariable analyses performed to identify prognostic variables. Results Thirty-nine patients (14 female) were identified, with a median age at presentation of 34 (range 17-78). Lower extremity was the most common primary site, followed by pelvis, chest, and abdomen. All EES were high grade and 12 (31%) patients had distant metastatic disease (mets) at presentation. In the majority of patients (n=22) treatment included resection of the primary plus CT and/or RT. 17 patients underwent primary CT and/or RT but not resection; 12 of these presented with mets. CT consisting of standard VAC and VP-16/Ifosfamide, was given to 37 patients (95%), and RT to 20 (51%). Mean follow up time was 34mos (range 2-137), and no patient was lost to follow up. Overall Survival (OS) at 5yrs was 46%, with no significant difference seen between the resection and no-resection groups (Table). During follow-up, 3/27 (11%) patients developed mets, and 1/22 (5%) resected patient had a local recurrence. Of the 4 non-resected patients who had cCR after what had been planned as neoadjuvant CT/RT, none have recurred as of last follow-up. Metastatic disease at presentation was the only significant predictor of OS in MVA (Table). Conclusions While we continue to recommend resection of the primary tumor as part of multimodality therapy for adult EES when technically feasible, these data suggest that a non-operative approach may be appropriate in a select group of patients who achieve cCR after CT/RT.

n	OS @5 yrs (actuarial, %)	HR	p-value
Resection 22	61	0.27	0.093
No resection 17	29		
Mets at presentation 12	14	10.58	0.002
No mets at presentation 27	83		

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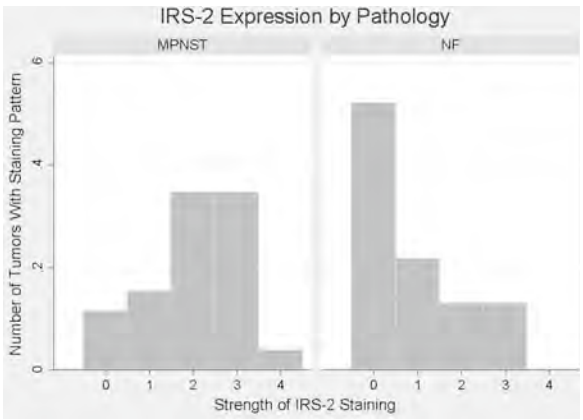
IRS-2 Expression is Elevated in Patients with MPNST: A Potential Therapeutic Target C. Shaw,[1]* S.R. Grobmyer,[1] W.G. Cance,[2] J.D. Reith,[1] S.N. Hochwald.[1] *1. University of Florida, Gainesville, FL; 2. Roswell Park Cancer Institute, Buffalo, NY.*

Background Interactions between focal adhesion kinase (FAK), insulin receptor substrate 1 (IRS-1), and insulin receptor substrate 2 (IRS-2) are known to play a role in tumorogenesis. Novel drugs to inhibit these pathways are emerging and will be sarcoma subtype-specific. As a result, defining the expression in select tumors is important in order to formulate therapeutic approaches to refractory neoplasms such as malignant peripheral nerve sheath tumors (MPNST). Methods Fifty-three patients with malignant peripheral nerve sheath tumors and neurofibromas who were treated at our institution from 1994-2005 were identified. Immunohistochemical staining for multiple key oncogenic proteins was performed on tumors and the sections were evaluated in a blinded fashion by a sarcoma pathologist (JDR). Data were analyzed using two-sample Wilcoxon rank-sum testing. Histograms were used to graphically examine data. Results Twenty-eight patients with malignant peripheral nerve sheath tumors (MPNST) and twenty-five patients with neurofibromas (NF) were analyzed. 88% of MPNSTs expressed IRS-2 compared to 48% of NF. IRS-2 expression was significantly higher in MPNSTs than in NFs (p = .0009, see figure). However, IRS-1 was significantly higher in NF than MPNST (p = .0283). A trend toward an increase in focal adhesion kinase (FAK) expression in MPNST was seen (p= .11). No difference was seen between MPNST and NF when evaluating the expression of phosphorylated FAK, vascular endothelial growth factor receptor 3, insulin-like growth factor receptor 1, nor neurofibromatosis 1. Conclusion Malignant peripheral nerve sheath tumors have elevated levels of IRS-2 and decreased IRS-1. A trend toward an increase in FAK staining with MPNST was also observed compared to neurofibromas. These data demonstrate for the first time that IRS-2 and FAK may contribute to malignant transformation of neurofibromas and are potential therapeutic targets in MPNST.



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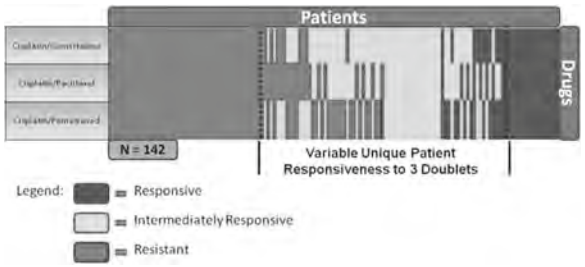
Assessment of In Vitro Chemoresponsiveness to Platinum Based Chemotherapy Doublets May Lead to Improvements in "Individualized" Therapy for Resected Non Small Cell Lung Cancer (NSCLC) M.J. Schuchert,[1]* R.J. Cerfolio,[2] R.J. McKenna,[3] L.R. Glassman,[4] M. Dylewski,[5] R.J. Landreneau.[1] *1. Cardiothoracic Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA; 2. University of Alabama at Birmingham, Birmingham, AL; 3. Cedars Sinai Medical Center, Los Angeles, CA; 4. North Shore University Hospital, Great Neck, NY; 5. South Miami Hospital, Miami, FL.*

Introduction: It is widely believed that there is clinical equivalence among many platinum-based chemotherapy doublets used for adjuvant therapy of resected non-small cell lung cancer (ECOG 1505), based upon randomized clinical trials treating advanced stage NSCLC (Schiller et al. NEJM 2002). We postulated that in vitro tumor chemo-responsiveness of resected NSCLC to commonly used "platinum-based" chemotherapy doublets may differ between patients. Methods: Viable tumor specimens from 142 surgically resected NSCLC were tested with an in vitro chemoresponse assay for 3 primary platinum-based chemotherapy doublets used today (cisplatin/gemcitabine, cisplatin/paclitaxel, cisplatin/pemetrexed). Tumors were categorized as pan-responsive, uniquely responsive to one or two of the doublets, or non-responsive to all three doublets tested based on a log dose response curve. Results: Pan-resistance to the three doublet regimens was seen in 49/142 (35%) of tumors and pan-sensitivity in 53/142 (37%). In 40 patients (28%), tumor demonstrated a heterogeneous, unique pattern of response, with 26 patients responsive to 2 of 3 of the agents, and the remaining 14 responsive to only 1 of the 3 doublets (6 to cisplatin/gemcitabine and 8 to cisplatin/pemetrexed). The Figure depicts a chemoresponse map, with each bar along the horizontal axis representing an individual patient response to a particular doublet listed on the vertical axis. The mid-zone of the map is populated with patients having uniquely variable

responses to the three doublets tested [Figure]. Conclusions: Chemoresponse testing importantly identifies pan-resistance in a significant minority of tumors tested with commonly used platinum-based therapies employed today. Among these patients, more novel experimental therapies may be indicated. Another large subset of tumors may have variable and unique chemoresponse patterns identified by in vitro testing, which may guide the selection of patient-specific platinum-based doublets leading to improved results with adjuvant chemotherapy for non-small cell lung cancer.



