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SOCIETY OF SURGICAL ONCOLOGY
63rd ANNUAL CANCER SYMPOSIUM

March 3-7, 2010
America's Center & Renaissance Grand Hotel
St. Louis, MO

The following is an outline of presentations and events scheduled during the Society of Surgical Oncology's 63rd Annual Cancer Symposium, March 3-7, 2010, in St. Louis, MO.

Wednesday, March 3

7:30 am – 5:30 pm	Colorectal Cancer and Liver Metastases for the Community Surgeon (includes hands-on workshop) Registration required
6:30 – 8:00 pm	*Dinner Symposium:* Genetic and Genomic Testing in Colorectal Cancer - Making a Difference in the Clinic

Thursday, March 4

8:00 – 10:00 am	Breast Cancer Controversies – More vs. Less
	Update on the Management of Gastric Cancer for the Surgeon
10:30 am – Noon	Comparative Effectiveness: Implications and Opportunities for the Surgical Oncologist
	New Concepts in Image-Guided Cancer Therapy
1:00 – 3:00 pm	Great Debates in Surgical Oncology
3:30 – 5:00 pm	Practice-Changing Clinical Trials
	Minimally Invasive Hepato-Pancreato-Biliary Oncological Surgery: Interim Assessment of a Maturing Field
5:30 – 7:00 pm	Burn-Out Among Surgeons: What Is It? Who Is At Risk? How to Respond?
	Quality Measurement in Cancer Care Delivery
7:30 – 9:00 pm	Welcome Reception at the Renaissance Grand Hotel

Friday, March 5

6:15 – 7:15 am	Meet the Professor Breakfasts *(Fee: $45)*	
7:30 – 7:45 am	Opening Announcements	
7:45 – 8:45 am	Plenary Session I	(Abstracts #1-4)
8:45 – 9:30 am	SSO Presidential Address: "Certification in Surgical Oncology," Fabrizio Michelassi, MD	
10:00 – 10:45 am	Plenary Session II	(Abstracts #5-7)
10:45 – 11:00 am	Annual Heritage Presentation honoring Murray F. Brennan, MD	
11:00 – 11:15 am	2008–2010 Clinical Investigator Award Presentations	
11:15 am – Noon	American Cancer Society/SSO Basic Science Lecture: "The Cancer Epigenome: Origins and Translational Implications," Stephen Baylin, MD	
1:00 – 3:00 pm	Parallel Sessions	
	* Gastrointestinal Cancer	(Abstracts #8-15)
	* Breast Cancer	(Abstracts #16-23)
	* Melanoma	(Abstracts #24-31)
	* Endocrine/Head & Neck	(Abstracts #32-39)
3:00 – 3:30 pm	Poster Discussion Session	
3:30 – 5:30 pm	Cancer Forum I	(Abstracts #40-46)
	A Practical Approach to Capturing Your Practice Dollars: From A to D/C	
	Controversies in the Management of Pancreatic Carcinoma	
6:00 – 8:00 pm	*Dinner Symposium:* The Role of the Surgical Physician Extender in Patient Navigation	

Saturday, March 6

6:30 – 7:30 am	Meet the Professor Breakfasts *(Fee: $45)*	
7:45 – 8:45 am	Plenary Session III	(Abstracts #47-50)
8:45 – 9:00 am	2008–2010 Clinical Investigator Award Presentations	
9:00 – 9:45 am	James Ewing Lecture: "Surgical Oncology in the Genomic Era: Doing More with Less," Richard L. Schilsky, MD	
10:15 – 11:15 am	Plenary Session IV	(Abstracts #51-54)
11:15 am – Noon	John Wayne Clinical Research Lecture: "Colorectal Cancer Outcome Improvement in Europe: Updated Results of Trials and Population-Based Outcome Registration," Cornelis J. H. van de Velde, MD, PhD	
1:00 – 3:00 pm	Cancer Forum II	(Abstracts #55-61)
1:00 – 3:00 pm	Parallel Sessions	
	* Gastrointestinal Cancer	(Abstracts #62-69)
	* Breast Cancer	(Abstracts #70-77)
	* Sarcoma	(Abstracts #78-85)
	* Quality Improvement/Clinical Outcomes	(Abstracts #86-93)
3:00 – 3:30 pm	Poster Discussion Session	
3:30 – 5:00 pm	*Susan G. Komen for the Cure® Symposium:* Controversies in the Management of Young Women with Breast Cancer	
	Potential Therapeutic Targets for Clinical Trials	
5:30 – 6:30 pm	Annual SSO Business Meeting	
7:00 – 10:00 pm	President's Reception and Banquet	

Sunday, March 7

7:00 – 8:45 am	*Breakfast Symposium:* Optimizing Outcomes in Gastrointestinal Neuroendocrine Tumors	
9:00 – 11:00 am	Contemporary Issues and Controversies in Cancer Disparities	

ABSTRACTS

Accepted for
PLENARY and PARALLEL SESSIONS

63rd Annual Cancer Symposium
Society of Surgical Oncology
March 3-7, 2010
St. Louis, Missouri

1

A Novel Targeted Biotherapeutic for Treatment of Pancreatic Cancer X. Qi,[1]* Z. Chu,[1] M.B. Palascak,[2] R.S. Franco,[2] K.F. Stringer,[1] S.A. Ahmad.[2] *1. Human Genetics, Cincinnati Children's Hospital Research Foundation, Cincinnati, OH; 2. University of Cincinnati College of Medicine, Cincinnati, OH.*

Introduction: Despite exhaustive efforts to map the genetic alterations associated with pancreatic cancer, few promising drug targets have been reported. We have discovered that pancreas cancer abnormally express phosphatidylserine (PS) rich domains on their cell membrane. These PS rich domains can be targeted as a novel therapeutic strategy. Methods: We have developed a biotherapeutic agent composed of a lysosomal protein Saposin C (SapC) and a phospholipid dioleoylphosphatidylserine (DOPS) which we assembled into cancer-selective nanovesicle particles (SapC-DOPS). A distinguishing feature of the SapC-DOPS nanovesicles is their high affinity for PS-rich membranes. The cytotoxic effects of SapC-DOPS targeting PS rich domains were measured using the MTT assay and survival curves were calculated using an orthotopic model in nude mice. Results: MTT assay revealed that SapC-DOPS induced a greater than 50% cytotoxic effect in 3/8 pancreas cancer cell lines. This cytotoxic effect correlated to the level of PS expression based on Annexin-V labeled flow cytometry. cfPac-1-Luc cell lines were than used for an orthotopic tumor model in nude mice. Mice were than treated with either SapC-DOPS via tail vein injection for ten treatments (n=6) or PBS as control (n=6). We observed that nanovesicle-treated animals survived until they were sacrificed at day258. PBS treated controls had a median survival of 65 days (p=0.0149). Luminescence imaging detected no evidence of tumor in any of the four nanovesicle treated animals. This was confirmed at necropsy. Furthermore, using a double-tracking method in living mice, we showed that fluorophore-tagged nanovesicles were specifically targeted to orthotopically-implanted, bioluminescent pancreatic tumors. No adverse behavioral, physical, or histopathologic (10 major tissues) changes were discernible, even at high chronic doses. Conclusion: We have demonstrated a novel biomarker for pancreatic cancers that can effectively be targeted utilizing cancer selective nanovesicles. The direct confirmation of tumor-targeting by SapC-DOPS provides powerful new evidence in support of our goal to develop the nanovesicles as a novel treatment for pancreatic cancer.

2

Trends in Centralization of Cancer Surgery K.B. Stitzenberg,[1]* N.J. Meropol.[2] *1. Surgery, UNC-CH, Chapel Hill, NC; 2. Case Western Reserve University, Cleveland, OH.*

INTRODUCTION: The relationship between procedure volume and clinical outcomes has led many to advocate centralization of cancer procedures at high volume centers (HVC). In previous work using data from 3 Northeastern states, we found a trend towards extensive centralization of esophageal and pancreatic procedures over the past decade but little evidence of centralization for colorectal procedures. We hypothesize that similar patterns have occurred nationwide. METHODS: The Healthcare Cost and Utilization Project National Inpatient Sample is a weighted sample of ≈20% of all US inpatient discharges. Using data from 1999-2007, we examined trends in hospital procedure volume for all extirpative esophageal, pancreatic, and colorectal cancer procedures. Low (LVC), medium, and high volume terciles were defined based on previously established standards: colon ≤37, 38-68, ≥69/yr; esophagus ≤3, 4-13, ≥14/yr; pancreas ≤4, 5-15, ≥16/yr; rectum ≤11, 12-27, ≥28/yr. RESULTS: 351,846 cases met inclusion criteria (256,157 colon; 6355 esophagus; 17,760 pancreas; 71,574 rectum). The proportion of pancreatectomies performed at LVC decreased from 25.0% in 1999 to 11.6% in 2007, p<0.001. Esophagectomies at LVC decreased from 34.6 to 18.2%, p<0.001. Smaller shifts occurred for colon and rectum: 27.9%-24.6% (p<0.001) & 25.2%-20.8% (p<0.001). These trends are also reflected in rising median procedure volumes. Figure. In 2007, HVC tended to be teaching hospitals (colon 69%, esophagus 100%, pancreas 100%, rectum 86%) and were seldom located outside urban areas (colon 1.4%, esophagus 0%, pancreas 5.6%, rectum 0%). Paradoxically, for esophagus and pancreas, urban patients in 2007 were more likely than others to undergo surgery at a LVC (OR 1.1 & 1.24, p<0.001). Throughout the study period for all organ sites, uninsured (OR 1.46-1.85) and Medicaid (OR 1.18-1.69) patients were more likely to have surgery at LVC (p<0.001). CONCLUSIONS: Nationwide, esophageal and pancreatic cancer procedures have been shifting away from LVC. In contrast, there has been little movement toward centralization for colorectal cancer procedures. Travel distance is not the only barrier to centralization, as patients living in urban areas often obtain surgery at LVC.

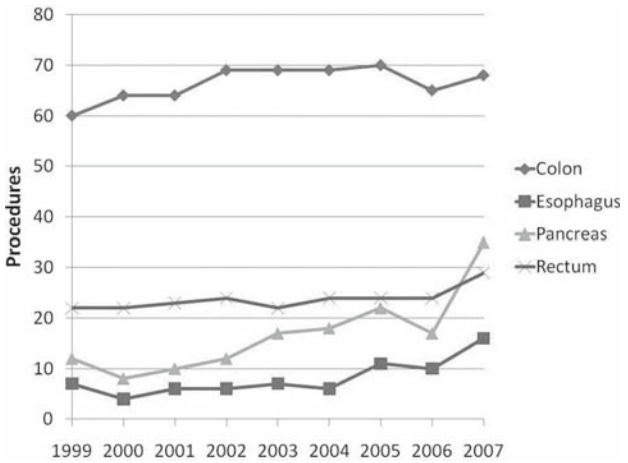


Figure. Annual median procedure volume. Values should be interpreted as hospital procedure volume for the 50th percentile of all patients.

3

Invasive IPMN and MCN: Same Organ, Different Outcomes? H. Kargozaran,* V. Vu, P. Ray, S. Bagaria, X. Ye, G. Singh. *Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA.*

Pancreatic cystic neoplasms have variable malignant potential, and surgery remains the best option for invasive lesions. But is surgery equally effective? We used a national cancer registry to compare the natural history of invasive mucinous cystic neoplasm (MCN) versus invasive intraductal papillary mucinous neoplasm (IPMN) after resection. The Surveillance, Epidemiology, and End Results (SEER) database (1991-2006) was queried to identify all cases of resected invasive MCN and IPMN between 1991 and 2006. Patient demographics, tumor characteristics, node status, and survival rates were recorded, and factors predicting survival were identified using log rank analysis and multivariate Cox regression model. Of 238 MCN cases and 771 IPMN cases, 71% and 48%, respectively, were women (P < 0.0001); mean age was 61 years and 64 years, respectively (P = 0.01). Racial distribution was similar. Most (73%) IPMNs were in the head of the pancreas; most (58%) MCNs were in the body and tail (P < 0.001). Pancreatoduodenectomy was more common for IPMN (73% vs. 35%, P < 0.001); distal pancreatectomy was more common for MCN (42% vs. 13%, P < 0.001). Mean tumor size was 7.0 vs. 4.5 cm for MCN vs. IPMN (p < 0.0001). IPMNs were more likely to be high grade (26% vs. 20%, P = 0.001) and associated with nodal involvement (44% vs. 23%, P < 0.001). Although overall survival rate was higher for invasive MCN (Table), node-positive IPMN had a survival advantage at 2 years (33% vs. 19%, P = 0.004) and 5 years (13 % vs. 10 %, P = 0.006), whereas node-negative MCN had a survival advantage at 2 years (71% vs. 60%, P = 0.05) and 5 years (54% vs. 40%, P = 0.01). Multivariate analysis identified age > 66 years (HR 1.37, P =0.004), positive nodes (HR 1.47, P = 0.006), high tumor grade (HR 1.70, P < 0.001), and higher stage (HR 1.21, P = 0.001) as predictors of worse outcome. Demographic and tumor-related differences in invasive IPMN and MCN may account for the better outcome in MCN, especially early-stage disease (Table). However, nodal involvement confers a worse prognosis in MCN than IPMN. These findings can guide management of postoperative systemic therapies for the two malignancies.

Stage	No. of Patients		Survival Rate					
			2 Years		p value	5 Years		p value
	IPMN	MCN	IPMN	MCN		IPMN	MCN	
All	771	238	47%	58%	0.025	27%	44%	0.001
Stage IA	34	9	54%	100%	0.082	39%	*	ns
Stage IB	182	85	67%	87%	0.002	49%	72%	0.002
Stage IIA	133	43	51%	47%	0.727	25%	33%	0.629
Stage IIB	282	36	33%	21%	0.033	14%	13%	0.057
* inadequate 5-year follow-up								

4

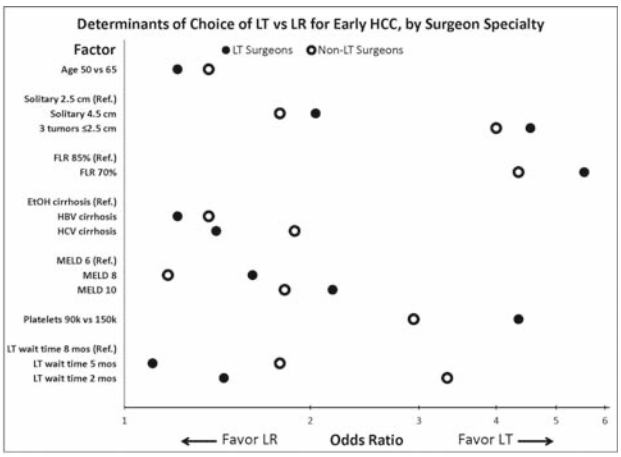
Extremity high grade soft tissue sarcoma (STS): outcomes in patients with primarily negative vs. positive converted to negative microscopic margins following re-excision G.J. Lahat,* D. Tuvin, K. Torres, B. Feig, J.N. Cormier, K.K. Hunt, P.W. Pisters, D. Lev, R.E. Pollock. *MDACC, Houston, TX.*

Introduction: In that R0 resection is optimal for STS control, we compared outcomes of primary R0 patients to those with R1 margins converted to R0 margins after re-excision to see if this practice policy was warranted. Methods: Prospectively accrued data were analyzed for all primary high grade extremity STS patients (n=403) who had complete macroscopic resection at our institution from 1996-2007. Outcomes analysis was performed for patients with primary R0 margins, primary R1 converted to R0 margins after re-excision, and those with final R1 margins (+/- re-excision). Results: Multivariable analysis identified R1 margins as an independent risk factor for local recurrence (HR: 3.97, p=0.05), distant metastasis (HR: 1.86, p=0.02), and STS-specific mortality (HR: 1.73, p=0.01). Of 403 patients, 203 patients (50.4%) had primary R0 margins, 146 (36.2%) were converted from R1 to R0 margins by re-excision, and 54 (13.4%) had final R1 margins. Age > 65 years (HR: 3.22, p=0.02), size > 5cm (HR: 1.73, p=0.03), and undifferentiated pleomorphic STS histology (HR: 4.86, p=0.01) as independent risk factors for R1 margins. Patients with primary R0 margins had prolonged distant metastasis free survival (DMFS) as well as disease specific survival (DSS) rates versus those with R1 converted to final R0 margins after re-excision (5Y DMFS, 88% +/-3.3 vs 66% +/- 4.2; p<0.0001); 5Y DSS, 86% +/-3.6 vs 69% +/-3.5; p=0.0004). However, local recurrence free survival (LRFS) was comparable (5Y LRFS, 86% +/-3.3 vs 80% +/- 4.5; p=0.16). Patients with final R1 margins had significantly shorter 5Y DMFS (52%, p=0.04), DSS (49%, p=0.002), and LRFS (74%, p=0.05) rates compared to patients converted from R1 to R0 status by re-excision. Conclusions: Patients with primary R0 margins had improved DSS and DMFS compared to patients with R1 converted to R0 margins after re-excision whose DSS and DMFS in turn was superior to those with final R1 margins whether or not re-excised. Without discounting the effects of STS biology,, a policy of resection/re-resection to R0 margins appears warranted if feasible.

5

Understanding Surgical Decision-Making in Early Hepatocellular Carcinoma H. Nathan,[1]* J.F. Bridges,[2] R.D. Schulick,[1] A.M. Cameron,[1] K. Hirose,[1] B.H. Edil,[1] C.L. Wolfgang,[1] D.L. Segev,[1] M.A. Choti,[1] T.M. Pawlik.[1] *1. Department of Surgery, The Johns Hopkins University School of Medicine, Baltimore, MD; 2. The Johns Hopkins University School of Public Health, Baltimore, MD.*

Introduction: Initial therapy for early (Milan-criteria) hepatocellular carcinoma (E-HCC) in well-compensated cirrhosis is controversial; little is known about how surgeons make this decision. We sought to identify patient- & surgeon-level factors that most influence choice of surgical therapy for E-HCC. **Methods:** Structured interviews of practicing surgeons identified key factors in E-HCC decision-making: age, tumor number/size, future liver remnant (FLR), cirrhosis etiology, MELD, platelet count, & liver transplant (LT) wait time. Case scenarios that systematically varied these attributes were presented in a web-based survey. Surgeons were asked to choose among initial treatment options for each case: liver resection (LR), radiofrequency ablation (RFA), or LT. Data were analyzed using multilevel multinomial logistic regression. **Results:** Of 336 respondents, 85% were at academic centers. Surgical training varied: 26% surgical oncology, 43% hepatobiliary, 64% LT. Most surgeons performed LR (94%) & RFA (79%) for E-HCC in practice; fewer performed LT (54%). In case scenarios, RFA was infrequently chosen (7%). Choice of LT vs LR varied by specialty. Practicing LT surgeons chose LT in 63% of cases (31% LR), while non-LT surgeons chose LR in 50% (41% LT, P<0.001). In regression analyses, clinical factors that most influenced choice of LT vs LR included FLR 70% vs 85% (OR 4.76), 3 tumors ≤2.5 cm vs solitary 2.5-cm (OR 4.33), & platelet count 90k vs 150k (OR 3.53) (all P<0.001). However, surgeon specialty (LT vs non-LT, OR 5.02, P<0.001) had a larger impact than any of these patient-level factors. Furthermore, LT & non-LT surgeons weighed certain clinical factors—such as HCV, MELD, & LT wait time—very differently (Figure, as visualized by the horizontal spread of points). Even within the same specialty, there was significant surgeon-to-surgeon variation (OR 5.7, P<0.05). **Conclusions:** This study is the first to analyze surgical decision-making in E-HCC. Choice of therapy is influenced more strongly by the surgeon's training & skill set than by the patient's disease. These data demonstrate significant variation in decision-making in E-HCC & should stimulate efforts to standardize care.



6

Update on DCIS Outcomes from the American Society of Breast Surgeons Accelerated Partial Breast Irradiation Clinical Trial Registry J.S. Jeruss,[1]* H.M. Kuerer,[2] P.D. Beitsch,[3] F. Vicini,[4] M. Keisch.[5] *1. Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL; 2. MD Anderson Cancer Center, Houston, TX; 3. Dallas Breast Center, Dallas, TX; 4. William Beaumont Hospital, Royal Oak, MI; 5. Miami Brachytherapy Center, Miami, FL.*

Introduction: Since the initial reports on use of accelerated partial breast irradiation (APBI) for treatment of DCIS, additional follow-up has accumulated. We hypothesize that the use of APBI would continue to be well tolerated, associated with a good cosmetic outcome, and a low risk for recurrence for patients with ductal carcinoma in situ (DCIS). Methods: From 2002-2004, 194 patients with DCIS were enrolled in a registry trial and deemed eligible for study to assess the use of APBI. Follow-up data was available for all 194 patients. Median follow-up was 52.2 months; 65 patients had at least 5 years of follow-up. Data obtained included patient, tumor and treatment related factors, recurrence incidence, device associated adverse events and cosmetic outcomes. Results: 2 patients (1%) had positive margins, 21(11%) had close margins and 171(88%) had negative margins at the completion of surgical therapy. 87 patients (45%) had the balloon brachytherapy applicator placed at time of lumpectomy; 107 patients (55%) had the device placed post-lumpectomy. In the first year of follow-up, 16 patients developed a breast infection; method of device placement was not associated with infection risk. 46 patients developed a seroma which was associated with applicator placement at the time of lumpectomy (p=0.001). Cosmesis was rated Excellent/Good versus Fair/Poor for >85% of each follow-up group annually for the past 5 years. Device to skin distance, method of device placement, infection and seroma were examined and were not associated with cosmetic outcome. 4 patients (2%) had an

ipsilateral breast recurrence and 1(0.5%) had recurrence in the breast and axilla, with a 5-year actuarial local recurrence rate of 3.40%. Positive/close margins (p=0.01) and age <50 at diagnosis (p=0.009) were associated with risk for local recurrence. Conclusions: After additional follow-up time, APBI continues to be well tolerated for patients with DCIS. Utilization of APBI may make lumpectomy possible for some women who would otherwise choose mastectomy because of standard radiation therapy associated barriers.

7

Mitotic Rate Predicts Sentinel Lymph Node Involvement in Melanoma: Impact of the 7th Edition AJCC Melanoma Staging System A.S. Caudle,* M.I. Ross, V.G. Prieto, C.L. Warneke, J.E. Lee, M.M. Johnson, J.M. Gardner, R.E. Royal, J.N. Cormier, A. Lucci, J.E. Gershenwald. *MD Anderson Cancer Center, Houston, TX.*

Background: The new 7th edition AJCC melanoma staging system added mitotic rate (MR) in defining T1b melanoma (at least 1 mitosis/mm2), reflecting its importance as an independent predictor of survival. The goal of this study was to determine whether mitotic rate predicts SLN involvement. Methods: A retrospective review of a prospective database of patients (pts) with cutaneous primary melanoma who underwent SLN biopsy between 1997-2009 at a comprehensive cancer center was performed. Univariate and multiple covariate logistic regression techniques were used to determine the effect of clinicopathologic factors included in the 7th edition AJCC melanoma staging system on SLN involvement. For this analysis, MR was dichotomized as in the AJCC staging system (<1 mitosis/mm2 vs. >=1 mitosis/mm2). Results: 2514 pts with complete clinicopathologic information were included. Overall, 943 (37%) were T1, 729(29%) T2, 549 (22%) T3, and 295 (12%) T4. In univariate analyses, clinicopathologic factors including Breslow thickness (T stage), ulceration, primary anatomic site, and male gender were associated with a positive SLN (PSLN). When stratified by the new AJCC criteria, pts with MR >= 1 were more likely to have PSLN than those with MR <1 (OR 4.34, 95% CI 3.32-5.65, p<.0001). PSLN was found in 9% (70/738) of pts with MR <1, 19% (95/502) with MR=1, 34% (281/824) with MR 2-5, 37% (111/300) with MR 6-10, and 48% (38/79) with MR >15. In multivariate analysis using the covariates listed previously, MR >=1 (vs <1) was an independent predictor of PSLN (OR 3.52, 95% CI 2.65-4.67, p<.0001). In multivariate analyses performed within each T-category, MR >= 1 was an independent predictor of PSLN in T1 and T2 strata only (OR 2.09 for T1, 95% CI 1.22-3.57, p=.007; OR 1.86 for T2, 95% CI 1.15-2.99, p=.01). Conclusions: Mitotic rate, as defined by the AJCC, is an important independent predictor of SLN involvement, and may explain in part its prognostic significance for survival. Since MR is particularly significant in thin melanomas, these data support the use MR in defining at-risk patients who may be offered SLN biopsy.

8

A Prospective Comparison of Cytoreductive Surgery plus Heated Intraperitoneal Chemotherapy and Early Postoperative Chemotherapy Vs. Heated Intraperitoneal Chemotherapy Alone in the Treatment of Peritoneal Carcinomatosis W.P. Francis,[1]* L.A. Mack,[3] W.J. Temple,[3] T. Hamilton,[2] M.A. Frankson.[4] *1. Surgery, Princess Margaret Hospital, Nassau, New Providence, Bahamas, The; 2. University of Calgary, Calgary, AB, Canada; 3. Tom Baker Cancer Centre, Calgary, AB, Canada; 4. University of the West Indies, Nassau, New Providence, Bahamas, The.*

Introduction: The management of peritoneal carcinomatosis continues to evolve. Two common treatment protocols include cytoreductive surgery (CS), hyperthermic intraperitoneal chemotherapy (HIPEC) with mitomycin C, followed by early postoperative intraperitoneal chemotherapy (EPIC) with 5FU compared to CS and HIPEC with oxaliplatin combined with intravenous 5FU. Our hypothesis is that the use of intraperitoneal oxaliplatin without EPIC will lead to shorter patient length of stay (LOS) and reduced major complications. Methods: A prospective database of consecutive patients undergoing CS, HIPEC and EPIC (Group 1) were compared to those with CS and HIPEC (Group 2). Primary outcome measures included LOS and Grade III/IV complications. Patient, tumor, and perioperative variables including age, gender, pathology, peritoneal cancer index (PCI), and in-hospital mortality were prospectively recorded. Results: Both groups were similar with respect to age, gender, pathology and PCI. 155 consecutive patients were explored; 24 were unresectable receiving no HIPEC or EPIC. Group 1 consisted of 88 patients and 43 in Group 2. Median length of stay for group 1 was 23 ±10.82 days and group 2 was 16 ±12.39 days; (p<0.001). Overall, 44.3 % of patients developed a complication. Complication rates in group 1 versus group 2 were 42.0% and 48.8% respectively (p=0.46). However, complication grades were significantly higher in group 1 (p<0.001). Conclusion: In our experience, HIPEC alone with oxaliplatin results in a clinically and statistically significant reduction in length of stay and decreased grade of complications. Disease-free and overall survival continues to be prospectively followed with no significant differences noted between groups 1 and 2 thus far.

9

Evolution of Laparoscopic Liver Resection in 300 Patients J.F. Buell,[1]* G. Brock,[1] M. Marvin,[1] M. Thomas,[1] S. Rudich,[2] T. Doty,[2] K. Bilinski,[1] K. Ravindra,[1] S. Barve,[1] G. Neff,[1] L. Marsano,[1] A. Barve,[1] C. McClain,[1] K. McMasters.[1] *1. Surgery, University of Louisville, Louisville, KY; 2. University of Cincinatti, Cincinatti, OH.*

Laparoscopic liver resection evolved over the last decade, from minor peripheral resections to major anatomical resections with adaption into cancer and cirrhotics. This study aims to evaluate the evolution of laparoscopic liver resection after 363 resections in 300 pts. Methods: Retrospective analysis of a prospectively collected database with IRB approval. Pt demographics, tumor characteristics and outcomes were examined using ANOVA and multivariate analysis based on intent to treat. Results: 600 patients were referred for evaluation of a hepatic mass, with 300 pts (146 presumed malignancy and 154 symptomatic) laparoscopically resected. 37 pts were cirrhotic, 16 had prior open hepatic resections, with 77 pts undergoing major resection. Pre op diagnosis included: Colorectal n=40, Non colorectal n=34, Hepatoma n=62, cholangiocarcinoma n=10, hemangioma n=52, adenoma n=19, FNH n=26, cyst n=39, other n=23. There were four conversions encountered all within the first 100 patients. Smaller tumors were approached in cirrhotics with a higher mortality rate (8% vs. 1%; p<0.01). Major resections were performed for larger tumors (7.8 vs. 4.3 cm; p<0.001) resulting in longer operative times (3.0 vs. 2.5 hrs; p<0.001), higher transfusion requirements (12% vs. 5%; P<0.05) and complication rates (30% vs. 14%; p<0.001). Mortality was equivalent with a trend toward improved margins. Median follow up was 30 months. Local recurrence in the resection bed occurred in 1.6% of cases. In field and distant recurrences were identified in 7.9%, and 4.7% of cases. Complication rates were higher in the last 100 cases which correlated with a higher incidence of cirrhotic and major lobar resections. The most common complication was ileus (n=6;21%). Conclusions: During our experience, laparoscopic liver resection realized improvements in shorter operative times, lower transfusion requirements, and increased surgical margins. The last 100 patients witnessed a rise in the management of cirrhotic patients, lobar resections and redo hepatectomies. This current series confirms that laparoscopic liver resection has evolved in utility with outcomes comparable to most modern series of open hepatic resection.

	Cancer	Cirrhosis	Major	Prior	Age	Size	EBL	OR Time	Transfusion	Morbidity	Margin	Mortality
100	47%	2%	25%	2	51	4.9cm	150cc	3 hrs	8%	14%	0.9cm	3%
200	49%	7%	24%	2	56	5.5cm	150cc	2.5 hrs	8%	14%	0.8cm	1%
300	50%	28%	28%	12	55	5.3cm	150cc	2.0 hrs	4%	28%	1.3cm	1%
p-value	NS	<.001	NS	<.001	<.01	<.01	NS	<.001	<.001	<.01	<.01	<.01

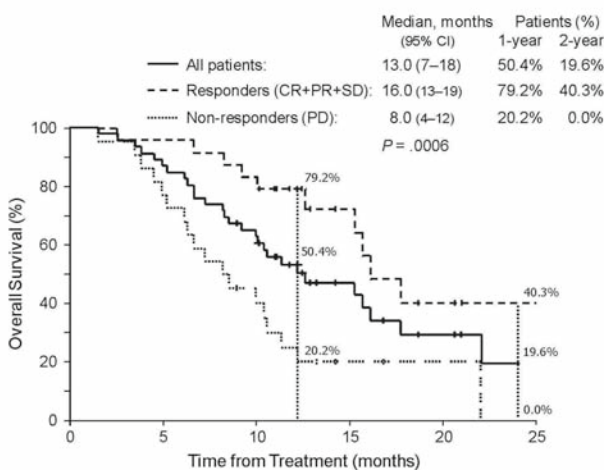
10

Multicenter Phase II Clinical Trial of Yttrium-90 Resin Microspheres Alone in Unresectable, Chemotherapy Refractory Colorectal Liver Metastases M. Cosimelli,[1]* R. Mancini,[1] F. Izzo,[2] F. Fiore,[2] R. Golfieri,[3] E. Giampalma,[3] M.G. Diodoro,[1] I. Sperduti,[1] E. Melucci,[1] M. Mottolese.[1] *1. Istituto Regina Elena, Rome, Italy; 2. G. Pascale Cancer Institute, Naples, Italy; 3. Malpighi Hospital, Bologna, Italy.*

Introduction: This phase II study evaluated prospectively the efficacy and safety of radioembolization in patients with unresectable, liver-dominant colorectal liver metastases who had failed prior oxaliplatin- and irinotecan-based chemotherapy. **Methods:** Eligible patients had adequate hepatic, hemopoietic and renal function, and an absence of major hepatic vascular anomalies and hepato-pulmonary shunting. Gastroduodenal and right gastric arteries were embolized prior to hepatic arterial administration of a single treatment of yttrium-90 resin microspheres (SIR-Spheres; Sirtex Medical Limited, Syd-

ney, Australia) (median activity 1.7 GBq; range 0.9–2.2 GBq). **Results:** Of 50 eligible patients, 76% had received ≥4 lines of chemotherapy. Most presented with synchronous (stage IV) disease (72%), >4 hepatic metastases (58%), 25-50% replacement of liver volume (60%) and bilateral spread (70%). Baseline analysis of neoplastic cells (n=26) found 96% were positive for p53, 81% for Survivin and 42% for bcl-2. A high Ki67 index was recorded in 74% of 19 patients. Using RECIST, 1 patient (2%) had a complete response, 11 (22%) a partial response, 12 (24%) stable disease, 22 (44%) progressive disease, and 4 (8%) were non-evaluable. Median overall survival was 13 months (95%CI, 7–18). Pre- and post-treatment analysis of biopsies (n=13) found favorable changes in all biomarkers following radioembolization; although these changes were only significant (p=0.05) for p53 and bcl-2. Two patients were sufficiently down-staged to enable potentially curative resection of ≥3 segments. Early and late (>48 hour) WHO G1–2 adverse events (mostly fever and pain) were observed in 16% and 22% of patients, respectively. One patient died of renal failure at 40 days and another of liver failure at 60 days. **Conclusions:** Radioembolization produced meaningful response rates and disease stabilization in patients who had exhausted all standard therapeutic options. Further investigation earlier in the course of the disease is warranted to consolidate the treatment response with modern chemotherapies and to increase the number of patients eligible for resection.

Figure 1. Kaplan-Meier plots of overall survival following radioembolisation in all patients (n = 50); and among responders (CR + PR + SD; n = 24) and non-responders (PD; n = 22).



11

Cyst Fluid Mucin Levels Predict Dysplasia in Intraductal Papillary Mucinous Neoplasms of the Pancreas (IPMN) A.V. Maker,* N. Katabi, M. Gonen, R. DeMatteo, M. D'Angelica, Y. Fong, W. Jarnagin, M. Brennan, P. Allen. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: There are no reliable markers of dysplasia in patients with incidentally discovered intraductal papillary mucinous neoplasms of the pancreas (IPMN). IPMN dysplasia may be associated with mucin protein (MUC) expression and histopathologic subtype. We hypothesize that MUC expression in pancreatic cyst fluid and serum can identify lesions with high risk of malignancy. **Methods:** Cyst fluid and patient serum were collected at the time of pancreatectomy between 2005 and 2009. Forty patients with pathologically confirmed IPMN were included. Samples were grouped into low risk (low grade dysplasia, n=6; or moderate dysplasia, n=15) and high risk groups (high grade dysplasia, n=14; or carcinoma, n=5). Mucin expression (MUC1, MUC2, MUC4, and MUC5AC) was assessed utilizing enzyme-linked immunosorbent assays. **Results:** MUC2 and MUC4 cyst fluid concentrations were elevated in high risk vs. low risk groups (10 ± 3.0 u/mL vs. 4.4 ± 1.2 u/mL, p=0.03; 20.6 ± 10.6 u/mL vs. 4.5 ± 1.4 u/mL, p= 0.03, respectively). MUC1 and MUC5AC levels in cyst fluid were not different. Evaluation of corresponding serum samples revealed higher levels of MUC5AC from high risk patients compared to low risk patients (19.9 ± 9.3 u/mL vs. 2.2 ± 1.1 u/mL, p=0.04). Histopathologic subtype of IPMN was significantly associated with the grade of dysplasia (see table), and the intestinal subtype was associated with increased MUC2 cyst fluid concentrations (13.8 ± 6.5 u/mL vs. 4.1 ± 0.9 u/mL, p=0.02). **Conclusions:** In this study, high risk IPMN contained elevated cyst fluid concentrations of MUC2 and MUC4, and increased serum levels of MUC5AC. High-risk IPMN also displayed a distinct mucin expression profile in specific histologic subtypes. These data, if validated, may allow surgeons to more appropriately select patients for operative resection.

Mucin Cyst Fluid Concentration and Histologic Subtype by Degree of Dysplasia

Degree of Dysplasia	Pancreatic Cyst Fluid Concentration (u/mL)		Histologic subtype		
	MUC 2*	MUC 4*	Intestinal*	Pancreatobiliary*	Gastric*
Carcinoma or High grade	10	20.6	100%	100%	9%
Low or Moderate	4.4	4.5	0%	0%	91%

* *p<0.05*

12

Survival and Health-Related Quality of Life Following Cytoreductive Surgery plus Hyperthermic Intraperitoneal Chemotherapy for Disseminated Peritoneal Cancer of Colonic Origin A.R. Hill,* R.P. McQuellon, G.B. Russell, P. Shen, J.H. Stewart, E.A. Levine. *Wake Forest University Baptist Medical Center, Winston-Salem, NC.*

Introduction: Peritoneal carcinomatosis of colonic (PCC) origin is a life-threatening diagnosis. Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CS + HIPEC) offers patients the prospect of long-term survival with alleviation of symptoms; however, health-related quality of life (HRQOL) among survivors is significantly affected. The purpose of this study was to monitor HRQOL before and after treatment with CS + HIPEC for PCC. **Methods**: Patients completed questionnaires at baseline (BL) and after surgery at 3 (T2), 6 (T3), and 12 (T4), months. Questionnaires consisted of demographic information, Functional Assessment of Cancer Therapy - Colon (FACT-C), Brief Pain Inventory, SF-36 Medical Outcomes Study Survey, and Center for Epidemiologic Studies - Depression Scale. A chart review identified post op complications. Time trends were assessed with SAS PROC mixed model. **Results**: Sixty two patients [mean age 53.4 yrs (SD=12.2)(range, 29-80); 47% f)], were assessed at BL. Median survival was 18 mos., with 85% ± 5% at T3, 71.3% ± 6.3% at T4. Fifty two percent had no post op complications. Emotional well being (p=.0007) improved with borderline effects for social well being (p=.065) and the colon subscale (p=.061) of the FACT. Significant effects were seen for role physical, bodily pain, and social functioning. Incidence of depressive symptoms was 41%, 25%, 37% and 33% at BL, T2, T3, and T4, respectively. Pain scores increased above BL at T2, but decreased below BL at T3 and T4. At T1 and T2, 54% and 26%, respectively, of patients reported that pain did not interfere with their ability to walk around. HRQOL scores of survivors improved over time. **Conclusions**: CS + HIPEC for PCC results in short term decrements in HRQOL for the first 3 months following surgery due to complications that may affect short-term recovery; however, HRQOL can be maintained or improved after 3 months. This suggests that patient-support interventions should focus upon the first few months after surgery to accelerate improvement of HRQOL.

13

The basic helix-loop-helix transcription factor ASCL1 mediates oncogenic transformation in gastrointestinal neuroendocrine tumor cells Y. Wang,* D.B. Donner, E.K. Bergsland, R.S. Warren, E.K. Nakakura. *University of California San Francisco, San Francisco, CA.*

Introduction: Neuroendocrine tumors (NETs) derived from the gastrointestinal (GI) tract frequently metastasize. Current therapy has limited efficacy in shrinking tumors. Earlier diagnosis and more effective therapies are needed but require a better understanding of GI NET biology. The basic helix-loop-helix transcription factor ASCL1 is overexpressed in human GI NETs. However, the function of ASCL1 in GI NET carcinoma is not known. Methods: To evaluate the effect of ASCL1 in its native cellular background, we used retroviral-mediated RNAi to knock down endogenous expression of ASCL1 in GI NET cells. Effective knock down of ASCL1 transcript and protein levels were

evaluated by qRT-PCR and Western blot analysis, respectively. The effect of ASCL1 knock down on oncogenic transformation in GI NET cells was determined by soft agar and xenograft tumor formation assay. Results: After infection and puromycin selection of GI NET cells, we found that ASCL1-RNAi effectively knocked down both ASCL1 transcript and protein levels. Compared with control infected cells, we observed that GI NET cells harboring the ASCL1-RNAi construct were significantly restricted in their colony forming efficiency (P = 0.003) by soft agar assay. In xenograft tumor formation assays, control cells formed large tumors in immunodeficient mice. In contrast, ASCL1-RNAi-infected cells formed significantly smaller xenograft tumors (P = 0.014). Conclusions: ASCL1 is critical for oncogenic transformation in GI NET cells. Further studies to identify ASCL1 downstream genes involved in the oncogenesis of GI NETs may result in clinically tractable targets for diagnosis and treatment of patients with GI neuroendocrine carcinoma.

14

Adjuvant Chemotherapy and Recurrence in Pathologically Node-negative Rectal Cancer After Neoadjuvant Chemoradiation and Total Mesorectal Excision A. Govindarajan,* M.R. Weiser, P.B. Paty, L.K. Temple, J.G. Guillem, W.D. Wong, G.M. Nash. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

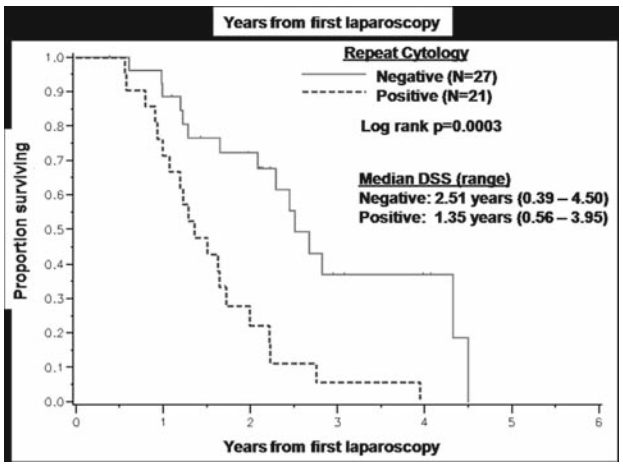
Introduction: Adjuvant chemotherapy is typically recommended for rectal cancer patients treated with neoadjuvant chemoradiation and radical surgery, irrespective of pathologic stage. However, there are little data examining the impact of adjuvant chemotherapy in patients with relatively favorable pathologically node-negative tumors after combined modality therapy (ypN0). Methods: We conducted a retrospective cohort study using a prospectively collected database. The study population included all rectal cancer patients treated with neoadjuvant chemoradiation and curative surgery (R0 resection) from 1993 through 2003, who had ypN0 tumors. Kaplan-Meier and multivariable Cox regression models were used to examine the association between use of adjuvant chemotherapy and recurrence-free interval, adjusting for confounders. Analyses were stratified a priori by pathologic stage to assess for possible differential effect sizes. Results: Overall, 324 ypN0 patients were identified; 57 did not receive adjuvant chemotherapy (17.6%). Compared to patients who received chemotherapy, these patients were older (63y vs 60y, p=0.03), had more distal tumors (5.1cm from anal verge vs 6.6cm, p<0.0001), and lower ypT-stage (p=0.04). At a median follow-up of 69 months, 49 patients had a cancer recurrence (37 distant recurrences). The risk of recurrence was associated with pathological stage – 2.7% ypT0 (2/73), 12.3% ypT1-2 (16/130), 24.2% ypT3-4 (29/120) - but not with receipt of adjuvant chemotherapy (p=0.32). When stratified by ypT-stage (ypT0-2, ypT3-4), adjuvant chemotherapy was not significantly associated with recurrence-free interval in either stratum in univariable or multivariable analyses (pT0-2 subgroup: HR 1.0, 95% CI 0.32-3.2, p=0.99; pT3-4 subgroup: HR 0.71, 95% CI 0.23-2.2, p=0.55). Conclusion: The recurrence rates for ypT0-2N0 rectal cancer after neoadjuvant chemoradiation and total mesorectal excision are low, even in the absence of adjuvant chemotherapy. Large prospective trials are needed to better define the magnitude of benefit from adjuvant chemotherapy after combined modality therapy for rectal cancer in this subgroup.

	Adjuvant chemotherapy (n=267)	No adjuvant chemotherapy (n=57)	Univariable p-value
Age (median)	60	63	0.03
Gender (% male)	65.5	63.2	0.73
Distance from anal verge (mean)	6.6	5.1	<0.0001
Poor differentiation, %	6.0	5.3	0.83
Lymphovascular invasion, %	4.4	1.8	0.35
Node-positive by ultrasound, %	55.5	43.2	0.34
Final pathological stage, %			0.037
ypT0	21.0	31.6	
ypT1-2	39.0	45.6	
ypT3-4	40.0	22.8	
5-year recurrence-free interval, %			
ypT0	98.2	94.4	0.41
ypT1-2	90.9	87.7	0.92
ypT3-4	75.0	84.6	0.64

15

Impact of Positive Peritoneal Cytology on Outcome in 291 Patients with Gastric Cancer J.J. Mezhir,* D.C. Coit, L.M. Jacks, M.A. Shah, M.F. Brennan, V.E. Strong. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Positive peritoneal cytology is a predictor of poor survival in patients with gastric cancer. Our aim is to more clearly define the natural history of this cohort. **Methods:** From 1993 to 2009, 1,241 patients with gastric cancer underwent staging laparoscopy with peritoneal washings; 291 (23%) had positive cytology. Multivariable Cox regression was performed to determine factors predictive of disease specific survival (DSS) at the time of initial staging laparoscopy. **Results:** There were 198 patients who had either peritoneal or visceral metastases discovered at laparoscopy and are designated M1-Cyt+. The remaining 93 patients had M0-Cyt+ disease (defined as cytology positive but no visible visceral or peritoneal metastases). The median DSS was 1 year (CI 0.9 to 1.1) for the entire cohort; all but one patient had died of disease by 58 months after initial diagnosis. Independent predictors of worse DSS were tumor location (antrum best, diffuse worst) and M-status (M1-Cyt+ median DSS 0.8 years versus M0-Cyt+ 1.3 years, p<0.0001). Poor performance status predicted worse DSS (HR 2.78, CI 1.9–3.9, p<0.0001). Seventy-two patients (25%) were selected for resection of primary tumor: T1/2=11(15%), T3=55(76%), T4=6(8%), 86% had nodal metastases. Resected patients were more often M0 (72% vs. 19%, p<0.0001). Of the 261 patients who were treated initially with chemotherapy, 48 (18%) underwent repeat laparoscopy. Of these, 21 patients had persistent positive cytology and had significantly worse DSS than the 27 patients who converted to negative cytology (**Figure**). **Conclusions:** Patients with M0-Cyt+ disease exhibit significantly longer DSS than those with M1-Cyt+ disease; tumor location and performance status further predict DSS in advanced gastric cancer. Although long-term survival in patients with positive cytology is extremely uncommon, those who convert to negative cytology after chemotherapy exhibit significant improvement in DSS.



16

Consequences of Axillary Ultrasound in T2 or Greater Tumors for Patients with Invasive Breast Cancer M.C. Lee,[1]* J. Eatrides,[2] A. Chau,[1] J.V. Kiluk,[1] N. Khakpour,[1] W.B. Carter,[1] C. Laronga,[1] C.E. Cox.[1] *1. Comprehensive Breast Program, Moffitt Cancer Center, Tampa, FL; 2. University of South Florida College of Medicine, Tampa, FL.*

Introduction: Axillary ultrasound (AUS) with needle biopsy [fine needle aspiration (FNA) or core] of abnormal nodes is used for diagnosis of nodal disease in newly-diagnosed breast cancer patients (pts). Our hypothesis is that routine AUS for invasive breast cancer >2cm on clinical examination reduces the need for sentinel node biopsy (SLNB). Materials and Methods: A prospective single-institution database of invasive breast cancer pts receiving AUS between 2004 and 2009 was reviewed. 212 pts received AUS at diagnosis; pts with incomplete records, clinical tumor size <2cm, or AUS after definitive surgery were excluded. An additional contemporaneous cohort of pts without AUS having clinical T2 (cT2) or greater disease and SLNB were identified as a

control. Clinicopathologic data were recorded for both groups. Simple Kappa coefficient and Chi-square statistical analyses were performed. Results: Of the pts with >cT2, 153 pts had AUS at diagnosis compared to 508 controls. Median age of the AUS group was 53.7 (range 22.8-85.8) vs 53.8 years (range 26.7-91.6); median AUS tumor size was 3.8cm (range 1.0-20.0) vs 2.5cm (range 0.1-11.0). One hundred twenty of 153 (78.4%) AUS pts had a needle biopsy; 88/120 (73.3%) had a positive (pos) result, avoiding SLNB (p<0.0001). After AUS, 65 patients had SLNB: 33 pts had a negative (neg) AUS and 32 pts had a neg needle biopsy. Of these 65 pts, 23 pts (35.4%) had a pos SLNB; 15/33 had a neg AUS and 8/32 had a neg needle biopsy (figure 1). One hundred and one of 153 had CALND compared to 310/508 controls (p = 0.30). The sensitivity and specificity of AUS was 86.2% and 40.5%. The sensitivity of AUS combined with needle biopsy was 89.3% with 100% specificity. Of the study group, 70/153 (45.8%) had neoadjuvant chemotherapy. Conclusions: Axillary US and FNA significantly reduces SLNB use in pts presenting with cT2 or greater invasive breast cancer and may impact the decision for neoadjuvant chemotherapy. AUS should be considered part of the routine evaluation of newly diagnosed breast cancer pts with a cT2 or greater breast lesion.

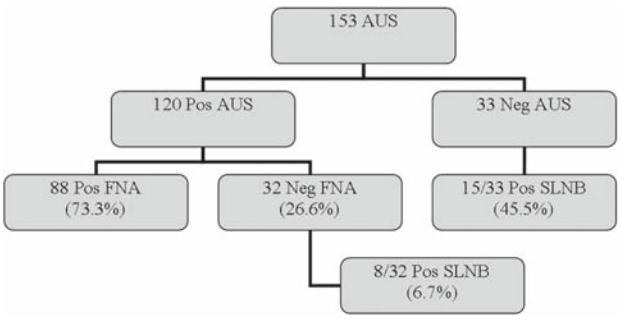
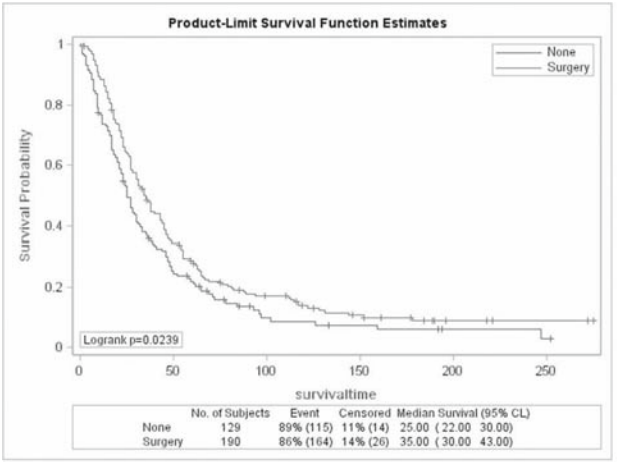


Figure 1: Use of Sentinel Node Biopsy after Axillary Ultrasound and Axillary Needle Biopsy

17

Survival Benefit of Surgery in Stage IV Breast Cancer Patients?
A. Holt,* R. Nelson, L. Kruper. *City Of Hope, Duarte, CA.*

Background: There is no standardized surgical treatment for patients who present with Stage IV breast cancer. Traditionally surgery has been palliative, with primary treatment being systemic therapy with cytotoxic and/or hormonal agents. Several retrospective studies have sited an improved overall survival (OS) with extirpation of the primary tumor. We sought to determine if surgery in Stage IV breast cancer patients confers a survival advantage. Methods: We identified 319 female patients, diagnosed with denovo Stage IV breast cancer, between 1985-2004. Data was collected from a prospectively maintained database, and included age, tumor characteristics, type (chemotherapy and hormonal) and year of systemic treatment, surgical margin status, and number and location of metastatic sites. Kaplan Meier curves were generated and the log-rank test compared differences in overall survival. Results: 190 patients (60%) underwent resection of the primary tumor. Patients undergoing surgery for their primary tumor had a median survival of 35 months versus 25 months for those who did not (p=0.024). Margin status did not impact survival. The median OS for patients with estrogen receptor (ER) positive tumors was 43 versus 23 months for those with ER negative tumors (p=0.009). Patients with metastases at one site versus multiple sites had a median survival of 35 versus 23 months (p=0.002). Inflammatory breast cancer patients had a median survival of 19 versus 35 months for those without (p=.0031). In multivariate analysis including surgical treatment, histology type (invasive vs inflammatory), age group (<50 vs >50), ER status, systemic therapy, and number of metastatic sites (single vs multiple), significant factors associated with improved OS were non-inflammatory histology type (p= 0.0011), ER positive status (p=0.0195) and single metastatic site (p=0.0141). Conclusion: The improved overall survival seen in Stage IV breast cancer patients undergoing surgical resection is primarily attributed to favorable tumor and clinical characteristics, not to surgical intervention. A randomized clinical trial is needed to ensure that the survival benefit seen in patients undergoing surgery is not due to selection bias.



18

Local Control Following Single Dose Intraoperative Radiotherapy Prior to Partial Mastectomy for Early Stage Breast Cancer
D.W. Ollila,* R.J. Kimple, N. Klauber-DeMore, C.M. Kuzmiak, D. Pavic, J. Lian, C.A. Livasy, W.M. Chiu, D.T. Moore, C.I. Sartor. *Univ of NC at Chapel Hill, Chapel Hill, NC.*

Introduction: For breast cancer patients, multiple techniques for delivering partial breast radiotherapy are available. We have previously presented our technical details (Annals of Surgical Oncology, 2007) of delivering partial breast irradiation with a single fraction of intraoperative radiotherapy (IORT) targeting the tumor in situ immediately prior to partial mastectomy. This study details our completed, single institution phase II trial, including local control rates. Methods: An IRB-approved, DSMB-monitored phase II trial was performed with the following inclusion criteria: women age 48 or older, ultrasound-visible invasive ductal cancers <3 cm, clinically negative axillary nodes. IORT was delivered using a mobile electron irradiator, including a 1.5-2 cm radial margin and a 1 cm deep margin, received 15 Gy and immediately underwent partial mastectomy. Ipsilateral breast recurrence was classified as true/marginal, elsewhere, or regional. Kaplan-Meier methods were used to estimate survival functions and exact 95% confidence intervals are reported. Results: Between 2003 and 2007, 71 women underwent IORT with a median follow-up of 3.0 years. For patients with tumor-involved or close margins additional therapy was required, 7 patients underwent total mastectomy and 11 received whole breast radiation. Four women experienced pathologically confirmed invasive ipsilateral breast failures (1 new primary, 3 margin recurrences) for an actuarial three-year local control rate of 49/53 (94.8%; 95% CI: 84.2% - 98.3%). Three year adjusted overall survival for patients treated with only IORT was 91%, and breast cancer-specific survival was 100%. Conclusions: Intraoperative radiotherapy delivered to an in situ tumor is feasible, but our three-year local control rate is concerning. Possible changes to this technique to improve local control rates include better preoperative imaging (MRI) and improved IORT delivery (larger cone size, increased dose).

19

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

Background: Despite reduced morbidity associated with sentinel lymph node (SLN) biopsy as compared to axillary lymph node dissection (ALND), lymphedema remains a clinically relevant complication. We hypothesized that a higher number of lymph nodes (LN) removed during SLN biopsy procedure is associated with a higher risk of lymphedema. Patients and Methods: 600 patients with clinically node negative invasive breast cancer who underwent SLN biopsy for axillary staging from June 1998–May 2003 were prospectively studied. Circumferential bilateral upper extremity (UE) measurements 5 cm below and 10 cm above the olecranon process were performed preoperatively

and at follow-up 3 to 8 years after surgery. Correlation between change in ipsilateral UE measurements (corrected for change in contralateral measurements) and number of LN removed were examined using the Spearman rank correlation coefficient. Association between presence of lymphedema (defined as >2cm change) and number of LN removed was calculated by Wilcoxon rank sum test. Results: At a median follow-up of 5 years, 5% of patients had developed lymphedema (defined as >2cm change). Factors associated with lymphedema included greater body weight and BMI, and post-operative infection or injury. There was no association between the number of LN removed and either change in UE measurements (Fig 1a,b) or in the incidence of lymphedema. Among patients with lymphedema (n=31) as compared to those without, mean (3.9 vs 4.2), median (4 vs 3) and range of (1-9 vs 1-17) number of LN removed were similar (p=0.93). Conclusion: In this prospective study of 600 women undergoing SLN biopsy, there is no correlation between number of LN removed and either change in UE circumference or incidence of lymphedema. These data suggest that other factors such as disruption of the lymphatic channels as a result of complete resection of the axillary fat pad during ALND play a larger role in development of lymphedema than does number of LN removed.

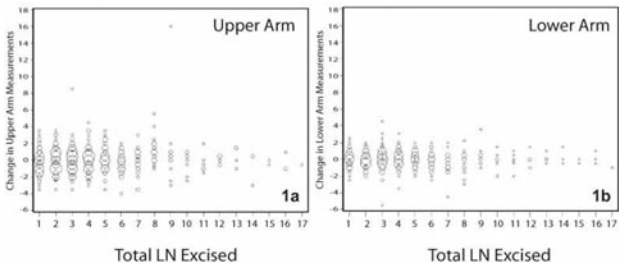


Figure 1a,b: Scatter/bubble plot of upper arm (a) and lower arm (b) measurements and number of nodes excised (a. corr=0.06, p=0.12; b corr=-0.04, p=0.31). The size of the bubbles is determined by the number of observations at the same coordinates. A large bubble indicates many observations at the same coordinates while a small bubble indicates one or a small number of observations.

20

Disseminated tumor cells in histologic subtypes of Stage I- III breast cancer patients A. Lucci,* S. Krishnamurthy, A. Lodhi, C. Hall, B. Singh. *Surgical Oncology, University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction.Triple receptor negative(TRN)[basal]breast cancers are higher grade tumors that are more likely to metastasize. Recurrences after 5 years are rare in TRN patients.Conversely,late recurrences are seen in ER positive(luminal)cancers. Disseminated tumor cells (DTCs) may be responsible for late(>5 years). We compared rates of DTCs in basal and luminal subtypes.Methods.We prospectively evaluated 250 stage I-III breast cancer patients at a single institution from 2004 to 2009.DTCs were assessed from bilateral bone marrow aspirates using anti-CK antibody cocktail(AE1/AE3, CAM5.2, MNF116, CK8 and 18)following cytospin.The presence of ≥1 CK positive cells meeting morphologic criteria for malignancy was considered a positive result for DTCs. Pathologic complete response (pCR) was defined as lack of residual invasive disease in primary tumor and regional lymph nodes after neoadjuvant chemotherapy (NAC).Statistical analyses used chi-square and Fischer's exact test. Results.Median f/u was 28 months. Fifty-eight patients had TRN and 127 had luminal cancers. Mean age was 51 y for TRN and 52 y for luminal subtypes. Twenty-five percent (10/41)of TRN patients and 27% (26/95) of luminal subtype had DTCs; P= NS.pCR occured in 14%(8/58) of TRN but only 3%(4/127) of luminal cancers after NAC. TRN patients were more likely to have pCR (14%) 8/55 as compared to those positive for any single receptor ;8% (15/195) P=0.041. Luminal subtype were less likely to achieve pCR 2% (3/125); as compared to non-luminal sybtype (15%)19/125 ;P=0.001.Interestingly, All TRN patients had complete eradication of DTCs after pCR whereas 33%(1/3)luminal subtype patients had DTCs;P=NS.Conclusions. Approximately 25% of stage I-III breast cancer patients with either luminal or TRN subtype had DTCs. Patients with TRN subtype were more likely to have pCR and complete eradication of all DTCs whereas patients with luminal subtype were less likely to have pCR and some had persistent DTCs after NAC. Further study including survival analyses is needed to determine if DTCs are responsible for late recurrences in the luminal subgroup .

21

Minimal Disease in the Sentinel Lymph Node: How To Best Measure Sentinel Node Micrometastases To Predict Risk of Additional Non-Sentinel Lymph Node Disease S. Kumar,* M. Bramlage, L.M. Jacks, J.I. Goldberg, S.M. Patil, D.D. Giri, K.J. Van Zee. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

Background: Volume of disease in the sentinel node (SLN) is a significant predictor of additional nodal metastasis in a woman with breast cancer. The objective of this study was to assess incidence of residual non-SLN disease in a large cohort of women with minimal SLN metastases, and to compare 3 methods of SLN micrometastasis measurement to determine which best predicts residual disease on axillary dissection (ALND). **Methods:** Of 7665 consecutive patients undergoing SLN biopsy, 505 patients with micrometastasis (N1mi) or isolated tumor cells (ITCs, N0(i+)) who underwent completion ALND and had complete data were identified. All SLNs were evaluated by 3 different volume of metastasis measurement methods: AJCC N stage, method of detection (frozen section, routine H&E, serial H&E, IHC) and maximum number of cells in a single section (1-100, 101- 999, ≥1000). Multivariable logistic regression models were used to predict the presence of additional disease in non-SLNs. **Results:** 251 (50%) patients had N0(i+) and 254 (50%) had N1mi disease by the current AJCC staging system. Overall, 12% of those with N0(i+) and 20% with N1mi disease were found to have additional positive non-SLNs on ALND. On multivariate analyses, age, tumor type and nuclear grade, multifocality, estrogen receptor status, number of negative and positive SLNs, primary tumor size, and extranodal extension were not significant. Only lymphovascular invasion (OR>2.2, p<0.01) and size of nodal metastasis as assessed by any method of measurement (AJCC, method of detection, and maximum number of cells (p=0.03, 0.04, and 0.02, respectively)) were significantly correlated with the presence of additional non-SLN disease. All 3 models had similar goodness-of-fit (Akaike information criteria=442, 442, 441; deviance=420, 416, 417; C-index=0.675, 0.680, 0.676, respectively). **Conclusions:** A non-negligible proportion of women with only SLN micrometastasis or ITCs have additional non-SLN disease at ALND. Assessments of SLN volume of disease by 3 different methods of measurement are equivalent for prediction of additional non-SLN metastases.

22

Ductal Carcinoma-in-Situ of the Breast Treated with Accelerated Partial Breast Irradiation Using Balloon Based Brachytherapy P.Z. Israel,[1]* F.A. Vicini,[2] A.B. Robbins,[1] P. Shroff,[1] K.L. Haile,[3] K.A. Grier,[4] M. Lyden.[5] *1. The Breast Center, Marietta, GA; 2. William Beaumont Hospital, Department of Radiation Oncology, Royal Oak, MI; 3. WellStar Kennestone Hospital, Department of Radiation Oncology, Marietta, GA; 4. WellStar Cancer Data Center, Marietta, GA; 5. BioStat International, Inc., Tampa, FL.*

Methods: One hundred twenty-six cases of DCIS seen and treated with APBI using balloon based brachytherapy constitute the study population. The median age at diagnosis was 59 years (range, 37-82) with 21% younger than age 50. Nuclear grade distribution was 52.5%, 41.4%, and 6.1% high, intermediate and low, respectively. 86% of patients had estrogen receptor positive DCIS. The median tumor size was 6 mm (range, 1-26). Margins of excision were negative in 98.4% of patients. A total of 87 patients (73.1%) were placed on adjuvant tamoxifen or arimedex. Results: With a median follow-up of 24 months (range, 0.7-73.9), three (2.4%) ipsilateral breast tumor recurrences (IBTRs) developed for a 2-year actuarial rate of 0.81%. Recurrences developed 4.8, 24.7 and 24.9 months after treatment. A subset analysis of the first 50 consecutive patients treated was performed. With a median follow-up of 40 months (range, 15.6-73.9), one IBTR developed for a 3-year actuarial rate of 2.15%. Conclusions: DCIS treated with APBI using balloon based brachytherapy produced results similar to those with invasive cancer treated with APBI as well as DCIS treated with whole breast irradiation.

23

Early Evidence of Better Cosmetic Outcome after Intra-operative Radiotherapy compared with External Beam Radiotherapy for Early Breast Cancer: Objective Assessment of Patients from a Randomised Controlled Trial M. Keshtgar,[1]* N.R. Williams,[1] T. Corica,[2] R. Hedges,[2] C. Saunders,[2] D. Joseph.[2] *1. Royal Free and UCL Medical School, London, United Kingdom; 2. Sir Charles Gairdner Hospital, Perth, WA, Australia.*

Introduction The international randomised TARGIT Trial started accrual in 2000 to determine if there is equivalence between the novel technique of IORT [intra-operative radiotherapy with Intrabeam® (Carl Zeiss, Germany)] and conventional external beam radiotherapy (EBRT) in women with early breast cancer. The main outcome measure is risk of local relapse within the treated breast. We report here the one-year data from a sub-protocol assessing cosmesis in a sub-set of 118 patients participating in the TARGIT Trial from one centre (Perth, Australia). **Methods** Frontal digital photographs from 118 patients (60 IORT, 58 EBRT) taken one year after completion of breast conserving surgery were assessed blinded to allocated treatment arm using specialist software (BCCT.core 2.0, INESC Porto, Portugal) which produces a composite score (Excellent, Good, Fair, Poor) based on asymmetry, colour and scar. This study had a power of 80% to detect a difference in proportion of outcome from 85% to 60% at p = 0.05 with 56 patients per group. **Results** Median age at randomisation was 61 (IQR 56-67) years; photographs were taken median 11 months after surgery; all patients were free from recurrence. The categories Excellent and Good; Fair and Poor; were combined. Results are shown in Table 1. More patients randomised to IORT had Excellent or Good cosmetic outcome, compared with those randomised to EBRT (76.7% versus 60.3%), difference 16.3% (95%CI -0.2% to 32.8%). **Conclusion** These results indicate that the cosmetic effects of targeted radiotherapy using Intrabeam® are better than those obtained with conventional EBRT, one year after surgery.

Table 1. Cosmetic outcome by randomised treatment (n=118)

	Excellent or Good	Fair or Poor
IORT	46	14
EBRT	35	23

Chi-Square = 3.6502, p = 0.056, df = 1

24

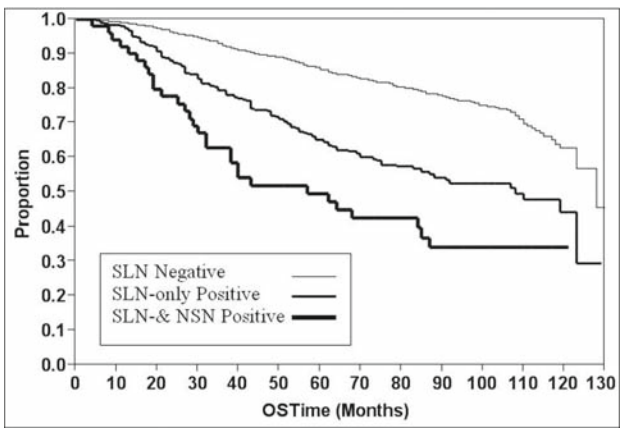
The Analysis of Molecular and Pathologic Prognostic Factors in Melanoma Patients with Positive Sentinel Lymph Node (SLN) Biopsy after Completion Lymph Node Dissection (CLND): Multi-Marker Reverse Transcriptase-Polymerase Chain Reaction (MM-RT-PCR) Assay in Lymphatic Drainage (LY) and SLN Tumor Burden P. Rutkowski,[1]* Z.I. Nowecki,[1] A.C. Van Akkooi,[2] J. Kulik,[1] W. Michej,[1] J.A. Siedlecki,[1] A.M. Eggermont,[2] W. Ruka.[1] *1. Soft Tissue/Bone Sarcoma and Melanoma, Cancer Center-Institute Warsaw, Warsaw, Poland; 2. Erasmus University Medical Center – Daniel den Hoed Cancer Center, Rotterdam, Netherlands.*

Purpose: We assessed molecular (presence of melanoma cells markers in LY) and pathological features (SLN tumor burden according to Rotterdam criteria, metastases microanatomic location) and correlated them with survival and melanoma prognostic factors. Methods: We analyzed 369 consecutive SLN-positive patients after CLND (212 axillary,146 ilio-inguinal LND; median Breslow thickness 4.0mm). In 320 patients we obtained data on SLN microanatomic location/tumor burden (only 6 cases had metastases<0.1mm); in 138 we additionally analyzed 24-hr collected LY after CLND [MM-RT-PCR with primers for tyrosinase, MART1(MelanA) and uMAGE mRNA (27.5% positive samples)]. Median follow-up time was 41 months. Results: According to univariate analysis following factors had negative impact on overall survival(OS): higher Breslow thickness (p=0.03), ulceration (p<0.001), higher Clark level (p=0.01), male gender (p<0.001), metastatic lymph nodes>1 (p<0.001), nodal metastases extracapsular extension (p<0.001), inguinal basin involvement (p<0.001), micrometastases size ≥0.1mm (p=0.001) and positive LY MM-RT-PCR (p=0.001). SLN tumor burden showed linear correlation with increasing Breslow thickness (p=0.01). 5-year OS rates for SLN tumor burden <0.1mm,0.1-1.0mm and >1.0mm were 80%/66%/41%, respectively; and for positive and negative LY MM-RT-PCR 48%/0%, respectively. The independent factors for shorter OS (multivariate analysis): male gender, primary tumor ulceration, extracapsular invasion, inguinal basin involvement and, in additional model including molecular analysis –positive MM-RT-PCR results (HR 2.5) and primary tumor ulceration(HR 2.0). Similar results were demonstrated for disease-free survival(DFS) data. Conclusions: SLN tumor burden categories according Rotterdam criteria showed correlation with OS after CLND. The positive result of LY MM-RT-PCR assay demonstrated additional prognostic value in SLN-positive melanoma patients, showing significant correlation with shorter DFS/OS.

25

The Prognostic Significance of Non-Sentinel Lymph Node Metastasis in Melanoma R.E. Brown,[1]* M.I. Ross,[2] M.J. Edwards,[3] R.D. Noyes,[4] D.S. Reintgen,[5] L. Hagendoorn,[6] A.J. Stromberg,[7] R.C. Martin,[1] K.M. McMasters,[1] C.R. Scoggins.[1] *1. University of Louisville, Louisville, KY; 2. University of Texas, MD Anderson Cancer Center, Houston, TX; 3. University of Cincinnati, Cincinnati, OH; 4. LDS Hospital, Salt Lake City, UT; 5. Lakeland Regional Cancer Center, Lakeland, FL; 6. Advertek, Inc, Louisville, KY; 7. University of Kentucky, Lexington, KY.*

INTRODUCTION: Traditionally, the total number of positive lymph nodes (LN) has been used in the staging of melanoma. We hypothesized that metastasis beyond the sentinel lymph nodes (SLN) to the non-sentinel nodes (NSN) is an important predictor of survival. METHODS: Analysis was performed of a prospective multi-institutional study that included patients with melanoma ≥1.0 mm in Breslow thickness. All patients underwent SLN biopsy; completion lymphadenectomy was performed for patients with SLN metastasis. Disease-free survival (DFS) and overall survival (OS) were computed by Kaplan-Meier analysis; uni- and multivariate analyses were performed to identify factors associated with differences in survival among groups. RESULTS: A total of 2335 patients were analyzed with a median follow-up of 68 months (range: 1-135 months). We compared 3 groups: Group 1: SLN negative (n=1988); Group 2: SLN-only positive (n=296); and Group 3: both SLN and NSN positive (n=51). The 5-year DFS rates were 85.5%, 64.8%, and 42.6% for Groups 1, 2, and 3, respectively (p<0.0001). The 5-year OS rates were 85.5%, 64.9%, and 49.4%, respectively (p<0.0001). On univariate Cox regression analysis, significant independent predictors of decreased OS included: SLN and NSN positivity, increased total number of positive LN, increased ratio of positive LN count to total LN count, increased age, male gender, increased Breslow thickness, presence of ulceration, Clark level ≥ 4, and non-extremity primary site (in all cases, p<0.01). Lymphovascular invasion, number of involved nodal basins, presence of a vertical growth phase, and evidence of regression were not significant predictors of OS. When total number of positive LN and NSN status were evaluated in a multivariate Cox model with other univariate predictors, NSN status remained statistically significant (p<0.001), while the total number of positive LN and LN ratio did not. CONCLUSIONS: This is the first study to demonstrate NSN metastasis as an independent prognostic factor in melanoma patients. This supports the concept that the SLN acts as the first line of defense against metastasis in melanoma and that metastasis past the SLN predicts a poorer prognosis.



Overall Survival Among Groups

26

Tumor Dormancy in Melanoma S.T. Steen,* D. Morton, X. Ye, M. Faries. *John Wayne Cancer Institute, Santa Monica, CA.*

Introduction Melanoma dormancy, characterized by long periods of subclinical disease, may be the result of indolent biology or endogenous host control. We hypothesized that demographic and pathologic variables are associated with melanoma dormancy and might suggest mechanisms for delayed recurrence or tumor reactivation. Methods We queried our 15,000-record melanoma database for patients who underwent surgical nodal staging of stage I/II primary cutaneous melanoma between 1971 and 2009, and subsequently developed early (< 3 years) or late (> 10 years) recurrence. T-test and Chi-square test were performed to compare patient-related (age, sex) and tumor-related (location, thickness, ulceration) characteristics of early recurrence (ER) and late recurrence (LR) groups. The patterns of recurrence and overall survival between groups were also analyzed. Results Of 6,849 patients treated for stage I/II melanoma, 3,332 had a nodal staging procedure. Of this group, 58 (1.7%) developed LR and 297 (8.9%) developed ER. Univariate analysis showed that patients with recurrence after dormancy (LR) were significantly younger and had thinner, less ulcerated tumors (Table). Age and Breslow were significant when dichotomized at 50 years and 2 mm, respectively. Sex was not significant. Head/neck primaries tended to be in the ER group, but multivariate logistic regression analysis identified age and Breslow thickness as the only factors significant for tumor dormancy. Recurrences were more likely to be distant for the LR group and locoregional for the ER group (Table). Despite a prolonged disease-free interval, the LR group did not have prolonged survival from the time of recurrence. Multivariate Cox regression model showed that thinner Breslow depth and locoregional recurrence were significantly associated with survival from first recurrence. Conclusion Although LR after extended dormancy is associated with younger age and thinner, non-ulcerated primary lesions, the prognostic benefit of these low-risk characteristics appears to disappear when dormancy ends. This suggests that a change in either tumor biology or host response allows malignant escape and subsequent growth equivalent to that of tumors with aggressive phenotypes at diagnosis.

	Age at Primary Dx	% Female	Primary Site %			Mean Breslow (mm)	% Ulcerated	Recurrence Type %	
			Extremity	Trunk	Head/neck			Stage III	Stage IV
ER	53	33	34	35	31	3.1	38	45	54
LR	45	29	34	48	17	1.5	15	22	78
p-value	0.0001	0.56	0.064			<0.0001	0.0023	0.0011	

27

Recurrence of Head and Neck Melanoma is not Affected by Reducing Margins of Wide Local Excision (WLE) J.D. Wayne,* J.Y. Kim, V. Rawlani, D.W. Buck II, S.A. Johnson. *Department of Surgery, Feinberg School of Medicine, Chicago, IL.*

INTRODUCTION: The proximity of head and neck melanomas to critical anatomical structures requires surgeons to achieve a balance between adequate margins of excision and the functional and cosmetic needs of patients. Although the National Comprehensive Cancer Network's Clinical Practice Guidelines state that wide local excision(WLE) margins may be modified to accommodate individual anatomical considerations, no evidence evaluating the safety of this practice exists. This study sought to determine the risk and risk factors of recurrence associated with reducing margins of WLE in head and neck melanoma. METHODS: 69 cases of head and neck melanoma were treated by WLE and followed prospectively. 40 WLE were performed according to current practice guidelines (0.5cm for in situ lesions, 1cm for lesions <1.0mm thick, 1-2cm for lesions 1.01-2.0mm thick, and 2cm for lesions >2.01mm thick). Reduced margins (0.5cm for lesion <1.0mm thick, 1.0cm for lesion >1.0mm thick) were utilized in 29 cases to preserve critical anatomical structures such as the eyelid, nose, mouth and auricle. RESULTS: The local recurrence rate was 8.7% over a mean follow-up period of 22.8 months. Reducing margins of WLE from 1.0cm to 0.5cm for lesions less than 1.0mm thick (p=0.465) or from 2.0cm to 1.0cm for lesions greater than 1.0mm thick (p=0.500) did not increase local recurrence rates. In this study, the clinical stage (p=0.001), Breslow depth (p=0.029), Clark stage (p=0.001), histological stage (p=0.001) and primary vs. secondary lesion status (p=0.044) significantly affected recurrence rates. The type of melanoma (p=0.404), initial pathology margin status (p=0.390), location (p=0.717) and sentinel lymph node biopsy results (p=0.648) or lymph node dissection (p=0.685) did not affect recurrence rates when proper margins were utilized. CONCLUSION: This study suggests that margins of WLE may be safely reduced in melanomas, which are in close proximity to critical structures of the head and neck without affecting local, regional or distant recurrence rates. Larger prospective clinical trials specific to the surgical management of head and neck melanomas are indicated.

Margins in Head and Neck Melanoma

Wide Local Excision Margins in Head and Neck Melanoma						
Breslow Depth	Clinical Margin (cm)	Number	Local Recurrence	Significance	Overall Recurrence	Significance
In situ	0.5**	16(23.2%)	0 (0.0%)		2 (12.5%)	
< 1.0mm	0.5	7 (10.1%)	0 (0.0%)	p=0.741	1 (14.3%)	p=0.636
	1.0*	19(27.5%)	1 (5.3%)		2 (10.5%)	
1.01 - 2.0mm	1.0*	7 (10.1%)	0 (0.0%)	p=0.533	1 (14.3%)	p=0.382
	2.0*	7 (10.1%)	1 (14.3%)		3 (42.9%)	
2.01-4.0mm	1.0	4 (5.8%)	1 (25.0%)	p=0.778	2 (50.0%)	p=0.727
	2.0*	4 (5.8%)	1 (25.0%)		2 (50.0%)	
> 4.01mm	1.0	3 (4.3%)	1 (33.3%)	p=0.714	2 (66.7%)	p=0.715
	2.0**	2 (2.9%)	1 (50.0%)		1 (50.5%)	
Minimal Wide Local Excision Margins in Head and Neck Melanoma.						
< 1.0mm	0.5	23(33.3%)	0 (0.0%)	p=0.465	3 (13.0%)	p=0.603
	1.0	19(27.5%)	1 (5.3%)		2 (10.5%)	
> 1.0mm	1.0	14(20.3%)	2 (14.3%)	p=0.500	5 (35.7%)	p=0.500
	2.0	13(18.8%)	3 (23.1%)		6 (46.2%)	

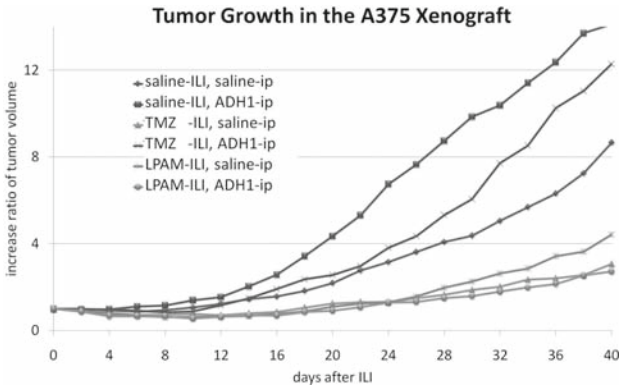
* NCCN recommended wide local excision margins based upon categorical level 1 evidence.
** NCCN recommended wide local excision margins not based upon categorical level 1 evidence.

28

Targeting N-Cadherin to augment the efficacy of regional chemotherapy: a potential double edged sword? H. Toshimitsu,* J.C. Padussis, R. Turley, C.K. Augustine, D.S. Tyler. *Surgery, Duke University, Durham, NC.*

Introduction: ADH-1 that targets N-Cadherin has been demonstrated to be effective in altering vascular permeability leading to increases in drug delivery to tumors and augmented anti-tumor responses. Given N-Cadherin's central role in tumor invasion and migration, we set out to determine if there could be potential pro-tumor effects associated with targeting this adhesions protein. Methods: The melanoma xenografts, A375, DM443, DM738, and DM733, were grown in the hindlimb of nude rats. After receiving either ADH-1 or saline via introperitoneal (ip), the rats underwent isolated limb infusion (ILI) with melphalan (LPAM), temozolomide (TMZ), or saline via the femoral vessels. Tumor volume was measured after ILI. Results: The effect of ADH-1 was initially examined. By comparing the tumor growth between saline-ILI+ADH-1-ip and saline-ILI+saline-ip, ADH-1 had no effect on the DM738 xenograft did have a small anti-tumor effect on the xenografts DM443 and DM733 tumor as compared to saline. Surprisingly, the administration of ADH-1 in the A375 xenograft led to a marked augmentation in tumor growth (p=.0009). The administration of ADH-1 in conjunction with a LPAM-ILI augmented the tumor response over LPAM alone in all 4 tested xenografts. In contrast when a TMZ-ILI was performed using the A375 xenograft, the anti-tumor efficacy of TMZ was markedly decreased by the additional administration of ADH-1 (p=.0012). While LPAM administration could overcome the growth augmenting effects of ADH-1, leading to a net reduction in tumor growth compared to controls, the addition of TMZ to an animal treated with ADH-1 had little effect, despite having a marked effect if used alone (Figure). Conclusions: Targeting ADH-1 may augment the growth of some melanoma xeongrafts. While ADH-1 appears to improve the activity of concurrently administered regional LPAM, it appeared to markedly interfere with the effectiveness of regionally administered TMZ. Vascular targeting agents should be utilized cautiously in conjunction with regional chemotherapies as they in some cases

may augment tumor growth in a fashion that can not be overcome by concurrently administered regional chemotherapeutics.



29

Growing Experience with Videoscopic Inguinal Lymphadenectomy (VIL): Moving Towards Better Outcomes K.A. Delman,* D.A. Kooby, M. Rizzo, K. Ogan, S.K. Maithel, V. Master. *Surgical Oncology, Emory University School of Medicine, Atlanta, GA.*

Introduction: Inguinal lymphadenectomy (IL) is associated with frequent (up to 50%) and potentially devastating incision-related morbidity. Our initial feasibility study of VIL for melanoma showed appropriate anatomic dissection and equivalent nodal yield as the open procedure. We report our growing experience with VIL and perioperative outcomes. **Methods:** Under an IRB-approved protocol, patients with inguinal nodal metastases were offered VIL. Procedures were performed via 3 ports: one at the apex of the femoral triangle, a second medial to the adductor muscle and a third lateral to the sartorius muscle. Femoral vessels were skeletonized and all lymphatic tissue within the femoral triangle to 5 cm above the inguinal ligament on the external oblique aponeurosis was resected. Specimens were removed through the apical port. Clinicopathologic and outcome data were recorded. **Results:** 38 VILs were performed in 26 patients: 14 had unilateral VILs for melanoma. 12 had bilateral VILs for neuroendocrine, extrammary Paget's or varied genitourinary malignancies. 6 patients (37.5%) were female, median age was 60 years (range 16-74), median BMI was 30 (range 19-53). Median operative time was 165 minutes (range 75-245 min), median LOS was 1 day (range 1-14), and median drain duration was 14.5 days. Median nodal yield was 11 (range 3-24), and the largest node removed was 5.6 cm. Wound complications were observed in 8 cases (21%): 6 cases (16%) developed cellulitis without any wound dehiscence, 1 patient developed a seroma, and 1 diabetic patient had mild skin necrosis which resolved with minimal care. **Conclusions:** Videoscopic lymphadenectomy is an alternative approach to traditional inguinal lymphadenectomy. In our growing experience, node retrieval is identical to and wound complications are substantially lower than that reported using an open approach. Further comparative analysis of VIL and traditional IL is ongoing.

30

Morbidity and length of stay with complete lymph node dissection in melanoma: results of MSLT1 trial M.B. Faries,[1]* J.F. Thompson,[3] H.J. Wang,[2] D.L. Morton,[1] M. MSLT Study Group.[1] *1. John Wayne Cancer Institute, Santa Monica, CA; 2. UCLA Biostatistics Department, Los Angeles, CA; 3. Sydney Melanoma Unit, Sydney, NSW, Australia.*

Introduction: The Multicenter Selective Lymphadenectomy Trial 1 (MSLT1) has confirmed that sentinel lymph node dissection (SLND) prevents progression of regional nodal metastases to higher N stage and improves disease-free survival. Prior single institution retrospective series have suggested that early removal of nodal disease is associated with decreased morbidity relative to delayed dissection of clinically evident disease. In a prospective, multicenter trial conducted at specialized melanoma centers, we evaluated the hypothesis that early removal of nodal disease would diminish the morbidity of complete lymph node dissection (CLND). Methods: The Multicenter Selective Lymphadenectomy Trial (MSLT1) enrolled 2001 patients with melanoma and randomized to SLND with immediate CLND if the sentinel node contained metastasis (early CLND), or to wide local excision alone with nodal observation and CLND upon clinical nodal recurrence (delayed CLND). Morbidity and length of stay were prospectively recorded and are compared here among patients undergoing early and delayed CLND. Wilcoxon rank sum and Chi-squared were used as appropriate. Results: 225 patients underwent early CLND after a positive SLND and 132 underwent delayed CLND after clinical nodal recurrence. The demographic (gender) and pathologic characteristics (tumor site, Breslow, ulceration, Clark level)of these patients were similar although the immediate CLND group was slightly younger (mean 50 vs. 54 years). The risk of lymphedema was substantially increased in the delayed CLND group (12.4% vs 20.4%, p=0.04). Length of stay was also significantly longer among patients undergoing delayed CLND (mean 8.3 vs. 9.9 days, p=0.02). Conclusion: Both the risk long-term morbidity and the length of hospital stay associated with CLND is significantly increased if the procedure is delayed until clinical presentation of nodal metastases. The use of SLND is therefore important not only to provide prognostic information and improve disease-free survival, but also to decrease the risk of CLND morbidity among those with nodal metastases.

31

Negative Predictive Value of a Nomogram to Predict Sentinel Node Status in Melanoma Patients S. Pasquali,[1]* S. Mocellin,[1] L.G. Campana,[1] A. Vecchiato,[2] E. Bonandini,[3] M.C. Montesco,[3] P. Del Fiore,[2] D. Nitti,[1] C.R. Rossi.[2] *1. Dpt. of Oncological & Surgical Sciences, University of Padova, Padova, Italy; 2. Istituto Oncologico Veneto, IRCCS, Padova, Italy; 3. Dpt. of Pathology, University of Padova, Padova, Italy.*

Introduction: About 80% of patients currently undergoing sentinel node biopsy (SNB) have negative lymph node: in the absence of conclusive evidence of a SNB-associated survival benefit, these patients may be overtreated. Here we tested a nomogram created at the Memorial Sloan-Kettering Cancer Center (MSKCC) available on line in predicting sentinel node (SN) status to avoid SNB procedure in patients at low-risk of lymph node metastasis. Methods: The clinico-pathological data (age, tumor site and thickness, Clark level and ulceration) of 769 retrospective patients who underwent SNB were reviewed. Patients in which SNB was performed according to the inclusion criteria of MSKCC (Breslow > 1 mm or < 1 mm with Clark level IV-V; n=543) were tested in the nomogram to assess the probability of SN involvement. With the aim of maximizing the negative predictive value (NPV) and reducing the rate of SNB procedures though minimizing the error rate, we considered patients with a probability scored by nomogram ≥ 0.1 at risk of having a positive SN. With this threshold we classified patients as true negative (TN), false negative (FN), true positive (TP) and false positive (FP); NPV predictive value was calculated along with positive predictive value (PPV), specificity, sensitivity, accuracy, SNB rate reduction and overall error rate. Results: Median age and tumor thickness were 53 years and 1.8 mm, respectively. SN was positive in 147 patients (27%). The MSKCC nomogram classified 135, 13, 134 and 262 patients as TN, FN, TP and FP, respectively. The NPV, PPV, specificity and sensitivity were 91.2%, 33.8%, 91.1% and 34% respectively, with an accuracy of 49.4%. Therefore, the SNB reduction and overall error rates were 27.2% and 2.3%, respectively. Discussion: MSKCC nomogram can preoperatively identify about one out four patients who might be spared SNB, with an acceptable error. Notably, correspondence could be found in these results within the findings of a previous experience on others predictive models. If validated in large prospective series, these tools might be implemented in the clinical setting for improved patient selection for SNB.

32

Adrenal Neoplasm Masquerading as Adrenal Hemorrhage L. Benavente Chenhalls,* M.L. Richards, A. Vella, G.B. Thompson, C.S. Grant, D.R. Farley. *Mayo Clinic Rochester, Rochester, MN.*

Background: There are few reports of adrenal hemorrhage (AH) associated with neoplasm and no evidence to support the management of these patients. This study assesses the clinical and pathological impact of AH in the setting of incidental adrenal neoplasms to establish proper management strategies. Hypothesis: Incidental adrenal neoplasms that are associated with adrenal hemorrhage are often malignant. Patients and Methods: Patients admitted over a 25-year period with a diagnosis of AH and incidental adrenal neoplasm were reviewed. Results: Incidental adrenal neoplasms were reported in 17/217

(8%) patients presenting with adrenal hemorrhage. The most common presenting symptom was abdominal pain (n=7), six patients (35%) were asymptomatic. In 12 patients the adrenal tumor was metastatic. Five primary adrenal neoplasms were identified: adrenocortical carcinoma (ACC, n=4), pheochromocytoma (1). All primary adrenal tumors were unilateral; 8/12 metastatic lesions were unilateral. Risk factors for AH were present in 5 patients. Computed tomography (CT, n= 13) was the primary imaging modality with masses ranging from 6.8-11.0 cm (mean, 9.1cm). Twelve patients were managed by surgical resection (adrenalectomy-5, radical nephrectomy-5, adrenalectomy/bowel resection-1, and laparotomy and packing-1). Two patients were managed conservatively with the diagnosis obtained from CT-guided biopsy. Three patients died before any intervention. One patient (Pheochromocytoma) was alive at 19-year follow-up. Actual survival time ranged from 9 days to 7.8 yrs (median, 329 days). The four patients with ACC had a median survival of 37 mo (range, 3 mos-5.5 yrs). Median survival for 12 patients with metastatic tumors was 297 days. Conclusion: Most patients with AH and neoplasm will have metastatic tumors to the adrenal glands. These patients do not typically present in hemorrhagic shock, allowing for adequate preoperative evaluation for function and assessment for primary tumors. Long-term survival is rare and the effect of AH on survival is uncertain.

33

Sentinel Lymph Node Biopsy for Thyroid Cancer: 10 Years of Experience at a Single Institution D.K. Cunningham,[1]* K.A. Yao,[2] R.R. Turner,[1] F. Singer,[1] A. Van Herle,[3] A. Giuliano.[1] *1. John Wayne Cancer Institute, Santa Monica, CA; 2. University of Chicago, Chicago, IL; 3. St. John's Hospital, Santa Monica, CA.*

INTRODUCTION: The feasibility of sentinel lymph node biopsy (SLNB) for identifying occult nodal metastases in thyroid cancer has been demonstrated in small studies. We hypothesized that occult disease in the SLN accurately predicts metastases in non-sentinel lymph nodes, and should be included in a management algorithm for this disease. METHODS: A retrospective chart review of patients undergoing total thyroidectomy with SLNB from 1998 thru September 2009 was conducted. Pre-operative ultrasound and clinical exam of the neck were performed. Intra-tumoral injection of blue dye was used to identify the SLN. If the SLN was positive for a macrometastasis on frozen section, a central neck dissection (CND) was performed. Locally advanced disease, previous thyroid surgery, and lymphadenopathy on pre-operative imaging or intra-operative palpation were exclusion criteria. RESULTS: Two hundred four patients (80%) were female and 52 (20%) were male. Ninety-six patients (38%) < 45 years of age, and 160 (62%) were older than 45. There were two-hundred thirty (90%) papillary, 12 (4.5%) follicular, 4 (1.5%) medullary, and 10 (4%) Hurthle cell carcinomas. Tumors were < 2.0 cm (T1) in 174 patients (68%), 2-4 cm (T2) in 56 patients (22%), and > 4.0 cm (T3) in 26 patients (10%). In 236 (92%) patients at least 1 blue SLN was identified; this node was positive for tumor on frozen section in 55 (23%) patients, with an additional 37 nodes positive on final pathology, for a total of 92 (39%). Of the 55 patients with a metastasis on frozen section, 48 patients (87%) underwent central neck dissection. Of these 48 patients, 35 (73%; p<0.0006) had a non-sentinel node metastasis. CONCLUSION: The presence of occult nodal metastasis in sentinel lymph nodes from thyroid cancer predicts a greater than chance (50%) likelihood of non-SLN metastasis and should be included the management algorithm for the disease. Clinical trials with long-term follow-up are now warranted to determine if the SLN procedure for thyroid cancer may serve as an endpoint for therapy when the SLN does not harbor disease.

34

Prophylactic Central Neck Dissection and Local Recurrence in Papillary Thyroid Cancer: A Meta-analysis T. Zetoune,* X. Keutgen, D. Buitrago, H. Shao, B. Zhu, M. Mazumdar, T.J. Fahey, R. Zarnegar. *Weill Cornell Medical College, New York, NY.*

Authors:Zetoune T., Keutgen X., Buitrago D., Shao H., Zhu B., Mazumdar M., Fahey TF, Zarnegar R. Background: The effectiveness of prophylactic central neck dissection (pCND) in the management of patients with papillary thyroid carcinoma (PTC) to prevent local recurrence is controversial. Methods: By performing a meta-analysis to assess the effect of pCND on local recurrence in PTC, 5 studies were identified that compared the local recurrence rates of PTC in patients without clinically detectable nodal disease in patients undergoing thyroidectomy + pCND (Group A) to those undergoing thyroidectomy only (Group B). All five studies were retrospective analyses. A meta-analysis was performed using the fixed effects method. Recurrence in was documented by imaging, thyroglobulin detection or reoperation. Location of recurrence was identified in either the central neck compartment (CNC) or the lateral neck compartment (LNC). Results: 1,264 patients were included: Group A (396) and Group B (868). Follow-up ranged from 24 to 97 months. The overall recurrence rate in Group A was 2.02% vs. 3.92% in Group B (OR=1.049, 95% CI: 0.476-2.31). The recurrence rate in the CNC in Group A was 1.86% compared to 1.68% in Group B (OR=1.31, 95%CI: 0.44-3.91). The recurrence rate in the LNC in Group A was 3.73% compared to 3.79% in Group B (OR=1.21, 95%CI: 0.52-2.75). There was no significant difference in the odds ratio in the local recurrence between the two groups. Conclusion: To date there is no convincing evidence in the literature suggesting that pCND in the surgical management of PTC is associated with a decreased local recurrence rate.

35

Pheochromocytoma: Increased incidence of asymptomatic presentation R. Lewis,[1]* K. Ebede,[2] D. Han,[1] D.L. Cohen,[1] D.L. Fraker.[1] *1. University of Pennsylvania Health System, Philadelphia, PA; 2. Ohio State University Medical Center, Columbus, OH.*

Introduction: Pheochromocytomas are neoplasms of the adrenal medulla defined by excess catecholamine excretion. The classic symptoms at presentation are hypertension and the triad of palpitations, headache, and diaphoresis. Increasingly incidentally diagnosed, we reviewed our experience with pheochromocytomas, evaluating symptomatology at presentation. Methods: An institutional database of 136 consecutive pheochromocytomas resected between January 1997 and August 2009 was retrospectively reviewed. Age, gender, familial syndromes, tumor dimension, invasive features, symptoms on presentation, and type of surgical treatment were analyzed. Results: The average age was 45, 56% were women, and 7% (10) were familial. The majority (60%, 81 of 136) of patients presented without any of the classic triad of symptoms; 18% (24) had only 1 of 3 symptoms, 15% (20) had 2 of 3, and only 8% (11) had the full triad (palpitations, headache, diaphoresis). 75% of the patients had hypertension, but it was typically mild and well controlled. Pathologic examination found lympho-vascular, capsular, or lymph node invasion in 30%. Regression analysis found no relationship between tumor size, invasive features, gender, or symptoms. However, symptoms correlated with age, becoming progressively less symptomatic as patients became older (p<0.05). The majority of patients had adrenal masses up to 11 cm diagnosed as true incidentalomas on imaging for unrelated reasons. Three pts had known incidentalomas between 1 and 4 years with no symptoms, resulting in delayed diagnosis. Conclusions: This cohort demonstrates the clinically variable and very frequently asymptomatic presentation of contemporary pheochromocytoma. With increasing use of CT, MRI scan, and PET scans, the incidence asymptomatic pheochromocyomas is likely to increase. All adrenal masses need evaluation with plasma and urine catecholamines.

36

What is the Clinical Utility of Recurrent Laryngeal Neuromonitoring during Thyroidectomy? K.A. Stevens,[1]* L.R. Henry,[2] L.B. Horst,[3] N.P. Solomon,[3] G. Coppit,[3] C.D. Shriver,[3] A. Stojadinovic.[3] *1. Naval Medical Research Center, Silver Spring, MD; 2. National Naval Medical Center, Bethesda, MD; 3. Water Reed Army Medical Center, Washington DC, DC.*

Background: Voice changes after thyroidectomy are common, and not always related to recurrent laryngeal nerve (RLN) injury. The utility of RLN neuromonitoring in preventing non-RLN related adverse voice outcomes is unknown. Methods: Prospective multi-dimensional voice assessment was conducted on patients undergoing thyroidectomy with and without RLN neuromonitoring before, 1-4 weeks, and 6 months postoperatively. Negative voice outcome (NVO) was diagnosed based upon combinations of patient-reported (Voice Handicap Index, Voice Case History), videolaryngoscopic, acoustic (Dysphonia Severity Index), and clinician-perceived (Consensus Auditory Perceptual Evaluation of voice) vocal quality. Groups with and without neuromonitoring were compared for early and late outcome differences. Of the 91 patients studied, 51 had the RLN(s) only encountered at operation, and 40 had neuromonitoring combined with RLN(s) visualization. Results: The two study groups were similar with regard to age, gender, smoking history, preoperative voice symptoms, extent of operation, and diagnosis, and were different only

in preoperative DSI scores. Six-month follow-up data was complete in 71, of whom 9 (12.7%) had NVO. There was no difference in NVO between neuromonitored and non-monitored patients at 1-4 weeks (27.5% and 30%; p=0.820) and 6 months (13.3% and 12.2%; p=0.999) after thyroidectomy. There was no difference in rate of NVO, laryngoscopic diagnosis, acoustic outcome, patient-reported or clinician-perceived quality of the voice. Neuromonitoring was associated with an increase in mean operative time of 50 minutes. Conclusion: Recurrent laryngeal neuromonitoring is associated with increased operative time, but does not appear associated with improved voice outcome after thyroidectomy. Larger prospective trials are warranted to definitively ascertain the utility of neuromonitoring. Disclaimer: The opinions expressed herein are those of the authors and do not necessarily reflect the policy or position of the US Navy, US Army, the Department of Defense, or the US government.

37

Fine needle aspiration cytology for nodular thyroid disease: Room for improvement D. Han,* R. Lewis, R.R. Kelz, D.L. Fraker. *Surgery, University of Pennsylvania Health System, Philadelphia, PA.*

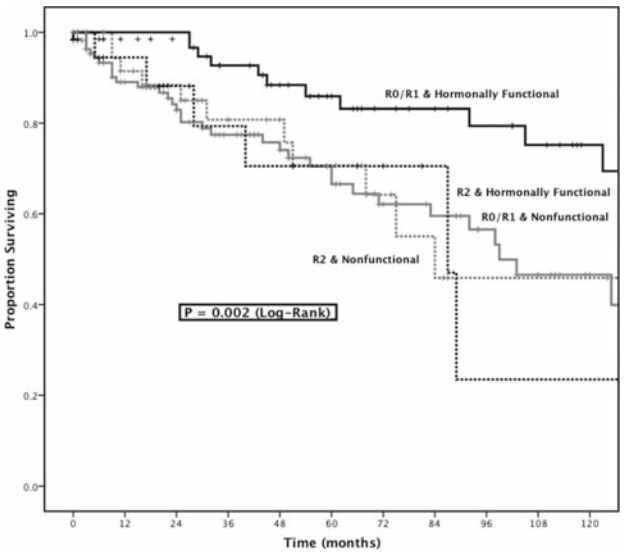
INTRODUCTION Fine needle aspiration (FNA) cytology has been the diagnostic gold standard in the management of thyroid nodular disease for over 30 years. We reviewed a large single surgeon's experience to evaluate the sensitivity and specificity of this standard technique in current series. METHODS Between December 1996 and August 2009, 2360 patients had thyroid resections with 1986 patients having surgery for nodular thyroid disease. Preoperative characterization of FNA were identified as malignant (papillary, medullary, or anaplastic carcinomas), follicular with papillary features, follicular neoplasm (including Hurthle cell), Cannot rule out follicular neoplasm, benign hyperplastic nodule, or non-diagnostic. We retrospectively correlated these preoperative interpretations with final pathology. RESULTS The results are summarized in the attached table. CONCLUSION FNA for thyroid nodules is very sensitive in identifying malignancies with an extremely low false negative rate, and very good at identifiying benign hyperplastic nodules removed for pressure symptoms. However, the largest population of patients undergoing thyroid surgery in this series (1015 pts with follicular neoplasm) had either surgery that was not indicated (the 30% of patients with hyperplastic nodules) or possibly inadequate surgery (the 22% of patients with follicular variant of papillary thyroid cancer). More and more thyroid nodules are discovered incidentally, and with an ever increasing number of FNA biopsies, improved techniques to differentiate hyperplastic nodules, true follicular neoplasms, and follicular variant of papillary thyroid cancer are needed.

		Final Pathology						
		N	Benign Adenoma	Benign Non-neoplastic	Papillary Thyroid Carcinoma	Follicular Carcinoma	Medullary Thyroid Carcinoma	Anaplastic Thyroid Carcinoma
FNA Result	Malignant	459	0%	0.5%	92%	2%	4%	1.5%
	Follicular with Papillary Features	170	15%	8%	71%	6%	0%	0%
	Follicular Neoplasm	1015	39%	30%	22%	9%	0%	<1%
	Cannot rule out Follicular Neoplasm	150	35%	47%	12%	6%	0%	0%
	Benign Hyperplastic	133	15%	85%	0%	0%	0%	0%
	Non-Diagnostic	59	24%	45%	25%	3%	0%	3%
Total		1986	26%	27%	40%	6%	1%	<1%

38

Surgical Management of Hepatic Neuroendocrine Tumor Metastasis S.C. Mayo,[1]* M.C. De Jong,[1] C. Pulitano,[2] B.M. Clary,[3] S.K. Reddy,[3] T.C. Gamblin,[4] D.A. Kooby,[5] C.A. Staley,[5] R.D. Schulick,[1] M.A. Choti,[1] G. Mentha,[6] J. Strub,[6] R.B. Adams,[7] T.W. Bauer,[7] A. Ferrero,[8] L. Capussotti,[8] T.M. Pawlik.[1] *1. Department of Surgery, 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.*

INTRODUCTION: The management of hepatic neuroendocrine tumor (NET) metastasis remains controversial with some surgeons advocating an aggressive approach while others have adopted a more conservative strategy. We sought to define the efficacy of the surgical management of hepatic NET metastasis and determine factors predictive of survival in a large multi-center cohort of patients (pts). METHODS: 339 pts undergoing surgical management for hepatic NET metastasis from 1977-2008 were identified from an international database of 8 major hepatobiliary centers. Clinicopathological data were analyzed and survival was assessed using Kaplan-Meier and Cox regression models. RESULTS: Most pts had a pancreatic (40%) or small bowel (25%) NET primary. The majority of pts (60%) had bilateral liver disease and 33% had a hormonally active tumor. At the time of surgery, 263 pts (78%) underwent hepatic resection, 10 (3%) ablation alone, and 66 (19%) resection + ablation. Major hepatectomy was performed in 151 pts (45%). Margin status was R0/R1 in 79% of pts; 21% underwent an incomplete (R2) debulking. Carcinoid was the most common NET histological sub-type (56%). The median survival was 125 months with an overall 3, 5, and 10-yr survival of 82%, 73%, and 54%, respectively. Of those pts who underwent an R0/R1 resection, 58% recurred with a mean time to recurrence of 23 months. Univariate factors associated with worse survival included high grade NET (HR=2.9), R2 margin status (HR=1.5), lymph node metastasis (HR=2.1), synchronous disease (HR=1.8), unknown location of primary NET (HR=2.3) and nonfunctional NET hormonal status (HR=2.2) (all P<0.05). Pts with hormonally functional NET who had an R0/R1 resection benefited the most from surgery. In contrast, there was no difference in survival following R0/R1 vs R2 resection for nonfunctional NET (Figure). On multivariate analyses, synchronous disease (HR=1.6) and non-functional NET hormonal status (HR=2.3) remained predictive of worse survival. CONCLUSIONS: Surgical management of hepatic NET metastasis is associated with long-term survival but a high rate of recurrence. Patients with low grade, functional hepatic metastasis benefit the most from surgical management.