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COX2 expression predicts resistance to chemoradiotherapy in esophageal squamous cell carcinoma Y. Akutsu,* N. Hanari, M. Mori, Y. Yoneyama, N. Ikeda, A. Komatsu-Akimoto, S. Endo, Y. Miyazawa, G. Yusup, H. Matsubara. *Department of Frontier Surgery, Chiba University, Chiba, Japan.*

Back ground and purpose: The overexpression of COX2 was correlated with carcinogenesis, tumor progression and prognosis, and increased COX2 expression was correlated with radiation resistance. However, no correlation between the COX2 expression and resistance to chemoradiotherapy for esophageal squamous cell carcinoma has so far been characterized. The purpose of the present study was to evaluate whether COX2 expression is an indicator of resistance to chemoradiotherapy in esophageal squamous cell carcinoma and the feasibility of COX2 as a biomarker for CRT. Methods: Fifty-eight patients who were diagnosed with esophageal squamous cell carcinoma from biopsy samples were enrolled in the present series. All patients underwent concurrent chemoradiotherapy in a neoadjuvant setting, followed by radical esophagectomy. COX2 expression was evaluated by immunohistochemical staining and statistically compared with the histopathologic findings in surgically resected specimens. Results: The rate of responders was 87% for weak expression of COX2, 62% for moderate expression, and 30% for strong expression, and there was a close correlation between COX2 expression and the response rate Kendall's Tb=0.396, p=0.001). In the univariate analysis, negative or weak expression of COX2 was found to significantly correlate with CRT response (odds ratio 6.296, 95% CI 1.580–25.096). In the multivariate analysis, weak expression of COX2 (30% or less) was found to be an independent prognostic factor (odds ratio 6.534, 95% CI 1.535–27.803, p=0.011). Conclusion: The COX2 expression predicts resistance to chemoradiotherapy in esophageal squamous cell carcinoma, and it is also a feasible biomarker for evaluating the CRT response.

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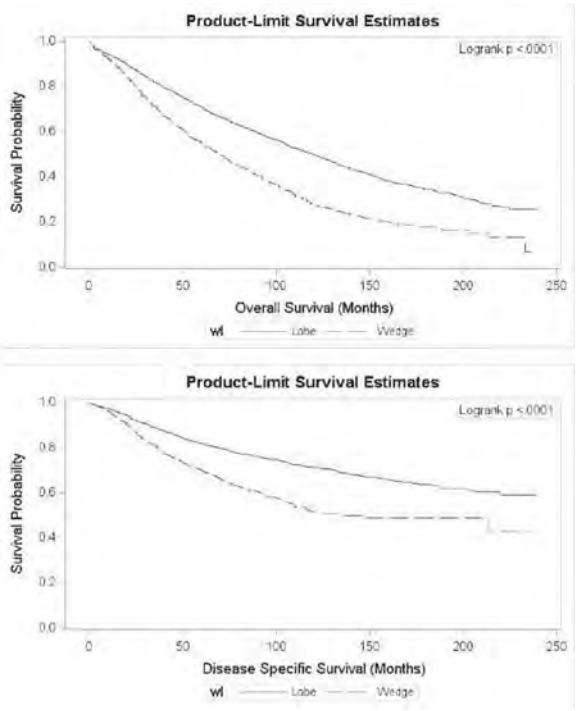
Is Sublobar Resection Adequate for Stage IA (< 2 cm) Non-Small Cell Lung Cancer? R. Sharma,* M. Demmy, A. Groman, E. Dexter, M. Hennon, C. Nwogu, T. Demmy, A. Miller, S. Yendamuri. *Roswell Park Cancer Institute, Buffalo, NY.*

Background: Extent of resection for stage IA (< 2 cm) non-small cell lung cancers (NSCLCs) is controversial and a large multi-center prospective trial (CALGB 140503) is underway to address the issue. In the meantime, this question was addressed using the Surveillance Epidemiology End Results (SEER) database. Methods: Patients with a history of one resected Stage I lung cancer < 2 cm after 1987 were selected, excluding unknown histology, small cell lung cancer, radiation or more extensive resection than lobectomy. Overall survival (OS) and disease specific survival (DSS) associated with lobectomy and sublobar resection were compared using multivariate proportional hazards methods controlling for age, gender, race, grade and number of lymph nodes examined (LNE). P values <0.01 were deemed statistically significant. Analyses were repeated using a propensity-matched sample. Results: Overall, 7006 patients fit our selection criteria, 1701(24.3%) of whom had sublobar resection. Multivariate analysis controlling for age, gender, race, grade and number of LNE showed patients with lobectomy had a better OS and DSS prognosis than those with sublobar resection {hazard ratio (CI) : OS = 0.8(0.72-0.88) ; DSS = 0.79 (0.68-0.91)}. In the full sample, Kaplan Meier analysis showed better median OS and DSS for patients with a lobectomy vs patients with sublobar resection (OS=120 m vs. 69 m, Logrank p<0.001; DSS = not reached vs.136 months, Logrank p<0.001; Figure 1). Multivariate Cox regression performed on a propensity-matched group confirmed superior survival of patients with lobectomy vs. sub-lobar resection {hazard ratio (CI): OS = 0.75(0.65-0.85); DSS = 0.71 (0.59-0.85)}. Conclusions: Lobectomy confers an overall and disease-specific survival benefit for patients with even small (< 2 cm) non-small cell lung cancers when compared to sublobar resection. The greater improvement in OS than DSS in the comparison groups may be due to patient selection bias for extent of resection, as patients with low cardiopulmonary reserve are typically chosen for less extensive resections. These observations should be verified in a prospective trial.



Survival Estimates for Overall Survival (OS) and Disease Specific survival (DSS)

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Anastomotic Leak Does Not Affect Ability to Receive Adjuvant Treatment R.W. Farmer,* C.R. St. Hill, K.M. McMasters, C.R. Scoggins, R.C. Martin. *University of Louisville, Louisville, KY.*

Background: Esophageal anastomotic leak is associated with high morbidity and mortality and potentially lethal if not recognized promptly and treated aggressively. While many studies have attempted to delineate the surgical techniques associated with lower rates of anastomotic leak, few have attempted to determine its long term effects on supplemental therapy and patient quality of life. Methods: We reviewed our prospective 350 patient esophageal-gastric database and found 164 esophageal anastomoses performed from 1994 to 2009. We compared clinical, pathologic, and outcomes data in the perioperative period between patients clinically or radiographically diagnosed with anastomotic leak and those without. We then compared their postoperative courses of adjuvant treatment, morbidty/mortality, and quality of life measured by Karnofsky performance status and EORTC score. Statistical correlations were calculated with Chi-Square, T-test, Kaplain-Meier, ANOVA, and Cox Regression analyses. Results: Of 164 patients receiving esophageal anastomses for cancer, 35 (21.3%)

developed anastomotic leak. These groups were similar in preoperative history, preoperative staging, and type of tumor. Type of operation and variations in operative technique did not significantly affect leak rate. Patients with a leak were more likely to require intraoperative transfusion (57.1% vs 34.1%, p=.013). As expected, they had a greater prevalence of perioperative complications to include pneumonia (48.6% vs. 16.3%, p=.001), pulmonary embolus (14.3% vs 4.3%, p=.043), ileus (11.4% vs. 1.6%, p=.006%), empyema (11.4% vs. 0%, p < .001), and catheter related blood stream infections (8.6% vs. 0%, p = .001). Despite this increase in perioperative morbidty, there was no statistically significant difference with ability to receive adjuvant therapy (28.6% vs. 38.0%, p=.303), quality of life (average Karnofsky score 93.2 vs. 93.1, p=.984), or survival at 6 months (60% vs. 69.8%, p=.273). Conclusion: Anastomotic leak after oncologic resection does not preclude adjuvant therapy and, when managed appropriately, does not affect long term performance status or survival.

Clinical Outcomes of Esophageal Leak and Follow Up Data

Factors Analyzed	Leak N = 35 (21.3%)	No Leak N = 129 (78.7)	P value	Significant (Y/N)
Blood Transfusion	20 (57.1%)	44 (34.1%)	.013	Y
Length of Stay - ICU (median,mean)	10, 10.6	4.5, 10.3	.006	Y
Pneumonia	17 (48.6%)	21 (16.3%)	>.001	Y
Pleural Effusion	5 (14.3%)	6 (4.3%)	.043	Y
Ileus Beyond Expected	4 (11.4%)	2 (1.6%)	.006	Y
Empyema	4 (11.4%)	0	>.001	Y
CVC related BSI	3 (8.6%)	0	.001	Y
Stricture	3 (8.6%)	10 (7.8%)	.874	N
Dilation	2 (5.7%)	2 (1.6%)	.158	N
Dysphagia	2 (5.7%)	11 (8.5%)	.586	N
Adjuvant Rx	10 (28.6%)	49 (38.0%)	.303	N
Karnofsky Score (avg @ 6 mos. f/u)	93.2	93.1	.984 (sem 1.95 / 2.54)	N
Karnofsky Score 80 +	17 (89.5%)	65 (92.9%)	.627	N
Alive with Dz/No Evidence Dz @ 6 months	21 (60%)	90 (69.8%)	.273	N

P296

Utility and accuracy of Endobronchial ultrasound in mediastinal staging of lung cancer W.D. Bolton,* R.J. Johnson, C. Schammel, K. Banks, S. Hutcheson, W. Wall, B.L. Johnson, J.E. Stephenson. *Surgical Education, Greenville Hospital System, Greenville, SC.*

Background: Endobronchial ultrasound (EBUS) is an emerging technology for mediastinal evaluation which is less invasive than cervical mediastinoscopy, the traditional gold standard. The purpose of our study is to evaluate the utility and accuracy of EBUS as a diagnostic and staging tool at our regional teaching institution. Methods: We retrospectively reviewed the institutional thoracic surgery database for all patients undergoing EBUS between 2008 and 2010. Results: 130 patients underwent EBUS during this time period: 59 patients underwent diagnostic EBUS alone; 57 patients underwent staging EBUS alone; 14 patients had both a diagnostic and staging EBUS. Level 4L, 4R, and 7 were all sampled in 25 (41.0%) of the 61 diagnostic EBUS procedures. Additional levels (11, 10, 3 or 2) were sampled in 23 (37.7%) procedures. Diagnostic EBUS yielded a diagnosis of: non-small cell lung cancer- n=15; other cancer- n=15; sarcoid/granulomatous- n=7; benign lymphoid tissue- n=35; and nondiagnostic specimen- n=1. Two patients (3%) had a false negative diagnostic EBUS. Both false negative studies sampled levels 4L, 4R, and 7. The sensitivity and specificity of diagnostic EBUS was 93% and 100%. For staging EBUS, patients 71% had three lymph node stations sampled and 29% had two lymph node stations sampled. Two patients (3%) had a false negative staging EBUS. Less than three stations were sampled secondary to: nodal size less than 3mm- n=19 and technical difficulty- n=1. The sensitivity and specificity for staging EBUS was 94% and 100%. For those with 3 or more node stations sampled, sensitivity and specificity were 90% and 100%. When 2 node stations were sampled, sensitivity and specificity were both 100%. Conclusion: We found that EBUS is a highly accurate and minimally invasive manner in which to both diagnose mediastinal masses and stage the mediastinum. Given the increasing availability of EBUS, it seems likely that this technology will have a more significant role in the management of patients with lung cancer in the future.

P297

Advancing thoracoscopic lobectomy (VATSL) at a community teaching hospital B.G. Dalton,* H.R. Yoon, R.B. Hird, R.K. Orr, C.L. Nguyen. *spartanburg regional medical center, Spartanburg, SC.*

Introduction: Although VATSL for early lung cancer is gaining popularity, most procedures are performed in the university teaching hospital setting. The purpose of our study is to investigate the safety and feasibility of introducing VATSL to a community teaching hospital which has no previous history with this procedure. Methods: We reviewed 74 consecutive patients undergoing VATSL by a single surgeon with first assistance from general surgery residents from July 2006 to September 2009. Data regarding preoperative patient characteristics, indication for resection, anatomic location of tumors, pathologic staging, postoperative complications, estimated blood loss (EBL) and 30-day mortality were analyzed. Results: VATSL was successfully completed in 71 of 74 patients (95.9%). Of the 3 conversions, two were secondary to bleeding and the other because of tumor size. The average operative time was 248 ± 72 minutes and the average blood loss was 264 mL. Comparison of average EBL for the first 37 patients with the most recent 37 patients demonstrated a difference of 356 ml versus 172 ml (p=0.02). NSCLC was the indication for resection in 66 of 74 patients (89%) and most tumors were staged as pStage I (65%). Of the patients undergoing lobectomy for NSCLC, 57.6% were diagnosed by intra-operative wedge resection and frozen section analysis (FS) followed by immediate formal lobectomy. Complications occurred in 24.3% of patients with supraventricular dysrhythmias and pneumonia being most common. Only three patients (4.1%) required blood transfusions during their hospitalization and there were no operative deaths. The 30-day mortality was 1.4% (1/74) and occurred in a kidney transplant patient who developed pneumonia and sepsis. Conclusion: Our data suggest the safety and feasibility of introducing VATSL into a community teaching hospital setting. However, a learning curve exists for teaching this procedure to general surgery residents as evidenced by our improved blood loss data. Furthermore, the utility of intra-operative wedge resection with FS followed by immediate lobectomy appears to be a successful strategy for timely diagnosis and treatment of early stage NSCLC.

P298

Laparoscopic resection of residual retroperitoneal tumor mass of non-seminomatous testicular germ cell tumors; a new promising treatment approach C.. Ozturk,* R.J. Van Ginkel, H.S. Hofker, J.A. Gietema, R.M. Krol, H.J. Hoekstra. *Surgical Oncology, UMCG, Groningen, Groningen, Netherlands.*