Overall survival after hepatic resection of neuroendocrine hepatic metastasis stratified by the margin status (R0/R1 vs R2) on final pathology and the hormonal activity of the tumor (Functional vs Nonfunctional).

39

Vitamin D deficiency increases the risk of postoperative hypoparathyroidism following thyroidectomy in malignant disease C.S. Landry,* E.G. Grubbs, R. Berri, J.E. Lee, N.D. Perrier. *Surgical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX.*

Introduction: Temporary hypoparathyroidism is a common complication following central neck surgery(CNS). The cause is often devascularization, unintentional resection or inadvertent thermal injury of the parathy-

roid glands. Medical management is burdensome. The relationship of Vitamin D (Vit D) levels and parathyroid hormone(PTH) levels is well described. The purpose of this study was to assess whether the preoperative Vit D level in patients undergoing CNS increases the risk of hypoparathyroidism. Methods A prospective, endocrine surgery database at a single, tertiary care center was retrospectively analyzed. Consecutive patients undergoing CNS[thyroidectomy with or without central neck dissection(CND)] from 7/2006 to 10/2008 were included. Pre and postoperative biochemical parameters, and operative and pathologic reports were recorded. Preoperative Vit D deficiency was defined as a serum 25OH Vit D less than 30ng/ml. Patients had biochemical assessments at 5 pm on the evening of the procedure and 12 hours later. Temporary hypoparathyroidism was defined by a repeatedly undetectable PTH. Permanent aparathyroidism was defined by undetectable PTH at six month follow-up. Univariate and multivariate analyses were performed. Results 86 consecutive patients underwent CNS; 62(72%) had thyroid cancer. 36(42%) patients had a Vit D deficiency, and 8(9%) patients had temporary hypoparathyroidism. No patient was aparathyroid at the 6 month follow-up visit. Among the 62 patients with thyroid cancer,47(76%) had a concurrent CND. Patients who were deficient in Vit D had significantly lower postoperative PTH levels than patients who were not Vit D deficient ($p<0.04$). Patients with malignant disease ($p=0.04$) or CND ($p=0.004$) were more likely to have postoperative temporary hypoparathyroidism. No patient developed a hypocalcemic crisis. Conclusion Patients with preoperative Vit D deficiency and malignant thyroid disease who undergo a CND, are at highest risk for temporary hypoparathyroidism following CNS. Consideration should be given to preoperative Vit D replacement therapy for deficient patients undergoing CNS to avoid this complication.

40

The Use of Antigen Specific Listeria Monocytogenes for Immunotherapy Against Hepatic Colorectal Metastases K. Olino,[1]* S. Wada,[1] B. Edil,[1] X. Pan,[1] K. Meckel,[1] W. Weber,[1] J. Slansky,[2] K. Tamada,[3] D. Pardoll,[1] R. Schulick,[1] K. Yoshimura.[1] *1. Johns Hopkins Medical Institutions, Baltimore, MD; 2. University of Colorado Health Sciences Center, Denver, CO; 3. University of Maryland, Baltimore, MD.*

Introduction: Listeria monocytogenes (LM) is a gram positive bacterium which generates strong innate and adaptive immune responses in the liver. In order to treat colorectal hepatic metastases with immunotherapy, we developed an attenuated strain of LM that did not express tumor antigen (LMD) and one that did express tumor antigen (LMD-AH1). Methods: Isolated hepatic metastases were generated in Balb/c mice and then treated with intraperitoneal injections of 0.1 x LD50 LMD or LMD-AH1 on postoperative days 3, 6 and 9 and compared to mice given no treatment. We analyzed immune cell populations in the liver with flow cytometry to define the activity, specificity and kinetics of primary and memory T cell responses. We performed survival analysis and tumor re-challenge with CT26 given after initial hepatic metastasis via both flank and pulmonary metastases challenge. Log-rank test for survival and 2-way ANOVA were used for statistical analysis. Results: Mice treated with LMD-AH1 showed 90-day survival of 90% while LMD alone showed 50% survival, while no untreated mice survived (Figure 1). Along with increased survival, the mice treated with LMD-AH1 had the highest a) number of tumor specific CD8+T cells in the liver, b) activation status as measured with interferon gamma staining and c) cytolytic activity as measured by an in vivo cytotoxic T cell assay. Upon re-challenge of survivors, mice initially treated with LMD-AH1 demonstrated strong durable T cell responses having both lower tumor volumes after both flank ($p=0.03$) or pulmonary metastasis re-challenge (57% survival $p=0.04$). Most importantly, prior to tumor re-challenge, mice treated previously with LMD-AH1 had the highest number of CD8+ AH1 specific CD8+ central and effector memory T cells which underwent expansion following tumor re-challenge. Conclusion: Treatment with a tumor antigen expressing strain of LM is a) an effective treatment for metastatic colorectal cancer to the liver, b) is a potent stimulator of primary cytotoxic CD8+ T cell tumor specific responses, and c) generates antigen specific memory providing lasting immunity to tumor.

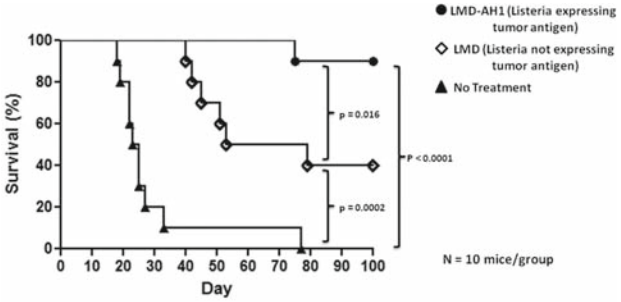


Figure 1

41

The Dual Functionality of Monoclonal Antibodies Derived from Immunogenic Tumor Associated Antigens M. Arlen,[1]* P. Arlen,[2] A. Bristol,[2] J. Luka,[2] J. Kantor,[2] X. Wang,[2] R. Gupta.[2] *1. Surgery, NSUH, Great Neck, NY; 2. Neogenix Oncology, Great Neck NY, NY.*

Introduction: We have developed a new class of monoclonals developed against immunogenic proteins (TAA's) expressed in human cancers. These mAbs serve a dual role including the early recognition of these TAA's that serve as diagnostic markers and the targeting of these diagnostic markers for tumor destruction. Method: We have isolated and characterized several human TAA's found to induce both cellular and humoral responses. These antigens derived from colon, lung and pancreas cancers, were used to develop hybridomas. Chimeric mAbs were also produced and found to demonstrate strong immunogenic responses against the corresponding malignancies. ADCC in excess of 50 % as well as tumor apoptosis was defined for each of the monoclonals. Monoclonal NPC-1, found to be extremely active in pancreatic and colon Ca failed to demonstrate target antigen in normal adjacent tissue Results: Monoclonals that were developed against TAA's from colon/pancreatic cancer as well as squamous cancer of the lung/cervix, were studied in detail in terms of biodistribution, tissue cross reactivity and cytokine release. Chimeric versions of the mAbs as well as humanized forms were shown to enhance ADCC and induce apoptosis. Because of their relatively low toxicity, rapid targeting of human tumor cell lines (in-vitro) and their ability to destroy established xenograft transplants (in-vivo) within days of delivery, these mAb's appear ideal for treating metastatic tumors. Chimeric NPC-1 is now being produced GMP for initiating clinical trials in pancreatic cancer patients having failed all standard forms of therapy.. Immunohistochemical studies have indicated that expression of the tumor antigens as target proteins occur several months before phenotypically appearing malignant cells can be identified . Conclusions : Protein derived mAbs can define the presence of malignant cellular transformation several months prior to phenotypic expression of malignancy. Such mAbs also have the capability of inducing apoptosis in both recurrent and metastatic malignancies expressing the tumor antigen.

42

TOP2A Expression is Associated with Metastasis and Essential for the Survival of Liposarcoma Cell Lines R.M. Gobble,* L.X. Qin, C. Angeles, S. Ugras, E.R. Brill, P. DeCarolis, R. O'Connor, S. Singer. *Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

Topoisomerase IIα (TOP2A) inhibitors have shown variable efficacy in the treatment of patients with advanced liposarcoma (LS). We sought to determine the association of TOP2A gene expression with metastasis across LS subtype and delineate its role in liposarcomagenesis. U133A expression profiling was performed on 140 primary LS samples, and a multi-gene predictor for distant recurrence free survival (DRFS) was developed. TOP2A expression was measured by qRT-PCR. Lentiviral short-hairpin RNA knockdown of TOP2A gene expression was performed in dedifferentiated (DDLS8817) and myxoid/round cell (ML2308) cell lines and adipocyte derived stem cells (ASC). Proliferation, apoptosis, and invasion assays along with immunoblotting to confirm TOP2A knockdown were performed. TOP2A gene expression was a significant predictor of DRFS with a 38% 5-year DRFS for patients with high TOP2A expressing tumors compared to 82% 5-year DRFS for patients with low TOP2A expressing tumors (HR1.9,$P<0.00001$). TOP2A gene expression was elevated 4-fold in well-differentiated, 42-fold in dedifferentiated, 8-fold in myxoid, 28-

fold in myxoid/round cell, and 85-fold in pleomorphic LS compared to normal fat on U133A expression profiling and 75-fold in DDLS8817 and 69-fold in ML2308 compared to ASC on qRT-PCR. TOP2A knockdown decreased proliferation 68% in DDLS8817 and 50% in ML2308 compared to Scr control (P<0.005). TOP2A knockdown increased apoptosis in DDLS8817 (52.2%vs.17.1%,P<0.0005) and ML2308 (43.3%vs.13.2%,P<0.0005) compared to Scr control. There was no difference in apoptosis or proliferation with TOP2A knockdown compared to Scr control in ASC. TOP2A knockdown decreased the invasiveness of DDLS8817 (34.3%vs.81.2%,P<0.0001) and ML2308 (27.3%vs.73.8%,P<0.0001) compared to Scr control. Immunoblotting verified TOP2A knockdown. Upregulation of TOP2A gene expression in LS is associated with reduced DRFS independent of subtype. Suppression of TOP2A gene expression decreases proliferation, invasion and induces apoptosis in LS cell lines. These results highlight the promise of developing strategies that target TOP2A gene expression in LS that over-express TOP2A.

43

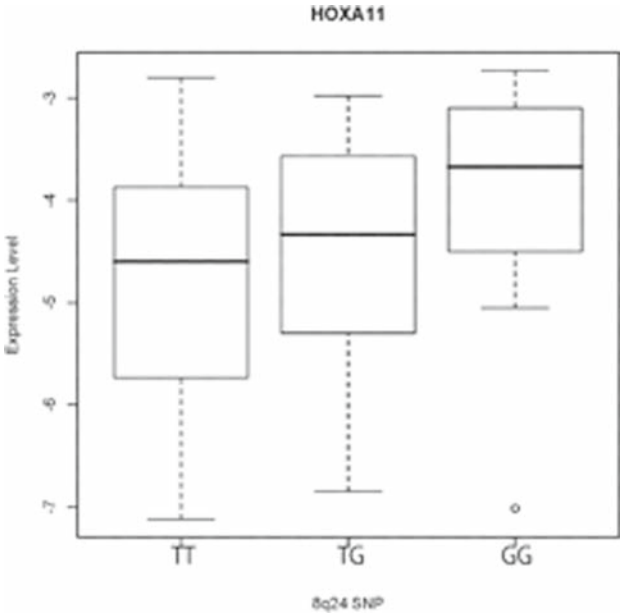
In vivo tumor targeting by functionalized dendrimer nanoscale complexes M.A. Alcala,[1]* C.M. Shade,[2] H. Uh,[2] K. Gogick,[2] R.A. Modzelewski,[1] D.L. Bartlett,[1] Y.J. Lee,[1] S. Petoud,[2] C.K. Brown.[1] *1. Surgery, University of Pittsburgh, Pittsburgh, PA; 2. Department of Chemistry, University of Pittsburgh, Pittsburgh, PA.*

Background: Regional therapies are emerging as effective treatment modalities for the 80% of colorectal patients with inoperable metastatic hepatic malignancies. We propose using dendrimer-based nanotechnology to selectively target tumors and enhance the therapeutic index. We established a method to cannulate the gastroduodenal artery (GDA) in an in vivo rat model of hepatic colorectal metastases and deliver a poly(amidoamine) (PAMAM) dendrimer with europium (Eu-G3P4A18N), to obtain tumor targeting with the intention to develop clinical applications for regional therapies. Methods: Livers of WAG/RijHsd rats were previously implanted with a 25 mg piece of CC531 colorectal tumor, and allowed to grow to 1.5 x 1.5 cm. The livers were subsequently perfused with the Eu-G3P4A18N dendrimer via the GDA using a catheter. In vivo imaging of the targeted tumors was captured by using confocal microscopy and a charge-coupled device (CCD) camera, which was fitted with a 610 nm and a 30 nm band pass emission filter. Livers were excited using 5-Watt LEDs, emitting at 450 nm. Results: The Eu-G3P4A18N dendrimer, synthesized with glycine-4-amino-1,8-naphthalimide, was designed to be stabilized against photobleaching. Within 4 seconds of infusion of the Eu-G3P4A18N dendrimer via the GDA into the liver in situ, the tumor displayed a fluorescent signal that was much higher than that of the background fluorescence. The fluorescence signal retention time was also observed in vivo at different time points in rats; 0 h, 4 h, 24 h and 72 h. Confocal microscopy has demonstrated that the Eu-G3P4A18N dendrimer was associated around the aberrant vasculature of the tumor but not around the normal vasculature of the liver. Conclusions: We have successfully established an in vivo metastatic liver tumor model in the rat and the delivery of a fluorescent imaging agent via GDA cannulation. The Eu-G3P4A18N dendrimer lacks photobleaching characteristics and also demonstrates tumor selectivity by utilizing the aberrant tumor vasculature. It also offers versatility by acting as a scaffold for the delivery of agents to the tumor and holds the potential to decrease systemic toxicity due to its targeting capability.

44

Identification of the target gene enhanced by Wnt/TCF binding to the common predisposition SNP rs6983267 at chromosome 8q24 in colorectal cancer cases K. Mimori,[1]* K. Yamamoto,[1] T. Sato,[1] K. Yamada,[7] M. Watanabe,[5] M. Kusunoki,[9] Y. Moriya,[6] S. Kudo,[4] H. Mochizuki,[8] K. Sugihara,[3] M. Mori.[2] *1. Medical Institute of Bioregulation, Kyushu University, Beppu, Oita, Japan; 2. Graduate School of Medicine, Osaka University., Suita, Japan; 3. Graduate School of Medicine, Tokyo Medical and Dental University, Tokyo, Japan; 4. Northern Yokohama Hospital Showa University, Yokohama, Japan; 5. Kitasato University School of Medicine, Sagami, Japan; 6. National Cancer Center, Tokyo, Japan; 7. Takano Hospital, Kumamoto, Japan; 8. National Defense Medical College, Tokorozawa, Japan; 9. Mie University, Tsu, Japan.*

Background: Recent study disclosed that homozygosity for the G allele of rs6983267 at 8q24 increases colorectal cancer (CRC) risk, and rs6983267 affects a binding site for the Wnt-regulated transcription factor TCF4, which activates c-MYC expression. However, the previous study showed no significant association between the GG allele and MYC expression. In the current study, we verified the risk of rs6983267 for CRC in Japanese cases, and searched for target genes other than MYC transcribed by the binding TCF4-Wnt signal. Material and method: 1) We organized multi-institutional collaboration study to perform TaqmanPCR for the SNP at rs6983267 in 1758 CRC cases and 2962 control. Genotyping and assignment of the alleles were done with GENOTYPER programs. 2) In order to establish expression profile of malignant cells specifically from 146 cases of primary CRC tumors, we applied laser-microdissection (LMD) and applied for Human Whole Genome Oligo DNA Microarray Kit (Agilent Technologies, Santa Clara, CA, USA). Results: 1) We disclosed that variants of rs6983267 on 8q24 is the susceptible risk marker for Japanese CRC cases (minor allele frequency; 0.38 (case) and 0.35 (control), OR (95%CI); 1.16 (1.06-1.27)). 2) Among TCF4 target genes, we disclosed that HOXA11 demonstrated the best concordant correlation significantly with three genotypes at rs6983267. The expression level of HOXA11 with CRC cases with genotypes, TT, TG and GG were log-4.77, -4.52 and -3.90, respectively (p=0.006). Second to HOXA11, expression level of MYC increased along with three genotypes, log-4.77(TT), log-4.52 (TG) and log -3.90 (GG), respectively (p=0.0089). HOXA11 was significantly higher expression in right side of CRC than that in the left side tumors (p<0.05). Discussion: We verified common variants on 8q24 that confer increased susceptibility to colorectal cancer in Japanese 4720 samples. We verified that MYC expression was concordantly associated with the risk (homozygous G) allele. Moreover, we identified HOXA11 as a possible mechanism to made an adequate explanation for the higher risk for oncogenic process toward CRC.



Expression of HOXA11 among 3 genotypes at the SNP

45

A Monoclonal Antibody to Secreted Frizzled Related Protein 2 Inhibits Angiosarcoma Differentiation and Migration N. Klauber-DeMore,* E. Hilliard, S. Siamakpour-Reihani, B. Bone, E. Rossi, D. Ketelsen, C. Patterson. *University of North Carolina at Chapel Hill, Chapel Hill, NC.*

Background: We recently reported the discovery of a novel angiogenesis factor, secreted frizzled related protein 2 (SFRP2) that is strongly expressed in human angiosarcoma and the mouse SVR angiosarcoma cell line. Silencing of SFRP2 in angiosarcoma cells resulted in inhibition of angiosarcoma tube

formation, and therefore targeting SFRP2 in angiosarcoma may be a therapeutic strategy. The purpose of this study was to generate a monoclonal antibody to SFRP2 (SFRP2 MAb) and to evaluate efficacy on SVR angiosarcoma differentiation and migration in vitro. Methods: Generation of a monoclonal antibody to SFRP2: Mice were immunized against an 18 AA peptide sequence of the SFRP2 protein. The spleens were removed and fused with myeloma cells and plated in HAT selection media. Hybridomas were subloned and screened with ELISA for the 18 AA peptide and for functional activity. Angiosarcoma tube formation: Matrigel was solidified into a 96-well plate. SVR angiosarcoma cells were suspended with 150 μl of SFRP2 MAb in HAT media, or HAT media alone and plated onto Matrigel at a concentration of 10,000 per well and incubated for 8 hours. Results were quantified by counting the number of branch points. Angiosarcoma migration: SVR angiosarcoma cells were plated at 10,000 per well into a 96-well plate and allowed to become confluent. The wound was formed using a 1 mL pipette tip and 150 μl of SFRP2 MAb in HAT media, or HAT media alone was added to the cells. Migration distance was measured using a 1 mm ocular ruler at time points between 16 and 32 h. Statistical analyses was performed with a 2-tailed t-test. Results: Angiosarcoma tube formation assay: The SFRP2 MAb inhibited SVR angiosarcoma tube formation by 87% compared to control (n=3 per group, $p < 0.0001$, Fig. 1). Angiosarcoma migration: Control SVR angiosarcoma cells migrated 0.75 mm ± 0.08 at 25 hours compared to those treated with SFRP2 MAb which migrated 0.48 mm ± 0.04 at 16 hours, n=4 per group, p= 0.003. Conclusion: A monoclonal antibody to SFRP2 effects angiosarcoma differentiation and migration in vitro. Future studies will evaluate the efficacy of the SFRP2 MAb on angiosarcoma xenograft growth in vivo.

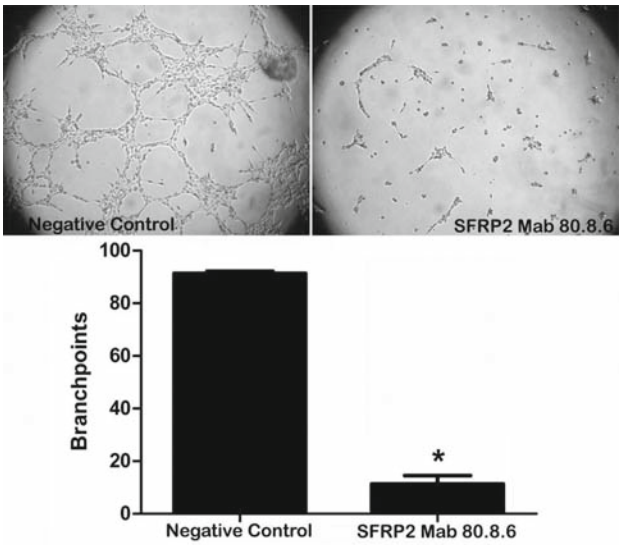


Fig. 1. SFRP2 MAb subclone inhibits angiosarcoma tube formation in vitro. Negative control contains the secletion media for the monoclonal antibody. N=3 per group, *p<0.0001.

46

Anti-tumor immune responses in human sarcomas V.P. Balachandran,* L.M. Ocuin, M.J. Cavnar, H. Obaid, R.P. DeMatteo. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

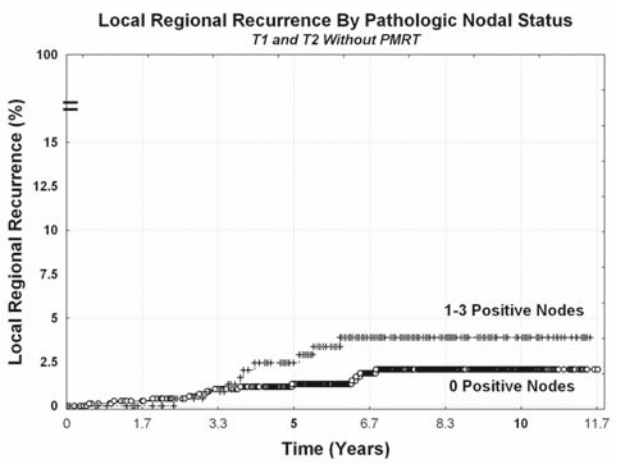
Introduction Spontaneous anti-tumor immune responses have been demonstrated to correlate with overall survival in multiple human cancers and form the rationale for the development of immune based therapies. However, the role of immune responses in sarcomas is yet to be determined. We examined immune cell infiltration in gastrointestinal stromal tumors (GISTs), the most common intestinal sarcoma. Methods Patients undergoing elective resection of primary and metastatic GIST were included in the study. Matched blood and tumor specimens were compared for the presence of immune cells. Immune cells were isolated from blood using ficoll centrifugation and from the tumor through mechanical digestion and filtration. Immune cells were identified and characterized based on cell surface and intracellular markers using flow cytometry. T cells were defined as CD3+CD56-. Regulatory T cells (T regs) were defined as CD3+CD56-CD4+FoxP3+. For functional assays, T cells were polyclonally restimulated in vitro for 4 hours followed by intracellular staining for cytokines. Results Untreated human GISTs (N=10) demonstrated striking infiltration by several immune cells. T cells represented the largest fraction, accounting for 30% of intra-tumoral lymphocytes. T cells were comprised of 75% CD4+ T cells and 25% CD8+ T cells. CD8+ T cells demonstrated higher expression of CD25 and CD69 compared to autologous blood CD8+ T cells, suggesting intra-tumoral CD8+ T cell activation ($p < 0.01$). T regs accounted for < 10% of CD4+ T cells in the blood and were expanded to > 20% within the tumor ($p < 0.01$). Upon in vitro restimulation, 60% of intra-tumoral CD4+ T cells produced IL-4 and < 10% of produced IFN-γ ($p < 0.01$). Similarly, < 10% of CD8+ T cells produced IFN-γ on in vitro restimulation. Conclusion Untreated human GISTs are infiltrated by activated CD8+ T cells and FoxP3+ regulatory T cells with putative suppressor function. Intra-tumoral T cells however demonstrate an immunosuppressive Th2 phenotype, producing IL-4 and not IFN-γ on restimulation. T cell based immunotherapies to enhance spontaneous immune responses are a possible therapeutic option for the treatment of refractory GIST.

47

Present day local-regional recurrence rates (LRR) in patients with T1 and T2 breast cancer (BC) with 0 and 1 to 3 lymph node (LN) metastases following mastectomy without radiation R. Sharma,[1]* I. Bedrosian,[1] A. Lucci,[1] R.F. Hwang,[1] L.L. Rourke,[1] T.A. Buchholz,[2] W. Qiao,[3] F. Meric-Bernstam,[1] A.M. Gonzalez-Angulo,[4] S.J. Kronowitz,[5] G.V. Babiera,[1] E.A. Mittendorf,[1] S. Krishnamurthy,[6] K.K. Hunt,[1] H.M. Kuerer.[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; 3. M.D. Anderson Cancer Center, Department of Biostatistics, Houston, TX; 4. M.D. Anderson Cancer Center, Department of Breast Medical Oncology, Houston, TX; 5. M.D. Anderson Cancer Center, Department of Plastic Surgery, Houston, TX; 6. M.D. Anderson Cancer Center, Department of Pathology, Houston, TX.*

Landmark studies demonstrating the survival advantage of post mastectomy radiation (PMRT) in women with 1-3 positive LNs come from trials completed over 2 decades ago (1961-1989). These studies reported 5 and 10 y LRR rates of 20-25%. The purpose of this study was to determine the present-day LRR to better gauge the potential benefit of PMRT in women with 1-3 LN mets treated in the current era. **Methods:** Clinical and pathologic factors from 1,022 women identified from the prospective BC Management Database were analyzed. Patients (pts) who had T1-T2 tumors and 0-3 pos LNs treated with primary surgery including margin-negative mastectomy and SLN biopsy or axillary dissection from 1997-2002 were studied. *No pts in the cohort received PMRT or neoadjuvant therapy.* Fisher's exact test and Kaplan-Meier analysis were used. **Results:** Median age was 55 yr, 79% had T1 and 21% had T2 tumors, 26% had 1 to 3 pos LNs, and 77% of pts received adjuvant chemotherapy and or hormonal therapy. At a median f/u of 94 mos (95% CI 88 to 94), LRR occurred in only 2.13% (n=22) of total pts: 11 chest-wall (CW), 1 CW/internal mammary (IM), 6 supraclavicular, 2 IM, 1 axillary/supraclavicular, and 1 IM/supraclavicular. Overall, 8% of patients in this series died of BC. The relationship between pathologic nodal status and development of LRR is shown in the Figure. The 5 and 10 y LRR rates for those pts with 0 pos LN (74%; n=753), 1 pos LN (18%; n=180), 2 pos LN (7%; n=69), and 3 pos LN (2%; n=21) were 1.2 and 2.4%, 2.4 and 3.2%, 3.1 and 6.7%, and 0%; respectively (P=0.16). Patients who were younger than 40, had T2 tumors with nodal mets, and had ER negative tumors had significantly higher chances of LRR (P<0.01). **Conclusions:** Local-regional recurrence rates are extremely low following primary mastectomy for T1 and T2 breast cancer with 0 to 3 positive LNs. The indications for use of PMRT in pts treated with present day primary surgery

and systemic adjuvant therapies should be reexamined in this era of improved imaging, pathologic assessment, and a better understanding of BC biologic subtypes.



48

Final Results of a Prospective Multi-Center Phase II Trial of Systemic ADH-1 in Combination with Melphalan via Isolated Limb Infusion (M-ILI) in Patients with Advanced Extremity Melanoma
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Background: ILI with melphalan dosing corrected for ideal body weight (IBW) is a well tolerated treatment for patients with in-transit extremity melanoma with an approximate 29% CR and 40% overall response rate as published in recent multicenter experience. ADH-1 is a cyclic pentapeptide that disrupts N-cadherin adhesion complexes. ADH-1 when given systemically in a preclinical model with regional melphalan demonstrated synergistic antitumor activity and had minimal toxicity in a Phase I trial with M-ILI. This report summarizes the final results of the multicenter Phase II trial with this combination of agents. Methods: AJCC stage IIIB or IIIC extremity melanoma patients were treated with 4000mg of ADH-1 administered systemically on Day 1 and 8 in addition to standard dose M-ILI corrected for IBW on Day 1. Drug pK, and N-cadherin IHC staining were performed on pretreatment tumor from patients. The primary endpoint was response at 12 weeks determined by modified RECIST. Results: 45 patients were enrolled over 15 months at 4 institutions. In field responses included 17 CRs (38%), 11 PRs (24%), 5 SDs (11%), and 7 PDs (16%). Five patients were non-evaluable for response. The OR rate was 62% and at a median follow-up of 20 months, 9 patients have sustained CRs over 12 months. Of 39 patients, 17 have developed disease outside the region of infusion (median time to progression 12 weeks). N-cadherin was detected in 20 of 29 (69%) pretreatment tumor samples. Grade IV toxicities included CPK elevation (4), arterial injury (1), neutropenia (1), acute respiratory distress syndrome (1), pneumonitis (1), and pulmonary infiltrate (1). There were no limb losses or compartment syndromes. Conclusion: This is not only the first prospective multi-center phase II ILI trial but also the first to incorporate a targeted agent in an attempt to augment anti-tumor responses. Targeting N-cadherin may represent a novel strategy for treating melanoma as well as a way for improving the efficacy of regionally delivered chemotherapeutic agents.

49

Diagnostic and prognostic significance of FOXC1 expression in basal-like triple negative breast cancer
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INTRODUCTION: Because we recently found that FOXC1 is critical for the aggressive phenotype of basal-like (BL) triple-negative breast cancer (TNBC), we hypothesize that FOXC1 might be an independent surrogate clinical marker of BLTNBC. We therefore used gene and tissue microarrays to examine the prognostic and diagnostic potential of FOXC1. **METHODS:** First, FOXC1 and 11 other suggested markers of BLTNBC were compared based on gene expression levels in 9 independent microarray datasets derived from analysis of primary tumors from 1693 patients. Second, protein expression of FOXC1 was examined by immunohistochemical staining (IHC) of a 96-sample microarray containing normal and cancerous breast tissue. Third, specificity of FOXC1 protein for BLTNBC was assessed by IHC of 100 TNBC archival tissue samples. Three independent data sets were analyzed for overall survival (n=649), time to distant metastasis (DM) and site of DM (n=344). **RESULTS:** Gene expression microarray datasets showed that FOXC1 was superior to αB-crystallin, moesin, CD109, p-cadherin, EGFR, CK5, CK14, CK17, c-Kit, ITGB4 and FOXC2 for diagnosis of BLTNBC (univariate Wilcoxon rank test, $p<0.0001$; multivariate logistic regression, $p=0.0003$). Tissue microarray analysis and archival tissue IHC showed that FOXC1 was as accurate but possibly more sensitive than other markers for diagnosis of BLTNBC. FOXC1 expression was significantly associated with poor overall survival in all patients ($p=0.0001$, n=295; $p=0.04$, n=232; $p=0.009$, n=122) and in node-negative patients ($p=0.0003$, n=295). FOXC1 expression was associated with shorter time to DM (21.3 mos vs. 33.2 mos, $p<0.01$) and with metastasis to brain ($p=0.0035$) and lung ($p=0.01$) in preference to bone ($p=0.0001$), which is characteristic of BLTNBC. **CONCLUSIONS:** FOXC1 is a powerful surrogate marker of BLTNBC with high diagnostic and prognostic significance. Previously reported findings support FOXC1 as a candidate for targeted therapy; the current findings support a large-scale prospective trial to validate and confirm FOXC1 as the diagnostic and prognostic marker of choice for BLTNBC.

50

Comparisons of demographics, burnout and career satisfaction of 407 surgical oncologists (SO) with 7454 surgeons from other specialties: an American College of Surgeons(ACS) survey
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INTRODUCTION: Burnout is a syndrome of emotional exhaustion and depersonalization that leads to decreased effectiveness at work. The SSO conducted a pivotal survey involving 549 members on burnout in 2006* (with an incidence of 28.2%), while the ACS conducted a similar survey in 2008 in conjunction with the Mayo Clinic Survey Research Center involving 7905 respondents, of which 407 were surgical oncologists. METHODS: The ACS survey evaluated demographic variables, practice characteristics, career satisfaction, burnout, and quality of life (QOL). Burnout and QOL were measured using validated instruments. RESULTS: Results are shown in the Table. Notable differences in demographics were that surgical oncologists were younger, more likely to be female, have younger children,practiced fewer years,had less nights on call, while they worked more hours, were more likely to be in an academic practice, be paid on a salaried basis, and had more time for non-patient activities. Compared to surgeons from all other specialties, SO had the same incidence of burnout, suicide ideation, and quality of life measures, but a lower incidence of depression, and better indices of career satisfaction. Comparison of surgical oncologists' responses from the 2006 SSO and the 2008 ACS survey showed remarkable similarities (data not shown). CONCLUSION: This data provides a frame of reference for valid comparisons of burnout, QOL, and career satisfaction indices for the surgical oncology community relative to all other surgical specialties. It is useful for better understanding of emotional and

career development issues that are more specific to the practice of surgical oncology. *Kuerer HM et al. Career satisfaction, practice patterns and burnout among surgical oncologists. Ann Surg Oncol. 2007;14:3043-3053.

Comparison of Surgical Oncologists with Other Surgical Specialties

Charactoristics	Surgical Oncologists (#407)	Other Surgical Specialists (#7454)	p value
Age (median)	49.9 yrs	51.7 yrs	0.0060
Women	26.4%	12.6%	<0.0001
Years in practice	15	18	0.0001
Hours worked/wk	62.6	59.1	0.0001
Hours in OR/wk	17.7	17.2	0.0600
Nights on call/wk	2.1	2.6	<0.0001
Private practice	27.8%	55.2%	<0.0001
Salary only	28.4%	21.3%	<0.0001
Salary plus bonus	39.7%	30.3%	<0.0001
Burned out	36.1%	39.8%	0.1386
Screen depression+	24.3%	30.2%	0.0114
Suicide ideation in past 12 months	4.9%	6.5%	0.2170
Would become a physician again	78.8%	73.7%	0.0111
Would become a surgeon again	75.1%	70.3%	0.0412
Recommend that their children become an MD	59.5%	50.0%	0.0060

51

A nomogram for predicting the risk of local recurrence after breast conserving surgery for DCIS U. Rudloff,* L.M. Jacks, J.I. Goldberg, C.A. Wynveen, E. Brogi, S. Patil, K.J. Van Zee. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

Background: While the mortality associated with DCIS is minimal, the risk of ipsilateral breast tumor recurrence (IBTR) is relatively high. Radiation therapy (RT) approximately halves the risk of IBTR and is considered standard treatment after breast conserving surgery (BCS), although RT has never been proven to improve survival, and in itself carries rare but serious risks. Individualized estimation of IBTR risk would assist in decision-making regarding the use of RT in women with DCIS treated with BCS. Methods: From 1991 to 2006, 1,868 consecutive patients treated with BCS for DCIS were identified. A multivariate Cox proportional hazards model was constructed using data from the 1,681 in whom data were complete. Ten clinical, pathological, and treatment variables were built into a nomogram estimating probability of IBTR at 5 and 10 years after BCS. The model was validated for discrimination and calibration using bootstrap resampling. Results: The DCIS nomogram for prediction of 5- and 10-year IBTR probabilities demonstrated good calibration and discrimination, with a concordance index of 0.704 (bootstrap-corrected 0.688) and a concordance probability estimate of 0.686. Factors with the greatest influence on risk of IBTR in the model included adjuvant RT or endocrine therapy, age, margin status, number of excisions, and treatment time period. Conclusions: The DCIS nomogram integrates 10 clinicopathologic variables to provide an individualized risk estimate of IBTR in a woman with DCIS treated with BCS. This tool may assist in individual decision-making regarding various treatment options and help avoid over- and undertreatment of non-invasive breast cancer.

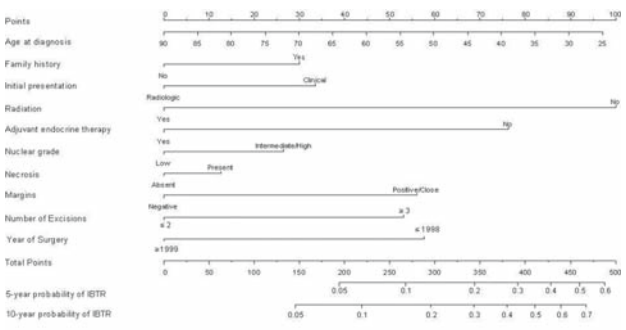

Figure 3. Nomogram for predicting 5-year and 10-year probability of IBTR.

Concordance probability: 0.686 (bootstrap validated: 0.671)
AUC/C-index: 0.704 (bootstrap validated: 0.688)

52

Phase II Comparison Study of Intraoperative Autotransfusion for Major Oncologic Procedures M. Bower,* S. Ellis, C.R. Scoggins, K.M. McMasters, R.C. Martin. *Surgical Oncology, University of Louisville, Louisville, KY.*

Introduction: Intraoperative autotransfusion (IA) of filtered salvaged blood has been widely accepted in cardiovascular surgery, but it has been avoided in oncologic surgery because of possible tumor cell dissemination. Through a prior Phase I study, we demonstrated that malignant cells are not present in blood adequately filtered for IA. The aim of the current study was to assess the rate of recurrence and outcomes of patients undergoing IA during major oncologic procedures. Methods: A Phase 2, IRB approved, prospective evaluation was conducted between 1/06-8/08 of patients undergoing hepatectomy, pancreatectomy, esophagogastrectomy, and retroperitoneal sarcoma resections. Quality of life(QoL) based on the Functional Assessment of Cancer Therapy-Anemia was assessed at regular intervals. The decision to use IA at surgery was based on the amount of available filtered blood and the preoperative hemoglobin (Hgb). Results: Ninety-two patients were enrolled with median age of 56 years (range 35-76). The most commonly performed procedures were hepatectomy (47%), Whipple (26%), and esophagogastrectomy (9%). The median pre-operative Hgb was 13.1 (range 9-16), and the median estimated blood loss was 350 (range 20-4000). Thirty-two (35%) patients received IA, with median amount of IA of 255ml (range 117 to 1499ml). Multivariate analysis identified that patients with pre-operative Hgb >11g/dl (p=0.02) and blood loss of 400-900mL (p=0.03) benefited from IA with a reduction in post-operative blood transfusion rate. Mean QoL scores were highest at the initial post-operative visit (80) and then showed a decrease at 6 weeks (73, p=.08), 3 months (74, p =.05) and 6 months (75, p=.002). Patients with discharge Hgb<9g/dl showed a trend toward lower QoL scores compared to patients with discharge Hgb>9g/dl. At a median follow up of 18 months, the rates of recurrence in the IA and the non-IA groups were equivalent (38% vs. 39%, p=.9). Conclusions: Intraoperative autotransfusion is safe and effective in major oncologic procedures and does not adversely impact recurrence rates. Furthermore, degree of discharge anemia does not lower postoperative QoL in this subset of patients.

53

Sentinel Node Biopsy and Immediate Lymphadenectomy for Occult Metastases versus Nodal Observation and Delayed Lymphadenectomy for Nodal Recurrence: Fourth Interim Analysis of MSLT-I D. Morton,[1]* J.F. Thompson,[2] A.J. Cochran,[3] R. Elashoff.[3] *1. John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, CA; 2. Sydney Melanoma Unit, Camperdown, NSW, Australia; 3. University of California at Los Angeles, Los Angeles, CA.*

Introduction: We developed sentinel node biopsy (SNB) to identify patients whose primary cutaneous melanoma is associated with occult regional nodal metastasis; these patients might benefit from immediate complete lymphadenectomy. MSLT-I is a 17-center randomized trial to evaluate the prognostic value and therapeutic impact of SNB in patients with clinically localized cutaneous melanoma. Methods:Patients were stratified by Breslow thickness and randomly assigned in a 40:60 ratio to wide excision (WE) followed by nodal observation (WEO), or to WE plus SNB followed immediately by CLND if the sentinel node (SN) contained tumor (+) by histopathology. Results:From 1/1/94 to 3/31/02, 797 patients were assigned to WEO and 1204 patients were assigned to SNB. The fourth interim analysis was undertaken at a median follow-up of 72.1 months. At 10 years melanoma-specific survival for all randomized patients with trunk and extremity primaries was 78.1% for SNB vs. 71.0% for WEO (P=0.046; HR=0.73). For 1.2-3.5 mm primaries, 10-year disease-free survival was 72.5% with SNB vs. 64.2% with WEO (p=0.005; HR=0.74); for primaries >3.5 mm, rates were 47.4% vs. 37.9%. SN tumor status was the most important factor for 10-year survival of SNB patients: survival was 85.4% for 944 SN- patients vs. 63.2% for 122 SN+ patients (p<0.0001, log rank). By 10 years nodal metastases were identified in 20.5% of SNB patients and nodal recurrence had developed in 20% of WEO patients. Ten-year survival was significantly higher after immediate CLND for SN+ than delayed CLND for clinical nodal recurrence (63.2% vs. 36.5%; P=0.001, log rank; HR=0.49). Conclusions:SNB staging of intermediate-thickness primary melanomas provides important prognostic information and identifies patients who may benefit from immediate lymphadenectomy. Survival rates are significantly higher after immediate CLND for occult nodal metastases than nodal observation and delayed CLND upon nodal recurrence. SNB

should become standard for staging, prognostic assessment and treatment planning in primary melanoma. Supported by NIH CA29605.

54

Primary Hyperparathyroidism with Negative Preoperative Imaging Still Most Commonly Caused by a Solitary Parathyroid Adenoma
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Introduction: Negative pre-operative imaging in primary hyperparathyroidism (pHPT) is often implicitly equated with multiglandular disease. We examined preoperative imaging and final pathology in a highly successful single surgeon series of patients with pHPT to assess this correlation. Methods: A retrospective study was performed on 1006 patients who underwent preoperative imaging and parathyroid surgery at a single center between 1998 and August 2009. Details of pre-operative imaging, peri-operative findings, and final pathology were examined. Results: All 1006 patients included in the study had a preoperative 99mTc-SestaMIBI scan, ultrasound, or both. There were 8 (0.8%) operative failures, defined as persistent hypercalcemia or elevated PTH. 97% of patients underwent a 99Tc-SestaMIBI scan, 30% an ultrasound. 40% of studies failed to localize. On final pathology, 85% of patients had a single adenoma, 10% a double adenoma, and 6% sporadic four-gland hyperplasia. The relationship between preoperative imaging status and final pathology is in the attached table. In patients with a positive pre-operative study, 89% had single adenoma, 7% double adenoma, and 4% hyperplasia. Patients witha negative study had 80% single adenoma, 12% double adenoma, and 7% hyperplasia. Overall, pre-operative imaging had a sensitivity of only 60%, with a positive predictive value (PPV) of 81%. For single adenoma, the sensitivity and PPV were 65% and 88%, but only 31% and 47% for double adenoma, and 5% and 7% for hyperplasia. Conclusions: Despite opinion that negative imaging means multiglandular disease, most (80%) of these image negative patients will still have a single adenoma on final pathology. Pre-operative imaging, while helpful in directing surgical approach, is not accurate enough to prevent the use of an adjunct, such as intra-operative PTH measurement, or four gland exploration.

Preoperative imaging's predictive value in primary hyperparathyroidism

		N	%	True Positives	%	Negative and False Positives	%
Final Pathology	Single Adenoma	845	85	505	60	340	40
	Double Aenoma	96	10	22	23	74	77
	Sporatic Hyperplasia	57	6	2	4	55	96

55

b-catenin is a promising therapeutic target in dedifferentiated liposarcoma A.M. Crago,* P. DeCarolis, C. Antonescu, N. Socci, S. Singer. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: β-catenin is downregulated during normal adipogenesis, but is over-expressed in dedifferentiated liposarcoma (DDLS) compared to well-differentiated liposarcoma (WDLS) and normal fat. This study sought to examine the role of β-catenin signaling in liposarcomagenesis. Methods: Affymetrix U133 microarray analysis was performed on 61 DDLS, 52 WDLS and 17 normal fat samples. An shRNA lentiviral system was employed to inhibit β-catenin expression in a DDLS cell line (DDLS8817), a WDLS cell line (WD0082), and in adipocyte-derived stem cells (ASC). Proliferation, apoptosis, and gene expression were assayed by CyQuant, annexin staining, and RT-PCR, respectively. Results: RNA expression profiles based on microarray data and a hand-curated set of 34 genes coding wnt/β-catenin signaling molecules were able to discriminate DDLS from WDLS and normal fat using a principle component analysis ($p<10^{-15}$). Western blots of cell line protein extracts showed elevated levels of β-catenin in DDLS8817 compared to WD0082 and differentiated ASC. Proliferation in DDLS8817 cells, but not ASC treated with β-catenin inhibitor FH535 was reduced 66% (p=0.05). β-catenin activity was also inhibited using shRNA (78% reduction in knockdown (KD) vs. scramble control, p=0.04). Proliferation was reduced 71% in the β-catenin KD (p=0.02), and correlated with induction of the cell cycle regulator p27. A 3-fold increase in apoptosis was also observed in DDLS8817 KD (35 vs. 10% in control, p=0.04). Abrogation of β-catenin expression (by 93 and 78%, respectively) did not induce apoptosis in WD0082 (12 vs. 16%) or in ASC (12 vs. 9.7%); the effect is specific to DDLS8817. Also consistent with induction of a more indolent phenotype, DDLS8817 KD grown in differentiation media had increased expression of adipogenic markers C/EBP-α (310%), PPAR-γ (153%), FABP4 (152%), and perilipin (187%) as compared to control. Conclusion: β-catenin activation is essential for proliferation, survival and maintenance of an undifferentiated adipogenic phenotype in DDLS cells, suggesting therapies targeted against β-catenin could be effective in treating DDLS.

56

Molecular Profiles of Pancreatic Cystic Neoplasms: The K-homology domain containing protein (KOC) may be an accurate test for malignant cystic lesions A. Briggs,* R. Wilcox, A.E. Noffsinger, J.C. Barreto, M.C. Posner, K.K. Roggin. *Surgery, University of Chicago, Chicago, IL.*

Introduction: Pancreatic cystic neoplasms (PCN) represent a spectrum of tumors that range from the purely benign serous cystadenomas (SCN) to premalignant mucinous tumors (MCA) and intraductal papillary mucinous neoplasms (IPMN), which may be benign or malignant. Previous studies have failed to accurately identify which PCN are malignant. Preoperative identification of malignant PCN is important, as it would allow for true selection of patients most likely to benefit from surgical resection. The K-homology domain containing protein (KOC) is an oncofetal RNA binding protein that has been previously shown to be over expressed in the majority of pancreatic adenocarcinoma and dysplastic lesions. KOC-expression has not been reported in PCN. Methods: All PCN resected between 1995 and 2007 were reviewed by two GI pathologists. Tissue microarrays were constructed and stained with monoclonal antibodies to KOC, mucin proteins (MUC1, MUC2, MUC5AC and MUC6), and CDX2 (a marker of intestinal differentiation). The intensity and distribution of staining was recorded and analyzed. Results: Sixty-two PCN cases were identified: 37 IPMN, 15 MCA, seven SCN, one mucinous carcinoma, and two non-neoplastic/simple mucinous cysts. Overall, one-third of the resected PCN contained invasive cancers (21/62). MUC1 was expressed in 14/20 (70%) of malignant IPMN, compared to 47% of benign IPMN (Table). CDX2 was seen in the majority of IPMN with intestinal components. KOC identified 16/20 cancerous IPMN (sensitivity=80%, positive predictive value 84%); only four malignant IPMN had positive KOC-staining (specificity=82%). Just 1/15 MCN and 0/7 SCN had positive-KOC staining. Conclusions: KOC appears to be a promising marker to detect invasive cancers arising in PCN. The molecular profiles for mucin genes and CDX2 were consistent with those previously reported in the literature. We plan to quantify KOC-levels in banked cyst fluid and test these findings in a larger dataset to determine if KOC can assist with clinical decision-making in patients with PCN.

Table. Summary of PCN immunohistochemistry for KOC, MUC proteins, and CDX2.

	KOC	MUC1	MUC2	MUC4	MUC5AC	MUC6	CDX2
Benign IPMN (N=17)	18%	47%	47%	47%	94%	94%	47%
Malignant IPMN (N=20)	80%	70%	45%	60%	100%	85%	70%
MCN (N=15)	7%	53%	6%	40%	47%	73%	20%
SCN (N=7)	0%	57%	0%	28%	0%	71%	0%

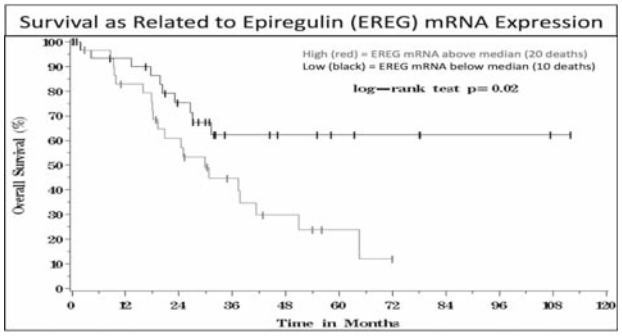
57

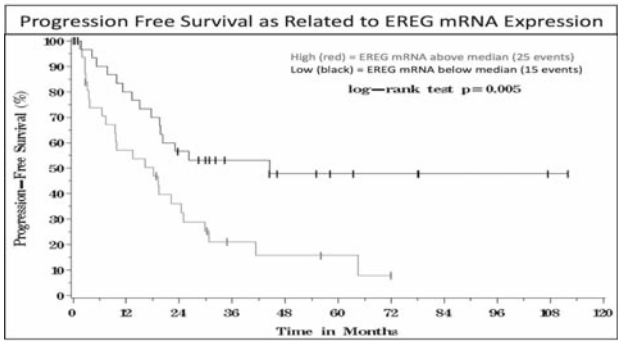
Paradoxical Effects of Smo Proto-Oncogene Overexpression in Hepatocytes J.K. Sicklick,[1]* J. Wang,[2] J. Huang,[2] W. Chen,[2] A.M. Diehl.[2] *1. Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; 2. Gastroenterology, Duke University Medical Center, Durham, NC.*

Hedgehog (Hh) activation occurs in hepatopancreatobiliary cancers. We have shown that overexpression of the Smoothened (Smo) proto-oncogene mediates c-myc expression in hepatomas and that Smo mRNA levels correlate with tumor size. We identified the K575M (KM) Smo SNP in a cirrhotic liver/hepatoma which activates Hh signaling (SSO, Abst 44, 2008). We hypothesized that Smo overexpression in hepatocytes confers a growth advantage.

METHODS: AML-12 hepatocytic lines were generated with empty pFLAG-CMV-3 vector (EV), vector with wild-type Smo (WtS), or vector with KM Smo (KMS). Assays for cell viability, proliferation (BrdU), and apoptosis (caspase-3/7 activity) were performed (48-72 h, N=4). Using real-time RT-PCR, mRNA expression of Hh components was studied in the lines and non-neoplastic livers/hepatomas. RESULTS: At baseline, AML-12 cells express Smo, Gli1 and Gli2 mRNA suggesting the capacity for Hh signaling. Compared to EV, overexpression of WtS led to a 14.1-fold decrease in viability (P<0.0001) while KMS resulted in a 1.2-fold decrease. Congruently, overexpression of WtS resulted in a 6.3-fold decrease in proliferation (P<0.0001) while KMS led to a 1.1-fold decrease. Overexpression of WtS also led to a 9.5-fold increase in apoptosis (P<0.05) while KMS led to a 3.6-fold increase (P<0.05). Wt Smo overexpression decreased Gli2 mRNA, a proliferation factor in hepatoma lines, by 4.3-fold while KM Smo overexpression increased Gli2 mRNA by 10.1-fold. Gli2 was upregulated in 63.6% (7/11) of comparisons between KM and Wt livers and in 91.8% (9/11) of comparisons between KM and Wt tumors. CONCLUSION: Smo overexpression alters the viability of hepatocytes by decreasing cell proliferation and increasing apoptosis. This is partially achieved though altered expression of the Gli2 transcription factor. The effects of Wt Smo may be important in the maintenance of hepatocyte homeostasis. In contrast, the KM Smo SNP upregulates Gli2 in vitro and in vivo and restores cell viability/proliferation. For the first time, we show that in benign tissue Smo acts through the Hh pathway to promote apoptosis and block proliferation while in malignant cells Smo overexpression has been shown to promote tumor growth.

	Viability	Proliferation	Apoptosis	Gli2 mRNA
Empty Vector	1.0	1.0	1.0	1.0
Wt Smo	↓(14.1)	↓(6.3)	↑(9.5)	↓(4.3)
K575M Smo	↓(1.2)	↓(1.1)	↑(3.6)	↑(10.1)





58

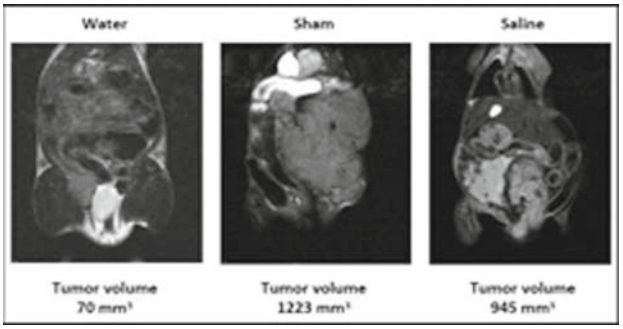
Epiregulin mRNA Expression in Colorectal Hepatic Metastases is Associated with Survival Post Partial Hepatectomy M.B. Smith,* A.S. Caudle, L.S. Caskey, M.O. Meyers, D.T. Moore, B.F. Calvo. *UNC Hospitals GI SPORE GRANT P50 CA 106991, Chapel Hill, NC.*

BACKGROUND: Primary colorectal carcinomas (CRC) overexpress human epidermal growth factor receptor type 2 (HER2) and HER3, as well as HER family ligands amphiregulin (AREG) and epiregulin (EREG). As these receptor-ligand complexes are potent mitogens, our aim was to determine if HER receptor or ligand mRNA expression in CRC liver metastases impact clinical outcome. METHODS: 65 CRC metastases from partial hepatectomies, and patient-matched normal liver were analyzed via qRT-PCR for receptors (HER1-4) and ligands (AREG, EREG, HRG, EGF, TGFa, HB-EGF). Cox analysis was used to assess the impact of individual variables on survival. Covariates associated with survival were evaluated by log-rank. RESULTS: Median follow-up for survivors was 32 months. Of the receptors and ligands evaluated, only HER3, EREG, and AREG mRNA expression were associated with decreased overall survival (OS) (HER3 p=0.08, EREG p=0.006, AREG p=0.06). When modeled together, high EREG expression remained associated with poor OS (p=0.006). Patients with above median EREG expression had shorter survival with 5-yr OS of 24% versus 62% in those with below median expression (p=0.02). Above median EREG expression was also associated with shorter progression free survival (3-yr PFS of 21% vs. 53%; p=0.005). There were no significant differences in clinical or pathologic variables between these two groups. Tumors expressed receptors HER 1-3 and ligands AREG and EREG at much higher levels than surrounding normal liver. Mean EGFR expression was increased 6 fold in tumors (95%CI=3 to 11), 21x for HER2 (95%CI=11 to 41), 25x for HER3 (95%CI=13 to 47), 40x for AREG (95%CI=27 to 101), and 76x for EREG (95%CI=42 to 139). CONCLUSIONS: CRC hepatic metastases with high EREG mRNA levels are associated with decreased post-hepatectomy OS and PFS. This finding appears independent of standard clinical predictors. Both AREG and HER3, which is potently activated by EREG, are also associated with decreased OS in univariate analysis. Significantly higher receptor and ligand levels in tumor, as opposed to surrounding liver, suggests that signaling by these HER receptor-complexes is tumor driven.

59

Peritoneal Lavage with Distilled Water is Tumoricidal: Science or Legend? F. Ito,* M. Seshadri, E. Ong, M. Alassas, J.M. Kane III, J.J. Skitzki. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

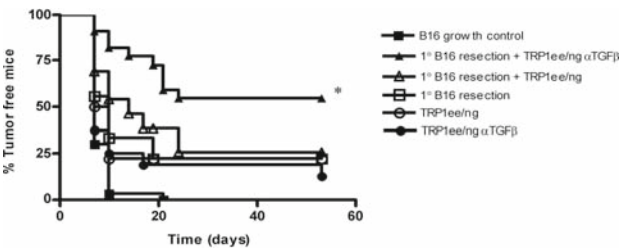
Background: Inadvertent contamination of the peritoneal cavity with viable tumor cells at the time of surgery may contribute to the development of carcinomatosis. The potential tumoricidal efficacy of peritoneal lavage with distilled water (DW) compared to normal saline (NS) was investigated. Methods: *In vitro* modeling consisted of a fixed concentration ($1x10^5$/ml) of the murine colon adenocarcinoma cell line (CT26) incubated with DW or NS, and harvested at varying time points (5, 15 and 60 minutes) and osmolarities (0 ~ 300 Osm/L). Tumor cell viability was assessed with the nuclear dye 4', 6-diamidino-2-phenylindole (DAPI). *In vivo*, BALB/c mice were injected intraperitoneally with $1x10^4$ CT26 in 50 μl of buffered saline. After 15 minutes for tumor cell distribution, mice were anesthetized, the peritoneal cavity was opened and retracted in a fixed, coliseum fashion. Precisely 3 ml of DW or NS (5 mice/group) was distributed intraperitoneally for 15 minutes with constant, controlled agitation on a programmable shaker. Control mice underwent tumor injection and sham laparotomy but no peritoneal lavage. MRI was used to noninvasively measure intraperitoneal tumor burden at day 27. The mice were followed until tumor growth caused a moribund status, and survival was assessed. Results: *In vitro*, tumor cells were still viable after 60 minutes in NS, but not after 15 minutes in DW. The tumoricidal activity was inversely osmolarity dependent and highest with DW (0 Osm/L). *In vivo*, MRI demonstrated significantly lower intraperitoneal tumor burden in the DW lavaged mice as compared to control mice or NS (Figure). At day 30, overall survival was 100% for the DW lavaged mice as compared to 0% for the NS or control groups. Conclusions: Even brief exposure to DW can dramatically decrease tumor cell viability *in vitro* and *in vivo*. This also translated into a decreased peritoneal tumor burden and improved survival in a murine carcinomatosis model. These findings have potential clinical implications for the treatment of inadvertent tumor contamination during surgery.



60

Perioperative immunotherapy is protective against melanoma recurrence in a mouse model E.C. Bellavance,* J.E. McCracken, J. O'Sullivan, A. Zloza, F. Kohlhapp, M.C. Posner, J.A. Guevara-Patino. *Surgery, University of Chicago, Chicago, IL.*

Introduction: Although surgical excision of early melanoma is curative, local and distant recurrences are a significant cause of cancer morbidity and mortality. We and others have observed that hosts rejecting primary melanomas develop effective memory immune responses against recurrent tumor challenges. The purpose of this study was to design an effective and clinically applicable approach to prevent melanoma recurrence by inducing anti-tumor immune memory responses with DNA vaccination in the perioperative period. Methods: C57BL6/J mice bearing palpable B16 melanoma tumors were treated in one of three ways: vaccination 3 times over 15 days with DNA encoding a selectively mutated tyrosine related protein (TRP1ee/ng), vaccination with anti-TGFβ monoclonal antibody (αTGFβ), and no treatment. At the time of second vaccination, tumors (~5mm in diameter) were resected. A second group of tumor-naïve mice were similarly treated with TRP1ee/ng ± αTGFβ. To assess for tumor protection, mice were re-challenged with B16 thirty days after final vaccination. Mice undergoing primary B16 resection alone and untreated tumor-naïve mice (B16 growth control) were tumor-challenged at this same time point. Tumor growth was assessed every two days over two months. Results: Greater than 50% of mice treated perioperatively with TRP1ee/ng and αTGFβ were tumor-free >50 days from tumor re-challenge, compared with 20% of mice undergoing primary tumor resection alone (see figure). Vaccination and tumor resection without TGFβ blockade resulted in 25% protection from tumor re-challenge. Less than 25% of tumor-naïve mice vaccinated ±αTGFβ remained tumor-free. All B16 growth control mice developed tumors within 21 days of tumor inoculation. Conclusions: Perioperative DNA vaccination with TGFβ blockade prevents the recurrence of a highly aggressive and immune-suppressive mouse melanoma cell line. Induction of anti-tumor memory responses with DNA vaccination at the time of primary tumor resection may provide the basis for the development of effective adjuvant therapies against melanoma recurrence.

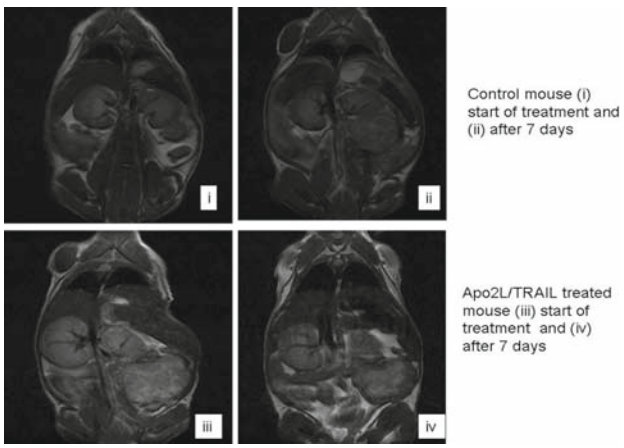


Percent of tumor-free mice over time after tumor challenge,* p<0.01 compared to B16 growth control.

61

Apo2L/TRAIL Inhibits Growth of Patient Pancreatic Tumors in a Metastasizing Orthotopic Xenograft SCID Mouse Model R. Sharma,* S. Buitrago, R. Pitoniak, J.F. Gibbs, B.L. Hylander, E.A. Repasky. *Roswell Park Cancer Institute, Buffalo, NY.*

Introduction: We have previously shown that subcutaneously established patient pancreatic tumor xenografts undergo apoptosis after treatment with Apo2L/TRAIL. We undertook this study to evaluate the response of these tumors and their metastases in an orthotopic model. Methods: An orthotopic model was established by disaggregating donor tumor xenografts and injecting cells with matrigel into the mouse pancreas. After 4-8 weeks, when tumors were established, Apo2L/TRAIL (500μg/dose) was administered daily by intraperitoneal injection; controls received saline. When palpable tumors were present in all control mice, the experiment was terminated. Final pancreatic weights were compared. To assess the response of metastases, tumors were imaged by MRI. Primary tumor volume, number and size of detectable metastases were determined. Results: Tumors which underwent significant growth inhibition in response to Apo2L/TRAIL treatment in a subcutaneous model, also exhibited significant tumor growth inhibition in the orthotopic model. Significant inhibition of the primary tumor was observed in three different patient tumors (mean pancreatic weight of the control vs. the treated group): Tumor #1, 0.421g vs.0.203g (p=0.002); #2, 0.404 g vs. 0.189g (p=0.01) and #3, 0.2202 g vs. 0.1470g (p=0.01). To assess the efficacy against metastatic disease, a tumor was selected in which predictable metastases to the liver were observed by 13 weeks. When orthotopic tumors were established, the animals were imaged by MRI and the size of the primary and metastases were quantified. After one week of treatment, the animals were re-imaged revealing that the volume of primary tumors in treated mice decreased by 44.75% while those in controls increased by 87.75%. Concomitantly, the volumes of metastatic lesions in the treated group decreased by 68.57% while those in the control group increased by 55.90%. Conclusions: Apo2L/TRAIL is effective in treating patient pancreatic tumors in an orthotopic xenograft model. Primary tumors and liver metastases underwent significant regression. This data supports the development of Apo2L/TRAIL as a therapy for pancreatic cancer.



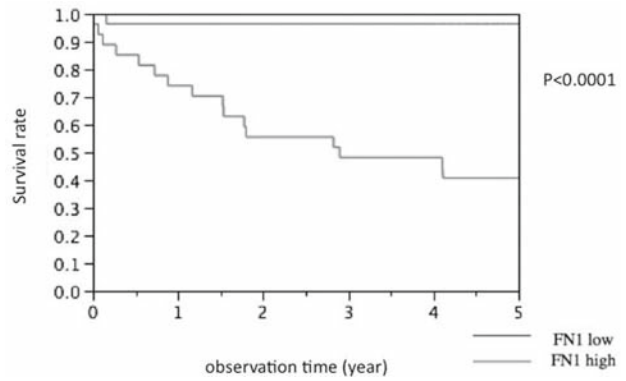
Representative T2 weighted MRI scans

62

FN1 is an independent prognostic marker and a susceptible indicator of chemotherapy in esophageal cancer T. Sudo,[1]* K. Mimori,[1] T. Yokobori,[1] M. Iwatsuki,[1] F. Tanaka,[1] M. Mori.[2] *1. Medical Institute of Bioregulation, Kyushu University, Beppu, Japan; 2. Department of Surgery, Graduate School of Medicine, Osaka University, Suita, Japan.*

Background: Fibronectin (FN1) is a predictive marker for metastasis in solid cancers. Besides, FN1 expressing cancers were resistant against anti-tumor agents. FN1 expression analysis is not fully conducted in esophageal cancer. Methods: 1) Fifty-five esophageal cancer patients who underwent esophagectomy were enrolled. Quantitative FN1 expressions were investigated using real time RT-PCR. Immunohistochemistry was performed to verify the

location of the FN1. Statistical analysis was performed to elucidate the correlation between FN1 expression and clinicopathological features. 2) Comparison to 30 cases without chemotherapies, another subset of 20 samples who underwent neoadjuvant chemotherapy were collected and immunohistochemistry was performed. Results: In real time RT-PCR analysis the average FN1 level in esophageal cancer was 1.01±2.13. The median value of 0.202 as a cut off line and patients were divided in two groups of FN1 high group (n=28) and low group (n=27). In FN1 high group, tumor size was larger ($p<0.0001$) than low group. FN1 high group showed wider range lymph node metastasis than low group ($p=0.021$). FN1 high group presented higher rate of distant metastasis ($p=0.034$). FN1 high groups' pathological stage was worse than low group ($p<0.0001$). The 5-years survival rate of the FN1 high group was worse than low group. The univariate and multivariate analysis revealed that the FN1 expression was strong independent prognositic factor equal to lymph node metastasis. Immunohistochemical staining presented that FN1 was strongly expressed tumors' invasion front. 2) In neoadjuvant group the FN1 was expressed higher than non-chemotherapy group. There were significant association between the expression of FN1 and the incidence of chemotherapy resistant ($p<0.05$). Discussion: FN1 is one of the epithelial mesenchymal transition (EMT) related genes, whose expression was quite correlated with esophageal cancers' malignancy. FN1 was also highly expressed in neoadjuvant chemotherapy patient. Neoadjuvant chemotherapy might worsen the capability of malignant behavior in cancer cells to more aggressive one with EMT change.



63

Chemotherapy After Portal Vein Embolization Protects Against Tumor Growth During Liver Hypertrophy Prior to Hepatectomy for Cancer C. Fischer, W. Jarnagin, K. Brown, M. D'Angelica, A. Covey, R. DeMatteo, S. Tuorto, L. Schwartz, G. Gatrejdman, N. Kemeny, Y. Fong.* *Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

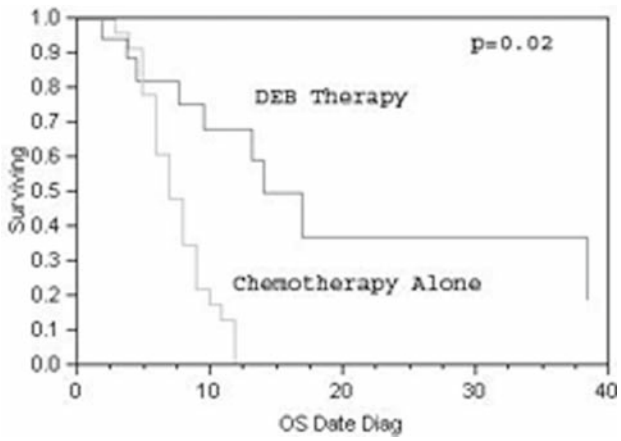
Background: Portal vein embolization (PVE) is an effective method for enhancing growth of intended remnant liver prior to major hepatectomy. There has been concern that liver growth after PVE may stimulate tumor growth during the period prior to hepatectomy. We had previously demonstrated that liver hypertrophy occurs after PVE even when cytotoxic chemotherapy is administered. We hypothesized that such administration of chemotherapy would in fact be beneficial in preventing growth of tumor. Methods: To assess the effects of chemotherapy given in the one month following PVE, we assessed by CT scans the size of 208 lesions in 71 consecutive patients with hepatic colorectal metastases subjected to PVE. 53 tumors in 18 patients undergoing chemotherapy in the month post-PVE were compared to the remaining 158 tumors in 53 patients not receiving chemotherapy. Lesions in both the embolized and non-embolized lobes of the liver prior to and one month following PVE were measured and response evaluation criteria in solid tumors (RECIST) applied to assess disease status. Results: One-third of lesions progressed after PVE when no chemotherapy was administered. This did not differ according to whether tumors were ipsilateral or contralateral to the portal vein embolization. When chemotherapy was administered, there was a significantly lower rate of progression. Conclusions: Chemotherapy after portal vein embolization attenuates progression of cancer.

	No Chemo	Chemo	P
Stable or regression	67%	81%	
Progression	35%	19%	0.03

64

Precision Hepatic Arterial Irinotecan Therapy in the Treatment of Unresectable Intrahepatic Cholangiocarcinoma: Optimal Tolerance and Prolonged Overall Survival S.C. Schiffman,* C.R. Scoggins, K.M. McMasters, R.C. Martin. *University of Louisville, Louisville, KY.*

Background: Unresectable intrahepatic cholangiocarcinoma (ICC) carries a poor prognosis and currently there are no established chemotherapeutic treatments to prolong survival. The purpose of this study was to assess the efficacy of drug-eluting bead (DEB) therapy by transarterial infusion in combination with systemic therapy in unresectable ICC. Methods: A prospective, multi-center, multi-national study of ICC patients, who received hepatic arterial DEB therapy. These patients were compared to patients who received chemotherapy alone. Results: Twenty-six patients with unresectable ICC were treated with DEB. Ten patients (38.5%) had recurrent ICC after prior radiofrequency ablation(n=3) or hepatectomy(n=7). Twenty patients (80%) had received prior chemotherapy mostly of gemzar(n=8) or oxaliplatin(n=6). The percent of overall liver involvement was < 25%(n=9), 26-50%(n=12), and > 50%(n=4). Ten patients (40%) had sites of extrahepatic disease located at lymph nodes(n=5), bone(n=2), peritoneum(n=1), lung(n=1) and mouth(n=1). A total of 42 treatments were administered. Of these, 35(83.3%) utilized irinotecan and 7(16.7%) used doxorubicin. Eight were administered in combination with systemic chemotherapy of FOLFOX(n=4) or gemzar(n=4). The median doses delivered were 75 mg of irinotecan and 150 mg of doxorubicin. Twelve patients (48%) received a second treatment and 4 patients (16%) received a third treatment. The median length of stay was 23 hours (23-72 hours). Adverse reactions were reported in 8 patients(30.7%). Of these, 7(87.5%) were minor (less than grade 3). One patient died from hepatorenal syndrome. One patient was down staged to resection. After a median follow up of 22 months the median overall survival of a multi-therapeutic regimen with DEB therapy was 17.5 months, as compared to chemotherapy alone which was 9.3 months in the historical data($p=0.02$). Conclusion: Bead therapy is safe and effective in patients with unresectable ICC. There is a significant survival benefit when DEB therapy is utilized as adjunctive therapy as compared to chemotherapy alone.



Overall survival of patients treated with adjunctive DEB therapy compared to those treated exclusively with chemotherapy

65

Defining Venous Involvement in Borderline Resectable Pancreatic Cancer Y. Chun,* J.C. Watson, B.N. Milestone, J.P. Hoffman. *Fox Chase Cancer Center, Philadelphia, PA.*

INTRODUCTION: Pancreatic adenocarcinoma impinging the superior mesenteric and/or portal vein (SMV-PV) is classified as borderline resectable, and preoperative chemoradiation is recommended to increase the margin-neg-

ative resection rate. There is no consensus on what degree of venous impingement constitutes borderline resectability. METHODS: All patients undergoing potentially curative pancreatectomy for pancreatic adenocarcinoma were reviewed. Venous involvement was classified by preoperative arteriogram according to Ishikawa types: (I) normal, (II) smooth shift without narrowing, (III) unilateral narrowing, (IV) bilateral narrowing, (V) bilateral narrowing with collateral veins. RESULTS: Between 1990–2007, 105 patients underwent resection of pancreatic adenocarcinoma involving the SMV-PV (Table). Seventy-two patients received preoperative chemoradiation, while 33 did not. Patients receiving preoperative therapy had significantly longer median overall and disease-free survival rates of 24 and 20 months, compared to 15 and 13 months for patients without preoperative therapy (P<.05). Preoperative chemoradiation was associated with a higher R0 resection rate and negative lymph nodes (both P<.001) but did not affect the need for vein resection. When stratified by Ishikawa types, preoperative therapy was associated with improved overall survival among patients with types II and III but not types IV and V. Similarly, the correlation between preoperative therapy and R0 resection rate was observed only in patients with Ishikawa types II and III. CONCLUSIONS: Preoperative therapy for borderline resectable pancreatic adenocarcinoma is associated with higher margin-negative resection and survival rates in patients with Ishikawa types II and III tumors, defined as a smooth shift or unilateral narrowing of the SMV-PV. Patients with bilateral venous narrowing were less likely to benefit from preoperative treatment.

Ishikawa classification of venous involvement in pancreatic adenocarcinoma (n=105)

Ishikawa type	Clinicopathologic features			
	Vein resection, n (%)	R0 margin, n (%)	Positive lymph nodes, n (%)	Median overall survival, mo
II, n=14	1 (7%)	8 (57%)	5 (36%)	28
III, n=50	21 (42%)	23 (46%)	22 (44%)	22
IV, n=33	13 (39%)	10 (30%)	18 (55%)	19
V, n=8	6 (75%)	4 (50%)	4 (50%)	30

66

Lymph node resection in laparoscopic distal pancreatectomy is equivalent to the open operation N. Newman,* B.H. Edil, M.A. Makary. *Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, MD.*

Introduction: While advantages of laparoscopic distal pancreatectomy have been described, the procedure has been largely avoided for cancer since it is unknown if the associated lymphadenectomy is equivalent. We reviewed our experience to see if the two techniques had equivalent lymphadenectomy. Methods: We retrospectively collected lymph node counts in resected specimens among open and laparoscopic distal pancreatectomy and splenectomy specimens at our hospital over a three-year period (June 2006-June 2009). A control group, matched by gender and cancer stage, was identified among patients who had the comparable open operation by the same surgeons. Results: We identified 20 laparoscopic distal pancreatectomy and splenectomy procedures (mean age=62.5 years, 63% female) and 26 open procedures (mean age=60.2 years, 53.8% female). There was no difference in the mean lymph node count in the laparoscopic group (15.2 nodes, range 0-68) and the open group (16.4 nodes, range 0-38) (p<0.05). Conclusions: Laparoscopic resection of the distal pancreas can achieve the same lymph node resection rate as the open operation, and therefore should be considered as an option in select patients with malignancy.

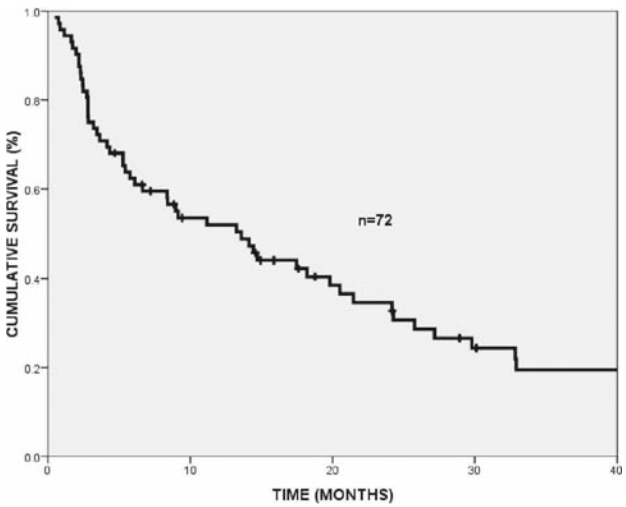
Laparoscopic versus open lymph node retrieval for distal pancreatectomy

Variable	Overall	Lap	Open
Number of Cases	46 (100%)	20 (42.2%)	26 (57.8%)
Age (years)	61.4 (range 31-84)	62.5 (range 31-84)	60.2 (range 34-83)
Male	20 (42.2%)	8 (36.8%)	12 (46.2%)
Female	26 (57.8%)	12 (63.2%)	14 (53.8%)
Examined Lymph Nodes	15.8 (range 0-68)	15.2 (range 0-68)	16.4 (range 0-38)
Involved Lymph Nodes	3.6% (range 0-8 nodes)	2.5% (range 0-5 nodes)	4.7% (range 0-8 nodes)
Tumor Size	3.74cm (range 0.3-16cm)	2.65cm (range 0.8-6.5cm)	4.83cm (range 0.3-16cm)
Positive Margin	7 (15.6%)	2(10%)	5 (19.2%)

67

Intra-arterial Iodine-131-Lipiodol for Unresectable Hepatocellular Carcinoma T.C. Chua,* F. Chu, S.P. Butler, R.J. Quinn, D. Glenn, D.L. Morris. *UNSW Department of Surgery, St George Hospital, Sydney, NSW, Australia.*

Background Hepatic artery administration of Iodine-131-Lipiodol serves as a modality that delivers targeted radiation therapy to hepatocellular carcinoma. Its efficacy has been promising from trials conducted in the adjuvant setting after hepatic resection. Further investigation of its role in the palliative setting is warranted. Methods Retrospective review of 72 patients with unresectable hepatocellular carcinoma treated with Iodine-131-Lipiodol and followed-up by the St George Hospital Sydney's Hepatobiliary service. Patients received a median of one treatment (range, 1 to 2) at a median dose of 1.0 Gbq (range, 0.5 Gbq to 2.0 Gbq). Efficacy of treatment was determined based on overall survival as the end point using the Kaplan-Meier method. Results Sixty men and 12 women with a mean age of 65 years (SD=11) underwent iodine-131-lipiodol treatment. The median follow-up period was 9 (range, 1 to 122) months. There were 52 deaths (72%). Median overall survival after treatment was 14 months; 1-, 2-, and 3-year survival rate was 52%, 33% and 20% respectively. Factors associated with survival include the AJCC stage (p=0.03), BCLC stage (p=0.05), CLIP score (p=0.008), tumor size (p=0.01), extrahepatic disease (p<0.001), previous surgery (p=0.02), and response to treatment (p<0.001). The response to treatment was identified through a multivariate analysis as the single independent predictor for survival [Hazard Ratio (95% CI); 3.5 (2.2 to 5.4); p<0.001]. Conclusion Encouraging survival outcomes may be derived through administration of Iodine-131-Lipiodol in patients with unresectable hepatocellular carcinoma. The overall success of treatment may be determined by the response to treatment.



68

Resection for Klatskin Tumors: Curative or Palliative? R.M. Cannon,[1]* M. Thomas,[1] K. Bilinski,[1] R. Kaikaus,[1] K. Ravindra,[1] S. Rudich,[2] S. Appana,[1] A. Barve,[1] T. Doty,[2] T. Shaquor,[1] G. Brock,[1] M. Marvin,[1] S. Barve,[1] C. McClain,[1] W. Jones,[1] K. McMasters,[1] J.F. Buell.[1] *1. Surgery, University of Louisville, Louisville, KY; 2. University of Cincinatti, Cincinatti, OH.*

Introduction: The management of hilar cholangiocarcinomas (Klatskin tumors) remains challenging, with conflicting reports of the value of surgical resection. The purpose of this analysis was to evaluate the outcome of pts undergoing resection for these tumors. Methods: Retrospective analysis of prospectively collected database was approved by the IRB. Patient demographics and tumor characteristics were examined through a multivariate analysis and Cox Regression Modeling. Tumor resectability, tumor recurrence and patient survival were assessed. Results: 100 consecutive Klatskin's tumor pts were enrolled over a 16-year period, with a median follow-up of 31 mo.

The study group was comprised of 58% males, 92% Caucasians, and the median patient age was 63 years. The most common presentation was jaundice (85%), wt loss (50%) or abdominal pain (21%). Median laboratory values at patient presentation included: bilirubin 6.2 mg/dL, Alk Phos 475 IU/L, and Ca 19-9 of 258. Of 89 pts with ERCP brushings and washings, 32 (36%) had tumor-positive cytology. Of 82 pts who were explored, 51 (62%) were resected: 31 with R0 and 20 with R1 resections. Lobar resection was performed in 43 (84%) of the resected patients. The 30-day mortality rate was 11%; the complication rate was 52%. During the second era of 50 resections the resectability rate increased (34% vs. 68%: P<0.001) as did the percentage of R0 resections (35% vs. 73%: P=0.008). Nineteen (37%) pts recurred in either the liver or lung. On Cox regression analysis, factors significantly associated with improved overall survival included resection (vs. no resection), negative margin status, negative lymph node involvement, lobar resection and second era of resection. (p<0.05). Conclusions: Although only a minority of pts with Klatskin tumors are able to undergo an R0 resection, these patients have a reasonable chance of long-term survival. The resectability rate has risen over the last decade with increased clinical experience at specialty centers, although the morbidity and mortality associated with resection of these tumors is substantial.

	N	1 year survival	3 year survival	5 year survival	HR (95% CI) p-value
Resected	51	63%	36%	33%	0.23(0.1-0.5) <0.001
No Resection	49	10%	2%	0%	
R0	31	73%	60%	52%	2.98(1.4-6.2)
R1	20	50%	10%	10%	

69

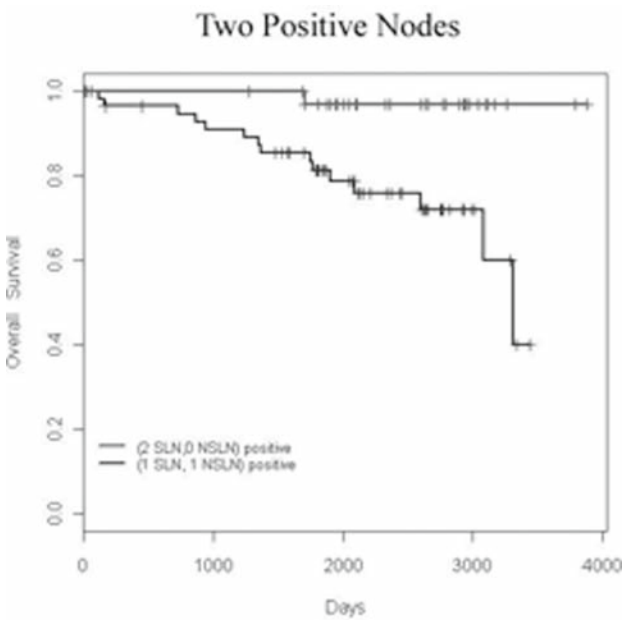
ANN Analysis to Identify MicroRNA Expression Patterns in Colorectal Cancer K. Chang,[1]* N. Miller,[1] E. Kheirelseid,[1] G. Ball,[2] M.J. Smith,[1] M. Regan,[1] O.J. McAnena,[1] M.J. Kerin.[1] *1. Surgery, National University of Ireland, Galway, Galway, Ireland; 2. Nottingham Trent University, Nottingham, United Kingdom.*

Introduction: Mi(cro)RNAs are non-coding molecules which post-transcriptionally regulate gene expression. Dysregulation of miRNA expression play an important role in carcinogenesis. MiRNAs hold much potential as novel diagnostic biomarkers, prognostic indicators and therapeutic targets. The purpose of this study was to profile the expression patterns of miRNAs in colorectal cancer (CRC) and to investigate association between miRNAs expression and clinicopathological parameters. Materials and methods: MiRNA expression profiling was performed on a cohort of 20 paired tumour and normal tissues with stage II CRC. Stepwise Artificial Neural Network (ANN) analysis was applied to relative expression data. Differentially expressed miRNAs were validated by RQ- PCR in an expanded cohort of 102 tissue specimens of varying stages from 58 patients. Eight candidate miRNAs were chosen for validation. Results: Thirty-three miRNAs were identified as differentially expressed in tumour compared to normal tissues. Array and RQ-PCR expression displayed strong correlation (Pearson's R range 0.489-0.916, p value range 0.000-0.039). ANN analysis identified 3 miRNA-signature predictive of tumour status. In the validation RQ-PCR cohort, expression of specific miRNAs was found to be associated with tumour aggressiveness (mucinous phenotype and poor differentiation), and distant metastasis. Conclusion: This study demonstrates that microarray technology and ANN analysis reliably identifies biologically relevant miRNAs associated with colorectal cancer specifically. Differential miRNA expression on the basis of tumour status implicates these miRNAs in both oncogenesis and tumour suppression. Association of specific miRNAs with clinicopathological features indicates their biological relevance and highlights their potential for development as clinically significant biomarkers to better stratify patients at increased risk of disease recurrence to guide adjuvant therapy.

70

Distribution of Axillary Lymph Node Metastases in Breast Cancer Predicts Mortality Better Than the Number of Positive Nodes J.W. Jakub,* K.L. Bryant, M. Huebner, T.L. Hoskin, J.C. Boughey, C. Reynolds, A.C. Degnim. *Surgery, Mayo Clinic, Rochester, MN.*

Introduction:In breast cancer a direct relationship exists between prognosis and the number of lymph nodes involved with metastatic disease. This study was undertaken to determine if metastatic disease confined to the sentinel lymph nodes (SLN) has a better prognosis than metastatic disease spread to nonSLNs, regardless of the number of nodes involved. Methods:The study group consists of 449 patients with a positive SLN who underwent complete node dissection (CLND). Cox proportional hazards regression models were used to assess the association of the number of positive SLNs and nonSLNs with overall survival (OS) and disease free survival (DFS). Results:The median number of SLNs (2) and the median number of nodes identified following CLND was no different (17, 18) in both the SLN positive only group (n=253) and the group with nonSLN involvement (n=196). In patients with disease confined to the SLNs, as the number of positive SLNs increased the OS and DFS remained the same. Once disease was spread beyond the SLN, both DFS and OS were negatively impacted. Among the patients with nonSLNs disease, there was no significant association between survival and the number of positive SLNs. However, mortality increased with the number of nonSLNs involved with metastatic disease. A direct comparison was undertaken of patients with 2 positive nodes. Group 1 had all disease confined to the SLNs (2 positive SLNs), Group 2 had nonSLN disease (1 positive SLN and 1 positive nonSLN). Despite both having an identical number of positive nodes, the estimated overall survival rates (95% CI, number still at risk) at 1, 3, and 5 years were 100% (100-100; 34), 100% (100-100; 34), and 96.9% (91.0-100; 29) for group 1 compared with 96.4% (91.7-100; 53), 90.9% (83.5-98.8; 49), and 81.1% (71.2-92.4; 36) for group 2 (p=0.004, Figure 1). Conclusion: The number of regional nodes involved with metastatic disease does not impact DFS and OS if all disease is confined to the SLNs. NonSLN involvement negatively influences OS. If these findings are validated in a larger data set, specifying SLN versus non-SLN involvement should be considered in breast cancer staging.



71

Double-Blinded, Placebo Controlled Prospective Randomized Trial Evaluating the Efficacy of Continuous Paravertebral Catheter Anesthesia with Paravertebral Block in Breast Cancer Surgery

C.C. Buckenmaier III,[1] K.H. Kwon,[1] R.S. Howard,[2] G.M. McKnight,[1] C.D. Shriver,[3] A. Stojadinovic.[3]* *1. Regional Anesthesia and Pain Management Initiative, Anesthesia & Operative Service, Walter Reed Army Medical Center, Washington DC, DC; 2. Department of Clinical Investigation, Division of Biostatistics, Walter Reed Army Medical Center, Washington DC, DC; 3. Clinical Breast Care Project, Walter Reed Army Medical Center, Washington DC, DC.*

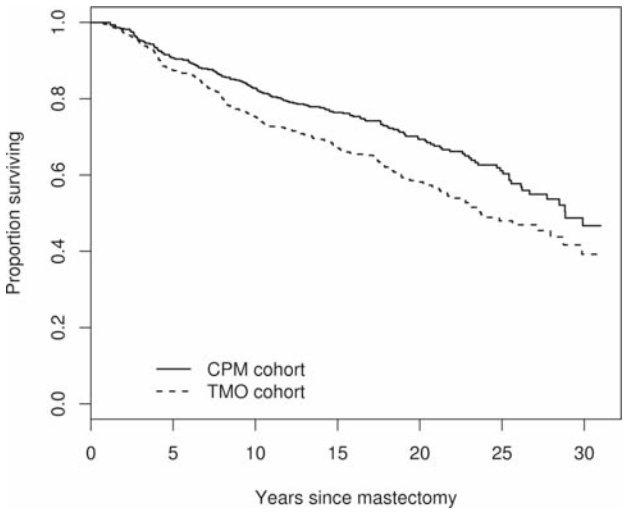
Background: Paravertebral block (PVB) is an effective alternative to general anesthesia for breast cancer surgery. Continuous paravertebral catheter (CPVC) anesthesia may extend post-operative analgesia and improve quality of early post-operative recovery of breast cancer patients. Purpose: This double-blinded prospective randomized trial was conducted to compare degree of pain, nausea, mood, level of symptom distress, and time to return to normal daily activity between PVB and CPVC+PVB in patients undergoing breast cancer surgery. Patients and Methods: Between July 2003 and April 2008 we randomly assigned 94 (73 evaluable) patients in a 1:1:1 ratio with early breast cancer to single injection PVB followed by CPVC infusion of 0.1% or 0.2% Ropivacaine versus placebo (Saline) for 48 hours post-operatively for unilateral breast cancer surgery without reconstruction. The primary study endpoint was the degree of pain, nausea, mood state, level of symptom distress, and recovery time. Results: Of the 468 patients assessed for eligibility 94 consented and 21 with incomplete data or follow up were excluded, leaving 73 subjects for analysis. There was no statistically significant difference in degree of post-operative pain, nausea, mood state, level of symptom distress or return to normal activity among the three study groups. Conclusion: Although it is possible that modest sample size may have masked a significant advantage for the addition of continuous paravertebral catheter anesthesia to paravertebral block, the current study fails to support the use of continuous paravertebral catheter anesthesia in patients undergoing operative treatment for breast cancer.

72

Contralateral prophylactic mastectomy is associated with a survival advantage in high-risk women with a personal history of breast cancer

J.C. Boughey,[1]* T.L. Hoskin,[2] T.A. Sellers,[3] A.C. Degnim,[1] M.J. Kasner,[4] L.C. Hartmann,[5] M.H. Frost.[4] *1. Surgery - Mayo Clinic, Rochester, MN; 2. Biomedical Statistics - Mayo Clinic, Rochester, MN; 3. Moffitt Cancer Center, Tampa, FL; 4. Women's Cancer Program - Mayo Clinic, Rochester, MN; 5. Medical Oncology - Mayo Clinic, Rochester, MN.*

Introduction: The aim of this study was to investigate whether contralateral prophylactic mastectomy (CPM) plus therapeutic mastectomy (TM) is associated with a survival advantage in high risk women with breast cancer compared with TM alone. Methods: We report long term follow up overall survival data on two cohorts initially established to evaluate risk of contralateral breast cancer (CBC). 442 women with stage I or II breast cancer and a family history of breast cancer who underwent TM and CPM at our institution between 1964 and 1993 were evaluated and compared to a cohort of 442 patients matched on age at mastectomy, tumor stage, nodal status, and year of mastectomy who underwent TM only. Results: At a median follow-up of 17.6 years, 3 CBCs (0.7%) developed in the CPM cohort and 37 (8.4%) in the TM only cohort. This represented a 93% decreased risk of CBC (HR=0.07, 95% CI: 0.02 to 0.23, $p < 0.0001$). This result remained strongly significant after adjustment for age, stage and nodal status. 154 women in the CPM group and 191 women in the TM alone group have died for 10-year overall survival estimates of 83% and 75% in the CPM and TM alone groups, respectively (HR = 0.71, $p = 0.002$, see figure 1). This difference in overall survival persisted (HR = 0.75, 95% CI: 0.60 to 0.93, $p = 0.01$) after adjustment for age, stage, nodal status, first-degree family history, ER and PR status, tamoxifen use, chemotherapy, radiation therapy, and prior oophorectomy. Other variables significant in this multivariable model included age ($p < 0.0001$), stage ($p = 0.007$) and having > 2 positive nodes vs negative nodes ($p < 0.0001$). In a separate model, recurrence modeled as time-dependent covariate was a strong predictor of death (HR = 11.7, 95% CI: 9.3 to 14.8, $p < 0.0001$). Conclusion: In this retrospective cohort study CPM was associated with improved all cause survival. Further studies are required to evaluate this finding, as design issues and selection bias may contribute to the apparent survival benefit.



Kaplan Meier overall survival curve of CPM compared to TM alone

73

Margin Index: A New Method for Prediction of Residual Disease Following Breast-Conserving Surgery

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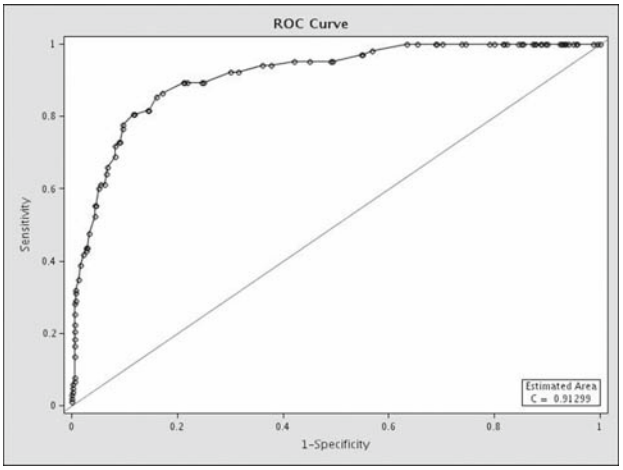
Background: Margin status is a risk factor for local recurrence, but no one agrees on what is an optimum margin. We hypothesized that the optimum margin should depend on the original size of the tumor as well as tumor characteristics. We therefore propose that "Margin Index", a relationship of the margin obtained to the size of the tumor, is a better predictor of residual disease upon re-excision than margin alone. Methods: We reviewed our surgical database and identified 472 consecutive patients with Stage I-II breast cancer who were treated with breast-conserving therapy (BCT) from 1998-2008 who also underwent re-excision for close margins. Margin index was calculated as follows: Margin Index = Closest margin (mm) / Tumor size (mm) x 100 A receiver operating curve was created using the derived margin index and the presence or absence of any residual disease in the re-excision specimen. Sensitivity and specificity values were calculated at various margin indices to determine the optimum margin index. Results: Of the 472 patients who underwent re-excision for close margins, 103 (22%) had residual disease in the re-excision specimen. The calculated margin index predicted the likelihood of residual disease in the re-excision specimen, whereby the lower the margin index, the higher the likelihood of residual disease. The optimum margin index was >5; the risk of residual disease for a margin index >5 was only 3.8%. The sensitivity and specificity of a margin index cut-off of 5 was 89% and 75%, respectively. The overall c index for the receiver operating curve was 0.91 (see Figure). There were no significant differences between patients who had residual disease in the re-excision specimen versus those who did not according to patient age, tumor size, tumor grade, estrogen/progesterone receptor and Her2neu status, histology type, or nodal status. Conclusions: Margin index is a reliable method for the prediction of residual disease following attempted BCT with close margins. This simple calculation may be helpful for identifying patients who require re-excision prior to radiation therapy and those who may be able to forego additional surgical interventions.



74

Breast cancer risk in women with pseudoangiomatous stromal hyperplasia (PASH) A. Degnim,[1]* D.A. Visscher,[2] R.A. Vierkant,[1] J.C. Boughey,[1] D.C. Radisky,[3] S.S. Anderson,[1] V.S. Pankratz,[1] M. Frost,[1] L.C. Hartmann.[1] *1. Mayo Clinic, Rochester, MN; 2. University of Michigan, Ann Arbor, MN; 3. Mayo Clinic, Jacksonville, FL.*

Introduction: Pseudoangiomatous stromal hyperplasia (PASH) is a recently described benign histologic entity in breast tissue. Its relationship to breast cancer risk has not been characterized. Methods: The histologic presence of PASH was evaluated with pathological review of archival specimens of 9065 women who underwent benign surgical breast biopsy from 1967-1991 at a single institution. PASH was defined as a localized area of fibrosis containing clusters of benign spindle cells and cleft-like spaces, resembling ectatic vessels. Subsequent breast cancers were identified via medical records and a questionnaire. Relative risks were estimated using standardized incidence ratios (SIR), comparing the observed number of breast cancers with those expected based on Iowa SEER data. Results: Among 9065 women, 579 (6.4%) had a predominant histologic finding of PASH. Compared to women without PASH, those with PASH were younger, were more likely to have a palpable mass indicating biopsy, and had less lobular involution (all p<0.0001), while they did not differ by family history of breast cancer or degree of epithelial proliferation. With a mean follow-up of 18.5 years, 823 breast cancers occurred - 34 among women with PASH (5.9%) and 789 in those without PASH (8.8%). Women with PASH had a lower risk of breast cancer (SIR 1.03, 95% CI 0.71 to 1.44) than those without PASH (SIR 1.54, 95% CI 1.43 to 1.65), p=0.01. After statistical adjustment for degree of involution and epithelial proliferation, the strength of association remained the same (p=0.01). Lower levels of breast cancer risk for the PASH subgroup persisted in analyses stratified by age, biopsy year, indication for biopsy, epithelial proliferation, involution, and family history. There was no significant difference in breast cancer risk among women with PASH who had a palpable mass indicating biopsy versus a mammographic finding that led to biopsy. Conclusions: PASH is found in a minority of women undergoing benign surgical breast biopsy. Despite the clinical concern generated by palpable density often associated with PASH, this histologic finding carries no higher risk of subsequent breast cancer than the general population.

75

Risk Factors for False Negative (FN) Sentinel Lymph Node (SLN) Biopsy Performed After Neoadjuvant Chemotherapy (NeoCTX) in Patients Presenting with Node-Positive Breast Cancer A. Kolli,* T.M. Breslin, M.S. Sabel, K.M. Diehl, V.M. Cimmino, A.E. Chang, L.A. Newman. *University of Michigan, Ann Arbor, MI.*

Background: Accuracy of SLN biopsy following neoCTX has been debated. Our goal was to identify risk factors for having a FN SLN after neoCTX among pts presenting with node-positive disease. Methods: We examined 169 pts with node positive disease documented by fine needle aspiration (FNA) or SLN from 1998-2009. Final nodal status was documented at the time of definitive surgery after neoCTX by ALND in all pts and concomitant SLN biopsy in 64 pts. Results: Median age was 48 yrs; avg tumor size 42mm. Of the 169 initially node positive pts, 46 (27.2%) were identified by SLN and 123 (72.8%) were identified by FNA. After delivery of neoCTX, 64 (37.9%) pts were downstaged to node-negativity; pts initially diagnosed by FNA were more likely to have residual nodal disease compared to pts initially diagnosed by SLN (69% vs. 44%; p=0.002). There were 5 FN SLN after neoCTX (7.8%). Pts with larger tumors (ÿ5cm) at presentation were more likely to have a FN SLN (7% vs 1%; p=0.03). Statistically non-significant trends were seen for higher FN rates in pts <50 (4.2% vs 2.1%); no correlations were observed between FN rate and histology; mode of initial node biopsy; or extent of response in the breast. Only one FN case occurred in the last five years of the study. Conclusions: We found that SLN biopsy performed after neoCTX is accurate in pts presenting with node-positive breast cancer, regardless of whether the initial node-positive status is determined by pre-treatment SLN or FNA biopsy. Pts with larger tumors at presentation are more likely to have a FN SLN, consistent with possible tumor emboli and CTX treatment effect. Accuracy of the procedure appears to be associated with a learning curve. Pts with initial SLN biopsy are less likely to have residual nodal disease after neoCTX, probably because the initial SLN were the only sites of metastatic disease in a subset of cases. These findings are relevant to the ACOSOG neoCTX and SLN biopsy protocol.

76

Tumor Sampling Variables Affect Reproducibility of Predictive Gene Expression Signatures in Breast Cancer B.R. Untch,* M. Abdelgadir Adam, C.L. Tebbit, J.R. Marks, J.A. Olson. *Surgery, Duke University Medical Center, Durham, NC.*

Introduction: Variation in tumor sampling and processing may influence application of gene expression signatures. The effect of variability on predictive signatures must be evaluated for their clinical utility to be realized. Methods: Twenty-four paired core biopsy breast cancer samples were collected from 12 patients. Five patients donated sequential tumor samples, once at the time of diagnostic radiologic biopsy (R) and again at the time of surgical resection (S). Another 5 patients donated paired specimens that were frozen immediately (non-ischemic, NI) or held for 2 hrs at room temperature (ischemic, I). Two patients had parallel samples subjected to RNA amplification to compare signatures from amplified (A) and unamplified (UA) RNA. Array data was generated on Affymetrix U95AV2 Genechips. Using binary regression analysis, predictions were performed on paired samples for chemosensitivity (adriamycin and 5-FU) and oncogenic pathway activation (Myc and Src). Further, two validated gene signatures from the literature (on similar microarray platform) were applied to the paired samples. Results: Adriamycin chemosensitivity predictions in the R/S, NI/I, and A/UA sample pairs were concordant in 5/5, 5/5, and 1/2 cases, respectively. 5-FU chemosensitivity predictions in the R/S, NI/I, and A/UA sample pairs were concordant in 3/5, 3/5, and 0/2 cases, respectively. Myc oncogenic pathway predictions in the R/S, NI/I, and A/UA sample pairs were concordant in 5/5, 5/5, and 2/2 cases, respectively. SRC oncogenic pathway predictions in the R/S, NI/I, and A/UA sample pairs were concordant in 3/5, 3/5, and 2/2 cases, respectively. Pearson correlation coefficients were performed on the P53 and "Death-from-Cancer"(DFC) signatures. For p53 the R/S group had an r value of 0.6, A/UA had an r value of 0.8 and NI/I had an r value of 0.99. For DFC R/S samples had an r value of 0.98, A/UA was 0.94, and NI/I was 0.86. Conclusions: Core biopsy sample source, ischemic time, and amplification conditions can significantly effect gene expression in breast cancer. The process of applying predictive signatures to clinical samples should be carefully standardized..