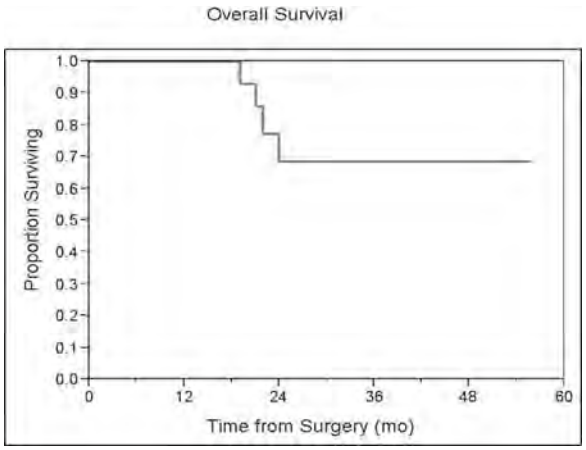
Background: Resection of residual retroperitoneal tumor mass (RRRTM) after cisplatin based polychemotherapy in advanced nonseminomatous germ cell tumor (NSTGCT) is a major part of the combined treatment. Methods: At the University Medical Center Groningen, 146 consecutive patients, with disseminated NSTGCT were treated with cisplatin based polychemotherapy between 2005-2010. Laparoscopic RRRTM was performed in patients with RRTM < 5 cm ventral or lateral from aorta and/or cava located. 42 patients fulfilled the criteria for laparoscopic resection, median age was 27 (range 17-59) years. Stage according to Royal Marsden classification prior to chemotherapy treatment: IIA 25%, IIB 45%, IIC 10%, stage IV with lymph node status N2 20%. Results: Median duration of laparoscopy was 201 (range 122-325) minutes. Median diameter of RRRTM 20 (range 5-47) mm. Laparoscopic resection was successful in 36 patients (86%). Conversion was necessary in five patients (12%); three due to bleeding, and two due to obesity. One non-planned hand-assisted procedure also had to be performed (2%). Histological examination of the specimens revealed fibrosis or necrosis in 15 patients (35.7%), mature teratoma in 25 patients (59.5%) and viable tumor in 2 patients (4.7%). Median period of hospitalization was one day (range 1-7). During a median follow-up of 32.5 (3-57) months, two patients developed a recurrence (4.7%). Conclusion: Laparoscopic RRRTM after chemotherapy for disseminated testicular cancer is feasible in selected patients, resulting in a short hospital stay and neat cosmetic results. However long term follow-up data with respect to recurrence rate should be awaited to prove the final oncologic efficacy.

P299

Laparoscopic Distal Gastrectomy for Gastric Cancer: Institutional Experience with 38 Consecutive Patients and Oncologic Outcomes

J. Ho,* E. Kachikwu, R. Nelson, A. Pigazzi, J. Ellenhorn. *City of Hope National Medical Center, Duarte, CA.*

Introduction The application of laparoscopy in the surgical treatment of gastric cancer has become more popular in recent years. Most of the published series are from Asia and few report on survival. Our objective was to elucidate the safety, efficacy, and oncologic outcomes of laparoscopic distal gastrectomy in patients with gastric cancer. Methods The medical records of all patients who underwent laparoscopic distal gastrectomy at City of Hope National Medical Center between 6/2005 and 8/2010 were retrospectively reviewed. Relevant data analyzed included patient demographics, operative parameters, complications, recurrence, and survival. Results A total of 38 consecutive patients were identified. Thirty-four of the 38 patients had a diagnosis of gastric adenocarcinoma. Median age was 70 years (35-96). Median operative time was 379 min (228-583). Median EBL was 200 ml (10-900). Seventeen of the 38 laparoscopic distal gastrectomy cases employed robotic assistance in lymph node dissection. The median number of lymph node retrieval was 23.5. Twenty-two cases included D2 lymph node dissections, 14 cases were D1 dissections, and 2 cases involved D0 dissections. All intended D2 dissections had greater than 15 nodes retrieved. Median hospital stay was 6 days (3-39). Morbidity and mortality rates were 11% and 0%, respectively. Of the 34 patients with gastric adenocarcinoma, histological staging revealed 1 patient had stage 0 disease, 25 had stage I, 7 had stage II, and 2 had stage III. Median follow-up was 12 months (0.5 to 58). Cancer recurrence occurred in 2 patients (6%). The 3 year overall survival is 69% and disease specific survival is 90%. The median survival has not been reached. Conclusions Laparoscopic distal gastrectomy is feasible and safe and can be performed in patients with gastric cancer with excellent surgical and oncologic outcomes.



P300

The Moffitt Prognostic Model for Prediction of Survival after Pancreaticoduodenectomy

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Background The AJCC staging for pancreatic cancer is relatively non-discriminatory for prediction of survival after resection. At the Moffitt Cancer Center a prognostic score for patients with localized pancreatic cancer (AJCC ≤ IIb) has been developed. In the Moffitt Prognostic Index (MPI) patients are grouped in 5 risk categories on the basis of extra-pancreatic tumor extension, degree of differentiation and lymphatic invasion. The aim of this study is to assess the MPI's predictive value in an independent cohort of patients who underwent pancreaticoduodenectomy (PD) at the New York University. Methods From our retrospective pancreatic adenocarcinoma database of 248 patients, we identified and grouped by MPI category patients with AJCC stage ≤ IIb who underwent PD (1990-2009). Differences between groups were evaluated using ANOVA and chi-squared test. Overall survival (OS) for each group was estimated using the Kaplan-Meier method and compared using the log-rank statistic. Results Among 131 patients with stage Ia-IIb cancer, MPI could be calculated for 126 (96%). Only few patients fell in MPI lower-risk groups 1-4 (respectively 1, 4, 3, 22), while the majority (96, 76.1%) fell in MPI group 5 (poor prognosis). The 5 groups were similar in demographics, underlying comorbidities, laboratory data, ASA score and ECOG performance status. There were no differences in operative time, blood loss, intra- and post-operative complications, length of stay, 30-day mortality. Pathology revealed more advanced stage in groups 3 to 5 (p=0.001). At mean follow-up of 18 months, there was no difference in median OS across MPI groups (respectively 19, 6, 16, 17, 12 months, p=0.91). Of note, AJCC staging did correlate with median OS (respectively 43, 12, 16, 11 months in stages Ia to IIb, p = 0.004). Conclusions In our experience the MPI performed worse than AJCC staging as a prognostic tool. The clustering of patients in the worst-prognosis group defied the very purpose of prognosis discrimination. Furthermore, in our experience MPI did not correlate with overall survival in patients undergoing DP for early-stage (≤ IIb) pancreatic cancer.

P301

CD133-positive circulating tumor cells (CTC) independently predict prognosis of patients undergoing liver resection for colorectal cancer metastatic disease

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Background Radical surgery is the mainstay of treatment for liver metastasis from colorectal cancer. Although this is the only potentially curative approach, the prognosis of these patients is often dismal. The identification of patients with high risk of disease recurrence after surgery is crucial to select those who might most benefit from adjuvant chemotherapy. Patients and methods Patients undergoing hepatic resection of liver metastatic disease from colorectal cancer were considered eligible. Selective gene expression profiling of metastatic disease, peripheral blood (withdrawn at the time of surgery) and normal samples (cultured fibroblasts and PBMC) was performed by means of quantitative real time PCR. Univariate and multivariate survival analysis (Cox proportional hazard model) was used to correlate the transcriptional level of seven genes (cytokeratin-19, cytokeratin-20, CEA, VEGF, EGFR, CD133 and Survivin) with patients' prognosis. Results Fifty patients were enrolled at our institution between 2003 and 2008. Radical (R0) and microscopically non-radical (R1) resection was achieved in 29 (58%) and 21 (42%) patients, respectively. At univariate survival analysis, radical resection and the expression of cytokeratin-19, Survivin and CD133 in the peripheral blood were significantly associated with patient prognosis. More importantly, at multivariate survival analysis only radical resection (hazard ratio [HR]: 6.0, 95% confidence interval [CI]: 2.5-14.2; P<0.0001) and CD133 gene expression in the peripheral blood (HR: 1.2, CI: 1.1-1.3; P<0.0001) were retained by the Cox model. Finally, the expression of CD133 resulted significantly higher in tumor samples as compared to normal tissues (including PBMC), which rendered this gene a potential marker of circulating tumor cells. Conclusions The identification in the peripheral blood of CD133 positive CTC as an independent prognostic factor in patients with liver metastasis from CRC represents an important step on the way to improve the therapeutic management of this disease.

P302

Nationwide Trends in Diagnosis and Outcomes of Gastrointestinal Stromal Tumors in the Era of Targeted Therapy

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Introduction: Gastrointestinal stromal tumors (GISTs) have historically been inconsistently categorized in tumor registries. Discovery of c-kit expression in 1998 allowed for more precise diagnosis, and use of tyrosine kinase inhibitors for GIST in 2000 marked a new era in management. We examined nationwide trends in the diagnosis, management, and outcomes of GIST in this post-imatinib era. Methods: Patients ≥18 years old with GIST were identified in the SEER database 1998-2007, using the GIST-specific code. After a period of steady increase, incidence stabilized after 2001. Trends from 2002 to 2007 were examined. Univariate and multivariate analyses were performed. This cohort was further divided into 2002-2004 and 2005-2007 for survival analysis by Kaplan-Meier methods and Cox proportional-hazard ratios. Results: 3604 patients were identified. There was a dramatic increase in diagnoses from

1998 to 2001 (109 to 376 cases, p<0.001), but no significant change from 2002 to 2007 (p=0.572). During this period of stable incidence (2002-2007), the proportion of patients recommended for surgery continued to decrease (85.2% to 80.1%, p<0.001), while utilization of radiation (1.1% by 2001) remained relatively constant (p=0.101). Anatomic distribution remained stable (p=0.529), with stomach (52.9%) and small bowel (29.3%) predominating. There was also no change in stage distribution (p=0.811). Late stage, black race, and advanced age were predictive of not receiving resection. Female sex, younger age, local disease, later year of diagnosis, and resection were associated with lower risk of death. Survival for patients diagnosed in 2005-2007 improved over 2002-2004 for both unresected (p=0.027) and resected (p=0.010) groups. Resection was an independent predictor of survival in both periods (p<0.001). Conclusions: Incidence of GIST as identified in the SEER database has stabilized 2002-2007, likely reflecting more accurate diagnosis. Survival for both resected and unresected patients has improved since the introduction of imatinib, and continues upward. These population-level findings confirm the significant benefit of surgical therapy beyond clinical trials.

P303

Single Nucleotide Polymorphism of Fibronectin-1, Determining Tumor Shape and Malignant Behavior in Colorectal Cancer Cases
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Background: The depressed flat surface lesion is not easy to find out at the routine colonoscopy for the screening of colorectal cancer (CRC). It is useful for screening of the depressed lesion by finding genes to determine shape of tumors, and the clinical significance of the molecule was unveiled. **Patients and Methods:** A total of 146 primary colorectal cancer patients were enrolled. Tumor cells were specifically collected from primary lesion by laser microdissection system (LMD) and total RNA was extracted. We performed microarray analysis by the Human Whole Genome Oligo DNA Microarray Kit. To evaluate SNPs, we extracted genomic DNA of peripheral blood from 64 patients of CRC. We performed SNP array analysis by Affymetrix analysis. **Results:** Microarray analysis identified *Fibronectin1 (FN1)* gene as a significantly different expressing genes between the group of "Depressed type tumors and lesions, such as 0-IIb, 0-IIc, 0-III, type 2 and type 3 tumors" and the group of "Elevated type tumors, such as 0-Ip, 0-Isp, 0-Is, 0-IIa, and type 1 tumors". There were three probes on *FN1* gene, and were commonly up-regulated significantly in depressed type lesions than that of elevated type tumors (q value: 5.17x10-3, fold change; 32.4). Replication of *FN1* expression was validated by qRT-PCR analysis in another subsets of 144 cases of CRC and IHC study, and the *FN1* abundant CRC cases indicated significantly higher incidence of lymphatic permeation, large size of tumors. SNP array analysis indicated that CRC cases with genotype GG at SNP (rs6707530) showed significantly higher *FN1* expression than 23 cases with other genotype (p<0.05). **Discussion:** *FN1* at 2q34 is involved in cell adhesion, migration and metastasis as a tumor with mesenchymal phenotype. Abundant expression of *FN1* might enforce cancer cells invading into deeper layers, which would eventually define the shape of tumors. The finding of the SNP allows us to predict the presence of depressed tumors in colorectal epithelium before the colonoscopy by blood samples, which helps us to discover the disease easily.

P304

Prognostic factors for perioperative morbidity, mortality and long-term survival after resection for colorectal liver metastases (CRLM)
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Objective:Up to 60% of patients with colorectal cancer eventually develop liver metastases during the course of their disease. Surgical resection remains the only potentially curative treatment for patients with CRLM. The aim of this study is to investigate how our results of liver resection for CRLM relate to the literature. Patients and methods: Patients treated with liver resection for CRLM were selected from a database containing all patient data of 176 liver operations in 156 patients performed between 1995 and 2010 in our hospital. Results: It involved 104 patients, 73 (70%) men and a mean age of 65.7 years 48 (46%) major resections (≥ 3 liver segments) were performed. The mean operative time was 177 (±60) minutes. 39 (38%) patients received blood transfusions. The median length of hospital stay was 11 (6-47) days. There were 54 complications in 29 patients (28%). Two of the 104 patients died because of postoperative complications (1.9%). Only major resection was an independent predictor for complications. The overall 5-year survival rate was 42% (SE 8), the disease-free 5-year survival rate 19% (SE 7). Among the tested variables the presence of extrahepatic metastases (p = 0.006) revealed an important negative independent prognostic factor. Also combination therapy with neoadjuvant chemotherapy (p = 0.014) and neoadjuvant and adjuvant chemotherapy (p <0.001) were negative independent prognostic factors for overall survival. Liver resection combined with RFA was a negative independent risk factor (p =0.004) for the disease free 5-year survival.Conclusion: Liver surgery can be performed safely in our non-academic liver center given the perioperative morbidity and mortality rates of 28% and less than 2%. The 5-year overall and disease-free survival rates are similar to those mentioned in literature. The indication for liver resection in patients with extrahepatic disease activity and greater overall tumor burden should be weighed carefully.

P305

Early recurrence after simultaneous colorectal and hepatic resection is associated with poor prognosis in synchronous colorectal liver metastasis
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Background: Under the policy of simultaneous resection of colorectal primary and synchronous colorectal liver metastases (SCRLM), early recurrence (ER) is a major problem after resection. Because ER might reflect systemic disease at presentation, patients likely to have a risk of ER should offer upfront chemotherapy before hepatectomy. The aim of this study was to investigate the relationship between ER after SCRLM resection and overall survival and to clarify the predictive factors of ER after resection. Methods: A retrospective analysis was performed for 195 consecutive patients who underwent simultaneous resection of colorectal primary and SCRLM between 1980 and 2004. ER was defined as recurrence < 6 months after resection. Results: All patients had no chemotherapy both preoperatively and postoperatively and 148 (76%) had a recurrence. Overall survival of patients with recurrence within 6 months after SCRLM resection was significantly worse than that of patients with recurrence after more than 6 months (P < 0.01). Maximum size of SCRLM 2.5cm or more, number of SCRLM 4 or more and intrahepatic bilateral distribution was significantly associated with ER after hepatectomy. Conclusion: ER after simultaneous colorectal and liver resection correlates with a poor prognosis. For patients with SCRLM, upfront simultaneous surgery should be confined to the very selected cases, and It is recommended to perform neoadjuvant chemotherapy when a patient has large size, large number or intrahepatic bilateral distribution of SCRLM.