77

Metaplastic Breast Cancer: To Radiate or Not to Radiate? W.H. Tseng,* S.R. Martinez. *Surgical Oncology, University of California at Davis, Sacramento, CA.*

Introduction: Treatment-related outcome data are limited for metaplastic breast cancer (MBC), which has been associated with poor prognostic factors. We hypothesized that radiation therapy (RT) would improve overall

survival (OS) and disease specific survival (DSS). Methods: We used the Surveillance, Epidemiology, and End Results (SEER) database to identify patients with MBC diagnosed between1988-2006. Univariate analyses of patient, tumor, and treatment-specific factors on OS and DSS were performed using the Kaplan-Meier method and differences among survival curves assessed using the log rank test. Variables included patient age, race, histologic subtype, tumor grade, tumor size (T stage), lymph node status (N stage), presence of metastasis (M stage), hormonal receptor status, type of surgery, and use of RT. Cox proportional hazards models utilized all covariates from univariate analysis. Risks of overall and breast-specific mortality were reported as hazard ratios (HR) with 95% confidence intervals (CI). Results: Among 1,589 patients, 10 year OS and DSS were 54.5% and 69.2%. Histologic subtype, tumor grade, T, N, and M stage, surgery type, and RT demonstrated significant OS and DSS differences on univariate analysis ($p<0.001$). 54.8% of patients received mastectomy and 41.2% of patients received lumpectomy. RT was given to 615 (38.7%) of patients (23.8% of mastectomy patients and 61.8% of lumpectomy patients). RT provided an OS (HR 0.63, CI: 0.50-0.80; $p<0.001$) and DSS (HR 0.70, CI: 0.53-0.91; $p<0.01$) benefit in the entire cohort. When stratified according to type of surgical procedure, the survival advantage attributable to RT persisted. RT provided an OS (HR 0.50, CI: 0.33-0.77 $p<0.002$) and DSS (HR 0.52, CI: 0.32-0.86; $p<0.01$) benefit in lumpectomy patients and an OS (HR 0.65, CI: 0.47-0.89; $p<0.007$) and DSS (HR 0.69, CI: 0.48-0.99; $p<0.05$) benefit in mastectomy patients (see Table 1). Conclusions: RT significantly reduces mortality in MBC in patients undergoing mastectomy or lumpectomy. Use of RT in MBC should be evaluated in the setting of a clinical trial to confirm or refute these findings.

Table 1. Hazard Ratios of Radiation Therapy on Multivariate Analysis among Several Surgical Cohorts

Cohort	OS HR	CI 95% / p value	DSS HR	CI 95% / p value
Entire Cohort (n=1,589)	0.63	0.50-0.80; p<0.01	0.70	0.53-0.91; p<0.01
Lumpectomy Only (n=655)	0.50	0.33-0.77; p=0.002	0.52	0.32-0.86; p=0.01
Mastectomy Only (n=871)	0.65	0.47-0.88; p=0.007	0.69	0.48-0.99; p=0.048

78

Treatment of Advanced Dermatofibrosarcoma Protuberans (DFSP) with Imatinib Mesylate and with or without Surgical Resection

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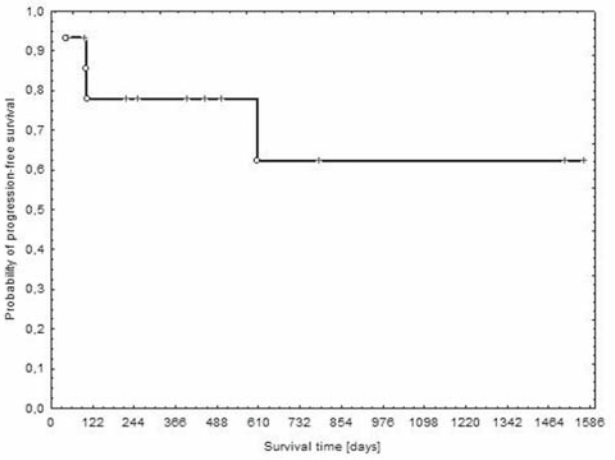
Introduction: Dermatofibrosarcoma protuberans (DFSP) is rare soft tissue sarcoma of skin characterized by a specific translocation t(17;22)(q22;q13). The aim of the study was analysis of patients with advanced DFSP patients treated with imatinib and with or without surgery in clinical practice outside trials. Patients and Methods: We analyzed data of 15 patients (6 male, 9 female; median age 56 years) with locally advanced/initially inoperable and/or metastatic DFSP treated with imatinib 400-800 mg daily between 12/2004 and 06/2009. All diagnoses were confirmed cytogenetically (FISH). Median follow-up time 16 months (range: 4-81). Results: Metastases were present in 6 cases (2 – lungs, 2 – soft tissues, 2 – lymph nodes). Fibrosarcomatous transformation (FS-DFSP) was confirmed in 7 patients (47%). 2-year progression-free survival (PFS) rate was 60% [Fig.1], 2-year overall survival (OS) rate was 78% (median time for PFS/OS was not reached). The best overall responses were: 10 partial responses (67%, including 5 FS-DFSP - 1 progressed during follow-up), 2 stable disease (13%) and 3 progressive diseases (20%). Seven patients (47%) underwent resection of residual disease and remain free of disease. Conclusions: We have confirmed profound antitumor effect of imatinib in DFSP harboring t(17;22) with long-term responses. Imatinib therapy may lead in some cases to resectability of the tumor or diminishing possible disfiguring.

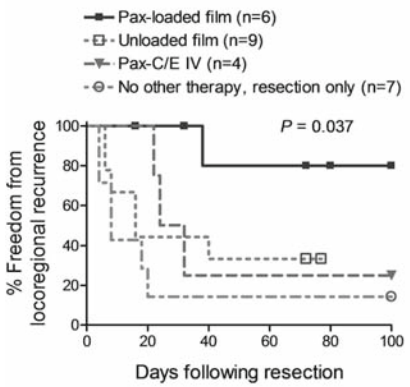


79

Paclitaxel-Eluting Polymer Film Reduces Locoregional Recurrence in Mouse Model of Sarcoma: A Novel Investigational Therapy

R. Liu,[1]* J.E. Wade,[1] J.B. Wolinsky,[2] J.H. Winer,[1] P.J. Catalano,[3] A.J. Wagner,[3] M.W. Grinstaff,[2] Y.L. Colson,[1] C.P. Raut.[1] *1. Brigham and Women's Hospital, Boston, MA; 2. Boston University, Boston, MA; 3. Dana-Farber Cancer Institute, Boston, MA.*

Background: Locoregional recurrence is observed in up to 50% of patients after macroscopically complete (R0/R1) resections of retroperitoneal sarcomas (RPS). For RPS, chemotherapy does not reduce locoregional recurrence, and radiotherapy remains investigational. We evaluated the efficacy of a novel drug-eluting film *in vitro* and in a mouse model of recurrent sarcoma. **Methods:** Flexible poly(glycerol monostearate-co-caprolactone) films (10x8mm) were synthesized with and without 300μg paclitaxel (Pax-film and unloaded film). Cytotoxicity was assessed *in vitro* by exposing films to freshly plated CS-1 (human chondrosarcoma) cells. Tumors were induced *in vivo* by subcutaneous flank injection of $2.0x10^6$ CS-1 cells in nude mice. Following R0/R1 resection, mice were randomized to 1 of 4 treatment arms: 1) Pax-film implant, 2) unloaded film implant, 3) paclitaxel 300μg IV, or 4) no other therapy. **Results:** *In vitro*, Pax-films reduced cell viability to <6% when measured longitudinally at 6 time points up to 60d while unloaded films did not (77-100% viable) ($P<0.001$, *t*-test). *In vivo*, primary tumors were resected 14-28d after CS-1 injection. Tumor size (890 ± 326 mm^3, mean ± SD) and body weight (2d and 4d after resection) were similar in all 4 arms. Locoregional recurrence (any tumor within a 5mm perimeter of the film edge) was observed in 1 of 6 mice (17%) treated with Pax-film (seen at 38d), 6/9 mice (67%) treated with unloaded film (median time to recurrence, or TTR, 16d), 3/4 mice (75%) treated with paclitaxel IV (median TTR 28d), and 5/7 (71%) mice with no therapy (median TTR 8d) ($P=0.037$, log-rank). Distant metastases (lung) were observed in 0/6, 2/9 (22%), 2/4 (50%), and 3/7 (43%) mice in the 4 arms, respectively. Median overall survival was not reached for Pax-film, and was 63d, 81d, and 31d in the 3 remaining arms, respectively ($P=0.156$, log-rank). **Conclusions:** Tumor bed implantation of slow-eluting Pax-films after R0/R1 resection reduced locoregional recurrence rates in a mouse model of recurrent chondrosarcoma. This represents a potentially novel therapy for improving local control for sarcomas in locations such as the retroperitoneum.

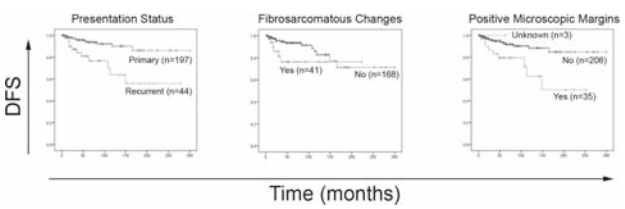


Implantation of Paclitaxel-loaded film after tumor resection reduces local recurrence (P = 0.037).

80

Dermatofibrosarcoma Protuberans (DFSP): Predictors of Recurrence and Response to Neoadjuvant Therapies R.C. Fields,* S. Singer, M.F. Brennan. *Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

INTRODUCTION: DFSP is a soft tissue malignancy with high rates of local recurrence, especially the fibrosarcomatous variant (FS-DFSP). The rare nature of this tumor has precluded large studies to identify biologic factors associated with more aggressive tumors. We examine clinicopathologic factors associated with disease-free survival (DFS) in patients with localized, resectable DFSP and evaluate the response to neoadjuvant therapy in patients with advanced DFSP. METHODS: Patients treated for DFSP were identified in a prospectively maintained database from 1982 – 2008. Patient, tumor, pathologic, and treatment factors associated with DFS were analyzed using the log rank test and Cox regression analysis. Kaplan-Meier analysis was performed to determine DFS. RESULTS: 244 patients with DFSP were included (197 primary tumors, 44 local recurrences, 3 metastatic disease). 98% underwent wide resection as their initial treatment. Median follow-up was 57 months. 23 patients had a local recurrence with a median time to recurrence of 35 months. 6 patients recurred with distant metastases. Actuarial 5-year DFS was 91%. On univariate and multivariate analysis, presentation with local recurrence, presence of FS-DFSP, and positive microscopic margins were associated with recurrence ($p < 0.001$ for all, see Figure). 22 patients with unresectable local recurrence or metastatic disease recurrence were treated with non-surgical therapy (14 radiotherapy, 4 tyrosine kinase inhibitor (TKI) only, 2 conventional chemotherapy only, 2 chemotherapy plus TKI). Radiation and TKI therapy resulted in objective clinical or radiographic partial responses, but no complete responses, in all patients. CONCLUSIONS: DFS after treatment for DFSP is strongly predicted by the presence of the FS-DFSP variant, margin, and presentation status. When possible, the treatment for recurrence is re-excision. TKI's and radiation, are effective agents for local recurrence and metastatic disease not treatable by resection, but should be considered palliative. No data exists to support the use of these modalities for adjuvant treatment in high-risk patients outside the context of a clinical trial.



Disease-free survival (DFS) segregated by presentation status, presense of fibrosarcomatous changes, and margin status in patients treated for dermatofibrosarcoma protuberans (DFSP)

81

Limb Preservation with Isolated Limb Infusion for Unresectable Non-melanoma Cutaneous and Soft Tissue Malignancies K.K. Turaga,[1]* G.M. Beasley,[2] R.J. Gonzalez,[1] K.A. Delman,[3] G.D. Letson,[1] D. Cheong,[1] D.S. Tyler,[2] J.S. Zager.[1] *1. H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; 2. Duke University, Durham, NC; 3. Emory University, Atlanta, GA.*

Introduction: Advanced, unresectable non-melanoma cutaneous and soft tissue malignancies (CSTM) including sarcomas (STS) of the extremities can pose significant treatment challenges. Previous single institution studies have shown 53-90% response rates to Isolated Limb Infusions (ILI). We report our experience including response and limb preservation using ILI in CSTM. **Methods:** We identified 16 patients (pts) with CSTM who underwent 17 ILI's with melphalan and dactinomycin from 2004-09 in 3 institutions. Outcome measures included limb preservation and in-field response rates. Regional toxicity was measured using the Wieberdink (WBD) scale and serologic toxicity via serum creatinine kinase (CK) levels. **Results:** Median age was 71 years (range, 19-92 years), and 50% were female. Five pts (31%) had pleomorphic undifferentiated sarcoma, 4 pts (25%) had Merkel cell (MCC), and 3 (19%) had epitheliod sarcoma. One pt each had Kaposi's, myxoinflammatory fibroblastic sarcoma, squamous cell carcinoma (SCC) and a sarcoma NOS. Table 1 summarizes intraoperative and perioperative parameters. The median length of stay (LOS) was 7 days (range, 3-10) . Twelve of 17 (71%) of the ILIs resulted in WBD grade I -II toxicity, 4 ILIs (24%) led to grade III toxicity; 1 (5%) patient developed grade IV toxicity. No patient developed grade V toxicity. Median serum CK was 227 U/l and 2292 U/l and the median LOS was 5.5 and 8 days for upper and lower extremity ILIs respectively. All but one pt had successful limb preservation resulting in 94% limb preservation. Of the 14 evaluable pts at least 3 month follow up, the in field overall response rate was 78% (36% complete and 42% partial). One pt had a repeat ILI after progressive disease after an initial partial response. One pt has stable disease and 2 have progressed in field.. The overall 3 month progression free response rate is 86%; 100% in pts with MCC and SCC, while it is 78% for pts with STS. **Conclusions:** ILI provides an attractive alternative therapy for regional disease control and limb preservation in pts with limb threatening CSTM. Short term response rates appear encouraging yet durability of response is unknown.

Table 1: Outcomes of patients with unresectable non melanoma cutaneous and soft tissue malignancies after an ILI.

Characteristics	Upper Limb (N=8)	Lower Limb (N=9)
Mean Limb Volume (±SD)	2.3 (±0.6)	7.0 (±2.7)
Melphalan Dose (mg)	18.5 (±6.3)	40.3(±11.5)
Dactinomycin Dose (mcg)	231 (±61)	567(±187)
Dose adjusted for corrected Ideal Body Weight*	83%	85%
Intraoperative Papaverine Administration	62%	67%
Median Ischemia Time (mins)	59(46 to 99)	56(46 to 81)
Perfusate Blood Gas (30 min)		
Median Base Excess (meq)	-14.7(-10.1 to -24)	-9.7 (-3.3 to -14.9)
Median PaO2 (mmHg)	15.7 (5.6 to 36)	5 (5 to 21)
Mean pH	7.04 (6.8 to 7.10)	7.14 (6.98 to7.28)
Median Peak CPK (U/ml)	227 (69 to 5448)	2292(70 to 7170)
Median Day of Peak of CPK	2 (1 to 6)	6(2 to 8)
Median Length of Stay	5.5 days (3 to 9)	8 days (5 to 10)
WBD Toxicity		
Grade I-II	6 (75%)	6 (67%)
Grade III-V	2 (25%)	3 (33%)
Overall Response Rate (CR+PR)	83% (50%+33%)	75% (25%+50%)
Merkel Cell Ca	100% (100%+0%)	100% (50%+50%)
Squamous Cell Ca	100% (0%+100%)	-
Soft Tissue Sarcoma	75% (25%+50%)	67% (17%+50%)

* Data missing on 4 patients, 2 for each extremity

82

Revisiting the role of surgery in the management of abdominal desmoid tumors S. Siddique,* R. Kandel, C.J. Swallow, R.A. Gladdy. *Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada.*

Introduction: Desmoids can be locally aggressive and complete resection may compromise function; the ideal management is controversial. The aim of this study is to evaluate outcomes in patients with abdominal desmoids managed by surgery alone, surgery + other modalities, or a variety of non-operative strategies. Methods: Between 1980 and 2009, 189 patients with intra abdominal or abdominal wall desmoids were assessed at our institution, which specializes in the management of hereditary GI cancer. Management included surgery (S), chemotherapy (C), hormonal therapy (HT) and/or radiation therapy (RT), or observation alone. Results: Median patient age was 36 yrs (14 to 77) and 74% were female; 90% presented with primary tumor. The majority of desmoids were sporadic (58%) but 79 occurred in FAP (42%); 56% of tumors were intra abdominal and 44% in the abdominal wall. Of the 91 women with sporadic tumors, all 24 of the recently pregnant patients (within 2 yrs) had abdominal wall desmoids. 94 patients had surgery as part of their treatment consisting of: surgery alone (n=67), S+C or HT (20), S+RT (5), S+RT+C (2). 95 patients had non-operative therapy consisting of HT (34), C (4), C+HT (10), RT (1) or clinical/radiologic observation alone (46). Surgery was less frequent in FAP patients (40% vs. 55% in nonFAP, p=0.02). The median tumor size with smaller in those resected vs. not (7.0 vs. 8.3 cm, p=0.03). Early in this experience, there were 4 desmoid-related post-op deaths, all in FAP patients. Median follow-up time from initial assessment was 65 mos (1 to 331 mos). Overall 5 yr survival was 93% in patients managed with resection ± other modalities, and 99% in those treated non-operatively (p=ns). In the 22 women with postpartum abdominal wall desmoids initially managed non-operatively, 8 required subsequent resection for symptomatic progression. Conclusions: The long-term survival is excellent for abdominal desmoids regardless of treatment strategy. Surgical management should be considered in patients with progressing disease after a period of observation or failure of other modalities. Non-operative management is appropriate in postpartum abdominal wall desmoids.

83

Testicular/Scrotal Soft Tissue Sarcomas: Confusing Presentation and Diverse Biologic Behavior R.D. Bennett,[2] J.M. Kane.[1]* *1. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY; 2. University at Buffalo School of Medicine, Buffalo, NY.*

Introduction: Soft tissue sarcomas (STS) of the testicular/peritesticular (TES), spermatic cord (SPC), and scrotal (SCR) areas are uncommon and may often be confused with testicular cancer. Given the diverse biologic behavior, optimal treatment and outcome are not well defined. Methods: Retrospective review of 24 patients treated at a single institution from 1971-2008. Demographics, tumor features, surgical and adjuvant therapy, and outcome were evaluated. Results: Median age was 31.5 years (range 5-76) and 96% were Caucasian. Median tumor size was 4.5 cm (range 0.8-12.9). Primary tumor site was 37.5% TES, 33.3% SPC, 25% SCR, and 4.2% unclear. Tumor histology was 33.3% leiomyosarcoma (LMS), 29.2% embryonal rhabdomyosarcoma (ERM), 20.8% non- embryonal rhabdomyosarcoma (RMS), 12.5% liposarcoma (LIP), and 4.2% synovial sarcoma (SS). Nine patients (37.5%) underwent orchiectomy to make the diagnosis; 6 via an inguinal incision. Nodal metastases were present at diagnosis in 25% (5 ERM and 1LMS) and distant metastases in 12.5%. For non TES location, the testicle was preserved in 40% (5 SCR and 1 SPC). 41.7% received adjuvant radiation. 66.7% received systemic chemotherapy at some point. Median follow-up was 33.6 months (range 1.5-420). The site of first recurrence was local in 4 patients (2 successfully salvaged with additional surgery), nodal in 1 patient, and distant in 5 patients. Disease status at last follow-up was 37.5% no evidence of disease, 4.2% alive with disease, 4.2% alive unknown, 8.3% dead without disease, and 45.8% dead of disease. Survival by tumor histology was 71.4% for ERM, 50% for LMS, 40% for RMS, 66.7% for LIP, and 100% for SS. Survival for SCR location was 83.3%. Conclusions: A high index of suspicion for testicular/scrotal STS, especially in older patients not likely to have testicular cancer, could potentially avoid a suboptimal surgical approach such as an inguinal incision. SCR STS appears to behave similarly to STS at other non-genitourinary anatomic locations. Even with nodal metastases, survival for ERM/RMS was reasonable following multimodality therapy.

84

Dose Reduction in Isolated Limb Perfusion for Soft Tissue Sarcoma of the Extremities is Safe and Effective in Terms of Long-term Patient Outcome M.L. Hoven- Gondrie,* E. Bastiaannet, R.J. Van Ginkel, A.J. Suurmeijer, H.J. Hoekstra. *University Medical Center Groningen, Groningen, Netherlands.*

Introduction. The optimal dose of TNF-α for isolated limb perfusion with TNF-α and Melphalan (TM-ILP) is not well established. Dose reduction is associated with less systemic toxicity and seems to be effective in terms of response rate and short-term patient outcome. Data on long-term patient outcome are however not widely available. Methods. From 1991 to 2008, 101 TM-ILPs were performed for a locally advanced soft tissue sarcoma of the extremity. After 58 TM-ILPs, perfusion duration was shortened from 90 to 60 minutes. In 27 TM-ILPs a reduced dose TNF-α (1 or 2 mg instead of 3 or 4 mg) was used. Pathological response rate, quality of surgery and long-term patient outcome were evaluated. Results. Complete response rate after reduced-dose TM-ILP was 11.1% vs 25.7% after standard-dose TM-ILP. Adjusted for perfusion duration, no significant difference in overall response rate (CR/PR) was found (59.3% vs 83.8%, OR 2.9, 0.7-12.9, p=0.15). There was no difference in quality of surgery with 76.8% R0- resections after reduced-dose TM-ILP vs 79.2% after standard-dose TM-ILP (p=0.97). Limb salvage was 85.2% in the reduced-dose group vs 73.0% in the standard-dose group (HR 1.6, 0.5-4.8, p=0.38). With a median follow up of 76 (range 2-203) months, 53 patients (52.5%) were still alive .Disease specific 5-year survival was not different between low-dose and standard-dose TM-ILP; 58.8% vs 49.2%, (HR 1.4, 0.7-2.9, p=0.38). There was no difference in local recurrence free 5-year survival (95.8% vs 80.5%, HR 4.4, 0.6-34, p=0.15) and distant metastases free survival (36.4% vs 54.2%, HR 0.91, 0.4-1.8, p=0.78). Conclusions. Dose reduction in TM-ILP had no significant impact on pathological reponse rate, quality of surgery and limb survival. 5-Year local recurrence free survival, distant metastases free survival and disease specific survival are not compromised by reduced-dose TM-ILP. Dose reduction in TM-ILP seems to be safe and effective in terms of long-term patient outcome.

		High dose TNF	Low dose TNF	Risk, p-value	Adjusted for perfusion duration
		%	%		
Response	NC Overall response (PR/CR)	16.2 83.8	40.7 59.3	OR 3.5 (1.3-9.5) p=0.012	OR 2.9 (0.7-12.9) p=0.15
Resection	R0 R1 R2	76.8 18.8 4.4	79.2 16.7 4.2	p=0.97	
Limb Salvage	Yes No	73.0 27.0	85.2 14.8	HR 1.6 (0.5-4.8) p=0.38	
5-Year local recurrence free survival		80.5 (67.5-88.8)	95.8 (73.9-99.4)	HR 4.4 (0.6-34) p=0.15	
5-Year distant metastases free survival		54.2 (40.6-66.0)	36.4 (10.9-63.1)	HR 0.91 (0.4-1.8) p=0.78	
5-Year Disease specific survival		49.2 (36.9-60.4)	58.8 (34.4-76.8)	HR 1.4 (0.7-2.9) p=0.38	

85

Conditional Survival of Extremity Soft Tissue Sarcoma: Results Beyond the Staging System H.M. Parsons,[1]* W.B. Al-Refaie,[2] T.M. Tuttle,[1] E.B. Habermann.[1] *1. Department of Surgery, University of Minnesota, Minneapolis, MN; 2. Minneapolis Veteran Affairs Medical Center, Minneapolis, MN.*

Background: With growing attention to adult cancer survivorship, current staging and prognostic estimates provide limited information for long-term survivors of extremity soft tissue sarcoma (ESTS). We assessed determinants of survival in adults surgically treated for non-metastatic ESTS conditional on specific survival periods. Methods: We identified 6,215 persons aged >18 in the Surveillance Epidemiology and End Results program who were surgically treated for non-metastatic ESTS from 1991-2006. We used Cox proportional hazards regression to assess demographic, tumor and treatment factors associated with 10-year sarcoma-specific survival (SSS) at diagnosis and conditional on surviving three and five years post-diagnosis. Results: At the time of diagnosis, age, tumor and treatment factors predicted SSS. While increased age significantly predicted worse SSS for all age groups at diagnosis (HR

3.78 for ages >81 vs. 18-35; p<0.05 for all), the effect of age became non-significant as survival time increased, except for the oldest group (>81 years). Tumor and treatment factors continued to be important predictors of SSS for all periods of conditional survival. Larger tumor size predicted worse SSS, even five years post-diagnosis (HR 2.1 for tumors 5.1+cm vs. < 5cm; p<0.05). Additionally, high grade tumors increased mortality risk for all conditional survival periods. The favorable survival effect in persons with myxoid liposarcomas disappears over time, whereas leiomyosarcomas present more than three times the mortality risk compared to malignant fibrous histiocytomas for all three survival periods. Finally, persons who underwent limb amputation were at three times the risk of mortality for all conditional survival periods (Table). Conclusions: In this large population-based experience of ESTS survivors, age >81, tumor and treatment factors continued to affect long-term survival, whereas the effect of age dampens over time. These estimates provide clinicians important counseling information for changing risk factors as survival time increases. Conditional survival can help streamline future surveillance programs and provide insights into the design of adult survivorship care.

Table: 10-Year Sarcoma Specific Risk of Death for Surgically Treated ESTS Patients

	Overall HR	HR (Conditional on Surviving 3 Years)	HR (Conditional on Surviving 5 Years)
Age			
18-35	Ref.	Ref.	Ref.
36-50	1.37*	1.23	1.08
51-64	1.51*	1.15	0.8
65-80	2.29*	1.56*	1.41
>81	3.78*	3.18*	3.19*
Tumor Size (cm)			
0-5	Ref.	Ref.	Ref.
5+	2.61*	1.93*	2.1*
Unknown Size	1.58*	0.91	1.07
Tumor Grade			
Low Grade	Ref.	Ref.	Ref.
High Grade	3.94*	2.08*	1.79*
Unknown Grade	2.25*	1.49*	1.24
Histology			
Malignant Fibrous Histiocytoma	Ref.	Ref.	Ref.
Leiomyosarcoma	1.13	1.99*	3.14*
Myxoid Liposarcoma	0.63*	0.89	1.08
Other	1.31*	1.46*	1.87*
Treatment			
Limb Sparing Surgery(LSS) Alone	Ref.	Ref.	Ref.
LSS+Radiation	1.01	1.3	1.53
Amputation Alone	1.95*	2.51*	3.31*
N	6215	3483	2322

Note: Regressions also adjusted for patient sex, race, SEER Registry and diagnosis year; HR- Hazard Ratio
* P-value <0.05

86

Prognostic value of pain and quality of life in patients with locally recurrent rectal cancer Y. You,* H. Habiba, G.C. Chang, M.A. Rodriguez-Bigas, J.M. Skibber. *University of Texas M.D. Anderson Cancer Center, Houston, TX.*

Background: Surgical salvage for locally recurrent rectal cancer (LRRC) carries a high morbidity rate but offers the only chance of survival gain in select patients. In addition to oncologic results, knowledge of patient-reported outcomes may aid in treatment selection. We hypothesized that pain and quality of life (QOL) in patients with LRRC impact overall survival (OS). Methods: Pain and QOL were prospectively assessed in 105 patients treated for LRRC at a single-institution, using the validated Brief Pain Inventory (BPI) and the Functional Assessment of Cancer Therapy-Colorectal (FACT-C) questionnaires. In 54 patients enrolled and followed from initial evaluation, relationship between pre-treatment pain, QOL and OS were examined. Results: Patients received surgical therapy of curative intent (60%), surgical palliation (12%), or nonsurgical treatment (28%). Median OS was 7.1, 1.7 and 2.4 years respectively (curative vs. palliative: p<0.0001; curative vs. nonsurgical: p=0.006; palliative vs. nonsurgical, p=0.261). The overall QOL (FACT-C total) and pain intensity reported by patients surviving at different time points after diagnosis of LRRC are summarized below. Compared to curative resection or nonsurgical treatment, surgical palliation showed a trended toward lower QOL at 9 months (FACT-C curative, palliative, or nonsurgical: 95, 53, or 104; p=0.0512). For the 54 patients assessed from diagnosis, pretreatment pain intensity and pain inference scores significantly correlated with FACT-C (Spearman's p<0.0001). After controlling for age and gender, median OS was independently predicted by pain intensity (score ≤ 3 vs. ≥ 4: 4.1 vs. 2.0 years; p=0.025) and treatment group (curative, palliative, vs. nonsurgical: 4.3, 1.7, vs. 2.4 years; p=0.0002). Conclusion: Curative surgery offered prolonged survival, but significant pain exists among long-term survivors and should be a focus of survivorship care in this patient population. Nonsurgical treatments led to similar survival outcomes as surgical palliation but may help preserve QOL. Patient's baseline pain has prognostic value and should be assessed to aid in treatment selection.

	Baseline	3 month	6 month	9 month	1 year	2 year	3 year	8 year
No.	54	37	29	29	29	31	16	5
FACT-C	102 (87, 114)	98 (84, 105)	99 (93, 113)	101 (87, 110)	96 (81, 114)	102 (82,112)	98 (70, 116)	104 (65, 114)
No.	46	36	26	27	12	8	3	3
Pain Intensity	1 (0, 3)	2 (0, 4)	1 (0, 4)	2 (0, 4)	2 (0, 3)	3 (1, 5)	5 (3, 5)	7 (4, 8)

No. indicates number of patients with available survey data. Scores reported as median (interquartile range).

87

Preoperative Factors Predict Morbidity After Pancreaticoduodenectomy: Creation of a NSQIP Nomogram D.Y. Greenblatt,* E. Winslow, V. Rajamanickam, R. Rettammel, C.S. Cho, S.M. Weber. *Department of Surgery, University of Wisconsin, Madison, WI.*

Introduction: Pancreaticoduodenectomy (PD) has long been associated with high rates of morbidity and mortality. Several high-volume centers have reported markedly improved outcomes with the procedure. The objective of this study was to identify preoperative risk factors for serious complications after PD, and to construct a risk-stratification nomogram. **Methods:** Patients who underwent elective PD from 2005-2007 were identified from the American College of Surgeons National Surgical Quality Improvement Project (NSQIP) Participant Use Data Files. Multivariate logistic regression identified predictors of serious complications and adjusted odds ratios were calculated. Using the highly associated preoperative variables identified, a nomogram was created to estimate the risk of serious complications after PD. This prediction tool was validated using 2008 NSQIP data. **Results:** Of 2,750 patients who underwent PD, 746 (27.1%) suffered a serious complication within 30-days. The most frequent complications were sepsis (16.9%), surgical site infections (12.5%), and respiratory complications (9.9%). Rates of 30-day reoperation and mortality were 7.4% and 2.8%, respectively. The mortality rate was significantly higher in patients who had a serious complication (9.4% vs. 0.4%, p<0.001). After adjusting for preoperative risk factors, significant predictors of morbidity included age, race, body mass index, chronic obstructive pulmonary disease, peripheral vascular disease, bleeding disorder, disseminated cancer, and serum albumin. These variables were used to construct a preoperative risk-stratification nomogram. **Conclusion:** In this sample drawn from over 180 academic and community hospitals nationwide, more than one in four patients suffered a serious complication after PD. Complications were associated with high rates of 30-day reoperation and mortality. Preoperatively-determined patient-specific risk factors predicted perioperative morbidity. The resulting nomogram may be used to help estimate the risk of complications for patients undergoing PD, as well as for risk adjustment when comparing surgical outcomes.

Significant predictors of 30-day serious complication after pancreaticoduodenectomy. Odds ratios are adjusted for variables which differed significantly in univariate analysis between the complication and no complication groups: age, gender, race/ethnicity, body mass index (BMI), functional status, dyspnea, chronic obstructive pulmonary disease (COPD), coronary artery disease, peripheral vascular disease (PVD), bleeding disorder, disseminated cancer, WBC, creatinine, alkaline phosphatase, and albumin.

Characteristic	Adjusted OR (95% CI) for Serious Complication
Age 80 years and older	1.89 (1.25 - 2.86)
BMI 30 to 49 kg/m2 (obese)	1.46 (1.14 - 1.88)
COPD	1.67 (1.05 - 2.65)
PVD	2.62 (1.19 - 5.79)
Bleeding disorder	2.42 (1.34 - 4.39)
Disseminated cancer	1.89 (1.10 - 3.26)
Albumin < 2.5 g/dL	2.02 (1.23 - 3.32)

88

Assesment of ACS-NSQIP's Predictive Ability for Adverse Events after Major Cancer Surgery D. Borja-Cacho,[1]* H.M. Parsons,[1] E.B. Habermann,[1] D.A. Rothenberger,[1] W.G. Henderson,[2] W.B. Al-Refaie.[1] *1. Surgery, University of Minnesota, Minneapolis, MN; 2. University of Colorado, Aurora, CO.*

Background: The American College of Surgeons National Surgery Quality Improvement Program (ACS-NSQIP) has improved operative outcomes in the US. However, its applicability to oncologic resections at ACS-NSQIP hospitals has not been fully explored. We assessed the ability of factors currently collected by ACS-NSQIP to predict adverse short-term operative events after major cancer surgery. Methods: Using pre- and intra- operative factors gathered by the 2005-2008 ACS-NSQIP, we constructed logistic regression models to determine their ability to predict 30-day mortality, prolonged length of stay (LOS), major complications or an increased number of complications in patients undergoing major thoracic, abdominal or pelvic oncologic procedures. We assessed each model's predictive ability using the c-index. Results: Over 15,700 patients underwent major thoracic, abdominal or pelvic oncologic resections at 211 hospitals over three years. While the mortality rate was relatively low (2.6%), nearly 24% of patients experienced major operative complications. However, up to 43% of patients with prolonged LOS did not have any major complication noted in the database. Further, our model predicting complications showed poor overall predictive ability compared to those predicting mortality and LOS (c-index < 0.67 vs. 0.80 and 0.73, respectively) (Table). When stratified by procedure (esophageal, pancreatic, or lung resection), the complication model's predictive ability again remained less accurate than models predicting 30-day mortality or prolonged LOS. These results remain unchanged after additional sensitivity analyses. Conclusions: Current ACS-NSQIP variables show low predictive ability for adverse operative events after major oncologic resections. Addition of some disease- and operation-specific variables may be an important consideration in the further evolution of the NSQIP to allow more utility in making predictions of adverse outcomes for specific types of major oncologic resections.

Logistic regression models of short-term operative outcomes after major oncologic resection

	30-day mortality	Prolonged LOS	Increased total number of complications	Major operative events
Number of events	398	3721	4549	3903
Total sample size	15709	14841	15709	15709
Event rate	2.6%	25.1%	29.7%	24.8%
C-index of model	0.804	0.733	0.663	0.672

89

Minimally Invasive Surgery is Underutilized for Colorectal Disease C.N. Robinson,* G.J. Chen, C.J. Balentine, C.L. Marshall, D. Anaya, A. Artinyan, D. Albo, D.H. Berger. *Baylor College of Medicine, Houston, TX.*

BACKGROUND: The Clinical Outcomes of Surgical Therapy Group (COST) trial published in 2004 demonstrated that minimally invasive surgery (MIS) for colorectal cancer provided equivalent oncologic results and better short-term outcomes when compared to open surgery. Prior to this, MIS only comprised approximately 3% of colorectal cancer cases. We hypothesize that there would be a dramatic increase in the use of minimally invasive techniques for colorectal cancer following this publication. METHODS: The National Inpatient Sample database was used to retrospectively review minimally invasive and open colorectal resections from 2005- 2007. ICD-9 specific procedure codes were used to identify colorectal cancer resections and laparoscopy. Chi square was used to compare the proportion of laparoscopic cases per year. Cramer's V was used to measure the strength of association. RESULTS: Upon review of 50,628 cases for colon disease, 4.4% (n=2220) were performed laparoscopically (Table 1.). In 2006 and 2007, there was a gradual increase in the percentage of laparoscopic cases from 5.0% (n=2539) to 5.6 % (n=2880). For rectal disease, of the 9,650 cases performed in 2005, only 0.9% (n=274) were performed laparoscopically. The use of MIS for rectal disease remained relatively unchanged from 1.2% (n=360) to 1.4% (n=411) between 2006 and 2007. Specifically for colon cancer, there was no significant change from 2005 to 2007 (5.3% vs. 7.19%, p<0.031). The utilization for rectal cancer remained stable (1.0% vs. 1.4%, p<0.007). The use of MIS for benign disease was also very low, and remained flat for both colon (3.6% vs. 4.4%, p<0.017) and rectal disease (0.8% vs. 1.4%, p<0.002). Despite being a significant change, the effect size of this increase was small as determined by Cramer's V (0.031)(Table 1.). CONCLUSION: Adoption of minimally invasive techniques for the treatment of colorectal cancer has been slow. This is not likely due to fears of worse cancer related outcomes from laparoscopic resections. Additional studies to evaluate barriers to adoption of minimally invasive colorectal cancer resection are warranted.

Table 1. The trend in minimally invasive surgery (MIS) for benign colorectal lesions and cancer from 2005-2007.

	2005	2006	2007	P-value	Cramer's V
COLON					
Proportion of MIS cases	4.4%	5.0%	5.6%	p< 0.001	0.023
Benign disease	3.6%	4.1%	4.4%	p< 0.001	0.017
Cancer	5.3%	6.2%	7.1%	p< 0.001	0.031
RECTAL					
Proportion of MIS cases	0.9%	1.2%	1.4%	p< 0.001	0.026
Benign disease	0.8%	1.4%	1.4%	p< 0.002	0.035
Cancer	1.0%	1.1%	1.4%	p< 0.007	0.022

90

Improving on National Quality Indicators of Breast Cancer Care in a large public hospital as a means to decrease disparities for African American women M. Rizzo,[1]* H. Bumpers,[2] J. Okoli,[2] D. Senior-Crosby,[3] S. Hearn,[3] R. O'Reagan,[4] A. Zelnak,[4] S.G. Patterson,[2] S.G. Gabram.[1] *1. Department of Surgery Emory University School of Medicine, Atlanta, GA; 2. Department of Surgery Morehouse University School of Medicine, Atlanta, GA; 3. Avon Comprehensive Breast Center at Grady, Atlanta, GA; 4. Hematology Oncology Winship Cancer Center, Atlanta, GA.*

Introduction In April 2007, the National Quality Forum (NQF)endorsed the first nationally recognized hospital-based performance measures for cancer care. We chose to study two breast cancer(BC)indicators. Radiation therapy is administered within 365 days of diagnosis for women receiving breast conserving surgery (BCS) and combination chemotherapy is considered or administered within 120 days of diagnosis for women with the American Joint Committee on Cancer (AJCC) T1cN0M0, Stage II and III, and hormone receptor negative BC. Methods Tumor Registry and medical records were used to identify patients and their demographics and treatments, including dates. After reviewing data from 2005 and 2006, the following changes were implemented: a dedicated nurse practitioner in medical oncology was hired, the radiation oncology social worker attended weekly multidisciplinary conferences for continuity and coordination of care. Patient navigators were trained and conducted support groups for patients regarding multi-modal care. Results A total of 213 female patients under age 70, were diagnosed and treated with Stage I, II, or III breast cancer at our center in years 2005-06 and 2008. 189 (89%) were AA women. Of the total, 86 (40.3%) qualify for adjuvant radiation therapy and 77

(36%) for adjuvant chemotherapy. Overall, 70 patients (81.3%) received radiation therapy and 59 (76.6%) received adjuvant chemotherapy. After our implementations, patients receiving radiation therapy increased from 78.2% in 2005 to 95.8% in 2008 per NQI. The number of patients who received or were offered adjuvant chemotherapy per NQI increased from 72.4% in 2005 to 87.5% in 2008. These improvements approach National Comprehensive Cancer Network (NCCN) NQI data: 96% for radiation and 91% for chemotherapy indicators. Conclusions NQF BC indicators provided a mechanism to improve care and compliance to treatment in our center and compare favorably with NCCN results. Raising awareness of these indicators in multidisciplinary conference, hiring dedicated personnel and educating patients has led to major improvements in our BC quality of care.

91

Comparison of a novel favorable pathology model with stage (clinical or pathologic) or biopsy Gleason score for predicting biochemical recurrence M.J. Donovan,* F. Khan, V. Zubek, D. Powell, J. Alter. *Aureon Laboratories, Yonkers, NY.*

INTRODUCTION: We have developed a pre-operative clinical-tissue based integrative (systems pathology) model to predict Favorable Pathology (FP) outcome of prostate cancer using the diagnostic biopsy specimen and pretreatment clinical variables from men treated by radical prostatectomy (RP). FP is a composite endpoint which includes: <= pT2, no Gleason grade 4 or 5 in the prostatectomy and a biochemical recurrence (BCR) free PSA level (<0.01) post RP. We sought to compare the FP model with both clinical and pathologic stage for predicting BCR, defined as a single PSA value >0.4ng/ml. METHODS: Paraffin-embedded prostate needle biopsy tissue from 255 men with cT1c – T3 (84.7% <=cT2a, 10.5% cT2b/c, 4.8% cT3) cancer treated with RP and followed for median 8 years was evaluated. Pathologic stage was 25.9% <=pT2a, 50.2% pT2b/c, and 23.9% pT3. A multivariate model for predicting FP was developed integrating pre-treatment clinical variables with quantitative biometric features derived from the needle biopsy. The univariate concordance index (CI) was used to estimate performance. RESULTS: Variables including clinical and pathologic stage, biopsy Gleason score and outcome (BCR) were obtained from the cohort. The probability of having a FP was based on a previously developed feature set which included two clinical (pretreatment PSA and biopsy Gleason score) and four tissue characteristics; one which measures the amount and dynamic range of Androgen Receptor protein in tumor epithelial nuclei, one which measures the degree of Ki67 and two features which quantify the overall cellular architecture of the tumor. The cTNM predicted BCR with a univariate CI of 0.54 (p= 0.08), pTNM CI was 0.59 (p= 0.0017) and the biopsy Gleason score CI was 0.62 (p<0.001). By comparison the FP model CI was 0.69 (p<0.001). CONCLUSION: Systems based pretreatment models which integrate biometric features of the patient's diagnostic prostate needle biopsy and clinical data were more accurate than stage (either clinical or pathologic) or biopsy Gleason score for predicting BCR.

92

Standardization and Documentation of Surgical and Pathologic Variables in a Multi-Institutional Trial of Adjuvant Therapy for Pancreatic Cancer: Results From ACOSOG Z5031 M.H. Katz,[1]* N.B. Merchant,[2] S. Brower,[3] M. Campbell,[4] M. Posner,[5] L.W. Traverso,[6] R.A. Abrams,[7] V.J. Picozzi,[6] P.W. Pisters.[8] *1. Surgery, UC Irvine, Orange, CA; 2. Vanderbilt University Medical Center, Nashville, TN; 3. Memorial Health University Medical Center, Savannah, GA; 4. Mayo Clinic, Rochester, MN; 5. University of Chicago, Chicago, IL; 6. Virginia Mason Medical Center, Seattle, WA; 7. Rush University Medical Center, Chicago, IL; 8. UT-MD Anderson Cancer Center, Houston, TX.*

Introduction: Standardization of surgical technique and pathologic assessment of the specimen is crucial to the interpretation of studies evaluating adjuvant therapies for resectable pancreatic cancer (PC). The purpose of this study was to critically evaluate surgical and pathological quality control and documentation in a national trial of adjuvant therapy. Methods: Operative and pathology reports of patients enrolled on ACOSOG Z5031– a multi-institutional protocol of adjuvant chemoradiation following pancreaticoduodenectomy (PD)– were rigorously evaluated by four surgical oncologists. Surgical and pathologic variables with the potential to influence staging or outcome were analyzed. Results: 80 patients reported to have undergone R0 (75%) or R1 (25%) pylorus-preserving (37%) or standard (63%) PD were recruited by 16 high-volume centers (range 1–13 patients/center). A search for metastases was documented in 96% of operative reports, but only 80% and 68% described evaluation of the liver or peritoneum, respectively. The proximity of the tumor to the superior mesenteric vein was reported in 69%; major vein resection was required in 9% and lateral venorrhaphy in 14%. The method of dissection along the superior mesenteric artery (SMA) was described in 71%: ultrasonic dissection (16%), stapler (23%), and clamp and cut (56%). SMA skeletonization was described in only 14% and absence of residual macroscopic disease after resection was documented in 24%. The surgeon reported marking the critical SMA margin in 25%, specimen inking was documented in 65% of cases and histologic evaluation of the SMA margin was reported in 47%. A median of 12 lymph nodes was obtained (range 1–49). TNM stage was documented in 49% of pathology reports and only 34% met basic College of American Pathologists criteria. Conclusions: Multi-institutional trials of adjuvant therapy after PD suffer from a lack of quality control of surgical technique, pathologic assessment of the specimen and associated documentation. Attention must be paid to these critical issues to facilitate analysis and interpretation of trial results.

93

Individual Item Analysis of Quality of Life Assessments Related to Laparoscopic-assisted Colectomy in the COST Trial 93-46-53 (INT 0146) C.H. Stucky,[1]* B.A. Pockaj,[1] P.A. Novotny,[2] J.A. Sloan,[2] D.J. Sargent,[2] M.J. O'Connell,[3] R.W. Beart,[4] J. Skibber,[5] H. Nelson,[2] J.C. Weeks.[6] *1. General Surgery, Mayo Clinic Arizona, Phoenix, AZ; 2. Mayo Clinic Rochester, Rochester, MN; 3. Allegheny General Hospital, Pittsburgh, PA; 4. University of Southern California, Los Angeles, CA; 5. MD Anderson, Houston, TX; 6. Dana Farber Cancer Institute, Boston, MA.*

Introduction: Laparoscopic-assisted colectomy (LAC) has been shown to minimally improve short-term post-operative quality of life (QOL) when compared with open colectomy. The question arises whether summated scores from multi-item QOL assessments are sufficiently sensitive to detect the true QOL benefits of LAC. The aim of this study was to determine whether specific subdomains of QOL items are more sensitive to QOL changes and patient outcome. Methods: Specific QOL variables were analyzed in 449 randomized patients from the COST Trial 93-46-53 (INT 0146) using stepwise linear regression models in an intention-to-treat analysis. Separate models were run for each endpoint and for changes: Day 2, Week 2, Month 2, and Month 18 after surgery. Survival was analyzed using Kaplan-Meier curves, log-rank tests and Cox proportional hazards models. Results: 449 colon cancer patients underwent LAC (230 total, 172 LAC and 58 LAC converted to open) and open colectomy (219). Baseline QOL was the most significant predictor of post-op QOL at every time point and every specific sub-domain QOL item. Table 1 shows where LAC was associated with better overall QOL and other sub-domain QOL items at various time points. Post-operative complications were associated with worse quality of life index at Week 2 but this resolved by Month 2. Patients with a low baseline QOL (≤50 out of 100) had worse health and fatigue at Week 2 and Month 2. Survival was not related to treatment or baseline QOL but was related to stage (p<0.0001), age (p=0.03), baseline health (p=0.0032), baseline support (p=0.001) and baseline outlook (p=0.01). Conclusions: Overall QOL represented by summated scores from multi-item assessments may not truly delineate the differences between surgical techniques. A more extensive analysis of specific QOL measures may describe potential benefits or disadvantages to a surgical procedure. A single-item baseline assessment of outlook appears to impact overall survival. This has been shown in other studies. Therefore, identification and early intervention of at-risk patients could lead to improved survival.

Table 1.

Dependent Variable	Time	p-value
Nausea Distress	Month 2	0.03
Appetite	Week 2	0.03
Appetite	Month 2	0.04
Pain Frequency	Month 2	0.04
Breathing	Day 2	0.05
Outlook	Month 18	0.0052
Overall QOL	Week 2	0.02
Overall QOL	Month 18	0.05

ABSTRACTS

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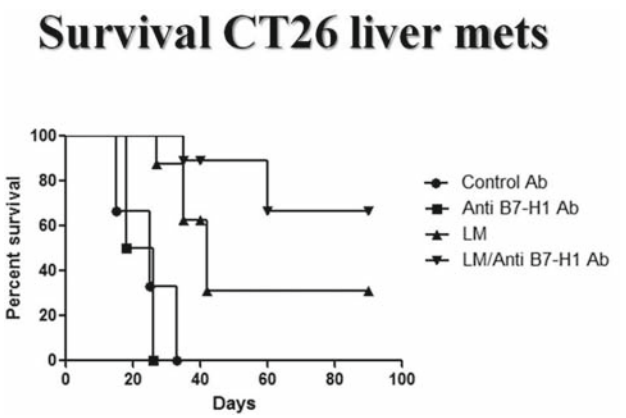
P1

Modulation of Immune Checkpoint B7-H1/PD-1 Interaction Improves Immunotherapy in the Treatment of Hepatic Colorectal Metastasis B.H. Edil,* K. Olino, X. Pan, S. Wada, W. Weber, D.M. Pardoll, R.D. Schulick, K. Yoshimura. *Surgery, Johns Hopkins, Baltimore, MD.*

Introduction: B7-H1 is expressed on dendritic cells (DCs), macrophages, T/B cells and various cancer cell lines. B7-H1 when bound to its T-cell receptor, programmed death-1 (PD-1) induces inhibition of T cell responses. These are potential targets of therapy in metastatic colorectal cancer as the cancer and the liver microenvironment express B7H1, while tumor infiltrating CD8+ T cells express PD-1. Cancer is able to exploit the B7H1-PD-1 inhibitory mechanism making the blockade of this interaction a potential enhancement of our already validated vaccine platform of doubly attenuated Listeria Monocytogenes (LM). Methods: Isolated hepatic metastases were generated in Balb/c mice and treated with intraperitoneal injections of 0.1 x LD50 of LM on postoperative days 3, 6, 9. In addition, intravenous injection of a mouse anti-mouse B7-H1 blocking antibody was given on days 4,7,10 and compared to mice given vaccine alone, antibody alone, and no treatment. We analyzed immune cell populations in the liver with flow cytometry to define the activity, specificity and kinetics. After blockade of B7-H1 we performed survival analysis and in vitro studies for T cell proliferation of activated T cells. Results: Mice treated with LM and B7-H1 showed a 60% survival, LM alone showed 30% survival, while antibody alone and untreated mice did not survive (Fig 1). We first demonstrated B7-H1 expression on colon cancer cell line CT26. We then found CD8+ T cells and conventional dendritic cells (cDC) treated with LM, showed an up-regulation of B7-H1. However, these receptors upregulation were both abgrogated when combined with B7H1 blocking antibody. When B7H1 blocking antibody was used alone, there was a decrease in B7H1 expression but an increased expression on PD-1 on CD8+ T cells. T cell proliferation assay in vitro showed sustained T cell activity with B7-H1 blockade even in the presence of tumor. Conclusion Blockade of B7-H1 is an effective method of overcoming immune evasion and improves the efficacy of LM vaccine in the treatment of metastatic colorectal cancer to the liver.



P2

WITHDRAWN

P3

The Relationship Between Notch1 and Akt-mTOR Signaling in Neuroendocrine Tumors S.C. Pitt,* R.J. Davis, R. Jaskula-Stzul, M. Kunnimalaiyaan, H. Chen. *University of Wisconsin, Madison, WI.*

Introduction: In neuroendocrine (NE) tumors, several signal transduction pathways, including the Notch1 and Akt-mTOR pathways, are known to effect tumorigenesis. We have previously shown that Notch1 activation suppresses tumor growth and NE marker expression in carcinoid and medullary thyroid cancer (MTC), but the relationship of this pathway to others remains unknown. In this study, we sought to determine the roles of Akt and mTOR in Notch1 signaling in NE tumors. Methods: BON-notch and TT-notch cell lines were created by stably transfecting a doxycycline-inducible Notch1 intracellular domain (NICD) into the carcinoid and MTC cell lines, BON and TT, respectively. To upregulate Notch1, cells were treated with doxycycline (0-1 μg/ml) for 48 hours. Activation of Notch1, Akt, and mTOR signaling was assessed by western blot analysis. Results: Treatment of BON-notch and TT-notch cells with doxycycline led to a dose-dependent increase in the levels of active, NICD. A comparable decrease in the NE markers achaete-scute complex like-1 (ASCL1) and chromogranin A also was observed. Activation of Notch1 signaling had no effects on the degree of Akt phosphorylation (Ser473), but decreased the levels of active, phosphorylated mTOR (Ser2448). In addition, increases in NICD expression did not alter levels of total Akt or total mTOR. To confirm the effects of Notch1 activation on mTOR signaling, we evaluated several downstream translational regulators, including p70 s6kinase (Thr389), eIf4G (Ser1108), 4E-BP1 (Ser65), and S6 ribosomal protein (Ser235/236). Notch1 upregulation also reduced phosphorylation of these translational regulators which act downstream of mTOR, demonstrating decreased mTOR activity. Conclusions: These results suggest that mTOR may be downstream mediator of Notch1 signaling in NE tumors that acts independently from Akt. Further investigation into possible synergy between Notch1 activators and mTOR inhibitors in NE cancers is warranted.

P4

Surgery enhances bone marrow derived cell mobilization and increases metastasis in a mouse melanoma model S. Lavotshkin,[1]* T.M. Theilen,[2] S.R. Granitto,[1] D. Rutigliano,[2] L. Rotman,[1] M.P. LaQuaglia,[2] R.N. Kaplan,[1] D. Lyden.[1] *1. Weill Cornell Medical College, New York, NY; 2. Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: We aim to show that surgery in the tumor setting acutely mobilizes bone marrow derived stem cells which home to future sites of metastasis, and foster distant tumor growth. This can explain the long-standing observation by Folkman and others, that removal of the primary tumor can be followed by the rapid growth of distant metastasis. Methods: C57BL/6 mice were flank-injected with B16-F10 melanoma cells fluorescently labeled with mCherry. Two types of surgery were performed on day 14 following tumor inoculation: primary tumor resection and a control sham operation, which involved tumor dissection without resection. Mice were sacrificed 17 days post-operatively and lungs were analyzed for metastatic burden, grossly, by QPCR and fluorescent microscopy. In a related experiment, mice were sacrificed four days post-operatively and analyzed for circulating progenitor cells by flow cytometry and colony-forming unit assays (CFUA). Results: Analysis of the mice that were operated on day 14 post-tumor inoculation showed an increase in metastatic lesions over tumor controls, both by gross observation and by fluorescent microscopy. In the sham surgery group, metastatic burden to the lung was greater when compared to the resected and the non-resected mice. This was confirmed by QPCR for mCherry, which showed a similar metastatic profile for the resected and non-resected groups, but a three-fold increase after sham surgery. Flow cytometric analysis of peripheral blood from four days after surgery showed an enhancement of circulating progenitor cell mobilization. Additionally the CFUA also demonstrated a 2.2 fold colony increase in the resection group, and a 1.5 fold increase in the sham surgery group, as compared to mice with no surgical intervention, representing an enhancement in circulating progenitor cells. Conclusion: Our data supports that surgery in the advanced tumor setting leads to an increase in metastasis, not only due to a loss of the primary tumor's regulatory control, but also due to an acute mobilization of bone marrow derived progenitor cells.

P5

CD4+ lymphocytes transduced with an MHC class I receptor can mediate tumor regression following adoptive cell transfer T.L. Frankel,* W. Burns, S.A. Rosenberg, R.A. Morgan. *National Cancer Institute, Bethesda, MD.*

Introduction: Adoptive cell transfer (ACT) of peripheral blood lymphocytes (PBL) genetically modified to express a melanoma associated antigen (MAA) specific T cell receptor (TCR) can mediate tumor regression in patients with metastatic melanoma. Because the current method of retroviral transduction involves use of both CD8+ and CD4+ cells, the consequence of introducing an MHC class I restricted TCR into CD4+ T-cells requires further investigation. Methods: A CD8 co-receptor independent TCR was cloned from a TIL specific for the MAA tyrosinase. The TCR was then modified to contain

the murine cytoplasmic signaling domain. Following transduction of sorted CD4+ or CD8+ splenocytes with the murinized TCR, cells were adoptively transferred into tumor bearing HLA-A2 trangenic C57/BL6 mice. Tumors were measured for 24 days and then mice were sacrificed. Histologic examination of the eyes was used to assess autoimmunity. Results: Mouse splenocytes were harvested from C57/BL6 mice and sorted in to CD8+ and CD4+ cells using antibody coated beads (purity 97%). After transduction with a murinized TCR, both subsets of splenocytes were able to secrete IFN-G following co-culture with HLA-A2 transgenic murine melanoma cell line B16-A2 (18,765pg/ml vs 21,345pg/ml for CD8+ and CD4+, respectively), but not the HLA-A2 negative line B16. Following ACT of separated and transduced splenocytes, there was tumor regression seen in both the mice receiving the CD8+ and CD4+ cells (figure 1). There were no observed instances of uviitis to suggest autoimmunity. Conclusion: ACT with PBL modified to express a cloned TCR has proven a safe and effective tool in the treatment of metastatic melanoma. Until now, the biologic significance of placing an MHC class I restricted receptor into a CD4+ cell has been unknown. We have demonstrated that CD4+ cells adopt a Th-1 like cytokine profile and can mediate the same anti-tumor effect as CD8+ cells without evidence of autoimmunity.

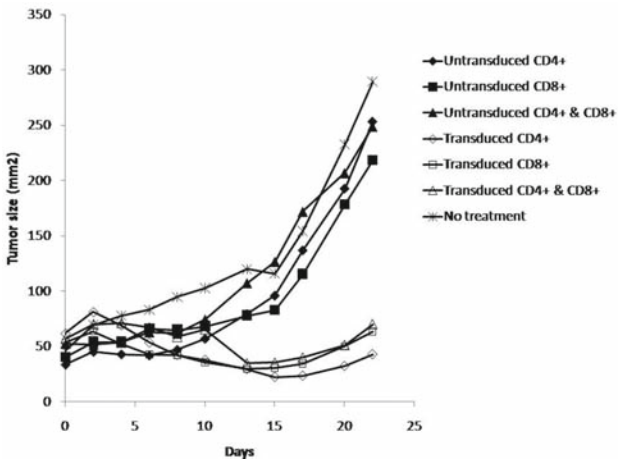


Figure 1: Tumor measurement following ACT (day 0) of untransduced and transduced CD4+ and CD8+ mouse splenocytes.

P6

Pancreatic Cancer-Associated Fibroblasts and ErbB3-mediated Tumorigenesis J.S. Liles,[1]* A. Frolov,[1] P. Kulesza,[2] J.D. Christein,[1] M.J. Heslin,[1] J.P. Arnoletti.[1] *1. Department of Surgery, University of Alabama at Birmingham, Birmingham, AL; 2. Northwestern University - Department of Pathology, Chicago, IL.*

Pancreatic cancer contains a large desmoplastic component, and the interactions between stromal fibroblasts and carcinoma cells are relatively unknown. We have demonstrated that ErbB3 influences pancreatic cancer cell response to Epidermal Growth Factor Receptor (EGFR) inhibition with erlotinib. We sought to investigate the impact of pancreatic cancer-associated fibroblasts (PCAF) on carcinoma cell proliferation and the role that EGFR and its heterodimer partner, ErbB3, play in this interaction. PCAF primary cultures were established from surgical specimens and immortalized with hTERT expression. Serum-free conditioned media (CM) from PCAF was collected for analysis and *in vitro* stimulation of AsPC-1 pancreatic cancer cells. AsPC-1 murine subcutaneous xenografts were developed with and without PCAF. Mice were treated with erlotinib and tumor volume was assessed. Xenograft expression of ErbB3 and its downstream signaling effectors was analyzed. *In vitro*, PCAF secreted neuregulin-1 (NRG-1), a potent ErbB3 ligand, and treatment of AsPC-1 cells with PCAF CM promoted cellular proliferation ($p<0.001$). This proliferative effect was abrogated by NRG-1 antibody inhibition ($p<0.001$). In AsPC-1 cells, NRG-1 rich CM induced phosphorylation of ErbB3 and AKT, and this signaling cascade was completely inhibited by an ErbB3 blocking peptide. *In vivo*, murine subcutaneous xenografts containing PCAF had greater volume than those lacking PCAF ($p<0.05$). Tumor volume directly correlated with the amount of PCAF present ($p<0.01$). Tumors containing PCAF exhibited more desmoplasia and strong NRG-1 expression which stimulated ErbB3 signaling as evidenced by phospho-ErbB3 and phospho-AKT protein expression. Following erlotinib treatment, the anti-tumor effects of EGFR inhibition were markedly less pronounced in the PCAF-containing murine xenografts ($p<0.05$). PCAF-secreted NRG-1 promotes pancreatic cancer tumorigenesis via ErbB3 and confers resistance to the anti-proliferative effects of erlotinib-induced EGFR inhibition. We have identified the NRG-1/ErbB3 axis as an attractive target in the attempt to disrupt the tumorigenic stromal-epithelial interactions within the pancreatic cancer microenvironment.

P7

High Throughput Oncogene profiling in Intraductal Papillary Mucinous Neoplasm (IPMN) of the Pancreas N. Lubezky,[1]* Y. Cohen,[3] M. Ben-Haim,[1] R. Nackache,[1] S. Marmor,[2] G. Rechavy,[3] J.M. Klausner.[1] *1. Department of Surgery B, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; 2. Istitute of Pathology, Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; 3. Cancer Research Center, Sheba Medical Center, Tel-Hashomer, Israel.*

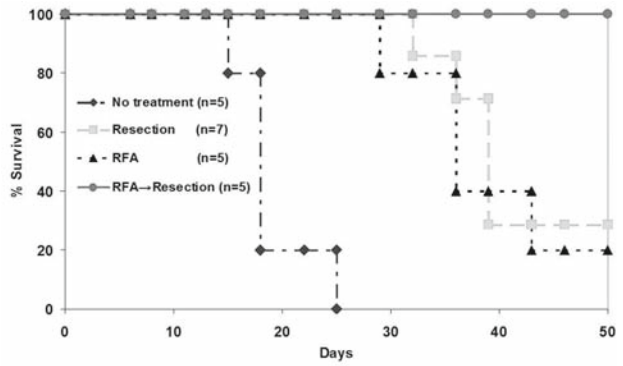
Background: The histological variety of IPMN and the presence of premalignant dysplatic cells in the pancreatic tissue surrounding the invasive component is an excellent system to study the genetic alterations involved in tumor development. The specific mutations leading to the development of the various histologic grades of IPMN (hyperplasia, atypia, invasive cancer) have been partially characterized. Methods: high throughput analysis of 323 oncogenic hotspot mutations in 22 tumor related genes (ABL, AKT1,2, BRAF, CDK4, CTNNB1, EGFR, ERBB2, FGFR1,3, FLT3, H-ras, JAK2, KIT, K-ras, MET, N-ras, p53, PDGFRA, PIK3CA, PTEN, RET), using a chip-based matrix-assisted laser desorption time-of-flight (MALDI-TOF) mass spectrometer (Sequenom, San Diego, CA) of DNA extracted from microdissected cells of low grade (n=14), borderline tumor(n=6), and invasive IPMN (n=7). For invasive cancers with a mutation, additional assays for the specific mutation were performed on the DNA extracted from microdissected IPMN dyplastic cells found in the background of the invasive lesion. Results: We identified 9 K-ras mutations (low grade, 2/14; borderline, 1/6; invasive, 6/7); 3 p53 mutations (low grade, 1/14; invasive 2/7); and 2 PIK3CA mutations (low grade, 1/14; invasive, 1/7). Hot-spot mutations in the other tumor related genes were not found. K-ras, p-53 and PIK3CA mutations present in the invasive cancer were absent in the adjacent premalignant cells in 50% of the cases. In one patient, K-ras mutation was present in the premalignant lesion, and absent in the invasive lesion. Conclusions: Of the 22 screened tumor related genes, only K-ras, p53, and PIK3CA mutations were found in IPMN, suggesting possible diagnostic and therapeutic targets for future studies. K-ras mutations are significantly more prevalent in invasive IPMN than in low grade and borderline IPMN. The variable existence of mutations found in invasive lesions also in the adjacent premalignant cells, and a patient in whom K-ras mutation was present in the precursor lesion and not in the adjacent invasive lesion, point to the heterogeneous nature of this tumor.

P8

Improved Survival with Pre-resectional Radiofrequency Ablation is associated with Enhanced CD8 T Lymphocyte Trafficking to Tumor-draining Lymph Nodes and Tumor Sites F. Ito,[1]* J.B. Muhitch,[2] T. Vardam,[2] M.M. Appenheimer,[2] D.T. Fisher,[2] W.C. Wang,[2] S.O. Gollnick,[2] S.S. Evans.[2] *1. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY; 2. Department of Immunology, Roswell Park Cancer Institute, Buffalo, NY.*

Background: While surgical resection is a cornerstone of cancer treatment, local recurrence continues to adversely affect outcome in a significant proportion of patients. Evidence that an alternative debulking strategy involving radiofrequency ablation (RFA) induces antitumor immunity prompted the current investigation of the efficacy of performing RFA prior to surgical resection in a murine tumor model. Methods: Mice implanted subcutaneously with a murine colon adenocarcinoma engineered to express hemagglutinin (CT26-HA; 100~500 mm^3) were treated with RFA (90°C, 1 min.), resection alone (day 10), or RFA (day 10) followed by resection (day 17). Tumor growth, local recurrence, and survival were assessed. Resected tumors were stained for infiltrating T cell subsets (CD4, CD8, and Foxp3). Trafficking of tumor (HA)-specific CD8 T cells to tumor-draining lymph nodes (TdLN) or tumors was investigated by short-term homing assays and intravital microscopy. Results:

Decreased local recurrence was observed following pre-resectional RFA (0-9%) compared to RFA (60-80%) or resection alone (40-75%) which was associated with significantly improved survival (P<0.0001). Immediately after RFA (6 hours-post), a marked increase in trafficking of naïve T cells was detected in TdLN, but not tumors or contralateral LN, thereby overcoming the repression in homoeostatic homing normally observed in TdLN. Elevated frequencies of antigen-specific CD8 T cells were detected within both TdLN and CT26-HA tumor ≥5 days after RFA. A strong increase in localization of CD4 and CD8 T cells, together with a concomitant decrease in Foxp3 regulatory T cells, was observed in resected tumor 7 days after RFA compared with resected tumor alone. Conclusions: Pre-resectional RFA significantly improved local control and overall survival. Evidence that RFA recruited antigen-specific CD8 T cells to TdLN and tumor microenvironment suggest that the underlying mechanism involves activation of adaptive tumor immunity. This treatment strategy can be readily extended to the clinic and should be considered an option for treating large tumors.



P9

Vaccinia Virus Mutant With Enhanced Extracellular Virion Production is a more effective Oncolytic Agent In the Presence of Humoral Immunity P. Thirunavukarasu,* M. Sathaiah, M. O'Malley, M. Gorry, J. Li, F. Austin, S. Guo, D. Bartlett. *University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Vaccinia Virus (VV), used in oncolytic therapy, forms 2 types of virions by replication - Intracellular mature virion (MV) and Extracellular Enveloped virion (EV), the latter responsible for remote infection. We attempt to characterize an enhanced EV-producing mutant VV and hypothesize that it would be a more effective vector in the presence of humoral immunity due to the presence of host derived envelope in EVs. Methods: By a single point mutation in A34R gene (responsible for EV retention) in dual gene deleted vaccinia (vvDD), a mutant virus (vA34R) was created. Reversing the mutation by recombination techniques, control virus (vCL) was made. Phenotype, cytotoxicity, viral replication, pathogenicity, remote spread and ability to evade humoral immunity were assessed using MC38(mouse colon cancer) and HCT116(human colon cancer) cell lines. Results: First, enhanced EV production was confirmed by formation of comet plaque phenotype, typical of EV producing mutants. Recovery of virus in the supernatant of infected cells was at least 10-20 fold higher with vA34R compared to vCL in HCT116 cells (3.5x104 pfu/ml vs 1x103 pfu/ml, $p < 0.05$) and MC38 cells (4.65x105 pfu/ml vs 2.15x104 pfu/ml, $p < 0.001$). MTT assays showed that vA34R was 45% more cytotoxic than vCL (cell viability 8.2% vs 14.9%, $p < 0.05$) at 48 hours in virus infected MC38 cells, compared to non-treated controls. In vivo studies with non tumor bearing nude mice show that vA34R is more pathogenic than vCL (median survival 60 days vs 120 days, $p < 0.05$). In vitro transwell models showed that virus released in the supernatant of vA34R-infected MC38 cells can infect MC38 cells in another well separated by artificial membranes, 10 fold more than vCL (9 pfu/well vs 103 pfu/well, $p < 0.05$). Addition of vaccinia immunoglobulin to the medium did not abate this 10-fold higher remote infection rate of A34Rm. Conclusion: Enhanced EV-producing mutant VV is more pathogenic, cytotoxic and replicates more with efficient remote spread of vaccinia to tumor cells in the presence of humoral immunity and hence may be a more effective viral vector for oncolytic therapy.

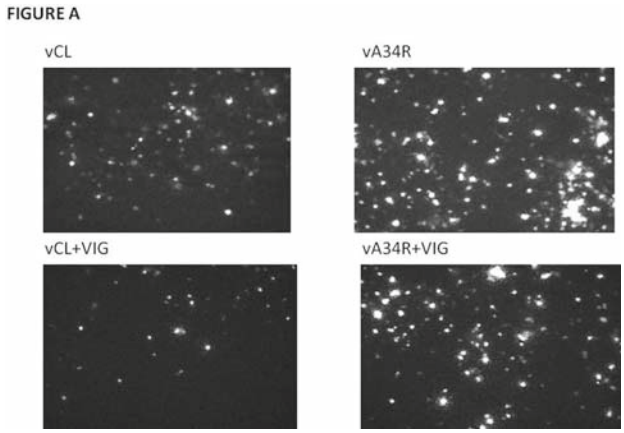


Figure A: Transwell assay showing increased viral expression in MC38 cells infected with vA34R compared to vCL with and without Vaccinia Immunoglobulin(VIG).

P10

Tyrosine Kinase Inhibitor Lapatinib Inhibits Cell Growth and Induces Apoptosis in Pancreatic Carcinoma Cells, and Exerts Synergistic Effects With Conventional Chemotherapy Agents S. Singla,* J.A. Pippin, J.A. Drebin. *Surgery, University Of Pennsylvania, Philadelphia, PA.*

Introduction: Patients with advanced pancreatic cancer have been traditionally treated with 5-fluorouracil (5-FU) and Gemcitabine (GEM) based regimens, with modest clinical benefit. Lapatinib, a dual erbB1 and erbB2 receptor tyrosine kinase inhibitor has shown significant activity against erbB1 and erbB2 expressing tumors of the breast. Since pancreatic cancers frequently overexpress these proteins, we investigated the cytotoxic effects of Lapatinib on pancreatic cancer cells, both alone and in conjunction with 5-FU or GEM. Methods: The human pancreatic cancer cell lines PANC1, ASPC and BXPC3 were used. Cells were treated with varying doses of Lapatinib in vitro. Effects on erbB1 and erbB2 phosphorylation, and on the downstream cell survival protein survivin were determined by western blotting. Cytotoxicity was determined by MTT assay. Apoptosis was measured using a Caspase 3 colorimetric assay. Similar dose-response Lapatinib experiments were conducted in the presence of varying concentrations of 5-FU or GEM and isobolograms were constructed to evaluate therapeutic synergy. Results: Lapatinib treatment of pancreatic cancer cells inhibited erbB1 and erbB2 phosphorylation in the range of 4 to 16 uM, a clinically achievable concentration. Lapatinib treatment also resulted in down-regulation of the cell survival protein survivin. Lapatinib treated cells showed dose-dependent inhibition of cell proliferation and induction of apoptosis at the same concentrations that blocked erbB1/erbB2 phosphorylation. Experiments evaluating combinations of Lapatinib and 5-FU or GEM demonstrated synergistic effects in inhibiting cell growth and inducing apoptotic cell death of pancreatic cancer cells. Conclusion: Simultaneous inhibition of erbB1 and erbB2 tyrosine kinases using Lapatinib inhibits pancreatic cancer cell growth and induces apoptotic cell death. These effects occur at clinically achievable concentrations and are synergistic with the effects of the conventional chemotherapy agents 5-FU and GEM. These findings support further evaluation of Lapatinib for the treatment of pancreatic cancer.

P11

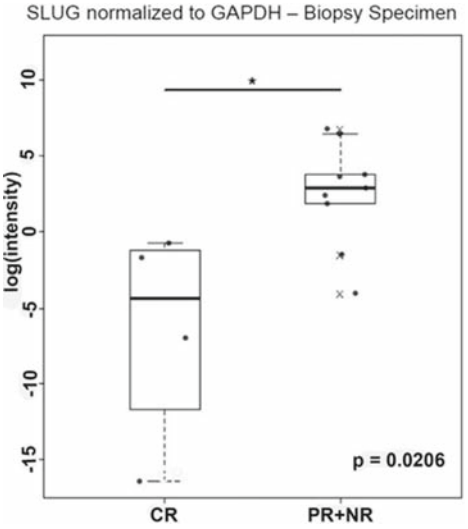
Ischemia Modulates Tumor Growth and Spread in a Murine Lung Cancer Model: The Role of Host Immunity E.G. Sheu,* K. Wakatsuki, S.M. Oakes, F.D. Moore, Jr.. *Brigham and Women's Hospital, Boston, MA.*

Introduction: Chronic hypoxia and inflammation are well known to influence tumor progression. In normal tissues, ischemia triggers an inflammatory response mediated by self-reactive natural antibodies, complement activation, and mast cells. We hypothesize that tumor ischemia initiates a similar inflammatory response that promotes tumor growth and spread. **Methods:** The Lewis lung carcinoma (LLC) cell line was implanted into wild-type C57BL/6 mice or knockout mice deficient in lymphocytes and antibodies (Rag1 -/-), complement (C3 -/-), or mast cells (Kit^{W}-$Kit^{W/v}$). Subsequently, ischemia was transiently induced by external tourniquet ligation of the tumor bearing hind limb. Primary tumor size was followed for 3-4 weeks. At sacrifice, lung metastasis and primary tumor weight were measured. Immunohistochemistry for natural antibody, complement, and activated caspase-3 was performed. **Results:** In wild-type mice, ischemic treatment of LLC resulted in a 33% increase in primary tumor size as compared to controls ($p < 0.0001$), despite histologic and biochemical evidence of tumor apoptosis, necrosis, and natural antibody deposition. In contrast, ischemic injury caused a 4-5 fold reduction in LLC lung metastasis as compared to sham or control injured mice ($p<0.001$). In Rag1 -/- knockouts, ischemia lost its ability to augment primary tumor growth but continued to inhibit LLC lung metastasis (four fold decrease, $p<0.05$). In both C3 -/- and Kit^{W}-$Kit^{W/v}$ mice, ischemic enhancement of LLC tumor growth was preserved. Formation of lung metastasis was reduced in C3 -/- and Kit^{W}-$Kit^{W/v}$ knockouts, even in the absence of ischemia. **Conclusions:** Ischemia enhances LLC tumor growth and inhibits lung metastasis. Enhanced primary tumor growth following ischemic injury requires host antibodies and/or lymphocytes. Mast cells and the complement cascade may play a role in spontaneous LLC metastasis.

P12

The Role of Epithelial to Mesenchymal Transition in Colorectal Cancer Therapeutic Resistance E.R. Camp,* S.G. Vaena, V.J. Findlay, J.P. Stokes, E.G. Hill, D.N. Lewin, N.F. Esnaola, D.J. Cole, D.P. Turner, D.K. Watson. *Surgery, Medical University of South Carolina, Charleston, SC.*

Mechanisms of therapeutic resistance 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. We hypothesized that Slug, a transcriptional regulator of EMT, may mediate therapeutic resistance in CRC. Methods: DLD-1 and 5-Fluorouracil resistant DLD-1 (5-FU rDLD-1) human colon cancer cells were compared for EMT properties. Motility was assessed by a Boyden chamber assay. Molecular alterations were assessed by Western Blot, real time RT-PCR (qRT-PCR), and immunofluorescence. Stable Slug-vector transfected DLD-1 cells (Slug DLD-1) were compared to empty-vector transfected cells (empty DLD-1) for properties of EMT and sensitivity to 5-FU as determined by the sulphorhodamine (SRB) test. Medical records and RNA samples obtained from pre-treatment, paraffin embedded tissue specimens from 15 patients with locally advanced rectal cancer were retrospectively analyzed to assess the relationship between Slug expression and response to neoadjuvant 5-FU based chemoradiation (chemoRT). QRT-PCR was performed for Slug expression normalized to GAPDH. Results: 5-FU rDLD-1 cells demonstrated increased features of EMT relative to parental DLD-1 cells, including greater than 2-fold enhanced invasion ($p<0.001$), suppressed E-cadherin expression and 2-fold increased Slug expression. Similarly, the Slug DLD-1 cells demonstrated enhanced EMT with altered morphology, motility, and decreased E-cadherin expression compared to empty DLD-1 cells. Slug DLD-1 cells demonstrated decreased 5-FU sensitivity compared to empty DLD-1 cells ($p=0.03$). Among the 15 rectal cancer patients, there were 4 complete (CR), 5 partial (PR) and 6 non (NR) responders following neoadjuvant chemoRT. By qRT-PCR, Slug expression was significantly increased in the PR and NR patients relative to CR ($p=0.02$). Conclusions: Molecular changes consistent with EMT are associated with therapeutic resistance in CRC. Slug expression results in in vitro chemoresistance and may represent a marker of response to neoadjuvant therapy in CRC.



P13

Soluble Factors in the Chemoresistant Colorectal Cancer Secretome D. Bose,[1]* F. Tozzi,[1] L. Zimmerman,[2] M. Herynk,[1] F. Fan,[1] S. Samuel,[1] A. Parikh,[2] R. Slebbos,[2] E. Petricoin,[3] D. Liebler,[2] L.M. Ellis.[1] *1. MD Anderson Cancer Center, Houston, TX; 2. Vanderbilt University, Nashville, TN; 3. George Mason University, Fairfax, VA.*

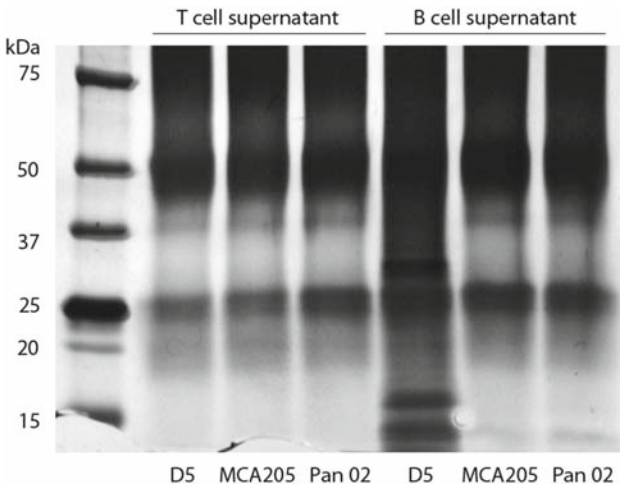
Introduction: Long term survival in patients with metastatic colorectal cancer (CRC) is limited by the development of chemoresistance. In prior studies, we found that conditioned media from oxaliplatin-resistant HT29 cells (OxR) could mediate growth and chemoresistance in chemonaive parental HT29 cells in vitro. We sought to identify the soluble factors in conditioned media that are potential targets to overcome this paracrine cell survival mechanism. Methods: Parental HT29 cells (Par) were grown in increasing concentrations of oxaliplatin generating OxR cells. Proteins from conditioned media (CM) were analyzed by liquid chromatography – mass spectrometry (LC-MS), and spectral counts were compared. Antibody-conjugated bead technology as well as ELISAs were used to obtain cytokine profiles of CM. Finally, reverse phase phosphoproteomic arrays (RPPA) were used to determine signal transduction pathways activated in cells treated with CM. OxR cells were injected into nude mice to determine the paracrine effect of Par tumors growing on the opposite flank. Results: OxR CM contained 53 upregulated proteins compared to Par CM (log 2 ratio>2, p value<0.05, and false discovery rate <0.2) by LC-MS analysis, including factors involved in extracellular matrix remodeling such as MMP7, and growth factors such as lipocalin 2, progranulin, and semaphorin 3B. Cytokine profiling demonstrates significant increase in stem cell factor/c-Kit ligand ($p=0.02$) and decrease in TRAIL ($p=0.008$) and IL-10 ($p=0.04$). RPPA analysis demonstrated early phosphorylation of EGFR and MEK1 followed by GSK, PTEN, and mTOR activation. OxR tumors induced faster and larger tumor growth of contralateral tumors indicating a systemic effect. Conclusions: Analysis of soluble factors from chemoresistant CRC cells demonstrates the presence of numerous potential mediators of cancer cell survival that may act in not only an autocrine/paracrine manner but also systemically.

P14

Identifying Tumor-Associated Antigens Recognized by Therapeutic B Cells Used in Adoptive Immunotherapy J.P. Namm,* Q. Li, J. He, D.M. Lubman, A.E. Chang. *Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: We have reported that the adoptive transfer of B cells derived from tumor-draining lymph nodes (TDLN) mediates tumor regression independently and in synergy with T cells in mouse models. In addition to antigen presentation, B cells produce tumor-specific IgG2b that bind and lyse tumor cells in the presence of complement. We hypothesize that these therapeutic antibodies (Ab) target tumor cells by specific interactions with tumor-associated antigens (TAA) expressed on tumor cell surfaces. We aim to identify the antigens (Ag) recognized by tumor-specific Abs. Methods: C57BL/6 mice were inoculated with D5G6 melanoma cells to induce TDLN. T and B cells were

purified from the TDLN and were activated with anti-CD3/anti-CD28/IL-2 or LPS/anti-CD40 respectively. As the activated T and B cells were used for adoptive transfer into tumor-bearing mice, we collected the culture supernatant as our Ab source for TAA identification. After incubating tumor cell lysates with T or B cell culture supernatant, the Ag-Ab complexes generated in the immunoprecipitation (IP) were resolved on SDS-PAGE. We cut and digested the specific bands for peptide analysis by mass spectroscopy. Results: The purified and activated D5 TDLN B cells produced significant amounts of Ab (158±7, 375±12, and 47±4 ng/ml of IgM, IgG, and IgG2b respectively by ELISA). The T cell culture supernatant had no detectable levels of Ab and was used as a cell culture control. After IP and SDS-PAGE, D5 TDLN B cell-produced Abs recognized six specific bands (31, 30, 17, 16, 14, and 13 kD) from the D5 lysate which were absent in the lysate of the control tumors (MCA205 and Pan 02). Mass spectroscopy on these six bands expressed by D5 tumors suggested a set of Ab-recognized surface proteins which includes 40S/60S ribosomal proteins and histones (H1.2, H2A, H2B, H3.2, and H4). Conclusions: The role of B cells as effector cells in tumor immunotherapy is continuing to emerge. Identification and characterization of TAA recognized by therapeutic B cell-produced Abs may provide additional mechanisms of B cell-mediated tumor regression and offer novel immunotherapy strategies in conjunction with effector T cells.

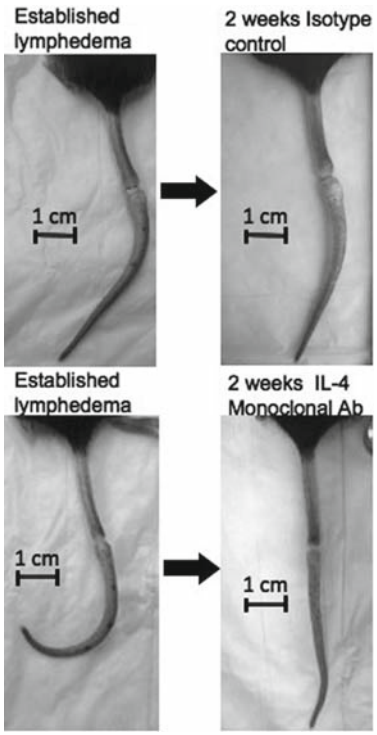


SDS-PAGE showing six specific bands at 31, 30, 17, 16, 14, and 13 kD after immunoprecipitation of D5 TDLN B cell culture supernatant with D5 tumor lysate.

P15

Inhibition of IL-4 leads to resolution of lymphedema and fibrosis in a mouse model T. Avraham,* S. Daluvoy, E. Kueberuwa, J. Zampell, B.J. Mehrara. *Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Lymphedema is chronic extremity swelling and fibrosis that affects nearly 30% of breast cancer patients who undergo lymphadenectomy. Although surgery is clearly the initiating event, the pathological mechanisms that result in some patients developing lymphedema remain unknown. Methods: We developed a surgical mouse model that enables us to determine the effects of transient or sustained lymphedema on inflammation and immune responses. Based on the known roles of CD4 cells in the regulation of other fibrotic disorders, we explored the role of a T-cell response in general, and Th2 differentiation in particular on the pathological changes associated with lymphedema. We then blocked IL-4, a cytokine necessary for Th2 differentiation, using a monoclonal antibody, and evaluated its effects on fibrosis, lymphedema, and lymphatic function. Results: Similar to clinical lymphedema, sustained experimental lymphedema resulted in a chronic inflammatory reaction consisting predominantly CD4+ T-helper cells. Furthermore, IHC and WB analyses demonstrated that sustained stasis resulted in a mixed Th1-Th2 response whereas transient stasis was associated with only a Th1 response. Application of our surgical model to athymic nude mice demonstrated that pathological fibrosis resulting from sustained lymphedema is T-cell dependent. Inhibition of Th2 differentiation in animals with lymphedema using a monoclonal antibody against IL-4 resulted in a marked reduction in tail edema (-36% in tail volume vs +3%, $p<0.02$), improved lymphatic function, and resolution of inflammatory reaction when compared with animals receiving isotype control. Reduction in fibrosis was grossly evident and statistically significant ($p<0.01$). Conclusions: Similar to other fibroproliferative disorders, lymphedema is associated with a CD4+ T-cell dominant chronic inflammatory reaction. Targeted inhibition of Th2 differentiation with an IL-4 monoclonal antibody can reverse the pathologic changes associated with sustained lymphedema in this model with resolution of swelling and fibrosis. These results suggest that modulation of lymphedema associated inflammatory represents a potential novel therapeutic approach.



Treatment of mouse tails with established lymphedema with an IL-4 blocking monoclonal antibody for two weeks resulted in grossly apparent, near complete resolution of both lymphedema and fibrosis.

P16

Human Melanomas are Sensitive to Inhibition of Polyamine Synthesis E.C. Hsueh,* Y. Zhang, G. Peng. *Saint Louis University, St. Louis, MO.*

Defect in urea cycle enzyme expression has been observed in human melanoma cells. Ornithine, a urea cycle substrate, is also the key substrate for polyamine synthesis. We hypothesized that inhibition of key polyamine synthesis enzyme, ornithine decarboxylase (ODC), would have negative growth effect on human melanoma cells. Ten human melanoma cell line cells were evaluated. Western blot were performed using polyclonal goat anti-ODC, or rabbit mAB anti-GAPDH. Quantitative real-time PCR were performed using TaqMan Gene Expression Assay (Applied Biosystems). GAPDH served as control. The siRNA duplexes targeting ODC and a scrambled control siRNA were designed and synthesized (Santa Cruz, CA) and transient transfections were performed. Cell Proliferation Assay was performed using Cell Titer Blue cell proliferation Assay according to the manufacturer's protocol. The cells were treated with or without various concentrations of DFMO or Rapamycin or combination then incubated up to 96 hours. For comparison between groups, the student's t test was used and $p< 0.05$ was considered to be statically significant. Variable expression of ODC was observed in human melanoma cells. Significant over-expression of ODC was observed in four of the ten human melanoma cell lines have over expression of ODC on Western blot analysis and RT-PCR analysis. Dose-dependent growth inhibition of human melanoma cells

were observed following DFMO treatment ($p<0.05$) and correlated with suppression of ODC expression levels. Suppression of ODC by siRNA also resulted in significant growth inhibition of the human melanoma cell lines. The combination of mTOR pathway inhibition with Rapamycin and polyamine synthesis inhibition with DFMO had additive growth inhibitory effect but no synergism was observed. Inhibition of polyamine synthesis may play a role in human melanoma treatment. The combination of polyamine synthesis inhibition and mTOR pathway inhibition has additive effect on growth inhibition of human melanoma cells.

P17

Fas Ligand Expression Increases Safety and Tumor Selectivity of Vaccinia Virus P. Thirunavukarasu,* M. Sathaiah, M. O'Malley, M. Kavanagh, F. Austin, H. Zeh III, S. Guo, D. Bartlett. *University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Vaccinia virus (VV) used in oncolytic therapy displays a yet unexplained innate tumor tropism. Attempts to further increase its tumor selectivity often result in reduced tumor cytotoxicity. Fas receptor(Fas), expressed to some extent in most normal cells can lead to apoptosis on binding to Fas Ligand (FasL). We hypothesize that VV expressing membrane-bound FasL (mFasL) increases safety and tumor selectivity by abortive infection in normal cell types, while maintaining its oncolytic effects. Methods: By inserting murine FasL gene in thymidine kinase(tk) gene locus of WR strain of VV(vJS6), mFasL expressing VV (vvFL) was made. Infecting MC38 (mouse colon cancer) and B16(mouse melanoma) cells which are Fas+ and Fas- respectively, with vJS6 and vvFL each, apoptotic activity was measured by TUNEL assay. Viral pathogenicity in non tumor bearing nude mice, tumor progression after subcutaneous delivery of virus-infected cells and virus recovery from in vivo tumors was measured for both viruses in both tumors. Results: Western blot confirmed mFasL expression in vvFL-infected but not in vJS6-infected non cancerous CV1 cells. Flow cytometry confirmed Fas+ and Fas- status of MC38 and B16 cells respectively. TUNEL assays revealed positive apoptosis in vvFL-infected MC38 cells only with no or minimal apoptosis in vJS6-infected MC38, vJS6-infected B16 and vvFL-infected B16 cells. Median survival of non tumor-bearing nude mice was 8 times longer with vvFL infection than with vJS6 (120 days vs 15 days, $p<0.0001$), proving safety of vvFL in normal cells. Although median tumor viral recovery of vvFL at 4 days is 100-fold lower than vJS6, tumor size at 13 days was smaller in vvFL-treated than vJS6-treated (18mm3 vs 263mm3, $p=0.0001$) and non-treated (18mm3 vs 1207mm3, $p=0.0001$) MC38 bearing mice. There was no difference in tumor viral recovery or tumor size in B16 tumors. Conclusion: vvFL is less pathogenic to normal cells, replicates equally well in FasR- tumors and reduces tumor progression more effectively in FasR+ cancers, compared to its parent virus vJS6. FasL armed VV is equally effective, safer and more tumor selective and hence a potential vector for oncolytic therapy in future.

P18

A new oncolytic poxvirus expresses tetracycline-inducible GM-CSF for cancer therapy F. Austin,* M. Gorry, M. O'Malley, M. Sathaiah, P. Thirunavukarasu, J. Li, Z.S. Guo, D.L. Bartlett. *Surgical Oncology, University of Pittsburgh, Pittsburgh, PA.*

Introduction: The regulation of therapeutic genes in an oncolytic poxvirus is a desired treatment for cancer. The tetracycline operon (tetO) has been utilized successfully in mammalian cells to regulate gene expression, and GM-CSF has been widely used as an immunostimulatory cytokine in immunotherapy. The aim of this study was to design a oncolytic poxvirus in which the production of GM-CSF was regulated by tetracycline. Methods: A new dual gene deleted vaccinia virus, vTet12, was created. Several modifications of the vaccinia promoter driving GM-CSF expression were studied in order to determine optimal up-regulation. Secreted GM-CSF levels were determined by ELISA assays in multiple cells lines, infected at MOIs from 0.1 to 1.0, after exposure to levels of doxycline ranging from 0 to 1000 ng/mL. The production of TetR and GM-CSF mRNA over time was determined by quantitative RT-PCR. Results: Multiple viral constructs were examined for up-regulation of GM-CSF production by doxycycline ranging from 0.5 to 28-fold over base line. The initial ELISA data showed two viral constructs that demonstrated significant up-regulation in both A2780 and HeLa cancer cells. One virus (vTet12) containing the gm-csf gene under the control of a viral p7.5 late promoter containing 12T and 4 TetO sites, can induce up to a 28-fold increase in GM-CSF production in the presence of 1000 ng/mL of doxycycline in A2780 cancer cells at 24 hours post infection. Cells infected by vTet12 induced by 1000 ng/mL of doxycycline, showed production of GM-CSF mRNA as early as 6 hours and continued to show a significant level of up regulation at 12 hours compared with the uninfected tumor cells and infected cells not exposed to doxycycline. Conclusion: This new oncolytic poxvirus shows inducible expression of GM-CSF by doxycycline in cancer cells. It may be a valuable virus for combined oncolytic virotherapy and immunotherapy for cancer.

P19

Cytokine levels correlate with immune cell infiltration after anti-VEGF therapy in preclinical mouse models of breast cancer C.L. Roland,* K.D. Lynn, J.E. Toombs, S.P. Dineen, R.E. Schwarz, D.G. Udugamasooriya, R.A. Brekken. *UT Southwestern Medical Center, Dallas, TX.*

Introduction: Myeloid-derived suppressor cells (MDSC) are a population of immature myelomonocytic cells that have been shown to suppress antigen-specific immunity and attract regulatory T cells, which promote tumor growth. We have shown a reduction in MDSC infiltration into xenografts following anti-VEGF therapy. Here, we use two breast cancer models to explore the effect of anti-VEGF therapy on immune cell infiltration, specifically MDSCs and intra-tumoral cytokine levels. Methods: Therapy was initiated in SCID mice bearing established MDA-MB-231 or BALB/c mice bearing 4T1 breast tumors. Mice were treated with control or an anti-VEGF therapy (Table 1). At the time of sacrifice, immune cell infiltration was evaluated by immunohistochemistry and cytokine levels were evaluated using ELISA and electrochemiluminescence. Results: In MDA-MB-231 tumors, treatment with agents that selectively inhibit VEGFR1 and VEGFR2 (bev and GU81) resulted in elevated levels of intra-tumoral IL-1β and MDSC accumulation. Furthermore, changes in IL-1β levels in response to anti-VEGF therapy were highly correlative with changes in MDSC infiltration. Interestingly, in the 4T1 immunocompetent model of breast cancer, changes in intra-tumoral IL-1β levels correlate negatively with changes in MDSC infiltration after three weeks of therapy. These findings indicate a possible bimodal effect of IL-1β on MDSC infiltration, with low levels of IL-1β inducing MDSC infiltration and increased levels following anti-VEGF therapy inhibiting MDSC infiltration. Finally, we looked at serum levels of IL-1β as a potential biomarker of response to anti-VEGF therapy. For animals treated with mcr84 or GU81, we found that decreases in serum levels of IL-1β were highly correlative with changes in tumor size after anti-VEGF therapy. Conclusions: We have demonstrated differences in the ability of anti-VEGF therapy to modulate immune cell infiltration, intra-tumoral and serum cytokine levels depending on the mechanism of VEGF inhibition. Furthermore, we have identified a possible biomarker for assessing the efficacy of anti-VEGF therapy in breast cancer patients.

Anti-VEGF Agents

Agent	Class	Target	Target Species
r84	Human Ab	VEGF (blocks VEGFR2 only)	Mouse & Human
mcr84	Murine chimeric Ab	VEGF (blocks VEGFR2 only)	Mouse & Human
bevacizumab	Humanized Ab	VEGF (blocks VEGFR1 and VEGFR2)	Human
RAFL-2	Rat Ab	VEGFR2	Mouse
GU81	Peptoid	VEGFR1/2	Mouse & Human
sunitinib	Small molecule	VEGFR1/2, cKit, PDGFRβ	Mouse & Human

Ab: antibody; VEGF: Vascular endothelial growth factor; VEGFR1: VEGF receptor 1; VEGFR2: VEGF receptor 2; PDGFRβ: Platelet-derived growth factor receptor β.

P20

WITHDRAWN

P21

WITHDRAWN

P22

Gene Expression Analysis of a Notch1 Overexpression Model of Medullary Thyroid Carcinoma M. Roy,* P. Geiger, G. Kennedy, M. Kunnimalaiyaan, H. Chen. *Surgery, UW, Madison, WI.*

Background: We have identified Notch1 as a tumor suppressor in neuroendocrine tumors (NETs) including medullary thyroid cancer (MTC); however, the exact molecular mechanism is unknown. We sought to perform a gene expression analysis study to elucidate the downstream targets of Notch1 that mediate its tumor suppressor role in NETs. Methods: Human MTC (TT) cells were used to create a doxycycline –inducible active NOTCH1 (TT-Notch cells). TT-Notch cells were treated with doxycycline for 48 hrs and induction of Notch1 was confirmed by Western blot (Notch1 and ASCL1) and qPCR (Hes1 and Hes5). Quality and quantity of RNA samples were determined on an Agilent 2100 Bioanalyzer using the RNA Nano Labchip (Agilent, Palo Alto, CA). RNA was reverse-transcribed into cDNA using specific primers that contained a sequence complementary to an oligo attached to a dendrimer containing Cy-3 or Cy-5 dye molecules. The labeled cDNA from both the treatment group and from its corresponding control were then mixed and hybridized to the whole human genome oligo microarray. Image acquisition was done using a DNA Microarray Scanner G2565 BA (Agilent). Results: The data was analyzed on EDGE. Initially untreated TT cells were used as the reference and expression of approximately 700 genes were altered in the TT and TT-Notch treatment groups using ANOVA ($p<0.05$). Next, we used Student's t-test to subtract effects of doxycycline using TT cells treated with doxycycline as a reference ($p<0.01$) and generated a list of approximately 130 genes that were up or downregulated due to Notch1 induction in MTC. Analysis of these 130 genes revealed several novel as well as known pro-tumorigenic and anti-tumorigenic molecules as downstream targets of Notch1 in MTC such as PLAU (plasminogen activator, urokinase), BCL2 (B-cell lymphoma protein 2), GDF15 (growth differentiation factor 15), MMP11 (matrix metalloproteinase 11), LOXL2 (lysyl oxidase-like 2). Conclusion: Here for the first time, we have explored the downstream molecules of Notch1 in MTC using microarray technique. Our goal is to further validate this data to identify novels targets of Notch1 that either promote or inhibit tumor formation in MTC.

P23

Expression patterns of Notch1 and its ligands in well differentiated thyroid cancers X. Yu,* A. Lund, M. Kunnimalaiyaan, H. Chen. *Endocrine Surgery Research Laboratories, Department of Surgery, and the University of Wisconsin Carbone Cancer Center, University of Wisconsin School of Medicine and Public Health, Madison, WI.*

Background: Notch1, a multifunctional transmembrane receptor, acts either as an oncogene or as a tumor suppressor depends on the cellular contexts. Previously, Notch1 has been shown to be a tumor suppressor in neuroendocrine tumors including medullary thyroid cancer. However, the expression levels of Notch1 and its ligands remain unknown for the well differentiated thyroid cancers which account for the majority of all thyroid cancers. This study aims to evaluate the expression patterns of Notch1 and its ligands Jagged1, Jagged2 and DLL1 in well differentiated thyroid cancers for their clinical correlations. Methods: Both cancer and contralateral non-cancer tissue samples were obtained from 9 patients with thyroid cancers. Nine patients with multiple nodular goiters were recruited as control. The mRNA levels of Notch1, Jagged1, Jagged2 and DLL1 were quantified using real-time PCR from the tissues as well as additional five thyroid cancer cell lines. Results: Of the 9 cancer patients, 7 are with papillary thyroid carcinoma and 2 with follicular thyroid carcinoma. Notch1 expression levels in cancer tissues were significantly down-regulated compared with benign and non-cancer tissues ($p=0.04$ and 0.025 respectively). In addition, Jagged1 and DLL1 showed much lower levels in cancer tissues than the correspondence non-cancer tissues ($p=0.123$ and 0.036 respectively), but not did Jagged2 ($p=0.933$). Decreased Notch1 revealed a trend to correlate with a higher TNM stage. Interestingly, among 5 cell lines, FTC236, which is metastatic follicular cancer cell line, demonstrated the lowest Notch1 level. Conclusion: Notch1, together with its ligands Jagged1 and DLL1 is down regulated in well differentiated thyroid cancers indicating that the Notch1 signaling may be required for dedifferentiation. This result supports our earlier findings that Notch1 functions as a tumor suppressor in neuroendocrine tumors and may also hold true in well differentiated thyroid cancers.

P24

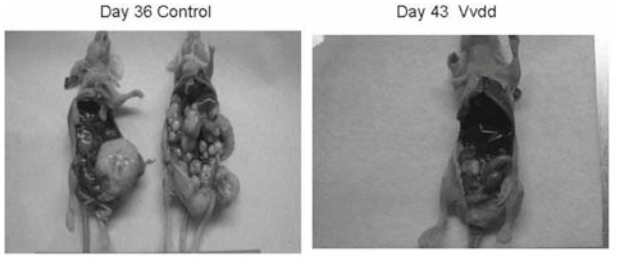
STAT2 Activation is Required for HPP1-Mediated Tumor Suppression J.M. Hernandez,* A. Elahi, D. Shibata. *GI Oncology, Moffitt Cancer Center and Research Institute, Tampa, FL.*

Background: HPP1 is a novel tumor suppressor gene that is epigenetically silenced in the majority of colorectal cancers. We have previously demonstrated that HPP1-mediated tumor suppression requires activation of STAT1 (Signal Transducers and Activators of Transcription). Given its cooperative function with STAT1 in interferon (IFNα) signaling pathways, we sought to determine the contribution of STAT2 to the growth suppressive effects of HPP1. Methods: We have previously stably transfected HPP1 into HCT116 cell lines and have shown growth suppression. Gene expression profiles associated with the ectopic expression of HPP1 were generated using the Affymetrix U133 Plus 2.0 GeneChip. RT-PCR and Western Blot analyses were used to determine the expression and activation of STAT2. Functional STAT promoter binding was quantified using a luciferase reporter plasmid containing ISRE-(Interferon Stimulated Regulatory Elements) promoter elements. The effects of siRNA-mediated knockdown of STAT2 was assessed by proliferation, cell cycle distribution and growth in soft agar assays. Results: Microarray analysis revealed that ectopic expression of HPP1 resulted in upregulation of both STAT1 (+7.6 fold) and STAT2 (+1.5), as well as numerous interferon-inducible genes. Both upregulation and activation of STAT2 in HPP1-transectants (HCT-HPP1) were confirmed. STAT2 knockdown in HCT-HPP1 cells resulted in increased proliferation ($p=0.05$), reduced G1/G0 cell cycle fraction and a restoration of growth potential in soft agar ($p=0.01$) as compared to controls. HCT-HPP1 cells demonstrated a significant increase in STAT1:STAT2 heterodimer ($p=0.03$) binding, which is critical for IFNα signaling. Treatment of HCT-HPP1 with escalating doses of IFNα resulted in incremental induction of STAT2 activation, and concomitant reduction in proliferation ($p=0.03$) with an increase in G1/G0 cell cycle arrest. Conclusion: STAT2 is necessary for HPP1-associated growth suppression and mediates these effects predominantly via STAT1:STAT2 heterodimeric activation of IFNα signaling pathways and the subsequent upregulation of interferon-inducible genes.