P306

INSULIN-LIKE GROWTH FACTOR 1 AND ITS RECEPTOR CORRELATES WITH OBESITY STATUS IN ESOPHAGEAL ADENOCARCINOMA TUMOURS
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Introduction: Obesity has been strongly implicated in the pathogenesis of esophageal adenocarcinoma. In this context, the insulin-like growth factor (IGF-1) axis warrants exploration. Methods: Samples from 100 patients diagnosed with esophageal adenocarcinoma with prospective clinicopathological, follow-up and obesity status data were collected. Adipocyte conditioned media (ACM) was created by co-culture of oesophageal cancer patient's omental or subcutaneous fat in media for 72 hours. ELISA was used to measure levels of free IGF-I in ACM (n=55) and serum (n=100) and of circulating total IGF-I levels using an acid precipitation pre-treatment (n=24). mRNA expression of IGF-IR and IGF-I was determined by qPCR in resected tumour samples (n=70). Immunohistochemistry (IHC) determined IGF-1R expression in human tumour sections (n=40) and tissue microarrays (n=200). Results: ACM is a source of IGF-1. There was a significantly increased total IGF-I level in the serum of overweight patients but free IGF-1 was unchanged. Gene expression analysis revealed positive significant correlations between IGF-IR and IGF-I in tumours

and obesity status ($p<0.05$). IGF-I levels correlated moderately IGF-IR expression ($\rho=0.465$, $p=0.001$). In resected oesophageal tumour IHC sections, no statistical difference between intensity of IGF-1R expression and BMI or stage was observed. However, higher intensity IGF-1R staining was observed in the leading edge of adenocarcinomas. This was replicated in tissue microarray immunohistochemistry. Conclusion: This study suggests an important role for the IGF axis in esophageal adenocarcinoma and a relationship between the IGF axis and obesity status. Phase I trials of IGF axis inhibitors may be indicated in these patients.

P307

Treatment of Recurrent Hepatocellular Cancer after Liver Transplant: Is There Hope? N.N. Nissen,* V. Menon, A. Annamalai, B. Boland, F. Poordad, J. Fair, T. Tran, J. Ryan, A. Klein, S. Colquhoun. *Comprehensive Transplant Center, Cedars-Sinai Medical Center, Los Angeles, CA.*

Introduction: Liver transplantation (LT) has been increasingly utilized as a treatment for hepatocellular cancer (HCC). Unfortunately, the immunosuppression accompanying LT is thought to make recurrence of HCC rapidly fatal. Methods: We reviewed treatments and outcomes for recurrent HCC after LT at a large academic medical center with an active LT program. 127 patients underwent deceased or living donor liver transplant (LT) for HCC between 2002 and 2010. 14 Patients developed recurrent HCC and are evaluated further in this report. Results: Recurrent HCC developed at a mean of 20 months and median of 14 months after LT. Sites of recurrence included liver alone (3), extrahepatic single site (8) and extrahepatic multifocal (3). Treatments utilized included decrease in immunosuppression (13), addition of the mTOR inhibitor sirolimus (6), resection of recurrence (5), locoregional hepatic therapy (4) and systemic therapy with sorafenib (5) or other agents (4). Overall survival measured from the time of LT for patients with HCC recurrence was 85% at 1 year and 55% at 3 years. Overall survival measured from time of diagnosis of recurrent tumor was 64% at 1 year and 39% at 3 years (Figure). Patients with recurrence within 1 year of LT (n=6) had more rapid disease progression than those with later recurrence. Of these 6 patients, 2 were diagnosed before 2006 and died within 2 months. The remaining 4 patients were diagnosed in 2009 and all have survived over 12 months, possibly owing to increased use of systemic therapies. Conclusions: Recurrent HCC after LT can be treated with a multidisciplinary approach with modest short-term survival. Application of the same modalities used to treat HCC in the non-transplant patient seems to be justified when treating recurrent HCC after transplant, but we should continue to develop new strategies for these patients.

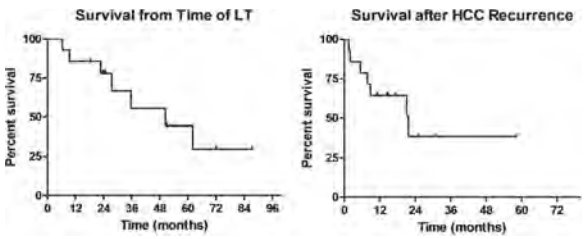


Figure: Patients with Recurrent HCC After Transplant

P308

The Analysis of Mucin in Surgically Removed Colon Cancer Specimens M. Johnson, E.W. Martin,* H. Ding, C. Hitchoock. *Surgery, The Ohio State University Medical Center, Columbus, OH.*

Introduction: Immunohistochemical analysis is an important asset in providing information about surgical specimens. With cancer being the second most common cause of death worldwide and colorectal cancer being the third most common form of cancer, it is important to have complete information on the status of surgical specimens. This study addresses the status of mucin expression in colon cancer specimens. Methods: Pathology slides from 21 patients with advanced colorectal cancer were utilized for analysis. These slides were analyzed with six different antibodies including MUC 1, MUC 2, MUC 4, MUC- 5AC, MUC 6 and B 72.3. Regions of interest included the distant margin and tumor to normal colon interface. Results: Percentages of positive staining were obtained from the different antibodies in the areas of interest. 18 of 21 tumors stained positive for at least one type of MUC. 15/21 were MUC 2 positive, 12/21 were MUC 4 positive, 7/21 were MUC 1 positive, 4/21 were MUC 6 positive and 0/21 were MUC-5AC positive. There is apparent increased TAG-72 antigen expression in colon epithelial cells that are in close proximity to tumor with 20/24 staining positive compared to 3/35 at the margin. In addition, when retrospectively addressing survival using the Social Security Death Index and internal hospital records, there were 3/21 patients alive. MUC positive patients seem to have a lower tendency of survival. For example, the survival ratio of patients with MUC1, MUC2, MUC4, MUC6 are 0/7, 2/15, 1/12, 0/4 respectively. On the other hand, the survival ratio of patients negative MUC1, MUC2, MUC4, MUC6 are 3/14, 1/5, 2/7, 3/16. No samples demonstrated MUC-5AC positivity. Notably, 3/3 alive patients had specimens that stained negative for MUC 1 antibody and 10/18 of the deceased patients had specimens that stained negative for MUC 1 antibody. Conclusions: Cancerous tumors in the colon may alter mucin expression in colonic epithelial cells. The majority of the colon cancer specimens showed positivity for MUC. The result of this study suggests that patients with colon cancer without the presence of MUC may have an increased survival compared to those with MUC positivity.