P25

Modified Vaccinia Virus Improves Survival in a Murine Peritoneal Carcinamatosis Model A.A. Mavanur,* D.L. Bartlett. *Division of Surgical Oncology, UPMC, Pittsburgh, PA.*

INTRODUCTION: A highly tumor-selective vaccinia virus (vv) with an engineered double deletion (DD) of the thymidine kinase (tk) and vaccinia growth factor genes with potential oncolytic viral activity has been previously described. The tk and vaccinia growth factor gene deletions in intra-tumorally administered vaccinia virus help to restrict its replication and cytolytic activity to tumor cells with large nucleotide pools and tumor cells with activation of the EGFR-Ras pathway. We present our experience with the effect of this virus on LS174T cells, a mucin producing colon cancer cell line in a murine model. METHODS: In vitro cytotoxicity assay was performed to assess the sensitivity of the cell line to Vvdd. Subsequently, an in vivo survival study was performed by injecting 1 million LS174T cells suspended in PBS intraperitoneal(I.P) in nude mice to establish tumor. On day three one group (n=10) was injected with 1x108 PFU of Vvdd I.P and the control group (n=10) was injected with PBS. The mice were followed with serial weight and girth measurements. The median survival in both groups was computed and compared. RESULTS: On the In vitro cytotoxicity assay, 60% of the cells were killed on exposure to Vvdd at a MOI of 1 at 72 hours. Analysis of the vivo results revealed median survival in the control group was 32 days as compared to 68 in the group injected with Vvdd. This difference was highly statistically significant ($p<0.0001$). Upon euthanasia, an autopsy of the mice was performed to assess tumor burden (Fig 1). CONCLUSIONS: We conclude that LS174T cells are sensitive to Vvdd in vitro and in vivo studies demonstrate that modified vaccinia improves survival in a murine peritoneal carcinamatosis model. REFERENCES: 1. J. Andrea McCart, Jerrold M. Ward, John Lee, Yun Hu, H. Richard Alexander, Steven K. Libutti, Bernard Moss, and David L. Bartlett. Systemic Cancer Therapy with a Tumor-selective Vaccinia Virus Mutant Lacking Thymidine Kinase and Vaccinia Growth Factor Genes. CANCER RESEARCH 61, 8751–8757, December 15, 2001



P26

Effects of Microwave (MW) Ablation on Blood Vessels A.B. Ross,* P. Manley, J. Coe, C. Ladtkow. *Interventional Oncology, Covidien, Boulder, CO.*

BACKGROUND Previous work describes the impact of hepatic vasculature on microwave ablation (MWA) geometry and efficacy, but information on MWA-mediated damage to vessels is limited. OBJECTIVE This is a multimodal study describing the impact of MWA therapy on neighboring vasculature. METHODS Computer simulations (COMSOL, Burlington, MA) of MWA temperatures were substantiated with data from three experimental groups: (1) a ground bovine liver bench model with fluid pumped through modeled blood vessels, (2) in vivo porcine with two hours post-MWA survival, and (3) in vivo porcine with seven days post-MWA survival. All microwave ablations were created by water-cooled MW antennas (Covidien, Boulder, Colo.). Thermal probes measured temperatures at the walls, interior and outlets of vessels in ex vivo experiments. Microwave ablations for in vivo experiments were created next to hepatic vessels of various sizes. RESULTS Temperature increases in fluid flowing through modeled vessels (ex vivo) depended primarily on vessel size and flow rate. Ground-liver temperature immediately adjacent to the vessel wall depended primarily on distance of the vessel to the MW antenna. Temperature rises inside vessels >3 mm were less than 5°C in both COMSOL simulations and ex vivo tests. In vivo acute results demonstrated partial and occlusive thrombosis in two of eight vessels <3 mm and 0/8 in vessels >3 mm. Chronic results showed thrombosis in zero of nine vessels. Ablation histology showed thermal damage to liver parenchyma up to and including the walls of nearby vessels. This damage up to the vessel walls was in agreement with the high temperatures measured at the vessel wall during ex vivo testing and COMSOL simulation, and also with previous findings suggesting limited heat sink effect with MWA. CONCLUSION Simulation and ex vivo tests showed high temperatures up to the boundary of vessels, but limited temperature rises within the flowing fluid during MWA. In vivo results confirmed these findings.

P27

Sphingosine Kinase 1; a New Target against Breast Cancer M. Nagahashi,* S. Ramachandran, O. Rashid, S. Milstien, S. Spiegel, K. Takabe. *Virginia Commonwealth University, Richmond, VA.*

INTRODUCTION: Sphingosine kinase 1 (SphK1) is one of the essential regulators of the potent bioactive sphingolipid mediator, sphingosine-1-phosphate (S1P). S1P promotes cancer cell survival, proliferation and angiogenesis. Expression of SphK1 is up-regulated in breast cancer, and associated with cancer progression. The aim of this study is to explore the therapeutic implications of targeting SphK1 for breast cancer treatment. We examined the effects of a newly developed isozyme-specific SphK1inhibitor, SK1-I, which does not inhibit other sphingosine kinases, in contrast to pan-SphK inhibitors. METHODS: 4T1-luc2 cells, a murine breast cancer that expresses ER-Beta, GPR30, Her2/neu, and that produces luciferase, were used. Western blotting, qPCR, luciferase assay, and colony formation assay were used to investigate SphK1 expression and responsiveness to SK1-I. RESULTS: qPCR demonstrated that 41-luc2 cells overexpress mRNA of SphK1, SphK2, S1P receptor 1, S1P receptor 2, and S1P receptor 4. Downregulation of SphK1 using siRNA targeted to a specific sequence of SphK1 mRNA (siSphK1) suppressed the growth of 4T1 cells detected by luciferase assay. The efficiency of siSphK1 in the knockdown of SphK1 mRNA in these cells was confirmed by Western blotting. Luciferase assay revealed that SK1-I inhibited 4T1 cell proliferation in a dose dependent manner. This result was consistent with colony formation assay using SK1-I on 4T1 cells. Of note, SK1-I inhibited 4T1 cell growth synergistically with the chemotherapeutic drug doxorubicin as determined by luciferase assay. CONCLUSIONS: Our results support the notion that SphK1 is an important factor in breast cancer progression and suggest that an isozyme-specific inhibitor of SphK1 deserves consideration as a new therapeutic agent for this disease. This therapeutic approach has the potential to overcome some of the major limitations of conventional chemotherapy, and may thus constitute a promising strategy for future applications in breast cancer therapy.

P28

Comparative Proteomic Analysis of 5-Fluorouracil and Oxaliplatin Resistant Colorectal Cancer Cells D. Bose,[1]* F. Fan,[1] L. Zimmerman,[2] R. Slebbos,[2] A. Parikh,[2] D. Liebler,[2] L.M. Ellis.[1] *1. MD Anderson Cancer Center, Houston, TX; 2. Vanderbilt University, Nashville, TN.*

Introduction: Chemoresistance occurs in nearly all patients with metastatic colorectal cancer (CRC), and mechanisms to reverse chemoresistance remain elusive. We tested the hypothesis that CRC cells resistant to 5-fluorouracil (5FUR) and oxaliplatin (OxR) exhibit proteomic profiles that may identify previously unrecognized mediators of resistance. Methods: Parental HT29 cell (Par) cells grown in increasing concentrations of 5-FU and oxaliplatin generated 5FUR and OxR cells. Protein from cell lysates were analyzed by liquid chromatography – mass spectrometry (LC-MS), and spectral counts were compared. Ingenuity pathway analysis was used to identify sets of proteins defined by canonical pathways and functions. We defined significance as a fold change > 2, p-value ≤ 0.05, and a false discovery rate ≤ 0.2. For pathways and functions, significance was defined by a p-value ≤ 0.05 by Fisher's Exact Test. Results: Forty-nine molecules were increased and 188 molecules were decreased in 5FUR cells vs. Par cells. In OxR cells, 803 molecules were increased and 653 molecules were decreased vs. Par cells. In 5FUR cells, pathways involving oxidative phosphorylation, inositol metabolism, actin cytoskeleton signaling, regulation of actin-based motility by Rho, and ATM signaling were significantly altered vs Par cells. In OxR cells, pyruvate metabolism, integrin signaling, caveolar-mediated endocytosis signaling, and mitochondrial dysfunction were among the most altered vs Par cells. Comparison of 5FUR and OxR cells revealed differences in RNA post-transcriptional modification, ERK/MAPK, RAN, and chemokine signaling. Conclusions: Chemoresistant CRC cells exhibit proteomes that reflect specific survival pathways, with many previously unrecognized potential mediators of resistance. Further studies are necessary to validate newly identified potential chemoresistance factors.

P29

WITHDRAWN

P30

HIF-1a Regulates VEGF-C Expression and is Required for Lymphangiogenesis J. Zampell,* S. Daluvoy, T. Avraham, E. Kueberuwa, A. Yan, B. Mehrara. *Surgery, Memorial Sloan Kettering, New York, NY.*

Introduction: Although HIF-1α is a key regulator of angiogenesis, the effects of this molecule on lymphangiogenesis remain largely unknown. Recent studies have demonstrated a correlation between HIF-1α and VEGF-C in clinical samples containing metastatic deposits suggesting that these molecules interact to regulate lymphatic metastasis. The goal of this study was therefore to determine the mechanisms by which HIF-1α expression regulates lymphangiogenesis. Methods: We utilized a mouse tail model of lymphatic regeneration in which the superficial and deep lymphatics are excised microsurgically. Following surgery, HIF-1α activity was blocked by administration of YC1, a well described small molecule inhibitor of HIF-1α. Lymphangiogenesis was evaluated and correlated with expression patterns of VEGF-A and VEGF-C. Transgenic mice containing a luciferase-HIF-1α fusion protein were used to precisely localize patterns of HIF-1α expression over time and across gradients of lymphatic fluid stasis. Finally, the role of tissue hypoxia in regulation of HIF-1α and lymphangiogenesis was characterized by pimonidazole staining. Results: Inhibition of Hif-1α markedly delayed lymphangiogenesis and led to significant increases in tail edema. This was evidenced by decreased numbers of lymphatic vessels, dilated lymphatics, and fewer markers of lymphatic differentiation. Additionally, impaired lymphangiogenesis resulting from HIF-1α destabilization was associated with significantly decreased tissue expression of VEGF-A and VEGF-C. Patterns of HIF-1α expression correlated with a gradient of hypoxia across the wound as assessed by pimonidazole staining and appeared to be independent of lymphatic fluid flow/stasis.

Conclusions: Our data provide evidence that HIF-1α directly regulates lymphangiogenesis through modulation of VEGF-C and VEGF-A. This regulation occurs along a hypoxic gradient rather than changes in lymphatic fluid flow or stasis. These findings are important as they demonstrate that HIF-1α expression is necessary for induction of VEGF-C expression and lymphatic regeneration and may provide a means to regulate lymphangiogenesis during metastases or wound healing.

P31

Molecular characterization of breast cancer progression: early lesions are not genetically advanced R. Ellsworth,[1]* J.D. Weyandt,[2] J.L. Fantacone-Campbell,[3] B. Deyarmin,[2] D.L. Ellsworth,[2] J.A. Hooke,[3] 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: Columnar cell lesions (CCL) and atypical ductal hyperplasia (ADH) frequently coexist and share molecular changes with in situ and invasive components, suggesting that CCL and ADH may be precursors to breast cancer. These conclusions are, however, largely based on studies examining CCL and ADH from patients diagnosed with more advanced disease. Thus, allelic imbalance (AI) was assessed in pure CCL or ADH specimens to characterize molecular changes in early breast lesions. Methods: DNA samples were obtained from laser microdissected CCL (n=42) or ADH (n=31) lesions without concurrent in situ or invasive disease. AI was assessed at 26 chromosomal regions commonly altered in breast cancer. Data was analyzed using Fisher's exact and Student's t-tests using a cutoff of $P<0.05$ to define significance. Results: The average AI frequency was 6.2% (range 0-20%) in CCL and 6.1% (range 0-25%) in ADH. The highest levels of AI were on chromosomes 17q12-q21 in CCL (15%) and 8q24 in ADH (23%); ~33% of early lesions did not have any detectable genetic changes. Levels of AI for both CCL and ADH were significantly ($P<0.0001$) lower than those found in in situ or invasive disease. Genetic changes characteristic of more advanced in situ and invasive disease, especially changes on chromosome 16q and 17p, were infrequent or non-detectable in pure early lesions. Conclusions: Pure CCL and ADH lesions demonstrate lower levels of genetic alterations than DCIS, invasive carcinomas or early lesions from cancerous breasts. Alterations characteristic of advanced disease were not found in lesions from non-cancerous breasts. While data generated from synchronous lesions has been used as support for a model of evolution from CCL and ADH to in situ and invasive disease, pure early lesions are, in fact, not genetically advanced and molecular profiles do not support these lesions as obligatory precursors to more advanced disease. Given the molecular differences between pure and synchronous lesions, current models of disease initiation and progression based largely on data generated from cancerous breasts must be re-evaluated.

P32

Basal phenotype predicts worse survival in HER2-positive breast cancer patients S.P. Bagaria,[1]* P.S. Ray,[1] J.M. Shamonki,[2] A.P. Chung,[1] X. Cui,[3] A.E. Giuliano.[1] *1. Department of Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA; 2. St. John's Health Center - Department of Pathology, Santa Monica, CA; 3. John Wayne Cancer Institute - Department of Molecular Oncology, Santa Monica, CA.*

INTRODUCTION Many studies have shown that HER2-positive and basal-like breast cancers are distinct groups associated with the poorest outcomes. Recent reports suggest that there exists a subtype of tumors which manifest both HER2 overexpression and basal-like markers. We sought to define the clinical impact of basal phenotype on HER2-positive breast cancers. **METHODS** A prospectively maintained breast cancer database was used to identify and retrieve archived paraffin-embedded sections for 138 tumors from 220 consecutive patients with HER2-positive, primary invasive ductal breast cancer diagnosed between 1995 and 2008. Whole tissue sections were immunostained for basal markers, CK 5/6 and CK 14. Expression of basal-like markers was correlated with age, tumor size, lymph node status, and tumor grade. Multivariate analysis was performed (adjusting for age, tumor size, lymph node status, tumor grade, hormone status) to understand the relationship of basal phenotype on survival. **RESULTS** Among the 138 HER2-positive patients, 57 (41%) were estrogen receptor (ER) negative of whom 13 (23%) expressed basal markers (HER2-basal). No ER positive patient (n=81) expressed basal markers. Compared to HER2-non-basal, HER2-basal patients were significantly older and were more likely to have lymph node metastasis and a high tumor grade. The 5-year overall survival rate for HER2-basal patients was 62% compared with 93% for HER2-non-basal patients ($p=0.003$). Multivariate analysis revealed that basal phenotype predicted worse 5-year overall survival (hazard ratio, 8.1; 95% confidence interval, 1.9-33.7; $p=0.004$). **CONCLUSIONS** Basal-like marker expression in HER2-positive breast cancer patients strongly prognosticates worse survival. Assessment of basal marker expression in HER2-positive breast cancer to define HER2-basal patients may need to be considered in developing a treatment plan.

P33

Does florid lobular carcinoma in situ behave like a precursor lesion of invasive lobular carcinoma? S.P. Bagaria,[1]* J.M. Shamonki,[2] P.S. Ray,[1] A.E. Giuliano.[1] *1. Department of Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA; 2. St. John's Health Center, Department of Pathology, Santa Monica, CA.*

INTRODUCTION Lobular carcinoma in situ (LCIS) is considered a risk factor for invasive lobular carcinoma (ILC) but not a precursor lesion. Florid LCIS (F-LCIS) is an architectural subtype of LCIS. Although F-LCIS does not express E-cadherin, its distended ductules and frequent luminal necrosis give it the histological appearance of ductal carcinoma in situ (DCIS). Since DCIS is a known precursor of invasive ductal cancer, could F-LCIS behave like a precursor of ILC? **METHODS** Our center conducted an extensive retrospective review of archival specimens, pathology reports and clinical records for LCIS cases diagnosed between 1991 and 2000. Excluded were patients with invasive cancers other than ILC. All cases were evaluated for the florid subtype and for ILC. Breast cancer subtype(s) was correlated with clinical endpoints and pathologic characteristics. **RESULTS** Of the 213 patients, 172 had classical LCIS (60% with ILC) and 41 had F-LCIS (83% with ILC). The percentage of grade 1, 2, and 3 lesions was 37%, 32%, and 32%, respectively, for F-LCIS; and 73%, 18%, and 9%, respectively, for classical LCIS. Classical LCIS had a diffuse pattern, whereas F-LCIS appeared as discrete foci adjacent to the ILC. The presence of classical LCIS or F-LCIS did not change the size, lymph node status, lymphovascular invasion, or hormone receptor status of ILC. There were no differences in overall survival according to architectural subtype of LCIS for those patients with and without ILC. **CONCLUSIONS** Our results indicate that 83% of patients with F-LCIS have concurrent ILC lesions that are often in close relationship with the primary tumor. One-third of F-LCIS lesions are high grade. These findings suggest that F-LCIS is often adjacent to ILC and warrants clinical treatment as a precursor for ILC.

P34

Disparities in Reconstruction Rates after Mastectomy A. Holt,* L. Duan, K. Henderson, L. Bernstein, J. Ta, J. Ellenhorn, L. Kruper. *City Of Hope, Duarte, CA.*

Background: Few studies have examined factors influencing whether breast cancer patients undergo reconstruction, either immediate or delayed, after mastectomy. This study examines variables associated with the use of reconstruction in four Southern California counties: Los Angeles, Orange, San Bernardino and Riverside. Methods: Postmastectomy reconstruction rates were determined from the California Office of Statewide Health Planning and Development hospital discharge database over a 5-year period from 2003-2007. International Classification of Disease-9 codes were used to identify patients undergoing reconstruction after mastectomy. Differences in reconstruction rates were examined by calendar year, age, race/ethnicity, insurance status and hospital characteristics. Odds ratios (OR) and 95% confidence intervals (CI) were calculated by logistic regression. Results: 2936 patients had mastectomy with or without reconstruction in 2003, increasing to 3,151 in 2007. Women under age 40 years had the highest rates of immediate reconstruction compared to other age groups. Compared with Caucasians, African Americans were half as likely to undergo immediate reconstruction after mastectomy (OR=0.49, 95%CI=0.38-0.62). Patients with private insurance were more likely than patients with Medi-Cal to undergo immediate reconstruction vs. mastectomy only (OR=7.12, 95%CI=6.04-8.39; $p<0.0001$). Teaching hospitals were nearly twice as likely to perform immediate reconstruction vs. mastectomy only compared to non-teaching hospitals. Patients undergoing procedures at NCI-designated comprehensive cancer centers were more likely to undergo flap vs. implant reconstruction (OR=2.76, 95%CI=2.15, 3.56) than patients undergoing procedures at other

hospitals. Delayed reconstruction was offered only at a small number of hospitals; the number increased from 22 to 35 hospitals over the 5-year period. Conclusion: Although the rate is increasing, only a minority of patients undergo reconstruction following mastectomy. Insurance status, race/ethnicity, and type of hospital appear to be significant factors limiting the use of reconstruction.

P35

The Role of Axillary Staging in Women Diagnosed with Microinvasive DCIS (DCISM) J.M. Pimiento,* M.C. Lee, N.N. Esposito, J.V. Kiluk, N. Khakpour, W.B. Carter, G. Han, C. Laronga. *H. Lee Moffitt Cancer Center, Tampa, FL.*

Objectives: Axillary staging via sentinel node biopsy (SLNB) in patients (pts) with DCISM is routinely performed but remains controversial with regards to the risk-benefit. Our objective is to determine clinicopathologic features associated with a higher risk of SLN-positive (pos) disease in pts with DCISM. Methods: A prospective, single-institution database of 19,084 newly diagnosed breast cancer pts treated from 1996-2009 was reviewed for a diagnosis of DCISM (invasive tumor <0.1cm), identifying 124 pts. Pts with incomplete records or no SLNB were eliminated. After exclusions, 90 pts were evaluable. Age, clinicopathologic data, and follow-up (F/U) were recorded. Statistical analysis was by Spearman correlation and logistic regression. Results: Of 90 pts, 30 (33%) were diagnosed by CNB, 34 (37%) by excisional biopsy, and 26 (29%) were upstaged from DCIS on CNB to DCISM at final operation. Three of 30 pts (10%) with DCISM on CNB were upstaged to invasive cancer on final pathology and eliminated from further analyses. Median age at diagnosis was 58.9 yr (range: 30-89). Lumpectomy was performed in 39 pts (45%) and mastectomy in 48 pts (55%). Mean number of SLN was 2.59 (SE 0.17). 6 pts of 87(6.9%) with DCISM as final diagnosis had a SLN-pos (4 lumpectomies, 2 mastectomies). There was no correlation with any clinicopathologic features, including palpable mass, grade, necrosis, or age at diagnosis (p=0.55 / 0.504 / 0.17 / 0.059). All 6 SLNB-pos pts had a complete axillary dissection; 2 pts had additional disease. Median F/U time was 74.2 mos (range: 2-169). In-breast recurrence was seen in 3 pts (5%), regardless of SLN status (p= 0.17) or correlation to DCIS grade or necrosis (p=0.16 / 0.78). There were no axillary recurrences. 2 pts developed distant metastasis; 1 died of disease. Overall survival was 94.2% at 5yrs for DCISM and 100% for DCISM with nodal disease (p=0.97). Conclusion: DCISM comprises 0.6% of pts at our institution. There is a low likelihood of nodal spread, however, a lack of identifiable clinicopathologic features associated with a positive SLNB precludes selective SLNB utilization.

P36

Post-excision mammography (PEM) has a limited role in assessing for residual disease (RD) after BCS M. Morrogh,* R. Sakr, E. Kueberuwa, A. Park, T.A. King. *MSKCC, New York, NY.*

Re-excision is standard practice for patients with inadequate margins after BCS yet there is no consensus on what defines an adequate margin, and re-excision is often negative for RD. In the setting of malignant calcifications, PEM may be used to assess for RD. The aim of this study was to assess the value of PEM after BCS in the setting of close/negative margins. METHODS Of 4235 patients underwent breast cancer surgery at MSKCC from Jan 2001-Dec 2003, 540(13%) presented with suspicious calcifications and underwent definitive BCS. Margin status was reported as: positive at ink, close<2mm, or negative>2mm. PEM +/- re-excision was performed at the surgeon's discretion. RESULTS Of 540 cases, 293(54%) had DCIS and 247(46%) had invasive disease (initial margin status: positive 71(13%), close 192(36%), negative 277(51%)). In total, 336/469(72%) patients with close/negative margins underwent PEM. Utilization of PEM did not vary with tumor type, but re-excision rate did (DCIS 42% vs INV 29%,p=.007). Of 192 patients with close margins, 146(76%) underwent PEM which was positive in 45(31%). 90% of patients with positive PEM underwent re-excision vs 70% with negative PEM and 20% with no PEM (p<.0001), yet positive PEM was not associated with a higher yield of RD. The NPV of PEM in this setting was 68%. Of 277 patients with negative margins, 192(69%) underwent PEM which was positive in 36(19%). Again, positive PEM increased the re-excision rate compared to negative or no PEM (97% vs 7% vs 3%,p<.0001) yet did not increase the yield of RD. The NPV of PEM in this setting was 73%. At a median follow up of 66 mos, the overall rate of LR among patients with close/negative margins was 6%. Margin status (close/negative) or re-excision did not influence LR. CONCLUSION For patients with malignant calcifications excised with close or negative margins, PEM was used selectively and was associated with higher rates of re-excision.While negative PEM accurately excluded RD in the majority of cases, positive PEM was not associated with a higher likelihood of finding RD in patients with close/negative margins and LR rates were not impacted by re-excision in this select group of patients.

Margins	n	DCIS N=260	Invasive N=209	Any Local recurrence
Close Margins	49	31 (63%)	18 (37%)	2 (4%)
Re-excision +	70	43 (61%)	18 (39%)	7 (10%)
Re-excision -	71	39 (54%)	33 (46%)	8 (11%)
No re-excision				
Negative Margins	16	11 (69%)	5 (31%)	1 (6%)
Re-excision +	33	22 (67%)	11 (33%)	0
Re-excision -	224	114 (50%)	114 (50%)	4 (2%)
No re-excision				

P37

The Impact of Breast Density on the Presenting Features of Malignancy N. Arora,[1]* L.M. Jacks,[2] T. King,[2] M. Stempel,[2] S.M. Patil,[2] M. Morrow.[2] *1. Surgery, NYPH-Cornell, New York, NY; 2. Memorial Sloan-Kettering Cancer Center, New York, NY.*

Mammographically dense breast stroma is associated with an increased risk of breast cancer. Limited mammographic visibility of tumors in dense stroma has also led to speculation that these malignancies may present at more advanced stage with worse prognosis. This study was undertaken to examine the relationship between breast density and presenting features of cancer. Methods: Data were obtained from a prospectively-maintained, single-institution database of 628 invasive breast cancers in patients treated between October 2005 and June 2007. Mammographic density was evaluated using BI-RADS classification (1=fatty, 2=scattered fibroglandular, 3=heterogeneously dense, 4=very dense). Patients were grouped as having fatty (BI-RADS 1+2) or dense (BI-RADS 3+4) breasts. Chi-square and multivariate logistic regression were used for statistical analysis. Results: The majority of patients were classified as BI-RADS 3 (61%), while a score of 1, 2, and 4 were assigned to 5%, 23%, and 11% of patients, respectively. Patients with dense breasts were younger and more likely to have mammographically occult tumors than those with fatty breasts(p<0.0001 for both). Controlling for patient age, no differences were identified in tumor size, grade, LVI, node positivity, or molecular subtype between dense and fatty groups(see Table). Tumors in dense breasts were more likely to have EIC (p=0.02) but there was no difference in mastectomy rate between groups. For BI-RADS 4 patients, there was a trend towards more lobular and non-ductal histologies when compared to all others(p=0.06). These patients were also more likely to undergo mastectomy, however this difference did not persist after controlling for age. Conclusions: Breast cancers in patients with dense breasts share the same clinical and molecular profiles as those in fatty breasts. Despite limitations in mammographic visibility, increased density is not associated with more advanced stage presentation or aggressive features. The trend towards lobular and special phenotypes in those with very dense breasts further supports that density does not predict worse outcomes and should not be considered a contraindication to breast conserving therapy.

Table. Age-adjusted comparison between breast density and clinicopathologic variables

Clinicopathologic variables	Fatty (1+2) N (%)	Dense (3+4) N (%)	p-value
MEDIAN AGE(range)	62 (30 - 84)	53 (29 - 91)	NA
MAMMOGRAPHIC FINDINGS			<0.0001**
Normal	2 (1%)	59(13%)	
Distortion	8 (5%)	41 (9%)	
Calcifications	20 (11%)	95 (21%)	
Mass	145 (82%)	253 (56%)	
Unknown	1 (1%)	4 (1%)	
MEDIAN TUMOR SIZE (range)	1.5 (0.1 - 11.0)	1.4 (0.1 - 10.0)	0.71
MULTICENTRIC/FOCAL	43 (24%)	135 (30%)	0.43
LYMPHOVASCULAR INVASION(LVI)	55 (31%)	159 (35%)	0.86
HISTOLOGIC GRADE			0.14
I	10 (6%)	16 (4%)	
II	28 (16%)	101 (22%)	
III	117 (66%)	277 (61%)	
Unknown	4 (2%)	42 (9%)	
NA	17 (10%)	16 (4%)	
EXTENSIVE INTRADUCTAL COMPONENT (EIC)	16 (9%)	86 (19%)	0.02**
TUMOR TYPE			0.88
Ductal/mixed	152 (86%)	389 (86%)	
Lobular	20 (11%)	52 (12%)	
Special	4 (2%)	11 (2%)	
MOLECULAR SUBTYPE*			0.51
Luminal A	128 (73%)	338 (75%)	
Luminal B	17 (10%)	38 (8%)	
Her 2	7 (4%)	23 (5%)	
Basal	24 (14%)	53 (12%)	
NODES POSITIVE			0.67
0	97 (55%)	255 (56%)	
1-3	55 (31%)	136 (30%)	
4+	24 (14%)	61 (13%)	
OPERATION			0.40
Mastectomy	67 (38%)	206 (46%)	
Breast Conservation	109 (62%)	246 (54%)	

*Molecular Subtype defined by immunohistochemistry of ER, PR, and HER 2. **Statistically significant

P38

Are mastectomy rates really increasing in the United States?

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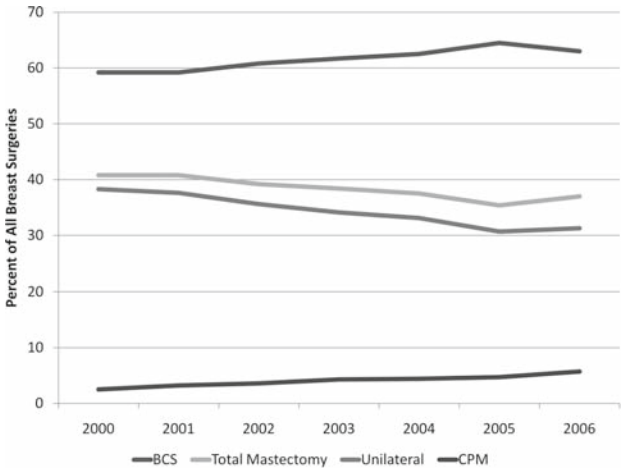
Introduction: Following the NIH Consensus Statement in 1991, breast conserving surgery (BCS) became more common while mastectomies decreased. However, several recently published single-institution studies have reported an increase in mastectomies since 2003. We conducted a population-based study to evaluate national trends in the surgical treatment of breast cancer (BCS, unilateral mastectomy or contralateral prophylactic mastectomy (CPM)) from 2000 through 2006. Methods: Using the Surveillance, Epidemiology, and End Results (SEER) database, we conducted a retrospective cohort analysis of women undergoing surgical treatment for breast cancer. We evaluated variation in BCS, unilateral mastectomy, and CPM rates over time by demographic and tumor factors. We additionally constructed logistic regression models to identify time trends and patient and tumor factors associated with each surgical treatment. Results: We identified 233,754 patients diagnosed with ductal carcinoma in situ (DCIS) or stage I-III invasive breast cancer from 2000-2006. The proportion of women treated with BCS increased slightly from 59.2% in 2000 to 63.0% in 2006 ($p<0.0001$). Total mastectomy use, a combination of unilateral and CPM, decreased over time. While unilateral mastectomies were clearly decreasing (from 38.3% to 31.3%), the proportion of CPMs more than doubled (2.5% to 5.7%). Women age 18-39 had the lowest rates of BCS and the highest rates of CPM of any age group; this group also experienced the largest increase in the proportion of CPMs over the study period (from 5.8% in 2000 to 16.4% in 2006). Multivariate analyses showed that women were more likely to receive BCS (OR=1.51 for 2006 vs. 2000, $p<0.0001$) and CPM (OR=2.03 for 2006 vs. 2000, $p<0.0001$) over time, after adjusting for patient and tumor factors. Conclusions: While several recently-published single-institution studies reported that mastectomy use has increased since 2003, our population-based analysis found decreased use of unilateral mastectomy and an increase in CPM use from 2000-2006. Variations in referral patterns and patient selection are potential explanations for these differences between single institutions and national trends.



Recent Trends in the Surgical Treatment of Breast Cancer

P39

Ipsilateral Breast Cancer Recurrence after Transverse Rectus Abdominal Muscle (TRAM) Reconstruction

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Introduction: The local recurrence rate after mastectomy is reported to be less than 10% and is similar with immediate reconstruction. The objective of this study was to identify characteristics of TRAM flap recurrence at a single institution with a limited number of surgeons. Methods: Medical records for patients with immediate TRAM reconstruction for breast cancer were retrospectively reviewed. We defined local recurrence as a biopsy proven mass in the reconstructed breast, ipsilateral axilla, or ipsilateral chest wall. The time to recurrence was calculated from the date of the surgery to the date of the biopsy. Results: From 1998-2008, 423 immediate TRAM reconstruction for breast cancer were performed. We identified 15 patients (3.5%) (age 34-59, median 45.5) with biopsy proven TRAM recurrence. All patients had clear margins (≥ 1 mm) at the time of the original surgery. The median follow-up time was 78.2 months (range 20.17–164.53 months).The majority of patients were Caucasian (68.7%). Younger patients age <40 (n=3), developed TRAM recurrence earlier compared to older patients > 50 (n=6), 20.9 months vs. 51.4 months, respectively. All recurrences were detected by physical examination performed by either the patients or the surgeon and confirmed by biopsy. TRAM recurrences presented as a palpable mass (n=13, 86.6%) followed by a non-specific change in the exam. The majority occurred in the subcutaneous tissue (n=13, 86.6%) and 2 occurred beneath the TRAM. Overall, the average time to detect the recurrence was 35.01 months; for chest wall recurrences this was longer, at 65.1 months. Breast imaging was done in 6 patients and only after clinical suspicion. All patients were staged after the TRAM recurrence and 5 (30%) were found to have metastatic disease. Conclusion: The majority of the TRAM recurrences were detected by routine physical examination. Recurrences that occur deep to the chest wall were diagnosed later than superficial recurrences. Since all local recurrences following TRAM were detected clinically, we do not recommend routine imaging of the reconstructed breast.

P40

Radiologic presentation of breast papillary lesions M. Lowe,[1]* J. Park,[2] L. Pan,[3] S.G. Gabram,[1] M. Mosunjac,[2] M. Rizzo.[1] *1. Department of Surgery, Emory University School of Medicine, Atlanta, GA; 2. Pathology and Laboratory Medicine, Atlanta, GA; 3. Biostatistics, Atlanta, GA.*

Background: The clinical management of breast intraductal papilloma (IDP) remains controversial. The objective of this study was to identify radiologic predictors of malignancy in a large cohort of solitary benign IDP diagnosed on core needle biopsy (CNB) who underwent surgical excision. Methods: Mammographic and sonographic data was collected using the Bi-rads (Breast Imaging reporting and Data System) categories. The location of IDPs was categorized as central or peripheral. The upgrade rate was defined as a change in the surgical specimen to a lesion of greater clinical significance. Logistic regression model and Fisher's exact test were applied to correlate upgrade with radiological characteristics. Results: From 2000 to 2007, we identified 126 patients with benign solitary IDP who underwent surgery within 6 months from the core biopsy. Of those, 31 (24.6%) were upgraded ($p<0.001$); 16(51.6%) to ADH, and 15 (48.4%) to DCIS. All patients had an abnormal mammogram or ultrasound, Bi-rads 4 or 5 that prompted the core biopsy. Upgraded IDPs were located centrally in 13 patients and peripherally in 18 patients. The radiologic presentations of these 31 IDPs included: breast mass or nodule, microcalcifications, or abnormal density as shown in Table 1. Both univariate and multivariate analysis showed that central location was predictive of upgrade to a lesion of greater clinical significance ($p=0.03$ in both analyses). Conclusions: We recommend routine mammogram and surgical excision of all IDPs identified on CNB because 24.6% of benign solitary IDP at CNB were upgraded to either ADH or DCIS. Only central mammographic location was a predictor of upgrade. TABLE 1

Radiologic presentation of 31 benign intraductal papilloma that upgraded to ADH or DCIS

TOTAL n=126	Upgrade to ADH or DCIS n=31 (24.6%)	OR(95% CI)	p-value
Location			
Central n=34(27%)	13(38.2%)	2.55(1.07-6.03)	0.03
Peripheral n=92(73%)	18(19.6%)		
Radiologic presentation*			
Mass n=63(45.9%)	12 (19.0%)	1.54 (0.68-3.49)	0.30
Density n=10 (7.2%)	4 (40.0%)	0.46 (0.12-1.73)	0.25
Microcalcifications n=63(46.9%)	15 (23.4%)	1.14 (0.51-2.56)	0.76

*The total number of radiologic presentation is 137 because 11 patients with microcalcifications had a breast mass or a density associated with microcalcifications.
OR=Odds Ratio
CI=Confidence Interval

P41

Intraoperative Imprint Cytology of Sentinel Nodes in Patients with Breast Cancer – Costly or Cost Effective? J.P. Kaminski,* D. Case, M. Howard-McNatt, K.R. Geisinger, E.A. Levine. *Surgical Oncology, Wake Forest University School of Medicine, Winston-Salem, NC.*

Background: Sentinel lymph node (SLN) biopsy is now a standard of care for breast cancer patients. Intraoperative imprint cytology (IIC) reveals results to the surgeon, which can lead to a lymphadenectomy under the same anesthetic for a positive SLN. Thus a positive IIC can spare the patient a second operation and charges associated with it. The aim of this study is to assess the cost-effectiveness of IIC in breast cancer patients. Methods: This study evaluated ninety-eight patients who underwent a SLN biopsy between July 2008 and May 2009. Each patient was divided into one of three populations based on the results of IIC and permanent sections: (1) true-negative (TN) IIC, (2) true-positive (TP) IIC, and (3) false-negative (FN) IIC. Total charges per hospital visit were extracted retrospectively and added to each patient. Statistical analysis was used to determine the charge differences between each population. Results: Metastases were identified in 26 (27%) of 98 patients. Of these, 18 (18%) patients were detected by IIC. Thus, the TN IIC population was composed of 72 patients, the TP IIC population was composed of 18 patients, and the FN IIC population was composed of 8 patients. No false-positive results were identified. The median total charges per patient for each population were the following: (1) $14,764.62 (2) $19,025.89 and (3) $29,750.64. The total charges among the three populations were statistically significantly different ($p<0.05$). There was more than a $10,000 difference in total charges per patient between the node positive population that did not benefit from IIC (FN) and the node positive population that did benefit from IIC (TP). The cost of evaluating two SLNs using IIC is $131 at our institution. Conclusions: IIC is a cost-effective evaluation of breast cancer patients. The difference in total charges between the two populations (FN and TP) far outweighs the actual cost of the IIC. Further, in addition to the reduced costs incurred by the patient and the hospital, IIC can spare the patient the psychological and physical stress of a second operation.

P42

Molecular Breast Imaging in the preoperative surgical workup of women with biopsy proven breast cancer J.C. Boughey,[1]* M.K. O'Connor,[2] C.B. Hruska,[2] L. Neal,[3] J.W. Jakub,[1] A.C. Degnim,[1] R.W. Maxwell,[4] C.L. Tortorelli,[4] D.J. Rhodes.[3] *1. Surgery, Mayo Clinic, Rochester, MN; 2. Nuclear Medicine - Mayo Clinic, Rochester, MN; 3. Internal Medicine - Mayo Clinic, Rochester, MN; 4. Breast Imaging - Mayo Clinic, Rochester, MN.*

INTRODUCTION Molecular Breast Imaging (MBI) is a nuclear medicine technique that images technetium 99m (Tc99) sestamibi uptake in the breast using dual head Cadmium-Zinc-Telluride gamma cameras. We report preliminary results from a prospective clinical trial evaluating the role of preoperative MBI in women with biopsy proven breast cancer. The aim of this study is to evaluate the ability of MBI to detect additional disease over that detected by mammography. METHODS Eligible women with biopsy-proven breast cancer underwent MBI using 30mCi Tc99 sestamibi. Patients with MBI studies showing suspicious uptake other than the known cancer underwent additional diagnostic studies (second look ultrasound and MRI) and biopsy as indicated. The impact of MBI findings on the surgeon's treatment was evaluated prospectively. Pathologic findings at surgery were correlated with the MBI. RESULTS 50 patients with biopsy-proven cancer on this prospective study have undergone MBI and surgery. MBI identified additional disease in 14 cases (28%) compared to mammography. In 4 patients with a mammographically occult palpable mass, the cancer was visualized on both ultrasound and MBI (4/50 = 8%). Of the 46 women with cancer seen on mammogram, 6 had an additional separate focus of breast cancer on MBI but not visible on mammogram (6/50 = 12%). These additional foci of disease were also seen on MRI and changed surgical treatment from breast conservation to mastectomy. In 3 patients, MBI detected a significantly greater extent of disease than mammography (3/50 = 6%). This larger volume of disease was also seen on MRI and changed the surgical treatment plan from breast conservation to mastectomy. In all cases the MBI and MRI findings were consistent with the final pathology. In 1 patient (2%) MBI prompted a contralateral percutaneous biopsy followed by excisional biopsy for atypia. CONCLUSION In women with biopsy-proven breast cancer, MBI detected additional confirmed pathological disease compared to mammography in 28% of cases and altered surgical treatment in 20% of women. MBI may be a clinically useful imaging modality in the preoperative workup of women with breast cancer.

P43

Usefulness of pre-operative axillary ultrasound in early stage breast cancer patients J. Cools-Lartigue,[1]* N. Trabulsi,[1] A. Sinclair,[2] A. Meguerditchian,[1] B. Mesurolle,[1] R. Fuhrer,[2] S.H. Meterissian.[1] *1. McGill University Health Center, Montreal, QC, Canada; 2. Department of Epidemiology, McGill University, Montreal, QC, Canada.*

INTRODUCTION: Axillary lymph node (ALN) status is the most important prognostic factor in early stage breast cancer. Axillary ultrasound is being used increasingly as a means of determining ALN status prior to surgery. The purpose of this study was to determine the sensitivity, specificity, and accuracy of axillary ultrasound in a consecutive series of breast cancer patients. METHODS: Axillary ultrasound is used routinely at our institution and this study is based on clinical, imaging, and laboratory data collected for a consecutive series of patients with early-stage breast cancer between 2005 and

2007. Axillary ultrasound findings were reported as normal, suspicious/abnormal, enlarged, and multiple/lymphadenopathy. To evaluate ultrasound performance, normal was compared to any abnormality. Lymph node status (positive or negative) was recorded for all sentinel and non-sentinel nodes examined following axillary dissection. The data were summarized and cross-tabulated, and test characteristics were calculated. RESULTS: Data were collected on 354 patients. The mean patient age was 57.8 years [range: 22 – 97], with invasive ductal cancer in 68%, estrogen receptor positive in 78%, progesterone receptor positive in 60%, Her-2-neu positive in 12% and positive axillary nodes in 48%. The ultrasound was normal in 61%, suspicious/abnormal in 22%, enlarged in 12% and multiple in 4.8%. Axillary node status was not available for 15 patients. The sensitivity and specificity of any ultrasound abnormality in identifying positive ALN status in these patients (339 pts) were 62 % (95%CI 54.8 – 69.7%) and 86 % (81.1 – 91.4%) respectively. The positive predictive value was 81 % (74.1 – 87.8%) and negative predictive value was 71% (64.7 – 77.0%). The overall accuracy was 74 % (69.6 – 79.1%) Accuracy improved with number of positive nodes (> 3 vs < 3, p<0.0001) and size of metastatic disease (> 2mm vs < 2mm, p<0.0001). CONCLUSIONS: Although operator-dependent, ultrasound of the axilla has an accuracy of greater than 70% in this series of patients. Ultrasound is easy to perform and may offer the potential to avoid unnecessary sentinel node dissection.

P44

Novel STAT3 inhibitor in the Treatment of Breast Cancer
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Background: Signal Transducer and Activator of Transcription 3 (STAT3) is a cytoplasmic protein shown to be essential for malignant transformation and progression of many human cancers. Persistent increased activity of STAT3 is found in more than 40 to 60% of primary breast cancers and is responsible for chemotherapy-resistance in both primary and metastatic breast cancers. We have identified novel STAT3 inhibitors by computational modeling and virtual ligand screening from the National Cancer Institute (NCI) chemical libraries. Of the initial targets Compound 48 (C48), a small molecule STAT3 inhibitor was selected for further testing. Methods: In vitro testing were performed in STAT3 over-expressing mouse (C3L5) and human (MDA 468) breast cancer cell lines. Cell viability was assessed by MTT assay. Syngeneic mouse breast cancer model (C3H/HeJ – C3L5) was used for in vivo testing. Mice, bearing subcutaneous tumors were either treated with daily intraperitoneal injections of vehicle or C48 (100 mg/kg or 200mg/kg) for three weeks. Tumor size and weights were measured. STAT3 inhibition was analyzed by western blot analysis. Results: Compound 48 treatment of both human and mouse breast cancer cell lines resulted in cell death in a dose dependent fashion(p<0.05). In vivo treatment with C48 was well tolerated and resulted in significantly decreased tumor growth as evidenced by decreased tumor size in animals treated with 200mg/kg of C48 when compared to the vehicle-treated controls (n=6/group, p<0.05). Western blot analysis of the C48 treated cells and resected tumors demonstrated inhibition of STAT3 phosphorylation, a key step in the activation of STAT3 (data not shown). Conclusions: We have identified a novel STAT3 inhibitor with significant anti-tumor effects both in vitro and in vivo. Further work is being focused on developing additional novel STAT3 inhibitors with structural modification to increase their therapeutic efficacy.

P45

Cumulative Findings from the E75 Peptide Vaccine Adjuvant Trials in Breast Cancer
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Background: We have vaccinated breast cancer (BCa) patients with a single, HLA-A2/A3 restricted immunogenic peptide (E75, HER2/neu,369-377) vaccine in phase I/II clinical trials. E75 was given with GM-CSF to clinically disease-free BCa patients after standard multi-modality therapy. The vaccine is safe and effective in stimulating clonal expansion of E75-specific CD8+ T-cells. Currently, we report the efficacy of the vaccine to prevent recurrence based on intention-to-treat and subset analyses. Methods: E75+GM-CSF was given intradermally x6 monthly inoculations to the vaccine group (VG) while unvaccinated control patients (CG) were followed prospectively. Studies included both node positive (NP) and node negative (NN) BCa patients expressing all levels of HER2/neu (IHC 1-3+). The trials were dose escalation/schedule optimization trials with monitoring for local/systemic toxicities. Due to waning immunity, a voluntary booster program, with boosting every 6 months was initiated mid-trial. Clinical recurrences were documented with 5 year follow-up. Results: 187 BCa patients were enrolled in vaccine trials. 106 (56.7%) patients were HLA-A2/A3-positive and assigned to the VG, while 81 (43.3%) were HLA-A2/A3-negative and followed in the CG. There were no significant prognostic differences between the groups except more ER/PR negativity in the VG (p=0.04). With a median follow-up of 52 and 57 months, the recurrence rate (RR) is 10.4% and 14.8% in the VG and CG, respectively (p=0.27). Since boosters were not included initially, 24 mo landmark analysis revealed a RR of 7.2% and 12.3% in the VG and CG, respectively (p=0.19). In subgroup analysis, the vaccinated patients who benefited most compared to controls were NP (13% vs 19% RR, p=0.40), HER2/neu low-expressors (6.3% vs 15.7% RR, p=0.22), optimally dosed (2.9% vs 14.8% recurrence, p=0.08), and boosted (0% vs 9.2% with early recurrences prior to booster program omitted, p=0.17). Conclusion: The E75+GM-CSF vaccine is safe, well tolerated and may be able to prevent BCa recurrences. A phase III trial has been designed targeting NP, HER2 low-expressors and with optimal dosing and booster inoculations to maximize potential benefit.

P46

Axillary Lymph Node Response after Neoadjuvant Chemotherapy in Triple Negative Breast Cancer
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Introduction: Neoadjuvant chemotherapy is the standard of care for locally advanced breast cancer. It is estimated that 25% of patients who present with node positive disease convert to node negative status after neoadjuvant chemotherapy. However, the axillary response rate after neoadjuvant chemotherapy has not been defined in triple negative breast cancer (TNBC). Methods: A retrospective review was used to identify patients diagnosed with stage II and III breast cancer who received neoadjuvant chemotherapy from Jan 2000 to Oct 2008. Patients with TNBC were identified and data was collected on patient age, tumor characteristics, pre-chemothrapy axillary staging,type of surgical staging procedure, and post chemotherapy axillary lymph node response and survival. Results: 136 patients with known tumor profile were treated with neoadjuvant chemotherapy. 40 out of 136 (29%) were triple negative. The median age of the triple negative patients was 48 years (range: 33-84) with 57% being African-American and the remaining 43% being Caucasian. The median follow up was 15 months with 26 patients (65%) being deceased and 14 (35%) alive. Average number of nodes removed was seven. 67% of patients (26/ 40) had clinically positive nodes before chemotherapy. 62% (16/26) continued to have pathologic positive nodes after chemotherapy, while 38% (10/26) converted to node negative status. 14 patients (33%) had clinically negative nodes of which 12 (86%) remained node negative after chemotherapy and 2 (14%) had positive nodes on surgical excision. Neoadjuvant chemotherapy was found to downstage 11 of 40 (28%) patients after resection. There was no significant difference in overall survival between patients who converted to node negative as compared to patients who remained node positive after neoadjuvant chemotherapy (p= 0.665). Conclusion: A Significant number of patients with triple negative breast cancer achieved eradication of axillary lymph node metastasis after neoadjuvant chemotherapy. Axillary lymph node conversion did not affect overall survival. Sentinel lymph node biopsy can be selectively considered in TNBC after neoadjuvant chemotherapy.

P47

Breast MRI Tumor Size as a Predictor of Response to Neoadjuvant Chemotherapy
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Introduction: Neoadjuvant chemotherapy (NACT) can be used in breast cancer to decrease tumor size, making breast conserving surgery more feasible. Accurate pre-operative measurement of tumor response would be beneficial for surgical planning. We examined the utility of breast MRI in evaluation of tumor response following NACT. Methods: A retrospective review of our breast MRI database between January 2006 - September 2009 was performed. Of the 667 newly diagnosed breast cancer patients (pts), only those pts who

underwent NACT and had a pre-NACT and post-NACT breast MRI were further analyzed. Age, tumor characteristics, lymph node status, type of surgery, invasive tumor size on pre-NACT and post-NACT MRI tumor size and final pathology results were collected. Statistical analyses were performed using chi-square test. Results: One hundred and forty pts underwent NACT for clinical N1 disease or tumor size larger than T1. Eighty-one pts had post-NACT MRI and comprise the study cohort. The median age was 50yrs (range 24-82). The median invasive tumor size as determined by pre-NACT MRI was 3.7cm (range 0.9cm-10cm). The median post-NACT size was 1.1cm (range 0cm-10cm). The median pathologic invasive tumor size (ypT) was 1.2cm (range 0cm-10.4cm). The median size difference of MRI versus ypT was 0.7cm (range 0cm-4.2cm). Forty-nine of 81 pts (60%) had mastectomy regardless of tumor response, and 32/81 pts (40%) had lumpectomy. Thirty-two pts who had lumpectomy had tumor size within 0.7cm (range 0cm-4.2cm) of MRI predicted tumor size. The concordance correlation coefficient between measurements by MRI and ypT was 0.80; (95% CI: 0.69 - 0.87); ($p< 0.0001$). Post-NACT MRI was found to have a positive predictive value of 91% and a sensitivity of 83%. The negative predictive value was 60% and the specificity was 75%. Conclusion: Breast MRI appears to be a useful modality to predict tumor response in breast cancer patients undergoing NACT. The use of MRI may aid in surgical planning and selection for breast conservation surgery.

P48

Response to Neoadjuvant Chemotherapy is Not Associated with Improved Results for Sentinel Lymph Node Biopsy in Patients with Inflammatory Breast Cancer S. Bloom,* H.S. Cody. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

INTRODUCTION: Sentinel lymph node (SLN) biopsy is standard care for axillary staging in breast cancer, but its role following neoadjuvant chemotherapy (NAC) is controversial, especially in the setting of inflammatory breast cancer (IBC). METHODS: We reviewed our SLN database from 1999-2004 and identified 112 patients who had SLN biopsy following NAC, including 37 patients with inflammatory breast cancer (IBC) and 75 with non-IBC. We compared the success rates of these groups, and examined the performance characteristics of SLN biopsy specifically in the IBC group. RESULTS: SLNs were less often identified for IBC than for non-IBC (62% vs 87%, p=0.003). All 37 patients with IBC had an axillary dissection, with a resulting false negative rate for SLN biopsy of 15%. Of the IBC patients, a clinical complete response (CR) was observed in 35% (13/37), while a pathologic CR in found in 5% (2/37). A pathologically negative axilla was identified in 16% (6/37). Comparing IBC patients who had a CR with those who did not, the success rate for SLN biopsy did not differ (69% vs 58%, p=0.51), the proportion of positive axillae was the same (85% vs 83%, p=0.92), and the false-negative rate was similar (25% (2/8) vs 8% (1/12), p=0.31). Of the 23 IBC patients with successful SLN biopsy performed by combined technique, the SLNs were identified by dye and isotope in 44% (12), by isotope alone in 48% (11) and by dye alone in 9% (2). CONCLUSIONS: Following NAC for IBC, the success rate of SLN biopsy is lower and the false negative rate is higher than for breast cancer patients in general, and for those who have had NAC for non-IBC. For patients with IBC, the presence of a clinical CR after NAC does not predict a higher success rate, a negative axilla, or a lower false negative rate. Under current NAC protocols, axillary dissection should remain standard care for patients with IBC.

P49

Are Increased Mastectomy Rates Based on Pretreatment MRI Findings Justified? Clive KS, Tyler JA, Barchie MF, Sutcliffe JB, Kirkpatrick AD, Banks KP, Bell LM, Saenger JS, and Peoples GE
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Introduction: Routine pretreatment breast MRI in newly diagnosed breast cancer patients remains controversial. Recent data from our institution demonstrated the feasibility of incorporating MRI without delay in treatment and lead to lower re-excision rates but higher mastectomy rates. In this study, we assessed whether the higher mastectomy rate based on MRI findings is justifiable. Methods: A retrospective review of our prospectively collected database of all new breast cancer patients since 2007 was undertaken. The database includes demographic, radiographic, pathologic, treatment and outcome parameters. 90 consecutive newly diagnosed breast cancer patients received pretreatment MRI at our institution. These patients were compared to 86 consecutive new breast cancer patients who did not receive an MRI. No other alterations were made during this period in our evaluation and treatment per NCCN guidelines. Results: Using standard imaging modalities, i.e. diagnostic mammography (DM) and ultrasound, our prior mastectomy rate was 26% (22/86). 90 consecutive patients received pretreatment MRI with 88 receiving operative intervention at our facility. Of these, 46/88 (52%) underwent mastectomy. The doubling of the mastectomy rate was largely due to MRI findings with 21/46 (46%) mastectomy patients having evidence of multifocal/multicentric (MF/MC) disease. Of these, 15/21 (71%) were confirmed to have MF/MC disease on surgical pathology. The sensitivity and specificity for MRI in detecting MF/MC disease was 71% and 83%, respectively, vs 10% and 97% with DM. For detecting lymphadenopathy (LAD), MRI demonstrated a sensitivity and specificity of 44% and 88%, respectively, vs 31% and 98% with DM. MRI was found to be the most accurate imaging modality for determining primary tumor size 68% of the time. Conclusions: Routine pretreatment MRI has been associated with a doubling of our mastectomy rate. This change has largely been due to MRI findings of MF/MC disease, LAD, and tumor size. These findings were confirmed with surgical pathology approximately 70% of the time.

P50

Intraoperative Injection of Low Dose 99mTc Sulfur Colloid for Sentinel Node Biopsy: An Aid to Resource Conservation E. Tran,[1]* B.J. Grube,[1] D. Cheng,[2] B. Killelea,[1] M. Rishi,[1] D. Lannin.[1] *1. Yale New Haven Breast Center, New Haven, CT; 2. Yale University, Department of Radiology, New Haven, CT.*

INTRODUCTION: Until fission-independent generators prove to be reliable for large-scale production, nuclear reactors remain the principal source of technetium-99m (99mTc). Their limited availability, high costs and large quantities of radioactive wastes raised the need for budgeting the use of 99mTc. Most institutions use between 0.5 to 1 millicurie of 99mTc sulfur colloid for sentinel lymph node biopsy (SLNB). A lower dose would help conserve this valuable resource. METHOD: A retrospective review was conducted of SLNB performed at a single academic breast center that used intraoperative intradermal injection of 0.25 millicurie of 99mTc sulfur colloid. RESULTS: At least one radioactive node was found in 995 of 997 (>99%) consecutive SLNB that were performed between Jan 1, 2003 and September 30, 2009. The mean number of SLN found was 2.25 (± 1.36). Of the 2 patients where a SLN was not found, one had previous breast reduction and a lower inner quadrant tumor, and the other had inflammatory breast cancer treated with neoadjuvant chemotherapy. Four additional patients had low initial counts and received a 2nd injection of 99mTc. Twenty four percent of SLNB resulted in at least one positive node, including 3% micrometastasis. An additional 3.7% had isolated tumor cells (N0i+). Radioactivity was detected in the axilla within 10 minutes of injection. A subset of 189 SLNB had 10-second gamma counts recorded, and the mean and median counts were 8190 and 3591 respectively (range 103 to 89,000) for the 1st SLN removed; 6768 and 3538 respectively (range 32 to 22,636) for the 2nd SLN. Nodes could be easily detected with gamma counts as low as 100 to 200. There was no significant difference in the rate of node positivity for nodes with greater vs. fewer than the median count (9% vs. 15%, $p = 0.26$) CONCLUSION: Intraoperative injection of radioisotope is convenient for the patient and the surgeon, and simplifies scheduling for the operating room and the nuclear medicine department. The use of low dose injection provides excellent results and may help reduce the demand for 99mTc, and thus the associated issues with its production.

P51

The Effect of Incision Choice on Outcomes of Nipple-Sparing Mastectomy Reconstruction J.Y. Kim,* V. Rawlani, S. Khan, N. Hansen, J. Fiuk, S.A. Johnson, E. Hirsch, N.A. Fine. *Department of Surgery, Feinberg School of Medicine, Northwestern University., Chicago, IL.*

INTRODUCTION: The indications for nipple-sparing mastectomy (NSM) are broadening as more breast surgeons accept the utility of preserving the nipple-areolar complex (NAC) in select cases of prophylactic and therapeutic mastectomies. A number of incision types are available to the mastectomy surgeon including the inframammary, lateral, and periareolar approaches. We endeavored to analyze the reconstructive outcomes associated with differing incisions. METHODS: Utilizing a single surgical technique, all NSM followed

by tissue expander implant reconstruction using acellular dermis performed between 2007 and 2008 were retrospectively reviewed. RESULTS: Thirty-seven breast procedures performed on 20 patients were analyzed. Periareolar incision caused significantly more nipple necroses than the lateral or inframammary incisions (38.1% vs. 6.3%, p=0.028). Breasts receiving radiation demonstrated a trend toward increased nipple necrosis (45.5% vs. 15.4%, p=0.066) and soft-tissue infection (36.4% vs. 7.7%, p=0.051). Breasts receiving chemotherapy demonstrated a modest trend towards more soft-tissue infections (23.1% vs. 12.5%, p=0.156). There was a trend towards increased breast size (weight of breast tissue excised) in cases demonstrating nipple necrosis (540.4 grams vs. 425.7, p=0.130). There was no difference in initial intraoperative fill volume (p=0.812), percent intraoperative fill volume (initial fill volume/final fill volume, p=0.694), or final fill volume (p=0.797) in breasts demonstrating nipple necrosis. CONCLUSION: The periareolar incision results in a higher rate of nipple necrosis following tissue expander-based reconstruction. There is a trend towards greater complications associated with radiation treatment. With the lateral and inframammary incision, NSM with a tissue expander-acellular dermis reconstruction results in acceptable cosmetic and reconstructive outcomes.

Table 1: Complication Rates from 37 Nipple Sparing Mastectomies Followed by Two-Stage Tissue Expander Implant Reconstruction

	Periareolar	Lateral or Inframmary	p-value
Number	21	16	
Nipple Necrosis	8(38.1%)	1(6.3%)	0.028
Complete	5(23.8%)	0(0.0%)	0.046
Partial	3(14.3%)	1(6.25%)	0.412
Infection	4(19.0%)	2(12.0%)	0.472
Hematoma	1(4.8%)	0(0.0%)	0.568
Seroma	0(0.0%)	0(0.0%)	-
Implant Migration	0(0.0%)	0(0.0%)	-
Capsular Contracture	0(0.0%)	0(0.0%)	-
Nipple Loss	5(23.8%)	0(0.0%)	0.046
Debridement	2(9.5%)	1(6.25%)	0.603
Explantation	4(19.0%)	0(0.0%)	0.091

P52

Comparison of Nodal versus Primary Her2/neu Expression in Node-positive Breast Cancer Patients C.E. Lago-Toro,[1]* E. Grujic,[2] A.R. Larsen,[1] L. Allen,[1] A.V. Barrio,[1] B. Sieling,[3] T. Fancher,[3] T.G. Frazier.[1] *1. Department of Breast Surgery, The Bryn Mawr Hospital, Bryn Mawr, PA; 2. Department of Pathology, The Bryn Mawr Hospital, Bryn Mawr, PA; 3. Department of Breast Surgery, St. Mary's Hospital, Waterbury, CT.*

Background: The Her2/neu gene is amplified in 25% of breast cancers denoting a poor prognosis. Evaluation of Her2 status is standard practice in patients with invasive breast cancer to assess responsiveness to trastuzumab. The goal of our study was to determine whether Her2 expression differed between the primary tumor and the axillary lymph node (ALN) in node-positive breast cancer patients. Methods: From 2003 to 2008, 50 female patients with node-positive invasive mammary carcinoma were identified. Immunohistochemistry (IHC) slides (of the primary tumor) for estrogen receptor (ER), progesterone receptor (PR), and Her2 overexpression were re-reviewed. The ALN blocks were submitted for IHC of ER, PR, and Her2 overexpression. These were compared with primary tumor ER/PR and Her2. Results: 46 of 50 patients identified had slides which were available for analysis, with 50% of primary tumors overexpressing Her2. 42 patients had invasive ductal carcinoma, 2 had invasive lobular carcinoma and 2 had mixed ductal/lobular. Her2 was concordant in 37/46 (80.4%) cases. In 8/9 cases, Her2 was overexpressed in the primary tumor, but not in the ALN metastasis. In 1 discordant case, Her2 was not overexpressed in the primary tumor and was 2+ on IHC in the ALN metastasis. With respect to hormone receptors, concordance for ER and PR was 43/46 (93.5%) and 36/46 (78.3%), respectively. ER expression was lost in the ALN in all 3 discordant cases. Of the 10 discordant PR cases, 7 expressed PR in the ALN when the primary tumor was negative and 3 lost their PR expression. Concordance for Her2, ER and PR between the primary tumor and ALN was found in 30/46 (65.2%) of cases. Conclusions: Her2 overexpression was lost in 8/46 (17.4%) of patients with node positive breast cancer. 1 case demonstrated equivocal expression in the ALN when the primary tumor did not express Her2. Loss of overexpression of Her2 in nodal metastasis may provide an explanation for trastuzumab resistance in select patients. A prospective study to evaluate clinical response to trastuzumab in patients in whom overexpression is lost in the ALN may impact future treatment recommendations.

P53

Validation of a Model to Predict Four or More Metastatic Axillary Nodes in Sentinel Node Positive Breast Cancer Patients B. Zendejas,* A.C. Degnim, T.L. Hoskin, C.A. Reynolds, D.R. Farley, J.C. Boughey. *Mayo Clinic, Rochester, MN.*

Introduction: Patients with metastases in four or more axillary lymph nodes (≥4+ALN) represent a subset of breast cancer patients at increased risk of local recurrence and who benefit from post-mastectomy radiation. A risk prediction model designed to identify such patients was published by Rivers et al from the University of Michigan and M.D. Anderson Cancer Center. We sought to evaluate the performance of this model in an independent patient population. Methods: We reviewed 455 breast cancer patients with positive sentinel lymph nodes who underwent completion axillary lymph node dissection at our institution. The estimated probability of ≥4+ALN was calculated for each patient using the Rivers model. The model performance was analyzed with the Hosmer-Lemeshow goodness-of-fit test and with the area under the receiver operating characteristic curve (AUC-ROC). We also estimated the sensitivity and negative predictive value (NPV) at probability cut-points of ≤5% and ≤10%. Results: Despite the fact that our patient cohort had a higher proportion of patients with ≥4+ALN (19% vs 14%) and more patients with worse prognostic features (tumor size, lymphovascular invasion and extranodal extension), the model demonstrated good calibration in our population based on the Hosmer-Lemeshow test (p=0.82). The discriminatory ability of the model resulted in an AUC of 0.81 (Figure 1). The mean estimated probabilities for those with and without ≥4+ALN were 0.41 (95%CI 0.35-0.47) and 0.15 (95%CI 0.13-0.17), respectively (p<0.0001). For predicted cut-off points of ≤5% and ≤10%, sensitivity and NPV estimates were 89.7% and 95.0%, and 86.2% and 94.5%, respectively. Conclusions: This study validated the Rivers model for prediction of ≥4+ALN using an external data set. The model performed well in our patient population and may be clinically useful to predict ≥4+ALN. However, its clinical utility is limited by the current controversy surrounding the use of post-mastectomy radiation for all node positive patients.

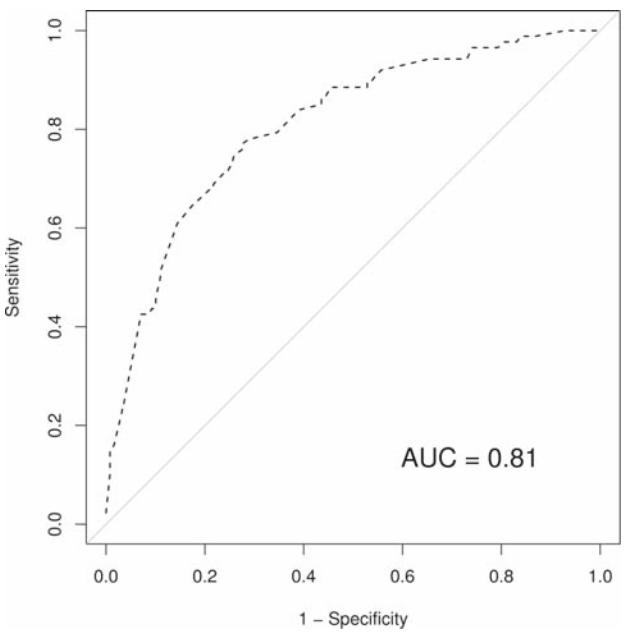


Figure 1. Receiver Operating Characteristic Curve

P54

Primary and Secondary Angiosarcoma of the Breast: A Review of 41 Cases J.S. Scow,[1]* C.A. Reynolds,[2] A.C. Degnim,[1] I.A. Petersen,[2] J.W. Jakub,[1] J.C. Boughey.[1] *1. Gastrointestinal and General Surgery, Mayo Clinic, Rochester, MN; 2. Mayo Clinic, Rochester, MN.*

Background: Angiosarcoma (AS) of the breast can be divided into primary (PAS) and secondary (SAS). The etiology of PAS is unknown. SAS develops following radiation therapy (RT) to the breast or chest wall for treatment of breast cancer (BC). Methods: With IRB approval all cases of breast AS were identified. Clinicopathologic factors were reviewed for each patient. Characteristics of PAS and SAS were compared. Results: AS was identified in 41 patients; PAS in 27 (66%) and SAS in 14 (34%). The median age of PAS patients was significantly lower than that of SAS - 43 years (range 26-74) vs 73 years (range 45-86) respectively (p<0.0001). Median time from RT to SAS diagnosis was 6.8 years (range 3.8-12). Median tumor size was 5.8 cm (range 1-18.5). PAS and SAS patients had a median tumor size of 7.0 (range 1-18.5) and 5.0 (range 1.2-12.2) cm respectively (p=0.7). Tumors were high grade in 33% of PAS and 82% of SAS (p=0.02). PAS was more likely to present with a mass while SAS typically presented with a rash (p<0.0001). All 27 PAS patients underwent mastectomy. Eleven (76%) SAS patients initially had lumpectomy for BC and all underwent mastectomy for SAS. Of three patients who had prior mastectomy and radiation for BC, two were treated with wide excision and one declined surgery for SAS. With a median follow-up of 2.3 years, 21 patients have died, 7 are alive with local or distant disease, 11 patients are alive and disease free and 2 are lost to follow up. Sixteen (76%) deaths were attributed to AS. Median time from diagnosis to death was 2.3 (range 1-13.5) and 5.4 (range 0.4-7.1) years for PAS and SAS respectively (p=0.9). Five year survival for PAS and SAS was 46% and 69% respectively (p=0.8) (see figure 1). There was no difference in survival based on tumor size (≥ 5 cm vs < 5 cm) (p=0.8). Conclusion: PAS occurs in younger patients than SAS. SAS occurs approximately 6.8 years after RT and is being seen with increased frequency in recent years. Mastectomy is the mainstay of treatment for both PAS and SAS. Local recurrence and distant metastases are common. Breast PAS and SAS are rare malignancies with poor prognosis and time to death is similar for both groups.

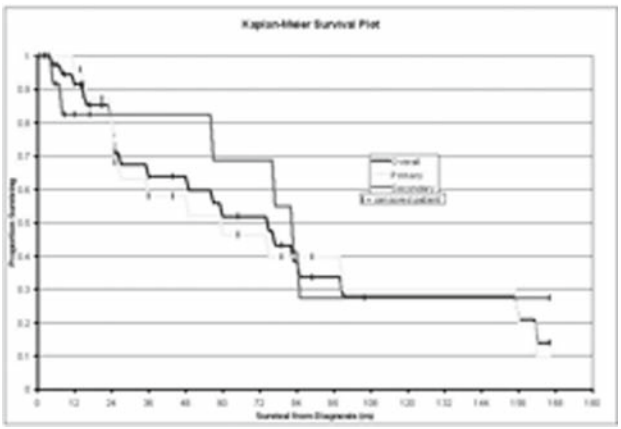


Figure 1. Kaplan-Meier plot of overall survival and survival of patients with primary or secondary angiosarcoma of the breast (p=0.8)

P55

Effect of Paget's Disease on Survival in Breast Cancer R. Layeequr Rahman,[1]* S. Crawford,[2] N. Rudolph,[1] M. Arredondo.[1] *1. Texas Tech University Health Sciences Center, Amarillo, TX; 2. UMass Medical School, Worcester, MA.*

Introduction: Paget's disease (PD) is associated with 1-3% of breast cancers. Stage of the underlying tumor is largely used for prognostication and PD without underlying tumor is staged as in-situ cancer. Presence of PD itself has not been studied as a biomarker with a potential to have bearing on the clinical outcome. Methods: The Surveillance, Epidemiology and End Results (SEER) database was queried to identify all patients with mammary PD and staged matched breast cancer patients without PD between 1973 and 2004. Prevalence of PD was determined within each stage of cancer. PD and non-Paget's disease (non PD) were compared in terms of age, estrogen receptor (ER), progesterone receptor (PR), type of surgery and radiation treatment. Survival was compared between PD and non PD group for each stage using log-rank testing. Regression analysis was used to analyze the effect of PD on survival. Results: One thousand five hundred and seven patients were diagnosed with mammary PD; whereas 301,714 patients had breast cancer without PD. The prevalence of PD within stage 0 thru stage 4 breast cancer ranged from 0.4 to 1%. The median age range in both groups was between 55 and 65 years. Thirty percent (455/1507) of patients in the PD group were ER negative and 35% (490/1507) were PR negative compared to 15.2% (45929/301714) and 23% (641579/301714) in the non PD group (p<0.0001). Mastectomy was done in 82% (1110/1507) of PD group vs. 45% (103726/301714) in the non PD group (p<0.0001) and radiation was used in 21% (309/1507) of PD group vs. 46% (125734/301714) of the non PD group (p<0.0001). The stage matched comparison of survival was significantly worse for PD group compared with the non PD group (table 1). Regression analysis of multiple factors revealed that the presence of PD was significantly associated with poorer survival (p<0.0001). Conclusion: There is dearth of data regarding the biological significance of mammary PD. Using stage matched comparison of survival curves between patients with and without PD, we demonstrated that the presence of PD is associated with significantly worse survival for all stages except stage 4 breast cancer.

Table 1: Effect of Paget's Disease on survival in Breast Cancer

Stage	Disease group (n)	5 year survival %	10 year survival %	P value
0	PD (287)	89.0	70.9	<0.0001
	Non PD (67,918)	96.3	88.3	
I	PD (456)	86.7	73.0	0.0011
	Non PD (112,560)	92.3	78.4	
II	PD (524)	77.3	57.5	<0.0001
	Non PD (93,751)	83.7	65.4	
III	PD (184)	50.6	27.3	0.0054
	Non PD (16,416)	59.6	38.4	
IV	PD (56)	18.4	11.0	0.775
	Non PD (11,069)	23.3	8.9	

PD = Paget's Disease of the Breast

P56

Can Axillary Node Dissection Be Omitted in a Subset of Patients with Low Local and Regional Failure? C. Barkley,[1]* J. Bellon,[1] B. Smith,[3] J. Wong,[1] M. Gadd,[3] A. Taghian,[3] E. Winer,[2] J. Iglehart,[1] J. Harris,[2] M. Golshan.[1] *1. Brigham and women's Hospital, Boston, MA; 2. Dana Farber Cancer Institute, Boston, MA; 3. Massachusetts General Hospital, Boston, MA.*

Background: Axillary node dissection is the standard of care in patients who have undergone sentinel lymphadenectomy (SLNB) with a positive sentinel lymph node (SLN). A certain subset of patients will not undergo completion axillary node dissection (ALND) for personal reasons, physician preference or a clinical trial. We present our recent experience in this group. Methods: We reviewed our prospectively maintained database of patients with invasive breast carcinoma who underwent sentinel node biopsy between 1999 and 2007. A total of 130 patients were identified who underwent 131 SLNB with a positive SLN and did not undergo completion ALND. We evaluated clinical data and adjuvant treatment patterns along with intermediate locoregional and distant events. Results: Of our 131 cases, median patient age was 50. 19% had (i+) disease, 53% had micrometastatic (N1mic) disease and 28% had macrometastasis (N1 or greater). The median number of positive nodes was 1 (mean 1.3) and the median number of nodes removed was 2 (mean 2.9). 72% had Stage I disease, 33% of tumors had lymphovascular invasion, 86% were ER positive, and 16% over-expressed Her2neu. Breast conserving therapy was performed in 78%; adjuvant chemotherapy was given to 82%, 81% received endocrine therapy and only 6% received trastuzumab. 88% of patients underwent radiation therapy; 66 patients (51%) had documented nodal radiation (50 were treated with 3 fields including axillary and supraclavicular fields, 14 were treated with high tangents, and specific information was not available for 2 patients). Median time to follow-up was 59 months. We observed no axillary recurrences; 2 patients (2%) had an in-breast recurrence and 9 patients

(7%) developed distant metastases. The median time to recurrence for patients who recurred was 24.5 months. Conclusions: In this selected group of 131 patients with a positive sentinel lymph node biopsy who did not undergo completion ALND, we observed no axillary recurrences. Long-term outcome and more importantly prospective randomized data are needed to identify a subset of patients with a positive sentinel node biopsy who do not require completion ALND.

P57

Clinical Utility of Routine Radiologic-Pathologic Correlation of Percutaneous Breast Biopsy Specimens E.W. Jernigan, B.K. Bednarski,* J.J. Yeh, D.W. Ollila, N. Klauber-Demore, K.D. Amos, C. Kuzmiak, M.O. Meyers. *University of North Carolina, Chapel Hill, NC.*

Introduction: Percutaneous breast biopsy is the most commonly performed diagnostic procedure for abnormalities detected on breast imaging. Although practice guidelines suggest close review of pathology from these procedures and comparison to radiographic findings to assure concordance, it is unclear how closely this recommendation is followed. At our institution, this is routinely done in a systematic way, however little is known about the impact of this practice on patient outcome. We sought to determine the incidence of discordance, the likelihood of malignancy in those with discordant biopsy and the clinical or radiographic features that might predict malignancy. Methods: Under IRB approval, all patients undergoing percutaneous breast biopsy at our institution in the year 2006 were identified. A retrospective analysis was performed to gather clinical, radiographic and pathologic data for all patients. Statistical analysis was conducted using Chi square and the Fisher exact test. Results: 594 biopsies were performed on 520 patients. Seventeen patients were excluded for lack of sufficient data leaving 577 biopsies for evaluation. 143 (24.7%) of the biopsies were malignant and 434 (75.2%) were benign. Of the benign lesions, 38 (8.7%) were deemed discordant. 29 surgical biopsies were subsequently performed and 8 (27.5%) revealed either atypia (n=4) or breast cancer (n=4). Analysis of predictors of discordance suggested that a family history of breast cancer (p=0.029), history of prior breast biopsy (p=0.009), and age >50 (p=0.03) were associated with discordance. There were no clinical or pathologic variables associated with malignancy. Discussion: Discordance between pathologic and radiologic findings after percutaneous breast biopsy was common, occurring in 9% of all biopsies performed. Importantly, for those patients deemed to be discordant, subsequent surgical biopsy altered clinical management in nearly 28%. These data highlight the importance of systematic review of percutaneous breast biopsy results and their corresponding imaging studies to ensure accuracy and identify patients who may need surgical biopsy.

P58

Early Stage Breast Cancer in Elderly Women - Can Radiation Therapy Safely Be Withheld Outside of a Clinical Trial Setting? S. Lillard,[1]* N. Watroba,[1] A. Miller,[2] S. Kulkarni,[1] S. Edge.[1] *1. Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY; 2. Roswell Park Cancer Institute - Department of Biostatistics, Buffalo, NY.*

Background: Recent studies have challenged the need for whole breast radiation in elderly women treated with lumpectomy, who have favorable tumor characteristics. It remains unclear if practices in community and academic settings, outside of the clinical trial arena, can generate equivalent results. We hypothesized that results similar to clinical trials can be obtained among elderly women with small, hormone receptor positive breast cancers, with lumpectomy alone outside of a clinical trial setting. Methods: A retrospective review of 181 cases of breast cancer in elderly women treated within a single, medium-volume, academic institution, between 1995 and 2007, with lumpectomy and endocrine therapy without radiation was undertaken to define the outcomes within our practice. Results: 179 women were treated over the 11 year period, with a mean age of 79 at the time of diagnosis. Most lesions were clinical stage I (88%), infiltrating ductal histology, ER positive (94%), with a median tumor size of 1.18 cm. Ninety-two percent of patients received endocrine therapy. Median follow-up time was 34 months. Local recurrence rate was 4.4%, and distant metastases occurred in only two patients. Fifty-eight patients died during the course of follow-up, only 4 of which were due to progressive disease. Overall survival at 5 years was 71%. Of those patients alive at the time of last follow-up, 111 (94%) were without disease recurrence. Of the 179 women, 74 (41%) had axillary lymph node surgery (axillary node dissection or sentinel lymph node biopsy). Those who had axillary surgery were less likely to die in the follow-up period (Hazard Ratio = 0.44). Conclusion: The risk of local recurrence in women over age 70 treated for hormone receptor positive breast cancer with lumpectomy and endocrine therapy without breast radiation in a practice setting outside a clinical trial is very low. This therapy may be considered as a part of routine practice for such women with small hormone receptor positive cancers.

P59

An Objective Parameter for Evaluation of Lymphedema J. Bulatova,* N.Z. Carp, J.L. Sabol, R.M. Ciocca, R.D. Smink. *general surgery, LH, Wynnewood, PA.*

INTRODUCTION: Lymphedema is a known complication of breast cancer surgery. However, no firm data exist defining the true incidence or magnitude of this problem. The purpose of this study was to evaluate the incidence of lymphedema in a single practice and to determine the variables that predict its development. METHODS: A retrospective review of 504 patients who underwent breast cancer surgery was conducted. Arm edema was assessed by immersion displacement technique and range of motion (ROM) by goniometric measurement of the angle between chest wall and elevated humerus. Demographic, anthropometric and treatment data were obtained by chart review. Statistical analysis was conducted to determine correlation between all variables as predictors for development of lymphedema. RESULTS: Evaluation of our data confirms the difficulty in objectively quantifying lymphedema. In order to standardize this process we created a new parameter called lymphedema index (LI). Control arm displacement (CAD) is subtracted from affected arm displacement (AAD) to achieve the "delta" (D). The LI is derived from the formula LI = D/CAD. Using the LI we found that 13% of our patients had significant lymphedema. There was no correlation between elevated LI and demographic or anthropometric data. These include age, race, BMI, cup size, interval since surgery, tumor stage, breast procedure, adjuvant therapeutic interventions, or complications (infection, seroma, hematoma). The only treatment modality affecting LI was axillary lymph node dissection (ALND) with removal of at least 10 lymph nodes (p<.001). Sentinel lymph node biopsy (SLNB) was not associated with increased arm swelling. No difference in ROM was noted. CONCLUSIONS: The incidence of lymphedema in our practice is 13%, less than most reported series. Significant increase in lymphedema was noted in patients undergoing ALND with removal of at least 10 nodes. No other correlation between any demographic, anthropometric, or treatment options was observed. No upper extremity dysfunction secondary to surgery was noted. We propose LI as a new objective measurement for evaluation of lymphedema. We recommend additional studies to validate this tool.

P60

Sentinel Node Frozen Section for Breast Cancer: Should it be done? M. Jamal,[1]* J. Rayment,[1] S. Doi,[3] A. Omeroglu,[2] A. Meguerditchian,[1] S.H. Meterissian.[1] *1. Department of Surgery, McGill University Health Center, Montreal, QC, Canada; 2. Department of Pathology, Montreal, QC, Canada; 3. Queensland University, Brisbane, QLD, Australia.*

INTRODUCTION: Recent reports are questioning the effectiveness of intraoperative Sentinel lymph node biopsy frozen section (ISNLFS) especially in avoiding a second surgical procedure. The aim of this study was to examine the sensitivity and accuracy of ISNLFS along with factors predictive of a positive ISNLFS. METHODS: We performed a retrospective review of all patients who underwent an ISNLFS for a T1-T3 N0 breast cancer at a single institution between 2005-2007. The Chi-square statistic and Fisher's exact test was used to determine significance in differences between groups for categorical variables. Binomial logistic regression was used for multivariate analysis. RESULTS: 176 patients underwent ISNLFS giving a total number of 376 sentinel nodes (SN). The mean patient age was 56.8 years (range 23-81) and each patient had on average 2.1 SN dissected (range 1-6). The median primary tumour size was 1.5cm (IQR 0.9-2.2; range 0.2-5.2). On final pathological analysis, 56/176 (31.8%) of patients had positive SN for metastatic carcinoma. Of these 56 patients, 32 were identified on ISLNFS, for an intraoperative per patient sensitivity of 57.1%. All (120/120) of the truly negative patients were correctly identified on ISLNFS (100% specificity). Overall, ISNLFS correctly identified the metastatic status of 152/176 patients (86% accuracy). Only lymphovascular invasion (LVI) (OR=12.1 [4.74-31.1]) and a larger primary tumour size (OR=1.76 [1.09-2.85]) were independent predictors of a positive ISLNFS

result. Nodes that contained micrometastases (<2mm) were 17.2 times more likely to be categorised as falsely negative on intraoperative analysis than those with metastatic lesions larger than 2mm (OR=17.2 [3.86-76.6]). Of the clinicopathological factors analysed in the present study, the presence of LVI (OR=8.47 [3.12-23.0], multifocality (OR=2.60 [1.05-6.46]) and primary tumour size (OR=1.69 [1.05-2.74]) were all independent predictors of a positive final SN biopsy result. CONCLUSIONS: We identified factors predictive of intraoperative and final SN positivity. ISLNFS is effective in eliminating the need for a second surgical procedure in the majority of patients.

P61

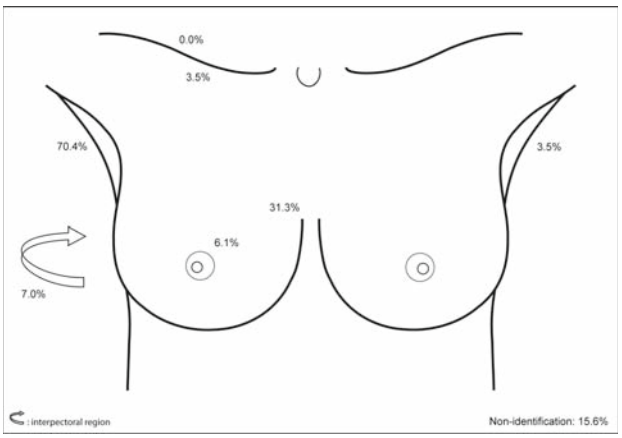
Poorer Survival in Male Breast Cancer is Attributed to Early-Stage Disease J.L. Gnerlich,[1]* S. Seelam,[2] E. Kimbuende,[2] A.D. Deshpande,[1] D.B. Jeffe,[1] J.A. Margenthaler.[1] *1. Department of Surgery, Washington University School of Medicine, Saint Louis, MO; 2. Saint Louis University School of Public Health, St. Louis, MO.*

Introduction: Studies suggest that males with breast cancer have a worse prognosis compared to females. We investigated patient and tumor characteristics accounting for these survival disparities. Methods: Using the 1988-2003 Surveillance, Epidemiology, and End Results (SEER) data, we conducted a retrospective, population-based cohort study of males and females diagnosed with breast cancer. Cox regression models calculated crude and adjusted hazard ratios (cHR, aHR) and 95% confidence intervals (CI) to compare overall and stage-specific breast cancer mortality between males and females, controlling for confounding variables in univariate tests. Results: Of 246,059 breast cancer patients, 1,541 (0.6%) were male and 244,518 (99.4%) were female. Compared with females, males were more likely to be black, married, diagnosed at an older age (65 vs. 60 years), diagnosed at advanced stages, and treated by mastectomy (each $p<0.001$). Male tumors were more likely to be a lower grade, estrogen receptor positive, progesterone receptor positive, and have nodal involvement (each $p<0.001$). Males were also less likely to receive radiation therapy ($p<0.001$). Overall, males were more likely to die from all causes (cHR 1.78, CI 1.64-1.93) at all stages of disease, except Stage IV breast cancer. Breast cancer-specific mortality was also higher in males compared to females (cHR: 1.42, CI 1.25-1.61). However, after controlling for confounders, males were more likely to die from their breast cancer compared with females only for Stage I disease (aHR 2.03, CI: 1.38-2.98). There was no breast cancer-specific survival disparity observed between males and females for in situ disease, Stage II-IV disease, or in unstaged patients. Conclusion: Men are more likely to die of other causes compared to women at all stages of non-metastatic breast cancer. Higher male breast cancer-specific mortality was identified in Stage I disease only, with no significant mortality disparities seen in other stages at diagnosis. Further studies should focus on the tumor biology characteristics and treatment of early-stage male breast cancer that may be contributing to this mortality disparity.

P62

Lymphatic Drainage Patterns from a Previously Treated Breast I.M. Van der Ploeg,* H.S. Oldenburg, E.J. Rutgers, M.J. Vrancken Peeters, B.B. Kroon, R.A. Valdés Olmos, O.E. Nieweg. *Surgery, The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands.*

Introduction: Lymphatic drainage patterns from the breast have been described in the past. Drainage may change after treatment of a breast or axilla and this may have implications for lymphatic mapping at a later stage. The aim of this study was to determine the lymphatic drainage patterns in breast cancer patients with a previously treated breast. Methods: Between January 1999 and November 2008, 115 sentinel node procedures were performed in breast cancer patients who had undergone treatment of the ipsilateral breast in the past. Lymphatic drainage patterns were analyzed based on pre-operative lymphoscintigrams and sentinel lymph node biopsy. Results: A sentinel node was found in 84% of the patients: in 81 patients (70%) in the axilla, 43 patients (37%) had drainage to more than one site and in eighteen patients (16%) no drainage was detected (figure). The percentage of drainage outside the axilla was higher than in a series of untreated breast cancer patients from our institution (51% versus 33%, p= 0.01). The 16% non-identification rate was also higher than the 3.1% in patients without previous treatment (p= 0.003). Four patients (3.5%) who had previously undergone an axillary dissection had lymphatic drainage to the contralateral axilla. Twelve patients (10%) had involved sentinel nodes. In ten patients, the positive sentinel node was harvested from the axilla and prompted completion dissection. The two other patients had a positive sentinel node in the contralateral axilla and were subjected to axillary node dissection on that side. No lymph node recurrences were observed during a median follow-up time of 39 months. Conclusion: Lymphatic mapping yields a lymph node in 84% of the breast cancer patients who have undergone previous treatment of the breast. Non-identification and extra-axillary nodes are more frequently encountered than in patients without treatment of the breast in the past. The finding of involved nodes suggests that sentinel node biopsy improves staging. Long-term follow-up will determine the sensitivity of the procedure in this specific situation.

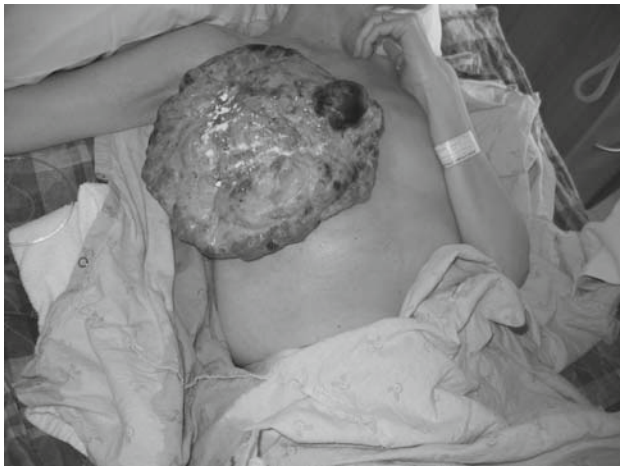


Lymphatic drainage was observed towards sentinel nodes in the axilla (level I and II), the internal mammary chain, the breast, the interpectoral region, the infraclavicular fossa (level III), the supraclavicular region and the contralateral axilla.

P63

Alternative Therapy Used as Primary Treatment for Breast Cancer Negatively Impacts Outcome E. Han,[1]* K. Steinbock,[2] N. Johnson,[2] N. Glissmeyer,[2] T. DelaMelena,[2] A. Wheeler.[2] *1. Surgery, OHSU, Portland, OR; 2. Legacy Health System, Portland, OR.*

Introduction: The use of complementary and alternative medicine (CAM) has escalated over the past decade, despite the fact that clinical studies validating the efficacy and safety of CAM remain sparse. Clinicians frequently encounter patients who reject standard treatment, but data on outcomes of patients choosing alternative therapies as primary treatment for breast cancer are also lacking. Methods: Breast cancer patients who refused or delayed standard treatments in favor of alternative therapies were identified over a 10-year period in a community surgical practice. Mean follow-up was 48 months. Chart reviews and telephone interviews were conducted when possible. For each patient, estimated 10-year survival given recommended treatment was calculated. Results: 62 patients were identified. The mean age was 54. Patients were stratified into 2 groups: those who declined/delayed surgery and adjuvant therapy when applicable (DS, n=23) and those who were non-adherent to surgery/adjuvant recommendations (NA, n=39). In the DS group, 79% experienced disease progression; 52% died of disease. Mean stage at initial presentation was 2; mean stage at re-presentation after primary treatment with alternative therapies was 3. Disease progression occurred in 77% of those in the NA group; 30.4% died of disease. The mean 10-year survival calculated for those who declined/delayed surgery and/or adjuvant therapy had they undergone recommended therapy was 61.6% v. the actual survival for those choosing alternative therapies as primary treatment of 48%. Conclusion: Alternative therapies used as primary treatment for breast cancer are associated with disease progression and death. Clinicians should be able to counsel patients on risks and benefits of alternative therapies. These data may aid patients who are delaying surgery or considering alternatives to standard treatment.



P64

Metaplastic Carcinoma(MPC) of the Breast: A Rare Entity with an Aggressive Clinical Course D.X. Choi,* M. Worman, S. Safdar, L. ODonoghue, X. Wang, C. Andrus, K.A. Skinner. *Surgery, University of Rochester Medical Center, Rochester, NY.*

MPC of the breast was defined as a distinct clinicopathologic entity in 2000. The purpose of this study was to define the clinical course of MPC. METHODS: Pathology archives were searched for cases of MPC between 1995 and 2009. Slides were reviewed to confirm the diagnosis. Medical records were reviewed to determine risk factors, presentation, treatment, and outcome. RESULTS: 22 patients(pts) with MPC were identified. Mean age was 62 years (range 36-89) and 82% were postmenopausal. 38% had a positive family history and one pt had a known BRCA1 mutation. Four pts (18%) had a prior or synchronous contralateral ductal cancer(Stage 0-1). 19% were screen-detected. 81% presented with a palpable mass. Mammography showed an irregular mass in 84% and a well-circumscribed mass in 16%. 36% underwent breast conserving surgery(BCS), 27% mastectomy (Mast) with reconstruction, and 36% Mast alone. Mean tumor size was 2.7cm. 14% were node positive. 43% were stage 1, 43% stage 2A, 5% stage 2B, and 5% stage 3. 10% of tumors were receptor positive and none overexpressed Her-2/neu. 55% were high grade. In 48%, the metaplastic(MP) component(spindle cell(sp) 80%, squamous(sq) 10%, chondroid 10%) was dominant, whereas the rest had focal MP changes. 68% received polychemotherapy(PCT)(75% anthracycline based, 17% taxane based, and 8% CMF regimen). Radiation(XRT) was given to 75% of BCS patients and 36% of Mast patients. Median follow-up was 44 months (range 3-135). Eight (36%) patients developed recurrence(REC) (3 local(LR), 1 regional+distant, and 4 distant only) with a median time to REC(TTR) of 15 months (range 6-46). 50% of BCS patients developed LR within 2 years. No LR were seen in Mast patients. Five year actuarial overall and disease-free survivals were 78.6% and 55.9%. CONCLUSIONS: MPC is an aggressive form of breast cancer with high LR rates if treated with BCS. Visceral REC was seen in 23%, despite PCT. Contralateral cancers were seen in 18% suggesting an increased risk. These data suggest that MPC are better treated with Mast than with BCS and that the contralateral breast should be followed closely. Better systemic therapies are needed to improve outcomes in patients with MPC.

Patient (Age)	REC Site	Surgery	XRT	PCT	MP Component	Grade	pT	pN	Stage	TTR(mos)
1 (49)	Liver	Mast	No	Yes	Focal/sp	High	2	0	2A	46
4 (71)	Breast	BCS	No	No	Entire/sp	Low	2	0	2A	23
6 (52)	Node, Lung	BCS	Yes	Yes	Focal/sp	High	2	0	2A	11
7 (46	Liver, Bone	Mast	Yes	Yes	Focal/sp	High	1	2	3	12
13 (88)	Breast	BCS	Declined	No	Entire/sp	High	1	0	1	11
16(63)	Lung, Bone	BCS	Yes	Yes	Focal/sq	Low	1	0	1	19
19 (63)	Breast	BCS	Yes	Yes	Focal/sp	High	1	0	1	17
20 (87)	Lung	Mast	No	Declined	Entire/sp	High	4	1	3	6

P65

Predictive value of BI-RADS classification for young patients G. Kennedy,* E. Avisar. *Surgery/Surgical Oncology, University of Miami, Miami, FL.*

Introduction: The Breast Imaging Reporting and Data System (BIRADS) is the standard grading tool for malignancy potential. BIRADS 4 or 5 and occasionally 3 will lead to a biopsy. The aim of this study was to assess the positive predictive value of mammography and/or ultrasonography(US)in women aged 50 years or younger based on the recommendations for biopsies and the final pathology results. Methods: We performed a retrospective analysis of all mammography and US reports issued from September 2005 to January 2007 at a large county hospital resulting in biopsies in women 18 to 50 years. Data collected included demographics, imaging modality, breast density, nature of the findings, BI-RADS grade and final pathology. Results: Four hundred and seventy-five biopsies in 395 patients were reviewed. A total of 43(9%) biopsies were malignant, 31(6.5%) invasive carcinomas and 12(2.5%) noninvasive. The positive predictive value of BI-RADS 3(n=11) was 9.1%, BI-RADS 4(n=440) 5.9% and BIRADS 5(n=24) 66.7%. Of the 168 biopsies recommended by both mammography and US 15(8.9%) were malignant. When US was the only tool (n=205) only 7(3.4%) were malignant whereas when mammography was the only tool(n=99) 20(20.2%) were malignant. 2/13 (15.4%) fat replaced breasts with suspicious findings resulted in malignancy compared to only 13/215(6%) moderate/heterogeneously dense breasts, and 6/41(14.6%) severely dense breasts. 26% of suspicious calcifications were malignant versus 6.8% of masses/nodules and only 3.6% of suspicious cysts. 4.3% of lesions reported as <1cm were malignant compared to 3.6% for lesions between 1 and 2cm and 11.8% for lesions above 2cm. None of the 40 biopsies performed on women age 18-29 were malignant versus 9/115(7.8%) for age 30-39 and 34/320(10.6%) for age 40-50. Conclusion:The positive predictive value of the current screening modalities diminishes markedly in women under the age of 50 and drops even more below the age of 40. Calcifications or masses larger than 2cm especially in fat replaced breasts should be biopsied but the current BIRADS criteria might have to be revised for other findings and younger patients.

P66

Is surgical excision necessary for radial scars diagnosed on percutaneous biopsy? C. Mercado, A. Guth,* J. Cangiarella. *Surgery, NYU School of Medicine, New York, NY.*

Introduction: Is surgical excision always necessary following diagnosis of a pure radial scar on image-guided percutaneous core biopsy? While excision is routinely recommended, some authors have suggested surveillance in the setting of benign radial scar. We undertook this study to examine the association of pure radial scars with malignant histologic findings on subsequent excision. Methods: Retrospective review of patients with pure radial scar diagnosed on percutaneous core needle biopsy. Cases accompanied by a second high risk lesion (atypical hyperplasia, papillary lesions, lobular carcinoma in situ) or malignancy were excluded. All lesions were surgically excised. The authors assessed the radiologic findings, histologic findings on core needle biopsy, and the findings at subsequent surgical excision. Results: 48 cases were identified (age range 36-74 years, mean age 52 years). 20 biopsies were performed for calcifications, 14 for mass lesions, 4 for architectural distortion, and 10 for enhancing lesions on breast MRI. At core-needle biopsy, lesions were diagnosed as radial scar and fibrocystic change (n=41), radial scar and fibroadenoma (n=3), and radial scar (n=4). Surgical excision revealed radial scar and fibrocystic change (n=17), radial scar with high-risk lesion (ADH, ALH, or LCIS)(n=7), radial scar and papilloma (n=3), radial scar and fibroadenoma (n=2), and rdial scar with low-grade DCIS (n=2). In 17 cases, no evidence of residual radial scar was seen at excision: these specimens consisted of fibrocystic change (n+10), fibrocystic change with ADH (n=3), fibrocystic change and papilloma (n=3), and intraductal papilloma alone (n=1). Conclusion: No invasive cancers were associated with pure radial scars in this series, while DCIS was seen in 2 patients (4%). The incidence of high-risk lesions was much higher (21%). Excision of pure radial scars remains necessary due to the low but present risk of finding malignancy at excision. Perhaps more importantly, it allows us to identify those patients with high-risk lesions who may benefit from increased surveillance and risk-reducing therapy.

P67

Meta-analysis of predictive factors for non sentinel lymph node metastases in breast cancer patients with a positive SLN R.F. Van la Parra,[1]* P.G. Peer,[2] M.F. Ernst,[3] K. Bosscha.[3] *1. Surgery, Gelderse Vallei Hospital, Ede, Netherlands; 2. Radboud University Nijmegen Medical Center, Nijmegen, Netherlands; 3. Jeroen Bosch Hospital, 's Hertogenbosch, Netherlands.*

Background: Over the last years, sentinel lymph node (SLN) biopsy has emerged as the minimally invasive alternative to routine axillary lymph node dissection (ALND) to stage breast cancer. Different clinicopathological variables, predictive of non sentinel node (NSN) metastases, have been identified to select those patients most likely to benefit from ALND when a positive SLN is found. The present study is a meta-analysis of the identified predictors of NSN metastases. Methods: A Medline search was conducted which identified 50 candidate studies. Original data were abstracted from each study and used to calculate odds ratios. The random-effects model was used to combine data and to determine the relative strength of the associations. Results: Fifty-six published series were included in the meta-analysis. The 6 individual characteristics found to be associated with the highest likelihood of NSN metastases are SLN metastases > 2 mm in size, extracapsular extension in the SLN, > 1 positive SLN, ≤ 1 negative SLN, tumour size > 2 cm, and lymphovascular invasion in the primary tumour. The histological method of detection, which is correlated with the size of metastases, had a correspondingly high odds ratio (4.37). Conclusions: We identified 6 factors predictive of NSN metastases that should be recorded and evaluated routinely in SLN databases. These factors should be included in a predictive model that is generally applicable among different populations.

P68

Significance of Fascin expression in high grade breast cancer B. Chikman,* R. Lavy, G. Tolstov, L. Habler, A. Kapiev, A. Halevy, J. Sandbank. *Assaf Harofeh, Zerifin, Israel.*

Background: Fascin, an actin-binding protein is frequently overexpressed in several types of cancer. The expression of fascin correlates inversely with estrogen and progesterone receptors expression in breast cancer and is remarkably more frequent in high grade tumors. The aim of this study was to evaluate the association of overexpression of Fascin with clinicopathological features and outcome in different biological types of breast cancer. Methods: 289 patients with high grade infiltrating duct carcinoma (grade 2-3 and grade 3) without previous neo-adjuvant therapy were selected and served as the basis for this study. Fascin expression was studied immunohistochemically and was considered positive in cases when more than 25% of tumor cells were stained. Results: Grade 3 tumors were more frequently Fascin positive compared to grade 2-3 tumors (61/200 pts - 30.5% vs 13/89 pts – 14.6%; p=0.005). Tumors with high proliferative rate measured by immunohistochemistry of Ki67 were also more frequently Fascin positive compared to tumors with low proliferative rate (34/111 pts – 38.7% vs 11/87 pts – 12.6%, p<0.001). Over-expression of Fascin was documented in 71.9% (46/64 pts) of triple-negative breast cancers, in 23.1% (6/26 pts) cases of Her2 positive tumors (ER-;PR-;Her2+), in 12.3% (18/146 pts) cases of Luminal A type tumors and in 7.5% (4/53 pts) with Luminal B type tumors (p<0.001). The added value of Fascin over-expression in triple-negative breast cancer was not associated with statistically significant additional deterioration of the outcome. On the other hand, in the group of patients with Luminal A type tumors the over-expression of Fascin was associated with significantly higher rate of recurrence compared to Fascin-negative tumors (38.9% vs 16.4%, p=0.048) Conclusion: Fascin expression was found in all biological types of breast cancer with significant predominance in the triple-negative group. The overexpression of Fascin among patients with Luminal A type breast cancer was shown to be an important predictor for worse prognosis.

P69

Clinical Series of Oncoplastic Mastopexy to Optimize Cosmesis of Large Volume Resections for Breast Conservation J. Bong,* R. Clapper, J. Parker, W.C. Dooley. *Breast Institute, University of Oklahoma, Oklahoma City, OK.*

Introduction: Oncoplastic mastopexy has been popularized as a method to hide the cosmetic effects of central or large volume resections associated with breast conservation surgery for breast cancer. Methods: This review was undertaken to study the uses and limitations of these techniques in providing adequate breast conservation lumpectomy for breast cancer of any stage in a single surgeon' s practice. All oncoplastic mastopexy reconstructions were analyzed in cases dating from March 2004 through May 2009. Results: One hundred and fifty patients had lumpectomies during this period associated with oncoplastic mastopexy reconstruction. The average age was 55 with a range of 26-85. Stage 0 breast cancer accounted for 33 cases and 127 cases were for invasive cancers stages 1-3. The most common oncoplastic techniques used were in order of frequency Bat wing mastopexy, parallelogram mastopexy, and Modified Wise pattern mastopexy. Positive or close margins (<2mm) were present in 33/150 (22%). Positive margins were most associated with + nodes, + LVI, ILC, use of neoadjuvant chemotherapy, larger initial T stage, + ER and younger age. Of these, only node + was statistically significant in this small series. Trends for the others were probably underpowered given the limited number of events. Ki-67 and her-2 status were not associated with positive margins at all. Positive margins were able to be managed by local re-excision of a solitary face of the prior resection wall in over 2/3 of cases to achieve negative pathologic margins. Conclusions: Oncoplastic mastopexy allows the surgeon to address large tumors or tumors in cosmetically difficult sites adequately for breast conservation. Careful margin marking and re-excision of close or + margins is still often feasible to achieve adequate negative margin with acceptable cosmesis in spite of the large initial volumes of resection.

P70

Cavity Shave Margins: Impact on Re-excision & Health Care Costs A. Unzeitig,* A. Kobbermann, D. Euhus, A. Moldrem, A.M. Leitch, J.V. Andrews, J. Huth, R. Rao. *Surgery, University of Texas Southwestern Medical Center, Dallas, TX.*

Intro Breast conserving surgery (BCS) requires complete tumor excision with negative margins.Current comprehensive pathologic analysis closely evaluates all margins, with 30-50% re-excision rates reported. Various techniques, including wire-localization alternatives, intra-operative margin review, & specimen mammogram have had mixed success in reducing re-excisions.These techniques typically require new equipment & may increase operative time. Also, there have been reports of significant specimen disorientation rateswith risk of re-excision of the wrong margin at 2nd surgery. Cavity shave margin (CSM) removal is a simple surgical technique utilizing existing equipment to potentially reduce re-excisions.This study evaluates the use of CSM to reduce re-excisions. **Methods** Single institution, retrospective review identified 522 cancers treated with BCS from 2005-2009.Patients underwent BCS with additional margins taken at surgeon discretion, or CSM.Data collected included demographics, pathology, neoadjuvant chemotherapy, surgeon, re-excision, & final surgery. **Results** 455 standard BCS & 67 BCS with CSM were compared. There were no statistically significant differences in pathology, localization, residual tumor at re-excision, extensive intra-ductal component, or neoadjuvant chemotherapy between groups.Overall re-excision rate was 43%.Most common reason for re-excision was DCIS close to a margin. Standard BCS group underwent 213 re-excisions (46.8%) while only 16 of 67 (23.9%) CSM's required reoperation (p=0.0003). Pathologic results from the standard BCS group revealed 143 of 213 (67.1%) patients could have been spared a 2nd operation with CSM, a total health care savings of $79,432 (Medicare 2009).The only other statistically significant difference was the rate of total mastectomy, more patients ultimately chose this in the standard BCS group (16%) (p=0.009) when compared to the CSM group (4%), even though these patients were not more likely to have residual tumor. **Conclusion** This study supports the use of CSM as an accessible and easily implemented technique that reduces re-excisions, costs, total mastectomy rates and allows the surgeon to be confident of the orientation of the margin re-excised.

P71

Modern Breast Imaging Predicts Risk of Malignancy in Patients with Bloody Nipple Discharge C.P. Bird,* N.K. Demore, D.W. Ollila, L.J. Tesche, B.J. Calvo, K.D. Amos, M.O. Meyers. *Dept of Surgery, University of North Carolina, Chapel Hill, NC.*

INTRODUCTION: Historical series as well as recent reports have associated a presenting complaint of bloody nipple discharge with breast cancer in as many as 20% of patients. We hypothesized that the risk of malignancy is lower in those patients who have an otherwise negative diagnostic workup in a comprehensive breast program. METHODS: Under IRB approval, we

reviewed 2,426 surgical breast biopsies performed at the University of North Carolina from July 1998 through December 2008. 157 biopsies were performed for bloody nipple discharge and included in this study. Clinical, radiographic and pathologic results were collected in all cases. Data was analyzed by Chi square or Fisher's exact test. RESULTS: All patients had either bloody or guaiac positive discharge. There were 64 premenopausal and 93 postmenopausal women. All had either a mammogram (99%) or a breast ultrasound (79%) performed. Positive findings were seen on 22% of mammograms, 47% of ultrasounds. There were 13 malignant diagnoses (8.3%) of which 11 were DCIS, 2 invasive carcinoma. Those with a positive mammogram were more likely to have a cancer than those without (21% vs. 5%; <0.001). Similarly, a positive ultrasound predicted the likelihood of cancer (11% vs. 6%; p<0.001). Other predictors of malignancy included age > 60 (p=0.01) and a family history of breast cancer in a first-degree relative (p=0.03). CONCLUSIONS: The incidence of malignancy associated with bloody nipple discharge in our series is lower than previously reported. Breast imaging findings were the most powerful predictors of malignancy in this group of patients, with a positive mammogram or ultrasound representing independent risk factors for cancer. In addition, younger patients were less likely to have cancer than older patients. These data may be important in counseling patients with bloody nipple discharge regarding the risk of malignancy and expectations of surgical biopsy.

P72

The effect of frozen section analysis on detecting micrometastases in sentinel lymph nodes in patients with breast cancer E. Madsen,[1]* L. Smeets,[1] T. Van Dalen,[1] J. Van Dalen.[2] *1. Diakonessenhuis Utrecht, Utrecht, Netherlands; 2. Erasmus University, Rotterdam, Netherlands.*

Background: Frozen section analysis of sentinel lymph nodes (SLNs) in patients with breast cancer enables axillary lymph node dissection during the same operative procedure. On the other hand, by frozen section analysis a part of the tissue of the SLN is sacrificed possibly affecting the chance of detecting micrometastases (size 0.2 – 2mm). Using a mathematical model the probability of missing micrometastases due to frozen section related tissue loss was calculated, if the SLN was examined according to the Dutch guidelines. Patients and methods: The dimensions and volume of twenty consecutive axillary SLNs in patients with cT1-2N0 breast cancer were measured. With SLNs the node is bisected, one frozen section is taken from the centre and examined directly. According to the Dutch guidelines 3 cuts from both halves, with a 250μm distance, are then taken and examined with haematoxylin and immunohistochemically. The amount of tissue that was wasted before a reliable cut fit for frozen section analysis could be examined, was calculated. Results: The median size of a SLN was 15 x 10 x 10mm (minimum: 10 x 7 x 5, maximum 25 x 20 x12mm). During frozen section analysis a mean tissue loss with a height of 350μm (72 – 644μm) was cut from the centre of the lymph node. Performing frozen section analysis affected the chance of detecting 0.2 and 2mm metastases (smallest and largest micrometastasis respectively). This loss of tissue from the centre of the node affected the chance of detecting a 0.2mm metastasis as follows: from 18% to 23% in a median SLN. For a 2mm micrometastasis the chances changed from 69% to 72%. This is described in table 1. Conclusion: Frozen section analysis results in loss of tissue from the SLN in patients with breast cancer. However, when the remaining tissue of the SLN is examined according to the Dutch protocol, frozen section analysis does not always influence the probability of detection in a negative way. This has to do with the fact that while tissue is lost from the centre, the outer areas of the lymph node are examined more thoroughly.

Pdetect[a] in micrometastases in a median SLN

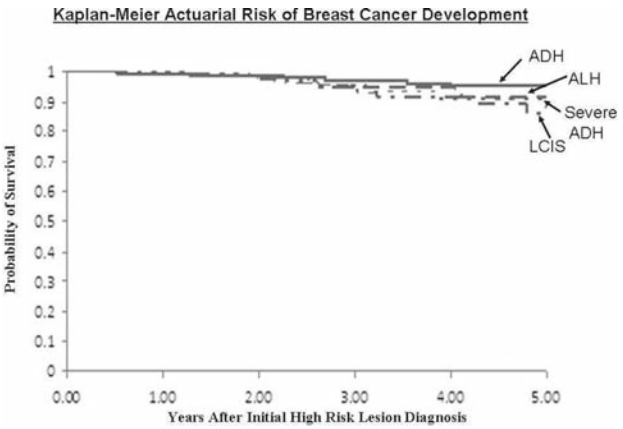
metastasis size	with FS [b] analysis	without FS [b] analysis
0.2mm	23%	18%
2mm	72%	69%

[a] Pdetect probability of detection; [b] FS frozen section

P73

The Utility of Natural Language Processing (NLP) in determining the Incidence of High Risk Breast Disease and the Subsequent Development of Breast Cancer E. Kim, MD,* J. Sharko, Ph.D., B. Drohan, MS, C. Roche, NP, Y. Zhou, MD, M. Specht, MD, M. Gadd, MD, B.L. Smith MD, Ph.D, K.S. Hughes, MD. *Massachusetts General Hospital, Department of Surgical Oncology, Boston, MA.*

There is limited data on the occurrence of breast cancer after high risk biopsies, and the review of free text path reports to identify these lesions is extremely time consuming. This study evaluated the incidence of severe ADH (borderline DCIS), LCIS, ALH and ADH, and the subsequent development of breast cancer. Cases were identified using NLP software. With IRB approval, 27,931 breast pathology reports, in 16,208 individuals, from 1/1990 to 6/2007 were retrospectively evaluated. Using NLP programmed for breast disease, we identified 1146 patients who were diagnosed with severe ADH, LCIS, ALH or ADH without a prior or concurrent history of breast cancer. We classified patients as having only the most severe diagnosis: severe ADH > LCIS> ALH > ADH. We identified which patients subsequently developed breast cancer. Patient's history and pathology data were analyzed, and NLP was evaluated for accuracy. Kaplan-Meier analysis estimated 5-year cancer risk for each diagnosis. NLP required 3 hrs to analyze the 27,931 reports and accuracy approached 99%. Using NLP, 1146 of 16,208 individuals were identified with high risk lesion, with the most important lesion being severe ADH in 192(1%), LCIS in 240(1%), ALH in 250(2%) and ADH in 464(3%). Average follow-up time for 1146 patients was 3.2yrs. Of 1146 patients identified with high risk lesions, 48 subsequently developed cancer. No statistical difference existed between lesion types in terms of the mean age at initial diagnosis (range: 48-58yrs) or time to subsequent cancer development (range: 45-62 months). Kaplan-Meier Actuarial risk of cancer development at 5 years for severe ADH was 13%(5yr); LCIS was 17%(5yr); ALH was 12%(5yr); and ADH was 7%(5yr). There was no statistical difference between Actuarial risks. NLP can accurately identify and categorize a large clinical data set efficiently. There was no difference in mean age at which these high risk lesions were diagnosed. Although there was no statistical difference between diagnoses, trends were identified that a larger data set might confirm.This approach can be used in the future for creating a larger data set.



P74

The Effect of Neoadjuvant Chemotherapy on Axillary Lymph Node Yield in Operable Breast Cancer Patients: a Review of the NCCN Database M.C. Lee,[1]* R.L. Plews,[2] J.V. Kiluk,[1] N. Khakpour,[1] B.. Rawal,[1] W.B. Carter,[1] C. Laronga,[1] L. Loftus.[1] *1. Comprehensive Breast Program, Moffitt Cancer Center, Tampa, FL; 2. University of South Florida College of Medicine, Tampa, FL.*

Introduction: A minimum of 10 level I/II axillary nodes is recommended for accurate staging in node-positive breast cancer patients (pts). Factors associated with lower lymph node (LN) yield at axillary node dissection (ALND) include neoadjuvant chemotherapy (NAC), age, and body mass index (BMI). The goal of this study was to assess the effect of NAC on LN yield at ALND in pts identified via the institutional National Comprehensive Cancer Network (NCCN) database. Methods: Our NCCN database was queried for breast cancer pts undergoing ALND from 2000-2008. Patients with stage 0 or IV

disease, bilateral breast cancers, outside axillary surgery, or treatment for other cancers were excluded. All ALNDs were performed by a fellowship-trained surgical or breast oncologist. Demographic, chemotherapy, and clinicopathologic data were collected. Age and BMI at diagnosis were calculated for each pt. Subset analyses of pts stratified by age, BMI, and stage were also performed. Statistical analyses used Student's T-test and ANOVA. Results: 238 NAC pts were identified as having ALND; an additional 903 pts with primary ALND were identified as a contemporaneous control. Median age of the NAC group was 49.6 years (range 22.6-79.6) with median BMI of 26.6 (range 18.4-49.4), compared to median age of 55.2 years (range 24.5-91.7) and median BMI of 26.3 (range 14.7-64.9) in the control. There was a significantly lower LN yield in pts undergoing ALND after NAC with a median 9.5 LN (range 5-46) compared to a median of 15.5 LN with primary surgery (range 4-64) ($p< 0.001$). NAC pts aged 51-60 ($p = 0.001$), those with BMI <18.5 or >24.9 ($p<0.05$), and pts with clinical stage II disease at presentation ($p = 0.001$) had significantly lower LN yields compared to controls. Conclusions: NAC is associated with a significantly decreased LN yield at ALND. Underweight (<18.5) or overweight/obese BMI (>24.9), age 51-60, and clinical stage II disease are also independently associated with lower LN yield at ALND after NAC. Further investigation regarding these findings is warranted.

P75

Simplified prognostic approach predicting disease progression in patients with high grade breast cancer B. Chikman, R. Lavy,* G. Tolstov, L. Habler, S. Vasyanovich, J. Sandbank, A. Halevy. *Assaf Harofeh Medical center i, Tel Aviv, Israel.*

Background: The outcome of patients with invasive breast cancer depends on the biological features of the tumor. Tumors with over-expression of Her2 are known to have poor prognosis. The triple-negative group of breast cancer is also associated with worse prognosis. Fascin is frequently over-expressed in basal-like type breast cancers. The aim of this study was to evaluate the prognostic significance of simultaneous evaluation of these two biological markers in patients with high grade breast cancer. Methods: 289 patients with high grade infiltrating duct carcinoma were included in this study. Her2 and Fascin expression were studied immunohistochemically. Results: 79/289 (27.3%) of patients were positive for Her2, while 210/289 (72.7%) were negative. Among patients with Her2-negative tumors 64/210 (30.5%) were positive for Fascin. Positivity to one or both of these markers (Her-2/Fascin) was found in 143/289 (49.5%) Expression of Fascin is more common in Her-2 negative tumors (64/210pts-30.5%) compared to the Her2-positive group (10/79 pts – 12.6%)($p=0.002$). Disease progression was documented in 28/79 Her-positive pts (35.4%), in 21/64 Fascin-positive pts (32.8%) and only in 24/146 pts (16.4%) who were negative for both Her2 and Fascin. Available data about site of first recurrence was in 48/74 patients. In Her-2 negative/Fascin-negative tumors the site of first relapse was: 4/14 (28.6%) loco-regional, 2/14 (14.3%) - visceral and 8/14 (57.1%) bone metastases. On the contrary, Her-positive and/or Fascin-positive tumors relapsed as follows: 9/34 (26.5%) loco-regional, 19/34 (55.9%) visceral and 6/34 (17.6%) bones, correspondently ($p=0.01$). Among patients with visceral metastases Fascin-positive tumors predominantly are associated with lung metastases (5/6 pts – 83.3%) and Her-2 positive tumors predominantly with liver or brain metastases (9/13 pts – 69.2%). Conclusion: Overexpression of Her2 and/or Fascin is highly predictive for recurrence. These two markers had additive significance, and both tend to predict visceral recurrence. Fascin expression is associated with lung metastasis while Her-2 positive tumors with liver and brain metastases.

P76

Nipple-Areola Complex Sparing Mastectomy is Technically Feasible for Risk Reduction and Early-stage Breast Cancer J. Wagner,[1]* R. Fearmonti,[2] L. Pantoja,[1] E. Beahm,[3] M. Crosby,[3] I. Bedrosian,[1] K. Hunt,[1] H. Kuerer,[1] F. Meric-Bernstam,[1] M. Ross,[1] B. Feig,[1] A. Lucci,[1] R. Hwang,[1] S. Krishnamurthy,[4] L. Feng,[5] M. Hernandez,[5] G. Babiera.[1] *1. M.D. Anderson Cancer Center, Department of Surgical Oncology, Houston, TX; 2. Duke University School of Medicine Division of Plastics and Reocnstructive Surgery, Durham, NC; 3. M.D. Anderson Cancer Center, Department of Plastic Surgery, Houston, TX; 4. M.D. Anderson Cancer Center, Department of Pathology, Houston, TX; 5. M.D. Anderson Cancer Center, Department of Biostatistics, Houston, TX.*

Background: Psychological effects of mastectomy for women with breast cancer have driven movements for optimal cosmesis while strictly adhering to oncologic principles. Although skin sparing mastectomy has been shown to be oncologically safe, questions remain regarding the use of nipple-areola complex (NAC) sparing mastectomy (NSM). We sought to evaluate the technical feasibility of NSM for patients undergoing mastectomy for early stage breast cancer and risk reduction. Methods: We enrolled 33 patients in a prospective clinical trial evaluating 54 NSM from 10/07 to 3/09 who were low risk for harboring occult nipple cancer (high risk and early stage breast cancer, unifocal, and at least 2.5cm from the nipple). NAC viability and surgical complications were evaluated. The NAC base was removed at surgery and subjected to intraoperative and postoperative pathologic assessment. Quality of life was assessed using the SF-36 item health survey. Results: Twenty-one bilateral and 12 unilateral NSM were performed in 33 patients; 37 (68.5%) for risk reduction and 17 (31.5%) for diagnosis of cancer. Pathologic stage ranged from 0-IIA. Mean age was 45.4 years (range 27-66) with a mean BMI of 24.8 kg/m2. Complications occurred in 16 (29.6%) NAC and 6 (11.1%) skin flaps. Twelve (22.2%) NAC and 1 (1.9%) skin flap were treated conservatively for necrosis. Operative intervention for necrosis resulted in 4 (7.4%) NAC removals and 5 (9.2%) skin flap debridements. Mean distance between tumor and base of the nipple was 6cm (range 3–9cm) in cancer patients. Two of the 17 (11.8%) breasts with cancer were found to have DCIS at the NAC margin necessitating removal at time of mastectomy. QOL assessments were completed by 20 of 30 patients that maintained the NAC. Patients compared favorably to the average of patients with chronic diseases. Conclusion: NSM is technically feasible with a low risk for NAC removal secondary to necrosis or intraoperative detection of cancer near the NAC in low risk patients. Thorough pathologic assessment is critical to minimize the likelihood of leaving residual disease. Long-term follow-up on local recurrence is crucial for determining safety.

P77

Sentinel Lymph Node Biopsy in Patients with Breast Cancer Using Superparamagnetic Iron Oxide and a Magnetometer M. Shiozawa,[2]* A. Lefor,[1] Y. Hozumi,[1] K. Kurihara,[2] N. Sata,[1] Y. Yasuda,[1] M. Kusakabe.[3] *1. Surgery, Jichi Medical University, Tochigi, Tochigi, Japan; 2. Oyama Municipal Hospital, Oyama, Tochigi, Japan; 3. University of Tokyo, Tokyo, Japan.*

Introduction: Sentinel lymph node biopsy (SLNB) is the standard of care for many patients with breast cancer, and is commonly done using the combination of a radioisotope (RI) and blue dye. However, throughout the world, many hospitals lack facilities for using RI. In this study, we developed a novel method using a superparamagnetic iron oxide tracer and a magnetometer instead of RI to perform SLNB. Methods: Following IRB approval, twenty patients with breast cancer participated in this study. Superparamagnetic iron oxide and patent blue dye were injected in the subareolar breast tissue. Following a few minutes of massage to promote migration of both magnetic tracer and dye, subcutaneous lymph nodes in the axilla were detected transdermally using the handheld magnetometer and harvested as the SLN. SLNB was followed by standard axillary dissection during the same operation in all patients. Results: Of the 20 patients (mean age, 56.0 ±10.7 years), there were 18 (90%) with invasive ductal Ca and 2 (10%) with DCIS. All patients had clinically negative axillae before surgery. No patient received preoperative treatment. The rate of detection of SLN was 85% (17/20) by the combination of blue dye and the magnetic tracer, and 80% (16/20) by blue dye alone. Six cases had metastases to the SLN. There was one false negative, resulting in a sensitivity of 5/6 (83.3%) and an accuracy of 16/17 (94.1%). SLN were successfully identified by the magnetic method in 14/20 (70.0%). In the first 10 cases, the detection rate by the magnetic method was just 5/10 (50.0%), but in the last 10 cases the detection rate improved to 9/10 (90.0%). There were no reactions to the tracer or complications in any patient. Conclusions: This is the first study to evaluate the use of a magnetic tracer to identify SLN in patients with breast cancer, and demonstrates that the technique is safe and effective. In some institutions, this new technique may alter the role of RI with further refinement and experience. Future studies will prospectively compare the effectiveness of magnetic detection to established techniques of identifying the SLNB.

P78

Contralateral Prophylatic Mastectomy in Breast Cancer Patients who Test Negative for BRCA mutations M. Howard-McNatt,* R. Schroll, G. Hurt, E. Levine. *Surgery, Wake Forest Baptist Medical Center, Winston-Salem, NC.*

Determination of BRCA 1/2 mutation carriers status has become increasingly important. At risk patients are offered genetic testing and counseling. BRCA 1/2 carriers are offered bilateral mastectomy and prophylactic salphingo-oophorectomy. Those who test negative typically do not undergo such extensive surgery. However, there is a cohort of women who still decide to have bilateral mastectomy at the time of their breast cancer diagnosis despite the fact that they test negative for the BRCA mutations. We sought to determine the factors that may influence these newly diagnosed breast cancer patients to choose bilateral mastectomies. METHODS: Genetic counseling and testing for the BRCA 1/2 germline mutations for 110 women with newly diagnosed breast cancer prior to definitive surgical treatment was performed between 2005- 6/2009. Patient demographics, tumor characteristics, surgical treatment and use of preoperative MRI were recorded. Chi-square analysis was performed on the data. RESULTS:The mean age was 45. The Stage distribution was DCIS 15%, Stage I 50%, stage II 10.5%, Stage III 21% and Stage IV 2%. Results revealed BRCA1/2 mutation in 36 (33%), variant of unknown significance in 7 (6%), and no mutation in 67 (61%) patients. In women who tested negative, 37% chose contralateral prophylactic mastectomies. In patients testing negative, only marital status was an independent predictor for receiving a contralateral mastectomy (married 34% vs. unmarried 1% p=0.02). There was no statistical difference in patients undergoing bilateral mastectomy with regard to race, age, ER/PR/Her-2/neu status, or parity. Only 25% of our patients received a pre-op. contralateral breast MRI; this did not alter rates of prophylactic mastectomies even if an abnormal MRI finding was seen (p=0.99). CONCLUSION:Increased rates of contralateral prophylactic mastectomies have been observed in women with negative BRCA results. In our study married women were more likely to choose this option. We continue to suggest genetic genotyping be performed in at risk patients prior to definitive surgery. These findings warrant further investigation.

P79

Breast Education in Residency J.P. Wilson,* S. Edge. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Breast cancer treatment has changed substantially with focusing of breast cancer surgery. This shift in care may affect training in breast disease for residents. The number of cases performed by residents completing residency has decreased. Also, the introduction of the sentinel lymph node biopsy has reduced the number of axillary dissections performed in training. This study examined the breast training of a cohort of applicants to surgical oncology fellowship training. A survey was administered to applicants interviewed by one fellowship training program in the fall 2009. The survey examined the type of training program, the volume of cases, and the comfort level of residents completing their training with surgical and diagnostic aspects of breast care. The survey was completed anonymously and was approved by the institutional review board. A total of thirty five applicants interviewed. The survey was completed by 29. Of these, 83% are completing residency in 2010. Fifty nine percent classified their programs as academic based, 38% as community based and 3% considered their programs mixed. Of these programs, 24.1% had dedicated breast services. Residents from programs with dedicated breast services noted that 86.7% of their breast training came from these services. Participants from programs with dedicated breast services received more training in both ultrasound and biopsy techniques. Nineteen programs were noted to have interdisciplinary clinic time including 100% of programs with dedicated breast services. Overall, participants had comfort levels above 8 (of 10) with breast related cases. However, for modified radical mastectomies and axillary lymph node dissections the comfort level dropped below 8. Participants were least comfortable discussing the medical management of breast cancer. Participants from programs with a breast service had the highest comfort of any other group. Residents completing residency are uncomfortable operating in the axilla compared to the breast. In addition, they are least comfortable discussing the medical management of breast cancer. However, training in a program with a dedicated breast service appear to provide more training in medical management, ultrasound technique, and biopsy techniques.

P80

The diagnosis of parathyroid cancer after minimally invasive parathyroidectomy does not mandate further open radical surgery C.J. O'Neill,[1]* C. Chan,[1] J. Symons,[1] D.L. Learoyd,[2] A. Gill,[3] S.B. Sidhu,[1] L.W. Delbridge,[1] M.S. Sywak.[1] *1. University of Sydney, Endocrine Surgical Unit, Sydney, NSW, Australia; 2. Department of Endocrinology, Royal North Shore Hospital, St Leonards, Sydney, NSW, Australia; 3. Department of Pathology, Royal North Shore Hospital, St Leonards, Sydney, NSW, Australia.*

Introduction: Parathyroid cancer accounts for <1% of cases of primary hyperparathyroidism (PHPT). Distinguishing parathyroid malignancy from benign disease is difficult pre-operatively, intra-operatively and on histopathological examination. Despite improving diagnostic accuracy with immunohistochemistry for parafibromin and PGP9.5, proven metastatic behavior remains the gold standard of diagnosis. Minimally invasive parathyroidectomy (MIP) is widely performed in patients with PHPT and positive localization studies, thus, it is inevitable that parathyroid cancers will be encountered at MIP. We present our experience of this rare entity. Methods: A case-control study was performed of patients who underwent MIP, comparing those with a histopathological diagnosis of parathyroid cancer to a control group of consecutive patients with benign PHPT. All patients were identified from a prospectively maintained surgical database. Multiple regression analysis was undertaken to compare indicators of parathyroid malignancy. Results: Between May 1999 and June 2009, 1215 patients underwent MIP and a histopathological diagnosis of parathyroid cancer was made in 6 patients (0.6%). Staining for parafibromin and/or PGP9.5 was abnormal in 4 cases. Despite subsequent unilateral thyroid lobectomy and lymphadenectomy in 5 patients, no further malignancy was identified in any specimens. Compared to controls, pre-operative calcium ($p=0.002$), parathyroid hormone ($p<0.001$), and parathyroid gland weight ($p<0.001$) were significantly elevated in patients with malignancy. Conclusion: Parathyroid cancer remains difficult to predict pre-operatively and the necessity of en bloc resection debatable. Thus, the diagnosis of parathyroid cancer following a minimally invasive parathyroidectomy does not mandate further open radical surgery with thyroid lobectomy and lymph node clearance.

P81

Laparoscopic Adrenalectomy for Metastatic Disease – Improving Survival One Gland at a Time E.J. Mitmaker,* M.R. Vriens, R.H. Grogan, A. Harari, J. Gosnell, O.H. Clark, W.T. Shen, Q.Y. Duh. *Endocrine Surgery, University of California, San Francisco, San Francisco, CA.*

Introduction: Adrenal gland metastases are not uncommon in patients with a known primary extra-adrenal malignancy. Laparoscopic adrenalectomy for metastatic disease, once considered controversial, is now performed for cure or palliation. We sought to determine if laparoscopic adrenalectomy for metastases improves survival in these patients. Methods: We retrospectively reviewed our institution's experience and recorded lesion size, growth rate, TNM stage, disease-free interval (DFI - defined as time of surgical removal of primary disease to appearance of adrenal metastasis), age, gender, tumor location and site of primary malignancy. Patients with stage IV disease of matching primary tumors from the SEER database served as historical controls. Results: Between 1993 and 2009, 504 patients underwent adrenalectomy by a single surgeon and 44 were diagnosed with adrenal metastasis; 41 of these patients underwent laparoscopic adrenalectomy. Median tumor size was 4.6 cm. The most common primary tumors that metastasized were lung cancer, melanoma and renal cell carcinoma. Median overall survival was 60 months for all primary tumor types. Median disease-free survival differed significantly for primary tumors classified as Stage 1 before adrenal metastasis and those classified as Stage IV ($p<0.05$, ANOVA). Only DFI was associated with greater 3-year survival (> 12 months, 91.3% vs. < 12 months, 37.5%, $p < 0.005$, Fisher's exact test). Overall 5-year survival rates for our patients with lung or renal cell carcinoma were higher than those for historical controls; the rate for melanoma did not differ. Conclusion: Our study showed that laparoscopic adrenalectomy for metastatic disease improved survival in patients with adrenal gland metastases. Although the clinicopathological characteristics we examined lack prognostic significance, adrenalectomy apparently plays an important role in patients with a solitary adrenal metastasis. These findings suggest laparoscopic adrenalectomy may be appropriate for metachronous lesions in patients whose DFI is > 12 months. A lesser benefit may be found in patients whose DFI is < 12 months.

P82

Curative surgery for pancreatico-duodenal neuroendocrine tumors: the Tel Aviv experience O. Zmora,* Y. Kariv, J. Klausner. *Surgery, Tel Aviv Sourasky Medical Center, Ra'anana, Israel.*

Introduction: Neuroendocrine tumors (NET) of the pancreatico-duodenal (PD)complex consist of various subgroups according to their secretion profile. Our aim was to describe the unique diagnostic, curative surgical management and prognosis for the different subgroups. Methods: retrospective chart review of all 65 patients who were operated for PD NET (1994-2009). Results: There were 42(65%) non functional tumors, 18(27.5%) insulinomas, 3(4.5%) gastrinomas and 2(3%) parathyroid hormone (PTH) secreting tumors. 31% of the patients with non functional tumors were asymptomatic. The most sensitive imaging modality for the entire group was endoscopic ultrasonography (EUS). Computerized tomography (CT) was highly sensitive for detecting non functional tumors but had a low sensitivity for functional tumors. Distal pancreatectomy was performed in 32 patients, Whipple operation in 15, enucleation in 12 (all for insulinomas), total pancreatectomy in 2, deudenotomy in 2 and both distal pancreatectomy and enucleation from the pancreatic head in 2. Out of 41 patients with non functional tumors, 15 were metastatic (10 to regional lymph nodes only), 7 locally advanced and 5 with involved surgical margins. 2 out of 2 gastrinomas were metastatic (lymph nodes only), one with involved surgical margins. One out of 2 patients with PTH secreting tumors was metastatic. None of 12 insulinomas were metastatic. In one patient with insulinoma the surgical margins were involved. Long term follow-up for the entire group was available for 58 patients and shows 87% overall 5 year survival and 7 cases of recurrence: 5 among patients with non functional tumors, one in a patient with gastrinoma and one in a patient with a PTH secreting tumor. There were no recurrences in patients with insulinomas. Conclusions: functional PD NED tumors are best diagnosed using EUS and are cured successfully with surgery with an excellent prognosis, especially for insulinomas. Non functional tumors are readily demonstrated by CT, have a higher rate of metastases, involved margins and locally advanced disease and usually necessitate larger operations with a less favorable prognosis.

P83

Combination of Preoperative Ultrasonographic Mapping and Radioguided Occult Lesion Localization in Patients with Locally Recurrent/Persistent Papillary Thyroid Carcinoma S. Gorgulu,* E. Ozturk, S. Ilgan, R. Yildiz, O. Emer, A. Ayan, S. Deveci, E. Alagoz, M.A. Ozguven, T. Tufan. *Gulhane Military Medical Academy, Ankara, Turkey.*

INTRODUCTION Despite the excellent overall prognosis, up to 40% of patients with papillary thyroid cancer (PTC) will have a persistent or recurrent disease. Although surgery represents the main treatment, reoperation for persistent or recurrent PTC is complicated. This report presents our experience on a combination of preoperative ultrasonographic (US) mapping and radioguided occult lesion localization (ROLL) in patients with locally recurrent/persistent PTC. MATERIALS AND METHODS Results of 19 consecutive patients who underwent central compartment reoperation for recurrent/persistent PTC were evaluated in this prospective study. Patients included 8 men and 11 women, and their average age was 41 years (17-68 yrs). All recorded suspicious lesions in the central and lateral neck were biopsied under US guidance. In the morning of surgery, lesions were plotted on a sketch showing reference points. Lesions injected with Tc-99m macroaggregate albumin under US guidance. A unilateral or bilateral thyroid bed exploration was carried out based on the location of biopsy proven lesion with the guidance of the intraoperative gamma probe and neck map. The lymphoadipose tissues showing high count rates were resected and labeled separately for histopathologic study. RESULTS Despite extensive scarring in some patients probe safely guided to lesions. Non-injected tumor foci were searched and successfully resected in the light of the neck map that showing topographic relation of injected and non-injected lesions. Explored compartment searched for additional metastatic foci after the removal of all preoperatively depicted lesions. Among the total of 106 excised lesions, 88 metastatic foci ranging from 3 mm to 38 mm in largest diameter were recognized at the final histological examination. SUMMARY In conclusion, the use of preoperative US-mapping with ROLL in patients with nonpalpable recurrent/persistent PTC in central compartment is technically safer and more effective then nonguided approaches. Most important indication seems subcentimeter recurrences in central compartment after initial surgery.

P84

Post Operative Thyroglobulin Level: Significant Marker of Recurrent Papillary Thyroid Carcinoma R.C. Webb,* R.S. Howard, A. Stojadinovic, H.B. Burch. *Walter Reed Army Medical Center, Washington, DC, DC.*

BACKGROUND: Resection, I-131 ablation and thyroid hormone suppression represents present-day treatment of papillary thyroid carcinoma (PTC). Serum thyroglobulin (Tg) at the time of I-131 ablation may correlate with increased risk of recurrent PTC. PURPOSE: To determine the predictive value of post-operative Tg levels for recurrent PTC. METHODS: Retrospective analysis of serum Tg levels in 93 patients with non-metastatic PTC treated between 1983 and 2002. Analysis was conducted to estimate predictive value of Tg for recurrence. RESULTS: Tg level at time of I-131 ablation predicted persistent or recurrent PTC, independent of patient age or tumor size. Recurrence rates according to Tg was: Tg<2(n=22), 14%; 2≤Tg<10 (n = 35), 23%; Tg≥10 (n=36), 64% (P<0.0005). Negative and positive predictive values for a cutoff of Tg at <2 were 0.86 and 0.44, and were 0.81 and 0.64 for a cutoff of ≥10. CONCLUSIONS: Post-operative serum Tg correlates significantly with post-ablation disease recurrence in patients with non-metastatic PTC treated with modern multi-modality therapy. Patients with Tg≥10 at the time of I-131 require close clinical surveillance for recurrence.

P85

Population based review of Gastrointestinal Carcinoids
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Introduction: Recent studies suggest the incidence of carcinoid tumors is increasing. The impact of earlier detection and more aggressive treatment on survival is unclear. The purpose of this study was to determine the distribution, treatment and survival outcomes for gastrointestinal carcinoid tumors (GICT) seen at a tertiary cancer center in Alberta, Canada over a 15 yr period. Methods: A retrospective review was performed using the provincial cancer registry (1990-2005). Data was extracted and overall survival (OS) was calculated using the Kaplan Meier method. Multivariate analysis was used to identify factors predicting poor survival. Results: 320 patients were included (50% male). Median follow up was 46 months. Small bowel was the most common tumor site (44%), followed by appendix (21 %), colon (7%), stomach (7%) and rectum (7%). At presentation 42% had localized disease, 23% regional disease, and 35% metastatic disease. The proportion of patients with localized disease varied by site: appendix (94%), rectum (87%), stomach (74%), colon (58%), small bowel (18%), pancreas (13%). Most (72%) patients underwent surgery, and internal targeted radiotherapy was given to 67 patients with metastatic disease. Overall survival was 72% at 5 years and 57% at 10 years. On multivariate analysis, stage at presentation, age at diagnosis and site of tumor were significantly associated with poor overall survival. 5-year survival was 87% for localized disease, 81% for regional disease and 47% for metastatic disease (p<0.0001). Patients older than 50 had a 5-year survival of 65% versus 91% for those younger than 50. Of all sites, appendiceal tumors had the highest 5-year survival (84%) versus rectum (81%), stomach (79%), small bowel (74%), pancreas (67%), and colon (66%). All cases where the primary site was unknown (11%) had metastatic disease and the 5-yr survival was 34%. Conclusions: Our findings support other studies suggesting that the appendix is no longer the most common site of GICT. The proportion of patients presenting with localized disease varies considerably by site. Age, site and stage at presentation predict overall survival. The 5 year OS for GICT is approximately 70%.

Stage at Presentation and Survival by Primary Tumor Site

Primary Tumor Site	N (%)	1990 - 1997	1998-2005	Localized Disease	Regional Disease	Metastatic Disease	5-yr Overall Survival
STOMACH	23 (7%)	7 (5%)	16 (9%)	74%	13%	13%	79%
SMALL BOWEL	141 (44%)	56 (42%)	85 (46%)	18%	41%	41%	74%
APPENDIX	66 (21%)	36 (27%)	30 (16%)	94%	3%	3%	84%
COLON	22 (7%)	10 (7%)	12 (6%)	58%	18%	24%	66%
RECTUM	23 (7%)	9 (7%)	14 (8%)	87%	0	13%	81%
PANCREAS	8 (3%)	1 (1%)	7 (4%)	13%	25%	63%	67%
BILIARY	1 (0.3%)	0	1 (0.5%)	100%	0%	0%	N/A
MISSING	36 (11%)	15 (11%)	21 (11%)	0%	0%	100%	34%
	TOTAL = 320	TOTAL = 134	TOTAL = 186				

P86

Initial CA19-9 levels predict survival in patients with carcinoma of the pancreatic head, but not resectability U. Von Holzen,* F. Zhu, J.C. Watson, J.P. Hoffman. *Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: CA 19-9 is recognized as a tumor marker that successfully helps in the diagnosis of pancreatic cancer with a high specificity. We hypothesized that preoperative CA 19-9 levels may predict the R0 resectability and survival of patients with pancreas cancer. Methods: A retrospective review of all patients with adenocarcinoma of the pancreatic head who underwent resection at our institution between 2000 and 2008 was performed. CA 19-9 serum levels were adjusted for hyperbilirubinemia. Analysis for survival was performed using the Kaplan-Meier method. CA19-9 serum levels were grouped into 4 categories using quartiles. Cox proportional hazard model was used for multivariate analyses. Results: Between 2000 and 2008, 150 patients were treated. 57 patients underwent neoadjuvant treatment and 93 patients underwent resection without prior treatment. For patients who underwent neoadjuvant treatment, median initial (at diagnosis) CA19-9 levels were 63 U/ml for patients with negative margins and 130 U/ml for patients with positive margins. For patients without neoadjuvant treatment, median initial CA19-9 levels were 80 U/ml and 138 U/ml, respectively. There was no significant correlation between initial CA 19-9 and margin positivity for both groups. Median postoperative survival for patients who underwent neoadjuvant treatment was 14, 14, 15 and 9 months for preoperative CA 19-9 levels of <10.3, 10.3-37.5, 37.5-239.25 and >239.25, respectively, and x, 14, 19 and 14 months for initial CA 19-9 levels of <27.4, 27.4-96.8, 96.8-396.2 and >396.2, respectively. There was a significant association between initial CA 19-9 and overall survival (p=0.03), but not between preoperative CA 19-9 and survival. Conclusions: Initial CA 19-9 serum levels predict overall survival in patients with adenocarcinoma of the pancreatic head, but do not predict R0 resectability of these tumors.

P87

25-hydroxyvitamin D Status Does not Affect Intraoperative Parathyroid Hormone Dynamics in Patients with Primary Hyperparathyroidism J.T. Adler,* R.S. Sippel, H. Chen. *University of Wisconsin, Madison, WI.*

BACKGROUND: Deficiency of 25-hydroxyvitamin D (25OHD) is a stimulus for the secretion of parathyroid hormone (PTH). During surgery for primary hyperparathyroidism (PHPT), 25OHD deficiency may artificially elevate PTH and decrease the sensitivity of intraoperative PTH (ioPTH). We evaluated if 25OHD deficiency affects ioPTH measurements after surgical treatment of PHPT. METHODS: 885 patients underwent curative surgical treatment of PHPT. An adequate drop in ioPTH was defined as a greater than 50% PTH decrease 5, 10, or 15 minutes after resection. Patients with a 25OHD level below 25 ng/mL were considered to be deficient. Clinical measures were analyzed and correlated with 25OHD status. RESULTS: Of 351 patients with known 25OHD status, 198 (56%) patients were 25OHD deficient. There was no statistical difference between 25OHD deficient and sufficient patients in PTH (169±12 vs. 154±20 pg/mL), phosphorous (2.8±0.0 vs. 3.0±0.0 mg/dL), and alkaline phosphatase (104±5 vs. 101±6 U/L). As continuous variables, there was a positive correlation between PTH and calcium (r = 0.26), alkaline phosphatase (r = 0.60), and gland weight (r = 0.40, P <0.001 for all). There was also an inverse correlation between preoperative PTH and 25OHD (r = -0.13, P = 0.05). The average ioPTH decrease was not significantly different after 5 minutes (54.7±1.6 vs. 55.0±1.6%, deficient vs. sufficient), 10 minutes (65.8±1.2 vs. 67.3±1.2%), or 15 minutes (71.5±1.0 vs. 72.9±1.3%). 25OHD status did not affect when ioPTH indicated surgical cure after 5 (64.6 vs. 63.4%, deficient vs. sufficient), 10 (87.9 vs. 88.2%), and 15 minutes (99.5 vs. 98.7%). CONCLUSIONS: Lower 25OHD levels are correlated with higher PTH levels in patients with PHPT. Moreover, an elevated PTH is associated with a decreased calcium, alkaline phosphatase, and gland weight, suggesting that patients with 25OHD deficiency may have more severe disease. In this study, 25OHD status did not affect the average percent ioPTH drop or the rate of cure. Importantly, patients with 25OHD deficiency do not appear to have different ioPTH dynamics than those without 25OHD deficiency.

P88

Common Locations of Parathyroid Adenomas M.A. Moreno,[1] C.S. Landry,[1]* G.G. Callender,[1] K. Woodburn,[1] B.S. Edeiken-Monroe,[2] E.G. Grubbs,[1] D.B. Evans,[1] J.E. Lee,[1] N.D. Perrier.[1] *1. Surgical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, TX; 2. The University of Texas M. D. Anderson Cancer Center - Diagnostic Radiology, Houston, TX.*

Introduction: We have developed a nomenclature system that succinctly specifies the locations of parathyroid adenomas in the neck. This project reports our experience applying the system to a large, contemporary cohort of patients with parathyroid adenomas. Methods: A prospective, endocrine surgery database at a single, tertiary care center was retrospectively analyzed. A previously described nomenclature describing the 7 most common specific locations for parathyroid glands was utilized: sites A, B, and C describe superior glands, and sites D, E, F and G describe inferior glands. We reviewed the records of 271 patients who underwent parathyroidectomy for sporadic primary hyperparathyroidism between January 2006 and May 2008, and analyzed the effect of adenoma location during operative intervention and postoperative outcome. Results: Adenomatous gland locations were classified intraoperatively as A (adherent to posterior thyroid capsule) in 12.5% of cases; B (behind thyroid, in tracheoesophageal groove) in 17.3%; C (close to clavicle, prevertebral space) in 13.7%; D (directly over the recurrent laryngeal nerve) in 12.2%; E (easy to identify, near the inferior thyroid pole) in 25.8%; F (fallen into thymus) in 7.4%; and G (within thyroid gland) in 0.4%. More than one enlarged gland was present in 10.7% of patients, which usually involved coexistent enlarged type A and E glands. Type F glands were associated with a longer mean operative time (p<0.05), and type E glands with a higher rate of outpatient surgery (p=0.02). Normocalcemia at 6 months was achieved in 96.3% of patients with single gland disease. Conclusions: Our nomenclature system provides a simple way to describe the locations of parathyroid adenomas. Type E adenomas were associated with a higher rate of outpatient surgery, and type F adenomas with a longer operative time. Biochemical cure rates were comparable for all locations of single adenomas. Most importantly, this system has allowed surgeons, endocrinologists, radiologists, and pathologists to speak a common language when communicating about patients with hyperparathyroidism.

P89

Tyrosine Kinase Signaling in Malignant Pheochromocytoma/Paraganglinomas - Utilizing Sorafenib as a Therapeutic Agent K. Idrees,[1]* J.S. Liles,[2] M.B. Kraemer,[2] A. Warriner,[2] T.B. Vaughn,[2] C. Arguello,[2] F. Ovalle,[2] R. Rosenthal,[2] O. Hameed,[2] J.P. Arnoletti,[2] M.J. Heslin.[2] *1. Section of Surgical Oncology, Department of Surgery, University of Pittsburgh, Pittsburgh, PA; 2. University of Alabama at Birmingham, Birmingham, AL.*

B: Malignant pheochromocytomas (PCC) & paraganglionomas (PG) are generally resistant to conventional chemo- & radio-therapy, and are associated with a poor prognosis. Due to the vascular nature of these tumors, we sought to investigate the expression of angiogenic markers that might provide a molecular basis for targeted therapy in the treatment of malignant PCC/PG. M: 24 operatively-obtained PCC/PG specimens were analyzed for expression of vascular endothelial growth factor receptor (VEGFR) 1 & 2, platelet-derived growth factor receptor-beta (PDGFR-β) & insulin growth factor 1 receptor (IGF-1R) by western blotting. Additionally, downstream signaling targets were also evaluated. R: 21 PCC (2 malignant) and 3 PG were analyzed. Greater than 90% of the specimens demonstrated strong expression of VEGFR-1, VEGFR-2, or both, with no correlation between expression level and tumor

type. Detection of IGF-1R was inconsistent (6/24 no staining, 7/24 detectable, 11/24 strong), while strong staining for PDGFR-β was found in all (24/24) of the specimens. MAPK and PI3-K are known to be mediators of VEGFR-2 & PDGFR-β signaling and > 95% of the specimens demonstrated high levels of activated ERK1/2 & AKT, further confirming that VEGFR and PDGFR-β receptors are active in PCC/PGs. These in vitro findings provided a rationale to treat a patient with metastatic PCC (thoracic & abdominal disease) with sorafenib, a potent VEGFR/PDGFR-β tyrosine kinase inhibitor. After 6 months of therapy, the patient demonstrated a partial radiographic response (32% per RECIST), as well as improvement in clinical symptoms & stabilization of blood pressure. Of note, this tumor was also found to strongly express VEGFR-1 and 2 by immunohistochemistry. C: We have demonstrated that angiogenic signaling cascades are present and active in malignant PCC/PGs. These findings are further validated as targeting of VEGFR & PDGFR-β with sorafenib resulted in significant clinical response in a patient with malignant PCC. Although this is the first reported case of targeted therapy of malignant PCC using sorafenib, further in vitro analyses of these promising therapeutic targets are needed.

P90

The effect of parathyroidectomy on hypertension in patients with primary hyperparathyroidism N. Samm,* B. Zarebczan, R.S. Sippel, H. Chen. *University of Wisconsin, Madison, WI.*

Introduction: The pathogenesis of hypertension in patients with primary hyperparathyroidism remains unclear. The objective of this study was to evaluate the effect of parathyroidectomy on hypertension by comparing changes in blood pressure, medication dosage, and measurement of blood pressure pre and post surgery in patients diagnosed with primary hyperparathyroidism. Methods: A retrospective chart review was performed on all patients diagnosed with primary hyperparathyroidism who underwent a parathyroidectomy between October 2001 and December 2006 at a single institution. Charts were reviewed for patient demographics, documented pre and post surgery blood pressure measurements, blood pressure medications, and histological diagnosis of excised parathyroid tissue. Results: During this time period, 673 patients underwent parathyroidectomy, of whom 160 (24%) patients were diagnosed with hypertension and had complete data on pre and post procedure blood pressure measurements. Of the 160 study subjects, 121(75%) were found to have adenomas (75%), 17 (11%) had a double adenoma, and 21(13%) were diagnosed with hyperplasia. There was no statistically significant differences in the initial blood pressure between groups. After parathyroidectomy, 63(39%) patients required higher doses of medication, 67 patients maintained their current level of medication and 30 patients had a reduction in blood pressure medication post parathyroidectomy. Patients with a double adenoma were more likely to have a reduction in their blood pressure medication after surgery, in comparison to either the adenoma or the hyperplasia group. Conclusion: Parathyroidectomy appears to stabilize or improve hypertension in the majority of patients with primary hyperparathyroidism. Interestingly, patients with double adenomas were much more likely to have a reduction in anti-hypertensive medications after successful parathyroid resection.

	Increased BP medication	Same BP medication	Decreased BP medication
Adenomas	49	55	17
Double Adenomas	4	2	11
Hyperplasia	10	9	2
Cancer	0	1	0

P91

Bilateral Neck Exploration For Primary Hyperparathyroidism: Is It Still Relevant? R.A. Dilawari,* A. Porpiglia. *Surgery, University of Tennessee Health Science Center, Memphis, TN.*

Targeted or minimally invasive exploration has gained significant popularity in recent years, because of the ability to localize the abnormal gland with various localization technique especially sistamibi scan. The potential advantages cited for limited exploration are; smaller incision, shorter hospital stay, and potential avoidance of general anesthesia. The potential disadvantage is that multiglandular disease can be missed. Utilization of intra-operative PTH can help reduce the incidence of multiglandular disease. However, analysis of intra-operative PTH requires a minimum of 20 minutes for each specimen which adds to idle time in surgery. Method: Prospectively decided to explore both sides of neck during the waiting period of intra-operative PTH analysis and the data was analyzed retrospectively. There were 113 patients, 110 of them had sistamibi scan, 28 patients had US, and 26 patients had both. 83 of 110 were localized by Sistamibi scan (75%). Only 57 were correctly localized (69%). 81 patients had intra-operative PTH. Average drop of intra-operative PTH 75.4%. 4 patients who had intra-operative PTH drop has persistent elevated PTH. Average incision size was 5 cms. No recurrent laryngeal nerve injury. No reoperation. All patients discharged next day. Average OR time 88 minutes. Conclusion: None of the localizing modalities can identify all the abnormal glands. Even intra-operative PTH measurements, which is now standard of care can miss multiglandular disease. Localizing studies identified only 75% of cases and was accurate only 69% of the time. Planned bilateral neck exploration can be done through small incision, with low morbidity and may decrease the chances of reexploration.

P92

A Comparison of the Ligasure and Harmonic Scalpel in Thyroid Surgery: A Single Institution Review B. Zarebczan,* D. Mohanty, H. Chen. *University of Wisconsin, Madison, WI.*

Introduction: Over the last few years many surgeons have begun to utilize the ligasure device or harmonic scalpel to perform thyroid surgery. Several papers have demonstrated the benefits of these devices over traditional hand-tying techniques. The purpose of this study was to examine our institution's experience with the ligasure device and harmonic scalpel during thyroid surgery and to compare mean operative times and complications associated with each device. Methods: A retrospective chart review was performed on all patients, who underwent thyroid surgery using either a ligasure device or harmonic scalpel at a single institution between December 2005 and August 2009. Charts were reviewed for patient demographics, type of surgery performed, mean operative time, and complications such as recurrent laryngeal nerve injury and hypocalcemia. Results: During this time period 360 patients underwent thyroid surgery. Those who underwent a MRND or central neck dissection (n=67), underwent prior neck surgery (n=26), and those having a history of neck radiation (n=14) were excluded from the study. Of the 253 patients who were included, 133 underwent total thyroidectomy, with the ligasure device being used in 89 of those cases and the harmonic scalpel in 44 cases. The remaining patients underwent lobectomy, 92 with the ligasure device and 28 with the harmonic scalpel. There was no difference in the weight of the glands removed during either procedure. There was a significant decrease in the operative time for both thyroidectomies and lobectomies when the harmonic scalpel was utilized. In regard to complications, there was no statistically significant difference in the number of transient recurrent laryngeal nerve injuries or in the number of patients developing hypocalcemia in the post-operative period. Conclusion: In this study, there was no difference in the rate of recurrent laryngeal nerve injury and hypocalcemia between the two devices. However, the use of the harmonic scalpel significantly decreased operative time for both thyroidectomies and thyroid lobectomies when compared to the ligasure device.

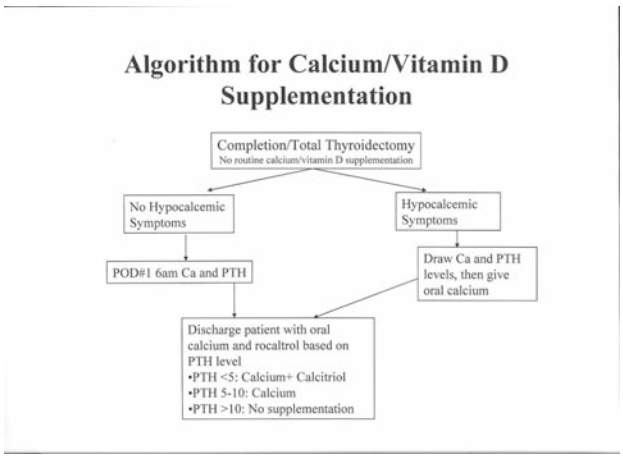
	TOTAL THYROIDECTOMY				THYROID LOBECTOMY		
	Wt(gms)	OR time(min)	RLN injury	Hypocalcemia	Wt(gms)	OR time(min)	RLN injury
Ligasure	40.9±33	74±16.3	3 (3.4%)	6 (6.7%)	27.9±38.1	42±14.1	6 (6.5%)
Harmonic	39.6±40.1	59±11.7	1 (2.3%)	3 (6.8%)	20.4±24.8	35±11.6	0
	P=NS	P<0.001	P=NS	P=NS	P=NS	P=0.001	P=NS

P93

Routine vitamin D supplementation following total thyroidectomy: An algorithm based on "morning after" parathyroid hormone levels A.K. Cayo,* T.S. Wang, J.S. Scheel, E.K. Krzywda, S.D. Wilson, T.W. Yen. *Surgery, Medical College of Wisconsin, Milwaukee, WI.*

Introduction: There are no evidence-based protocols for calcium and vitamin D supplementation after total thyroidectomy. This study examines the role of postoperative serum calcium (Ca) and parathyroid hormone (PTH) levels in predicting the need for long term vitamin D supplementation (DS). Methods: A retrospective chart review of patients undergoing completion/total thyroidectomy from 1/07-12/08 was performed. Ca and PTH levels were obtained the morning of postoperative day 1 (D1). Data collected included extent of surgery, final pathology, postoperative Ca (normal 8.4-10.5 mg/dL) and PTH levels (normal 14-72 pg/mL), and the duration of DS, using calcitriol.

Patients were divided based on D1 PTH levels: Group 1 (<5.0); Group 2 (5.0-10); Group 3 (10.1-20); and Group 4 (>20). Results: 104 of 145 patients who underwent completion/total thyroidectomy had D1 PTH levels. 26 patients were in Group 1 (median PTH <2.5; range <2.5-4.5), 12 in Group 2 (median PTH 8.2; range 5.2-10), 18 in Group 3 (median PTH 14.1; range 10.2-17.9) and 48 in Group 4 (median PTH 30; range 21-227). Ca levels did not differ among the groups. All 7 (7%) patients who required DS >1 month were in Group 1. Of these, 5 (71%) had thyroid cancer and 4 underwent lymphadenectomy; only 4 had subjective hypocalcemic symptoms. The positive predictive value (PPV) of D1 PTH <5.0 in predicting DS >1 month was 27% (sensitivity [SN] 100%, specificity [SP] 80%); this increased to 45% for patients with cancer (SN 100%; SP 78%) and 67% for patients with lymphadenectomy (SN 100%; SP 71%). The negative predictive value of D1 PTH ^ 5.0 for DS >1 month was 100%. The ability of D1 Ca to predict the need for DS >1 month was poor; the PPV for serum Ca <7.5, <8.0 and <8.5 ranged from 14-17%. Conclusion: D1 PTH levels, compared to D1 Ca levels, better predict the need for long term DS after thyroidectomy. A PTH level ^5.0 may identify patients who can be safely discharged without routine vitamin D supplementation. Based on these findings, we have implemented a PTH-based algorithm for calcium and vitamin D supplementation after completion/total thyroidectomy.



P94

Management of Follicular Thyroid Carcinoma Should be Individualized Based on Degree of Capsular and Vascular Invasion
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Introduction: Follicular thyroid carcinoma (FTC) includes a spectrum of neoplasms with varying propensity for metastasis. The aim of this study is to describe outcomes for follicular carcinoma following multimodality treatment, with reference to the degree of capsular and vascular invasion and to recommend a rational management approach based on these characteristics. Methods: Patients with histologically confirmed FTC were identified from a prospectively maintained database. Details of intervention and long-term outcome were obtained. Outcomes were compared between Group 1: minimally invasive FTC without vascular invasion; Group 2: minimally invasive FTC with angioinvasion; and Group 3: widely invasive FTC. Results: Between May 1983 and December 2008, 124 patients with FTC were identified. The overall disease-free survival rate was 84% at a median of 38 months follow-up. Disease-free survival was 97%, 76% and 46% respectively in Groups 1, 2 and 3, and significantly different between groups (p=0.006). Fourteen patients in this series (11%) developed distant metastases including 2 (3%) in Group 1 and 6 (12%) in Group 2. Only patients <45 years of age in Group 1 had 100% disease-free survival. After multivariate linear regression, age (p<0.001) and lymph node involvement (p=0.03) were the most powerful predictors of distant metastasis with tumor diameter (p=0.05) and vascular invasion (p=0.06) being less predictive. Conclusions: Survival is improved in those with minimally invasive compared with widely invasive FTC. In patients <45 years with minimally invasive FTC without angioinvasion, hemithyroidectomy may be adequate treatment. All other patients with FTC should undergo total thyroidectomy and radioactive iodine ablation.

P95

A Comparison Of Competing Lymph Node Staging Schemes In Resectable Gastric Cancer
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Background: New schemes for lymph node (LN) staging have been proposed to improve upon the well-described UICC/AJCC staging N category convention. The ratio-based system and the logarithmic odds (LODDS) score are two novel competing staging systems. We compared the UICC/AJCC staging with the ratio and LODDS systems in predicting overall survival (OS) in 10,887 resectable gastric cancer patients. Methods: In a large multiinstitutional US-based gastric cancer data set, we identified 10,887 non-metastatic resectable gastric cancer patients who had LNs examined between 1988-2001. We compared each subject's UICC/AJCC N stage category with the two novel staging schemes. After calculating quartiles for the two novel staging schemes, we analyzed the OS curves for each method. Our comparison metric was the log-rank chi-squared statistic, with large chi-squared statistics indicating improvement in N stage intercategorical discrimination. Results: Median (range) of follow-up was 7.6 years (1 month – 19 years), with an overall median survival of 2.0 years (95% CI: 2.0 – 2.1 years). With all patients combined, we found that the LODDS and LN Ratio methods performed similarly. However, both were notably superior to the traditional UICC/AJCC convention. In LN-positive patients only (N = 6,835), LODDS performed marginally better than the ratio method, with again both considerably superior to the UICC/AJCC convention (see Table). Conclusions: The two novel LN staging methods have a higher degree of discrimination utility than the UICC/AJCC N staging convention. These methods may have a role in reducing the prognostic impact of lymph node count variability, and carry the potential to more closely correlate nodal staging categories to outcomes in gastric cancer.

Log-rank chi-squared statistics for OS among three competing staging conventions

All Patients (n=10,887)		LN-positive Patients (n=6,835)	
Method	Chi-squared	Method	Chi-squared
LODDS	2492	LODDS	953
LN Ratio	2510	LN Ratio	912
AJCC N Stage	1856	AJCC N Stage	336

Greater chi-square statistics indicate improvement in N stage category discrimination

P96

R0 Resection After Induction Gemcitabine/Oxaliplatin/Cetuximab +/- Capecitabine-Based Chemoradiation For Locally Advanced Pancreatic Cancer
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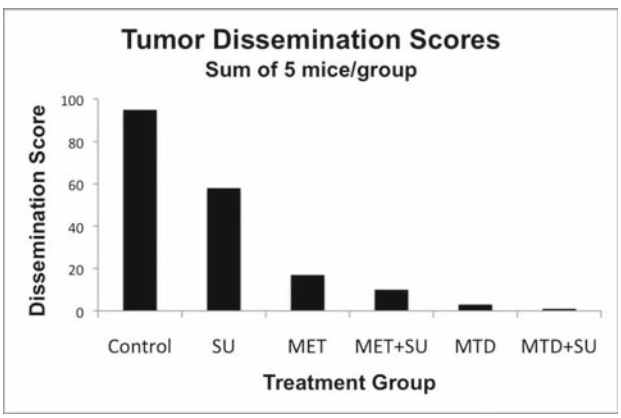
INTRODUCTION: Although chemoradiation (chemoRT) has been shown to improve median survival in patients (pts) with locally advanced pancreatic cancer (LAPC), few patients are "downstaged" to allow resection and therapy is rarely curative. We conducted a phase II trial of induction chemotherapy +/- chemoRT to optimize progression free survival (PFS), R0 resection rate, and overall survival (OS) in pts with LAPC. METHODS: Thirty nine pts with biopsy-proven LAPC (based on defined CT/MRI/ endoscopic ultrasound [EUS] criteria) received 6 cycles of gemcitabine 1,000 mg/m2 IV D1 and oxaliplatin 100 mg/m2 IV D2 every 14d combined with cetuximab 400 mg/m2 IV D1 followed by 11 weekly infusions of 250 mg/m2. Pts with complete/partial response (CR/PR) by CT/MRI/EUS underwent attempted surgical resection, while pts with stable disease (SD) received intensity modulated radiotherapy (IMRT, 54 Gy) with concurrent capecitabine (800 mg/m2 PO BID) followed by re-staging CT/MRI/EUS +/- attempted resection. RESULTS: Thirteen pts with borderline resectable and 26 pts with frankly unresectable LAPC were

enrolled between 3/06-11/08. Four out of 34 pts who completed induction chemotherapy (0%CR/17%PR/66%SD/17% progressive disease [PD]) and 9/26 patients who subsequently completed chemoRT (0%CR/0%PR/77%SD/23% PD) underwent surgical exploration. Twelve pts (8 borderline resectable, 4 frankly unresectable) underwent surgical resection consisting of either pancreaticoduodenectomy (11 pts) or extended distal pancreatectomy (1 pt). Six pancreaticoduodenectomy pts required vascular resection/reconstruction: 4 venous, 1 venous/arterial, and 1 arterial. Eleven pts (28% of all enrolled pts) underwent R0 resection, including 1 pt with a pathologic CR. At a median follow-up of 11.8 months, median PFS and OS were 9.1 (7.1, 16.1) and 12.9 (9.5, Inf) months, respectively. In pts who underwent R0 resection, median PFS/OS had not been reached. CONCLUSIONS: Induction chemotherapy with gemcitabine/oxaliplatin/cetuximab +/- capecitabine-based IMRT is well tolerated, results in a substantial R0 resection rate, and may significantly improve survival in pts with LAPC.

P97

Low Dose Metronomic Gemcitabine has High Antimetastatic Efficacy in an Orthotopic Mouse Model of Pancreatic Cancer H.S. Tran Cao,[1]* M. Bouvet,[1] E. Romney,[2] S. Kaushal,[1] A. Keleman,[2] G. Kim,[2] J. Fruehauf,[2] D.K. Imagawa,[2] R.M. Hoffman,[3] M.H. Katz.[2] *1. UC San Diego, San Diego, CA; 2. Surgery, UC Irvine, Orange, CA; 3. AntiCancer, Inc., San Diego, CA.*

INTRODUCTION: Therapies targeting metastasis of pancreatic cancer (PC) are ineffective. Low dose metronomic chemotherapy has suppressed growth of primary cancers but its antimetastatic efficacy is unknown. We report the efficacy of metronomic gemcitabine with and without tyrosine kinase inhibitor sunitinib on metastasis in an orthotopic model of PC. METHODS: Mice with highly metastatic, orthotopic PC tumorgrafts expressing red fluorescent protein were treated with intraperitoneal gemcitabine on a metronomic (1 mg/kg daily, MET) or maximum tolerated dose (150 mg/kg twice weekly, MTD) schedule with or without oral sunitinib (SU). Rates of metastasis, primary tumor growth and survival were evaluated. Primary tumor growth and metastasis were quantified by fluorescence imaging. RESULTS: Control mice with orthotopically-implanted MIA-PaCa-2-RFP fluorescent tumorgrafts died of local and widespread metastatic disease within 4 weeks. Gemcitabine at daily doses of 2 mg or greater led to toxicity and death within 1 month in mice without tumors but MET was well tolerated. Treatment of mice with established tumorgrafts with MET at 1 mg/kg daily for 2 weeks dramatically suppressed metastasis at multiple sites—an effect enhanced by SU ($p<0.05$). In contrast, primary tumor growth was inhibited by MET+SU ($p<0.05$) but not by either MET or SU alone. In a survival study, both MET and SU had a modest effect on survival compared to control but survival was limited by extensive primary tumor growth (med. survival 32d, 31d, 25d, respectively). MET+SU had a more pronounced effect on survival (med. survival 44 days, $p<0.05$). MTD with or without SU had the most favorable effect on primary tumor growth and survival but its antimetastatic effect was similar to that of MET+SU. Staining of primary tumors for vWF revealed an antiangiogenic effect of therapy. CONCLUSION: Antimetastatic activity approaching that of standard MTD gemcitabine is achieved with a total gemcitabine dose reduced 42 times using MET and is further enhanced by sunitinib. Our results suggest the clinical potential of this well-tolerated regimen against PC in the adjuvant and maintenance settings.



The extent of metastatic dissemination following 2 weeks of each therapy was scored by grading metastases on a 1 (microscopic) to 4 (large, macroscopic) scale at multiple sites. Column = sum of scores for 5 mice/group.

P98

Intensity Modulated Radiation Therapy in Hepatocellular Carcinoma and Cirrhosis: Evaluation of Radiological and Pathological Response S. Samaniego,* C. Gimenez, U. Katta, R. Roccio, C. Moorthy, S. Bentley-Hibbert, D. Wolf, M. Rodriguez-Davalos, M. Facciuto. *Westchester Medical Center, New York, NY.*

Introduction: Locoregional therapies may be applied to cirrhotic patients with hepatocellular carcinoma (HCC) who are awaiting liver transplantation (OLT) in an attempt to prevent tumor progression. However, data regarding the efficacy of locoregional treatments remain limited. Methods: From 2006-2009, 27 HCC patients (AJCC I and II) listed for OLT underwent intensity modulated radiation therapy (IMRT). 39 lesions were treated and assessed radiologically. Out of the 27 patients, 17 had OLT. The liver explants were analyzed and 22 lesions underwent pathological evaluation. Results: Radiation dosage varied from 2400cGy to 3600cGy with 62% of patients receiving 2800cGy over 2 to 4 fractions. The mean percentage of liver volume treated was 9%. The average time from IMRT to OLT was 4 months. Upon completion of OLT, tumors were studied for pathological response (0-29% necrosis=no response, 30-99%=partial response, and 100%=total response). Of the 22 pathologically evaluated lesions, 38% were responders. Radiological response was defined as complete (disappearance of all intratumoral arterial enhancement), partial (at least a 30% decrease in the sum of the longest lesion diameters, compared to baseline), progressive (an increase of at least 20% in the sum of diameters or appearance of new lesions), or stable (any case in between). In a cumulative analysis of all radiological imaging, 30% had complete response, 7% partial, 56% stable, and 7% had progression of disease. Multivariate analysis found dose fraction to be an independent predictor of radiological response ($p=0.036$, 95% CI 0.18; 0.94). For pathological response, no independent predictor was found, most likely due to small sample size. Side effects from IMRT were recorded in 3 of 27 patients (11%). Conclusion: IMRT in the setting of early HCC and cirrhosis has a comparable radiological and pathological response rate which is roughly equivalent, if not superior, to the response rate of other locoregional therapies. With possibly fewer side effects due to its very minimally invasive nature, IMRT can be viewed as an efficacious choice for local tumor treatment while awaiting OLT.

P99

Interferons Augment the Antitumoral Activity of Sorafenib in Human Pancreatic Cancer Cell Lines N.R. Billimoria,[1]* A.A. Arora,[1] S.S. Galoforo,[2] B. Marples,[2] G.D. Wilson,[2] M.J. Jacobs.[1] *1. General Surgery, William Beaumont Hospital, Royal Oak, MI; 2. Radiation Oncology, William Beaumont Hospital, Royal Oak, MI.*

Introduction: Interferons (IFNs) may be beneficial for pancreatic cancer therapy. Previous studies showed that their cytotoxic effects are mediated through IFN membrane receptors. The goal of this study was to assess whether IFNs augment the antitumoral activity of sorafenib in human pancreatic cancer cell lines by activating signal transduction pathways to reduce cellular proliferation and increase apoptosis. Methods: Four human pancreatic cancer cell lines with disparate receptor expressions were investigated (BxPc3, Capan1, MiaPaCa2, Panc1). Cell survival was measured after exposure to 3 chemotherapy agents (5FU, gemcitabine (Gem), sorafenib) and IFNs alone followed by combinations of IFNs+chemotherapy agents. Cellular viability was assessed by the methylthiazol tetrazolium assay; apoptosis assayed by caspase activation. Results: IFNs mediated cytotoxic activity only in cell lines expressing the corresponding receptor. The chemotherapeutic agents individually inhibited cell proliferation however, sorafenib had the most significant decrease in cell viability compared to 5-FU and Gem ($p < 0.05$) in 3 cell lines (MIAPaCa2, Capan1, and Panc1). The addition of IFN-alpha to sorafenib significantly decreased cell survival compared to sorafenib alone with $p < 0.05$ in MIAPaCa2 and BxPc3. In Capan1, although the combination of sorafenib + IFN-alpha had the lowest cell survival, the difference in cell survival between sorafenib alone and sorafenib + IFN-alpha was not significant. There was no survival difference by adding IFN-alpha to the Panc1 which was expected since these cells do not express the interferon receptor. Similar results were observed

when IFN-alpha was replaced with IFN-beta, and IFN-gamma. The apoptosis data correlated with the cell survival data in that there was more cell death (or decreased survival) with the combination treatment compared to the single agent. Conclusion: Addition of IFN to each chemotherapy agent augmented the antitumoral effects of the drug in IFN-receptor postive cell lines. Furthermore, the IFN-sorafenib combination caused the lowest cell survival by increasing apoptosis when compared to the IFN combinations with 5FU and Gem.

P100

Adjuvant Gemcitabine and Erlotinib for Resected Pancreatic Cancer P. Bao,[1]* R.K. Ramanathan,[3] A.J. Moser,[2] N. Bahary,[2] B.C. Lembersky,[2] D.L. Bartlett,[2] S.J. Hughes,[2] K.K. Lee,[2] H.J. Zeh.[2] *1. Stony Brook University Hospital, Stony Brook, NY; 2. University of Pittsburgh Medical Center, Pittsburgh, PA; 3. TGen, Scottsdale, AZ.*

Background: Combination gemcitabine and erlotinib has benefit for advanced pancreatic adenocarcinoma. Adjuvant use may improve outcome in resected patients. **Methods**: A single-center phase II trial of adjuvant biweekly gemcitabine (1500mg/m^2) over 4 months plus erlotinib (150mg/day) for 12 months was initiated. Eligibility included patients with margin-negative resection within 10 weeks of study treatment. Primary endpoint was time from treatment start to radiologic recurrence and sample size was powered to detect improvement in recurrence free survival (RFS) from 10 to 15 months. Secondary endpoints included overall survival (OS) and toxicity evaluation. Descriptive statistics were calculated and the Kaplan-Meier method used to analyze time-to-event data. **Results**: The study completed intended accrual of 25 patients with median age 66 years (range 34-81). Procedures included 20 pancreaticoduodenectomies and 5 distal pancreatectomies with 16 (64%) node-positive. Median time from resection to treatment start was 62 days (range 34-70). Median follow-up to date is 16.7 months (range 11-24) for subjects alive without disease. Ten subjects completed all intended therapy, 4 withdrew due to toxicity, and 1 remains on protocol. There were 16 recurrences observed at a median 8.5 months (range 1-28): 10 (62%) while on protocol; 5 (31%) after completing therapy; and 1 (6%) in a patient taken off protocol due to adverse events but on single-agent gemcitabine. The estimated median RFS was 21.5 months (95% CI 8.2, 24.5) with 1- and 2-year RFS of 56% and 28%, respectively. There have been 8 deaths from disease with estimated 1- and 2-year OS of 85% and 53%, respectively. Subjects experienced a median 3 (range 0-6) Grade 2 or higher toxicities at least possibly attributable to gemcitabine or erlotinib, with 32% requiring dose-reduction and 36% needing dose-holding of one or both drugs at some point during treatment. **Conclusions**: Early results show an increase in RFS for resected pancreatic cancer patients given a reasonably well-tolerated regimen of adjuvant gemcitabine and erlotinib. However, recurrence during therapy is frequently observed and thus an optimal adjuvant regimen remains elusive.

P101

Multiplexed cell signaling analysis of normal gastric mucosa, gastric metaplasia and invasive cancer reveals distinctive fingerprints of gastric cancer E. Mammano,[1]* F. Galdi,[1] E. Tessari,[1] M. Briarava,[1] A. Marchet,[1] G.M. Rossi,[1] P.L. Pilati,[1] G. Esposito,[2] M. Digito,[1] F. Farinati,[3] D. Nitti.[1] *1. Clinica Chirurgica 2, Department of Oncological ans Surgical Sciences, Padova, Italy; 2. Oncology Section, Department of Oncology and Surgical Sciences, Padova, Italy; 3. Departments of Surgical and Gastroenterological Sciences, Padova, Italy.*

Background. Gastric cancer is still one of the commonest malignancy in the world. The mechanism of gastric carcinogenesis is not well known. This tumor is believed to arise from a premalignant cascade thought to be initiated by chronic Helicobacter pylori (H.pylori) infection, that lead to intestinal metaplasia and subsequently invasive cancer. Deregulation of protein kinases are thought to play a critical role in development and progression of gastric carcinogenesis. Reverse phase protein microarray (RPMA) technology, provides a unique opportunity to understand the signaling network. Methods. We performed RPMA on human tissue biopsy to identify a phosphoproteomic profile of gastric carcinogenesis. 10 endoscopic biopsies from healthy subjects, 9 from subjects with gastric metaplasia and 10 from gastric cancer patients without lymph node metastases were collected at our Institution and immediately snap frozen. The cells were lysed and subjected to RPMA analysis. Using this technique, we measured the phosphorylation level of 52 key-signalling proteins. Molecular network analysis was performed using commercially available software. Results. The hierarchical two way cluster analysis identified three distinct phosphoproteomic profiles that segregate healthy subjects from gastric metaplasia and gastric metaplasia from gastric cancer. The signalling activation is mainly in the pathways that involve PKCs activation, those phosphorilation levels has an exponential growth from healthy mucosa to metaplasia and than to cancer. In addition we found that activation of MAPK pathways – a pathway involved in cell proliferation, differentiation, motility, and death- is distinctive of invasive cancer profile. Conclusions. Our results map the critical pathways involved in premalignant transformation from normal mucosa to metaplasia and to cancer. These findings may direct future investigation on prevention of invasive cancer development with protein kinase inhibitor.

P102

Tumor Size and Depth Predict Rate of Lymph Node Metastasis and Utilization of Lymph Node Sampling in Surgically Managed Gastric Carcinoids M.S. Saund,[1]* R.H. Al Natour,[1] Q. Huang,[1] V.A. Boosalis,[2] J.S. Gold.[1] *1. VA Boston Healthcare System/Brigham and Women's Hospital, West Roxbury, MA; 2. VA Boston Healthcare System/Boston University School of Medicine, West Roxbury, MA.*

Introduction: Radical resection with regional lymph node dissection is recommended for all sporadic gastric carcinoids. Local resection, however, is accepted for some carcinoids from other gastrointestinal sites (i.e. appendix and rectum). We sought to examine the relation of tumor size and depth to LNM in order to determine whether gastric carcinoids can be selected for local resection. We also sought to quantify the utilization of lymph node sampling (LNS). **Methods:** The Surveillance Epidemiology and End Results Registry was used to identify patients. The Pearson Chi-Square Test was used to assess significance. SPSS was used for statistical analysis. **Results:** 984 patients with localized gastric carcinoids who underwent cancer directed surgery between 1983-2005 were identified. Tumor size and depth predicted probability of LNM in these cases ($p<0.001$, $p<0.001$). While 2.0% of all tumors <1cm had LNM, the rate was 32% for tumors ≥2cm (Table). As patients who did not undergo LNS may have had LNM that was not identified, we examined the rate of LNM in patients who were selected to undergo LNS. In the subset of tumors that underwent LNS, even tumors <1cm had a 6.4% rate of LNM. The AJCC classification of tumor depth provided good stratification of the probability of LNM. 1.5% of all Tis tumors had LNM, while the rate was 80% for T4 tumors. For cases with LNS, even Tis tumors had an 11.8% rate of LNM. Tumors were subgrouped by both depth and size in order to attempt to find cases with a low risk of LNM. For Tis tumors, LNM was not seen for tumors <2cm. For T1 tumors that were <1cm, 3.4% had LNM (5.6% of T1 tumors <1cm with LNS). Excluding Tis tumors <2cm and T1 tumors <1cm, all other subgroups based on size and depth had rates of LNM >7%. Smaller tumors and superficial tumors were less likely to have LNS ($p<0.001$, $p<0.001$). Overall, only 21% of tumors had LNS. Excluding Tis tumors <2cm and T1 tumors <1cm, only 43% had LNS. **Conclusions:** Tumor size and depth predict LNM for gastric carcinoids. Local resection may be appropriate for Tis tumors <2cm and perhaps T1 tumors <1cm. LNS is underused for gastric carcinoids at risk for LNM.

Rate of Lymph Node Metastasis of Gastric Carcinoids Subgrouped by Tumor Size and Depth

	All depths	Tis	T1	T2	T3	T4
All sizes	61/727 (8.4%)	4/259 (1.5%)	9/185 (4.9%)	22/85 (26%)	13/26 (50%)	8/10 (80%)
<1cm	4/197 (2.0%)	0/89 (0%)	2/59 (3.4%)	2/5 (40%)	0/0	0/0
1-2cm	8/119 (6.7%)	0/23 (0%)	5/47 (11%)	2/25 (8.0%)	0/0	1/1 (100%)
≥2cm	41/130 (32%)	3/20 (15%)	2/27 (7.4%)	15/37 (41%)	12/25 (48%)	6/7 (86%)

P103

Additional prognostic information of DUPAN-2/Span-1 in CA19-9 negative pancreatic carcinoma K. Yamashita,* M. Waraya, M. Watanabe. *Surgery, Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan.*

Background We previously identified subgroups with long term survival in pancreatic cancer. This subgroup was identified by JPS stage, preoperative CA19-9 value (preCA19-9), and DPM (dissected pancreatic tis-

sue margin)(Waraya et al. Ann Surg Oncol, 2009). Our aim is to validate the prognostic significance of the independent prognostic factors allowing for other tumor markers including CEA, DUPAN-2, and SPan-1. Materials and Methods Registered is the 63 pancreatic cancer, which included all the parameters, and their prognostic relevance was validated in both a univariate and a multivariate prognostic analysis. Result JPS stage, preCA19-9, and DPM were reproducibly validated to be an independent prognostic factors. Patients with high values of preoperative DUPAN-2 and SPAN-1 also displayed poor prognosis (p=0.001 and p=0.002, respectively) as compared to those with low values, but CEA was not. preDUPAN-2 and preSPAN-1 were closely associated with preCA19-9 (p=0.0878 and p=0.0001, respectively), suggesting that all these carbohydrate antigens may represent the shared structure of tandem repeat of core mucin as a whole, however some patients clearly showed differential pattern of these biomarkers. Among preCA19-9 negative cases, cases with high values of either preDUPAN-2 or preSPan-1 showed significantly poor prognosis with those with triple negative cases (p=0.0006 and p=0.04, respectively), while preSPan-1 harbors a little weaker power for poor prognosis. Conclusion preDUPAN-2/preSPan-1 in addition to preCA19-9 may be useful biomarkers to predict poor prognosis of pancreatic carcinoma. Mucin which expresses either of carbohydrate antigens may play critical roles in carcinoma aggressiveness in pancreatic cancer.

P104

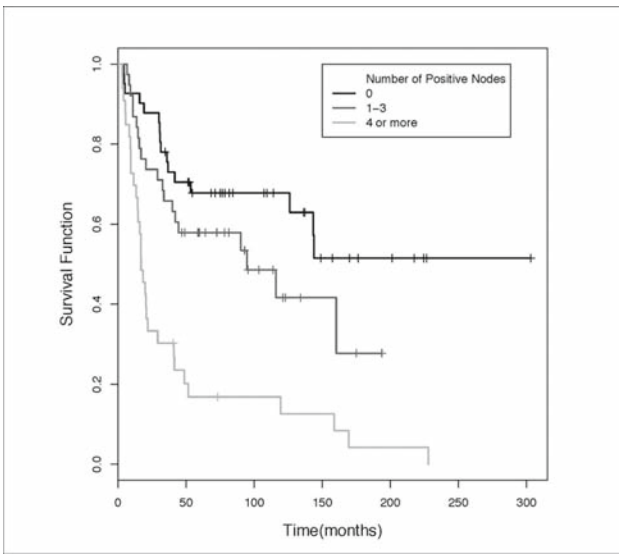
Anastomotic complications following Ivor Lewis esophagectomy in patients treated with neoadjuvant chemoradiation are related to radiation dose to the gastric fundus W.P. Ceelen,* C. Vande Walle, T. Boterberg, D. Van de Putte, Y. Van Nieuwenhove, P. Pattyn. *Ghent University Hospital, Ghent, Belgium.*

Introduction Neoadjuvant chemoradiation (CRT) is increasingly used in patients with locally advanced esophageal cancer. Some studies suggested that CRT results in increased overall surgical morbidity. No data are available on the influence of CRT on anastomotic complications following Ivor Lewis esophagectomy. Methods Clinical and pathological data were prospectively collected from all patients treated with neoadjuvant chemoradiation (36 Gy in 20 fractions combined with 5-FU and cisplatin) followed by Ivor Lewis esophagectomy. Using radiotherapy (RT) planning CT scans, target volumes were drawn encompassing the proximal esophagus region and the gastric fundus. Within these target volumes, dose-volume histograms were analysed to generate the D50 (total dose to 50% of the target volume). We studied the ability of the D50 to predict anastomotic complications (leakage, ischemia, or stenosis). Dose limits were derived using receiver operating characteristics (ROC) analysis. Results Fifty four patients were available for analysis. Radiotherapy resulted in either T or N downstaging in 51%; complete pathological response was achieved in 11%. In hospital mortality was 5.4% and major morbidity occurred in 36% of patients. Anastomotic complications (AC) developed in 7 patients (13%). No significant influence of the D50 on the proximal esophagus was noted on the anastomotic complication rate. The median D50 on the gastric fundus, however, was 33 Gy in patients with AC and 18 Gy in patients without AC (P = 0.024, Mann Whitney U test). Using ROC analysis the D50 limit on the gastric fundus was defined as 29 Gy. Conclusions In patients undergoing neoadjuvant CRT followed by Ivor lewis esophagectomy, the incidence of AC is related to the RT dose on the gastric fundus, but not on the dose received by the proximal esophagus. When planning preoperative RT, efforts should be made to limit the total dose on the gastric fundus.

P105

Duodenal Adenocarcinoma: Clinicopathologic Analysis and Prognostic Implications G.A. Poultsides,[1]* J.L. Cameron,[1] E.A. Sugar,[2] R. Tuli,[3] J.M. Winter,[1] R.H. Hruban,[4] T.M. Pawlik,[1] J.M. Herman,[3] B.H. Edil,[1] M.A. Choti,[1] C.L. Wolfgang,[1] R.D. Schulick.[1] *1. Department of Surgery, Johns Hopkins Hospital, Baltimore, MD; 2. Departments of Epidemiology and Biostatistics, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; 3. Department of Radiation Oncology & Molecular Radiation Sciences, Johns Hopkins Hospital, Baltimore, MD; 4. Department of Pathology, Johns Hopkins Hospital, Baltimore, MD.*

INTRODUCTION: Evidence to guide treatment strategy in duodenal adenocarcinoma is limited. This study intends to evaluate the risk associated with precursor lesions, identify prognostic factors and describe recurrence patterns after resection. METHODS: Between 1984 and 2006, 122 patients with duodenal adenocarcinoma (28 of which arising within an adenoma) and 58 patients with duodenal adenoma (without invasive cancer) underwent pancreaticoduodenectomy. Patients with neoplasms arising from the ampulla of Vater were excluded. Data on clinicopathologic factors and survival were analyzed. RESULTS: Invasive carcinoma was more common in adenomas > 3 cm in size (49% vs. 9%, p<0.001), or with a villous component (villous 54%, tubulovillous 47%, tubular 19%, p=0.003). In patients with invasive adenocarcinoma, overall survival after pancreaticoduodenectomy was 48% at 5 years and 41% at 10 years (median follow-up for survivors, 65 months). Poor tumor differentiation, margin involvement, and perineural invasion (all p<0.01), but not T stage (extension into the duodenal wall), tumor size, and receipt of adjuvant chemo-radiation, were associated with survival on univariate analysis. In addition, lymph node metastasis (63% of patients, p=0.04) and vascular invasion (39%, p<0.01) were independently associated with a reduction in overall survival. Furthermore, as the number of positive nodes increased from 0 to 1-3 to 4 or more, there was significant trend for worsening overall survival (p<0.01, Figure). Data on disease recurrence were available for 51 patients. Of 27 who recurred,16 (59%) had distant recurrence only, 5 (19%) had local recurrence only and 6 (22%) had both local and distant recurrence. CONCLUSIONS: Duodenal adenomas > 3 cm or with a villous component frequently harbor invasive carcinoma. In patients with duodenal adenocarcinoma, lymph node metastasis, and vascular invasion dictate outcome, which appears to be particularly dismal when 4 or more lymph nodes are involved. Therefore, appropriate lymphadenectomy for accurate staging is warranted. The predominantly distant pattern of failure after resection underscores the need for effective adjuvant systemic therapy.



Kaplan-Meier plot of overall survival following pancreaticoduodenectomy for duodenal adenocarcinoma stratified by the number of positive nodes (0, 1-3, 4 or more, p < 0.01).

P106

mir-675 is Overexpressed in Alpha-Fetoprotein-Secreting Hepatocellular Carcinoma J.M. Hernandez,* D. Shibata, B. Centeno, G. Bloom, W. Fulp, D. Chen, C. Timme, S. McCarthy, M. Gruidl, T. Yeatman. *GI Oncology, Moffitt Cancer Center and Research Institute, Tampa, FL.*

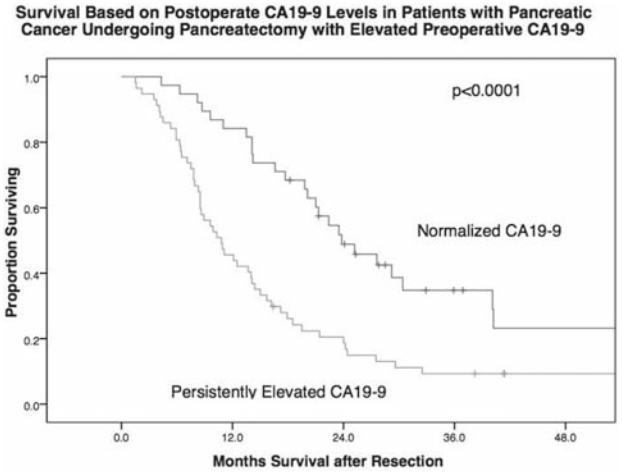
Background: It is estimated that up to 50-75% of hepatocellular carcinomas (HCC) are associated with elevated serum AFP levels. Although AFP-secreting tumors may have a more favorable prognosis, it is unclear whether they represent a distinct genetic entity. We have sought to establish and interrogate a differential gene expression profile comparing AFP-secreting and non-secreting tumors. Methods: From 2000-2009, we identified 27 patients having undergone resection for HCC and also consented to our tissue banking

protocol. These tumors (14 AFP-secreting and 13 non-secreting) were profiled using the Affymetrix 133 Plus 2.0 GeneChips. Pathway analysis software was used to identify altered biologic pathways. Expression validation was performed on a subset of seven patients (four patients with AFP-secreting and three with non-secreting tumors), using quantitative real-time PCR (RT-PCR). Results: At a false discovery rate of 0.2, we identified 418 genes differentially regulated between AFP-secreting and non-secreting tumors, which was independent of any associations with cirrhosis or hepatitis viral activity. H19, a maternally imprinted gene encoding the precursor for mir-675 (a heretofore uncharacterized miRNA), was found to be the most highly upregulated gene (>14 fold) in association with elevated serum AFP. In addition, we identified 23 downregulated biological pathways ($p<0.01$) involving substrate metabolism, and two upregulated pathways ($p<0.03$) involving cell adhesion for AFP-secreting tumors. We validated the overexpression of mir-675 with AFP secretion, demonstrating an average gene expression fold change of 12.5 for patients with AFP-secreting versus non-secreting tumors. Conclusions: HCC associated with elevated serum AFP demonstrates distinct alterations in gene expression and biologic pathways as compared to non-AFP-secreting tumors. Recently, the critical importance of microRNA in the tumorigenesis process has become apparent. Mir-675 is highly overexpressed in AFP-secreting HCC and further investigation of its role in the regulation of AFP expression and additional downstream targets is warranted.

P107

Failure of Normalization of CA19-9 Following Resection for Pancreatic Cancer is Tantamount to Metastatic Disease S.R. Abdel-Misih,* E.C. Ellison, S. Melvin, C.R. Schmidt, M. Bloomston, I. Hatzaras, P. Muscarella. *Surgical Oncology, Ohio State University Medical Center/Arthur G. James Cancer Hospital, Columbus, OH.*

Background: Common curative therapy for pancreatic cancer involves radical resection followed by gemcitabine-based chemotherapy. Often, clinical trials and second-line chemotherapy requires radiographic evidence of disease prior to initiation, potentially delaying needed therapy. We hypothesized that failure of CA19-9 levels to normalize within six months of primary therapy is prognostically equivalent to metastatic disease. Methods: From our pancreatectomy database, we identified 95 patients with pancreatic adenocarcinoma who had elevated CA19-9 levels prior to resection and CA19-9 levels measured after resection. Patients were grouped based on normalization or persistent elevation of CA19-9 levels six months after resection. CA19-9 levels normalized (<35u/ml) after resection in 38 (40%) and remained elevated in 57 (60%). Clinicopathologic characteristics were compared between these two groups using student's t-test and chi-square analysis. Survival curves were constructed using Kaplan-Meier method and compared by log-rank analysis. Results: The two groups were similar in terms of age, gender, comorbidities, tumor size, margin status, perioperative complications, and preoperative CA19-9. As expected, the postoperative mean (± SD) CA19-9 nadir was higher in the persistently elevated group(3534.17 ± 20321.27 vs. 17.61± 7.69, $p=0.290$). Patients with node-positive disease were less likely to normalize their CA19-9 compared to those without nodal metastases (28% vs. 60%, $p=0.0048$). Following resection, patients with persistently elevated CA19-9 had shorter median overall survival of 10.8 months compared to 23.8 months in patients with normalization of CA19-9 ($p<0.001$)(Figure). Discussion: Patients with node-positive disease are less likely to normalize CA19-9 within six months of resection. Persistent CA19-9 elevation after attempted curative resection confers shorter survival analogous to unresected disease and should be considered as recurrence for accrual to clinical trials or initiation of second-line chemotherapy.



P108

The clinicopathological significance of genomic aberrations of microRNA locus in colorectal cnacer patients S. Ishimaru,[1]* K. Mimori,[1] M. Mori.[2] *1. Institute of Bioregulation, Kyushu university, Beppu, Oita, Japan; 2. Osaka University, Beppu, Osaka, Japan.*

[Background] microRNAs (miR) are non-coding RNAs with 18-24 nts, which are known to regulate gene expression post-transcriptionally. Recently, it has been revealed that some miRs play important roles in cancer biology such as development, invasion, and metastasis. But, the significance of genetic aberration on miR locus, which is often found in cancer tissues, is not recognized yet. [Purpose] The aim of our study was to identify miRs with genetic aberration in cancer cells, and to investigate their effects on clinicopathological factors of colorectal cancer patients. [Material and Methods] Cancer tissues were collected from surgically resected samples of 117 colorectal cancer patients by laser microdissection (LMD) method. Genomic DNA and total RNA were extracted from the tissues, and then CGH array was performed with 7 normal colonic mucosa samples as standard. Correlation between genomic aberration of miRs and clinocopathological factors was analyzed to select candidate miRs. Expression of candidate miRs was examined by miR microarray and miR RT-PCR. [Results] miR-17-92a cluster and miR25-106b cluster showed genomic amplification (1.2 fold and 1.1 fold, respectively) and increased expression (8.2 fold and 10.7 fold, respectively). Genomic amplification and mRNA overexpression of these clusters had close correlation($r2=0.809$,$p=0.0376$, $r2=0.531$, $p=0.1628$, respectively), which meant that they were regulated more genetically than by epigenetic modifications. Genomic amplifications of these clusters had significant correlation with lymph node metastases and miR25-106b cluster low expression group showed better 5-year survival than high expression group. [Conclusion] Simultaneous changes of multiple miRs on relatively narrow range of genome can lead to crucial loss of protein regulation mechanisms and to influence cancer progression.

P109

Pancreas-Protocol Imaging at a High Volume Center Leads to Improved Preoperative Staging of Pancreatic Ductal Adenocarcinoma D.M. Walters,[1]* J.B. Stokes,[1] E.E. De Lange,[2] R.B. Adams,[1] T.W. Bauer.[1] *1. University of Virginia, Department of Surgery, Charlottesville, VA; 2. University of Virginia, Department of Radiology, Charlottesville, VA.*

Introduction. High quality preoperative cross-sectional imaging is vital to accurately stage patients with pancreatic ductal adenocarcinoma (PDAC). We hypothesized that imaging performed at a high-volume pancreatic cancer center with dedicated pancreatic imaging protocols and radiologists more accurately stages patients when compared to pre-referral imaging. Methods. We conducted a retrospective review of data from all patients with PDAC who presented to the surgical oncology clinic at our institution between June 2005 and August 2009. Patients were categorized as resectable, unresectable, or borderline resectable based on CT or MRI. The date of imaging and performing facility were recorded as well as resectability at the time of surgery.

For patients who had pre-referral imaging, we determined whether additional imaging at our institution changed management. Results. Two hundred twenty patients with PDAC were identified of which 166 had pre-referral imaging. Patients were selectively re-imaged at our institution based on the quality and timing of imaging at the outside facility. Average time from pre-referral imaging to repeat imaging was less than one month. Based on imaging, 105 (47.7%) patients were deemed resectable, 48 (21.8%) were deemed borderline resectable, and 67 (30.5%) were deemed unresectable. Of the resectable patients, 96 opted for resection. Seventy-nine of the 96 patients underwent preoperative imaging at our institution and of these 28% had unresectable disease at the time of surgery, compared to 47% of patients who only had pre-referral imaging (p=0.11). Re-imaging altered staging and changed management in 41% of patients. Among that group were 54 patients who were categorized as resectable on pre-referral imaging but on repeat imaging were deemed to be borderline resectable (n=26) or unresectable (n=28). Conclusions. Pancreas-protocol imaging at a high volume center improves preoperative staging and alters management in a significant proportion of patients with PDAC who undergo pre-referral imaging. Thus, repeat imaging with pancreas protocols and dedicated radiologists is justified at high volume centers.

P110

Improved Survival in Patients with Resected T1-3 N0-1 Pancreatic Adenocarcinoma Using Adjuvant Conformal or Intensity Modulated Chemoradiation and Intravenous Gemcitabine N. Hanna,* S. Yovino, N. Pandya, N. Horiba, P. Hausner, P. Darwin, E. Goldberg, W. Regine, H. Alexander. *Surgery, University of Maryland School of Medicine, Baltimore, MD.*

Introduction: The recent RTOG 9704 randomized controlled trial demonstrated improved survival using adjuvant external bean radiation therapy and intravenous (IV) Gem in high risk patients with pancreatic adenocarcinoma (PanCa). We reviewed our experience with this regimen using conformal or intensity modulated chemoradiation (IMRT) to confirm patient outcome at a single high volume center. Methods: From 10/2004 to 3/2009, 203 patients underwent pancreatic resection for suspected neoplasm of which 34 who had a pathologic diagnosis of T1-3 N0-1 PanCa and received adjuvant therapy at our institution were identified from a prospectively maintained database. Patients underwent pancreatic resection followed by conformal or IMRT to 50.4 or 59.4 Gy in 5 daily fractions per week. One cycle of IV Gem, 1000 mg/m2, q week x 3 every 28 days was administered pre-conformal or IMRT and for 4 to 6 cycles after. Patients were followed regularly for progression-free and overall survival (PFS and OS, respectively). Results: The mean age was 62 yrs (range: 35-83); there were 12 females (35%). Five patients had distal pancreatectomy/splenectomy and 29 had pylorus-preserving or classic pancreaticoduodenectomy with portal venous reconstruction in 7 (20.6%). Median number of sampled lymph nodes (LN) was 14; 32 patients (74%) had a T2-3 primary, 23 (68%) had LN metastases and 14 (41%) had a microscopic margin positive resection. At a median potential follow-up of 15 months, 17 patients have recurred; 5 locally, 6 with hematogenous metastases and 6 with both (3 lost to follow-up). The median actuarial OS is 30 months (Figure). Conclusions: These data validate the RTOG 9704 clinical trial results and suggest that conformal or IMRT and IV Gem results in a median OS comparable or better than previously reported using other regimens. This adjuvant regimen should be offered routinely to high-risk patients following resection of PanCa.

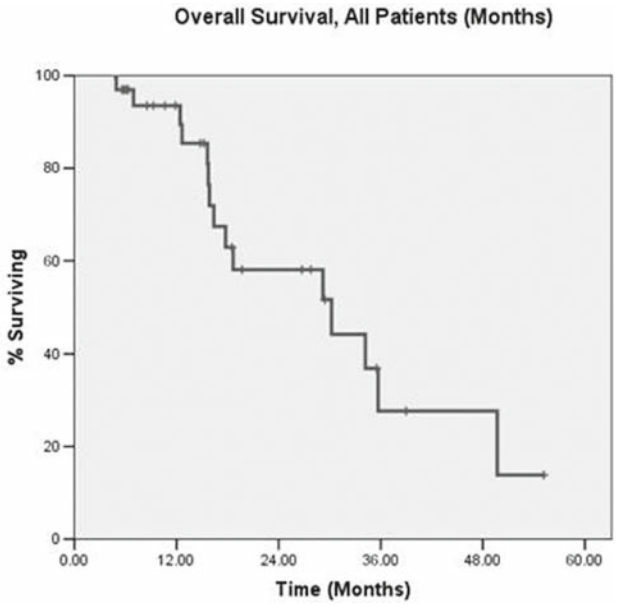


Figure. Overall survival of 34 patients with T1-3 N0-1 pancreatic adenocarcinoma following resection and adjuvant therapy.

P111

Clinical significance of miR-125b expression in colorectal cancer patients T. Yokobori,[1]* K. Mimori,[1] H. Kuwano,[2] M. Mori.[3] *1. Department of Surgery, Medical Institute of Bioregulation, Kyushu University, Beppu, Japan; 2. Gunma University, Maebashi, Japan; 3. Osaka University, Suita, Japan.*

Introduction. A role in carcinoma development of microRNA(miR) attracts attention in several kind of cancers including colorectal cancer. Recently, miR-125b was reported as miR which inhibits p53 translation in non-cancerous tissues (Genes Development 2009). To clarify the clinical relationship of miR-125b and p53 in cancer tissues, we examined the expression levels of miR-125b in clinical colorectal cancer samples. Methods. We performed taqman RT-PCR using a miR-125b specific primer in 89 colorectal cancer (T) and adjacent non-cancerous tissues (N), and examined the relationship of miR-125b expression and clinical significance including clinicopathological factors and prognosis. Next, we examined whether miR-125b expression is inversely proportional to the intensity of p53 immunoblots in colorectal cancer cell lines. Results. miR-125b expression levels in T (1.29 ± 1.755; mean ± s.d.) were significantly lower than in N (1.96 ± 1.59; p = 0.0086). With regard to overall survival, patients in the high miR-125b expression group (n = 45) had a significantly poorer prognosis than those in the low miR-125b expression group (n = 44) (five years survival rates; 58% vs 81%, p=0.0229). Clinicopathological factors differed significantly in the high miR-125b expression group. There was more deeper depth of tumor invasion (p = 0.037) than in the low miR-125b expression group. Multivariate analysis revealed that the high expression level of miR-125b in colorectal cancer tissue was an independent prognostic factor (p = 0.0265). The intensity of p53 immunoblots was weak in miR-125b overexpressing colon cancer cell lines. Conclusions. High expression level of miR-125 which targets p53 translation in colorectal cancer is a candidate promising prognosis marker, and it is suggested that miR-125b expression plays an important roles in colorectal cancer development.

P112

Prophylactic total gastrectomy for hereditary diffuse gastric cancer: surgical and pathological results P.K. Pandalai,[1]* D. Patel,[4] D.C. Chung,[2] G.Y. Lauwers,[3] S.S. Yoon.[5] *1. Department of Surgery Massachusetts General Hospital, Boston, MA; 2. Department of Medicine Massachusetts General Hospital, Boston, MA; 3. Department of Pathology Massachusetts General Hospital, Boston, MA; 4. Center for Risk Analysis Massachusetts General Hospital, Boston, MA; 5. Division of Endocrine and Oncologic Surgery Hospital of the University of Pennsylvania, Philadelphia, PA.*

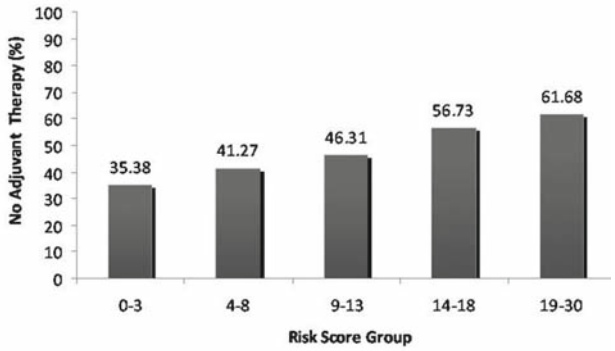
Introduction: Germline mutation of the CDH1 gene, which encodes for the E-cadherin adhesion protein, is rare, but confers a lifetime risk of hereditary diffuse gastric cancer (HDGC) of 67-83%. Endoscopy often fails to reliably detect early intramucosal signet-ring cell carcinoma characteristic of HDGC, and prophylactic total gastrectomy (PTG) has been advocated. Methods: Data were collected prospectively on 10 consecutive patients (pts) with CDH1 mutation undergoing PTG by one surgeon, which represents the world's largest single surgeon experience. Results: Ten pts (6 male, 4 female) were from 6 families and had a median age of 42 years (26-51 years). All pts had a strong family history of diffuse gastric cancer and tested positive for CDH1 gene mutation (4 missense, 1 frameshift, and 1 splice site). Median time from genetic testing to surgery was 3 months (1-7 months). All pts had an upper endoscopy or chromoendoscopy prior to surgery, with only one patient identified as having a focus of diffuse gastric cancer. All pts underwent a PTG with Roux-en-Y esophagojejunostomy. Median operating time was 213 minutes (187-308 minutes), no patient required blood transfusion, and length of stay was 7-8 days. One patient had an early postoperative complication (pulmonary embolism), and 3 pts had late complications (2 small bowel obstructions and 1 anastomotic stricture requiring dilation). Microscopic pathological analysis was performed on the entire gastric mucosa which required up to 490 sections. Only 1 patient had unremarkable pathology. Nine pts had 1-77 foci of noninvasive cancer, and 2 of these pts had 4-12 foci of T1 invasive cancer. For the 9 pts with at least 6 months follow-up, the median weight loss was 23% Conclusions: The majority of pts with germline CDH1 mutation have foci of noninvasive or invasive gastric cancer by middle age. Serial endoscopy provides inadequate screening, and PTG is the procedure of choice for definitive treatment. PTG can be performed safely by experienced surgeons, and long-term sequelae can be managed with multidisciplinary care.