P309

Outcomes Associated with Surgery for T4 Esophageal Cancer J.M. Pimiento,* J. Weber, S. Hoffe, R. Shridhar, M. Melis, J. McLoughlin, R.C. Karl, K.L. Meredith. *Moffitt Cancer Center, Tampa, FL.*

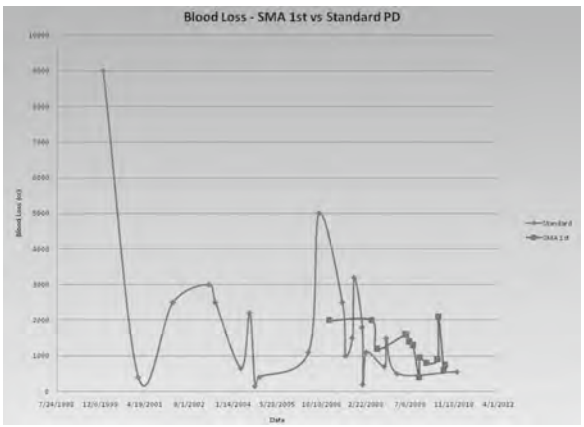
Background: Esophageal cancer often presents as locally advanced disease with 15% of patients having T4 tumors at diagnosis. Esophagectomy was often reserved for palliation given the dismal survival rates and high rates of R1/R2 resections. However, neoadjuvant therapy (NT) has the potential to significantly downstage esophageal cancers and thus increase complete resection rates. We report our experience with surgically resected T4 esophageal cancers. Methods: Using a comprehensive esophageal cancer database, we identified patients who underwent an esophagectomy for T4 tumors between 1994 and 2008. NT and pathologic response variables were recorded and response was denoted as complete (pCR), partial (pPR), and non-response (NR). Clinical and pathologic data were compared using Fisher's exact and chi-square while Kaplan Meier estimates was used for survival analysis. Results: We identified 39 patients with T4 tumors who underwent esophagectomy of which 38(97%) underwent NT. The median age was 61(31-79) years with a median follow-up of 32(5-97) months. There were 3(7.9%) pCR, 17(44.7%) pPR, and 18(47.4%) NR. R0 resections were accomplished in 37(94.9%). Two patients had incomplete resections. One patient had a R2 resection after NT and was deemed as NR, an additional patient had a R1 resection after NT and was a pPR with a residual 0.2cm tumor on permanent pathology. There were 14(35.9%) recurrences with a median time to recurrence of 19.5(4-71) months. In this group pCR represented 1(7.1%), whereas pPR and NR represented 6(42.9%), and 7(50%) respectively. The overall and disease free survival for all patients with T4 tumors was 28% and 34% respectively. Patients achieving a pCR had a 5-year overall and disease free survival of 43% and 47%, compared to pPR 30% and 21%, while there were no 5-year survivors in the NR cohort. Conclusions: T4 esophageal cancer often portends a dismal prognosis even after surgical resection. Historical incomplete resections and dismal survival rates often make surgery palliative rather then curative. However, we have demonstrated that neoadjuvant therapy and downstaging of T4 tumors leads to increased R0 resections and improvements in overall and disease free survival.

P310

Pancreaticoduodenectomy with Venous Resection Utilizing the SMA 1st Dissection Technique D. Bourgeois,* W.C. Conway, J. Bolton. *Ochsner Clinic Foundation, New Orleans, LA.*

Introduction: Recent data indicates pancreaticoduodenectomy (PD) with venous (SMV/PV) resection can be done with acceptable mortality/morbidity and results in survival comparable to PD without SMV/PV resection. In an effort to reduce blood loss (EBL) associated with this procedure, the "superior mesenteric artery (SMA) first" technique has been described. Here, we review our experience using the SMA 1st method during PD requiring venous resection. Methods: An IRB approved, retrospective review was conducted to identify patients undergoing a PD with venous resection for pancreatic head cancer at Ochsner Medical Center from 1997-2010; small venous side wall defects were not included. Data collected included patient and tumor characteristics and peri-operative outcomes. Cases in which the SMA 1st technique was used

were compared with those in which conventional dissection was utilized. Results: 37 patients underwent PD with vascular resection/reconstruction during the study period. The SMA 1st technique was utilized in 13 cases. Comparing the 24 patients undergoing conventional dissection to the SMA 1st group, median age and gender were similar (66 vs 68; 12 female vs 8). Tumor stage was not significantly different between the groups; conventional group had a 33% nodal positivity while the SMA 1st group had a 50% rate. Looking at peri-operative outcomes, the conventional group required a median of 3 units of blood (min 0, max 14), the surgery took a median of 10 hrs (6, 16.5), and median EBL was 1100 (150, 9000). The SMA 1st group required a median of 2 blood transfusions (0, 6), required 10 hrs (8.5, 12.5), and had a median EBL of 1200 (400, 2100). Mean EBL was 1700 and 1231 for the conventional group and SMA 1st group, respectively. Although these 2 groups of peri-operative outcomes were not significantly different, we are clearly seeing a reduction in EBL with the SMA 1st technique as more experience is gained (figure). Conclusion: The SMA 1st dissection technique facilitates PD with venous resection. In our early experience, a trend toward reduced EBL has been noted, likely related to the devascularization of the pancreatic head prior to venous resection it affords.



P311

Resection of At-Risk Mesenteric Lymph Nodes Improves the Outcome of Patients with Small Bowel Neuroendocrine Tumors
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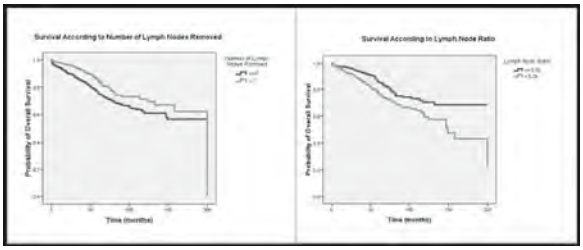
Background. Neuroendocrine tumors of the small intestine commonly metastasize to regional lymph nodes(LN). Single institutional reports suggest that removal of LNs improves outcome, but comprehensive data is lacking. We hypothesized that the performance and extent of lymphadenectomy reported in a large administrative database would be associated with improved survival. Methods. A search of the SEER database was performed for patients(pts) with jejunal and ileal neuroendocrine tumors from 1977-2004. Descriptive pt characteristics were collected to include age at diagnosis, gender, race, grade, primary tumor size, LN status, number of LNs resected, presence of distant metastasis, and operation. Statistical analyses were limited to pts with only 1 primary tumor to exclude pts with other malignancies. Univariate and multivariate analyses were performed to analyze the number of LNs resected and the LN ratio(LNR=number of positive LNs/total number of LNs removed) to determine the effect on cancer-specific survival. Results. We identified 3548 pts with jejunal or ileal carcinoid tumors. Of these, 1364 possessed 1 primary tumor; 1112 were alive and 252 died of disease with a median follow-up of 35 months. Removal of any LNs was associated with improved cancer-specific survival when compared to pts with no LN removal reported(p=0.0027). Among those who had any LN removed, a median of 8 LNs(381 pts had 0 LNs removed; data missing for 433 pts) were identified in resection specimens with a median LNR of 0.29(range 0-1). On multivariate analysis(adjusting for age and tumor size), pts with >7LNs removed experienced an improved cancer-specific survival over those with ≤7LNs removed(median survival not reached vs. 140months; HR=0.573 [0.402, 0.817],p=0.002). Increased LNR>0.29 was associated with a diminished cancer-specific survival(median survival 134months vs. median survival not reached; HR=1.497[1.043, 2.149],p=0.029). Conclusion. This review of a large number of surgical pts suggests that removal of mesenteric LNs at risk in conjunction with resection of the primary tumor will improve the survival of pts with small bowel neuroendocrine tumors.