P113

Adjuvant therapy for resectable pancreatic cancer: a simple prediction rule J.K. Smith,* S.C. Ng, J.P. Simons, Z. Zhou, S.A. Shah, T.P. McDade, J.F. Tseng. *Surgical Outcomes Analysis & Research, University of Massachusetts Medical School, Worcester, MA.*

Introduction: Adjuvant therapy benefits patients with resectable pancreatic cancer, but a substantial proportion of patients do not receive timely or complete adjuvant treatment. The objective of this study is to develop a simple prediction rule to identify patients less likely to receive adjuvant therapy, so that they have potential to be referred for neoadjuvant treatment or other optimization of care. Methods: Medicare-eligible patients ^ 65 years of age at time of pancreatic cancer diagnosis who underwent resection were identified from the SEER-Medicare linked database, 1991-2007. Primary outcome was receipt of adjuvant chemotherapy with or without radiation. Logistic regression and bootstrap methods were used to create a score for estimating likelihood of receiving adjuvant therapy; predictors included patient, procedure, and hospital characteristics. The prediction rule was derived with a randomly selected 80% of the cohort; the remaining 20% was used to validate the rule. Results: Among the total 3023 patients who underwent surgical resection for pancreatic cancer, only 1544 (51.1%) received adjuvant therapy. Median survival was improved for patients who received either neoadjuvant (18.2 months) or adjuvant therapy (16.3 months) compared to those who underwent resection only (10.3 months; p <0.0001). For the purposes of developing the prediction rule, patients who had already received neoadjuvant therapy (5.5% of all resected patients) were excluded. Factors included in the model were patient age, sex, Charlson comorbidity score, procedure type, and hospital teaching status. The prediction rule discriminated with a c-statistic of 0.61 and 0.62 in the derivation and the validation sets, respectively. Conclusions: We have generated a readily usable prediction rule to preoperatively calculate the probability that a patient who is able to undergo surgical resection for pancreatic cancer will go on to complete guideline-directed care with adjuvant therapy. The score can be calculated by hand or using a web-based calculator (example: www.umassmed.edu/surgery/soar/adjuvantprediction.aspx). This rule may be used to determine the optimal treatment strategy for individual patients.

Risk score calculation		Points
Age group	65-69	0
	70-74	7
	≥ 75	16
Charlson comorbidity score	0	0
	1-2	1
	≥ 3	9
Sex	Male	0
	Female	1
Planned procedure type	Distal/NOS	0
	Proximal	1
Hospital type	Teaching	0
	Non-teaching	3



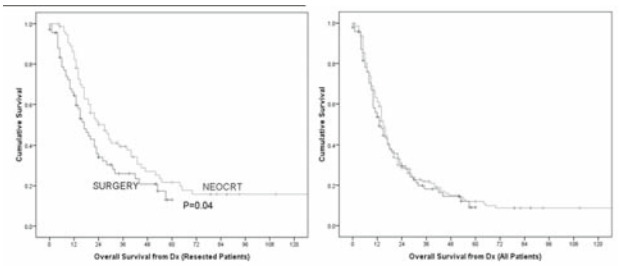
Risk score calculation for risk of not receiving adjuvant therapy following pancreatic cancer resection (available at: www.umassmed.edu/surgery/soar/adjuvantprediction.aspx)

P114

Does neoadjuvant therapy improve survival in patients with resectable pancreatic cancer? K.T. Papalezova,* V.M. Kim, S.S. Stinnett, D.G. Blazer III, B.M. Clary, T.N. Pappas, D.S. Tyler, R.R. White. *Surgical Oncology, DUMC, Durham, NC.*

Introduction: Retrospective series show pancreatic cancer pts who undergo resection after neoadjuvant chemoradiation therapy (NEOCRT) live longer than pts who undergo resection without NEOCRT, a difference that may be attributable to patient selection. Our goal was to compare survival between all pts with resectable disease who underwent NEOCRT or surgical exploration with "intent to resect". Methods: We retrospectively identified 237 pts with pancreatic head adenocarcinoma seen between 1999-2007 with enough data to be confirmed medically and radiographically resectable by NCCN criteria. Results: Ninety-three pts (39%) proceeded directly to exploration (SURGERY) due to lack of tissue diagnosis or patient/surgeon preference, and 144 pts (61%) initiated NEOCRT. The groups were similar in age and tumor size on imaging, but the NEOCRT group was more likely to have venous abutment (47 vs. 25%, p<0.01) and trended toward having a higher Charlson comorbidity index (p=0.09). In the NEOCRT group, 76 pts (53%) underwent resection, 29 (20%) had metastatic and 16 (11%) locally unresectable disease after NEOCRT, and 23 (16%) were not explored due to performance status or loss to follow-up. In the SURGERY group, 68 pts (73%) underwent resection (of whom 66% received adjuvant therapy), 17 (18%) had metastatic and 8 (9%) locally unresectable disease. In resected patients, the NEOCRT group had smaller path tumor size and lower incidence of positive lymph nodes than the SURGERY group but no difference in positive margins or need for vascular resection. Median follow-up in surviving pts was 30 mos. from diagnosis. Median over-

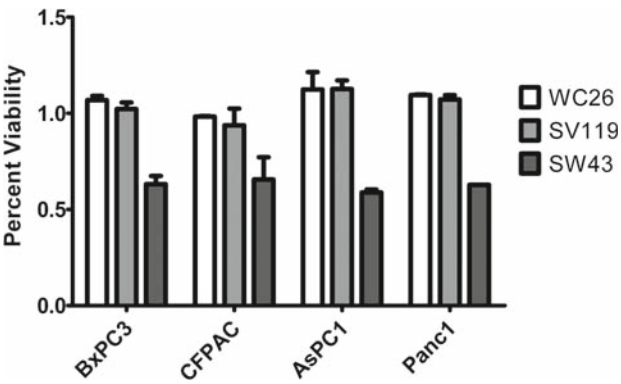
all survival (OS) in resected pts was 27 mos. in the NEOCRT group and 17 mos. in the SURGERY group (p=0.04, Figure left). Median OS in all pts was 15 and 13 mos., respectively, with superimposable survival curves (Figure right). Conclusions: Despite a lower resection rate, the NEOCRT group had similar survival to the SURGERY group, suggesting that NEOCRT allows better patient selection for resection. To demonstrate an effect on survival, a randomized trial is necessary to control for differences in patient/tumor characteristics that influence the decision to offer NEOCRT.



P115

The Novel Sigma-2 Receptor Ligand SW43 Induces Apoptosis in Pancreas Cancer J.R. Hornick,* D. Spitzer, P.S. Goedegebuure, R.H. Mach, W.G. Hawkins. *Washington University School of Medicine, St Louis, MO.*

Introduction: Pancreas cancer is an aggressive disease and effective treatment options are limited. We have previously shown that sigma-2 selective ligands preferentially bind to pancreas cancers and induce apoptosis with limited systemic toxicity. In order to indentify the best candidates for a clinical study we created and tested several derivatives of these ligands and identified a candidate compound (SW43) which has superior apoptotic activity. Methods: The human pancreas cancer cell lines CFPAC, BxPC3, AsPC1, and Panc1 were treated with 50uM of the sigma-2 receptor ligands WC26, SV119, SW43, or vehicle control. Cell viability was determined following a four hour treatment by cell density with crystal violet staining and CellTiter-Glo® Luminescent Cell Viability Assay (Promega). To examine apoptosis, cell lines BxPC3, CFPAC, and mouse pancreas cancer PanO2 were treated with 25uM ligand. Caspase-3 activity was screened by cleavage of Z-DEVD-AMC. Results: At this low dose and short time interval, viability had not significantly decreased for WC26 or SV119 while those treated with SW43 demonstrated a significant reduction in tumor viability, Figure 1 ($p<0.0001$ ANOVA). Viability expressed as a percent relative to vehicle control. Cell density was determined and is expressed as a percentage of density in the absence of treatment. Cell densities ranged from 86 to 107% after WC26 and 80 to 95% after SV119 treatment while cell density ranged from 36 to 57% after a single dose of SW43 treatment ($p<0.0001$). Caspase-3 activity was increased after SW43 compared to WC26 or SV119 treatment ($p=0.05$). Conclusions: SW43 is a more potent inducer of apoptosis in pancreas cancer cell lines when compared with other selective S2-ligands. We are currently testing the in vivo efficacy and toxicity profile of SW43 to see if this new S2-ligand has potential as a novel chemotherapeutic for the treatment of pancreas cancer.



P116

Irreversible Electroporation of the Liver and Liver Hilum in Swine K.P. Charpentier,* F. Wolf, M. Resnick, L. Noble, B. Winn, D. Dupuy. *Warren Alpert Medical School at Brown University, Providence, RI.*

Introduction: Thermal ablation by radiofrequency or microwave is an established therapy for selected patients with liver tumors. Limitations of thermal ablation include damage to adjacent structures and heat sink. Irreversible electroporation (IRE) is a novel, non-thermal form of tissue ablation which utilizes short pulses of high frequency electrical energy to kill cells. We undertook a study to compare intra-hepatic IRE with IRE of the liver hilum and to determine the ability of tetrazolium vital staining to predict the zone of ablation. Methods: Eight swine underwent 20 ablations of the liver and liver hilum with IRE. Treatment location and parameters are as shown in table 1. Monopolar probes were placed 2 cm apart. IRE treatments were performed 15 minutes (n=4), 30 minutes (n=4), 1 hour (n=4), 2 hours (n=4), 2 days (n=2) and 14 days (n=2) prior to sacrifice. The liver and porta hepatis were recovered. Tissue was analyzed grossly and by H+E and tetrazolium vital staining. Results: All animals survived. No major complications were encountered. Ablation zones were determined by H+E and tetrazolium staining (table). Tetrazolium staining accurately demonstrated the zone of ablation in all groups including animals sacrificed 15 minutes after ablation. Average ablation zone size is larger in the liver hilum compared to intra-hepatic ablations using the same treatment parameters. Hepatocyte necrosis occurs immediately adjacent to large central veins within the ablation zone. Large portal structures in the ablation zone are more resistant to the effects of IRE than surrounding hepatocytes. Conclusions: IRE is a novel ablation technique that can safely create predictable ablation zones in liver tissue. Our results suggest that IRE is not limited by heat sink and can produce cell necrosis immediately adjacent to large venous structures. Portal structures appear more resistant to the effects of IRE allowing ablations to be performed safely adjacent to these structures. Tetrazolium staining predicts the zone of IRE ablation as early as 15 minutes following treatment.

IRE ablation parameters and results

Location	N	Exposure	Voltage	Reverse polarity	Ablation Zone(cm)
Intra-hepatic	9	2.5cm	2,500	yes	2.95 +/- 0.31 x 1.5 +/- 0.44
Intra-hepatic	3	2.5cm	3,000	no	2.27 +/- 0.23 x 1.5 +/- 0.2
Intra-hepatic	4	2cm	3,000	yes	3.25 +/- 0.35 x 1.45 +/- 0.21
Liver hilum	4	2cm	3,000	yes	4.45 +/- 0.07 x 1.8 +/- 0

P117

Prospective Whole Mount Analysis of Rectal Cancer Following Combined Modality Therapy: Long-Term Oncologic Outcome J.J. Mezhir,* J.G. Guillem, J. Shia, E. Riedel, L.K. Temple, G.M. Nash, M.R. Weiser, P.B. Paty, W.D. Wong. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction It has been demonstrated that there is minimal residual disease distal to the gross tumor margin following preoperative combined modality therapy (CMT) for rectal cancer. Although this suggests that close resection margins are acceptable for sphincter preservation, the long-term oncologic impact is unclear. Using a comprehensive whole mount pathologic analysis, our aim is to determine the impact of resection margins on long-term oncologic outcome following CMT. **Methods** We prospectively enrolled 113 patients with EUS-staged locally advanced rectal cancer (T2-4 and or N1) following CMT and total mesorectal excision from 3/00 to 10/04. Pathologic analysis using whole-mount sectioning was performed and clinicopathologic variables were correlated with disease-specific survival (DSS). **Results** Tumors were located at a median of 7cm from the anal verge and sphincter preservation was performed in 80% of patients. Median distal margin of resection was 2cm and all distal margins were negative; 23 patients (20%) had distal margins ≤1cm. Median radial margin clearance was 1cm and six patients (5%) had a positive radial margin (defined as ≤1mm). Viable distal intramural tumor spread was found in 3 patients (2.7%) and in each instance was ≤ 1cm from the gross tumor edge. At a median follow-up of 68 months, 5-year actual DSS was 87% and 1 patient (0.9%) experienced a local recurrence (**Table**). Factors associated with worse DSS on univariate analysis included advanced T and N stage, mucinous tumors, and neurovascular invasion. Sphincter preservation did not

affect DSS. As continuous variables, tumor distance from the anal verge and the length of the circumferential and distal margins of resection were not associated with worse DSS. **Conclusions** The vast majority of patients with locally advanced rectal cancer in this study had no microscopic disease distal to the gross tumor edge following CMT. The length of distal resection margin was not associated with local recurrence or DSS, suggesting that patients may undergo sphincter preservation after CMT without compromising local control or long-term outcome.

Pathological Variables and Impact on Disease Specific Survival (DSS)

Categorical Variables(1)	(N, %)	5-year DSS(%) (95% CI)	p
All patients	113	87 (78 - 92)	-
Operation Low Anterior Resection Abdominoperineal resection	90 (80) 23 (20	90 (81 - 95) 76 (51 - 89)	NS
Pathologic Stage 0 I II III IV	18 (16) 29 (26) 27 (24) 29 (26) 10 (9)	100 100 86 (62 - 95) 79 (56 - 91) 50 (18 - 75)	**0.0008**
Mucinous Tumor No Yes	98 (87) 15 (13)	91 (82 - 95) 60 (28 - 81)	**0.02**
Neural or Vascular Invasion Absent Present	89 (79) 24 (21)	90 (80 - 95) 77 (80 - 95)	**0.02**
Continous Variables (2)	**Median (range)**	**5-year DSS (%) (95% CI)**	**p**
Distance from anal verge (cm)	7 (0 - 13)	-	NS
Radial margin (cm)	1 (0.1 - 2.8)	-	NS
Distal margin (cm)	2 (0.1 - 10)	-	NS

(1)-Log-rank test (2)-Cox proportional hazard regression

P118

Laparoscopic Liver Resection for Cirrhotic Patients with Hepatocellular Cancer: An Early Experience F. Alemi,* C. Freise, S. Kang, R. Hirose, J. Roberts, L. Stewart, C.U. Corvera. *University of California, San Francisco, San Francisco, CA.*

BACKGROUND: Surgical treatment of hepatocellular cancer (HCC) is challenging because most patients also suffer from underlying liver disease which limits the extent of resection. The ability to complete a resection laparoscopically offers these patients the well-established benefits of minimally invasive surgery. Here, we report our experience with laparoscopic liver resections in cirrhotic patients with HCC. METHODS: A retrospective review of a prospectively maintained database at a University setting identified cirrhotic patients who underwent laparoscopic liver resection. Outcome measures including patient characteristics, procedure type, operative time, blood loss, hospital stay, and complications were analyzed. RESULTS: 28 patients with HCC and severe but well-compensated cirrhosis were treated between September 2003 and June 2009. Mean age was 61 (range 37-81). There were 2 right hepatectomies, 8 left lobectomies, and 21 segmentectomies; 13 were anatomic resections. Three patients underwent multiple procedures during the same operation. Totally laparoscopic resections were carried out in 17 patients, 6 were hand-assisted, and 5 converted to limited laparotomy. Mean tumor size was 4.0 cm (range 1.2-9.5 cm). Median operative time was 317 minutes (range 131-915 mins), and median blood loss was 200 mL (range 20-3000 mL). Median hospital stay was 7 days (range 3-46). There were no deaths. Morbidities occurred in two patients: one developed hepatorenal syndrome not requiring hemodialysis, and the other developed renal insufficiency requiring long-term hemodialysis. Three patients developed minor wound complications. CONCLUSION: While the majority of hepatic resections continue to be done open, the laparoscopic approach is appealing in select patients with underlying chronic liver disease. Laparoscopic resection in this high-risk group can be done safely with an acceptable complication rate. The advantage of limited incisions in this high-risk group for wound complications is an important reason to consider a laparoscopic approach. Further data is necessary to determine if this approach should become the new standard of practice for this patient population.

P119

Is lymph node dissection with high ligation always necessary for right colon cancer? H. Kobayashi,* T. Higuchi, M. Enomoto, M. Yasuno, H. Uetake, S. Iida, T. Yoshimura, T. Ishikawa, M. Ishiguro, K. Sugihara. *Department of Surgical Oncology, Tokyo Medical and Dental University, Tokyo, Japan.*

INTRODUCTION: Lymph node dissection (LND) with high ligation is a standard technique for advanced right colon cancer in Japan. However, high ligation of the supplying arteries and draining veins for right colon cancer is sometimes complicated because of a variety of vascular branch. The aim of this study was to clarify the usefulness of LND with high ligation for right colon cancer. METHODS: We enrolled 1097 patients with curative resection for colorectal cancer at a single institution between 1991 and 2005. Among them, 197 patients underwent curative resection for T2-T4 right colon cancer. All patients received LND with high ligation. We evaluated the oncologic outcomes according to the distribution of lymph node metastasis (LNM). The distribution of LNM was classified as follows: n0, no LNM; n1, LNM adjacent to the colon or along the vascular arcades of marginal arteries; n2, LNM along the major vessels; n3, LNM near the root of the major vessels. RESULTS: The rates of LNM were 11.1%, 38.6%, and 58.0% in T2, T3, and T4 right colon cancer, respectively ($p<0.0001$). Among various parameters, depth of tumor invasion ($p<0.0001$), histologic type ($p = 0.0049$), lymphatic invasion ($p<0.0001$), and venous invasion ($p = 0.0038$) were risk factors for LNM in univariate analysis. Among these, T4 cancer ($p = 0.017$) and lymphatic invasion ($p = 0.0020$) were independent risk factors by multivariate analysis. Recurrence rates were 27.3%, 37.5%, and 57.1% in patients with n1, n2, and n3 LNM, respectively ($p<0.0001$). The distribution of LNM was associated with recurrence in T3 ($p = 0.0023$) and T4 ($p = 0.0013$) cancer. There was no n3 LNM in patients with T2 right colon cancer. The 5-year overall survival rates were 95.2%, 86.3%, and 65.0% in patients with stage I (T2), stage II, and stage III cancer ($p = 0.0055$) CONCLUSIONS: Among the patients with n3 LNM, 43% did not develop recurrence. LND with high ligation benefits some of the patients with extended LNM. The patients with T3-T4 right colon cancer are suitable candidates for LND with high ligation. However, those with T2 cancer may not need high ligation. A large-scale study will be necessary to clarify these issues.

P120

Functional outcome and Stricture rates with the use of circular stapler for esophagogastric anastomosis after esophagectomy G. Pines,[1]* I. Sifrony,[3] E. Melzer,[2] Y. Klein,[1] S. Machlenkin,[1] V. Buyeviz,[1] H. Kashtan.[1] *1. Surgery B, Kaplan Medical Center, Rehovot, Israel; 2. Kaplan Medical Center, Rehovot, Israel; 3. Hebrew University School of Medicine, Jerusalem, Israel.*

Introduction: Stapled esophagogastric anastomosis after esophagectomy is considered to be superior to traditional hand-sewn techniques. Is this study we compared the functional outcome and long term results of the use of circular staplers. Methods: Records of all patients who underwent esophagectomy between 2003-2008 were reviewed. Patients who underwent either colon transposition or linear stapler anastomosis were excluded. Esophagogastric anastomosis was done either hand-sewn or using a circular stapler. Benign anastomotic stricture was defined as a stenosis necessitating dilatation. Patients were interviewed regarding several foregut symptoms and eating habits. Results: 85 patients met the inclusion criteria. Median follow-up was 20 months. In 31 patients the anastomosis was hand-sewn and 54 patients had a stapled anastomosis. Anastomotic stricture occurred in 6 (19.3%) patients in the hand-sewn group and 7 (12.9%) patients in the stapler group. All 13 patients who had an anastomotic stricture had a cervical anastomosis. 31% (4/13) of patients who had anastomotic leakage developed a stricture, compared to 12% (9/72) of those who did not leak (NS). A stricture developed in 23% of patients who had a locally advanced disease compared to 9% who had an early disease (NS). All patients were treated successfully with dilations alone. Several risk factors were associated with stricture development, regardless of anastomotic technique: male gender, cervical anastomosis, anastomotic leak and locally advanced disease. 38 patients answered the questionnaire. Patients consumed a median of 4 (2-10) meals per day, most of them (n=24, 63%) had

no dietary restrictions. Meal size was reported to be smaller in all patients compared to pre-operative state. Mean symptom severity scores improved for all symptoms except regurgitation and choking (figure 1). Conclusion: Esophagogastric anastomosis using circular staplers is feasible and safe with acceptable morbidity. The use of circular stapler for anastomosis has comparable outcomes to hand-sewn anastomosis in regards of anastomotic stricture rates and functional outcome.

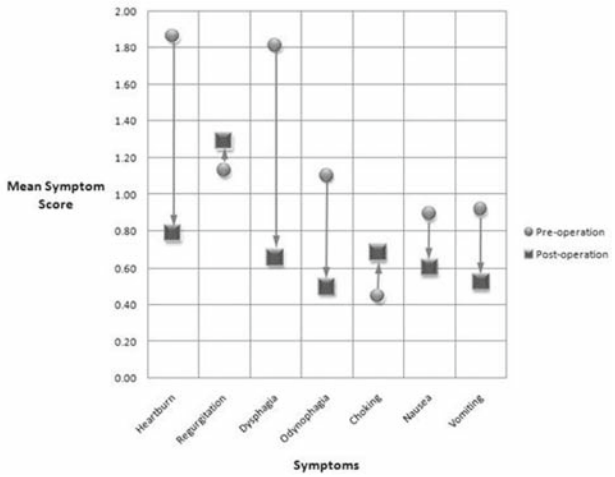


Figure 1. Pre to post-operative mean symptom scores

P121

Role of Fecal Diversion for Low Rectal Cancer Resection
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Background:Fecal diversion at the time of resection for rectal cancer has been an area of controversy. While the morbidity of anastomotic dehiscence may be mitigated by a defunctioning stoma, it is unclear if it is required for the majority of lower rectal anastomosis. Preoperative risk factors leading to anastomotic complications and indications for fecal diversion have yet to be clearly defined Methods:Using the American College of Surgeons-National Surgical Quality Improvement Project's (ACS-NSQIP) participant-use file, patients were identified who underwent low rectal resection with anastomosis for cancer at the 240 participating hospitals in 2005 - 2008. Demographic, clinical, and intraoperative variables and 30-day morbidity and mortality were collected. Patients were excluded if they underwent laparoscopic resection or emergent procedure Results:We identified a total of 1791 patients that underwent low rectal cancer resection. These patients were subdivided into 2 groups based on the level of the anastomosis. 1266 patients had a low pelvic anastomosis (LPA) and 525 patients had a coloanal anastomosis (CAA). In the LPA group, 606 patients had an ostomy and 660 had no ostomy performed. There were no differences noted in age, comorbidities and ASA class. There were no significant differences in wound complications, sepsis or septic shock. In the CAA group, 352 had an ostomy and 173 had no ostomy performed. There was no difference in age, sex, comorbidities and ASA class. There were no differences in wound complications, but in patients without fecal diversion, there was a significantly greater incidence of sepsis (8.6% vs 3.7%, p=0.023, OR 2.47), septic shock (3.4% vs 0.56%, p= 0.018, OR 6.29) and need for re-operation (11% vs 1.7%, p=0.0001, OR 7.15) Conclusion:Fecal diversion after low anterior resection for rectal cancer seems to provide no extra benefit outside a very low (coloanal) anastomosis, and may be associated with an increased cost and morbidity. While a defunctioning stoma in the setting of a coloanal anastomosis seems to be protective from post-op sepsis, septic shock and need for re-operation, it is likely overused in rectal cancer surgery and should be avoided in low risk patients

P122

Double Contrast-Enhanced Ultrasonography for the Preoperative Evaluation of Gastric Cancer: A Comparison to Endoscopic Ultrasonography with Respect to Histopathology
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Background: The purpose of this study was to compare the accuracy of endoscopic ultrasound (EUS) with double contrast enhanced ultrasound (DCUS) in the preoperative staging of gastric malignancies. DCUS is a transabdominal ultrasound technique utilizing both intravenous and intraluminal contrast to enhance sonographic visualization. Methods: This retrospective study included 162 patients with biopsy proven gastric cancer who underwent surgical resection as primary management of their malignancies. All patients underwent DCUS and EUS prior to surgical intervention with the results of the ultrasound findings compared with the pathological stages of the resected specimens. Results: Among the 162 gastric cancer patients, there were 42 cases of T1, 49 cases of T2, 56 cases of T3, and 15 cases of T4 tumors. The overall accuracy of DCUS and EUS for the determination of loco-regional tumor infiltration (T Staging) was 77.2% vs 74.7%. Comparison of ultrasound techniques revealed that DCUS was superior to EUS only for a tumor depth of T3 ($\chi 2$, p=0.025). Lymph nodes were correctly staged with DCUS and EUS in 78.4% and 57.4% of cases, respectively ($\chi 2$, p= 0.001). Using DCUS, the sensitivity of the technique was 78.4% with a specificity of 78.5%. In comparison, EUS had a sensitivity of 49.5% with a specificity of 69.2%. DCUS also detected a higher incidence of poorly differentiated (81.5% vs 42.6%) and signet ring cell type tumors (66.7% vs 44.4%). Conclusions: Double contrast-enhanced ultrasonography offers another noninvasive approach for the preoperative evaluation of gastric cancer. DCUS was comparable to EUS in tumor depth evaluation. DCUS offers an advantage in the detection of lymph node metastases, especially in poorly differentiated tumors. Based on our experience, it can be a valuable adjunct in the workup of patients with gastric cancer.

P123

Major Hepatic Resection for Hilar Cholangiocarcinoma (HC) – Has long-term survival changed?
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INTRODUCTION: Major hepatic resection, bile duct resection, and regional lymphadenectomy for HC are widely accepted as the preferred treatment for HC, although 5-year survival only approaches 30%. We updated our experience with HC to identify clinical and pathologic features associated with patient outcome and to determine if outcome has improved over time. METHODS: 84 consecutive patients underwent this surgical approach for HC between 1979 and 2006. Multivariable models to predict death and recurrence were constructed. RESULTS: Left and right hepatectomy was undertaken in 47 (56%) and 37 (44%) patients. Segment I was resected in 51%. R0 resection was achieved in 87%. Operative mortality was 11%. Overall morbidity was 64%, with 35% Clavien grade I/II and 29% Clavien grade III/IV. Median survival was 2.6 years with 1-, 3-, and 5-year survival rates of 81%, 43%, and 30%. Factors associated with death on univariate analysis were: male sex (p=0.03), positive margin (p=0.03), high tumor grade (p=0.05), increased tumor size (p=0.01), degree of cholestasis (p=0.006), and red blood cell transfusion (p<0.001). On multivariable analysis only red blood cell transfusion (p<0.001), tumor size (p<0.001), and lymph node metastases (p=0.028) were associated with death. HC recurred in 37 of 70 patients and were primarily loco-regional (62%). Median recurrence-free survival was 3.7 years. Factors associated with recurrence on univariate analysis were: hepatitis (p=0.04), positive margin (p=0.03), high tumor grade (p=0.02), and increased tumor size (p=0.04). On multivariable analysis only tumor grade (p=0.01) and size (p=0.02) were associated with recurrence. Neither caudate lobe resection nor adjuvant chemotherapy was significantly associated with patient outcome. No significant improvement in overall and recurrence-free survival was observed when comparing 46 patients operated during 1979-1997 to 38 patients operated during 1998-2006. CONCLUSION: 5-year survival of 30% supports major hepatic resection, bile duct resection, and lymphadenectomy for treatment of HC. Lack of improved survival over time further emphasizes the need for effective adjuvant therapy.

P124

Meta-analysis of Trials Comparing Minimally-invasive and Open Liver Resections for Hepatocellular Carcinoma A. Fancellu,[1]* A. Rosman,[2] V. Sanna,[3] G.R. Nigri,[4] L. Zorcolo,[5] M. Pisano,[6] M. Melis.[7] *1. Department of Surgery - Institute of Clinica Chirurgica, University of Sassari, Sassari, SS, Italy; 2. Section of Gastroenterology and Medicine Program, Mount Sinai School of Medicine and Bronx VAMC, New York, NY; 3. Department of Oncology, Azienda ASL n.1 Sassari, Sassari, SS, Italy; 4. Department of Surgery, Sapienza University of Rome, Roma, RM, Italy; 5. Department of Surgery, University of Cagliari, Cagliari, CA, Italy; 6. Department of Surgery, Ospedali Riuniti di Bergamo, Bergamo, BG, Italy; 7. Division of Surgical Oncology, New York University School of Medicine and NYHHS VAMC, New York, NY.*

Background: Recent literature suggests that minimally-invasive hepatectomy (MIH) for hepatocellular carcinoma (HCC) is associated with faster post-operative recovery and decreased morbidity compared to open hepatectomy (OH). However, previous reports have been limited by small sample size and single-institution design. To overcome these limitations, we performed a meta-analysis of studies comparing MIH and OH for HCC. Methods: A systematic literature review was conducted to analyze studies comparing MIH and OH. Variables were pooled only if evaluated by 3 or more studies. Both qualitative and quantitative data were pooled using a random-effects model. Endpoints included post-operative overall morbidity and mortality, blood loss, rate of transfusion, operative time, resection margins, and length of hospital stay. Results: Six studies comparing MIH and OH were considered suitable for the meta-analysis; the reports were primarily retrospective studies of comparable patients. A total of 159 patients underwent MIH and 294 had OH. Patients in the two groups were similar with respect to age, sex, rates of cirrhosis, hepatitis C infection, and tumour size. The MIH group had lower rates of hepatitis B infection than the OH group (odds ratio [OR]=0.38, 95% CI 0.19–0.74). There were no differences in type of resection performed (anatomic resection of one or more segments, or non-anatomic), use of the Pringle manoeuvre, operative time (194 vs. 185 min). The rate of positive margins was lower for the MIH group (OR=0.31, 95% CI 0.11–0.83). Patients undergoing MIH had less blood loss (difference 193 ml, 95% CI 75–311) and lower rate of transfusion (OR=0.33, 95% CI 0.20–0.57). Hospital stay was lower for MIH but the difference just missed statistical significance (-5.1 days, 95% CI -10.8–0.5, p 0.08). Peri-operative complications (OR=0.48, 95% CI 0.31–0.75) and 30-day mortality (OR=0.35, 95% CI 0.12–0.99) were reduced in MIH. Most studies reported similar survival and recurrence rates. Conclusions: Our meta-analysis indicates that MIH for HCC is feasible, safe and associated with reduced blood losses, transfusions, complications, and mortality when compared to OH.

P125

IPMN- Associated Cancers, Family History; Genetic Predisposition? N. Lubezky,[1]* M. Ben-Haim,[1] R. Nackache,[1] E. Brazowski,[2] I. Solar,[2] J.M. Klausner.[1] *1. Department General Surgery B, Tel-Aviv Medical Center, Tel-Aviv, Israel; 2. Institute of Pathology, Tel-Aviv Medical Center, Tel-Aviv, Israel.*

Background: Increased rates of extrapancreatic malignancies (EPM) in patients with Intraductal Papillary Mucinous Neoplasm (IPMN) of the pancreas are recently reported. Occurrence of IPMN in patients with familial history of pancreatic cancer, and in a patient with Hereditary Nonpolyposis Colon Cancer syndrome (HNPCC) has also been reported. Materials and Methods: Retrospective analysis of a prospectively collected database of 73 patients with histologically proved IPMN. Direct contact of all patients or relatives to obtain personal and familial cancer history. Comparison with a cohort of 120 patients operated for pancreatic ductal adenocarcinoma (PDAC). Evaluation of the common germline mutations in the BRCA 1 and 2 genes in available patients. Results: Rate of EPM in patients with IPMN was higher than in patients with PDAC (17% vs. 6.8%, P=0.04). Malignancies in first degree relatives were more common among patients with IPMN than patients with PDAC (56% vs. 40.6%, P=0.048). Patients with IPMN who had additional EPM, had a higher rate of first degree relatives with cancer compared with patients without EPM (84% vs. 36%, P=0.0015). This was most evident regarding colorectal cancer in first degree family members (38% vs. 3%, P=0.0015). 2 patients, both with family history of pancreatic cancer, were tested positive for the BRCA2 gene mutation (5% of tested patients, 8% of tested Ashkenazi patients, 33% of tested patients with family history of pancreatic cancer). One patient fulfilled all Amsterdam criteria for HNPCC. Conclusions: Patients with IPMN have an increased risk of EPM, and a high rate of family members with cancer, compared to patients with PDAC. Screening patients with IPMN and a personal or familial history of pancreatic or breast cancer for the BRCA 2 gene mutations is appropriate. Patients with IPMN and EPM have a high rate of malignancies in first degree relatives, especially colorectal cancer. This, and the fact that IPMN is found in patients with HNPCC, point to a possible role of the mismatch repair (MMR) genes in IPMN pathogenesis. Further studies are necessary to determine the role of BRCA 2, MMR genes and other genetic changes in the development of IPMN.

P126

Prospective Trial of Diagnostic Peritoneal Lavage to Detect Positive Peritoneal Cytology in Patients with Advanced Gastric Cancer K.K. Roggin,* M.D. McKee, J.J. Mezhir, E. Galka, M.C. Posner. *Surgery, University of Chicago, Chicago, IL.*

Introduction: Positive peritoneal cytology is an independent predictor of poor outcome in patients with gastric cancer. Diagnostic peritoneal lavage (DPL) is a rapid, cost-effective, and safe test to detect occult visceral injury in trauma patients. We hypothesized that DPL could safely and accurately assess the peritoneal cytology status of patients with advanced gastric cancer. Methods: Patients with advanced gastric adenocarcinoma undergoing diagnostic laparoscopy (DL) were enrolled into this IRB-approved study. DPL was performed on anesthetized patients prior to DL. Normal saline was instilled through a percutaneously inserted DPL catheter and sample of the fluid was collected for cytology (Cyt-1). Additional peritoneal washings obtained during DL were used as controls. Results: Twenty-seven patients were enrolled from 1/2007-9/2009. The majority of cancers were located in the gastroesophageal junction or cardia (19/27); eight patients had antral tumors. The median time to complete the DPL procedure was 15 minutes (range 5-35). DPL was technically successful (>10% of the instilled saline retrieved) in 24/27 patients (89%); three patients had adhesions precluding percutaneous access. There were no immediate or late (30-day) complications related to the DPL. Among the 24 evaluable cases, 13 had positive peritoneal cytology (54%). Positive Cyt-1 specimens matched control cytology in all 12 cases (Table). One of 12 cases with negative Cyt-1 had rare atypical cells on the final cytology. DL identified nine patients with gross peritoneal disease (M1); only six of those cases (66%) had positive cytology samples. Conclusions: DPL appears to be a safe and simple method of detecting occult intraperitoneal metastases in patients with advanced gastric cancer. In this study, DPL did not detect all patients with M1 disease. Minimally invasive techniques to sample peritoneal cytology may reduce costs, streamline staging workups, and facilitate accurate stratification of patients entering clinical trials involving neoadjuvant chemotherapy.

Table. Significance of cytology obtained during DPL relative to controls.

Sensitivity	12/13 (92%)
Specificity	11/11 (100%)
Positive predictive value	12/12/ (100%)
Negative predictive value	11/12 (92%)
Accuracy	23/24 (96%)

P127

Single Institution Experience of 215 Patients Comparing Accuracy of Endoscopic Ultrasound with Subsequent Pancreatic Surgery C. Boutros,* E.. Genova, M. Haniff, N. Toubia, P. Somasundar, N.J. Espat. *Division of Surgical Oncology, Roger Williams Medical Center, Providence, RI.*

Introduction: No consensus has been reached between the accuracy of pancreatic endoscopic ultrasound (EUS) and subsequent surgery. We investigated the accuracy of EUS and analyze factors associated with subsequent pancreatic surgery. Methods: Using IRB approved prospectively maintained data base, all patients undergoing pancreatic EUS over 20 months in a single institution were reviewed. Demographics, pathological features, EUS diagnosis and FNA cytology results were assessed. In patients undergoing pancreatic surgery, final pathology was compared to EUS diagnosis. Results: 215 patients undergoing EUS for a presumed pancreatic lesion were included. EUS was aborted in 9 patients. In the 206 patients in whom EUS was completed, no pancreatic lesion was identified in 65(31.5%). These patients were younger (59.2±16 vs.

66.4±14.1, p<0.05) but have no difference in sex or BMI compared to other patients. In 93 patients, EUS revealed a cystic lesion (CL); FNA rate 45%. 12 patients with EUS identified CL (13%) received surgery; the size of the CL was larger in the surgical group (3.4 cm±1 vs. 2.1±1.7, p<0.05) compared to the non surgical CL group, however there was no difference in the age, sex, BMI or FNA rate between the two groups. In 48 patients EUS revealed pancreatic mass (PM); FNA rate 62%. 16 patients with EUS identified PM (33.3%) had surgery. These patients had higher FNA rate (75% vs. 31%, p<0.05) but had no difference in age, sex, BMI and mass size compared to the non surgical PM group. 28 patients (13.6%) underwent surgery. Compared to the non surgical group, surgical patients were older (69.8±12.4 vs. 63.3±15.3, p<0.05) but had no difference in sex, BMI, lesion size and FNA rate. Compared to the final pathology diagnosis, the accuracy of the EUS diagnosis was 74% with or without FNA. For surgical patients with final pathology revealing pancreatic cancer the sensitivity and specificity of EUS was 88.8% and 100%, respectively. Conclusion: Routine EUS can preclude surgery in 31% of presumed pancreatic lesions. Sex, BMI and mass size were not associated with a higher surgical rate. FNA did not affect the accuracy of EUS diagnosis.

P128

Lymph node ratio is inferior to pN-stage in predicting outcome in colon cancer patients with high numbers of analyzed lymph nodes
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Objective: The number of positive lymph nodes (LN) and the total number of analyzed LN are strongly correlated with survival in colon cancer. Recently, the lymph node ratio (LNR), i.e. the number of positive LN divided by the number of analyzed LN, has been described as a strong outcome predictor. However, most of the published analyses have been conducted on series with relatively low total numbers of analyzed LN. Therefore, the objective of the present study was to evaluate the prognostic impact of LNR in colon cancer patients with high numbers of analyzed LN. Methods: One hundred sixty-six colon cancer patients underwent open colon resections and standard LN dissection. The number of analyzed LN and the number of positive LN were prospectively recorded. Median follow-up was 33.5 months (range 5.6-74.7 months). All node-positive, stage III patients were analyzed for this study. Patients were categorized into high LNR vs. low LNR with the median LNR used as cut-off point. Results: Fifty-seven patients (34.3%) were node-positive. The median number of analyzed LN in these patients was 23 (range 8-54), and the median LNR was 0.13 (range 0.03-0.67). Forty-two (73.7%) of 57 stage III patients received adjuvant chemotherapy, and 16 (28.1%) recurred during follow-up. The recurrence rate was significantly higher in pN2 (10/20, 50.0%) than in pN1 patients (6/37, 16.2%; p=0.012). Similarly, a trend towards a higher recurrence rate was seen in the high LNR group (11/28, 39.3%) compared to the low LNR group (5/29, 17.2%; p=0.082). Median disease-free and overall survival was 24.4 months (range 5.6-74.7) and 28.7 months (range 0.1-74.7), respectively. Disease-free and overall survival was significantly shorter in pN2 patients compared to pN1 patients (p<0.001, and p=0.004, respectively). Similarly, patients with a high LNR had a significantly shorter disease-free survival (p=0.014) and a trend towards worse overall survival (p=0.103). Conclusions: LNR is a good outcome predictor in node-positive colon cancer patients. However, LNR is inferior to pN-stage in predicting recurrence and overall survival in patients with high numbers of analyzed LN.

P129

Do Physician Attitudes Influence Treatment Patterns for Pancreatic Cancer? A. McKay, J. Lipschitz, J. Woodmass.* *Surgery; Community Health Sciences, University of Manitoba, Winnipeg, MB, Canada.*

Introduction Surgery appears to be an underutilized treatment option for pancreatic cancer. Nihilistic physician attitudes may be partly responsible. The objectives were to analyze physician attitudes towards this disease and to determine treatment patterns including rates of surgical referral in the Province of Manitoba. Methods A survey was administered to 480 specialists and family physicians to examine physician attitudes towards pancreatic cancer. Data from the Provincial Cancer Registry and other administrative databases was used to assess the treatment patterns of all patients diagnosed with pancreatic cancer between 2004 and 2006. Results The survey response rate was 43%. The majority of survey respondents considered surgery to be worthwhile. Fewer family physicians (41%) stated that surgical resection can cure a patient of pancreatic cancer than did surgeons (77%) (P = 0.002). Nearly 75% of family physicians estimated the surgical mortality rate to exceed 5% and a third estimated it to be greater than 10%. 413 patients were diagnosed with pancreatic cancer during the study period (see Table 1). Of the 124 patients with early stage disease (Stage I or II), 85 did not receive any treatment. 33 of these 85 (39%) patients did not receive surgical consultation. On univariate analysis, the patients who did not receive surgical consultation were older (mean age 81 vs. 68; p = 0.0001), but actually had less comorbidities than those who did (p = 0.006). On multivariate analysis only older age remained a predictor of not getting surgical referral (OR = 5.6, 95% CI = 1.5 – 21). Conclusions Most physicians stated that surgery is worthwhile when feasible. However, a proportion of physicians continue to overestimate the mortality and underestimate the long-term survival benefit. Potentially resectable patients who were not referred to a surgeon tended to be older, but did not have more advanced comorbidity. Although advanced age may justly account for some patients who did not receive a referral, it is reasonable to assume that other factors such as nihilistic physician attitudes are preventing some patients from being at least offered surgery.

Table 1. Pancreatic cancer patient demographics and treatment patterns

Characteristic		Stage of Disease*		
		Early (n=124)	Late (n=252)	Unknown (n=37)
Treatment				
	Surgery	28 (23%)	3 (1.2%)	4 (11%)
	Other	11 (8.9%)	40 (16%)	0 (0%)
	No Treatment	85 (69%)	209 (83%)	33 (89%)
Gender				
	Male	69 (56%)	123 (49%)	18 (49%)
	Female	55 (44%)	129 (51%)	19 (51%)
Age				
	Under 65	36 (29%)	85 (34%)	4 (11%)
	65 and Over	88 (71%)	167 (66%)	33 (89%)
Charlson Comorbidity				
	2 or Less	71 (57%)	63 (25%)	23 (62%)
	3 or More	50 (40%)	181 (72%)	12 (32%)
	Missing	3 (2.4%)	8 (3.2%)	2 (5.4%)
Residence				
	Urban	80 (65%)	159 (63%)	23 (62%)
	Rural	43 (35%)	91 (36%)	13 (35%)
	Missing	1 (0.8%)	2 (0.8%)	1 (2.7%)

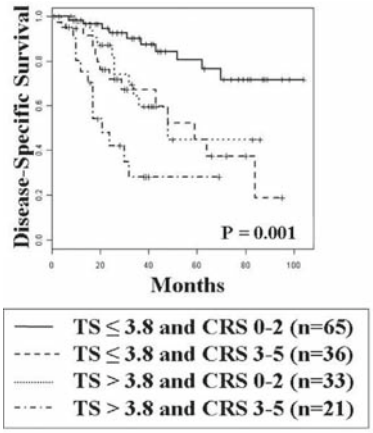
* Early Stage = AJCC Stage I and II
Late Stage = AJCC Stage III and IV

P130

Thymidylate Synthase Expression Improves Clinical Risk Score Prediction of Recurrence and Survival After Hepatic Resection of Metastatic Colorectal Cancer S.K. Maithel,[1]* M. Gonen,[2] H. Ito,[2] R.P. DeMatteo,[2] P.J. Allen,[2] Y. Fong,[2] L.H. Blumgart,[2] W.R. Jarnagin,[2] M.I. D'Angelica.[2] *1. Surgical Oncology, Emory University, Atlanta, GA; 2. Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Variation in tumor gene expression can predict resistance to chemotherapy in patients with hepatic colorectal cancer metastases. The prognostic relevance in patients treated with resection and modern chemotherapy is not known. Methods: Patients submitted to liver resection for metastatic colorectal cancer (mCRC) between 01/2000 and 10/07 and with adequate tissue for analysis were eligible. A clinical risk score (CRS, range 0-5) was calculated for each patient. RNA was extracted from H&E confirmed tumor isolates, and real-time PCR assessed quantitative expression of 12 genes with potential importance in chemotherapy resistance. They included thymidylate synthase (5-Fluorouracil), excision repair cross complementing gene-1 and xeroderma pigmentosum groups A-G (oxaliplatin), topoisomerase I (irinotecan), c-met, and hepatocyte growth

factor. Regression analysis assessed the association of gene expression with recurrence-free survival (RFS) and disease-specific survival (DSS) from the time of hepatic resection. Results: 155 patients with good quality tumor RNA [median RNA index number of 6.8 (normal value range 1-10)] were identified. Median follow-up was 32 mo for survivors and median CRS was 2. Eighty-seven patients (56%) received preoperative and 124 (80%) postoperative chemotherapy. Median RFS for all patients was 13 mo and 3-yr DSS was 69%. Median RFS and 3-yr DSS for patients with an elevated CRS (3-5) was lower (7 vs 18 mo, p<0.0001; 50% vs 80%, p<0.0001, respectively). Of the 12 genes studied, only elevated thymidylate synthase (TS) expression was associated with reduced RFS (HR1.16; 95% CI: 1.0–1.3; p=0.03) and shortened DSS (HR1.25; 95% CI: 1.0–1.5; p=0.03). Median RFS and 3-yr DSS for patients with elevated tumor TS expression was reduced (9 vs 15 mo, p=0.03; 48% vs 82%, p=0.001, respectively). TS expression had prognostic value that was independent of CRS on multivariate analysis (Figure). Conclusion: In patients with hepatic mCRC treated with resection and chemotherapy, elevated tumor TS expression improves outcome stratification based on the CRS, and appears to be a useful biomarker.



P131

Factors Predicting Response and Survival after Yttrium-90 Radioembolization of Unresectable Neuroendocrine Tumor Liver Metastases: A Critical Appraisal of 48 Cases A. Saxena,[1]* D.L. Morris,[1] T.C. Chua,[1] L. Bester.[2] *1. UNSW Department of Surgery, St George Hospital, Sydney, NSW, Australia; 2. St Vincent's Hospital, Sydney, NSW, Australia.*

Background Yttrium-90 (90Y) radioembolization is a promising treatment option for unresectable neuroendocrine tumor liver metastases (NETLM). This study is the first to evaluate the prognostic variables that influenced radiologic response and survival in patients with unresectable NETLM who were treated with 90Y radioembolization. As a secondary outcome, the impact of this treatment on serologic toxicity was assessed. Methods Forty-eight patients underwent resin-based 90Y radioembolization for unresectable NETLM at a single institution between December 2003 and May 2009. Patients were assessed radiologically and serologically at 1 month and then at 3 month intervals after treatment. Prognostic variables that affected response and survival were determined. The impact of this treatment on serologic toxicity over a 6-month period was assessed. Results No patient was lost to follow-up. The median follow-up for the patients who were alive was 41 months (range 5 to 63). The median survival was 35 months. On imaging follow-up, 26 patients (54%) had a good radiologic response. Five prognostic factors were associated with an improved survival: good radiologic response (p=0.003), low hepatic tumor burden (p = 0.022), female gender (p=0.022), well differentiated tumor (p=0.001) and absence of extra – hepatic metastasis (p<0.001). Three factors were associated with a good radiologic response: female gender (p=0.040), well differentiated tumor (p<0.001) and low hepatic tumor burden (p=0.041). There was a significant increase in the level of alkaline phosphatase over the 6-month period (p<0.001). Conclusions 90Y radioembolization is a promising treatment option for unresectable NETLM. Patients with low hepatic tumor burden, well differentiated tumor, female gender and no extra-hepatic disease benefit most from treatment.

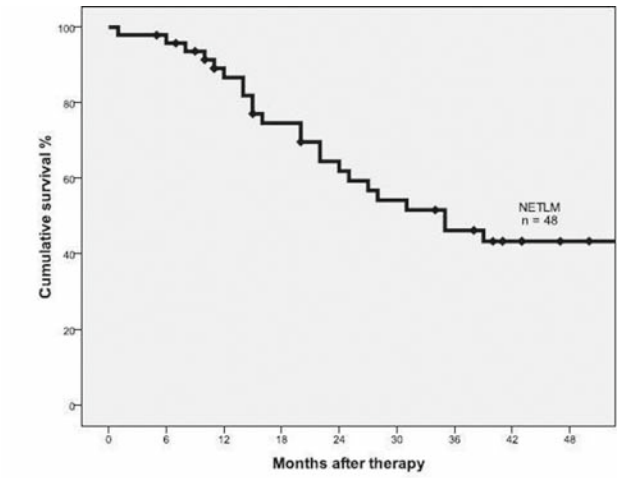
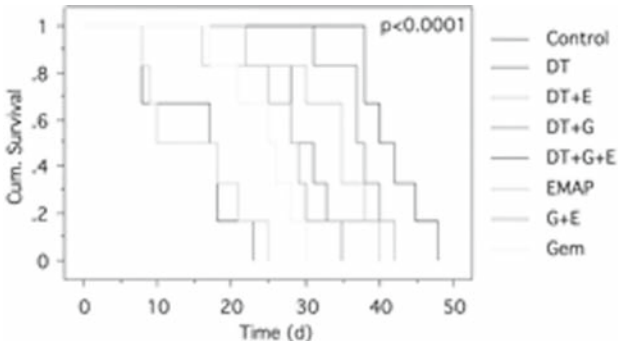


Figure 1. Overall survival after ^{90}Y radioembolization for neuroendocrine tumor liver metastases (n = 48).

P132

A combination approach to enhance taxane-based antitumor activity in experimental pancreatic cancer N. Awasthi, A. Kirane,* M.A. Schwarz, R.A. Brekken, R.E. Schwarz. *UTSW Medical Center, Dallas, TX.*

Background: Pancreatic ductal adenocarcinoma (PDAC) remains a leading cause of cancer related deaths. It is poorly responsive to gemcitabine (G), or other agents such as docetaxel (DT). Endothelial monocyte activating polypeptide II (EMAP, E) is an antiangiogenic cytokine that has been shown to enhance gemcitabine activity in PDAC. The present study tested combination benefits of EMAP, gemcitabine or docetaxel in experimental PDAC. Method: Human PDAC (AsPC-1) and endothelial cells (HUVECs) were grown in RPMI and E-Stim growth medium, respectively. Cell proliferation assays were performed using WST-1 reagent. Protein expression was determined by Western blotting. In vivo animal survival was evaluated in murine xenograft models after 3-week treatment with E, G or DT. Results: In vitro cell proliferation analysis of AsPC-1 cells showed no (E), modest (G, IC50 > 10μM) or major inhibitory effects (DT, IC50: 8μM); at 10μM concentration, percent inhibition in cell proliferation was 1.4, 40 and 60, respectively. Addition of E to G or DT had no additive antiproliferative effects. In HUVECs, E, G and DT had significant antiproliferative effects, with 59, 96 and 85 % inhibition at 10 μM, respectively. Addition of E to G and DT had significant additive antiproliferative effects. In HUVECs, E alone or in combination with G and DT caused an increase in apoptosis-related phospho-JNK protein expression. The in vivo animal survival study revealed that compared to controls (median survival: 17 days), E (14 d) had no benefit, G (25 d, p<0.02) and DT (29 d, p=0.006) alone extended the survival, and sequential treatment with DT first followed by G (37 d, p=0.0006) further extended survival. Addition of E to G, DT or the DT+G group enhanced survival in all settings (G+E: 28 d, DT+E: 35, DT+G+E: 40 d; p<0.05). Conclusion: In vitro, EMAP addition increased the antiproliferative effect of gemcitabine and docetaxel in endothelial but not in PDAC cells. In vivo, the benefit of DT+G was further enhanced by the addition of E. This combination therapy using antiendothelial EMAP represents a more effective therapeutic strategy for PDAC.



P133

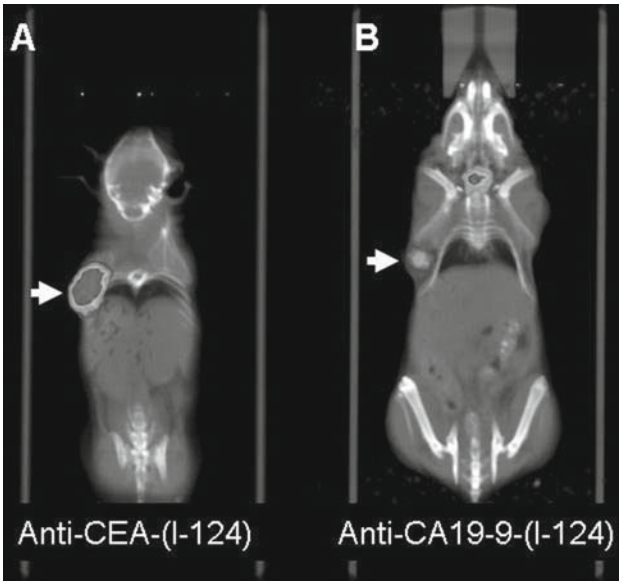
Multicentric study on robotic tumor-specific mesorectal excision for the treatment of rectal cancer A. Pigazzi,[1]* A. Patriti,[3] J.H. Baek,[4] F. Biffi,[2] J. Garcia-Aguilar,[1] L. Casciola,[3] F. Luca.[2] *1. general and Oncologic Surgery, City of Hope, Duarte, CA; 2. European Institute of Oncology, Milan, Italy; 3. Ospedale San Matteo degli Infermi, Spoleto, Italy; 4. Inha University College of Medicine, Incheon, Korea, South.*

BACKGROUND: laparoscopic rectal resection has been recently used for rectal cancer resulting in superior post-operative early outcomes compared with open anterior resection. Few studies investigating the role of robot-assisted tumor-specific rectal surgery (RTSRS) have been carried. The aim of the study was to verify on a multicentric basis the perioperative and oncologic outcome of RTSRS. METHODS: one hundred forty-three patients consecutively undergoing RTSR in three centers were reviewed. Pathologic data, postoperative and oncologic outcome measures were prospectively collected and analyzed by an independent researcher. RESULTS: a total of 112 restorative surgeries and 31 abdomino-perineal resections were carried out. Conversion rate was 4.9%, mean blood loss 283 ml and the mean operative time was 297 minutes. The mean number of harvested nodes was 14.1 (+/-6.5); mean distal margin was 2.9cm (+/- 1.8); negative radial margins were recorded in 142 cases. The 3-year overall survival rate was 97%, and no isolated local recurrences were found at a mean follow-up of 17.4 months. CONCLUSION: RTSRS is a safe and feasible procedure that may facilitate mesorectal excision. Randomized clinical trials and a longer follow-up are needed to evaluate a possible influence of RTSRS on patient survival.

P134

Radiolabeled anti-CA 19-9 and anti-CEA as PET imaging probes for pancreas cancer M. Girgis,[1]* V. Kenanova,[2] T. Olafsen,[2] K. McCabe,[2] A. Wu,[2] J.S. Tomlinson.[1] *1. UCLA - Department of Surgery, Los Angeles, CA; 2. UCLA - Crump Institute for Molecular Imaging, Los Angeles, CA.*

Background: Pancreas cancer is one of the most lethal cancers in which mortality approximates incidence. Sensitive and specific imaging of pancreas cancer should improve our ability to evaluate and apply our current treatments appropriately. The vast majority of pancreas cancers express tumor antigens CA19-9 and CEA which can be targeted with antibodies. The goal of this study was to determine the potential of these tumor antigens as targets for imaging pancreas cancer. Methods: Expression of CEA and CA19-9 was verified using flow cytometry on human pancreas cancer cell lines BxPC3 and Mia Paca. Immunohistochemistry was used to confirm in vivo xenograft expression. A previously engineered anti-CEA antibody fragment {Anti-CEA[scFv-Fc(310A)] }with a mutated FcRn binding domain to decrease serum half life and an intact murine anti-CA19-9(clone:NS-116-19-9) were labeled with a positron emitting radionuclide (Iodine-124) and injected intravenously into mice harboring an antigen positive xenograft (BxPC3) and a negative xenograft (MiaPaca). MicroCT and MicroPET scans were then performed at successive time intervals after injection. Radioactivity was measured in blood and tumor to provide objective confirmation of the microPET images. Results: Pancreas cancer xenograft imaging with anti-CEA-scFv-Fc-310A demonstrated an average tumor:blood ratio of 5.2 and positive: negative tumor ratio of 17.6 for experiments involving 3 mice. Additionally, imaging with anti-CA19-9 in 3 mice demonstrated an average tumor:blood ratio of 5 and positive: negative tumor ratio of 20. Conclusions: Molecular imaging of pancreas cancer should improve our ability to not only evaluate extent of disease but also improve our ability to evaluate the effect of our current and future therapies. The results of our study demonstrate that antibody based PET imaging of tumor antigens CEA and CA19-9 show great promise in achieving sensitive and specific molecular imaging of pancreas cancer.



Combined MicroPET/MicroCT Images: A) anti-CEA labeled with iodine-124; B) anti-CA19-9 labeled with iodine-124

P135

Management of Colorectal Liver Metastases in the Elderly Patient: A Decision Analysis S. Yang,[1]* S. Alibhai,[1] E. Kennedy,[1] N. Coburn,[2] C. Law.[2] *1. University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Health Sciences Centre, Toronto, ON, Canada.*

INTRODUCTION: Our population is aging rapidly and the incidence of liver metastases (LM) from colorectal cancer (CRC) is on the rise. When invasive strategies are considered, elderly patients are frequently subject to undertreatment both due to perceived risks of therapy and under-representation of the elderly in clinical trials. Recent evidence has shown hepatic resection to be a safe and effective option for elderly patients with LM. Commonly employed alternative strategies to surgery are supportive care, chemotherapy, and ablation. METHODS: A Markov decision model was built to examine the effect on quality-adjusted life expectancy (QALE) and life expectancy (LE) of four strategies – best supportive care (BSC), systemic chemotherapy (SC), radiofrequency ablation (RFA), and hepatic resection (HR). The baseline cohort included healthy 70 year-old patients presenting with LM following primary resection for CRC potential treatable by all strategies. All event and transition probabilities as well as utilities were derived from a comprehensive review of the literature. Deterministic and probabilistic sensitivity analyses were performed on all study parameters to assess the strength of the model. RESULTS: In the base case analysis, BSC, SC, RFA, and HR yielded QALE of 7.9, 15.3, 27.9, and 34.5 months, and LE of 11.3, 25.9, 38.0, and 40.1 months, respectively (Table 1). The model was sensitive to the probability of recurrence after hepatic resection, with RFA becoming the preferred strategy if monthly probability of recurrence is greater than 6.1%. In probabilistic sensitivity analysis, HR is preferred 70.1% of the time and RFA is preferred 29.9% of the time. CONCLUSION: The present model suggests that hepatic resection is the optimal treatment strategy for elderly patients with liver metastases. However, in older patients who have less favorable tumour characteristics, RFA may provide better QALE then other strategies.

Table 1. Expected value from base case deterministic analysis

Treatment Strategy	LE (months)	QALE (months)
Best supportive care	11.3	7.9
Systemic chemotherapy	25.9	15.3
Radiofrequency ablation	38.0	27.9
Hepatic resection	40.1	34.5

LE = life expectancy; QALE = quality-adjusted life expectancy

P136

Inaccuracy of Preoperative Classification of Pancreatic Cystic Neoplasms: Are We Improving? A.J. Russ,* E.R. Winslow, R.J. Rettammel, S.M. Weber, C.S. Cho. *Section of Surgical Oncology, University of Wisconsin School of Medicine and Public Health, Madison, WI.*

Introduction. Pancreatic cystic neoplasms (PCN) are being diagnosed with increasing frequency. The decision to resect is driven by the biological behavior of PCN subtypes, making accurate preoperative classification critical. Radiologic and endoscopic advancements have refined diagnostic evaluation, but the accuracy of preoperative PCN classification remains undetermined. Methods. We reviewed a prospective institutional database to identify contemporary patients who underwent pancreatectomy from 1999 through 2009 for a preoperative diagnosis of PCN(serous cystadenoma (SC), mucinous cystadenoma (MC), intraductal papillary mucinous neoplasm (IPMN), or cystadenocarcinoma (CA)). All patients were evaluated in a multidisciplinary clinic. Preoperative and pathological PCN classifications were compared and factors affecting the accuracy of preoperative diagnosis were determined. Results. Fifty-one patients underwent pancreatectomy for a preoperative indication of PCN between 1999 and 2009. Preoperative endoscopic ultrasonography was performed in 33% of cases before 2005 and in 70% after 2005. Operative management consisted of left pancreatectomy in 67%. Preoperative diagnoses were MC (37%), IPMN (22%), CA (20%), indeterminate (14%), and SC (6%); pathological diagnoses were MC (35%), IPMN (27%), SC (22%), CA (12%), and other (4%). Preoperative PCN classification was correct in 43% and preoperative classification of mucinous versus non-mucinous PCN was correct in 73%; this accuracy did not differ between the two eras. Among cases with incorrect preoperative classification, the pathological diagnosis was more often less aggressive (46%) than more aggressive (13%) than the preoperative diagnosis (p=0.043). The likelihood of identifying occult invasive malignancy not confirmed preoperatively was 6%. Conclusion. Despite ongoing advancements in preoperative diagnostic techniques, the ability to accurately classify PCN remains suboptimal. When incorrect, preoperative classification tends to overestimate the severity of diagnosis. The prevalence of occult invasive malignancy among PCN patients undergoing resection in a multidisciplinary setting is low.

P137

Impact of Temporary Stoma on Quality Of Life (QOL) of Rectal Cancer Patients Undergoing Treatment H.B. Neuman,[1]* S. Patil,[2] S. Fuzesi,[2] W.D. Wong,[2] M.R. Weiser,[2] J.G. Guillem,[2] P.B. Paty,[2] G.M. Nash,[2] K.N. Duhamel,[2] L.K. Temple.[2] *1. Surgery, Division of Surgical Oncology, University of Wisconsin, Madison, WI; 2. Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Data supports using a diverting stoma in rectal cancer patients with low anastomoses. However, little data exists on how temporary stomas impact QOL. Our objective was to prospectively evaluate QOL of rectal cancer patients with a temporary stoma. **Methods:** Patients with a temporary stoma were identified from a prospective single-institution longitudinal study of stage I-III rectal cancer patients undergoing sphincter-preserving surgery. Patients completed the EORTC C30/CR38 QOL scale preoperatively, at stoma closure, and 6 months later. A validated Stoma QOL scale evaluating factors relevant to stomate QOL was also administered at closure. Longitudinal trends on *a priori* selected subscales were performed with ANOVA. Correlations between Stoma QOL subscales and EORTC Global QOL were assessed with Pearson correlation coefficient. **Results:** Of eligible, consented patients, 76% completed at least one survey(n=60). Median age at diagnosis was 55(35-85) yrs, 55% men, 90% received neoadjuvant therapy. Tumors were located 8(0-15) cm from the anal verge and anastomoses hand-sewn in 37%. Stomas remained for median 190(54-490) days. Patient EORTC Global QOL was good(mean score 70/100). Of *a priori* identified EORTC QOL subscales, only Future Perspective improved over the study period(p=0.01); no change was seen in Physical(p=0.68), Social(p=0.81) or Role(p=0.23) function or Body Image(p=0.12). Most Stoma QOL subscales(4/6) were significantly associated with EORTC Global QOL at closure (table). When assessing individual items in subscales most highly correlated, leakage difficulty(38%), comfort in clothing(never/seldom 33%), and worry about privacy to empty pouch(32%) were common. **Conclusion:** EORTC Global QOL in rectal cancer patients undergoing treatment is good, remaining stable throughout the study, even with a stoma. However, stoma-related issues had significant association with EORTC Global QOL, suggesting that difficulty with a stoma may be detrimental. As some stoma-related factors impacting QOL may be modifiable, further clarification of these factors will be relevant in designing interventions to improve patient experience with a stoma.

Correlation of Stoma QOL Subscales with Global QOL

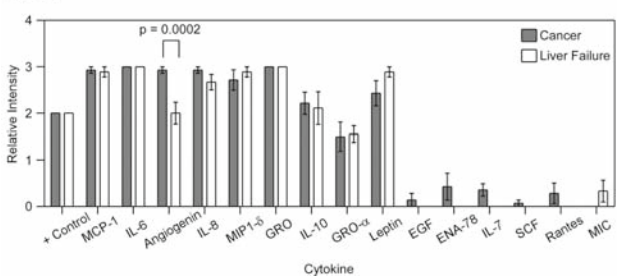
	R	P
Overall satisfaction with life	0.67	<0.0001
Work/Social Function	0.43	0.001
Sexuality/Body Image	0.37	0.02
Stoma Function	0.34	0.01
Financial Concerns	0.19	0.14
Skin Irritation	0.11	0.46

P138

Angiogenin and Leptin: Potential Targets for the Palliation of Peritoneal Ascites E.K. Cooley,* C.W. Lee, L.A. Lambert, B. Rajeshkumar, A. Tran, S. Shah, N. Anwar, G.F. Whalen. *University of Massachusetts Memorial Medical Center, Worcester, MA.*

Introduction: Patients with peritoneal ascites often suffer debilitating symptoms including life-threatening anorexia and cachexia. Symptom management is challenging and often inadequate, resulting in loss of quality of life (QoL). This study investigates the cytokine profiles of malignant and non-malignant ascites for potential targets for palliation and compares the QoL in both sets of patients. Methods: A prospective, observational study was conducted at an academic medical center. Ascitic fluid was collected from thirty adult patients undergoing paracentesis for symptomatic ascites (15 due to non-malignant liver failure; 15 due to gastrointestinal cancer). With IRB approval and patient consent, level of expression of 15 cytokines in ascites were determined using the RayBio® protein array. All patients completed FACT-G QoL questionnaires at the time of paracentesis. Relative intensity of cytokine expression was quantified using a 3-point scale. Cytokine expression profiles and QoL for cancer and liver failure patients were compared. Results: Eight of 15 cytokines were expressed with similar intensity in both malignant and non-malignant ascites. Angiogenin was significantly increased in malignant ascites (p=0.0002), and there was greater heterogeneity of cytokine expression in the malignant ascites. Cancer patients had significantly greater overall QoL scores compared with liver failure patients (mean total score 81.2 vs 68.4 out of possible 120, p=0.016). Functional well-being was significantly better in cancer patients, specifically in the area of work and the ability to sleep well. Conclusions: Targeted, more effective therapy is needed for the management of symptomatic ascites. Angiogenin was significantly higher in malignant ascites and may offer a target for anti-angiogenic therapy. The appetite suppressant, leptin, was elevated in both malignant and non-malignant ascitic samples and may be a potential target for palliation of ascites-related anorexia.

Figure 1.



P139

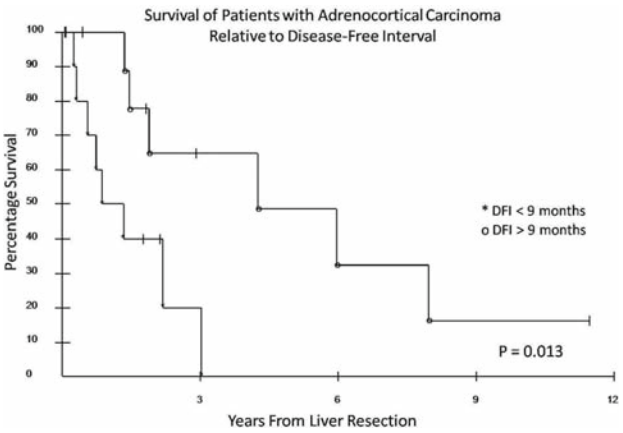
Isolated Pelvic Perfusion as Neoadjuvant Therapy for Advanced/Unresectable Malignancy H. Wanebo,[1]* J. Belliveau,[1] E. Gustafson,[2] M. DiSienna,[3] G. Begossi.[4] *1. Landmark Medical Center, Woonsocket, RI; 2. Miriam Hospital, Providence, RI; 3. Berkshire Medical Center, Pittsfield, MA; 4. Roswell Park Cancer Institute, Buffalo, NY.*

Introduction: Preoperative (or palliative) chemo radiation therapy (CRT) for advanced pelvic malignancy is often precluded by previous radiation. Isolated pelvic perfusion (IPP) provides high tissue drug levels to enhance resectability, survival in pts failing CRT +/- surgery. We performed 113 IPP in 78 pts (34 - palliation, 44 - preop therapy) using balloon occlusion technique. Methods: 42 pts had locally advanced irradiated rectal cancers, 26 had preop, 16 palliative therapy: 8 pts advanced anal cancer, 6 pts pelvic sarcoma. Other pts were melanoma (M 4pts), endometrial cancer (EC) 2, ovarian cancer (OC) 2, bladder cancer (BC) 1. A total of 113 isolated pelvic perfusions (60 min.) were done using 5FU, cisplatinum (CIS), Oxaliplatin (OX) mitomycin (10) for epithelial cancer, selected agents for M&S. (Adriamycin, Phenyl Alanine Mustard (PAM). High dose IPP with PAM (110/M2), Paclitaxel 60mg/M2 and Cisplatin 150mg/M2 was done in 6 pts; (3 required stem cell support) advanced M (4 pts), SCC (1 pt), Endometrial ca (1pt). Results: Palliatvie IPP in 16 advanced rectal cancer pts resulted in significant pain relief (1-4 months) in pts with narcotic resistant pain. Preoperative IPP in 26 locally advanced rectal cancer pts achieved CR in 2 pts, significant regression in 11 pts rendering them resectable: 7 had RO resections of 6 other pts, 4 refused, 2were medically excluded. Med. survival was 24 mos in 12 pts resectable pts vs. 8 mos in 12 non resectable pts. ($p<0.05$). It was 30 mos in advanced anal cancer pts (1pt survived >90 mos). Med survival was 20 months in 4 pts with recurrent EC/OC CA, (1 died NED >48 mos), 13 mos. in 4 advanced pts, 5 mos in 6 advanced sarcoma pts (4-34 mos-NED). Overall 17 pts of 44 pts (39%) were resected, 24 were amenable to palliative therapy after IPP. Conclusion: Isolated pelvic perfusion using a simplified balloon occlusion technique has promise in palliation or augmenting resectability of selected pts with advanced pelvic malignancy not amenable to conventional chemoradiation.

P140

Liver Resection for Metastatic Adrenocortical Carcinoma R.T. Ripley,[1]* A. Mathur,[1] C.D. Kemp,[1] R.E. Royal,[1] S.K. Libutti,[1] S.M. Steinberg,[2] B.J. Wood,[3] U. Kammula,[1] T. Fojo,[4] I. Avital.[1] *1. Surgery Branch, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, MD; 2. Biostatistics and Data Management Section, Office of the Clinical Director, Center for Cancer Research, National Cancer Institute, NIH, Rockville, MD; 3. Department of Radiology, Clinical Center, NIH, Bethesda, MD; 4. Medicine Branch, Center for Cancer Research, National Cancer Institute, NIH, Bethesda, MD.*

Background: Adrenocortical carcinoma (ACC) is a rare disease without effective chemotherapy. The aim of this study was to evaluate our experience with liver resection for metastatic ACC. Methods: Retrospective review of patients who underwent liver resection and radiofrequency ablation (RFA) for ACC from 1979 to 2009. Results: Twenty-seven patients were identified. No patients responded to systemic chemotherapy. 19/27 underwent liver resection. 11/19 and 8/19 had single and multiple liver lesions, respectively. 18/19 were rendered free of disease in the liver and 11/19 were rendered completely free of disease. 13/19 had synchronous extrahepatic-disease (EHD), 10/13 underwent synchronous EHD resection and 5/10 were rendered free of disease. 6/19 (32%) remained disease free in the liver (median follow-up 6.2 years). 8/27 underwent RFA; 7/8 became free of disease in the liver; 5/7 had EHD. Median overall survival and survival of patients who underwent liver resection were both 1.9 years (0.24 – 11.5+ yrs); 5-yr actuarial survivals were 29.3% and 28.7%, respectively. Disease-free interval (DFI) greater than 9 months from primary resection was associated with longer survival (4.1 vs. 0.9 yrs; $p = 0.013$). Synchronous metastatic disease at initial diagnosis, functional tumor status, number of hepatic metastases, adjuvant or neoadjuvant chemotherapy, EHD, and intra and extra-hepatic disease status were not statistically significantly associated with survival. Conclusions: This report is the largest single institution and reported series of liver resection and RFA for ACC. Given the lack of effective systemic treatment options, liver resection and RFA may be considered in selected patients with ACC metastatic to the liver with DFI longer than 9 months.



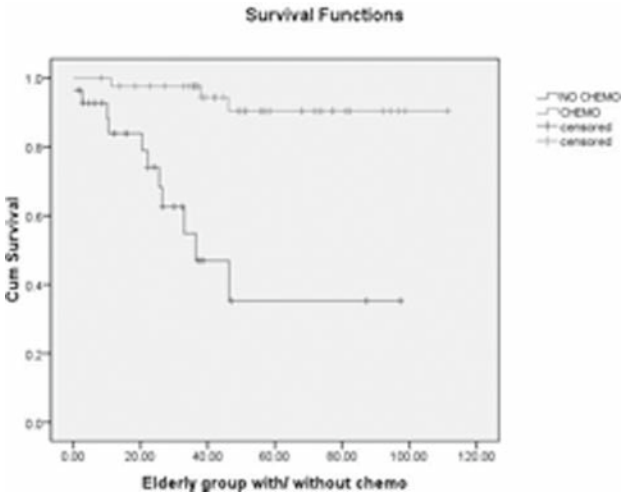
P141

WITHDRAWN

P142

Use of Adjuvant Chemotherapy in Elderly Colorectal Cancer Patients: A case-control study A. Mathieson,[1]* P.F. Ridgway,[1] Y.J. Ko,[2] A.J. Smith.[1] *1. University of Toronto, Toronto, ON, Canada; 2. Odette Cancer Center, Sunnybrook Health Sciences Center, Toronto, ON, Canada.*

Introduction: Advances in adjuvant chemotherapy in stage III colorectal cancer have led to significant survival advantages. With an aging North American population, it is unknown whether trial data are truly generalizable to elderly cohorts. Surgical and medical oncologists historically were reticent to submit this group to adjuvant therapy. We examine the contemporary application and tolerability of chemotherapy in the elderly. Methods: A single institution case-control retrospective review of a prospective database was conducted. Stage III colorectal cancer patients treated between July 1999 and December 2005 were included. The elderly group was those over 70 years and the control group was aged 50 to 70. Statistical analysis was conducted using the Mann-Whitney U test and Kaplan-Meier estimates with chemotherapy use as the primary outcome measure. Results: A total of 100 elderly patients and 118 young patients were identified in the institutional database. Twenty-nine elderly patients and 36 young patients were excluded as data were incomplete, or they declared stage IV prior to chemotherapy. 154 patients (71 elderly, 83 young) were analyzed. The rate of chemotherapy given to the elderly group was 61% versus 98.8% in the younger group ($p<0.001$). The rate of dose reduction in the elderly and young groups was 39.5% and 31.7% respectively ($p=0.38$). The adjuvant chemotherapy completion rate was 81.4% for the elderly and 80.4% for the young group ($p=0.90$). There was no clinical difference in ECOG score, ASA score, gender, nodes excised or number of positive nodes. Outcomes in the elderly group were significantly influenced by adjuvant therapy. The overall 5-year survival rate for the elderly group that received chemotherapy was 90.4% versus 35.2% ($p<0.001$) for those not given adjuvant therapy. Conclusion: Adjuvant chemotherapy is prescribed less frequently to elderly patients. Once started on chemotherapy elderly patients seem to tolerate chemotherapy well with increased survival. Age itself should not be contraindication to adjuvant chemotherapy and thus should be considered in all elderly patients.



Kaplan Meier curves for elderly patients treated with and without adjuvant chemotherapy

P143

Genes mediating Wnt and FGF signaling are potential biomarkers of diffuse-type gastric cancer P.S. Ray,[1]* S.P. Bagaria,[1] C. Moran,[1] A. Fleisig,[1] M. Shin-Sim,[2] X. Cui.[3] *1. Department of Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA; 2. Department of Biostatistics, John Wayne Cancer Institute, Santa Monica, CA; 3. Department of Molecular Oncology, John Wayne Cancer Institute, Santa Monica, CA.*

INTRODUCTION: Wnt and FGF signaling pathways are known to display crosstalk in a variety of cellular processes. Although their prognostic significance is unknown, the Wnt and FGF pathways have been implicated to play a functional role in gastric cancer. We sought to determine whether expression of specific genes, that mediate Wnt and FGF signaling, define a cluster of gastric cancer patients. **METHODS:** A publicly available 200-sample human gastric cancer gene expression microarray dataset was subjected to unsupervised hierarchical clustering which revealed three major clusters. Expression of Wnt and FGF pathway genes were analyzed with respect to clustering pattern. Genes displaying the highest correlation to one of three major clusters identified were then correlated with histologic subtype using a 112-sample independent gastric cancer dataset. We are conducting an extensive retrospective review of archival specimens and clinicopathologic outcomes for all patients diagnosed with gastric cancer. Immunohistochemical expression of select genes is correlated with clinical outcome. **RESULTS:** Highly specific clustering of Wnt and FGF pathway genes was observed in a subset characterized by loss of CDH1(E-cadherin). Of the approximately 180 genes relevant to Wnt and FGF signaling, SFRP1, FGFR1 and FGF1 were found to have the highest correlation coefficients with loss of CDH1 (0.44,0.39,0.45, respectively). In the second dataset, mean expression levels of SFRP1, FGFR1 and FGF1 were shown to be associated with diffuse-type gastric cancer ($p<0.00006$, $p<0.00008$, $p<0.06$). **CONCLUSIONS:** Our preliminary results show that expression of Wnt and FGF pathway mediators SFRP1, FGFR1 and FGF1 displayed independent correlation with loss of E-cadherin and diffuse-type gastric cancer. This strongly implicates the Wnt and FGF pathways in the biology of diffuse-type gastric cancer and may offer potential therapeutic targets.

P144

The ChemoFx Assay: Response of 31 Hepatopancreatobiliary Tumor Patients K. Lau,* N. Agee, I.H. Mckillop, D. Sindram, J.B. Martinie, D.A. Iannitti. *Carolinas Medical Center, Charlotte, NC.*

Introduction: Phenotypic chemoresponsive assays have been used to assess in vitro drug sensitivity/resistance in breast and ovarian cancer. No such data is currently available for hepatopancreatobiliary (HPB) maglignancies. This study sought to determine the potential for one such test system; the ChemoFx assay, to determine HPB tumor-drug responsiveness. Methods: Tumor specimens from 31 patients undergoing resection for HPB tumors were analyzed for drug responsiveness using the ChemoFx assay system. Results: 31 patients, were enrolled for evaluation (20 male/11 female). Using this approach we demonstrated that carboplatin exhibited the highest tumor cell sensitivity rate with 66% of pancreatic cancers (n=15) And 100% of colangiocarcinomas (n=7) being responsive. In the case of cells derived from hepatocellular carcinoma, the greatest responsiveness to chemotherapeutic agents was observed for gemcitabine (44%, n=9). Conversely, amongst the other agents tested, HPB-derived cells were least responsive to docetaxel, fluorouracil and oxaliplatin. Conclusion: Data from this study indicates that the ChemoFx assay can detect selective, chemotherapeutic drug responsiveness in HPB-derived tumor cells in vitro. Future analysis is now required to determine whether this approach can be used translationally to improve patient responsiveness to selective drug therapy regimes

P145

Regionalization of Pancreatic Resection for Malignancy in NY State and the Effect of Hospital Volume on Perioperative Mortality D.D. Cox,* A. Miller, S. Edge, B. Kuvshinoff. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

INTRODUCTION: The relationship between hospital case volume and perioperative mortality in pancreas resection is well documented. A statewide data from New York (1984-1991)showed that high volume hospitals had substantially lower operative mortality (5.5%) compared to low volume (18.9%)and that only 19% of patients had pancreatic cancer surgery at high volume hospitals. The current study uses the same Statewide Planning and Research Cooperative System(SPARCS) hospital data to determine the change in regionalization of pancreatectomy for cancer is occurring in New York State and the impact on perioperative mortality. METHODS: Hospital discharge abstracts were obtained from the SPARCS for all patients who underwent pancreaticoduodenectomy or total pancreatectomy for malignancy in New York between 2002 and 2007. Logistic regression analysis was used to determine the relationship between hospital and surgeon volume to perioperative mortality and length of hospital stay(LOS). RESULTS: A total of 3051 procedures were performed at 121 hospitals by 392 surgeons. Overall perioperative mortality was 143(4.7%),which was lower than 15 years earlier (12.9%). Most cases (58.6%) were done at high volume centers and 47.3% of procedures performed by high volume surgeons. Mortality and LOS at high volume centers was 2.9% and 14.7 days, respectively, compared to 12.2% and 25.4 days for minimal volume centers. Mortality and LOS for high volume surgeons was 2.6% and 14.6 days compared to moderate(4.0%, 17.6) and low (9.9%, 24.1) volume surgeons. Compared to hospitals and surgeons with high caseloads, the odds of death are 3.8 times higher in a minimal volume hospital($p<0.001$) and 3.6 times higher for low volume surgeons($p<0.001$). CONCLUSION: An increased proportion of pancreatic resections for malignancy in New York now occurs in high volume centers and by high volume surgeons. This has occured in the absence of imposed regulatory or legislative authority. The result is decreased mortality and LOS when compared to minimal volume centers and low volume surgeons.

Mortality Rates and Duration of Hospitalization After Pancreatic Resection, According to Hospital Volume From 2002 to 2007

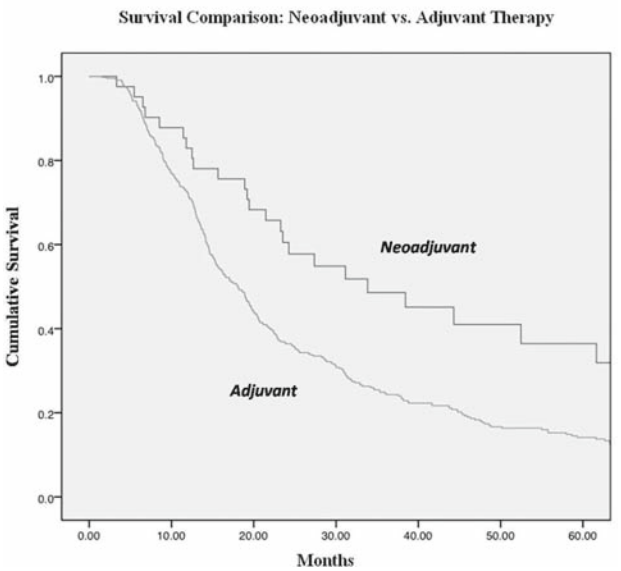
Hospital Volume (# of Pancreas Resections for Malignancy Performed(cases))	Total Number of Cases Performed	Percentage of Cases Performed(%)	Crude Mortality (%)	Mean Length of Stay (LOS)days
Minimal (<10)	238	7.8	12.2	25.4
Low (10-50)	765	25.1	5.9	20.9
Medium (51-80)	259	8.5	6.6	21.7
High (>81)	1789	58.6	2.9	14.7

P146

Neoadjuvant chemotherapy is superior to adjuvant treatment in resectable pancreatic adenocarcinoma A. Artinyan,[1]* D. Anaya,[1] B. Mailey,[3] J.D. Ellenhorn,[2] J. Kim.[2] *1. Baylor College of Medicine, Houston, TX; 2. CIty of Hope, Duarte, CA; 3. UC Irvine School of Medicine, Irvine, CA.*

Background: Preoperative systemic therapy has been used as a strategy for improving survival with operable pancreatic cancer. However, its benefit

in this setting is unclear. Our objective was to compare survival in patients receiving neoadjuvant versus adjuvant therapy for resectable pancreatic adenocarcinoma. Methods: The California Cancer Surveillance Program (CSP) Database identified 458 patients diagnosed with non-metastatic pancreatic adenocarcinoma between 1987-2006 who underwent definitive pancreatic resection and received systemic chemotherapy. The cohort was stratified into two groups: preoperative versus postoperative systemic therapy. Clinicopathologic characteristics of the two groups were compared. Overall survival was compared by treatment group using the Kaplan-Meier method and was stratified by extent of disease as well era of treatment (1987-1996 vs. 1997-2006). Multivariate Cox regression analysis was used to determine the benefit of preoperative systemic therapy, independent of other significant factors. Results: Of the 458 patients, 39 (8.5%) patients started chemotherapy preoperatively and 419 (91.5%) received postoperative treatment. There was no difference in age, sex, or primary tumor extent by treatment group (all p-values >0.05). However, there was a significantly lower rate of lymph node-positivity in the preoperative group (45% vs. 65%, p=0.011). The preoperative group had a significantly longer overall survival compared to the postoperative group (median survival 34 vs. 19 months, p=0.003). This difference was independent of tumor extent and node status and was most notable in the later era. On multivariate analysis, preoperative treatment was an independent predictor of improved survival (HR 0.62, p=0.030, 95% CI 0.40-0.96). Conclusion: This is the first population-based study to compare neoadjuvant vs. adjuvant systemic treatment in resectable pancreatic cancer. Neoadjuvant therapy is associated with a lower rate of lymph node-positivity and improved survival. It should be considered as an alternative to immediate surgery and may help select the group of patients most likely to benefit from resection.



P147

Laparoscopic Liver Surgery in Cancer Patients: Experience at a National Cancer Center R. Matteotti,* A. Gumbs, V. Siripurapu, J. Hoffman. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction:Oncological adequacy/safety of major liver resections is uncertain.Methods:Patients undergoing laparoscopic liver surgery were retrospectively analyzed.Intraoperative data final pathology and short-term clinical outcome were analyzed.Results:Forty-nine liver procedures were analyzed,47 were attempted,45(96%) completed laparoscopically.Median age 62(SD14.58),median BMI 27,95(SD3),ASA2.Fifteen underwent major resections (31%),27 minor resections(56%),7(13%)underwent either an ablation or liver biopsy.The major hepatectomy group constituted of 5 laparoscopic left hepatectomies (33%)10 right hepatectomies,8 completed laparoscopically (80%).4 of 49 patients(8%) had intraoperative complications, 2 requiring conversion. Conversion rate in major hepatectomies was 2/15(13%).Twenty-two percent had a postoperative complication.We had 1 bile leak. Lymph node dissection in the hepatoduodenal ligament was done in 19% of the patients(n=9).We never used portal clamping Preoperative portal vein embolization before major resections was done in 4%. Median EBL 403cc(SD741.4).Four patients required intraoperative blood transfusion.Median operative time 217 min(SD171.5).Frozen sections positive in 27% requiring re-resection during the same surgery. Margins positive in 6(15%.29 patients had stage 4 disease,n=21 colorectal c,n=3 gallbladder,n=1 renal,n=2 breast,n=2 neuroendocrine.Specimen values:Median Size(mm) 11(SD65.8),Median Volume(cc)802.1(SD 868.5),Median Weight (gr)625(SD 258.2),Median Distance tumor/margin(mm)7.5 (SD15.9)Mean hospital stay was 4 days(min 1, max 17) Thirty-day mortality 0%.Infectious complications n=1,intra-abdominal abscess,requiring drainage. Conclusions:Laparoscopic liver surgery at a major cancer center is safe and Median hospital stay and short term mortality are comparable to similar series in the literature reporting open procedures.Most importantly,a laparoscopic approach does not violate oncological principles intraoperatively,tumor visualization is excellent,adequate margins can be obtained. Many more cases and Long-term follow up data will be needed to compare laparoscopy to an open approach in terms of survival and quality of life.

P148

Association of Tumor Biology and Neoadjuvant Therapy with Actual Five Year Survival in Esophageal Carcinoma T. Kim,* K. Ben-David, S.R. Grobmyer, S.B. Vogel, S. Hochwald. *Surgery, University of Florida College of Medicine, Gainesville, FL.*

Background: Esophageal cancer in the United States carries a poor prognosis with an overall 5 year survival rate of less than 10%. Factors associated with actual 5 year survival exist in this disease are not well defined. Methods: Single institution retrospective review of esophageal resections from 1984 to 2004 revealed 266 patients with invasive esophageal cancer. Neoadjuvant therapy was given to clinically staged > or = to T2 or node positive tumors. We identified 50 (19%) actual 5 year survivors (long-term survivors) and, using logistic regression, identified factors associated with long term survival and compared demographic and clinicopathologic characteristics between the long-term and short-term survivors (<5 years). Results: For the entire cohort, the mean age was 65 ±10 years, 196 (74%) were male, and 162 (61%) received neoadjuvant therapy. Of note, there was no significant difference in the utilization of neoadjuvant therapy in long term vs short term survivors (58% vs 62%, respectively, p=0.64) Median survival was 7.8 (Range 5.7-10.5) vs. 1.0 (Range 0.3-2.0) years for long-term vs. short-term survivors, respectively. Comparing long-term to short-term survivors, age, sex, race, location and type of cancer, and type of operation were not significantly different. The long-term survivor group had a significantly higher rate of complete pathologic response to neoadjuvant therapy (69% vs 41%, p<0.001), lower pathologic T stage (T1 and T0) following chemoradiation, (83% vs 45%, p=0.001), higher incidence of pathologic N0 disease (97% vs 68%, p<0.001), favorable tumor differentiation, i.e. well or well to moderate (50% vs 8%, p=0.001), and absence of angiolymphatic (93% vs 69%, p<0.01) or perineural invasion (100% vs 85%, p=0.04). Conclusions: Actual 5 year survival is possible with combined modality therapy in patients with > or = T2 clinical disease. Response to multimodality therapy and less aggressive pathologic tumor types predict long term survival in patients with esophageal carcinoma.

P149

Allogeneic red blood cell transfusion following pancreaticoduodenectomy for ductal adenocarcinoma is associated with earlier recurrence and reduced survival P.J. Kneuertz,* C.K. Chu, S.K. Maithel, J.M. Sarmiento, K.A. Delman, C.A. Staley, D.A. Kooby. *Department of Surgery, Emory University School of Medicine, Atlanta, GA.*

Introduction: Allogeneic red blood cell transfusion (RBCT) is associated with adverse outcomes after cancer surgery, and timing of RBCT may be critical. We examined affects of RBCT during and after pancreaticoduodenectomy (PD) for ductal adenocarcinoma (DAC). **Methods:** A prospective database of all patients undergoing PD for DAC from 2000-2008 at a single center was reviewed. Factors influencing RBCT, recurrence free survival (RFS), and overall survival (OS) were assessed. Intraoperative (intraop) and postoperative (postop) RBCT were analyzed separately. 30 day deaths were excluded from the survival analysis. **Results:** Of 220 patients undergoing resection, 147 (67%) received RBCT: 103 (47%) intraop and 102 (46%) postop. Of patients who

received RBCT, more units were given postop than introp (3.8 vs 2.2). Transfused patients had more comorbities (48% vs 26%, p=0.002), lower preop albumin (2.9 vs 3.2 gm/dL, p=0.007), lower Hgb (11.8 vs 12.8 gm/dL, p=0.001), and higher peak bilirubin (8.4 vs 5.4 mg/dL, p=0.003), as compared with non-transfused. RBCT was associated with greater blood loss (718 vs 275 ml, p=0.001) and longer operations (342 vs 239 min, p=0.001). Tumor factors and margin status were not significantly different between the groups. Transfused patients had more postop infections (50% vs 23%, p=0.001), major complications (34% vs 10%, p=0.001) and longer hospital stays (16.2 vs 9.5 days, p=0.001). RBCT was associated with reduced OS (15 vs 20 mo; p=0.015). Postop RBCT had greater adverse impact on both RFS and OS (table). Controlling for age, BMI, comorbidities, tumor factors, and major complications; postop RBCT was independently associated with worse RFS (HR 3.2, 95%CI [1.8-5.7], p=0.001) and OS (HR 1.6, 95%CI [1.1-2.2], p=0.011). Intraop RBCT was not. **Conclusion:** Allogeneic red blood cell transfusion is associated with earlier recurrence and reduced survival in patients undergoing pancreaticoduodenectomy for ductal adenocarcinoma, especially when administered postoperatively. Future studies should investigate the impact of timing and methods of minimizing RBCT in pancreatic cancer surgery.

Survival for patients subjected to pancreaticoduodenectomy for ductal adenocarcinoma, excluding 30-day deaths.

Group (n)	Median RFS (months)	*P*	Median OS (months)	*P*
No RBCT (72)	15		20	
Any RBCT (144)	10	0.347	15	0.015
Any intraop RBCT(102)	12	0.541	15	0.039
Any postop RBCT (99)	8	0.038	14	0.003

P150

Pancreatic resection is a feasible therapeutic option for elderly patients G.J. Lahat,* R. Sever, I. Nachmany, N. Lubezky, M. Ben-Haim, R. Nakache, J. Koriansky, J.M. Klausner. *Sourasky medical center, Tel Aviv, Israel.*

Introduction: Compromised physiological reserve, comorbidities, and the natural history of pancreatic cancer may deny pancreatic resection from elderly patients. Our aim was to evaluate outcomes of elderly patients amenable to pancreatic surgery. Methods: The medical records of all patients who underwent pancreatic resection at our institution between 1995-2007 were retrospectively reviewed. Patient, tumor, and outcomes characteristics in elderly patients aged ≥ 70 years were compared to a younger cohort (<70y). Univariable and multivariable analyses were performed to identify prognostic factors. Results: Four hundred and sixty patients had pancreatic resection and are included in the study cohort; of them, 166 patients (36%) aged ≥ 70 years. Compared to patients younger than 70 years (n=294), elderly patients had more associated comorbidities; 72% vs. 43% (p=0.01) and a higher rate of malignant pathologies; 72.9% vs. 58.8% (p=0.002). Operative time and consumption of blood products were comparable, however, elderly patients had more post-operative complications 41% vs. 29.3% (p= 0.01), longer hospital stay; 26.2 vs. 19.7 days (p<0.0001), and a higher incidence of peri-operative mortality; 5.4% vs. 1.4% (p=0.01). Multivariable analysis identified age ≥ 70 years as an independent risk factor for shorter disease-specific survival (DSS) among patients who had surgery for pancreatic adenocarcinoma (n=224). Median DSS for patients aged ≥ 70 was 15 months (SE: 1.6) vs. 20 months (SE: 3.4) in the younger group (p=0.02). One, two, and 5-Y DSS rates for the elderly cohort of patients were 58.2%, 36.4% and 22.6%, respectively. Conclusion: Properly selected elderly patients can undergo pancreatic resection with acceptable post-operative morbidity and mortality rates. Long term survival is achievable even in the presence of adenocarcinoma and therefore surgery should be seriously considered in these patients.

P151

Lymph Node Micrometastasis (Micromets) Correlated to Other Prognostic Factors in Colon Cancer (CCa) S. Saha,* S. Sirop, M. Soni, A. Korant, B. Chakravarty, S. Pampanagouda, D. Wiese. *McLaren Regional Medical Center-Michigan State University, Flint, MI.*

Introduction: The impact of micromets in CCa remains controversial with a decreased three year survival when compared to node negative disease in a recent meta-analysis. We aimed to correlate the presence of micromets in CCa with other well established prognostic factors. **Methods:** Patients (pts) diagnosed with CCa between 1996-2006 underwent Sentinel Lymph Node Mapping (SLNM) at the time of surgery and were included in the study. SLNs were evaluated for the presence of micromets (0.2-2.0 mm) with Cytokeratin Immunohistochemistry. Retrospectively tumor blocks were evaluated for the presence of molecular markers.The presence of micromets was then correlated to these markers, as well as to the grade, stage, bone marrow micromets and total number of LNs harvested (<12 or ≥12). **Results:** A total of 272 pts were included. The mean age was 71 years and 51.5% of pts were male. Micromets were detected in 19 pts of node positive disease (20.5%). The presence of micromets did not correlate to the grade, presence of bone marrow micromets, or the total number of LNs (table 1). There was also no association between the presence of micromets and any of the molecular markers of the available tumor blocks, including p-53 mutation, Angiogenesis Index, DNA profile (Diploid versus aneuploid), Thymidylate Synthase, BCL2 mutation, and BAX mutation (table 1). **Conclusion:** Micromets did not correlate with any of the established prognostic factors in colon cancer, neither with tumor markers. Our correlation analysis concludes that micromets occur independently of other prognostic factors.

Table 1: Lymph node micrometastasis correlated to molecular markers and to established prognostic factors

variable		Micromets	Node Negative Disease	Total	P-Value
# of LNs	< 12	7	49	56	0.79
	>= 12	12	100	112	
	Total	19	149	168	
Grade	I	1	38	39	1.0
	II	17	103	120	
	III	1	9	10	
	Total	19	150	169	
BMM	Detected	1	7	8	1.0
	Not Detected	10	53	63	
	Total	11	60	71	
AI	Not favorite	0	12	12	0.32
	Favorite	6	39	45	
	Total	6	51	57	
MDR1 Mutation	Present	8	48	56	1.0
	Not present	7	47	54	
	Total	15	95	110	
DNA Profile	Diploid	6	50	56	0.78
	Aneuploid	8	55	63	
	Total	14	105	119	
TS	Present	9	53	62	0.7
	Not Present	2	19	21	
	Total	11	72	83	
BCL2 Mutation	Present	3	24	27	1.0
	Not Present	7	49	56	
	Total	10	73	83	
BAX Mutation	Present	7	46	53	0.42
	Absent	1	20	21	
	Total	8	66	74	
P-53 Product	Present	9	50	59	0.48
	Not present	6	41	47	
	Total	15	91	106	

AI = Angiogenesis index, BMM = Bone marrow micrometastasis, TS = Thymidylate Synthase, LN = Lymph node.

P152

Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Prevents Recurrence of Mucinous Ascites from Appendiceal Cancer L.A. Lambert,[1]* K.F. Fournier,[2] P.F. Mansfield.[2] *1. Surgical Oncology, UMass Memorial Medical Center, Worcester, MA; 2. M.D. Anderson Cancer Center, Houston, TX.*

Background: Mucinous ascites can significantly impact the quality of life in patients with appendiceal cancer not amenable to curative approach with HIPEC. HIPEC has been shown to prevent recurrence of malignant ascites from other gastrointestinal cancers, including gastric and colon cancer, however its role in the palliative management of patients with appendiceal cancer is often overlooked. This study evaluates the efficacy of HIPEC with mitomycin C (MMC) in preventing recurrence of mucinous ascites from appendiceal cancer. Methods: All patients undergoing cytoreductive surgery (CRS) and MMC-HIPEC for appendiceal cancer between January 1993 and June 2007 were retrospectively reviewed. Patients with mucinous ascites who underwent HIPEC after incomplete cytoreduction were identified. The incidence of recurrent ascites, morbidity, mortality and overall survival were determined. Results: 134 patients underwent CRS and HIPEC for appendiceal cancer were. Eight (6%) patients with mucinous ascites underwent HIPEC after CCR 2-3 cytoreduction. There were no peri-operative deaths and the rate of

Grade III/IV morbidity was 12.5%. The average volume of ascites was 4L (range 2-8.5 L). Median follow-up was 23.5 mos (range 4-65 mos). Median overall survival was 26 mos (range 16-65 mos). At the time of last follow-up, no ascites was visible by computer tomography in 5 patients (63%) and only minimal ascites was suggested in 3 (37%). No patient required treatment for ascites-related symptoms. Conclusions: This is the first study to specifically demonstrate that HIPEC prevents recurrence of mucinous ascites from appendiceal cancer. The role of HIPEC, with or without CRS, needs to be further assessed for palliation of mucinous ascites from appendiceal cancer in patients not amenable to curative intent.

P153

Multimodality Management of Neuroendocrine Tumors Metastatic to the Liver S. Celinski,* K.T. Nguyen, J.L. Steel, R. Mehra, J.W. Marsh, D.A. Geller, A. Tsung, T.C. Gamblin. *University of Pittsburgh, Pittsburgh, PA.*

Introduction: Neuroendocrine tumors (NET) are uncommon tumors which frequently metastasize to the liver. Aggressive management of metastatic disease has been advocated due to the indolent course of NET, however no effective systemic therapy is available. We sought to evaluate factors affecting survival in patients treated with transarterial chemoembolization (TACE) and/or surgery. Methods: Clinicopathologic data was retrospectively gathered from the records of 124 patients who underwent treatment of NET metastatic to the liver. Chi-square and Analysis of Variances were performed to test differences between groups. Survival was assessed using Kaplan-Meier survival analysis. Results: TACE was performed for 90 patients, surgery for 22 patients and 12 patients received both treatments. Mean survival of the entire sample was 60 months. No differences between treatment groups (TACE vs. surgery) were observed for gender, age, symptomatic presentation or location of the primary tumor. More patients undergoing surgery had their primary tumor resected than those undergoing TACE (83% vs. 17%). R0, R1 and R2 resection was achieved in 35%, 29% and 35% respectively. A significant difference in survival was seen comparing those undergoing TACE alone, surgery alone, and TACE combined with surgery. Median survival from initiation of treatment was 25 months for TACE, 97 months for surgery and not reached for combination therapy. (p=0.001). Patients younger than 50 years had better survival than those over 50 years whether they were treated with resection (mean survival 160 vs. 86 months) or TACE (mean survival 69 vs. 32 months). Using Cox regression analyses, predictors including age (younger or older than 50), resection of the primary tumor, and treatment type (TACE vs. resection) were entered into a model. The overall model was significant (p=0.001) with age (p=0.009) and treatment type (p=0.01) contributing significantly to the model. Conclusions: Long term survival is possible in patients with NET metastatic to the liver. Younger age and treatment with the combination of resection and TACE may contribute to improved survival.

P154

ROBOTIC TOTAL MESORECTAL EXCISION FOR RECTAL CANCER. A PROSPECTIVE ANALYSIS OF ONCOLOGICAL SAFETY AND SHORT-TERM OUTCOMES P. Bianchi,[1]* C. Ceriani,[1] A. Locatelli,[1] G. Zampino,[2] B. Andreoni.[3] *1. Minimally Invasive Surgery Unit, European Institute of Oncology, Milano, Italy; 2. Division of Medical Oncology. European Institute of Oncology, Milano, Italy; 3. Division of General and Laparoscopic Surgery. European Institute of Oncology, Milano, Italy.*

Background. Aim of this study is to evaluate feasibility, oncological safety and short-term outcomes of robotic total mesorectal excision (TME) in rectal cancer. Methods. From January 2008 to September 2009 30 patients with histological proven adenocarcinoma of middle and lower rectum were enrolled in a prospective data base. Mean age was 66 years, 21 were male, mean body mass index was 21. Twenty-one patients (70%) received an anterior resection and 9 (30%) an abdomino-perineal resection. In 16 patients (64%) a preoperative radio-chemotherapy treatment was performed. The Robotic system used was a four arms Da Vinci® Surgical System (Intuitive Surgical, Sunnyvale, CA, USA). Results. Mean operative time was 258.2 minutes, first bowel movements was 2.5 days, mean hospital stay was 6.8 days. Major complications with a reoperation occurred in 2 patients, one anastomotic leakage and one small bowel perforation. A protective ileostomy was performed in 16 patients (43.3%). The overall percentage of post-operative complications was 16%. None conversion to laparotomy was necessary. The number of lymphnodes harvested per patient was 19.7. Circumferential margin was less than 1 mm in 2/30 patients (6%), distal resection margin was free of disease in all the cases. No local recurrences occurred in the follow up period (mean: 10 months). The American joint commitee on cancer pathological stage was: 15 patients stage I, 8 stage II and 7 stage III. Conclusions. Robotic TME in rectal cancer is a safe and feasible operation. The oncological safety is respected and short-term outcomes are similar to the laparoscopic series. Further studies are justified to evaluate which, between open, laparoscopic and robotic, is the better technique in the treatment of rectal cancer.

P155

MULTIMODAL TREATMENTS FOR LIVER METASTASES FROM MELANOMA: EXPERIENCE OF A SINGLE INSTITUTION P.L. Pilati,* E. Mammano, E. Tessari, M. Briarava, G. Mattara, C.R. Rossi, D. Nitti. *Clinica Chirurgica 2, Department of Surgical and Oncological Sciences, Padova, Italy.*

Background: Hepatic metastases are found in 15%-20% of patients with cutaneous melanoma and more frequently in patients with ocular melanoma (40% at diagnosis and 25% during the lifetime). Chemotherapy alone has limited efficacy against melanoma liver metastases: the median survival is poor, varying from 5 and 7 months, with a 1-yr survival less than 20%. Based on these data, some authors have investigated the role of surgery as a better curative treatment for liver metastases from melanoma. Methods: Thirty-six patients with liver metastases from melanoma (6 patients with previous cutaneous melanoma and 30 patients with previous ocular melanoma) were treated at our Institute from 2000 to 2008. Ten patients (27.7%) (2 from cutaneous melanoma, 8 from ocular melanoma) received neoadjuvant chemotherapy, 13 patients (36.1%) (2 from cutaneous melanoma, 11 from ocular melanoma) received adjuvant chemotherapy. The median time to liver metastases was 22 months (range 11-158). They underwent different surgical procedures: patients with resectable disease underwent liver resection (R0) (9 patients, 25%); patients with unresectable disease underwent liver resection (R1-R2) plus hepatic artery catheter implantation (4 patients, 11.1%), hepatic artery catheter implantation (20 patients, 55.6%) or isolated liver perfusion (3 patients, 8.3%). Results: The perioperative mortality rate was 3.4%. The median overall survival was 15 months, the 1-yr and 2-yr overall survival were respectively 61.7% and 16.5%. The survival is higher when considering only the group of curative resections, with a median of 23 months, and 1-yr and 2-yr overall survival were respectively of 74% and 59.6%. In the group of unresectable patients the median overall survival was 14 months and the 1-yr and 2-yr overall survival were respectively 59.5% and 11.8%. Conclusions: Despite the general poor prognosis of patients with either ocular or cutaneous melanoma to the liver, radical surgery allows the best survival advantage, but other surgical treatments also may add a survival benefit in selected patients compared to the systemic chemotherapic treatment, achieving long-term survival (56 months).

P156

Splenectomy Ameliorates Hematologic Toxicity of Intraperitoneal Hyperthermic Chemotherapy R.D. Becher,* P. Shen, J.H. Stewart, G. Russell, T. Bradley, E.A. Levine. *General Surgery, Wake Forest University, Winston-Salem, NC.*

Background: Peritoneal carcinomatosis (PC) is a terminal disease which can be treated with cytoreductive surgery and intraperitoneal hyperthermic chemotherapy (IPHC). This approach has been associated with prolonged survival and improved quality of life in select patients. To date, there has been no study investigating the effect of splenectomy on hematotoxicity in patients undergoing IPHC. Methods: Between December 2003 and December 2007, 195 patients with peritoneal carcinomatosis underwent first IPHC at our institution. Patients underwent cytoreduction to resect all gross tumor; splenectomy was performed only when there was gross tumor involvement of the spleen. This was followed by IPHC using Mitomycin or Oxaliplatin with a standard protocol. The chemotherapy was delivered at 40°C for 120 to 150 minutes. Postoperatively, patients were treated with Neupogen when their white blood cell (WBC) counts were <4. Hematologic adverse events were graded using the common toxicity criteria scale from 0 to 5, with 5 being most severe. Results: 101 of the 195 patients underwent splenectomy (52%). Cytopenia contributed to death in four splenectomy patients (2.1%) and one non-splenectomy patient (0.5%). In splenectomy patients, the average WBC nadir was 6.04 (SD 3.27; 95% CI 5.39 to 6.68), the average platelet nadir was 172.0 (SD 81.9; 95% CI 155.0 to 189.0), and the average hemoglobin (Hb) nadir was 7.51 (SD 1.01; 95%CI 7.31 to 7.71). In patients who didn't undergo splenectomy, the average WBC nadir was 4.60 (SD 2.41; 95% CI 4.11 to 5.10), the average platelet nadir

was 164.1 (SD 73.0; 95%CI 149.2 to 179.1), and the average Hb nadir was 8.19 (SD 1.84; 95%CI 7.82 to 8.57). Neupogen was administered in 29% of splenectomy patients versus in 43% of non-splenectomy patients (p-value=0.043). Conclusions: Splenectomy appears to ameliorate the hematologic toxicity in patients with peritoneal carcinomatosis undergoing IPHC. Splenectomy statistically significantly reduces the number of patients who require post-operative growth factor support. While not an indication for splenectomy, such an effect should be considered when evaluating the need for splenectomy during IPHC.

P157

Radical Resection after Chemoradiation Therapy for Locally Recurrent Rectal Cancer (LRRC) M. Ikeda,* M. Sekimoto, N. Haraguchi, I. Takemasa, T. Mizushima, H. Ishii, H. Yamamoto, Y. Doki, M. Mori. *Department of Surgery, Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Suita, Osaka, Japan.*

Background and Purpose: Surgical treatment for LRRC is challenging. Radical resection of fixed recurrent tumor with adjacent organs such as, bladder and sacral bone in severe scarring tissues requires highly skilled surgical team. Even with experienced surgical team, local re-recurrence rate is very high. In order to reduce local re-recurrence, we have employed preoperative chemoradiation therapy (CRT) since 2004. The aim of this study was to evaluate the efficacy of preoperative CRT and radical surgery for the treatment of LRRC. Patients and Methods: Twenty-eight pts (median age 60 years old, 36-72) had preoperative CRT consisted of CPT-11, UFT, and LV. Radiation therapy was given to the pelvis with daily fractions of 2.0Gy 5 days a week for 5 consecutive weeks. Surgery was performed 3 to 6 weeks after the completion of CRT. Results: Pts background: There were 21 males, 7 females, median age 60, ranging 36 to 72. Low anterior resection/abdominoperitoneal resection was carried out in 12 pts, and total pelvic excenteration was performed in 15 pts. Twenty pts (71%) had concomitant sacral or pubic bone resection. Median operation time was 875 min (380-1350), and median blood loss was 5090g (640-17300). In order to prevent pelvic sepsis anal preservation was done in 15 pts, and omental flap for 13 pts, rectus abdominis myocutaneous (RAM) flap for 9 pts. R0 operation was achieved in 26 (93%) pts. One patient could not discharge and died of pelvic sepsis. Incidence of pelvic sepsis and abscess was 25% and 21%, respectively. At median follow up of 3 years, three-year overall survival, relapse free survival, local re-recurrence free survival rates were 68%, 45%, and 56%, respectively. Incidence of local re-recurrence rate and distant metastasis was 25 % and 43%, respectively. Conclusion: Radical resection after CRT for LRRC is feasible, and may provide good impact on local control. Another treatment strategy for distant metastasis is mandatory.

P158

Is (neo)adjuvant treatment necessary in stage II of low-rectal cancer patients subjected to abdominosacral amputation of the rectum (ASAR)? M. Bebenek,[1]* W. Tupikowski,[1] K. Cisarz,[1] A. Balcerzak,[1] L. Wojciechowski,[1] A. Stankowska,[1] R. Tarkowski,[2] T. Sedziak,[1] R. Szulc,[1] B. Bednorz,[1] B. Kapturkiewicz.[1] *1. 1st Department of Surgical Oncology, Regional Comprehensive Cancer Center, Wroclaw, Poland; 2. Department of Oncology, Wroclaw Medical University, Wroclaw, Poland.*

INTRODUCTION (Neo)adjuvant treatment is a standard treatment procedure in low-rectal cancer patients in stage II subjected to surgery. We have assessed if such treatment really influences the therapeutic results in cases operated on by means of abdominosacral amputation of the rectum (ASAR). METHODS Low-rectal cancer patients (T3–T4, N0, n=105), qualified for surgery and operated on by means of ASAR between April 15th, 1998 and April 18th, 2006, were subjected to analysis. Two groups of patients were distinguished for initial analysis: 1) those who besides the surgery did not receive any other treatment, and 2) those who received neoadjuvant or adjuvant therapy. The latter group was further divided into two subgroups depending on the protocol of combined treatment being applied (neoadjuvant or adjuvant treatment). The subgroups were compared in terms of 5-year overall survivals, local recurrence rates and postoperative morbidity. RESULTS Patients who received neoadjuvant (n=32) or adjuvant treatment (n=31) in addition to surgical therapy did not differ in terms of overall morbidity (p=0.063), local recurrence rates (p=0.142), or percentages of 5-year overall survivals (p=0.447) from those patients who underwent surgery only (n=42). There were also no differences in therapeutic results among the groups that underwent various protocols of combined treatment. CONCLUSION The use of combined treatment does not influence the therapeutic results achieved in stage II of low-rectal cancer patients, who were operated on by means of ASAR.

P159

Management of hemochromatosis associated hepatocellular carcinoma S.W. Cho,* J.W. Marsh, D.A. Geller, T.C. Gamblin. *Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: Hemochromatosis is a rare but well-known risk factor for hepatocellular carcinoma. However, there is a paucity of literature specifically focusing on presentation, management strategies and outcomes of patients with hemochromatosis who developed HCC. Methods: We performed a retrospective review of patients seen at our tertiary liver cancer center between 1990 and 2008 who were diagnosed with HCC in the setting of hemochromatosis. We examined their demographic data, mode of presentation, investigation and management strategies employed and treatment outcome. Result: 40 patients with HCC and hemochromatosis were identified during the study period. Median age at HCC diagnosis was 66 and male to female ratio was 37:3. Presentations included abdominal pain (n=10), detection by screening test (n=7), hepatic decompensation (n=7), HCC in the explant liver specimen (n=6) and others (n=10). Median duration of documented hemochromatosis before HCC diagnosis was 6 years. Five patients were diagnosed with hemochromatosis at the same time as HCC. Only nine patients had documented evidence of regular screening for HCC prior to diagnosis, despite the fact that 23 patients (58%) received regular phlebotomy. 21 patients had alpha fetoprotein level greater than 20ng/ml at the time of HCC diagnosis. Seven patients developed HCC without evidence of cirrhosis. Treatment included orthotropic liver transplanatation (n=10), hemihepatectomy(n=2), partial hepatectomy (n=3), transcatheter arterial chemoembolization (n=17), therasphere treatment (n=4) and radiofrequency ablation (n=2). Kaplan-Meyer Survival Analysis showed that median survival after HCC diagnosis was 13 months (s.e = 4.6 months) and 15 patients were alive at last follow-up. Conclusion: Hemochromatosis can lead to HCC after a prolonged period. Although the diagnosis of hemochromatosis was established in the majority of patients, HCC screening was not utilized in the majority of cases. Screening should be emphasized to allow for earlier diagnosis and provided greater therapeutic options.

P160

WITHDRAWN

P161

Laparoscopic vs. Open Surgery for Rectal Cancer.A NSQIP analysis S. Nurkin,* R. Kakarla, D. Ruiz, R. Jeganathan, J. Turner, H. Tiszenkel. *New York Hospital Queens / Weill Cornell Medical College, Flushing, NY.*

BACKGROUND:Previous trials suggest overall morbidity and mortality after laparoscopic assisted anterior resection (LAAR) and open anterior resection (OAR) for rectal carcinoma to be generally comparable. However, most societies currently favor open resection for rectal cancer, and laparoscopic resection is not recommended outside a clinical trial. The objective of this study was to compare short term operative outcomes following LAAR to OAR.METHODS: Using the American College of Surgeons-National Surgical Quality Improvement Project's (ACS-NSQIP) participant-use file, patients were identified who underwent anterior resection with low pelvic anastamosis for cancer at 228 participating hospitals in 2007. Patients were excluded if they underwent emergent procedures, were ASA class 5, had metastatic disease or proximal diversion (ileostomy or colostomy). RESULTS: Of the 577 patients who underwent elective anterior resection for cancer, 154 (26.7%) had LAAR and 423 (73.3%)had OAR. There were no significant differences in age, gender, Race, ASA class, preoperative chemotherapy or body mass index (BMI) between the two groups. Patients that had the open approach were more likely to have had preoperative radiation (10 % vs.18%, p= 0.028). Operative time was greater in the laparoscopic group compared to the open group (205min. vs. 177min, p=0.0005). Patients with LAAR had a lower likelihood of developing post-op sepsis (2.6% vs 7.1%, p= 0.045) and septic shock(0% vs 3.3%, p =0.026). Laparoscopic resection had less need for intraoperative blood transfusions(0.03 vs. 0.17, p= 0.0265). The average number of days from operation to discharge were less in the laparoscopic group compared to the open group (5.6 vs. 8.1 days, p=0.0001). CONCLUSION: Laparoscopic resection in the

short term appears to be a safe approach to rectal cancer. Although it has slightly increased surgical and anesthesia times, it has significantly lower morbidity, like post-operative sepsis, less blood transfusions, need for re-intubation and shorter lengths of hospital stay. Prospective trials are required before laparoscopy becomes the standard of care for this disease, and we stress the importance of accrual in ACOSOG-Z6051.

P162

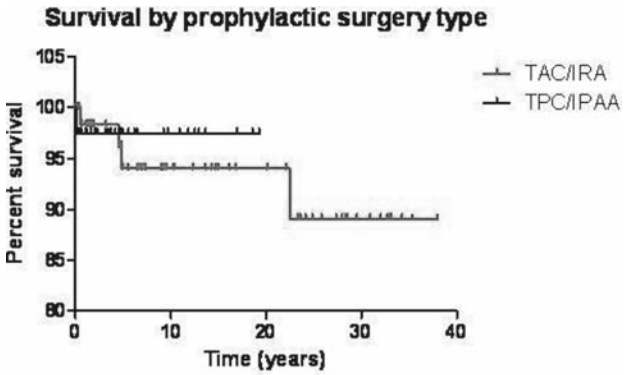
Number of Nodes Examined and the 12 Gene Colon Cancer Recurrence Score Predict Recurrence in Stage II Colon Cancer in 2 Independent Studies I.C. Lavery,[1]* M.J. O'Connell,[2] M. Lopatin,[3] G. Yothers,[4] K. Clark-Langone,[3] F. Baehner,[3] M. Lee,[3] S. Shak,[3] N. Wolmark.[2] *1. Cleveland Clinic, Cleveland, OH; 2. NSABP Foundation, Pittsburgh, PA; 3. Genomic Health, Inc., Redwood City, CA; 4. NSABP Biostat Center and University of Pittsburgh, Pittsburgh, PA.*

Background: Number of nodes examined is a prognostic factor included in the NCCN practice guidelines for stage II colon cancer. We assessed the prognostic value of nodes examined in conjunction w/ other variables including the 12-gene colon cancer Recurrence Score (RS) in stage II pts treated w/ surgery alone in an observational cohort from Cleveland Clinic (CC) and the NSABP C-01/C-02 study. Methods: Gene expression was quantitated by RT-PCR from 3x10μm manually microdissected fixed paraffin-embedded primary colon tumor sections. Cox regression models were used to examine the relationship between nodes examined, RS and recurrence risk. Results: Number of nodes examined was available for 630/635 pts(504 CC,126 NSABP). Median nodes examined was 18 (20 CC,11 NSABP) w/ 10% <6 nodes and 71% ≥12 nodes examined. Nodes examined increased with time in both studies (CC:65,75,76,88% pts w/ ≥12 nodes in 1981-5,1986-90,1991-5,1996-2000; NSABP:45,54% pts w/ ≥12 nodes in 1978-82,1983-8) and was significantly associated with recurrence risk as a continuous (HR=1.20 per 10 node decrease,p=0.005) and a categorical variable (HR=1.83 for <12 vs ≥12,p=0.003). Similar results were observed after controlling for age, tumor grade and surgery period. The relationship of nodes examined with recurrence risk was linear. Minimal association between RS and nodes examined (Spearman rho=-0.1) was observed. In a model w/ RS and continuous nodes, both RS and nodes examined were independent predictors of recurrence (p<0.001 and 0.01), w/ no significant interaction between RS and nodes examined (p=0.16). In a subset of CC patients w/ T stage and MMR available (n=468), RS and nodes examined remained significant independent predictors of recurrence in the presence of T stage and MMR status(p<0.001 and 0.028). Conclusions: Number of nodes examined and Recurrence Score are independent predictors of recurrence in stage II colon cancer following surgery, and both should be considered in risk assessment for the individual pt. Ongoing adoption of a target of at least 12 nodes assessed in clinical practice should be encouraged based on these results.

P163

Audit of a Single Institution Familial Adenomatous Polyposis Registry, 1971-2009 S. Dharmarajan,* G. Nandakumar, O. Wolff, S. Agarwal, J.W. Fleshman, A.Y. Lin. *Washington University, Saint Louis, MO.*

INTRODUCTION: Familial adenomatous polyposis (FAP) is a hereditary polyposis syndrome which untreated leads to colorectal cancer. Polyposis registries, together with prophylactic surgery, lead to increased life expectancy and reduction in colorectal cancer in FAP kindreds. The objective of this study was to report the experience of our institutional registry with FAP. METHODS: We performed a retrospective review of an institutional registry of families with FAP or attenuated FAP from January 1971 to September 2009. Data reviewed included patient demographics, genetic mutation testing, index colorectal operations and reoperations, and patient outcomes. The primary endpoint of the study was comparison of the durability of total abdominal colectomy with ileorectal anastomosis (TAC/IRA) versus total proctocolectomy with ileoanal pouch (TPC/IPAA) as prophylactic surgery for FAP. RESULTS: 207 patients from 155 families were identified. 166 (80%) had FAP, 25 (12%) had attenuated FAP, and 16 (8%) were not characterized. 70% of patients were diagnosed by family history while 26% were diagnosed due to symptoms. 61 patients (30%) underwent genetic testing, and of those, 40 (19%) had an identified mutation. As index operation for FAP, 64% underwent TAC/IRA, 31% underwent TPC/IPAA, and 5% had TPC with end ileostomy. 18 of the 91 (20%) patients who initially underwent TAC/IRA required completion proctectomy, with median time to completion proctectomy being 19.3 years, while only 1 (2%) patient who underwent TPC/IPAA required pouch excision (p=0.0067, RR=8.7). There was no difference in overall survival rates between TPC/IPAA and TAC/IRA with a mean followup of 9.4 years (p=0.79). CONCLUSIONS: Creation and maintenance of a polyposis registry facilitates identification of patients and at-risk family members, as 70% of patients in our registry were diagnosed secondary to positive family history. Rates of genetic testing are low, and barriers to access to genetic testing should be further investigated. Finally, TPC/IPAA is more durable prophylactic operation than TAC/IRA. However, TAC/IRA remains a valuable option in the surgical treatment of FAP.



P164

A Comparison of Hematologic Toxicity Profiles after Heated Intraperitoneal Chemotherapy with Oxaliplatin and Mitomycin-C K.I. Votanopoulos,* P. Shen, J.H. Stewart, G. Russell, E.A. Levine. *Wake Forest University, Winston Salem, NC.*

Background: Though peritoneal carcinomatosis (PC) of colorectal and appendiceal origin is consistent with metastatic disease complete cytoreduction with hyperthermic intraperitoneal chemotherapy (HIPEC) using mitomycin-C (MMC) can improve survival. A recent phase I study using hyperthermic intraperitoneal oxaliplatin has demonstrated its safety and appropriate dose. Herein is presented our institution's experience with the hematologic toxicities of the two agents. Methods: We performed a retrospective review of 187 patients with PC of colorectal or appendiceal origin who underwent HIPEC with MMC or oxaliplatin between Oct 2006 and Sep 2009. Hematologic toxicities were graded according to the NCI Common Terminology Criteria for Adverse Events Version 3.0. Filgrastim was routinely delivered when WBC was less than 4000; this WBC level is considered as the toxicity starting point for the purposes of this study. Results: From the 187 patients, 55 had oxaliplatin-based HIPEC while 132 patients received MMC. Splenectomy was performed in 96 (51%) patients due to disease involvement. Comparison of the splenectomy and non splenectomy groups by agent showed no differences in age, gender, race, or ECOG status. No statistically significant difference was observed in the rate of WBC toxicity comparing oxaliplatin and MMC perfused patients after splenectomy (14/28 (50%) vs. 22/67 (33%), p=0.16). The same was true for patients with spleen preservation (17/27(63%) vs. 34/65 (52%), p=0.37). In the non-splenectomy group, MMC was not associated with greater than grade 1 PLT toxicity (55% at 1) while oxaliplatin had 7% and 4% grade 2 and 4 toxicity, respectively (p=0.023). In the splenectomy group, grade 2, 3 and 4 PLT toxicities were observed in 4%, 0, and 3% MMC patients vs. 4%, 14%, and 4% oxaliplatin patients (p=0.016). Conclusions: Oxaliplatin-based HIPEC for peritoneal carcinomatosis of colorectal and appendiceal origin is associated with similar WBC toxicity and higher platelet toxicity compared to MMC-based HIPEC. These finding provide a conceptual framework for understanding hematologic toxicities associated with HIPEC for PC.

P165

Bowel Complications in Patients with Peritoneal Carcinomatosis of Appendiceal Origen Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy A. Sardi,* C. Omohwo, C.A. Nieroda, D.R. Holter, N. Athas, V. Gushchin. *Surgical Oncology, Mercy medical center, Baltimore, MD.*

Background: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is an extensive surgical procedure that includes peritonectomy and multiple organ resections. Bowel complications related to

anastomotic leaks and fistula formation are described in 3.8% to 11%. Other complications including diarrhea, dehydration, prolonged nausea and vomiting, high output syndrome, bowel obstruction, short gut syndrome and anastomotic bleed are less commonly described. The aim of this study is to analyze short and long term specific bowel complications related to CRS and HIPEC in patients with peritoneal carcinomatosis of appendiceal origin. Patients and Methods: A total of 102 patients presented for treatment. Four of these cases were unresectable. Bowel complications were studied in 98 procedures performed in 92 patients between January 1999 and December 2008. National Cancer Institute Common Toxicity Criteria (NCICTC) was used to categorize complications. Results: Grade III/IV complications were seen in 24% of patients. There was no operative mortality.Total number of bowel anastomosis was 121(range 0-5).No bowel fistula or anastomotic leaks ocurred. Sixty five patients (72.2%) had a complete cytoreduction (CC0-CC1.Median follow up was 20 months (R:2-101). The mean peritoneal cancer index score was 27. The bowel complications seen were diarrhea(14), dehydration(11), prolonged nausea and vomiting(8),high output syndrome(6), bowel obstruction(5), short gut syndrome(3), and post operative bleed at an anastomotic site(1).On univariate analysis, statistical significance was seen with the following variables; blood loss (p=0.03), duration of surgery (p=0.043), preoperative PCI >20 (p=0.03). Conclusion: CRS and HIPEC can be performed safely with a low incidence of anastomotic leaks and mortality even in patients with high volume disease. Long-term bowel complications can be significant; therefore an effort should be made to spare as much bowel as possible while performing a complete cytoreduction. A postoperative support program for these patients is essential to assure good outcome.

P166

Lymph Node Ratio and Recurrence in Sentinel Lymph Node Mapping vs Conventional Surgery in Colon Cancer M. Soni,* S. Saha, S. Sirop, A. Korant, B. Chakravarty, A. Singla, S. Pampanagouda, D. Iddings, D. Weise. *McLaren Regional Medical Center-Michigan State University, Flint, MI.*

Introduction: Lymph node metastasis remains the most important prognostic factor in resectable Colon Cancer (CCa). Sentinel Lymph Node Mapping (SLNM) has been shown to upstage up to 20% of patients(pts) to node positive status. Recently, the Lymph Node Ratio (LNR) has been shown to be a prognostic factor in stage III pts. Our study aims to correlate LNR to recurrence in SLNM vs Conventional Surgery(Conv Sx). **Methods:** A retrospective chart review of 119 pts undergoing SLNM and Conv Sx was undertaken. Final path was reviewed and only stage III pts were included in the analysis. LNR was calculated as the ratio of positive nodes to total nodes harvested for each patient. A minimum of 2 year follow up was studied for locoregional or distant recurrence. Pts with incomplete data and lost to follow up were not included. LNR and recurrence were compared among SLNM and Conv Sx pts. **Results:** Of a total of 119 pts, 58 and 61 underwent SLNM and Conv Sx respectively. Mean follow was 61 and 56 months in SLNM and Conv Sx respectively. There was no significant difference in demographics or T stage distribution between the 2 groups. Avg total nodes harvested were 16 vs 12.6 in SLNM and Conv Sx (p=0.007). In the SLNM group, 20% (12/58) of pts had only micrometastatic disease. Overall recurrence was 15.5%(9/58) vs 52% (32/61), p=.0001 in SLNM and Conv Sx. Overall LNR was 0.20 vs 0.31 in SLNM and Conv Sx. When LNR in recurrent vs non-recurrent tumors were compared in each group, recurrent Conv Sx pts had a statistically significant higher LNR than non recurrent Conv Sx pts (0.39 vs 0.22, p=.01). In the SLNM group, LNR was higher among recurrent tumors but without statistical significance (0.24 vs 0.19, p=0.45). **Conclusion:** LNR appears to be a prognostic factor among Stage III pts receiving Conv Sx but did not correlate with recurrence among SLNM pts. Recurrence is lower among SLNM pts possibly due to the diagnosis and treatment of micrometastasis with low volume disease.

Table 1: LNR and Recurrence in SLNM vs Conv Sx

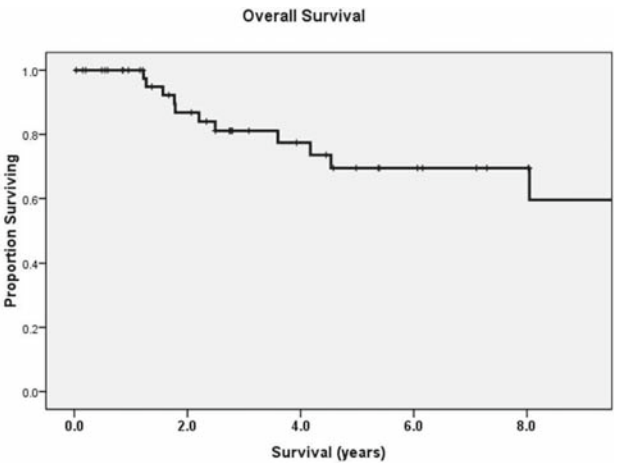
	SLNM	Conv Sx	p value
Avg. Total Nodes Harvested	16	12.6	0.007
Overall Recurrence	15.5%	52%	.0001
Overall LNR	0.20	0.31	0.015
	LNR in Recurrence	LNR in non-recurrence	
SLNM	0.24	0.19	.45
Conv Sx	0.39	.22	.01

SLNM=Sentinel Lymph Node Mapping, Conv Sx=Conventional Surgery, LNR=Lymph Node Ratio Avg.=Average

P167

Multi-cycle early post-operative intraperitoneal chemotherapy (EPIC) following cytoreductive surgery for appendiceal neoplasms with isolated peritoneal metastasis P.L. Wagner,* D. Jones, A. Aronova, P.B. Paty, G.M. Nash. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Although cytoreductive surgery (CRS) and intraperitoneal chemotherapy (IPC) are considered routine for the treatment of appendiceal neoplasms with isolated peritoneal metastasis, the optimal method of IPC administration has not been established. At our institution, patients who undergo complete CRS in this setting are treated with multiple cycles of early postoperative intraperitoneal chemotherapy (EPIC). Methods: Patients having complete CRS and EPIC with 5-fluoro-2'-deoxyuridine (FUDR) plus leucovorin (LV) for appendiceal neoplasms with peritoneal metastases from 1995 to 2009 were evaluated for 30-day morbidity, cancer recurrence, and survival. Disease recurrence and overall survival were compared using Kaplan Meier analysis. Median follow-up was 2.7 years (range, 0-12 years). Results: 50 patients (30 female), with a median age of 48 years (min-max, 26-66), underwent placement of IP catheter after complete CRS, followed by treatment with a median of 4 cycles (min-max, 1-9) of IP FUDR (1000 mg/m2 daily for 3 days) and leucovorin (240 mg/m2). The median hospital length of stay was 9 days (max, 29). Complications occurred in 34% of patients, with major complications in 12% (3 abdominal abscesses, 1 deep vein thrombosis, 1 abdominal hemorrhage, 1 IP port malfunction). There were no 30-day mortalities. The 5-year recurrence free interval was 43%. Among 22 patients with recurrence of disease, 17 recurred only within the peritoneum. Median overall survival was 9.8 years. Conclusions: CRS with multiple cycles of EPIC is safe and achieves survival results similar to the published outcomes of other IPC protocols, including hyperthermic intraperitoneal chemotherapy (HIPEC). Prospective trials are warranted to compare the various methods of IPC used in this clinical setting.



P168

Cytoreductive Surgery and Intraperitoneal Hyperthermic Chemotherapy Perfusion For Peritoenal Surface Malignancies: Effective, But At What Cost? A. Shaligram,[1]* G. Mann,[1] L. Mann.[2] *1. Surgery, University of Washington, Seattle, WA; 2. None, Seattle, WA.*

Introduction: Peritoneal carcinomatosis is seldom curable. Maximal Cytoreductive Surgery (CS) combined with Intraperitoneal Hypethermic Chemotherapy Perfusion (IPHC) has been used in efforts to improve oncologic outcomes, but is an aggressive therapy associated with high complication rates. Purpose: To review the oncologic outcomes, morbidity and mortality associated with CS/IPHC performed by a single surgeon at University of Washington Medical Center. Methods: IRB approved retrospective chart review . 50 consecutive patients undergoing 53 CS/IPHC (mitomicin C or cisplatin) treatments from June 2002 to May 2009 were included. Charts were reviewed for patient, tumor

and treatment factors. Morbidity was analyzed and graded, mortality and oncologic outcomes were assessed. Results: Median age was 57 (range 24-76) with 36 female patients. Most frequent pathological diagnosis was appendiceal neoplasm (62%), followed by colorectal cancer (16%), mesothelioma (14%), and other (8%). The median peritoneal carcinomatosis index was 12 (Range 0-36 of a possible 39). Complete gross cytoreduction was achieved in 91% of operations. Perioperative mortality was 8%. Almost half of all patients had some complication: major in 21%, and minor in 28%. Eleven percent developed an intra-abdominal abscess requiring drainage and eight percent developed an enterocutaneous fistula requiring parenteral nutrition and/or surgical repair. Median survival was 25 months. Conclusion: CS/IPHC for peritoneal carcinomatosis has a significant morbidity and mortality. Durable responses are possible, and it should be considered for select patients after careful consideration of risks.

P169

Incidence and occurrence pattern of second primary malignancies after resection of rectal carcinoid tumors K. Sato,[1]* T. Akasu,[1] S. Yamamoto,[1] T. Matsuda,[2] S. Fujita,[1] Y. Moriya,[1] Y. Saito.[2] *1. Colorectal Surgery Division, National Cancer Center Hospital, Tokyo, Japan; 2. Endoscopy Division, National Cancer Center Hospital, Tokyo, Japan.*

BACKGROUND Strategy of surveillance after resection of rectal carcinoid tumors has not been established yet. To establish strategy for efficient surveillance system, understanding of incidence and occurrence pattern of second primary malignancies is essential. Therefore, the aim of this study was to evaluate incidence and occurrence pattern of second primary malignancies after resection of rectal carcinoid tumors, retrospectively. METHODS Between 1970 and 2005, 145 patients with primary rectal carcinoid tumors were treated with endoscopic resection (n = 80), local excision (n = 39), and radical surgery (n = 26). There were 89 men and 56 women with a median age of 55 (range 27-85) years. This study included only patients followed for more than 3 years. Median follow-up time was 7.4 (range 3.2-32.1) years. Data from prospectively maintained database and medical records were evaluated retrospectively. RESULTS Median tumor size was 7 (range 2-100) mm. There were 138 pT1, 4 pT2, and 3 pT3 tumors. Histologic TNM staging (for rectal cancer) included stage I in 129 patients, II in 1, III in 13, and IV in 2. Eleven patients (8%) had been treated for malignant tumors (stomach, 3; uterus, 2; large bowel, 1; urinary bladder, 1; thyroid, 1; pharynx, 1; malignant lymphoma, 1) before resection of rectal carcinoid tumors. Twenty-two patients (15%) had synchronous malignancies (large bowel, 17; stomach, 4; lung, 1; pancreas, 1; malignant lymphoma, 1). Thirteen patients (9%) developed second primary malignancies (prostate, 4; stomach, 3; large bowel, 2; liver, 2; lung, 2). CONCLUSION Nearly 10% of patients develop second primary malignancies after curative treatment for rectal carcinoid tumors. The present results suggest the need for close surveillance of the gastrointestinal, genitourinary, and respiratory organs. Since the incidence of synchronous malignancies is also high, intensive screening for gastrointestinal, especially colorectal tumors before treatment is recommended.

P170

Oncologic efficacy of minimally invasive esophagectomy (MIE) after neoadjuvant chemoradiotherapy (NT) in esophageal cancer A.S. Khithani,* D. Christian, J.G. Barton, J. Jay, D. Jeyarajah. *Methodist Dallas Medical Center, Dallas, TX.*

Introduction: Minimally invasive techniques for esophagectomy have improved patient outcomes while maintaining oncologic principles. NT 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 MIE in patients who undergo NT at a non-university tertiary care center (NUTCC). Methods: MIE by combined thoracoscopic and laparoscopic approaches performed cooperatively by two surgeons between September 2005 and September 2009 were reviewed. The patients were studied as two groups, one group that received NT (Neoadjuvant group) and the other receiving no NT (Primary surgery group). Preoperative, intraoperative, postoperative, and histopathologic data were evaluated. Results: Forty two (42) patients underwent MIE for esophageal malignancies. Of these, 62% (26 patients) received NT. In the neoadjuvant group, 69% of patients were preoperative stage IIA, 8% were stage IIB, and 23% were stage III. The comparison between the 2 groups is shown in Table 1. Extension to a miniceliotomy was required in 2 patients, both from the neoadjuvant group. Four patients had positive margins, all from the neoadjuvant group. Conclusions: MIE can be safely performed after NT. Complete pathologic response can be achieved with a preoperative approach in 35% of patients with esophageal cancer. MIE should be considered as safe as open resection after preoperative treatment.

Table 1: Table showing comparison of perioperative outcome between two groups.

	Neoadjuvant group	Primary surgery group
No. of pts	26 (58%)	16 (42%)
OR time (mins)	263(range, 242-262)	271(range, 202-444)
Blood loss (mL)	300(range, 100-700)	200(range, 150-600)
Blood Transfusions	35%	13%
Length of stay (days)	10(range, 8-22)	11(range, 8-54)
Morbidity	62%	56%
Leak	0	0
Mortality	0	0
Complete pathologic response	35%	n/a

P171

The Delivery and Timing of Radiation Therapy Impact Survival in Patients with Rectal Adenocarcinoma Y. Akmal,[1]* A. Artinyan,[2] B. Mailey,[1] W. Lee,[1] S. Christopher,[1] S.P. Mckenzie,[1] A. Pigazzi,[1] J. Garcia-Aguilar,[1] J. Kim.[1] *1. General Oncologic Surgery, City Of Hope National Medical Center, Duarte, CA; 2. Baylor College of Medicine, Michael E. Debakey VA Medical Center, Houston, TX.*

Background: Although the delivery of radiation therapy is standard of care for locally advanced rectal cancer, a survival advantage and optimal timing of administration have been much debated. Moreover, current reports comparing neoadjuvant with adjuvant radiation therapy regimens have shown improvements in local disease control without an overall survival benefit. We examined the use of radiation therapy in the management of rectal cancer in a large population-based cohort. Methods: The Los Angeles County Cancer Surveillance Program (CSP) database was used to identify patients with local [T(1-2)N0] or regional [T(3-4)N0 or T(1-4)N(1-2)] disease who underwent curative-intent surgical resection for rectal adenocarcinoma between 1988 and 2006. Patients were stratified by receipt of radiation therapy (yes vs. no) and timing of radiation administration (neoadjuvant vs. adjuvant). Results: Using CSP 6,918 patients were identified. From this cohort, 2,819 (41%) patients received radiation therapy. After stratifying by extent of disease, radiation therapy improved survival for patients with local disease [median survival (MS) 156 vs. 137 months; log-rank, P=0.014) and regional disease (MS 72 vs. 55 months; log-rank, P<0.001). On multivariate analysis, radiation therapy independently predicted survival only in patients with regional disease (HR 1.12, 95% CI 1.01-1.25, P=0.031). When timing of radiation therapy was examined, neoadjuvant radiation was associated with improved survival compared with adjuvant radiation therapy for patients with local disease only (MS 160 vs. 153 months; log-rank, P=0.024). On multivariate analysis, adjuvant radiation therapy was an independent predictor of poorer survival in patients with local disease (HR 1.38, 95% CI 1.04-1.84, P=0.027). Conclusions: Our large population-based cohort study suggests that radiation therapy improves survival for patients with rectal adenocarcinoma. Furthermore, our results also suggest that the timing of radiation administration may influence overall survival. Accordingly, better efforts should be made to treat the large number of eligible patients who fail to receive radiation therapy.

P172

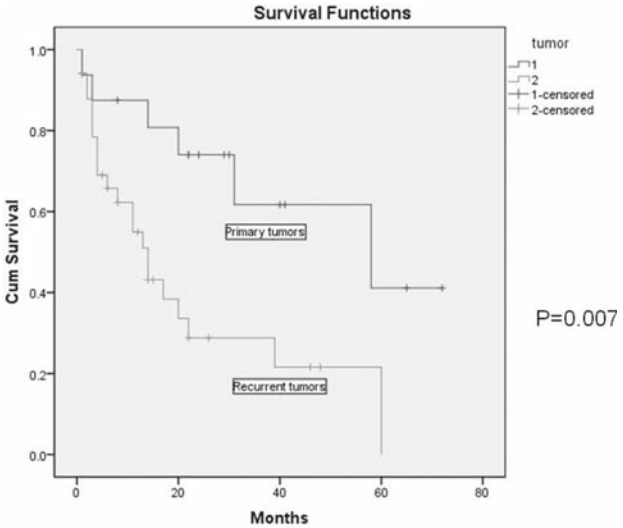
Hyperthermic Chemotherapy for Ovarian Cancer – Report of the HYPERO Registry C. Helm,[1]* S.D. Richard,[2] J. Pan,[1] D. Bartlett,[3] M.D. Goodman,[4] R. Hoefer,[5] S.S. Lentz,[6] E.A. Levine,[7] B.W. Loggie,[8] D.S. Metzinger,[1] B. Miller,[6] J.E. Spellman,[9] P.H. Sugarbaker,[10] S.N. Rai,[1] R.P. Edwards.[2] *1. James Graham Brown Cancer Center, Louisville, KY; 2. Magee-Women's Hospital, Pittsburgh, PA; 3. Division of Surgical Oncology, University of Pittsburgh Medical Center, Pittsburgh, PA; 4. Division of Surgical Oncology, Tufts Medical Center, Boston, MA; 5. Surgical Oncology Associates, Newport News, VA; 6. Division of Gynecologic Oncology, Wake Forest University, Winston-Salem, NC; 7. Division of Surgical Oncology, Wake Forest University, Winston-Salem, NC; 8. Division of Surgical Oncology, Creighton University, Omaha, NE; 9. Oncologic Surgery, Beebe Medical Center, Rehoboth Beach, DE; 10. Washington Hospital Center, Washington, DC.*

Introduction: Information on hyperthermic intraperitoneal chemotherapy (HIPEC) for invasive epithelial ovarian cancer (OC) is based on relatively small, heterogeneous studies. HYPERO is designed to collect and analyze a larger dataset gathered from multiple, collaborating institutions. Methods: Internet-based registry. Eligibility includes women with OC treated with HIPEC. Borderline and non-epithelial cancers are excluded. Data collected in format to allow analysis of both surgical and gynecological factors. Results:141 women eligible for analysis treated front-line (n=26), interval debulking (n=19),consolidation (n=12) and recurrence (n=83). Mean perfusion temperatures were inflow 38.5- 43.60C (median 41.90C) and outflow 36.9 – 42.90C (median 410C) for 30-120 minutes. Treatment was with platinum agent (n=72), mitomycin (n=53) or combination (n=14). Median follow-up 18 month (range: 0.3 to 140.5). 110 of 141 (78%) recurred and 87 died, three(0.5%) dying within 30 days of surgery. Median overall survival was 30.3m (95% CI:23.0-37.6. For recurrence (n=83) median survival was 23.5m (95% CI:16.4-30.6) despite 85% having widespread disease and 28.5% being platinum resistant. Factors significant for increased survival in multivariable analysis were sensitive to platinum response (p=0.048), completeness of cytoreduction scores of 1 or 0 (p=0.025), carboplatin alone or combination of two or more chemotherapy agents used (p=0.011) and duration of hospital stays of 10 of less days (p=0.021). Toxicity (%) included: any toxicity 69.6, grade 3 electrolytes 34.9, grade 3 creatinemia 7.9, infection/sepsis 20.6, gastro-intestinal 13.5, fistula 3.6 and wound 8.5. Toxicity overall was related to longer duration of surgery whilst wound and septic complications were related to maximum inflow temperature. Conclusions: HIPEC can be incorporated into treatment of OC with reasonable morbidity and mortality. It may well be improving outcome in recurrent disease – analysis of outcomes at other time-points still needs greater numbers. Carboplatin may be the best agent for platinum-sensitive recurrent disease. Continued research into HIPEC in OC should be encouraged.

P173

Open thermo-surgical ablation of inoperable primary or recurrent/metastatic abdomino-pelvic malignancies C. Gajdos,* M.D. McCarter, N.W. Pearlman. *University of Colorado, Aurora,, CO.*

Introduction: The treatment options for patients with inoperable (INOP) primary (PT) or recurrent/metastatic (RM) abdomino-pelvic (AP) malignancies are limited and these patients have a short lifespan. The purpose of our study was to determine the impact of a combined open radio-frequency ablation (RFA) and surgical debulking of otherwise INOP tumors. Methods: Fifty consecutive patients were identified from an IRB approved, prospectively collected database undergoing ablation for INOP AP malignancies via conventional surgical methods in a single institution between 07/2003 and 09/2009. Patients were selected for debulking if they had a dominant mass that caused significant symptoms. All tumors were debulked to the extent possible with a combination of serial application of conventional RF probe and surgical curettage/resection. Results: Sixteen patients had PT and 34 presented with a RM malignancy. The PTs were AP sarcomas (11 patients), colorectal cancer (CRC) (2) one gastric cancer, mucinous cystic pancreatic neoplasm and carcinoid. The RM tumors were CRCs (16 patients), AP sarcomas (13), and one prostate cancer, bladder cancer, melanoma, adrenal cancer and pseudomyxoma peritonei. Five out of the 16 patients with PT were explored at outside institutions and found to be unresectable. All patients in the RM group had prior surgical procedures and 16 out of 34 had more than 1 surgery with the second procedure aimed at recurrence resection. Twenty-two patients were alive and 28 died as of September, 2009. Follow-up ranged from 1 to 72 months. The median survival for patients who died was 9.5 months vs. 22 months for those who were still alive. The 5-year survival for all patients was 18%. Patients with a PT had a 5-year survival of 41% compared to no 5-year survivors in the RM group (the last patient died at 60 months in this group)(P=0.007) (Fig.1) Conclusions: Thermo-surgical ablation of PT and RM AP malignancies maybe associated with moderate long term survival in selected, symptomatic patients. Patients with ablated PTs have a significantly longer survival than patients who have ablation for RM disease.



P174

The Impact of Metastatic Lymph Node Ratio on Survival in Node-Positive Colon Cancer S. Bordoli,[2]* S.S. Kukreja,[2] J. Velasco,[1] T.J. Hieken.[3] *1. Surgery, NorthShore University Health System Skokie Hospital, Skokie, IL; 2. Rush University Medical Center, Chicago, IL; 3. Rush Medical College, Chicago, IL.*

Introduction: The degree of metastatic lymph node involvement after curative resection for Stage III colon cancer is the most important determinant of long-term survival. Recent data suggest that the total number of involved, negative and analyzed nodes and metastatic LN ratio (LNR) may have additional prognostic significance and clinical value. We undertook this study to explore the relationship of LNR to survival in colon cancer patients in our community teaching hospital. Methods: From our Cancer Registry, from 685 consecutive colon cancer patients undergoing curative resection between 1995-2007, we identified 184 stage III patients, followed a median of 4 years, who are the focus of this analysis. Data was verified by chart and pathology note review. Statistical analysis was performed with an SAS statistical software package. Results: The mean # of lymph nodes (LN) analyzed per patient was 15.8±0.63 (median 15) and 67.4% had ≥12 LNs. The mean # of metastatic LNs (LN+) was 4.02±0.29 (median 3, range 1 to 23). The mean LNR was 0.29±0.018 (range 0.026-1.0; quartiles ≤ 0.1, 0.11-0.2, 0.21-0.44 and >0.44). LNR correlated with # of LNs+ (R2=0.56) but not with # of LNs removed and was greater for patients who recurred (0.345±0.028 vs. 0.255±0.023, p=0.01). During follow up, 70/184 (38%) developed recurrence and 52/184 (28%) died of disease. Factors significantly affecting cancer-specific overall survival (CSS) included T stage (p=0.04), tumor grade (p=0.01), N stage (p=0.05), # of LNs+ (p=0.01), highest quartile LNR (p=0.002) and adjuvant chemotherapy (p=0.02). CSS was unaffected by patient gender, tumor location, preop CEA, # of LNs removed, whether ≥12 LNs were removed or # of negative LNs. In multivariate analysis LNR was the most significant factor predicting death from colon cancer (risk ratio 6.45, CI 1.55-22.7, p=0.01). Conclusions: In our series, LNR was a potent predictor of survival. LNR may be a beneficial addition to standard staging for Stage III colon cancer patients to identify patients at greatest risk of relapse, select those most likely to benefit from aggressive therapy and surveillance, and refine patient stratification within clinical trials.

P175

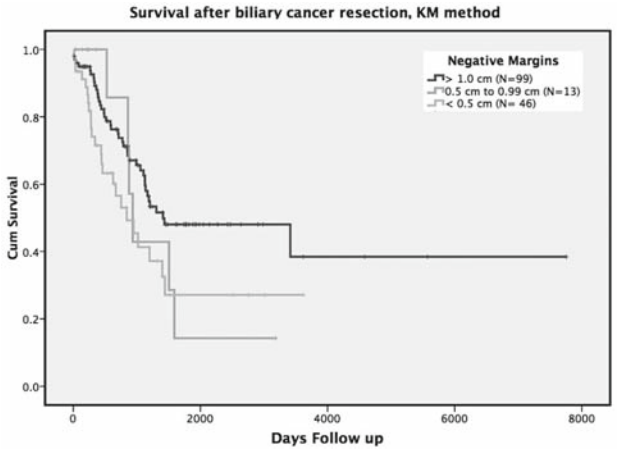
Gene expression profile related to cisplatin intrinsic resistance using our established anal canal squamous cell lines A. Takeda.* *Digestive Surgery, International University of Health and Welfare Hospital, Tochigi, Japan.*

Background: Platinum drugs resistance is a complex process based in the alternation of genes that belong to several pathways related to drug metabolism. To clarify these mechanisms, we analyzed gene expression profile using our established six anal canal squamous cell lines (SaTM-1) with different sensitivity to cisplatin (CDDP). The aim of this work was to compare gene expression profile between high and low IC50 lines to determine genes that might play a role as CDDP intrinsic resistance. **Methods**: In order to investigate susceptibility to CDDP, 3500 cells were treated with several concentration (2.5, 5, 7.5, 10, 15, 20, 50 µg/ml) for 24 hours. The relative number of viable cells was assessed using the CellTiter 96 AQueous Kit. Gene expression profile was analyzed through microarray technology using Affymetrix GeneChipR. The p values of the identified genes were evaluated by the difference in signal values between high and low IC50 group. Of these, genes having p value < 0.0001 were selected, then, greater 2.5-fold average signal values compared with those of low IC50 genes were selected. The final option was to obtain several genes with > signal values of 3000 from the high IC50 group. We finally performed to visualize and cross-validate the network among selected genes with pathway analysis with MetaCoreTM system.**Results**: The cytotoxic effects of CDDP showed different behavior, divided into two groups. The IC50 score of SaTM-1A, B and E were two-fold lower than those of SaTM-1C, D and F. Hierarchical clustering produced two major clusters. The significant p value was set at lesser than 0.0001 and defined 1463 genes below the p value. A total of 209 genes were selected which have greater two-fold average signal values between high and low IC50 groups. Of the 209 genes, the selected 36 genes with > 3000 of average signal values in high IC50 group are selected. Some of the genes identified were suggested to be potentially associated with the chemotherapeutic targets for CDDP.**Conclusions**: An expression profile showed to be related to CDDP intrinsic resistance, which should be validated to establish their potential role in treatment selection.

P176

Neoadjuvant and Adjuvant Therapy Does Not Improve Survival in Resected Biliary Cancers E.S. Glazer,* V.G. Ellis, E.K. Abdalla, J.N. Vauthey, S.A. Curley. *Surgical Oncology, M.D. Anderson Cancer Center, Houston, TX.*

Introduction: The use of neoadjuvant and adjuvant chemotherapy or radiotherapy is common with many human cancers. There is a paucity of data on multidisciplinary treatment of biliary cancers. We reviewed our experience with resected biliary tract cancers to determine if neoadjuvant or adjuvant therapy improved survival. Methods: A prospective database was queried to identify patients undergoing resection for gall bladder cancer (GBC) and cholangiocarcinoma (CC). Demographic, operative, and outcome/survival data were collected. Two-tailed Fisher's exact test and Student's t-test were used to determine significant differences between groups. Results: We identified 158 patients who underwent resection for primary GBC (n=63) and CC (n=95). The average age was 61.1 ± 11.9 years. Overall, survival was 55.1% at a median follow-up of 25.5 months (range 10 days to 21 years). 18.4% of patients received neoadjuvant chemotherapy, the majority being gemcitabine-based. Two patients received preoperative chemoradiotherapy. 48.7% of patients received adjuvant chemotherapy (majority being capecitabine-based), while 15.8% received postoperative chemoradiotherapy. In patients who received neoadjuvant therapy, surgical resection was delayed on average for 6.8 months ($p < 0.0001$). Immediate resection without neoadjuvant chemotherapy increased median survival from 24.3 months to 33.9 months ($p \sim 0.01$). Adjuvant therapy did not significantly prolong survival ($p >> 0.05$). Negative margins of at least 1 cm were associated with a Kaplan-Meier 5 year survival rate of 48.1%, margins of 0.5 cm to 0.9 cm resulted in a 14.3% rate, and margins less than 0.5 cm resulted in a 27.1%% rate ($p < 0.01$ using 1 cm cut-off limit). Conclusions: Early surgical resection of biliary malignancies with adequate tumor free margins provides the best probability for long-term survival. Currently, neoadjuvant or adjuvant therapy does not improve survival compared to resection alone indicating that more active and effective agents are needed.



Immediate resection of biliary cancers with margins greater than 1 cm offers the best probability for significant long-term survival ($p < 0.01$).

P177

Risk-adjustment models in assessing postoperative mortality following transthoracic esophagectomy in patients with esophageal cancer D.J. Bosch,[1]* B.B. Pultrum,[1] G.H. De Bock,[2] J.K. Oosterhuis,[3] M.G. Rodgers,[3] J.T. Plukker.[1] *1. Dept Surgical Oncology, University Medical Center Groningen, Groningen, Groningen, Netherlands; 2. University Medical Center Groningen, Dept. of epidemiology, Groningen, Groningen, Netherlands; 3. University Medical Center Groningen, Dept. of anesthesiology, Groningen, Groningen, Netherlands.*

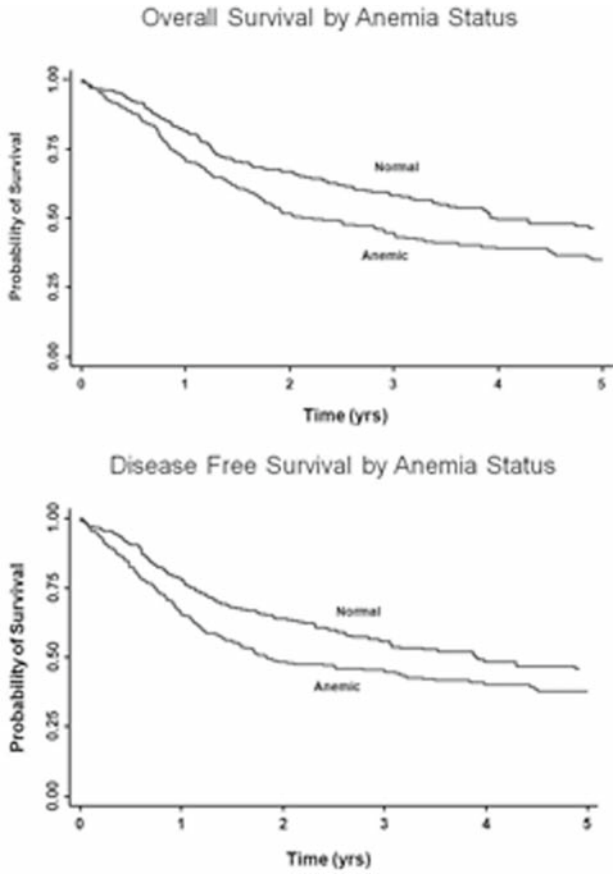
Introduction: To assess postoperative mortality after transthoracic esophagectomy we evaluated five frequently used risk-prediction models, including the P-POSSUM, O-POSSUM), the Charlson and its age adjusted score (ACCI) and the ASA score. Methods: Data of 278 consecutive esophageal cancer patients treated between 1991 and 2007 was analyzed to predict postoperative mortality, defined as in-hospital and 90-day mortality Data were analysed regarding calibration and discrimination. Hosmer and Lemeshow goodness-of-fit (HLG) test used for calibration and the area under the Receiver Operator Curve (ROC) for discrimination. Results: Observed postoperative mortality rate was 6.5% (18 patients). P- and O-POSSUM predicted 6.2% and 9.7%, respectively. The HLG test was applied to each risk-prediction model, respectively for P-POSSUM (p=0.035); O-POSSUM (p=0.529); Charlson score (p=0.659); ACCI score (p=0.270) and ASA score (p=0.210). The ROC curve indicated discriminatory power of 0.766 (95% CI:0.67-0.86) for P-POSSUM and 0.756 (95% CI:0.67-0.84) for O-POSSUM, but less in the other models: Charlson: 0.567 (95% CI:0.42-0.71), ACCI: 0.684 (95% CI:0.58-0.79) and ASA: 0.635 (95% CI:0.51-0.76). Conclusion: Postoperative mortality after esophagectomy is best predicted by O-POSSUM. However, in identifying patients at risk it still overpredicted postoperative mortality in all risk groups.

P178

Pre-operative anemia decreases survival after esophagectomy for cancer M. Melis,[1]* K.L. Meredith,[2] S. Hoffe,[2] R. Shridar,[2] J.M. McLoughlin,[3] J.M. Weber,[2] R.C. Karl.[2] *1. Surgery, New York University, New York, NY; 2. Moffitt Cancer Center, Tampa, FL; 3. Medical College of Georgia, Augusta, GA.*

Background Malignant diseases and their treatment are frequently associated with anemia. Anemia has been reported to reduce survival for a variety of cancers, including esophageal cancers treated solely with chemo-radiation. We sought to measure effects of pre-operative anemia on survival following esophagectomy. Methods According to the World Health Organization classification, anemia was defined as hemoglobin <13 g/dL in men or <12 g/dL in women. From our comprehensive esophageal cancer database of 541 patients we identified 259 anemic and 254 non-anemic patients that underwent esophagectomy. Differences between groups were evaluated with Pearson's $\chi 2$ or Fisher exact test as appropriate. Cumulative survivals were calculated by the Kaplan-Meier method; differences in survival were analyzed by log rank

method. The study end-points were overall and recurrence-free survivals. Results Four-hundred thirty men and 83 women (mean age 63 years, range 28-86) underwent esophagectomy during the period 1994-2008. Pre-operatively, 254 (49.5%) patients were anemic. Anemic patients presented more often with kidney disease (4.1% vs. 0.8%, p 0.01) and advanced esophageal cancer (Stage III 55.7% vs. 32.8%, p 0.001). They were more likely to receive neoadjuvant treatment (72.0% vs.40.5%, p 0.001), trans-hiatal surgery (26.4% vs. 18.5%, p 0.005) and peri-operative blood transfusions (58.7% vs. 44.4%, p 0.001). There were no differences between groups in terms of peri-operative morbidity or mortality. At median follow-up of 25 months, 5-year overall and recurrence-free survivals were significantly worse in anemic patients (respectively 37% vs. 46%, p 0.002 and 34% vs. 45%, p 0.002; see Figure 1). Multivariate analysis confirmed that anemia negatively affects survival, independent from other factors such as stage, administration of adjuvant treatment or blood transfusion (p 0.01). Conclusions In our experience, pre-operative anemia was independently associated with worse survival after esophagectomy for cancer. Our results are in line with other reports suggesting that anemia and resulting hypoxia may favor tumor progression, likely through enhanced tumor angiogenesis.



P179

Severe Electrolyte Disturbances After Hyperthermic Intraperitoneal Chemotherapy: Oxaliplatin Versus Mitomycin C

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Introduction: Oxaliplatin is increasingly used for hyperthermic intraperitoneal chemotherapy (HIPC) for patients with peritoneal metastases. The aim of this study was to review early electrolyte disturbances after HIPC with oxaliplatin versus mitomycin C. Methods: We evaluated the data of patients enrolled in a single-institution prospective clinical trial who underwent cytoreductive surgery and received HIPC with mitomycin C or oxaliplatin. We reviewed patient demographics, cancer pathology, operative course, HIPC administration, and postoperative electrolyte disturbances. Measured postoperative sodium values were corrected for systemic hyperglycemia using the correction formula: (measured Na+) x [(glucose-100/100) x 1.6]. Results: From January 2002 to April 2009 we performed 80 HIPC procedures. Sixty patients (75%) received mitomycin C (dose range 12.5-50 mg/m2) carried in lactated ringers solution. Twenty patients (25%) received oxaliplatin (dose range 300-400mg/m2) carried in 5% dextrose solution. The most common malignancies were appendix (n= 43, 53.8%) and colon (n=22, 27.5%). The table summarizes patient electrolyte data. Compared to mitomycin C, patients receiving oxaliplatin had significant 24-hour postoperative uncorrected hyponatremia ($p<0.001$), corrected hyponatremia ($p<0.001$), hyperglycemia ($p<0.001$), and metabolic acidosis ($p<0.001$). Hypomagnesemia was associated with both HIPC agents. We found no association between oxaliplatin dose and electrolyte disturbances. In the oxaliplatin group, corrected (mean 130.5) and uncorrected (mean 127.4) sodium levels were significantly lower than preoperative levels (mean 139.9, $p<0.001$); however, sodium levels returned to normal within 72 hours in 80% of patients. One patient developed severe cerebral edema related to post-HIPC hyponatremia. The 30-day mortality was 0% in both groups. Conclusion: Compared to mitomycin C, HIPC with oxaliplatin is associated with significant but predictable electrolyte disturbances; close monitoring with early correction is imperative to maximize perioperative care. Further studies are needed to provide mechanistic insight.

Preoperative and 24-hour postoperative electrolyte data

	Mitomycin C	Oxaliplatin
	n=60	n=20
	Mean	Mean
Preoperative Data		
Sodium	139.5	139.9
Glucose	116.3	101.7
Bicarbonate	26.9	26.5
Creatinine	0.93	0.82
Magnesium	2.0	2.1
Postoperative Data		
Maximum Uncorrected Sodium	135.6	127.4*
Maximum Glucose	162.6	288.1*
Maximum Bicarbonate	24.3	20.4*
Maximum Magnesium	1.3	1.2

*$p<0.05$

P180

CYTOREDUCTION AND HYPERTHERMIC INTRAPERITONEAL CHEMOPERFUSION IN WOMEN WITH HEAVILY PRETREATED RECURRENT OVARIAN CANCER

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Background We evaluated the use of cytoreductive surgery with hyperthermic intraperitoneal chemoperfusion (HIPEC) in patients with recurrent stage III ovarian cancer. Methods Extensive cytoreduction was followed by HIPEC using cisplatin or oxaliplatin. The extent of disease was scored using a simplified peritoneal cancer index (range 0-7). Results Forty-two women were treated from October 2002 until January 2009. Chemoperfusion with cisplatin was used in 59% of patients. A macroscopically complete resection was achieved in 50% of patients. No mortality occurred, and the major morbidity rate was 21%. After a mean follow up of 21 months, median overall survival (OS) was 37 months (95% CI 12.2-61.8) and median progression free survival was 13 months (95% CI 6.9-19.1). In univariate analysis, OS was influenced by completeness of resection, type of chemoperfusion drug, nodal status, and tumor grade. In a Cox regression model only completeness of resection (Hazard ratio 0.06-0.8, P = 0.022) and tumor grade (Hazard ratio 1.23-12.6, P = 0.021) were independent predictors of OS. Conclusion In selected patients with heavily pretreated recurrent ovarian cancer, cytoreduction combined with HIPEC provides a meaningful OS benefit with acceptable morbidity. Optimal

results are achieved in patients with a macroscopically complete resection and biologically favorable disease.

P181

Impact of Tumor Grade on Prognosis in Pancreatic Cancer: Should We Include Grade in AJCC Staging? N. Wasif,[1]* C.Y. Ko,[2] J. Farrell,[2] Z. Wainberg,[2] O.J. Hines,[2] H. Reber,[2] J.S. Tomlinson.[3] *1. Surgery, John Wayne Cancer Institute, Santa Monica, CA; 2. David Geffen School of Medicine at UCLA, Los Angeles, CA; 3. Greater Los Angeles VA Healthcare System, Los Angeles, CA.*

Introduction. AJCC staging of pancreatic cancer (PAC) is used to determine prognosis, yet survival within each stage shows wide variation and remains unpredictable. We hypothesized that tumor grade might be responsible for some of this variation and the addition of grade to current AJCC staging would improve prognostication. Methods. The Surveillance, Epidemiology, and End Results (SEER) database (1988-2000) was utilized to identify 8082 patients with resected PAC. The impact of grade on overall and stage specific survival was assessed using Cox regression analysis. Variables in the model were age, sex, tumor size, lymph node status, and tumor grade. Results. For each AJCC stage, survival was significantly worse for high-grade versus low-grade tumors. On multivariate analysis, high tumor grade was an independent predictor of adverse survival for the entire cohort (HR1.40, 95% CI 1.31- 1.48) as well as for Stage I (HR 1.28, 95% CI 1.07- 1.54), Stage IIA (HR 1.43, 95% CI 1.26-1.61), Stage IIB (HR 1.38, 95% CI 1.27- 1.50), Stage III (HR 1.28, 95% CI 1.02- 1.59) and Stage IV (HR 1.58, 95% CI 1.21- 2.05) patients. The addition of grade to TNM staging resulted in statistically significant and durable survival discrimination between all stages. Conclusions. Tumor grade is an important prognostic variable in PAC and has a magnitude of impact similar to tumor size (T Stage) and nodal involvement (N Stage). We propose a novel TNMG staging system incorporating grade into current AJCC staging for pancreas cancer. The improved prognostication is more reflective of tumor biology and may impact therapy decisions and stratification for future clinical trials.

P182

Comprehensive Pathologic Assessment of Pancreaticoduodenectomy Specimens A. Sasson,* C. Are, A. Lazenby, Q. Ly. *Univ of Nebraska Medical Center, Omaha, NE.*

Background: Optimal management of localized adenocarcinoma of the head of the pancreas is pancreaticoduodenectomy with microscopically negative resection margins (RO). Multiple studies have demonstrated the adverse impact of positive resection margins (R1) on patient outcome. Assessment of surgical margins is often limited to the pancreatic cut surface, common bile duct (CBD) and posterior margin (pancreatic tissue overlying the IVC. Tumor extension the SMA and portal and superior mesenteric veins (PV/SMV) is often the limiting factor preventing complete surgical extirpation. Objective: The purpose of the study was to evaluate a comprehensive examination protocol of pancreaticoduodenectomy specimens to determine the frequency of microscopically positive SMA and PV/SMV margins, collectively referred to as mesenteric margin. Methods: Between 2001 and 2009, 87 patients underwent pancreaticoduodenectomy for pancreatic adenocarcinoma, with removal of all gross tumor (RO, R1). Following resection, the surgeon, in the presence of the pathologist, oriented the specimen denoting the following margins; pancreatic cut margin, CBD, posterior margin, SMA and PV/SMV. Margins were considered positive if tumor was present at the inked surface. Results: Of the 87 specimens, 29 (30%) had microscopically positive resection margins. The frequency of positive margins was; PV/SMV (12), SMA (10), posterior (4), pancreatic (4) and CBD (3) Seven specimens (8%) had positive margins. In 16 specimens (18%), the only positive resection margins were the SMA or SMV/PV. More limited pathologic assessment of only the pancreatic, CBD and posterior margins would have resulted in a positive margin rate of 11%. The SMA or SMV/PV margin accounted for 67% of microscopically positive margins. Conclusions: The mesenteric tissue is the most frequently positive resection margin in patients with pancreatic cancer undergoing a pancreaticoduodenectomy. A limited examination would have failed to detect positive SMA or SMV/PV margins in nearly 20% of patients. Due to the clinical significance of microscopically involved margins, comprehensive examination to include the mesenteric margins is recommended.

P183

Role of laparoscopy in neo-adjuvant therapy for pancreatic adenocarcinoma A. Sasson,* C. Are, Q. Ly. *Univ of Nebraska Medical Center, Omaha, NE.*

Background: A staging laparoscopy has been shown to detect radiographically occult disease in approximately 15% to 25% of patients with pancreatic adenocarcinoma. The role of staging laparoscopy in the setting of neoadjuvant chemotherapy is not clearly defined. A staging laparoscopy prior to initiation of aggressive neoadjuvant therapy could be beneficial, however this is not universally agreed upon. Furthermore, the benefit of repeating the laparoscopy following completion of neoadjuvant therapy to exclude the progression of radiographically occult disease is unknown. Objective: To determine the value of a staging laparoscopy prior to and following completion of neoadjuvant therapy for pancreatic adenocarcinoma. Methods: A retrospective review of patients undergoing neoadjuvant therapy for radiographically resectable, borderline, or locally advanced pancreatic adenocarcinoma was performed. All patients were evaluated with a high resolution pancreas protocol computed tomography (CT) scan and had no evidence of metastatic disease. Patients were classified as resectable, borderline, or locally advanced based on a recent consensus statement. Results: From 2002 to 2009, 74 patients were evaluated for neo-adjuvant therapy with intent of potential resection. Sixty-five patients had a laparoscopy (n=56) or exploratory laparotomy (n=9) prior to initiation of therapy. Occult metastatic disease was identified in 13 patients (20%). Thirty-four patients completed therapy and had staging laparoscopy with 7 patients (21%) having metastatic disease. Overall, resection was possible in 16 (47%) patients. The remainder of patients were unresectable due to arterial involvement or distant lymphadenopathy. Conclusion: Staging laparoscopy prior to and following the initiation of neoadjuvant therapy in pancreatic adenocarcinoma identified approximately 20% of patients with radiographically occult disease.

P184

Single Incision Colectomy for Colon Cancer M.E. McNally,[1]* B.T. Moore,[2] K.M. Brown.[2] *1. General Surgery, University of Missouri-Kansas City, Kansas City, MO; 2. St. Luke's Hospital, Kansas City, MO.*

Background Laparoscopic colectomy has been shown to not be inferior to traditional open colectomy in disease-free and overall survival. Patients experience some benefit in length of stay and narcotic use. Single-incision colectomy (SIL-C) may offer additional benefit without compromising oncologic principles. Methods We retrospectively reviewed records of patients who underwent SIL-C and traditional laparoscopic colectomy (TLC) for malignant disease performed by a single surgeon. SIL-C consisted of a single port access device with traditional lateral to medial laparoscopic technique. Results Between January and October 2009, 26 SIL-C were performed for colon cancer. Forty-five TLC patients with malignant disease from the prior year were used as controls. Median age was 70 and 54% were female, with no differences between the groups. The median body mass index (BMI) was 27 (18.3-39.9) and 26 (16.6-71.4) for SIL-C and TLC respectively. The ASA class for the cohort was mostly II (53%). Twelve SIL-C (44%) and 21 TLC patients (46%) had previous abdominal operations. The median lymph node harvest was 15 (3-32) and 17 (0-35) for SIL-C and TLC respectively. The median estimated blood loss was 50ml for both groups. The median operative time was 114 minutes (range 59-268) and 135 minutes (range 45-314) for SIL-C and TLC respectively. Seven SIL-C required additional ports while five TLC required conversion to open technique. The median length of stay was 3 days (range 2-17) and 5 days (range 2-11) for SIL-C and TLC respectively (p=0.079). There were five significant postoperative complications in the SIL-C group and 16 in the TLC group, including 4 postoperative ileus and 1 leak. There were no postoperative deaths in the SIL-C group and two in the TLC group. One (3.7%) SIL-C required re-operation (cecal ischemia). One (2.2%) of the TLC required reoperation for an anastomotic leak. Patients with stage III disease or higher were more likely to have complications in both groups. There was no statistical difference between the two groups. Conclusion SIL-C can be used safely in selected colon cancer patients with no difference in blood loss, OR time, or lymph node retrieval. SIL-C patients may have a shorter LOS.

P185

The evolution of surgical management of ampullary adenomas: evaluation of a systematic approach in the era of endoscopic ultrasound. Breaux JA, Lee KK, Moser AJ, Zeh HJ, Hughes SJ, Gamblin TC University of Pittsburgh Medical Center, Pittsburgh PA

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Introduction: The optimal surgical management of adenomas of the ampulla of Vater is controversial. Our aim was to evaluate the effectiveness of a systemic approach to ampullary adenoma which includes selection for transduodenal ampullectomy (TDA) based on endoscopic ultrasonographic, pathologic, and intraoperative findings, with conversion to Whipple if necessary. Methods: We retrospectively reviewed EUS reports from 2001 to the present and identified patients found to have biopsy-proven benign adenomas of the ampulla not amenable to endoscopic resection. Retrospective chart review was used to collect data on operative procedure, final pathology, length of stay (LOS), morbidity, follow-up endoscopies and recurrence. Results: Twenty-six patients underwent surgery for ampullary adenoma from 2001 to present. Mean age was 68. Mean size was 21 mm. Seventeen patients were treated with TDA based on pre- and intra-operative findings. Seven were converted to Whipple, 4 for extensive adenoma, 1 for positive frozen section analysis, and 2 for suspicious findings on palpation of the lesion. One TDA patient early in our experience had extensive high-grade dysplasia on endoscopic biopsy and final pathology showed T1N0 adenocarcinoma. The patient refused completion Whipple and underwent chemoradiation. Sixteen of 17 patients selected for TDA had benign final pathology and at a median follow-up of 47 months, none had recurrent adenoma. Median LOS was 12 days in those converted to Whipple and 9 days for TDA (p=0.15). Morbidity data is shown in Table 1. Conclusions: A systematic approach to ampullary adenomas including preoperative evaluation with EUS, biopsy and careful intraoperative evaluation allows for the performance of transduodenal ampullectomy and conversion to Whipple when appropriate, with high concordance with final pathology results and low recurrence.

Table1. Morbidity grade for TDA and TDA converted to Whipple

Procedure/Morbidity	N
TDA	17
Grade 0	7
Grade 1	6
Grade 2	3
Prolonged Ileus	1
C. Difficile colitis	1
Pneumonia	1
Grade 3a	0
Grade 4a	1
MI/CHF	1
TDA converted to Whipple	7
Grade 0	1
Grade 1	1
Grade 2	1
Insulin dependence	1
Grade 3a	3
Pancreatic leak	3
Grade 4a Respiratory failure	1 1

P186

Tumor Location Does Not Impact Survival After Resection for Pancreatic Adenocarcinoma Despite Larger Tumors in the Tail

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Introduction: Convention dictates that patients with adenocarcinoma arising in the tail of the pancreas have shorter survival than patients with adenocarcinoma in the head of the pancreas. There is a paucity of early symptoms with cancers in the tail of the pancreas and patients present with larger tumors and experience shorter survival. This study was undertaken to determine differences in tumor characteristics and survival between resectable adenocarcinomas of the pancreatic tail and head. Methods: Since 1992, data has been prospectively collected on all patients undergoing pancreaticoduodenectomies or distal pancreatectomies (all with concomitant splenectomy) for adenocarcinoma. Survival comparisons were undertaken using Mantel-Cox survival curve analysis. Data are presented as median, mean ± SD. Results: Pancreatic resections for adenocarcinoma were undertaken in 253 patients; 220 patients underwent pancreaticoduodenectomy and 33 patients underwent distal pancreatectomy. Tumors in the head or body / tail were similar by T stage, N stage, AJCC stage, and margin status though tumors leading to distal pancreatectomy were larger (4 cm, 5 cm ± 2.3) than tumors leading to pancreaticoduodenectomy (3 cm, 3 cm ± 1.4; Mann-Whitney U-Test, p=0.005). Overall survival was similar after pancreaticoduodenectomy (17 months, 26 months ± 25.9) vs. distal pancreatectomy (15 months, 20 months ± 18.6; p=0.74). Survival at each location was impacted by T stage, N stage, AJCC stage, and margin status. However, comparing tumors in the head vs. body / tail, there were no differences in survival by T stage, N stage, AJCC stage, or margin status (Table). Conclusions: Survival is unsatisfactory though similar after resection of cancers in the head or body / tail of the pancreas, despite tumors in the body / tail being generally larger. Survival is improved, irrespective of location, by complete tumor extirpation (R0 resection). By most descriptors, adenocarcinomas in the body / tail or head of the pancreas are similar; margin status is the only operative factor over which surgeons' have control and complete tumor extirpation should be aggressively sought.

Margin	Distal Pancreatectomy with Splenectomy	Pancreaticoduodenectomy	p-value
R0	16 months, 20 ± 19.8 (n=26)	20 months, 26 ± 23.5 (n=55)	0.90
R1	11 months, 17 ± 14.4 (n=7)	13 months, 20 ± 27.6 (n=165)	0.95

P187

Laparoscopic Radiofrequency Thermal Ablation of Hepatocellular Cancer: Predictors of Survival H. Akyildiz, J. Mitchell, A. Siperstein, E. Berber.* *Cleveland Clinic, Cleveland, OH.*

Introduction: Radiofrequency thermal ablation (RFA) is an option for patients with unresectable hepatocellular cancer (HCC). The aim of this study is to report the long-term oncologic outcomes and predictors of survival after laparoscopic RFA for HCC. Methods: One hundred consecutive patients with HCC who were not candidates for a curative liver resection underwent laparoscopic RFA. The patients were followed up with quarterly chest and abdominal CT scans for the first 2 years and then biannually. Data were collected prospectively into an IRB-approved database. The relationship between demographic, clinical, laboratory, and surgical parameters and survival was assessed using univariate Kaplan-Meier survival and multivariate Cox Proportional Hazards model. Results: There were 83 men and 17 women, with a mean age of 68.2 ± 1.0. One hundred thirty-five laparoscopic RFA procedures were performed for 255 lesions (mean 1.9, range 1-5). Mean tumor size was 3.6 ± 0.2 cm (range 1-13 cm). Local recurrence was detected in 14%, new liver recurrence in 56% and new extrahepatic disease in 14% of the patients in follow up. The overall median Kaplan-Meier survival was 34.5 months and disease-free survival 12.5 months after RFA. Child class was the only predictor of survival in both univariate and multivariate analyses. Child's A patients had a median survival of 74 months, B patients 21.5 months and C patients 6.5 months after RFA (p<0.0001). Child's C patients had a 5- fold increased risk of mortality compared to Child's A patients (p<0.0001). Conclusions: This study describes which patients do best after RFA of HCC. Underlying liver function is the single predictor of survival in these patients.

P188

Pathologic non-responders after neoadjuvant chemoradiation for esophageal cancer demonstrate no survival benefit compared to patients treated with primary esophagectomy G.W. Dittrick,* K. Turaga, J.M. Weber, R. Shridar, S. Hoffe, M. Melis, J. Barthel, E. Eikman, M. Biagioli, R.C. Karl, K.L. Meredith. *H. Lee Moffitt Cancer Center, Tampa, FL.*

Background: Neoadjuvant chemoradiation (NCRT) followed by esophagectomy has become the preferred treatment for patients with locally advanced esophageal cancer. Survival is often correlated to degree of pathologic response to NCRT. The benefit of NCRT in patients who are found to be pathologic non-responders (pNR) has yet to be investigated. This study aims to evaluate survival in pNR to NCRT compared to patients treated with primary esophagec-

tomy. Methods: Using our prospectively maintained esophageal cancer database we identified patients treated from 1994-2009 with NCRT followed by esophagectomy who were pNR and patients who proceeded to primary esophagectomy. Clinical and pathologic data were compared using Fisher's exact and chi-square when appropriate while Kaplan Meier estimates were used for entire cohort as well as stage specific disease free (DFS) and overall survival (OS). Results: We identified 60 patients who underwent NCRT followed by esophagectomy who were pNR and 81 patients who underwent primary esophagectomy. Median DFS and OS were significantly decreased in pNR compared with those treated with primary esophagectomy (10 vs 50 months, $p<0.001$ and 13 vs 50 months, $p<0.001$, respectively). For patients with Stage II disease, median DFS and OS were similarly decreased in pathologic nonresponders (13 vs 62 months, $p<0.001$ and 31 vs 62 months, $p=0.024$, respectively). There were no differences in median DFS or OS for patients with stage III disease (10 vs 14 months, $p=0.29$ and 10 vs 19 months, $p=0.16$, respectively). Within each stage, there were no differences between groups for age, gender, race, histology, grade, margins, adjuvant chemotherapy, or lymph nodes resected. Conclusions: Pathologic non-responders to NCRT for esophageal cancer receive no benefit in DFS or OS compared to patients treated with primary esophagectomy. Furthermore, for patients with stage II disease, DFS and OS are significantly decreased in pNR. Further studies aimed at early identification of non-responders to NCRT are critical to improve outcomes for esophageal cancer.

P189

Laparoscopic Implantation of Radiofrequency Emitting Transponders in Stage III Pancreatic Tumors to Facilitate Radiation Therapy

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Includes video demonstration for presentation. Introduction: Patients with locally advanced (stage III) pancreatic cancer are often treated with a combination of chemotherapy and radiation. However, delivery of radiation therapy to the pancreas may be complicated by toxicity to adjacent structures. Advanced image-guided radiation techniques have evolved in order to maximize tumor dose and minimize exposure of adjacent organs, but are dependent on accurate delineation of tumor borders. Since respiration and patient motion can cause variations in location of the pancreas within the abdominal cavity, methods to more accurately define the position of a pancreatic tumor in four dimensions during radiation treatment are needed. We present initial results of a study in which laparoscopic placement of radiofrequency emitting transponders in the tumor was performed at the time of staging laparoscopy for stage III pancreatic tumors. Methods and Results: Patients with stage III pancreatic cancer provided signed informed consent to participate in this trial, which was approved by the University of Pennsylvania Health System IRB. The Calypso Localization system (Calypso Medical Technologies, Seattle, WA) was utilized. Using two or three laparoscopic port technique, dissection was carried out to identify the pancreatic tumor through the greater or lesser omentum. Three transponders were implanted around the tumor in each patient using a trocar-needle assembly. An abdominal x-ray was obtained intraoperatively to confirm transponder positioning. Laparoscopic implantation of transponders was successful in each of our first five patients. There was minimal blood loss and the procedure took less than 20 minutes. Subsequent evaluation of pancreas tumor positioning using the transponders through the respiratory cycle demonstrated a greater than expected degree of tumor motion. Conclusion: Real-time tracking of tumor position using radiofrequency transponders may result in more effective and less toxic delivery of radiation therapy to the pancreas. Placement of such transponders can be performed safely and efficiently during staging laparoscopy.

P190

Does the clinical outcome following resection for esophageal cancer treated with neoadjuvant chemoradiotherapy more closely follow the initial or post-treatment stage?

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BACKGROUND: Despite a growing body of evidence that neoadjuvant chemoradiotherapy improves overall and disease free survival in patients with stage II and III esophageal cancer, there is still no consensus on the best curative treatment. We postulate that the improvement in survival is due to the downstaging of the primary lesion following neoadjuvant therapy. METHODS: We performed a retrospective chart review for all patients undergoing surgical resection of esophageal cancer for cure at a large metropolitan based, university affiliated hospital from 1995 to 2007. A total of 322 patients with esophageal cancer were reviewed of which 91 either had neoadjuvant chemoradiotherapy and surgery (NEO n=31) or surgery alone (SURG n=60). 30-day mortality, 48-month survival, and 75-month survival were compared between the NEO and the SURG groups. We then analyzed the NEO group, comparing the initial stage with the post treatment stage in the pathologic specimens. RESULTS: 30-day mortality was 6.5% and 8% for the NEO and the SURG groups. 48-month and 75-month survival was 74% and 43% for the NEO group, and 40% and 28% for the SURG group. Downstaging of disease was observed in 65% of the patients in the NEO group as illustrated in the table below. Microscopic residual disease and complete pathologic response was observed in 42% of patients in the NEO group. The 48-month and 75-month survival for the NEO patients in Stage 0 were 88% and 75%, Stage I 88% and 50%, Stage II 71% and 29%, Stage III 60% and 20%, and Stage IV 33% and 0%. The 48-month and 75-month survival for the SURG patients in Stage 0 were 88% and 88%, Stage I 67% and 58%, Stage II 42% and 11%, Stage III 6% and 6%, and Stage IV 0%. CONCLUSIONS: 48-month and 75-month survival in the NEO group more closely paralleled the stage after chemoradiotherapy as compared with the initial stage. This suggests that downstaging the patients with neoadjuvant chemoradiotherapy improves survival.

Tumor Stage	SURG (n=60)	NEO (initial)(n=31)	NEO (pathologic)(n=31)
0	8	0	8
I	12	0	8
IIa	12	19	4
IIb	7	3	3
III	16	5	5
IV	5	4	3

P191

Polymorphism of the tandem repeat sequence in the thymidylate synthase gene is associated with tumor stage in colon cancer

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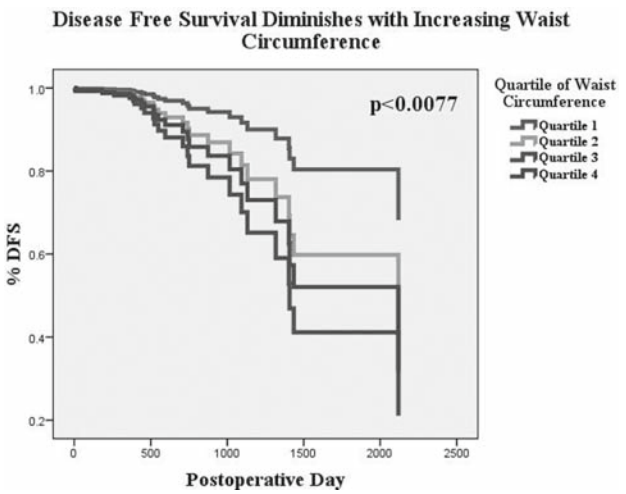
Introduction: Thymidylate synthase (TS) plays an important role in colorectal carcinogenesis and response to 5FU-based chemotherapy. TS expression can be modified due to polymorphisms in the 5'-untranslated region of the gene. Objective: to investigate the association between TS polymorphisms with clinicopathological characteristics of colon carcinomas. Methods: we retrospectively studied 89 individuals with high risk stage II (obstruction, T4 stage, presence of lymphovascular invasion or preoperative CEA > 5.0) and stage III patients submitted to curative intent surgery. DNA was extracted from paraffin embedded tumor tissues and sequenced. The polymorphism studied was the variation of the number of the repeated 28-bp sequences (3 or 2 repeats). Results: the frequency of the polymorphisms was: 2R2R in 22 cases (29.2%), 2R3R in 36 cases (40.4%), and 3R3R in 27 cases (30.3%). We did not find associations between the frequencies of these polymorphisms and age, gender, presence of lymphovascular invasion, or level of preoperative CEA. We find a significantly higher proportion of T4 tumors between the 3R3R genotype compared with the 2R2R and 2R3R genotypes (OR=2.69; 95% CI: 1.05 – 6.94; $p=0.04$). By the other hand, a significantly lower proportion of positive lymph nodes were found among patients with tumors presenting the 3R3R genotype, by comparing with the 2R2R and 2R3R subgroup (OR: 0.28; 95%CI: 0.10 – 0.72; $p=0.01$). Five-year disease free survival and overall survival were, respectively, 81% and 85% among patients with tumors presenting the 3R3R genotype, and 62% and 67% among patients with tumors presenting 2R2R or 2R3R genotypes. These differences were not statistically significant. Conclusions: in this sample,the TS polymorphic tumor genotype 3R3R was associated with lower risk of lymph node metastases in colon carcinomas.

P192

Fat Distribution and Quantity Predict Survival in Men with Rectal Cancer C. Balentine,[1]* C. Robinson,[1] C. Marshall,[1] J. Wilks,[1] K. Haderxhanaj,[2] J. Enriquez,[1] V. Bansal,[1] S. Sansgiry,[2] N. Petersen,[2] A. Artinyan,[1] S. Awad,[1] D. Albo,[1] D.H. Berger.[1] *1. Baylor College of Medicine, Houston, TX; 2. Michael E DeBakey Veterans Affairs Hospital, Houston, TX.*

BACKGROUND Elevated body mass index (BMI) has been linked to a two-fold increase in the incidence of colorectal cancer, but the relationship between BMI and survival after colorectal cancer resection is uncertain. This may be due to the fact that BMI fails to account for distribution and quantity of adipose tissue. Since direct measurement of adiposity has proven superior to BMI at predicting medical complications of obesity, we hypothesized that these measures would also be more accurate predictors of survival in rectal cancer. METHODS Retrospective review of an institutional colorectal cancer database at a tertiary care Veterans Hospital was used to identify consecutive cases of men undergoing elective resection of rectal adenocarcinoma from 2002-2009. Preoperative CT imaging was used to quantify intra-abdominal fat, subcutaneous fat, and waist circumference. BMI was calculated from the medical record. Cox regression analyses were used to determine association of obesity measures and survival after controlling for other factors. RESULTS From 2002-2009, 108 men underwent curative elective resection for rectal adenocarcinoma. Mean patient age was 64±0.98 years, and mean BMI was 28.7±0.47 kg/m^2. BMI did not significantly predict overall (HR 1.039, 95% CI 0.411-2.621, p<0.936) or disease free survival(HR 1.157, 95% CI 0.518-2.582, p<0.722) after adjusting for age, tumor stage, grade, ethnicity, smoking, and neoadjuvant therapy. However, greater waist circumference predicted decreased disease free survival (HR 1.07, 95% CI 1.02-1.12, p < 0.0077, Figure 1) and overall survival (HR 1.05, 95% CI 0.998-1.105, p<0.0621). Moreover, a higher ratio of intra-abdominal to subcutaneous fat was associated with improved disease free survival (HR 0.501, 95% CI 0.264-0.949, p<0.034) and overall survival (HR 0.378, 95% CI 0.165-0.863, p<0.0210). CONCLUSIONS Direct measurements of adipose quantity and distribution significantly predict overall and disease free survival in rectal cancer while BMI fails to differentiate prognosis. This provides the first evidence that direct measurement of adipose tissue is superior to traditional measures in predicting long-term cancer outcomes.



Survival in Rectal Cancer Decreases with Increasing Waist Circumference

P193

Survival after Hepatic Resection with or without Intra-Hepatic Chemotherapy in Non Colorectal Liver Metastasis M. Soni,* B. Chakravarty, A. Korant, S. Sirop, D. Wiese, S. Nagpal, T. Singh, S. Saha. *McLaren Regional Medical Center-Michigan State University, Flint, MI.*

Background: There is no definitive guideline for management of non-colorectal liver metastases (NCLM). A study was undertaken to evaluate the role of major hepatic resection (HR) with or without intra-hepatic chemotherapy (IHC) in patients (pts) with NCLM. **Methods:** Of the 90 pts evaluated for major liver resection of metastatic disease,26 were due to NCLM,15 pts underwent major HR with or without IHC. Survival rates of this group were calculated and correlated with or without IHC. Variables included age, sex, histology, primary tumor and number of metastasis. **Results:** Of these 15 pts (Median age – 69 yrs,M : F = 4:11),3 pts had left total, 4 had right partial, and 4 had left partial lobectomy. One pt had only ablation with resection and 3 pts had only infusaid pump. The most common primary site was breast (26.7%), followed by cholangiocarcinoma (20%) .The most common histology was adenocarcinoma(83.3%). Metachronous liver metastasis was found in 93% of pts. Overall median survival of the entire group was 18 months. Median survival for pts with HR only (n=6) was 10 months, compared to 39.5 months for pts with HR and IHC (n=6). The overall survival rate was 60 % at one year,40% at two-year and 26.7% at five-year follow up.One yr survival for pts with only HR(n =6),only IHC(n=3), and both (n=6) were 50%,33.3%, and 83.3% respectively. Three yr survival for pts with only HR,only IHC, and both were 16.7%,33.3% and 66.7% respectively **Conclusions:** Pts with NCLM who undergo IHC along with major resection or ablation survive longer than resection alone.A larger multicenter study is warranted.

Table 1: Demographics of the 15 patients with NCLM and the overall survival correlated to the use of intrahepatic chemotherapy.

Entire Group	Number	Median Age (years)	Male : Female	Unilobar : Multilobar disease	Most Common Primary	Most common Histology
	15	69	4:11	11:4	Breast Cancer	Adenocarcinoma
Overall median survival	Entire Group				18 months	
	Only Hepatectomies ; 6 pts (40%)				10 months	
	Hepatic Resection and Intrahepatic chemotherapy : 6 pts (40%)				39.5 months	

P194

Radiofrequency Ablation as Regional Management of Breast Cancer Liver Metastases M.A. Cassera, C. Hammill, R. Wolf, L.L. Swanstrom, P.D. Hansen.* *Hepatobiliary and Pancreatic Surgery Program, Portland Providence Medical Center, Portland, OR.*

Introduction: Selected patients with breast cancer liver metastases (BCLM) may benefit from surgical resection. The risks and traumatic impact, however, may outweigh the benefit in patients who have a poor overall prognosis. Laparoscopic radiofrequency ablation (RFA) allows for accurate staging and offers a low-risk definitive treatment of liver metastases. Methods: Between 12/1998 and 8/2006, patients with BCLM were offered laparoscopic RFA if they had 3 or fewer tumors, all < 4cm in size, and if they had no or stable extrahepatic disease. Data was reviewed retrospectively. Results: Fourteen patients underwent staging laparoscopy for BCLM. Seven patients were amenable to laparoscopic RFA and seven had extensive disease. In the laparoscopic RFA group, the mean number of tumors ablated was 2.3 (±1.9), tumor size was 2.3 cm (±1.7), operative time was 165 minutes (±44.9), and blood loss was 66 ml (±51). There was one complication, a PE which, required anticoagulation. With a mean follow-up of 32 months, there were no local recurrences, although five of the seven patients (71.4%) had disease progression within the liver at non-RFA sites. The median and mean times to progression were 4.9 and 17.7 months respectively. One-year and 3-year survival was 86% and 54% respectively in the laparoscopic RFA patients and 71% and 57% in the seven patients who underwent staging laparoscopy without laparoscopic RFA. Conclusion: While laparoscopic radiofrequency ablation is a safe and effective tool for the local control of breast cancer liver metastasis, most patients will develop regional metastases in a short period of time. We believe that there is no role for radiofrequency ablation in the treatment of multifocal breast cancer liver metastasis.

P195

Peri-operative blood pressure as a risk factor for anastomotic leakage in colorectal surgery K. Noordzij, I. Grossmann, W. Mastboom, J. Klaase, M. Lutke Holzik.* *Surgery, Medisch Spectrum Twente, Enschede, Netherlands.*

Introduction: Symptomatic anastomotic leakage after colorectal surgery results in a high incidence of morbidity and mortality. For many years research had been done on identifying potential risk factors for this. In this study we analyzed in literature described risk factors and our own formulated risk factors. Methods: In this prospective cohort study, previous in literature described

risk factors and our own formulated risk factors have been analyzed with the use of an unselected patient group. Thirty-eight peri-operative potential risk factors were scored and statistically analyzed. Results: Between January 2007 and August 2008, 333 primary colorectal anastomoses were created amongst 329 patients. The anastomotic leakage percentage was 9.3%. The leakage related mortality was 20%. Multivariate analysis showed two significant risk factors: 1)pre-operative hypertension and 2)the duration of the peri-operative hypotensive period. The definition of the peri-operative hypotension is formulated as the absolute period of a systolic tension less than 100 mm/Hg during the operation. The median time of the peri-operative hypotensive period in the group that developed an anastomotic leakage was 30 minutes in comparison to 15 minutes in the group that did not developed a leakage (OR: 1.02, 95% CI: 1.01-1.03, p = 0,007). Of the patients with pre-existing hypertension, whether or not corrected by the use of medication, 14.9% developed an anastomotic leakage compared to 6.4% of the patients without pre-existing hypertension (OR: 2.52, 95% CI: 1.13-5.63, p = 0.024). Hypotension may result in a reduced micro perfusion in the intestinal wall (ischemia), resulting in impaired healing and anastomotic leakage. Patients with pre-existing hypertension may be relatively hypotensive at an accepted peri-operative systolic tension of around 100 mm/Hg. This may increase their risk of anastomotic leakage Conclusion:These findings are clinical significant since peri-operative hypotension can be influenced by the anesthesiologist. Now we maintain a systolic blood pressure of at least 100mm/Hg during all colorectal procedures. Relative peri-operative hypotension may be an underestimated parameter

P196

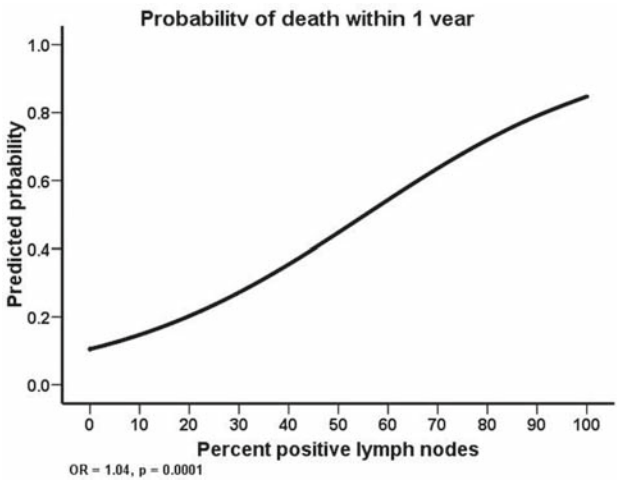
Major liver resection in the elderly; is it safe? S.W. Cho,* A. Tsung, D.A. Geller, J.W. Marsh, T.C. Gamblin. *Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: We aim to examine the safety of major liver resection in the elderly in a case-controlled manner. Method: Patients aged 70 or older (Group 1) were matched with those younger than 70 (Group 2) by the extent of liver resection and by operative indications. The study period was between July 2000 to July 2008 and only patients who underwent resection of at least two liver segments were included. 75 patients were identified in each group. Primary outcome measures were rates and severity of post-operative complications as measured by the Clavien classification. The secondary outcome measures were length of hospital stay and discharge destination. Results: Male to female ratio was 43:32 in both groups. The median aged was 76 (range: 70 to 86) and 56 (range 25-67) in Group 1 and 2, respectively. Significant differences between these groups were found in terms of ASA score ($p<0.001$), renal insufficiency ($p<0.001$), coronary artery disease ($p<0.01$), congestive heart failure ($p<0.03$), diabetes ($p<0.0001$), and hypertension ($p<0.001$). There were no differences in terms of BMI, COPD, preoperative total bilirubin, albumin, and INR. Liver resection performed included extended hepatectomy (n=4 in each group), right/left hepatectomy (n=24 (Group 1), n=23 (Group 2)), and bisegmentectomy (n=47 (Group 1); n=48 (Group 2)). There was no mortality in 90 days post-operative period in both groups. Overall complication rates were 44% in Group 1 and 33.3% in Group 2 ($p=0.18$). Minor complications (Grade 1 and 2) constituted majority of recorded complications in both groups (63.6% and 56%, respectively; $p>0.1$). Median length of hospital stay were 7 days in Group 1 and 6 days in Group 2 ($p<0.01$). 19 % and 1% of patients in Group 1 and Group 2 were discharge to rehabilitation facilities, respectively ($p<0.001$). Conclusion: Major liver resection can be performed in the patients aged 70 or older with similar rates and severity of complications as in the younger patients. Majority of morbidity was minor in both groups. However, older patients required a longer hospital stay and were placed in rehabilitation facilities more often prior to being discharged home.

P197

Mortality within twelve months after subtotal esophagectomy for cancer G. Pines,[1]* V. Buyeviz,[1] S. Machlenkin,[1] Y. Klein,[1] E. Idelevich,[2] H. Kashtan.[1] *1. Surgery B, Kaplan Medical Center, Rehovot, Israel; 2. Kaplan Medical Center, Rehovot, Israel.*

Introduction: Esophageal carcinoma has a poor prognosis. Surgery is still considered to be the mainstay of treatment for esophageal carcinoma. Some patients died of their disease within 12 months after esophagectomy. The aim of this study is to identify predictive factors for mortality within the first year after esophagectomy for esophageal cancer that may negate surgery in some patients. Methods: All patients who had undergone subtotal esophagectomy for cancer between 2003-2008 were included. Patients in whom follow-up preceded 12 months and perioperative mortality were excluded. Patients were assigned into two groups. Group A included all oncological mortality cases within 12 months of surgery. Group B included all patients who survived longer than 12 months following surgery. Results: Of 81 patients who met the inclusion criteria, 18 patients were assigned to group A and 63 to group B (median survival 10 and 25 months respectively). A higher proportion of patients were operated for pN1 disease in group A (72% vs. 33%, p=0.0004). R1 esophagectomy rate was higher in group A (61% Vs 22%, p=0.03). Metastatic lymph node ratio (LNR) was higher in group A (mean - 46% vs. 10%, p=0.0003). Multivariate analysis identified LNR as an independent risk factor for first year mortality (O.R. = 1.04, p=0.0001. 95%CI: 1.029 – 1.080, figure 1). No differences were found in pre-operative variables including age, gender, tumor histology, type of operation and administration or response to neo-adjuvant therapy. Conclusions: No pre-operative predictive factors for mortality were identified. Metastatic LNR was an independent risk factor for first year mortality after esophagectomy for cancer. pN1 disease and resection margin involvement were also identified as prognostic factors for first year mortality. Further research should be conducted to identify pre-operative mortality risk factors.



P198

Individual surgeon, pathologist and other factors affecting lymph node harvest in stage II colon carcinoma. Is a minimum of 12 examined lymph nodes sufficient? L. Stocchi,* V.W. Fazio, I. Lavery, J. Hammel. *Cleveland Clinic, Cleveland, OH.*

INTRODUCTION Insufficient lymph node harvest in presumed stage II colon carcinomas can result in understaging and worsened cancer outcomes. The purpose of this study was to evaluate factors affecting the number of lymph node examined and their corresponding impact on cancer outcomes. METHODS We considered all patients undergoing surgery alone for stage II colon cancer in our institution since 1976 and included in our colorectal cancer database. We compared lymph node harvests before 1991 and afterwards when the current standard of a minimum of 12 examined nodes was formulated. We analyzed variables affecting lymph nodes examined and their impact on cancer outcomes with reference to the standard of 12 nodes. RESULTS 901 patients were included. Mean follow-up exceeded 8 years. Laparoscopic technique and individual pathologist had no statistically significant association with the number of lymph nodes examined. Harvest of at least 12 nodes was related to surgery after 1991 (85% vs. 69%,$p<0.001$), right vs. left colon carcinomas

(85% vs. 72%, p<0.001) and individual surgeon (p=0.018). Length of specimen was also significantly associated with a number of at least 12 examined lymph nodes at different cutoffs of at least 30cm, 25cm and 20cm (86% vs. 72%, p<0.001; 84% vs. 68%, p<0.001; 82% vs. 66%, p<0.001, respectively). Increasing age was associated with fewer examined lymph nodes (Spearman correlation= -0.22,p<0.001). Less than 12 nodes and stage IIb independently affected OS (p=0.003 and p=0.022, respectively), DFS (p=0.010 and p=0.09, respectively), DSM (p=0.009 and p<0.001, respectively) and OR (p=0.13 and p=0.023, respectively). A minimal number of greater than 12 examined nodes had no significant effect on cancer outcomes. CONCLUSIONS Year of surgery, age of patient, tumor location, length of specimen and individual surgeon, but not pathologist affected the number of nodes examined. At least 12 examined nodes optimized cancer outcomes for stage II colon cancer. Our results do not support efforts to increase the minimal lymph node harvest in stage II colon cancer.

P199

Rt Vs Lt Colon cancer- Distinct tumors ? Gatot Inbar, Shapira Zahar, Lavy Ron, Chikman Bar,Halevy Ariel Division of surgery, Assaf-Harofeh Medical Center,Israel I. Gatot, Z. Shapira, R. Lavy,* B. Chikman, A. Halevy. *Assaf Harofeh Medical center i, Tel Aviv, Israel.*

Background: Recent studies of patients with colorectal cancer have suggested a Rt sided shift in the incidence of cancer .There are some differences between RT and LT colon cancer: embryologically the Rt colon originates from the Midgut while the Lt colon from the Hindgut. Few studies showed different gene expression. Right side colon cancer is associated with a 5% decrease in median survival compared to the left side. Aim To compare the pathological & histological characteristics between right and left colon cancer . Methods Retrospective study . We reviewed all the patients who underwent colectomy for primary colon cancer in our institute . Results : The study cohort is based on 823 patients, 426 Rt colectomy (52.8%),and 397 Lt colectomy (48.2%).We found no difference in sex, nodal status, lymphatic and vascular invasion. The main differences were in Mucinous component and mucinous tumors which were predominantly in the right sided tumors 13.1 % Vs 7 % . and Higher incidence of poorly differentiated tumors in right sided tumors 19% Vs 8.7 % . Less prominent differences were found in age (70 years Vs 68), tumor size (4.9cm Vs 4.4cm) and the percentage of T3-4 (88% Vs 82%) . Conclusions : Our data demonstrates some pathological differences between Rt & Lt colon cancer which might explain in part the poorer outcome that was reported by other researchers .