P312

Completion and toxicity rates of adjuvant chemotherapy in rectal cancer patients previously treated with neo-adjuvant therapy and resection
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Background: Adjuvant chemotherapy is recommended after rectal cancer surgery. Yet the success and complication rates of this adjuvant treatment are poorly studied. The purpose of this study is to determine the success rate and define the toxicity profile of adjuvant chemotherapy in rectal cancer patients previously treated with neo-adjuvant chemotherapy. Methods: Study Design is a retrospective review of patients from December 2002 – December 2007 from the City of Hope database. Data is available with 66 patients diagnosed with locally advanced rectal cancer treated with neo-adjuvant chemo radiation and resection. Data points analyzed included demographics, chemotherapy-related toxicity and survival. Results: Adjuvant chemotherapy was started in 35/66 (53%) of patients. In 31 (47%) cases, chemotherapy was not given because of patient refusal or physician preference. 9 patients were lost to follow-up. Follow-up ranged from 9-59 months with median follow-up of 27 months. In the 26 patients with adequate follow up there were a total of 165 episodes of toxic events ≧ grade 1. Most of the events were mild to moderate grade 1-2. In 10 patients (28%) 22 major toxicities ≧ grade 3 episodes were observed. The median Karnofsky performance scale (KPS) showed no significant difference in patients before and after adjuvant chemotherapy (p=0.071). The rates of 1-year, 3-year and 5-year survival were 100%, 90%, and 60%, respectively; corresponding disease free survival was 88%, 83%, and 69% respectively. Conclusion: These preliminary data suggest that only a fraction of rectal cancer patients previously treated with neo-adjuvant CRT complete a full course of adjuvant chemotherapy. Future studies will help confirm these preliminary findings and generate an outcome comparison between patients receiving and not receiving adjuvant therapy.

P313

Oncologic Outcomes Following Minimally-Invasive Distal Pancreatectomy for Pancreatic Adenocarcinoma: Matched Comparison with Open Resection
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Introduction: Multicenter data indicate that laparoscopic distal pancreatectomy (LDP) can be performed with safety equivalent to open DP (ODP) for benign pancreatic lesions. We performed retrospective analysis of 57 DP for PAC performed either laparoscopically or open to determine relative oncologic efficacy. Methods: Perioperative outcomes and cancer-specific survival in a consecutive series of 57 distal pancreatectomies (DP) for PAC between 2002 and 2009 were analyzed by intended procedure. Results: 32 LDP (56%) and 25 ODP (44%) were identified with 45 month median observation time. Based on intent-to-treat, the LDP and ODP groups were identical in preoperative patient factors like age and BMI as well as tumor characteristics by CT scan and EUS. Perioperative outcomes like estimated blood loss (EBL), transfusion, ICU admission, and length of stay were equivalent despite a 36% conversion rate. EBL in the completed LDP group was significantly reduced. There were no severe complications, reoperations, or perioperative deaths in either group.

The frequency and clinical significance of postoperative complications (Clavien scale) as well as the frequency (15/57, 23%) and severity (11/15 grade A,73%; 4/15 grade B, 27%) of pancreatic fistulae by ISGPF were similar. The rates of R0 resection (ODP 88%; LDP 81%), median lymph node harvest (ODP 11 IQR 12; LDP 10 IQR12), and distribution of AJCC pathologic stages were equivalent regardless of technique. 81% of patients received adjuvant treatment (ODP79%; LDP 83%). No differences in median progression-free (ODP 5.1 mo; LDP 6.0 mo) or overall survival (ODP 14.8 mo; LDP 19.0 mo) were observed. Similarly, no difference in the rates of local (8% ODP; 6% LDP), or local and systemic (16% ODP; 19% LDP) recurrences was identified. Conclusions: No selection bias was observed between the LDP and ODP groups based on preoperative patient factors or CT/EUS findings. A high-rate of margin-negative resection was maintained regardless of technique. We detected no evidence for inferiority of LDP compared to ODP on the basis of postoperative outcomes or long-term cancer survival data.

P314

Metastatic Tissue Has Decreased hENT1 Expression in Pancreatic Cancer Compared to Primary Tumor Q.P. Ly,* N. Chaika, A. Lazenby, S. Lele, C. Are, A.R. Sasson, K. Johnson. *Uinversity of Nebraska Medical Center, Omaha, NE.*

Background: Pancreatic cancer is the 4th leading cause of cancer related death with dismal survival. The majority of patients presented with unresectable disease. Even with surgical resection, 5 year survival is only 15%. Previous studies have shown that patients whose primary tumor expressed hENT1 had better survival than those whose tumor did not, especially when the patients were treated with gemcitabine (Gem). The aim of our study was to understand why those patients with hENT1 expressed pancreatic cancer still succumb even when treated with Gem. Method: We examined 16 Whipple specimens from patients with pancreatic cancer over the past 5 years using Immunohistochemistry for hENT1 expression. The slides were reviewed and scored by our pathologists for intensity and percent of cells stained. Clinicopathologic information such as stage, survival and recurrence were correlated to hENT1 score. We also developed a cellular in vivo model of acquired chemoresistance by exposing a normally Gem-sensitive pancreatic cancer cell line (MiaPaCa2) to increasing doses of Gem then maintained the cells at a drug concentration that is more than 1000 times higher than the cells' IC50. We compared the expression of hENT1 between the parental and the resistant progeny at the mRNA level using polymerase chain reaction (PCR) and at protein level using immunofluorescence. Results: We found that the expression of hENT1 did not correlate with stage, recurrence or survival. However, we were surprised to find that all specimens with nodal positivity showed decreased staining in the metastatic tissue when compared with the primary tumor. When we compared the expression of hENT1 in our parental and resistant MiaPaCa2 cells, hENT1 expression also inversely correlated with the development of resistance both at the RNA and protein levels. Conclusion: The results of our study demonstrate that a decrease or loss of hENT1 expression correlates with gemcitabine resistance. Interestingly, this loss was seen in surgically resected specimens. These findings may further explain why lymph node metastasis portent a worse prognosis beyond an increase in staging.

P315

A meta-analysis of laparoscopic versus open hepatectomy for malignant liver tumors B. O'Brien, Y.H. Kuo, J.M. Davis, E. Hagopian.* *Surgery, Jersey Shore University Medical Center, Neptune, NJ.*

Introduction : Previous studies have shown that laparoscopic hepatectomy is both safe and feasible for trained surgeons in carefully selected cases. The objective of this meta-analysis is to determine if the laparoscopic approach impacts survival in those operated on for malignancy as compared to an open traditional approach. Methods: Systematic review of the literature and meta-analysis of trials comparing laparoscopic and open hepatectomy published in PubMed and Medline were conducted. Comparative studies of laparoscopic and open hepatectomy for solid malignant tumors (hepatocellular carcinoma, cholangiocarcinoma, and liver metastases) in humans which reported survival (1-, 3-, or 5-year) met criteria for inclusion. Pooled odds ratios with 95% confidence intervals were calculated using fixed effect model. Results: Ten studies met criteria for inclusion including 7 retrospective-matched and 3 retrospective non-matched studies. These studies included a total of 763 patients : 325 underwent laparoscopic and 438 underwent open hepatectomy. The 1-, 3-, and 5-year survival rates following laparoscopic hepatectomy were 94%, 77%, and 60% as compared to open hepatectomy being 92%, 73%, and 55%. Those undergoing the laparoscopic approach did not show an increased risk of death (odds ratio [95% confidence interval] of mortality from comparing laparoscopic with open: 1-year =0.69 [0.37, 1.28], p=0.24; 3-years = 0.74 [0.50, 1.10], p=0.14; 5-years = 0.75 [0.49, 1.13], p=0.17). Conclusions: There is no difference in the 1-, 3-,and 5-year survival following laparoscopic versus open hepatectomy for malignant liver tumors. Therefore, laparoscopic hepatectomy is an acceptable alternative to open liver resection for malignancy in selected cases.

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