Accumulated data on 823 patients

	Rt sided colon cancer N=426;51.8%	Lt sided colon cancer N=397;48.2%	P value
Age	70	68	<0.001
Male sex N(%)	206(48.4)	196(49.4)	NS
Tumor size (CM)	4.92	4.43	<0.001
T stage			
T1 N(%)	11 (2.6)	20 (5.1)	
T2	41 (9.7)	48 (12.10	
T3-4	382(87.7)	328(82.8)	0.049
Nodal status			
No L.N examines	15.6	12.7	0.001
N0 N(%)	266(62.7)	237(60)	NS
N1	102(24.1)	101(25.6)	NS
N2	56(13.2)	57(14.4)	NS
Vascular invasion N(%)	39(9.2)	40(10.1)	NS
Grade			
I(well differentiated) N(%)	12(2.8)	29(7.5)	<0.001
II(moderately differentiated)	308(78)	326(83.8)	<0.001
III(poorly differentiated)	75(19)	34(8.7)	<0.001
Mucinous component	56(13.1)	28(7)	<0.001
Mucinous tumor	31(7.3)	8(2)	<0.001

P200

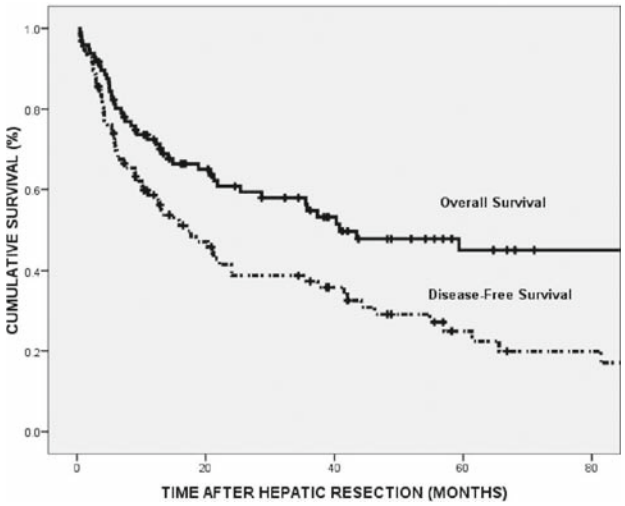
Tissue factor is associated with a prothrombotic state in pancreaticobiliary cancer (PBC) A.V. Patel,[1]* A.A. Khorana,[2] A. Bharthuar,[3] B.W. Kuvshinoff,[3] N. Mackman,[4] A. Hutson,[3] R.V. Iyer.[3] *1. Arizona Cancer Center, Tucson, AZ; 2. James P. Wilmot Cancer Center, Rochester, NY; 3. Roswell Park Cancer Institute, Buffalo, NY; 4. University of North Carolina at Chapel Hill, Chapel Hill, NC.*

Introduction: PBC is associated with a high risk for venous thromboembolism (VTE). Tissue factor (TF), the physiologic initiator of coagulation, is overexpressed in pancreaticobiliary cancer, and circulating TF may be responsible for the prothrombotic state. We hypothesized that PBC patients (pts) with VTE would have elevated systemic TF as compared to those without VTE. Methods: With IRB approval, demographic, treatment and clinical outcome-related information was obtained on all pts with PBC diagnosed from January 2005 to December 2008 with available clinical data and plasma in the institute biorepository. TF level was measured in de-identified samples using a previously established TF microparticle-associated procoagulant activity (PCA) assay. Clinical data was collected independently and merged with the TF- PCA for analysis. Results: The study population comprised of 117 pts. Demographics: M/F 52/65; median age: 65 years(range 40-85); race - caucasian 108, african-american 7, others 2; primary cancer - pancreas 80, hepato-biliary 34, unknown primary 3. VTE occurred in 49 pts (41%) [11 (22%) pulmonary embolisms, 14 (28%) deep venous thrombosis, 24 (49%) other sites of venous thrombosis]. Mean and median TF for the entire group were 2.15 and 1.20 pg/ml respectively. Pts with VTE had significantly elevated mean TF compared to those without (3.18 pg/ml vs 1.40 pg/ml). Elevated TF was associated with increased risk of primary or recurrent VTE, p=0.03, 95% OR=1.22, CI= (1.02, 1.47) in multivariate analysis. The corresponding area under the ROC curve, interpreted as a measure of diagnostic accuracy, was AUC=0.60. In a subset analysis of only pancreatic cancer pts, the difference between the mean and median TF in the VTE group (3.64 pg/ml and 1.34 pg/ml) remained significant compared to the non-VTE group (1.18 pg/ml and 1.11 pg/ml). No other variables were significant in the model. Conclusions: In pts with PBC, VTE occurrence rates are high. TF levels are significantly elevated in patients with symptomatic VTE in comparison to those without VTE. TF is a promising biomarker for identifying patients at risk for VTE and warrants further prospective study.

P201

Clinicopathological Determinants of Survival after Hepatic Resection of Hepatocellular Carcinoma in 97 Patients – Experience From an Australian Hepatobiliary Unit T.C. Chua,* A. Saxena, F. Chu, W. Liauw, A. Kokandi, J. Zhao, D.L. Morris. *UNSW Department of Surgery, St George Hospital, Sydney, NSW, Australia.*

Background Identification of clinicopathological determinants that predict for risk of recurrence and overall survival after undergoing potentially curative hepatic resection for hepatocellular carcinoma is a strategy towards personalizing therapy to improve outcome. Through evaluation of a centre's experience with treatment of a disease, determinants unique to the treated patient cohort may be identified. Methods Ninety-seven patients with hepatocellular carcinoma underwent liver resection. Clinical, treatment and histopathological variables were collected and evaluated using univariate and multivariate analyses with disease-free survival (DFS) and overall survival (OS) as the endpoints. Results The median follow-up period was 19 (range, 1 to 188) months from the time of hepatic resection. The median DFS and OS after RFA treatment was 17 and 41 months respectively. Five-year overall survival rate was 45%. Eight Independent factors associated with disease-free and overall survival were identified through a multivariate analysis. Three factors; Child Pugh Score (DFS p=0.045, OS p=0.001), histopathological grade (DFS p<0.001, OS p<0.001), and histological diagnosis of cirrhosis (DFS p<0.001, OS p<0.001) predicted for both disease-free and overall survival. Conclusion Integrating the knowledge of identified prognostic factors into clinical decision making may provide a clinicopathological signature that could identify patients at greatest risk of treatment failure such that novel interventions may be applied to improve the survival outcome.



P202

Survival benefit associated with surgery performed by a colorectal cancer surgeon in a cohort of stage III colon cancer patients aged 65 and older: an analysis using SEER-Medicare data

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Introduction: To date, no population study in the United States (US) has examined the evidence for a survival or other clinical benefit associated with surgery performed by a colorectal cancer (CRC) surgeon. This study aims to fill this gap. Methods: Linked registry and claims data from the Surveillance, Epidemiology and End Results (SEER) – Medicare dataset provided clinical, demographic, treatment, and mortality data on patients age 65 years and older diagnosed with incident Stage III colon cancer between 1997 and 2002, with associated claims data thru' 2004. All patients underwent surgery by a CRC surgeon or a non-CRC surgeon as identified from the Medicare claims data. The outcome of interest was colon-cancer specific mortality. Cox proportional-hazards regression models were used to estimate adjusted hazard ratios and evidence for selection bias was examined using propensity scores (PS). Results: 7,526 patients met the inclusion/exclusion criteria. The colon-cancer (all-cause) mortality rate was 28% (47%) and differed according to whether or not a CRC surgeon performed the surgery: 23% vs. 29%; p-value=0.002 (38% vs. 48%; p-value<0.001). The sample was 87% White and the median age was 78. The median number of nodes examined was 11 and differed according to whether or not there was a CRC surgeon involved (14 vs. 11; p-value<0.001). In covariate-adjusted analyses, there is a colon cancer – specific and all-cause survival benefit associated with CRC surgeon involvement (Table). The survival benefit was not present in a PS matched analysis (N=1,484) controlling for observed selection bias. Conclusion: This population study shows for the first time in the US that there is a survival benefit associated with surgery performed by a CRC surgeon for stage III colon cancer and that the survival benefit can be explained by differences in tumor stage characteristics such as total node count, T stage, and tumor location and medial oncology visits and receipt of adjuvant chemotherapy.

Adjusted hazard ratios (HR) for colon cancer-specific and all-cause mortality

Mortality	HR	CI	P
Colon	0.822	0.700-0.965	.017
All Cause	0.810	0.714-0.918	.001

P203

Role of Radiation Therapy and Lymphadenectomy in Outcomes for Patients with Rectal Cancer: Are We Under Treating the Elderly?

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Objective: Evaluate the impact of neoadjuvant radiotherapy and lymphadenectomy on survival of patients undergoing curative intent surgery for rectal adenocarcinoma (RAC). Methods: SEER data for patients with rectal adenocarcinoma from 2001-2006 were queried. Univariate and multivariate analysis were performed to determine 5-year overall and cause-specific survival (CSS). Results: Overall, 14,191 patients underwent surgical extirpation (low anterior resection LAR, abdominoperineal resection APR) with curative intent for RAC in the study period. Five year overall and disease free survival for entire cohort was 57% and 68% respectively. Multivariate analysis showed that radiation treatment (neoadjuvant or adjuvant), adequate lymphadenectomy (LN ≥ 12), and negative lymph node status, to be independent predictors of improved survival. Age > 65 was an independent predictor of poor prognosis. Further analysis of patients over 65yrs demonstrated a higher utilization of APR (30% vs 25%), lower frequency of adequate lymphadenectomy (40% vs 47%), and decreased utilization of either neoadjuvant or adjuvant radiotherapy (21% vs 37%)versus patients under 65 yrs. Conclusion: There is significant synergistic survival benefit for radiation therapy and adequate lymphadenectomy in all patients with RAC regardless of lymph node status or age. The benefit of radiation therapy appears equivalent when administered in a neoadjuvant or adjuvant setting. Worse prognosis in patients over 65yrs is likely partly due to failure to provide radiation therapy and adequate lymphadenectomy. Systems to assure higher utilization of radiation therapy and adequate lymphadenectomy are needed in patients over 65 yrs to improve outcomes.

P204

Surgical Management of Colorectal Cancer in Octogenarian and Nonagenarian Patients

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Background: Although surgical resection remains standard of care for early colorectal cancer (CRC), the outcomes for the elderly (≥80 yrs of age) have not been well-established. Our objective was to examine survival for elderly patients undergoing definitive surgical resection for CRC. Methods: All surgically resected patients with CRC treated in Los Angeles County from 1988 to 2006 were identified from the Los Angeles County Cancer Surveillance Program (CSP). Patients were categorized by age (18-50, 51-64, 65-79, and ≥80) and overall survival (OS) and disease specific survival (DSS) were compared. Results: Of 53,103 patients, 9% (N=4,741), 23% (N=12,124), 45% (N=24,006), and 23% (N=12,232) were 18-50, 51-64, 65-79 and ≥80 yrs of age, respectively. When age groups were compared, elderly patients were least likely to present with metastatic disease (20%, 18%, 15%, and 13% for the age groups, respectively, p<0.001), receive chemotherapy (55%, 43%, 27%, and 9%, respectively, p<0.001), or die from CRC (77%, 65%, 47%, and 37%, respectively, p<0.001). Younger patients demonstrated better OS and DSS than elderly (5-yr OS: 64%, 62%, 53%, and 33%, respectively; and 5-yr DSS: 70%, 70%, 69%, and 64%, respectively; p<0.001). After controlling for age and other established clinicopathologic characteristics, surgical resection independently predicted improved OS and DSS (HR: 0.40, 95% CI: 0.38-0.42, p<0.001; HR 0.41, 95% CI: 0.39-0.43, p<0.001, respectively). Conclusions: Nearly one-quarter of patients treated for CRC in LA County were ≥80 years of age. Although OS and DSS for elderly patients may be inferior compared to younger patients, surgical resection provides a durable survival benefit in the elderly. Curative surgical resection should be routinely considered in the management of CRC for elderly patients.

Comparison of surgically resected colorectal cancer patients by age

Factor	Age groups				p-value
	18-50	51-64	65-79	80-99	
Age (mean ± SD)	43 ± 6.2	58 ± 3.9	72 ± 4.2	85 ± 3.9	N/A
Gender N (%) Male Female	2,450 (52%) 2,291 (48%)	6,731 (56%) 5,393 (44%)	12,635 (53%) 11,371 (47%)	4,866 (40%) 7,365 (60%)	<0.001
Tumor location N (%) Ascending colon Transverse colon Descending colon Rectosigmoid junction Rectum	1,196 (26%) 324 (7%) 1,625 (35%) 534 (11%) 994 (21%)	3,338 (28%) 742 (6%) 4,265 (36%) 1,532 (13%) 2,147 (18%)	8,660 (36%) 1,766 (7%) 7,646 (32%) 2,568 (11%) 3,122 (13%)	5,531 (46%) 1,110 (9%) 3,430 (28%) 998 (8%) 1,037 (9%)	<0.001
Tumor size N (%) < 5cm ≥ 5cm	1,860 (59%) 1,320 (41%)	5,315 (63%) 3,091 (37%)	11,693 (66%) 6,007 (34%)	5,962 (65%) 3,197 (35%)	<0.001
Tumor grade N (%) Well Moderate Poor Unidfferentiated	348 (8%) 3,017 (67%) 1,080 (24%) 29 (1%)	1056 (9%) 8,172 (71%) 2,219 (19%) 62 (1%)	1980 (9%) 15,996 (70%) 4,696 (21%) 157 (1%)	928 (8%) 7,998 (68%) 2,685 (23%) 108 (1%)	<0.001
Lymph node status N (%) Negative Positive	2,017 (51%) 1,978 (49%)	5,579 (57%) 4,270 (43%)	11,934 (62%) 7,317 (38%)	6,524 (65%) 3,492 (35%)	<0.001
Extent of disease (N, %) Local Regional Distant	1,323 (28%) 2,436 (52%) 941 (20%)	4,044 (34%) 5,828 (48%) 2,170 (18%)	8,773 (37%) 11,547 (48%) 3,510 (15%)	4,464 (37%) 6,118 (50%) 1,564 (13%)	<0.001
Chemotherapy (N, %) No Yes	2,045 (45%) 2,498 (55%)	6,581 (57%) 5,042 (43%)	16,710 (73%) 6,216 (27%)	10,851 (91%) 1,038 (9%)	<0.001
Radiation (N, %) No Yes	3,852 (81%) 878 (19%)	10,382 (86%) 1,727 (14%)	22,017 (92%) 1,944 (8%)	11,861 (97%) 353 (3%)	<0.001
Cause of death N (%) Colorectal cancer All other causes	1,369 (77%) 410 (23%)	3,510 (65%) 1867 (35%)	6,927 (47%) 7,811 (53%)	3,598 (37%) 6,043 (63%)	<0.001
Vital status N (%) Dead Alive	1,779 (38%) 2,962 (63%)	5,377 (44%) 6,747 (56%)	14,738 (61%) 9,268 (39%)	9,641 (79%) 2,591 (21%)	<0.001

P205

Nodal Involvement as a Prognostic Factor For Stage IV Colon Cancer with or without Sentinel Lymph Node Mapping S. Sirop,* S. Saha, A. Korant, M. Soni, M. Arora, B. Chakravarty, D. Wiese, D. Eilander, S. Nagpal, T. Singh. *McLaren Regional Medical Center-Michigan State University, Flint, MI.*

Background: Colon cancer (CCa) patients (Pts) with stage IV disease at diagnosis may or may not have nodal metastasis (mets). Sentinel lymph node mapping (SLNM) upstages a significant number of pts compared to conventional surgery. We aimed to study the impact of nodal mets in stage IV CCa on the cancer specific survival after conventional surgery with or without Sentinel Lymph Node Mapping (SLNM). **Methods:** Two CCa databases were analyzed:The Surveillance, Epidemiology and End Result (SEER) database (pts that underwent conventional surgery) and the SLNM database (pts that underwent SLNM followed by oncological resection). Inclusion criteria were: stage IV CCa at the time of diagnosis with minimum follow up of five years. The primary outcome was cancer specific survival. Exclusion criteria included second malignancy, pts lost to follow up, unavailable data, or death secondary to other causes. Cancer specific survival was estimated and compared using the Kaplan Meier Curve and log rank test, respectively. **Results:** Between 1996-2003, 42,347 pts in the SEER database compared to 53 pts in the SLNM database were diagnosed with stage IV CCa at the time of surgery and were included in our analysis. Of these, 8896 pts in the SEER database and 6 pts in the SLNM database were excluded according to above mentioned criteria. In the SLNM database, two pts were found to have micrometastasis and were considered to have node positive disease. The three-year cancer specific survival rates for node -ve pts compared to node +ve pts were 33% versus 13% (P<0.0001) in the SEER database, and 66.7% compared to 25.7% in the SLNM database (P=0.001). The five-year cancer specific survival rates for node -ve pts compared to node +ve pts were 20% versus 7.4% (P<0.0001) in the SEER database and 33% versus 11.4% (P=0.02) in the SLNM database. The survival rates also correlated to the number of +ve LNs at the time of diagnosis. (Table 1) **Conclusions:** Stage IV CCa with nodal mets carries a worse prognosis compared to node negative disease. This applies whether or not SLNM was used. The number of LNs involved at the time of diagnosis is also a prognostic factor in stage IV CCa.

Table 1: Three year and Five year cancer specific survival in stage IV colon cancer: SLNM versus SEER

Cancer Specific Survival	SLNM			SEER		
	Included pts	3 year survival	5 year survival	Included pts	3 year survival	5 year survival
Stage IV T-N0-M1	12	66.7%	33.3%	4662	33.2%	20.5%
Stage IV T-N1-M1	11	45.5%	36.3%	5671	22.1%	12.2%
Stage IV T-N2-M1	24	16.7%	0%	23118	11.1%	6.2%

SLNM = Sentinel Lymph Node Mapping, SEER=Surveillance, Epidemiology and End Results
N1=1-3 LNs+ve; N2=>3 LNs+ve

P206

Body Fat Distribution is associated with Oncologic Outcomes of Total Mesorectal Excision for Rectal Adenocarcinoma N. Ballian,* M.G. Lubner, A. Munoz, C.P. Heise, G.D. Kennedy. *University of Wisconsin, Madison, WI.*

Introduction: Obesity increases the technical difficulty of pelvic surgery and is usually defined using the body mass index (BMI). Body fat distribution could predict surgical outcomes more accurately than BMI. The purpose of this study is to examine if body fat distribution affects technical difficulty, complications and oncologic outcomes (lymph node retrieval, negative microscopic resection margins) of total mesorectal excision (TME) for rectal adenocarcinoma. Methods: Adult patients undergoing TME for rectal adenocarcinoma at a tertiary referral center were retrospectively identified from a prospectively maintained database. Preoperative computed tomography scans were used to measure visceral (VFA) and subcutaneous fat area (SFA) at the level of the umbilicus. BMI, VFA, SFA and VFA/SFA ratio were examined for association with technical difficulty, complication rates and oncologic outcomes using logistic and ordinary least squares regression, with p≤0.05 defined as significant. Results: Between 1999 and 2009, 113 patients met inclusion criteria. Mean age was 59 years, 41% of patients were female and 74% received preoperative radiotherapy, which was not dose-adjusted for body fat distribution. Mean BMI, VFA, SFA and VFA/SFA ratio were 27.6, 108 cm2, 231 cm2 and 0.49 respectively. Increasing VFA and VFA/SFA ratio were associated with reduced lymph node retrieval (p=0.03 and p=0.009, respectively); their association with negative microscopic surgical margins neared but did not reach significance (p=0.06 and p=0.07, respectively). The association between increasing VFA/SFA ratio with earlier resumption of oral intake was also significant (p=0.05). BMI, VFA, SFA and VFA/SFA ratio were not associated with intraoperative blood loss, operative duration, complications, length of hospital stay, lymph node metastases or sphincter preservation (Table 1). Conclusion: Increased VFA/SFA ratio is associated with reduced lymph node retrieval and delayed resumption of oral intake in patients undergoing TME for rectal adenocarcinoma. Defining obesity using VFA/SFA ratio rather than BMI could more accurately predict oncologic outcomes in these patients.

Table 1: Means and p-values for association of obesity indices with perioperative and oncologic outcomes in 113 patients undergoing TME for rectal adenocarcinoma

	Mean±SD [range]	**BMI**	**VFA/SFA ratio**	**SFA**	**VFA**
Estimated Blood Loss (ml)	419±552 [50-5000]	0.17	0.10	0.93	0.30
Operative Duration (min)	215±78 [79-502]	0.82	0.93	0.79	0.37
Complication Severity	not applicable	0.19	0.69	0.17	0.97
Resumption of Oral Intake (median, days)	4 [1-14]	0.38	**0.05**	0.95	0.27
Length of Hospital Stay (median, days)	7 [3-26]	0.77	0.26	0.78	0.77
Positive Resection Margins	not applicable	0.45	0.07	0.63	0.06
Lymph Node Metastasis	not applicable	0.67	0.56	0.07	0.35
Total Lymph Nodes Resected	9.5±5.2 [0-24]	0.26	**0.009**	0.86	**0.03**
Abdominoperineal Resection	not applicable	0.56	0.50	0.56	0.31

TME: total mesorectal excision; SD: standard deviation; BMI: body mass index; n/a: not applicable; VFA: visceral fat area; SFA: subcutaneous fat area
Significant values in **bold**

P207

The Outcome Of Sphincter Preservation And Abdomino- perineal Resection Following Preoperative Chemoradiation in locally advanced low rectal Cancer W.M. Gawad,* M.M. Khafagy, S.M. Moneib. *Surgical oncology, National cancer Institute, Cairo, Cairo, Egypt.*

Background. The advent in surgical techniques alongside neoadjuvant chemo radiation enabled more patients with low rectal cancer to have sphincter preservation. Objective. The aim of this study was to compare the oncologic outcome in patients with locally advanced low rectal cancer treated by neoadjuvant chemoradiation followed by sphincter preservation as low anterior resection (LAR)/Double stapling coloanal anastomosis ; LAR/ Abdominoanal Intersphincteric resection-hand sewn anorectal anastomosis)and Abdominoperineal resection (APR). Methods We prospectively evaluated 115 patients with low rectal cancer from 2004-2008. Forty six patients (40%) were stage II and 69 patients (60%) were stage III low rectal cancer located 5 or less from anal verge. Patients received preoperative chemoradiation and total mesorectal excision. Sixty four patients 56% had sphincter preservation and 51 patients 44% Abdominoperineal resection (APR). Results Male: female ratio was 1.8:1.Tumours were located between 2.5-4.5 (mean 3-6)cm from anal verge. patients undergone APR were older with poorly differentiated tumours that showed less response to chemotherapy requiring extended resection. Complete resection with negative margins was obtained in 90% of patients, circumferential margins were positive in 22% (stage II 21%,stage III 35%). With a median follow up of 45 months, there were a total of 12 recurrences (10%) 4 in sphincter preservation and 8 in APR patients. Estimated 5- years recurrence-free survival for stapled anastomosis, abdominoanal Intersphincteric resection and APR were 81%,80% and 41% respectively (p=0.001).The 5 year actuarial survival rates(Kaplan –Meier) for sphincter preservation and APR were79% and 64% respectively. Conclusion In low rectal cancer, the sphincter preservation appears to have a superior outcome over APR due to a significant response to preoperative chemoradiation and Intersphincteric techniques of resection with no jeopardy to margins or outcome. APR is retained for patients with less response to chemoradiation and poorer outcome.

: Local recurrence and 5 years survival in relation to CRM involvement in

Sphincter Preservation	Percentage %	Local recurrence	5 years survival
CRM +ve	22.5%	17 %	57%
CRM-ve	77.5%	9%	78%

P208

Various prognostic nodal factors, adjuvant chemotherapy and survival among same cohort of colon cancer patient aged 65 and older: an analysis using SEER-Medicare data N.N. Hanna,[1]* E. Onukwugha,[3] M. Choti,[2] A. Davidoff,[3] I. Zuckerman,[3] V. Hsu,[3] D. Mullins.[3] *1. Surgery, University of Maryland, Baltimore, MD; 2. Johns Hopkins University, Baltimore, MD; 3. University of Maryland, School of Pharmacy, Baltimore, MD.*

Introduction: The prognostic effect of chemotherapy and various nodal measures (positive nodes, total node count and the positive lymph node ratio (PLNR)) in colon cancer patients has been separately established. It is unknown whether the cancer-specific survival benefit of chemotherapy differs across these nodal prognostic factors in the same cohort of patients. This information may help identify patients most likely to benefit from chemotherapy Methods: The retrospective analysis of linked Surveillance, Epidemiology, and Endpoints and Medicare data included patients aged 65 and older with Stage III colon cancer diagnosis between 1997 and 2002. We grouped patients according to the number of positive nodes (N1 and N2), total node count (≥12 and <12 total nodes), and PLNR (below the 75th percentile and at least at the 75th percentile of the PLNR). The outcome was colon-cancer specific mortality. Results: Only fifty-one percent (N=3,701) of the 7,263 patients received adjuvant therapy during this period. The mean (sd) number of total nodes examined was 13 (9) and positive nodes identified was 3 (3). Patients with N2 disease, < 12 total nodes examined, and a high PLNR had worse survival at 2, 3, and 5 years following colectomy. Utilization of chemotherapy demonstrated a colon cancer-specific survival benefit (HR at median follow up: 0.7; $p < 0.001$) that was consistent and statistically significant across the three nodal prognostic categories examined. Conclusions: The benefit of chemotherapy did not vary based on N stage, total node count or PLNR. The results favor a broad-based approach to increasing chemotherapy treatment rates in Stage III patients aged 65 and older rather than an approach that targets clinical subgroups.

Colon cancer mortality rates for treated and non-treated patients, stratified by N stage, total node count at least 12, and percentile of positive lymph node ratio (PLNR)

Variable	%	%
	N1 disease	N2 disease
No adjuvant treatment	31.1	48.1
Adjuvant treatment	15.7	31.9
p-value	<0.001	<0.001
	Total nodes < 12	Total nodes ≥ 12
No adjuvant treatment	37.1	34.6
Adjuvant treatment	21.9	19.4
p-value	<0.001	<0.001
	< 75th %ile of PLNR	≥ 75th %ile of PLNR
No adjuvant treatment	31.7	48.2
Adjuvant treatment	16.2	35.5
p-value	<0.001	<0.001

P209

Actionable indicators for short and long term outcomes in rectal cancer J.T. Plukker,[1]* M. Gort,[3] M. Broekhuis,[4] N.S. Klazinga,[4] R. Otter.[2] *1. Dept Surgical Oncology, University Medical Center Groningen, Groningen, Groningen, Netherlands; 2. Comprehensive Cancer Centre North East, Groningen, Groningen, Netherlands; 3. Faculty of Economics and Business, University of Groningen, Groningen, Groningen, Netherlands; 4. Department of Social Medicine, University of Amsterdam, Amsterdam, Amsterdam, Netherlands.*

Introduction: Although patient and tumor characteristics are important determinants for outcomes in rectal cancer care, actionable factors for improving these are still unclear. We assess the impact of surgeon and hospital factors which can actually be influenced to improve on postoperative complications, disease free (DFS) and relative survival (RS) in rectal cancer. Methods Data of 819 curatively operated rectal cancer patients, staged I-III and diagnosed between 2001 and 2005, were derived from the population-based Cancer Registry of the Comprehensive Cancer Center North East and medical record information. We performed logistic regression analysis to examine influence of relevant factors on postoperative complications and time from diagnosis to first treatment and Cox regression for DFS and RS analysis. Results Postoperative complications were dependent on type of surgery (p=0.024) and hospital volume (p=0.029). DFS was mainly influenced by stage (p<0.001) and time to treatment (p=0.018). Actionable indicators related to RS were type of surgery (p=0.011) and time to treatment (p=0.048). Time to treatment was found to be related to co-morbidity (p=0.007), preoperative radiotherapy (p=0.003) and referral for operation (p=0.048). Nevertheless, 18.2% unexplained variation in time to treatment remained on hospital level. Conclusions Optimal outcomes for rectal cancer care can be achieved by focusing on early detection and timely diagnosis, as well as adequate choice and timeliness of treatment in hospitals with optimal logistics for rectal cancer patients.

P210

Improper wound healing does not limit the application of abdominosacral amputation of the rectum (ASAR) in low-rectal cancer patients M. Bebenek,[1]* W. Tupikowski,[1] K. Cisarz,[1] A. Balcerzak,[1] L. Wojciechowski,[1] A. Stankowska,[1] M. Pudelko,[1] R. Tarkowski,[2] T. Sedziak,[1] R. Szulc,[1] B. Bednorz,[1] B. Kapturkiewicz.[1] *1. 1st Department of Surgical Oncology, Regional Comprehensive Cancer Center, Wroclaw, Poland; 2. *Department of Oncology, Wroclaw Medical University, Wroclaw, Poland.*

INTRODUCTION We have recently presented abdominosacral amputation of the rectum (ASAR) as a potentially valuable alternative to abdominoperineal resection (APR) in the surgical treatment of low-rectal cancer patients. The problem we frequently had to deal with, however, was whether or not the extent of the ASAR procedure affected increased morbidity due to problems in wound healing. The purpose of our presentation is to solve this problem by means of retrospective analysis of a group of patients who were subjected to ASAR. METHODS The analysis included 188 patients subjected to ASAR between April 15th, 1998 and March 31st, 2007. They were divided into two subgroups: cases operated on after neoadjuvant therapy and those subjected to

surgery alone. Surgical wound healing was monitored during the initial four weeks for acute complications and within one year after the operation for late complications. RESULTS No postoperative mortality or eventeration were recorded in any of the patients studied. Total frequency of acute wound healing complications amounted to 38 cases (20.2%), among which superficial infections (n=25) were the most frequent finding. In total, acute wound healing complications prolonged median hospitalization by two days (12 vs. 10) compared to the cases without any healing problems. Two cases of perineal hernia were recorded in ASAR-treated patients, but neither was symptomatic nor required surgical intervention. Impaired wound healing was significantly more frequent in the group given neodajuvant, long radiochemotherapy treatment. CONCLUSIONS Improper wound healing is infrequent in ASAR-operated patients and does not constitute a serious limitation for the application of this technique. Optimal healing of the surgical wound in ASAR-operated cases results mainly from an unhindered surgical approach with sharp and under direct-vision dissection along anatomical planes.

P211

Impact of Lymph Node Status on Survival in Patients with Resected Stage IV Colon Cancer S.P. Bagaria,[1]* P. Ray,[1] R.W. Beart,[2] D.A. Etzioni.[2] *1. Department of Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA; 2. Department of Colorectal Surgery, Keck School of Medicine, University of Southern California, Los Angeles, CA.*

INTRODUCTION For patients with non-metastatic colon cancer, lymph node status is a critical factor in determining prognosis and treatment. The importance of lymph node status among patients with stage IV colon cancer patients who undergo colon resection is unknown. **METHODS** Patients who underwent colon resection for stage IV colon cancer diagnosed 1992-2002 were identified from the SEER-Medicare database. The hospitalization during which these resections were performed was classified as elective, urgent, or emergent based on hospital report. Multivariate analyses were performed (adjusting for age, sex, race/ethnicity, Charlson score, and preoperative chemotherapy) to understand the relationship between 1) nodal status and 2) number of lymph nodes examined on survival. **RESULTS** We analyzed a total of 7,029 patients. Multivariate analysis revealed that patients with N1 or N2 disease (relative to N0) had worse overall survival. Greater numbers of examined lymph nodes were associated with better overall survival. **CONCLUSIONS** Patients with stage IV colon cancer who are N0 and those with higher numbers of examined lymph nodes have improved survival, although the mechanism for this is unclear. Regardless of mechanism, nodal disease in the presence of metastatic disease has prognostic importance, and may therefore need to be considered in developing a treatment plan.

	Elective		Urgent		Emergent	
	HR [95% CI]	P value	HR [95% CI]	P value	HR [95% CI]	P value
Nodes examined						
5-9 LNs vs. 1-4 LNs	0.72 [0.64-0.81]	<0.001	0.89 [0.77 - 1.03]	0.11	0.83 [0.71-0.96]	0.014
10-14 LNs vs. 1-4 LNs	0.63 [0.55-0.71]	<0.001	0.84 [0.72 - 0.98]	0.027	0.64 [0.55-0.77]	<0.001
15+ LNs. vs 1-4 LNs	0.60 [0.53-0.68]	<0.001	0.71 [0.61 - 0.82]	<0.001	0.70 [0.60-0.82]	<0.001
Nodal stage						
N1 vs. N0	1.26 [1.14-1.39]	<0.001	1.24 [1.08 - 1.41]	0.0018	1.25 [1.09-1.42]	0.0013
N2 vs. N0	2.08 [1.88-2.30]	<0.001	2.08 [1.82 - 2.37]	<0.001	1.89 [1.65-2.17]	<0.001

P212

WITHDRAWN

P213

Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Carcinomatosis of Varying Histology-Aggressive but safe R. Wong,* G. Jibara, F. Manizate, Y. Assadipour, S. Hiotis, S. Roayaie, M. Schwartz, D. Labow. *Surgery, Mount Sinai School of Medicine, New York, NY.*

Background: Cytoreductive surgery (CRS) with heated intraperitoneal chemotherapy (HIPEC) has gained acceptance in the treatment of peritoneal carcinomatosis. Clear indications for this aggressive approach, and for which malignancies it applies to, remains unclear. This series reports a single institution experience for CRS and HIPEC for varying malignancies. Methods: Between July 2007 and July 2009, a total of 69 patients underwent 71 cytoreductive procedures and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC)for peritoneal carcinomatosis at a single institution. Clinical data were prospectively collected. Univariate and multivariate analyses were performed to assess safety of procedures across histologies in our series. Results: There were 37 females and 32 males. The median age was 56 years (range, 18-77 years). The most common histology was colon cancer (n=25, 35%) followed by appendiceal cancer (n=20, 28.5%), gastric cancer (n=6, 8.5%), and hepatocellular cancer (n=4, 5.6%). The median operative time and estimated blood loss were 431 minutes (range, 175-815 minutes) and 500 mL (range, 50-6500 mL) respectively. The median hospital length of stay was 9 days (range, 4-99 days). The median initial Peritoneal Cancer Index (PCI) score was 16 (range, 0-37) and post-CRS PCI score was 3 (0-26). Optimal cytoreduction (CC 0 or 1) was achieved in 70.5% of cases. Major morbidity rate was 25.4% with a 30-day and in-hospital mortality were 1.4% and 4.2%, respectively. Clinical variables including number of anastomoses, operative time, estimated blood loss, extent of cytoreduction and histologic subtype were not independent risk factors for morbidity. Intraoperative blood transfusion was the only independent prognostic factor for major morbidity on multivariate analysis ($p<0.05$). Conclusion: Our single-institution experience of CS/HIPEC procedures for peritoneal carcinomatosis for different hisotologies demonstrates low 30-day perioperative mortality and acceptable rates of morbidity. Optimal cytoreduction was achieved in nearly 3/4 of cases. This series supports the safety of CRS and HIPEC in selected patients.

P214

Pancreatic resection in the 9th decade of life: not always a safe option for pancreatic malignancy I. Hatzaras,* C. Schmidt, P. Muscarella, W.S. Melvin, E.C. Ellison, M. Bloomston. *Surgery, OSU, Columbus, OH.*

Objective: To assess our institution's experience and outcomes with pancreatic resection in the setting of malignancy, in patients beyond their 9th decade of life. Methods: We retrospectively reviewed the clinical records of all patients undergoing pancreatic resection for malignancy. Demographics, laboratory, treatment and outcome data were gathered. Comparisons of groups were made by two-tailed student's t and the Wilcoxon rank sum tests for continuous data and contingency table analysis (chi-square and Fisher's exact test) where appropriate. Survival was analyzed using the Kaplan-Meier method and comparisons between groups were performed employing the log-rank test. Statistical significance was accepted at p-value<0.05. Results: There were 517 pancreatic resections for cancer in our institution from January 1990 to December 2007. Of these, 27 patients were older than 80. The distribution of clinical characteristics was similar between the two groups (table). The majority of patients undergoing pancreatic resection harbored a pancreatic adenocarcinoma at the head of the pancreas, hence the most common procedure performed was pancreaticoduodenectomy (398, 78%). There were no differences in the complication rates, length of stay, or perioperative mortality rates. While there was a trend towards shorter overall survival in patients over 80 (median 10.2 vs. 15.5 months), this was not statistically significant (p=0.08, figure). Conclusion: Pancreatectomy for malignancy in octogenerians is associated with increased perioperative mortality and decreased overall survival. While these findings were not statistically significant, the trend suggests that appropriate patient selection is critical in elderly patients.

Clinical characteristics of patients undergoing pancreatic resection in the setting of malignancy

	Age ≥80 N=27	Age <80 N=490	p
Female gender	13 (48.1%)	217 (44.3%)	0.69
Comorbidities	19 (70.4%)	306 (62.4%)	0.40
Mean Preoperative CA19-9 (SD)	1,032 (469.8)	1,057 (279.2)	0.49
Mean Tumor Size (SD)	3.6cm (1.7)	3.6cm (2.1)	0.98
Positive Margins	3 (11.1%)	76 (16.2%)	0.59
Mean hospital Stay (SD)	15.0 days (2.0)	13.3 days (0.42)	0.33
Mean ICU Stay (SD)	1.9 days (0.51)	1.8 days (0.11)	0.88
Complications	13 (48.1%)	202 (41.2%)	0.47
Perioperative Mortality	4 (14.8%)	41 (8.4%)	0.28

P215

Perioperative biochemical tests predict perioperative and disease-related mortality following pancreaticoduodenectomy J. Coates,* E. Brown, J. Russo, S. Chen, R. Canter, R. Bold. *UC Davis, Sacramento, CA.*

Introduction: Preoperative evaluation of patients planned to undergo pancreaticoduodenectomy (PD) may predict risk for mortality from short-term causes (ie procedure-related) or long-term causes (ie disease-related). Accurate identification of these patients may allow for more careful event-surveillance or therapeutic decision-making. We therefore evaluated whether perioperative biochemical testing prior to PD allows for stratification of perioperative and disease-related mortality. Methods: Using our institutional database, we identified 191 patients who underwent PD, of which 115 were for adenocarcinoma. Factors evaluated included preoperative and postoperative (ie POD#1) hematological studies, serum chemistry panels, liver function tests and the tumor marker CA19-9. Univariate analysis was performed by Chi-squared analysis or t-testing; Kaplan-Meier and Cox proportional hazards modeling were used for overall survival analysis. Results: The overall rate of hospital death was 2.6% and 30-day mortality was 3.7%. Factors associated with increased risk of perioperative mortality included preoperative anemia (hemoglobin <11.8 gm/dl; p=0.01) and renal insufficiency (creatinine > 1.0 mg/dl; p=0.03). In the postoperative period, a rising creatinine (increase of greater than 0.1 mg/dl); p=0.03) or falling white blood cell count (any decrease from preoperative value; p=0.03) also predicted an increased risk of short term mortality (Figure 1A). In patients with adenocarcinoma, elevated preoperative level of CA19-9 (ie >150) was associated with a shorter disease-related survival (17 vs. 10 months, p=0.003) (Figure 1B). Conclusions: Perioperative biochemical tests can be used to identify patients who are at elevated risk for perioperative and disease related mortality. Accurate identification of these patients may allow for direct intervention that may alter perioperative risk, such as correction of anemia or renal insufficiency. Furthermore, those patients with increased risk of disease-related mortality may be appropriate candidates for alternative therapeutic strategies and counseled appropriately about the benefit of surgical intervention.

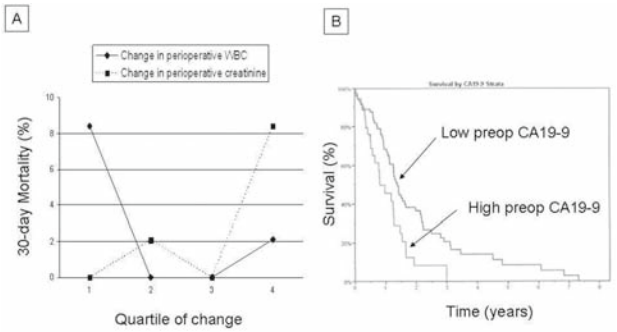


Figure 1: A) 30-day perioperative mortality of patients undergoing PD based on quartile of perioperative change (preoperative to POD#1) in either WBC (◆——◆) or creatinine (■——■), and B) Overall survival of patients undergoing PD for adenocarcinoma based on high (>150) or low (<150) preoperative CA19-9.

P216

Feasibility and safety of laparoscopic complete mesocolic excision for right colon cancer T. Akasu,* S. Yamamoto, K. Sato, T. Funada, S. Fujita, Y. Moriya. *Colorectal Surgery Division, National Cancer Center Hospital, Tokyo, Japan.*

BACKGROUND Recently, a concept of complete mesocolic excision (CME) for colonic cancer is proposed. CME aims at the separation of the mesocolon from the parietal plane and true central ligation of the supplying arteries and draining veins right at their roots and thus may result in reducing local recurrence. On the other hand, laparoscopic surgery has been well applied for colon cancer surgery. The aim of this study was to assess feasibility and safety of laparoscopic CME as compared to conventional lymph node dissection for right colon cancer. METHODS Between 2000 and 2008, 153 patients with primary right colon cancer underwent laparoscopic ileocecal resection (n = 65) or right hemicolectomy (n = 88). Patient characteristics and details of surgery are shown in the Table. CME is recommended for c-stage II or III tumors in the Japanese guidelines. In CME, the surgical trunk was first exposed and the ileocolic and right colic vessels were clipped and cut. Then the mesocolon was completely dissected from the retroperitoneum. RESULTS As shown in the Table, the patients with CME had more advanced tumors, longer operating time, and larger numbers of lymph node harvest as compared to those with conventional lymph node dissection. There were no patients with blood transfusion and mortality in both groups. In terms of morbidity and post operative recovery, both groups were comparable. CONCLUSION Laparoscopic CME for right colon cancer is feasible and safe and has the advantage of resecting more lymph nodes as compared to the conventional dissection.

	CME (n = 50)	Conventional (n = 103)	P value
No. of men	24	54	0.73
No. with age > 65 yrs	21	55	0.23
Stage 0/I/II/III	3/16/16/15	13/66/10/14	< 0.001
Median operating time	214 min	174 min	< 0.001
Median blood loss	34 mL	27 mL	0.18
No. with transfusion	0	0	-
No. with conversion	1	0	0.33
Median lymph node harvest	27	19	< 0.001
No. with complication	1	5	0.66
Median hospital stay	8 days	8 days	0.15

P217

Sphincter Preservation and Local Recurrence Using a Multimodal Algorithm for Treatment of Surgically Difficult Rectal Cancer R.J. Aragon,[1]* G.R. Machado,[2] I.J. Kuo,[2] A. Coutsoumpos,[3] K.B. Zmaj,[1] M.E. Reeves.[1] *1. Surgical Oncology, Jerry L. Pettis Memorial VA Medical Center, Loma Linda, CA; 2. Loma Linda University Medical Center, Loma Linda, CA; 3. Loma Linda University School of Medicine, Loma Linda, CA.*

INTRODUCTION: Achieving adequate local control while maintaining sphincter preservation (SP) are goals of curative rectal cancer surgery. Total mesorectal excision (TME) and neoadjuvant chemoradiation (NC) are treatment modalities that can decrease local recurrence rates. NC can also enable previously unsuitable patients to undergo sphincter-preserving operations. This study's objective is to evaluate the impact of a uniformly applied multimodal treatment algorithm on SP and local control in a surgically difficult population. METHODS: Data was collected prospectively from 2000-2009 in an all-male population undergoing curative resection for rectal cancer. Patients presenting with recurrent cancer were excluded. Close supervision and follow-up assured strict adherence to the algorithm. Patients were staged preoperatively with endoscopic ultrasound (EUS). Patients with stage 1 disease (≤T2 and N0) underwent resection and TME +/- ileostomy. If upstaged during surgery, they received postoperative chemoradiation. Patients with stage 2 or 3 disease (≥T3 or N1) received NC followed by resection and TME +/- ileostomy + postoperative chemotherapy. RESULTS: 94 male patients (median age-66) who underwent curative resection were included. Median follow-up was 37 months. SP rate was 80%. The local recurrence rate was 2%. Of patients with preoperative stage 2 or 3 tumors, 77% received NC. Reasons for not receiving NC included prior pelvic radiation and patient preference. Approximately 30% of patients who received NC experienced complete pathologic response. 52% of patients were determined to require an APR prior to treatment. However, 62% of these patients were converted to a sphincter-sparing operation. Median tumor distance from anal verge was 8 cm, and 23% of tumors were low cancers (<5 cm from anal verge). Protecting ileostomy was utilized in 25% of patients that had a distal anastomosis. Five-year overall survival (all stages) was 68%. CONCLUSION: In a surgically difficult rectal cancer population (males, narrow pelvis, low tumors), strict adherence to a multimodal treatment algorithm achieves good local control and sphincter preservation rates.

P218

Comorbidites should not preclude resection in Esophageal cancer: The role of Minimal Invasive Esophagectomy D. Christian,* A.S. Khithani, J.G. Barton, J. Jay, D. Jeyarajah. *Methodist Dallas Medical Center, Dallas, TX.*

Introduction: Minimal invasive surgery has been applied to esophagectomy with different approaches. However it continues to be associated with a high mortality. The aim of this study was to determine the safety and efficacy of MIE in patients with significant comorbidities and a high Charlson comorbidity score. Methods: MIE in the form of combined thoracoscopic and laparoscopic esophageal resections were performed cooperatively by two surgeons between September 2005 and Sept 2009. The Charlson comorbidity score was assigned to each patient. The Charlson score is used, to evaluate prognosis based on age and comorbid conditions. It indicates increased cumulative mortality with each increased level of the comorbidity. A Charlson score of 2 or more has been reported to be associated with 1.5 fold increase in postoperative mortality. Preoperative, intraoperative, and postoperative were evaluated. Results: Forty two patients underwent MIE for esophageal malignancies, 64% for adenocarcinomas, 24% for squamous carcinomas, and 12% for high-grade dysplasia with Barretts. There was a male predominance with a male to female ratio of 1:2.2. Mean age at presentation was 66 years(range 83-20). Comorbidities were documented in 79% of the study group, with 48% from ASA class III and IV each. Twenty six patients (62%) received neoadjuvant chemoradiotherapy. The median Charlson age-adjusted comorbidity index was 5.00(range 2-9). The median operating time was 270 minutes (range 192-462). The Median blood loss was 250 mL(range 100-700). Two patients (5%) required conversion to open celiotomy. The median length of hospital stay was 10 days (range 8-54). Three patients (7%) required a reoperation for wound problems. There was no mortality reported in the series. There was no post operative anastomotic leak. Conclusions: MIE can be performed with results that meet and exceed reported benchmarks. This technique may help to achieve low mortality and hence better safety even in the presence of significant co-morbidities.

P219

90% Hepatectomy With A Porto-Hepatic Shunt In A Canine Model: A Feasibility Study S.T. Steen,* W. Conway, C. Guerra, M. Shin, G. Singh. *John Wayne Cancer Institute, Santa Monica, CA.*

Introduction: After extended hepatectomy, portal venous inflow can produce shear stress that contributes to liver dysfunction. We postulated that a surgical shunt between the portal and hepatic veins (porto-hepatic shunt) could decrease shear stress on the liver remnant and thereby improve its function and regeneration. We used a canine model to design and test the feasibility of a procedure for 90% hepatectomy with and without a porto-hepatic shunt. Although several studies have investigated near-complete hepatectomy in a murine model, the canine model is more relevant for translational research. Methods: Eight mixed-hound canines (body weight, 20–30 kg; age, 8–12 months) were quarantined for 15 days. Two animals were then sacrificed for postmortem study of hepatic anatomy; results were used to design a procedure for removing all of the liver except portions of two lobes. This 90% hepatectomy procedure was tested under general anesthesia in the remaining animals, with (N=3) or without (N=3) a surgical porto-hepatic shunt. Animals were monitored postoperatively with serial liver function testing, and sacrificed on postoperative day 45. Liver regeneration was assessed as a percentage of overall body weight. Results: Extended hepatectomy removed four complete lobes and portions of the right lateral and caudate lobes. For the porto-hepatic shunt, the left portal vein branch was anastomosed to the left hepatic vein branch. All procedures were performed successfully. One no-shunt animal expired on the second postoperative day. Although the size of the population prevented detection of statistical differences in postoperative liver function or regeneration, shunted animals tended to recover faster than animals without a shunt. Conclusion: Our canine model allowed us to develop a reproducible and technically feasible procedure for 90% hepatectomy with or without a surgical porto-hepatic shunt. If the efficacy of shunting is validated in a larger canine population, it may increase the indications for extensive resection in patients with advanced hepatic malignancy.

P220

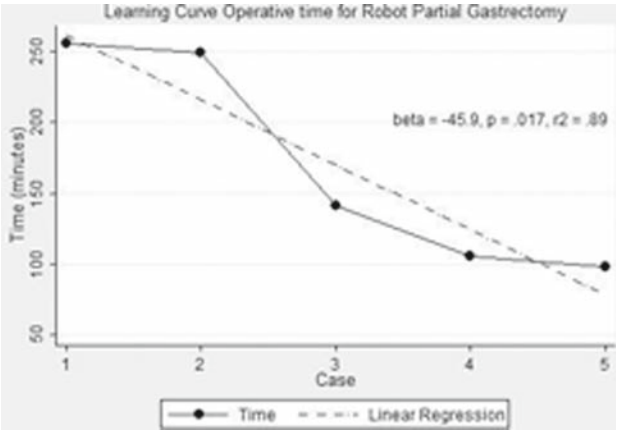
Does a Preoperatively Placed Percutaneous Endoscopic Gastrostomy Tube Impact Negatively on Eventual Esophagectomy? S.M. Foster,* M.H. Chung. *Grand Rapids Medical Education and Research Center, Grand Rapids, MI.*

INTRODUCTION: Esophagectomy remains the curative therapy for early esophageal carcinoma. We examined the impact of preoperative percutaneous endoscopic gastrostomy (PEG) placement in patients undergoing esophagectomy. METHODS: A retrospective chart review of one surgeon's experience with preoperative PEG placement in patients undergoing esophagectomy from 6/1/05 through 6/30/09 was performed. Data collected included preoperative therapy, stage of tumor, type of esophagectomy, preoperative PEG placement, gastric conduit suitability, anastomotic leak, morbidity and mortality (in-hospital or 30 day). RESULTS: Fifty-five patients were reviewed during the study period, 49 without PEG placement (PEG -) and six with placement (PEG +). The two groups were similar with regards to demographics, tumor stage, and type of esophagectomy performed. However, there were five (83.3%) neoadjuvant chemo/radiation patients in the PEG + group and 14 (28.6%) in the PEG - group. In both groups, the stomach was technically usable as an esophageal replacement. Each group had two patients with colon interposition. There were three esophagogastric anastomotic leaks in the PEG - group versus no leaks in the PEG + group. No one in the PEG + group leaked from their old PEG site. One mortality occurred in the PEG - group. CONCLUSIONS: It appears that preoperative PEG placement has no effect on performance of esophagectomy even if placement occurred without the surgeon's consent. However, further study should occur in this area. We recommend that patient care be coordinated in a multidisciplinary setting and that this procedure be discussed with surgeons prior to placement.

P221

The Learning Curve in Robotic Gastrointestinal Surgery A. Zemlyak,* P.Q. Bao, K.T. Watkins. *Surgery, SUNY Stony Brook, Stony Brook, NY.*

Background/Objectives: Minimal data exist on how robotics should be incorporated into a gastrointestinal surgery program and whether significant benefits such as seen in prostatectomy can be realized. The DaVinci robotic system was recently incorporated into our minimally invasive gastrointestinal surgery program. We evaluated our initial experience by looking at our most frequently performed procedure. Methods: A retrospective review was performed on robotic gastric wedge resections performed between 1/2009 and 9/2009. All tumors were exophytic in nature and locally resected. The gastrotomy was closed in two layers utilizing the robotic instruments. Results: Seven patients were identified four of which were female. Ages ranged from 38-83. Five had gastrointestinal stromal tumors (GIST) and two leiomyomas. Median (range) tumor size was 8 (2.7-13)cm. All tumors were resected with negative margin with the exception of a 13 cm tumor that had spontaneously ruptured and received neoadjuvant Gleevec. There was no observed morbidity or mortality. Median blood loss was 20 ml and there were no transfusions. Median (range) hospital stay was 1 (1-5) days. All patients were home by day 2 except the patient with ruptured GIST and multiple pre-existing conditions. Excluding two cases prolonged by additional procedures, one with added cholecystectomy and one who required intraoperative endoscopy to decompress his stomach after multiple failed attempts to place an orogastric tube, there was a definite early learning curve with significant improvement in OR times (graph). In earlier cases the robot was docked at the beginning and used for the entire procedure. At later points initial identification and isolation of the tumor was performed laparoscopically with tumor resection and closure being performed with the robot. Conclusions: There appears to be a definite early learning curve for the implementation of robotic surgery. In an established minimally invasive surgery program this learning curve seems brief. Further investigation is required to evaluate where robotic approaches offer any significant benefit.



P222

Sub-optimal Removal of Lymph Nodes for Malignant Colonic Polyps and Impact on Survival in the General Population

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Background Colonoscopic screening and appreciation of the adenoma-carcinoma sequence has led to increased detection of malignant colonic polyps (MP) and referral for surgical removal. Our goal was to assess the quality of surgical resection for MP as measured by lymph node (LN) retrieval and survival outcomes. Methods The Surveillance, Epidemiology and End Results (SEER) registry was queried to identify patients with MP treated by surgical resection from 1988-2003. Survival of patients was compared using Kaplan-Meier curves and Cox regression analysis used to identify predictors of survival. Results Of 17,953 patients undergoing surgical resection for MP the median number of LN retrieved overall was only 4. A significant proportion (33.4%) had no LN detected in the specimen (Nx). When compared to patients who had at least one LN examined (N), the Nx subset had a lower overall survival (OS) at 5 years (69% vs. 63%, p <0.001). In 12,061 of patients with T1 tumors, 48.6% were Nx and the OS difference at 5 years between N and Nx was more pronounced (75% vs. 64%, p <0.001). On multivariate analysis of the entire study population, having at least one node examined conferred a 27% benefit to OS at five years (Hazard Ratio 0.73, 95% CI 0.64-0.82). Conclusions Patients undergoing surgical resection for MP in the general population have poor LN retrieval, with an adverse impact on survival. Performance of adequate lymphadenectomy by surgeons is crucial to optimize survival outcomes for patients with these potentially curable lesions.

P223

Yttrium-90 Radiotherapy for Unresectable Intrahepatic Cholangiocarcinoma: A preliminary assessment of this novel treatment option

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Background There are no treatment options for unresectable intrahepatic cholangiocarcinoma (ICC) with proven efficacy. The objective of this study was to present data on the safety and efficacy of a novel treatment option, yttrium-90 (90Y) radioembolization for unresectable ICC. Methods Twenty-five patients underwent resin- based 90Y radioembolization for unresectable ICC between January 2004 and May 2009. Patients were assessed at 1 month and then at 3 month intervals after treatment. Radiologic response was evaluated with the Response Criteria in Solid Tumors (RECIST) criteria. Clinical and biochemical toxicities were prospectively recorded. Survival was calculated using the Kaplan-Meier method and potential prognostic variables were identified. Results No patient was lost to follow-up. The median follow-up was 8.1 months (range = 0.4 to 56). The median survival after the first 90Y radioembolization treatment was 9.3 months. Two factors were associated with an improved survival: peripheral tumor type (versus infiltrative, p = 0.004) and ECOG performance status of 0 (versus 1 and 2, p < 0.001). On imaging follow-up of 23 patients, a partial response to treatment was observed in 6 patients (24%), stable disease in 11 patients (48%) and progressive disease in 5 patients (20%). The most common clinical toxicities were fatigue (64%) and self-limiting abdominal pain (40%). Two patients (8%) each developed grade III bilirubin and albumin toxicity. One patient (4%) developed grade III alkaline phosphatase toxicity. Conclusion 90Y radioembolization may be a relatively safe and efficacious treatment for unresectable ICC. This treatment modality warrants further investigation in the absence of other effective therapeutic options for this disease.

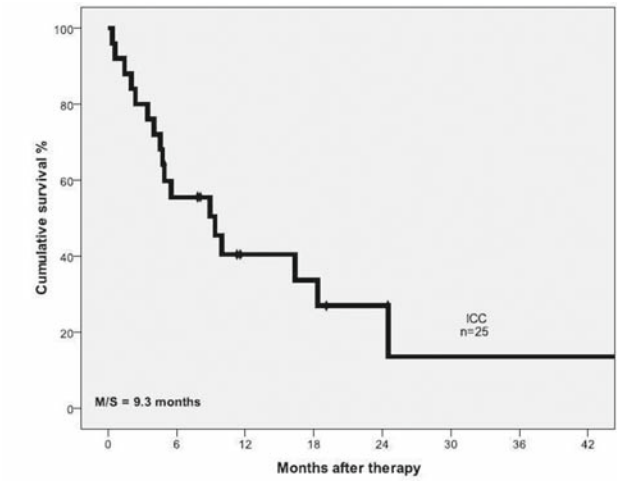

Figure 1. Overall survival after ^{90}Y radioembolization for intrahepatic cholangiocarcinoma (n = 25).

P224

Sentinel node biopsy combined with detection of micrometastasis in carcinoma of the buccal mucosa

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Introduction Carcinoma of the buccal mucosa is a common cancer in India, the incidence is particularly high in North India .This is a locally aggressive malignancy with a low propensity to nodal or distant metastasis. Presence of lymph node metastases in neck is considered as an adverse prognostic factor. Aim of this study was to evaluate role of sentinel lymph node biopsy by using blue dye and immunoshistochemistry for cytokeratin in identifying in occult metastasis in neck N0 neck in patients with carcinoma buccal mucosa. Patients and methods Between 2006 and 2008, 28 consecutive clinically and radiographically node negative previously untreated patients were enrolled in prospective study. In the operating room peritumoral injection of 2.5% isosulfan blue dye was given followed by dissection of blue node. All sentinel nodes found to be negative on histology were stained with cytokeratin antibody by immunoperoxidase method. Results Sentinel node was identified in 27 patients. A total of 37 nodes were harvested at an average of 1.3 nodes per neck. Sentinel nodes were distributed in five cases in level Ia, 14 cases in Level Ib, 8 cases in level IIa. Of the 37 harvested nodes 14 were positive and 23 were negative for metastases. One of the negative node was (3.7%) cytokeratin positive. Sensitivity of sentinel node biopsy was 100%.negetive predictive value is 100%, specificity was93.35 positive predictive value is 92.8%. Conclusions Sentinel lymph node biopsy with isosulfan blue was able to detect blue node with high sensitivity, with few false negative results .The results show that it can be reliably used to predict status of remaining nodal basin.

Distribution and positivity of sentinel node by tumor stage

Tstage	SLN found	SLN not found	SLNB positive	SLNB negative	HPE positive	HPE negative	sentinel only positive
T1	4	-	1	3	3	3	1
T2	9	-	4	5	4	5	1
T3	8	1	6	2	6	2	3
T4	6	-	3	3	3	3	1

SLN – Sentinel lymph node; SLNB – sentinel lymph node biopsy; HPE – histopathology of the rest of neck.

P225

Iodine Inhibits the Growth of Thyroid Cancer Cells via Cell Cycle Arrest and Mitochondrial-mediated Apoptosis G.G. Chen,* X.H. Liu, A.C. Vlantis, C.A. Van Hasselt. *The Chinese University of Hong Kong, Hong Kong, China.*

INTRODUCTION: Iodine has long been associated with thyroid tumorigenesis and therapy. However, the molecular mechanism involved remains poorly understood. METHODS: In this study, we investigated the anti-proliferative effect of iodine in 3 types of thyroid cancer cells by studying cell cycle, cell growth, apoptosis and related molecules. RESULTS: We observed that iodine induced G0G1 and G2M arrest and apoptosis in thyroid cancer cells. It appeared that apoptosis induced by iodine was mitochondrial-mediated, with the loss of mitochondrial membrane potential, Bak upregulation, caspase-3 activation and cytochrome c release. Iodine treatment decreased the level of mutant p53 including p53 with R273H mutant that possesses anti-apoptotic features, but increased the p21 level. The block of p21 significantly prevented iodine-induced apoptosis. Iodine also stimulated the activation of ERK1/2 as well as JNK1/2, the former of which turned out to be pro-apoptotic but the latter was anti-apoptotic. Surprisingly, iodine promoted instead of suppressing the expression of anti-apoptotic Bcl-xL. The increase of Bcl-xL was likely to compensate the damage induced by iodine since the inhibition of Bcl-xL accelerated iodine-mediated apoptosis. CONCLUSIONS: our data demonstrated that iodine induced mitochondrial-mediated apoptosis in thyroid cancer cells and this apoptotic pathway was involved in the up-regulation of p21, mutant p53, Bak and the activation of ERK1/2 and JNK1/2. The finding provides some solid molecular evidence to explain the epidemiological observation that iodine insufficiency promotes the thyroid tumor development. It may also reveal some novel markers for the treatment of thyroid cancer.

P226

Cervical Lymph Node Dissection for Metastatic Testicular Cancer M.G. Van Vledder,[1]* J.A. Van Der Hage,[2] W.J. Kirkels,[1] C. Verhoef,[1] J.W. Oosterhuis,[1] J.H. De Wilt.[3] *1. Erasmus MC - Daniel den Hoed Cancer Centre, Rotterdam, Netherlands; 2. Netherlands Cancer Institute - AVL, Amsterdam, Netherlands; 3. UMC St. Radboud, Nijmegen, Netherlands.*

Introduction: Testicular carcinoma is the most common form of cancer in young men. Approximately 40% of these patients will have extra retroperitoneal (ERP) metastases, which are localized in the cervical lymph nodes in only a minority of patients. Despite a generally good response to systemic chemotherapy, 30% of patients with advanced stage testicular carcinoma will have residual ERP masses requiring resection. Limited data is available concerning the incidence, surgical management and follow-up of neck metastasis arising from a testicular primary tumor. Patients and Methods: 665 patients that were referred to our tertiary referral cancer centre from January 1997 to June 2009 with the diagnosis of testicular cancer were retrospectively reviewed for the presence of cervical lymph node metastases. Patients who underwent concomitant surgical therapy were identified and analyzed. Clinical and pathological data were collected from patient records, including radiology and pathology reports. Furthermore, data on primary treatment strategy, chemotherapeutic regimens, timing of surgical procedures, complications, disease recurrence and follow up were collected. Results: 26 patients (4%) had cervical lymph node metastasis. The majority (n=19) had also other ERP sites involved. Nine patients (35%) underwent neck dissection. In six patients, this was indicated due to residual masses post chemotherapy. In three patients, cervical masses represented a late and distant relapse of previously treated disease. Viable germ cell tumor was found in the resected specimen only in these three patients. Seven patients are currently without evidence of disease. Two patients died of disseminated disease. Conclusion: Cervical lymph node metastases of germ cell tumors are rare. However, they are more commonly observed in patients with advanced stage disease. Cervical lymph node dissection can be safely performed both after chemotherapy and in the case of recurrent testicular cancer.

P227

Accuracy and Predictive Value of Diagnostic Biopsy in Cutaneous Melanoma C. Fusco,[2]* J. Boll,[3] J.E. Jones,[2] T.J. Hieken.[1] *1. Surgery, NorthShore University Health System Skokie Hospital, Skokie, IL; 2. Rush University Medical Center, Chicago, IL; 3. Rush Medical College, Chicago, IL.*

INTRODUCTION: Melanoma is diagnosed by a variety of biopsy types. While excisional biopsy is preferred, it is not always performed or possible. We undertook this study of our community surgical oncology practice to identify how frequently final tumor thickness and T stage increased after each type of diagnostic biopsy and how often this altered treatment recommendations. METHODS: From our Melanoma Registry, we identified 410 patients with clinically localized disease. Data were verified by chart and pathology report review to compare histopathology of the diagnostic biopsy and final wide local excision (WLE). 332 patients were suitable for analysis (44 had insufficient data and no WLE was done in 34). An SAS software package was used for statistical analysis. RESULTS: Median patient age was 65 years and 174 (52%) were female. Tumor site was extremity in 51%, trunk in 33% and head/neck in 16%. Initial biopsy type was excisional in 187/332 (56%), punch in 68/332 (21%), shave in 60/332 (18%) and incisional in 17/332 (5%). Biopsy margins were positive in 204/332 (61%) cases and varied with biopsy type: excisional-43%, punch-92%, shave-72% and incisional-100% ($p<0.0001$). Residual melanoma was present on WLE in 10% of patients with negative and in 53% with positive biopsy margins. Tumor thickness on WLE was greater in 53/332 (16%) of cases and tumor level increased in 26/332 (8%). T stage changed in 27/332 (8%) (excisional-3/187-2%, punch-16/68-24%, shave-4/60-7%, incisional-4/17-24%, $p<0.001$) and treatment recommendations in 21/332 (6%) (excisional-3/187-2%, punch-12/68-18%, shave-3/60-5%, incisional-3/17-18%, $p<0.001$) of patients. Change in treatment included wider margins in 71% and sentinel lymph node biopsy in 52%. CONCLUSIONS: In our study, most diagnostic biopsies were margin-positive regardless of technique and >50% of patients had residual melanoma on WLE. Despite this, a T stage change occurred in only 8% of patients, lead to a change in recommended treatment in only 6% of patients and varied markedly with biopsy type. This information is helpful in preoperative discussion with melanoma patients regarding a potential change in prognosis and the need for secondary procedures.

P228

Patterns of Recurrence in Melanoma and the Impact on Survival N. De Rosa,* J.E. Herndon II, J. Marcello, D.S. Tyler, R.P. Scheri, S.K. Pruitt, J.L. Wheeler, A.P. Abernethy. *Duke University Medical Center, Durham, NC.*

Background: The incidence of metastatic melanoma is increasing and no effective systemic therapy is available. Stratification of melanoma patients based upon longitudinal patterns of metastasis may provide an increasingly accurate predictive model for survival and may provide more comprehensive criteria for patient enrollment in clinical trials. The objective of this study was to identify patterns of metastatic recurrence and their associated survival by analysis of the prospectively collected data from 14,029 patients diagnosed with primary melanoma between 1970 and 2004 within our Melanoma Database. Methods: A retrospective review was performed to determine the sites of melanoma metastases, the most prevalent longitudinal patterns of recurrence, and the survival associated with various metastatic patterns. Patients initially diagnosed with clinical stage I or II melanoma that developed metachronous lesions were included in the analyses. Survival as defined by the time from metastatic diagnosis until death was calculated by the Kaplan Meier method. Results: Of 14,029 patients diagnosed with melanoma, 33% (N=4,636) of stage I and II patients developed metastases. The first metastatic site identified in these patients was lymph nodes (LN) (52.9%), local skin (17.5%), lung (9.9%), distant skin (5.1%), brain (4.6%), liver (3.2%), in-transit nodes (2.4%), bone (1.6%), other (1.6%), gastrointestinal (1.0%), and adrenal gland (0.2%). When metastases were identified in LN, recurrence at distant sites occurred in 15% of patients. When the initial site of metastasis was distant, subsequent recurrence was uncommon except in lung lesions which were associated with brain recurrence (2%). Median survival differences occurred based on patterns of disease recurrence (see Table). The highest median survival was observed in patients with distant skin metastases (14.6 years). Median survival decreased as the number of metastatic sites increased. Conclusions: Patterns of metastatic recurrence in melanoma affect median survival. Classification based on metastatic patterns of recurrence may provide increasingly accurate

stratification of patients for enrollment in clinical trials and comparison of outcomes data.

Metastatic recurrence patterns in 4636 patients with melanoma.

Metastatic recurrence patterns			N	%	Median survival (years)	95% Confidence Interval
1st site	2nd site	3rd site				
Distant skin			80	2%	14.6	(8.1, *)
Nodes			1044	23%	10.6	(8.4, 13.9)
Nodes	Brain		152	3%	1.7	(1.4, 2.0)
Nodes	Distant skin		115	3%	3.7	(2.3, 5.0)
Nodes	Local skin		102	2%	3.4	(2.0, 5.4)
Nodes	Liver		80	2%	1.3	(1.0, 1.7)
Nodes	Bone		48	1%	1.8	(1.4, 2.3)
Nodes	Lung		142	3%	1.9	(1.4, 2.8)
Nodes	Lung	Brain	44	1%	1.5	(1.3, 2.6)
Lung			172	4%	4.5	(3.6, 5.5)
Lung	Brain		77	2%	3.2	(2.9, 4.6)
Local skin			302	7%	9.9	(6.2, 13.5)
Local skin	Nodes		98	2%	2.5	(1.7, 9.3)
Brain			144	3%	3.3	(2.7, 4.0)
Liver			90	2%	2.6	(2.2, 3.6)

* Confidence interval unable to be determined as >50% of population remains alive at follow-up.

P229

Adoptive immunotherapy using effector T cells rendered insensitive to TGFb signaling J. Quatromoni, R.C. Koya, Y. Wang, J. Treger, J. Economou.* *surgery, ucla, Los Angeles, CA.*

Cytotoxic T cells entering the tumor microenvironment encounter immunosuppressive molecules such as transforming growth factor β(TGFβ) which can thwart an otherwise effective antitumor immune response. Using a well characterized murine model of adoptive immunotherapy (Pmel-1 mouse T cells which express a transgenic T cell receptor that recognizes the melanocytic differentiation antigen gp100 expressed on murine B16 melanoma), we tested the hypothesis that Pmel-1 CD8 T cells, genetically engineered to express a TGFβ dominant-negative (DN) receptor (which abrogates TGFβ signaling) would have superior antitumor activity. C57BL/6 mice with 4-8 day established B16 tumors underwent a myeloablative conditioning regimen (900cGy) supported with normal bone marrow. These mice then intravenously received activated Pmel-1 T cells, Pmel-1 T cells transduced with a TGFβ DN receptor using an ecotropic retrovirus, or no immune cells. TGFβDN-Pmel-1 T cells were on a cell-for-cell basis over 10x more effective in mediating B16 suppression. TGFβ DN T cells were consistently superior in cohorts of mice receiving adoptive cell therapy and supported by IL-2, gp100 peptide-pulsed dendritic cell or no supportive therapy. These results indicate that tumor-specific effector T cells can be genetically engineered to resist the immunosuppressive effects of TGFβ and have superior antitumor activity in vivo.

P230

Mitf expression is associated with improved survival in melanoma G.I. Salti,* K. Schaeffer. *Surgical Oncology, University of Illinois at Chicago, Chicago, IL.*

Microphthalmia transcription factor (Mitf) is involved in melanocyte development and differentiation. We previously reported that Mitf expression, as detected by immunocytochemistry, is an independent prognostic marker in patients with intermediate-thickness melanoma. The current study was undertaken to prospectively study clinical outcome in patients with melanoma whose Mitf expression is analyzed prior to surgical therapy between September 2003 and December 2006. One hundred patients were enrolled in the study. Mitf expression was evaluated by immunocytochemistry and analyzed visually. Slides were graded as follows according to the percentage of cells whose nuclei stained positive for Mitf: (a) 0, 0%; (b) +1, 1-25%; (c) +2, 26-50%; (d) +3, 51-75%; and (e) +4, > 75%. Median follow-up was 34 months. Mean thickness was 2.7 +/- 2.7 mm. Mean overall survival was 62.51 +/- 2.77 months. Mean disease-free survival was 53.38 +/- 3.17 months. Eighty seven melanomas stained positive for Mitf. By univariate analysis, mean overall survival and disease-free survival in patients whose melanomas did not express Mitf were 20.45 +/- 3.48 months and 15.75 +/- 3.36 months, respectively. This compares with 66.96 +/- 2.38 months and 58.12 +/- 3.09 months, respectively, for patients whose melanomas expressed Mitf ($P < 0.0001$ and $P < 0.0001$). These findings persisted in multivariate analysis. In addition, patients with detected Mitf expression had significantly fewer nodal metastases ($P = 0.017$). Our data suggest that Mitf is an important prognostic marker in patients with melanoma.

P231

Sentinel lymph node biopsy (SLNB) is a powerful predictor of recurrence for patients with cutaneous head and neck melanoma (CHNM) R.S. Sweeting,[1]* E.D. Routh,[2] M.O. Meyers,[2] P. Long,[2] J.S. Frank,[2] K.B. Stitzenberg,[2] K.D. Amos,[2] D.W. Ollila,[2] J.J. Yeh.[2]
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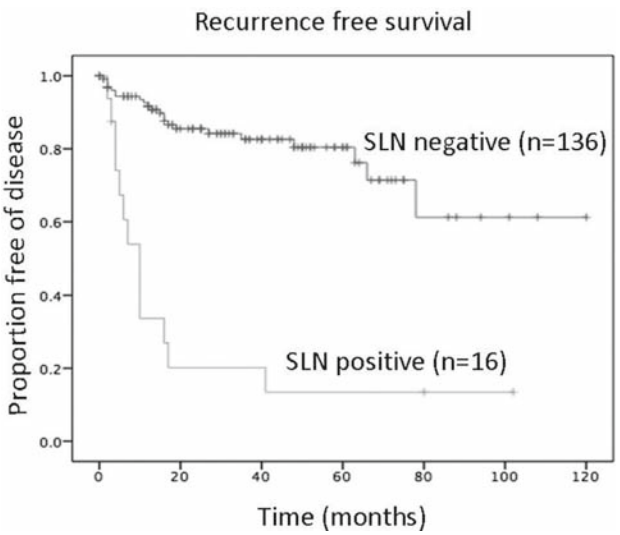
Introduction: Despite earlier findings from the SLN Working Group in CHNM, SLNB remains controversial due to variable lymphatic drainage patterns and anatomical challenges. Recent studies have suggested underutilization of SLNB in CHNM. The goals of this study were to evaluate the utility of SLNB in staging patients with CHNM. **Methods:** All clinically node-negative patients with CHNM undergoing SLNB from 1999-2007 were identified from a prospective, IRB-approved, single-institution database. Data were analyzed to determine the clinicopathologic factors associated with prognosis. **Results:** One hundred and fifty two patients underwent SLNB for CHNM. Median age was 67 (18-89) years, median Breslow depth was 1.5 mm (0.2-10.7), and 75% of the patients were male. The median follow-up time was 29 (0-120) months. Of the 152 patients who underwent SLNB, 16 (11%) had a positive SLN. Eighty one percent (13/16) of SLN positive patients recurred compared to 16% (22/130) of SLN negative patients. The 2 year recurrence free survival (RFS) rate was 94% in SLN negative compared to 20% in SLN positive patients ($p<0.001$). In a multivariable analysis, SLN status was the most powerful predictor of RFS (HR 7.8, [CI 3.1-19.4]). Ulceration (HR 2.4, [CI 1.1-5.1]) and Breslow depth (HR 1.3, [CI 1.0-5 1.5]) were also independent predictors of RFS. No patient (n=41) with a Breslow depth <0.95 mm had a positive SLN. For patients (n=86) with intermediate thickness melanoma, SLN status was an even more powerful independent predictor of RFS (HR 35.7, [CI 6.4-196.7]). **Conclusion:** Patients with positive SLNs in CHNM have a significant risk of disease recurrence. The prognostic value of a positive SLN in patients with CHNM is of greater magnitude than has previously been seen in non-CHNM patients. SLNB should be used routinely for patients with CHNM of ≥ 1.0 mm Breslow depth or with ulceration. More intense follow-up for these patients should be considered.



P232

Role of Sentinel Lymph Node Biopsy in Anorectal Melanoma

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Introduction: Although sentinel lymph node biopsy (SLNB) is well established for staging regional lymph node basins in patients (pts) with cutaneous melanoma, its role in anorectal melanoma (AM) has not been defined. We hypothesized that SLNB may contribute to the staging and clinical management of pts with AM. Methods: All pts with AM seen at a single institution from 1992-2006 were retrospectively identified using a tumor registry. Demographics, staging work-up, surgical technique, pathology, adjuvant treatment, locoregional recurrence (LRR), distant metastases and survival were evaluated. Results: 119 pts were identified. 40 who had their primary surgery elsewhere and 41 with regional/distant metastases were excluded. Of the remaining 38 pts, the overwhelming majority (n=35, 92%) underwent treatment of their primary by transanal excision (TE); only 3 (8%) required low anterior or abdominoperineal resection. SLNB was done in 19/35 pts (54%) who had TE; 11/19 had preoperative lymphoscintigraphy. SLNB was negative in 8, positive in 6, and not identified in 5 pts. Bilateral SLNs were identified and harvested in 4/14 pts. Of the 5 in whom no SLN was detected, 2 had rectal primaries and 1 had mesorectal drainage only. Adjuvant radiotherapy (XRT) was delivered to 31/35 pts; 26 (74%) received pelvic and bilateral inguinal XRT (30 Gy/5 fractions), while 5 with negative SLNB had selective XRT, omitting inguinal XRT. 16/35 (52%) pts also received adjuvant systemic therapy. At median follow-up (f/u) of 30.9 months, LRR, distant failure, no evidence of disease, or loss to f/u occurred in 6 (19%), 17 (55%), 6 (19%), and 2 (7%) pts, respectively. No pt with unilateral drainage recurred in the contralateral nodal basin. No pt who received selective XRT recurred in either inguinal nodal basin. Conclusion: TE followed by pelvic and bilateral inguinal XRT affords effective LR control in pts with AM. SLNB accurately assesses the pathologic status of nodal basins at risk. It may be most useful for pts with anal primary tumors (at or distal to the dentate line) rather than rectal sites. SLNB may facilitate selective use of adjuvant inguinal XRT and avoid associated morbidity in the subset of pts with a negative SLN.

P233

Electrochemotherapy: clinical outcome and predictive factors from a single institution experience on 50 melanoma patients

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Introduction: Electrochemotherapy (ECT) is a minimally invasive and efficient technique for palliating superficial metastases. So far, predictive factors of clinical outcome in melanoma patients treated with ECT have not been investigated. Methods: Fifty consecutive patients with in-transit metastases underwent 108 bleomycin-based ECT. Here we investigated on: toxicity, local response, response duration, impact on quality of life (QoL), predictive factors of local response, duration of response and survival. Results: The majority of patients (71%) were in TNM stage III disease. Fourteen patients had previously undergone isolated limb perfusion (ILP). Treatment was well tolerated. An objective response was observed in 48 out of 50 patients (complete response [CR], 47%). Twenty-seven patients underwent a second ECT and two patients received up to 6 ECT. Upon re-treatment CR rate rose to 64%. After a mean follow-up of 16 (range: 4–32) months, 6 of the 50 patients (12%) experienced local recurrence. On multivariate analysis, significant positive predictive factors of tumor response were decreasing tumor size (P=0.003) and the decreasing number of tumor nodules (P=0.02); the increasing number of ECT cycles was related with local control (P=0.02). Thickness of primary tumor was the only independent prognostic factor for survival (P=0.03). Through a non-validated, 8-items questionnaire (assessing wound healing and bleeding, aesthetic impairment, daily activities, social relations, pain, treatment satisfaction, acceptance of retreatment), 44 out of 50 (88%) patients reported a benefit in local disease-related complaints and in activity of daily living. Conclusions: ECT provides superficial tumor control thus preserving patients' QoL, and is safely applicable also in those with locally recurrent disease after ILP. Significant factors for local response were tumor size and the number of tumor nodules; local control was only affected by the number of ECT cycles. The individuation of new predictive factors, both patient- and treatment-related, would enable to predict which patients might benefit most from this treatment approach.

P234

Preoperative ultrasound is not useful for identifying nodal metastasis in melanoma patients undergoing sentinel lymph node biopsy

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Introduction The evaluation for regional nodal status using sentinel lymph node biopsy(SLNB) has been well accepted in melanoma patients(pts). Identifying nodal involvement using high resolution ultrasound(US) preoperatively may offer a less invasive staging method and minimize the delay to therapeutic lymphadenectomy. The purpose of the study was to assess the feasibility of using clinically targeted US (ie, US performed without lymphoscintigraphy localization of draining nodal basins) as a screening tool in patients prior to SLNB. Methods We reviewed 298 consecutive melanoma pts(473 basins) who underwent US prior to lymphoscintigraphy and SLNB. US findings of benign appearance or no visualized nodes were considered negative; all other findings were considered abnormal. Results Of 298 pts, 62 (21%) had a positive SLNB. 19 of these (31%) had an abnormal US, but in only 17 was the abnormal US in the same basin as the positive SLNB. Two pts had two node-positive basins but only one of these was abnormal by US. Two patients had an abnormal US and negative SLNB in one basin and a normal US and positive SLNB in a second basin. Therefore, only 15 pts had an abnormal US that corresponded to the node-positive basin. The US was negative in 43 pts who had a positive SLNB, including 5 pts who did not have US evaluation of the basin that was positive on SLNB. In 236 pts with a negative SLNB, the US was abnormal in 39(17%). Hence, we cannot be sure that the nodes in the 15 SLNB and US positive basins were in fact correctly identified by US. A non-draining basin underwent US 119 times and a draining basin was not imaged in 34 cases. The per basin and per patient sensitivity(26%, 24%) and specificity(88%, 83%) of US without prior lymphoscintigraphy localization were unacceptable, even in high risk subgroups (Table). Conclusions In our study, preoperative US without localization detected only at most 15 of 62 positive nodes in 298 patients. Thus, US is not recommended for preoperative evaluation of regional node status. Targeted preoperative US after lymphoscintigraphy may be more beneficial, but the cost effectiveness needs to be addressed.

Sensitivity and specificity of clinically targeted ultrasound without lymphoscintigraphy localization

		N	Sensitivity (%)	Specificity (%)
Overall	Patients	298	24	83
Overall	Nodal Basins	473	26	88
Breslow Depth (mm)	0-1	84	0	89
	1.01-2	210	11	89
	2.01-4	117	42	86
	> 4	62	33	91
Location of Nodal Basin	Neck	90	33	74
	Axilla	250	28	90
	Groin	100	22	96
	In-transit	33	0	97

P235

Novel Hand Held Intraoperative Radionuclide Imaging

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Introduction: Imaging for SLN identification is not optimal, specifically for areas where the injection site is close to the nodal basin or the target site is near physiologic radionuclide uptake such as bladder, salivary glands, brain and heart. A portable hand held gamma camera was devised with real-time computer imaging. Methods: Study of 50 melanoma, breast cancer patients. Goals were in-vivo localization of the SLN with camera, ex-vivo confirmation of radioactivity with the nonimaging probe and with the camera. Results:

Use of the camera was feasible and easy to use for trainees. We could identify additional SLN compared to probe particularly in the head and neck region. Conclusions: Use of the camera did not increase OR time and there was a trend toward increased ability in identifying SLN in difficult locations such as in the head and neck melanoma.

Clinical Feasibility

Cancer Type and Location	Patient #	Basins>1	Nonimaging Probe Neg	Camera Positive	Camera False Negative	Soft Tissue	Path Positive
Breast CA	11	0	0	11	0	1	1
Tunk or Extremity Melanoma	29	4	7	33	2	25	26
Head and Neck Melanoma	10	3	1	9	2	3	5
TOTAL	50	7	8	53	4	29	32

No statistical difference (paired t-test p<0.4) between probe and camera

P236

Metastectomy Improves Survival in Patients With Stage IV Melanoma; Time for a Second Look? N. Wasif,* S.P. Bagaria, P. Ray, D.L. Morton. *Surgery, John Wayne Cancer Institute, Santa Monica, CA.*

Introduction: Therapeutic choices for patients with Stage IV melanoma are limited with few long-term survivors. Studies on metastectomy in colon and breast cancer have repositioned surgery as a curative option for some. Our goal was to investigate the impact of metastectomy on survival in patients with metastatic melanoma. Methods: Patients with Stage IV melanoma were identified from the Surveillance, Epidemiology and End Results (SEER) database (1988-2006). Metastatic disease was sub-divided into M1a and M1b/M1c according to current AJCC staging. Patients who had metastectomy performed were compared with those that did not. Results: The median age of the study population (n= 4229) was 63 years and median survival was 6 months. Patients who underwent metastectomy (n = 1422) had an improved median and 5-year overall survival as compared to patients who did not (n= 2779); 12 months vs. 5 months and 16% vs. 7%, p <0.001). This improvement of survival following metastectomy was enhanced in patients with M1a disease (n= 1981); median survival of 14 months vs. 6 months and 5-year overall survival of 20% vs. 9%. Diagnosis between 2000-2006, younger age and white race were predictors of metastectomy. On multivariate analysis, metastectomy was an independent and significant predictor of survival (HR 0.47, 95% CI 0.43-0.52). Conclusions: Metastectomy in patients with Stage IV melanoma, especially M1a, may improve long term survival. In view of the lack of effective medical therapy, the role of surgery needs to be re-examined and the impact of metastectomy on survival confirmed by randomized trials.

P237

Age Disparities in Melanoma Treatment and Outcomes in the US A. Zemlyak,* P. Pugliani, H. Meng, C.R. Pameijer. *surgery, SUNY at Stony Brook, Stony Brook, NY.*

Background: Age has been variously reported as having no impact or a significant impact on the outcome of patients with melanoma. We used data from the SEER registries to determine the impact of age and other demographic factors on treatment and outcomes in patients with melanoma. **Methods**: The SEER public-use data file was used to identify patients with melanoma diagnosed between 1998 and 2003. A total of 33,291 patients were included. Overall survival was calculated using the Kaplan-Meier method, and hazard ratios were calculated based on Cox proportional hazards models. **Results**: The prevalence of thick melanoma increases with age. The rate of lymph node sampling decreases over the age of 70. While 40% of patients age 80 years or older presented with melanoma thicker than 1mm, only 17% had lymph node surgery. Among patients with thick melanoma (> 4mm), 43% did not have lymph node sampling. The recurrence rate increases with age, and is higher among patients who have no lymph node sampling versus those who do (4.3% vs 2.5% p<0.01). Both mortality and recurrence rates of melanoma increase steadily with age, with 11.2% of patients over 80 years old dying of melanoma, vs 4.5% of patients aged 20-30. **Conclusion**: There is a high rate of non-compliance with treatment guidelines in older patients and patients with deep melanoma. While age is a negative prognostic factor for melanoma, substandard treatment of older patients may play a role in their worse outcome.

Table 2: Rates of Lymph Node Biopsy and Positivity

Age	20-39	40-49	50-59	60-69	70-79	80+
Melanoma >1mm (%)	1155	1436	1740	1674	2055	1621
	20.0%	23.3%	25.8%	29.5%	32.0%	40.0%
LN Surgery (%)	1605	1892	2068	1790	1670	678
	29.0%	30.6%	30.7%	31.5%	27.0%	17.0%
Positive LN (%)	317	363	344	313	276	147
	27.4%	25.3%	19.8%	18.7%	13.4%	9.1%

LN Surgery includes SLNB and CLND. Positive LN is the % of patients with melanoma >1mm deep.

P238

Desmoplastic Melanoma- the Step-Child in the Melanoma Family? N. Wasif,* R.J. Gray, B.A. Pockaj. *Mayo Clinic Scottsdale, Phoenix, AZ.*

Introduction: Desmoplastic melanoma (DM) is a rare variant of melanoma with unclear biology and management options. Current knowledge is derived from single institution studies limited by small sample sizes. Our goal was to use a population database to study the natural history of DM, identify prognostic factors and the impact of treatment options. Methods: Patients with DM melanoma were identified from the Surveillance, Epidemiology and End Results (SEER) database (1988-2006). Demographic and prognostic factors for melanoma were extracted. Kaplan-Meier survival curves and log rank analysis were used to compare survival. Cox regression analysis assuming proportional hazards was used to identify predictors of survival. Results: The median age of the study population (n= 1735) was 69 years and overall survival at 5 years 65%. DM was more common in males (64.9%), most commonly found on the head and neck (50.8%), rarely involved lymph nodes (4%) and had a mean Breslow thickness of 2.98mm (SEM 0.7mm). None of the traditional prognostic factors such as Breslow thickness, Clark level, nodal positivity, ulceration or site predicted survival on univariate analysis. Patients who had a wide excision (WE) performed (>1cm) had improved survival compared to those who had a simple excision (SE) or no surgery of the primary (5 year survival of 67% vs. 60% vs. 45% respectively, p <0.001). Of the 505 patients (29.1%) undergoing sentinel node biopsy (SNB), only 14 (2.8%) were positive. The 134 (7.7%) patients who received post-operative radiation had a worse 5 year survival when compared to patients who did not (51% vs. 66%, p = 0.001). On multivariate analysis only receipt of radiation (HR 1.65 [95% CI 1.17-2.31]) and extent of resection (WE) correlated with survival (HR 0.47 [95% CI 0.32-0.69]). Conclusions: Desmoplastic melanoma does not share traditional prognostic factors with the melanoma family. The incidence of nodal involvement is too low to justify SNB and nodal positivity does not impact survival. Management should be surgical resection with wide margins to optimize survival. The adverse effect of radiation on survival probably reflects selection bias on the part of treating physicians.

P239

Primary Tumor Staining with ODAM, A Novel Biomarker, is Predictive for Stage III Melanoma S. Siddiqui,[1]* S.S. Gandhi,[1] C.T. Bruker,[2] K.D. Gray,[1] J.L. Bell,[1] D. Kestler,[3] J.M. Lewis.[1] *1. Department of Surgery, University of Tennesse, Knoxville, TN; 2. Department of Pathology, University of Tennessee, Knoxville, TN; 3. UT Human Cancer and Immunology Program, Knoxville, TN.*

INTRODUCTION: Odontogenic ameloblastic associated protein (ODAM) is a novel biomarker up-regulated in metastatic breast cancer that correlates with improved survival. The prognosis of melanoma is based on histologic factors of the primary tumor and nodal status. We hypothesize that ODAM is up-regulated in the primary tumors of patients with sentinel lymph node positive melanoma (Stage III). METHODS: After IRB approval was obtained, melanoma patients were retrospectively identified through our tumor registry. Histologic factors of the primary tumors were controlled for between cohorts of sentinel node positive and negative patients. Archived tissue was cut and stained with anti-ODAM antibodies. Immunohistochemical staining for ODAM was graded in blinded fashion by a single pathologist. Overall survival and ODAM staining results of primary tumors were compared between the two cohorts using Fisher's exact test. RESULTS: Complete medical records and adequate tissue samples were available for 26 patients. All patients were stage II or higher. Thirteen patients were in each lymph node cohort. Median Breslow thickness of

the node negative and positive patients was 2.45mm (range; 0.35 -7.0mm) and 2.5mm (range;0.32-16 mm), respectively. Primary tumors in the lymph node positive patients were significantly more likely to stain positive for ODAM (p = 0.0414) with 8/13(62%) lymph node positive patients staining positive for ODAM. Only 2/13(15%) of primary tumors in the lymph node negative patients stained positive for ODAM. Overall 5-year survival between node negative and positive cohorts was similar at 9(69%) and 8(62%), respectively. Subset analysis in lymph node positive patients found no statistically significant relationship between ODAM antibody positvity and 5-year survival and recurrence rates. CONCLUSIONS: ODAM is significantly up-regulated in the primary melanoma specimens of sentinel lymph node positive patients. This has important prognostic implications for this disease. Further investigation is warranted for this novel biomarker and its implications in overall survival for patients with melanoma.

P240

Bevacizumab Augmentation of Regional Melphalan in a Melanoma Xenograft Model J.C. Padussis,[1]* H. Toshimitsu,[2] C. Augustine,[2] D.S. Tyler.[1] *1. General Surgery, Duke University, Durham, NC; 2. Durham VA Medical Center, Durham, NC.*

Bevacizumab (BEV) mediated VEGF blockade effects alterations in tumor vessel physiology that allows improved delivery and efficacy of chemotherapy. We examined the ability of BEV to augment regional melphalan (LPAM) therapy in a melanoma xenograft model. The LPAM resistant human melanoma cell lines DM443 and DM738 were grown as xenografts in the hind limb of nude rats, and animals were assigned to one of four treatment arms (Table 1). Tumor size was measured and volume calculated daily. In a second cohort, Evans blue dye was used as a tracer to assay the permeability of peripheral vessels. After receiving BEV or saline, rats bearing DM738 xenografts underwent ILI, in which Evans blue dye was circulated. Tumor dye extraction was performed and absorbance measured. BEV treated tumors showed 30% less Evans blue dye penetration as compared to saline control. (p=0.03). This decrease in vascular permeability correlated with BEV's ability to augment LPAM's regional anti-tumor activity as measured by tumor growth delay over 30 days of treatment. In both xenografts tested, LPAM therapy alone was not significantly better than saline control, confirming the LPAM resistance of the xenografts. In DM443, tumor volume increased 426% from starting volume in the SAL/SAL cohort and 384% in the SAL/LPAM cohort (p=0.59). Similarly, in DM738, tumor volume increased 1820% in the SAL/SAL cohort and 1370% in the SAL/LPAM cohort (p=0.06). Tumors treated with BEV alone had a volume increase of 322% in DM443 and 1430% in DM738, which was not significantly better than saline therapy alone (p=0.13 and 0.11). However, when the combination of BEV and LPAM was given, tumor volumes reached only 209% in DM443, significantly better then LPAM or BEV alone (p= 0.02 and 0.03). Similarly, when BEV/LPAM was given to DM738 tumors, volumes reached only 637%, significantly better than LPAM or BEV alone (p= 0.005 and 0.004). Combination therapy of BEV/LPAM has a marked synergistic antitumor effect which appears related to altered vascular permeability leading to increased drug delivery. The use of BEV to augment regionally administered LPAM represents a novel strategy for improving response rates for in-transit melanoma.

Table 1: Treatment Arms

	Drug #1 (IP on days 0 and 3)	Drug #2 (Administered via isolated limb infusion on day 6)	Percent Growth on Day 30 (DM443)	Percent Growth on Day 30 (DM738)
Cohort #1 (SAL/SAL)	Saline	Saline	426%	1820%
Cohort #2 (SAL/LPAM)	Saline	Melphalan (90mg/kg)	384%	1370%
Cohort #3 (BEV/SAL)	Bevacizumab (5mg/kg)	Saline	322%	1430%
Cohort #4 (BEV/LPAM)	Bevacizumab (5mg/kg)	Melphalan (90mg/kg)	209%*	637%*

* reaches statistical significance when compared to Cohorts #1, #2 and #3

P241

Predictors of morbidity of inguinal lymph node dissection in patients with melanoma T. Kingham,* G. Karakousis, K. Panageas, C.E. Ariyan, M.S. Brady, D.G. Coit. *Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Completion lymph node dissection (CLND) is standard for patients with melanoma in a sentinel lymph node. The morbidity of inguinal CLND, however, is substantial. Recently, the role of CLND in the management of these patients has been questioned. We evaluated the morbidity of CLND in a recent cohort of patients to create a clinical risk score. **Methods**: Patients who underwent CLND were identified from a prospectively maintained melanoma database (1992-2008). Complications were recorded and significant factors associated with complications were used to create a clinical risk score. Independent samples t-test and Chi square analysis were used to determine significance. Lymphedema was defined as clinically significant edema more than 2 months after surgery. **Results**: One hundred and four patients were identified, of whom 61 (59%) had a total of 71 complications. Most complications (94%) were grade I or II but 5 patients required readmission. Thirty complications occurred more than 30 days from surgery. The most common complication was infection (n=33, 53%), followed by lymphedema (n=23, 37%) and seromas (n=11, 18%). Infection did not predict lymphedema. Older patients were more likely to have a complication (median 58 years vs. 47 years, p=.01). BMI was higher in the complication group (median=29) compared to the no complication group (median=24, p<.01). Patients who had a complication were likely to have a higher American Society of Anesthesiologists (ASA) score and all patients with coronary artery disease and/or diabetes (n=12) had a complication (p=.02). Males were more likely to have an infection (54% vs. 38%, p=.05). A clinical risk score was created utilizing these significant factors (Table 1). **Conclusion**: Predictors of complications include age, sex, BMI, coronary artery disease, diabetes, and ASA score. Complications are frequent after CLND; most are minor and almost half occur after 30 days. A clinical risk score may predict complications after CLND.

Table 1. Clinical risk score for complications after inguinal lymphadenectomy

Clinical risk score*	N	Number of patients with complications#
Low: 0-1 points	22	5 (23%)
Moderate: 2-4 points	45	29 (61%)
High: 5-7 points	23	20 (83%)

*Age≥54=2 pts, BMI≥27=2pts, ASA≥2=1pt, coronary artery disease or diabetes=1pt, male=1pt.
#p≤.001 based on Chi square analysis comparing percentage of complications between three risk score groups

P242

Can Lymphatic Drainage Patterns of Head and Neck Melanoma be Predicted? J.D. Jensen,[1]* R.J. Gray,[2] N. Wasif,[2] M.C. Roarke,[2] W.J. Casey,[2] P. Kreymerman,[2] B.A. Pockaj.[2] *1. Midwestern University, Glendale, AZ; 2. Mayo Clinic, Scottsdale, AZ.*

Background: The lymphatic drainage patterns of the head and neck is complex. Therefore, identification of the sentinel lymph node (SLN) for head and neck (H&N) melanoma can be challenging. Methods: A retrospective review of a prospective melanoma database was performed. All patients underwent preoperative lymphoscintigraphy. After 2007, patients also underwent SPECT/CT. Intraoperative SLN mapping included isosulfan blue injection. Primary melanomas were divided into the following anatomic locations: central face (central forehead, nose, and nasolabial folds), central scalp, lateral face (preauricular, mandible, cheek, lateral forehead,) ear, and neck. Standard anatomic neck lymph node station nomenclature (Ia, Ib, IIa, IIb, III, IV, Va, Vb, and VI) was used. The parotid was considered a separate site. Results: A total of 137 patients drained to 218 lymph node basins. Most patients were male (75%). The median age was 70 years (range 17-86). Mean Breslow thickness was 2.2 mm (range 0.5-9.0). The SLN identification rate was 97% with 12 patients (9%) having a SLN metastasis. The drainage patterns are summarized in Table 1. The majority of patients (88%) drained unilaterally. Bilateral drainage occurred in 14 patients (10%), and the majority of these were from central face or scalp lesions (34%). The majority of patients (58%) drained to only one neck level with the most common being level IIA (deep to the parotid gland, upper jugular) regardless of primary melanoma site. The other most common sites were parotid and level III (middle jugular). In the posterior neck almost all SLNs were in level Vb (near the spinal accessory nerve). In our cohort, no patients drained to level Ia. Two patients with neck melanomas drained outside of the neck: one to bilateral axillae and the posterior neck and one to an infraclavicular lymph node and unilateral neck. One patient drained only to the contralateral neck. Conclusions: H&N melanoma lymphatic drainage is often

found in surgically challenging locations. While the SLN locations are not consistent, H&N drainage occurs in patterns that, once known, can assist the surgeon and radiologist in SLN identification.

Neck Lymph Node Levels	Melanoma Location					
	Lateral Face N=46	Central Face N=11	Central Scalp N=36	Ear N=24	Neck N=20	Total N=137
Total Neck LN Levels	78	17	54	41	28	218
Parotid	24%	41%	6%	17%	4%	37
Ia	0%	0%	0%	0%	0%	0
Ib	13%	29%	6%	2%	0%	19
IIa	37%	29%	17%	40%	29%	68
IIb	1%	0%	22%	10%	0%	17
III	13%	0%	20%	10%	36%	35
IV	1%	0%	0%	0%	0%	1
Va	1%	0%	7%	2%	4%	7
Vb	8%	0%	22%	14%	21%	30
VI	1%	0%	0%	2%	7%	4

P243

Brain metastases in cutaneous head and neck melanoma

A.M. Huismans,* K.F. Shannon. *Melanoma Institute Australia, Sydney, NSW, Australia.*

Introduction: Of all cutaneous melanomas, 15 to 20% are located in the head and neck area. These melanomas show a poorer survival compared to melanomas located elsewhere. A possible explanation for this could be the high incidence of brain metastases in these patients. In this study we analysed the incidence of brain metastases in cutaneous head and neck melanoma (CHNM) and the risk factors for their development. Methods: We selected 1703 patients with AJCC stage I and II head and neck melanoma from our prospectively collected database. Patients with and without brain metastases were compared to assess risk factors for brain metastases and independent risk factors were determined by means of Cox regression analysis. Results: The incidence of brain metastases from CHNM was 7% compared with 5.5% for brain metastases from melanomas located elsewhere on the body. Patients with scalp melanoma developed brain metastases most often (13.8%). Independent risk factors for brain metastases were high Breslow thickness, the presence of ulceration, and location on the scalp. Patients with scalp melanoma, Breslow thickness >2.0 mm and ulceration had a 26% incidence of brain metastases. Patients with none or one of these risk factors developed brain metastases in only 4.6% of cases. Conclusion: The main reason for the high incidence of brain metastases from cutaneous head and neck melanomas is the contribution from primaries arising on the scalp. Important additional risk factors for brain metastases are high Breslow thickness and ulceration. Why melanoma on the scalp seems to be more aggressive remains unknown.

P244

Melanoma Pathology in the Community Setting: Are we meeting the NCCN minimum reporting criteria? J. Fox,* A. Loeb, J. Ouellette, P. Termuhlen, M. Hellan. *Surgery, Wright State University, Dayton, OH.*

Introduction: The pathology report is a key element in developing a treatment plan for patients with melanoma. The National Comprehensive Cancer Network (NCCN) guidelines identify 6 “minimal elements” to be reported. The purpose of this study is to assess the frequency with which these elements are reported in a community setting. Methods: We conducted a retrospective chart review from July 2008 – July 2009 for all patients referred to a surgical oncology practice for treatment of melanoma. Pathology reports were assessed for reporting of: Breslow thickness, ulceration, Clark level, mitotic rate, margin status and satellitosis. A Fisher’s exact test was used to evaluate for statistical significance between labs utilizing templates and those who do not. Results: Seventy-four charts met inclusion criteria. Reports were received from 13 labs, with 7 utilizing a reporting template. Overall, thickness was reported most consistently at 95.9%, followed by Clark’s level (79.7%), ulceration (66.2%), peripheral margins (66.2%), mitotic index (59.5%), deep margins (50.0%), and satellitosis (12.2%). Labs utilizing a reporting template were more likely to report ulceration (p=0.0061), peripheral margins (p=0.0061), deep margins (p=0.0242), and satellitosis (p=0.0001). Conclusions: Despite recommendations from the NCCN and available templates from the College of American Pathologists, and the Commission on Cancer, basic pathologic elements for melanoma are frequently not included in the final report. in the community practice setting. This is consistent with reviews across Europe, the UK, and Australia. As staging and indications for sentinel lymph node biopsy continue to evolve, pathology reports to guide clinical decision-making are lagging and need improvements.

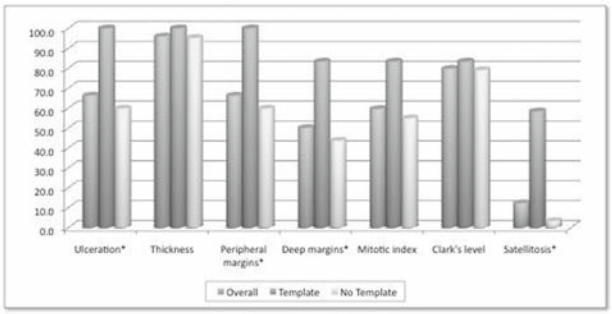


Figure 1. Reporting of NCCN minimal elements overall and by template utilization (*p=<0.05)

P245

Completion lymph node dissection in melanoma patients with a tumor-positive sentinel node does not increase the rate of local-regional recurrences H.J. Veenstra,* I.M. Van der Ploeg, M.W. Wouters, B.B. Kroon, O.E. Nieweg. *Surgery, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, Noord-Holland, Netherlands.*

Introduction: The main purpose of this study was to determine the occurrence of the various forms of local-regional recurrence in sentinel node positive melanoma patients. A comparison was made with the rate of local-regional recurrence in patients who underwent lymph node dissection for palpable metastasis. Factors associated with these recurrences were analyzed. Methods: Between December 1993 and December 2008, 141 patients with a tumor-positive sentinel node underwent completion lymph node dissection. The median follow up was 65 months. In the same period, a therapeutic node dissection for palpable nodal metastases was performed in 178 patients. A local recurrence was defined as a recurrence in contact with the primary tumor scar. Metastases within 2 cm of the scar were classified as satellites. Other recurrences up to the regional lymph node field were categorized as in-transit metastases. (Sub)dermal node field recurrences were listed as a separate category. Results: In the sentinel node positive patients, the local recurrence rate was 5%, the rate of satellite metastasis was 2% and for in-transit metastasis this was 15%. In patients with palpable nodal disease, these percentages were similar: 3, 2 and 14 respectively. The ten-year local-regional recurrence-free rate in the two groups was also similar (P=0.17). Starting with patients with in-transit metastasis up to the regional node field (P=0.39) and subsequently adding patients with (node field recurrences (P=0.42), satellite metastases (P=0.42) and local recurrences (P=0.17) did not result in a statistically significant difference between the two groups. Only Breslow thickness was predictive of local-regional recurrence in the multivariate analysis (P=0.02). Conclusions: Patients with a tumor-positive sentinel node and patients with palpable nodal involvement have a similar rate of local-regional recurrences following node dissection. The present study refutes the suggestion that a positive sentinel node followed by early node dissection predisposes for the development of loco-regional recurrences.

P246

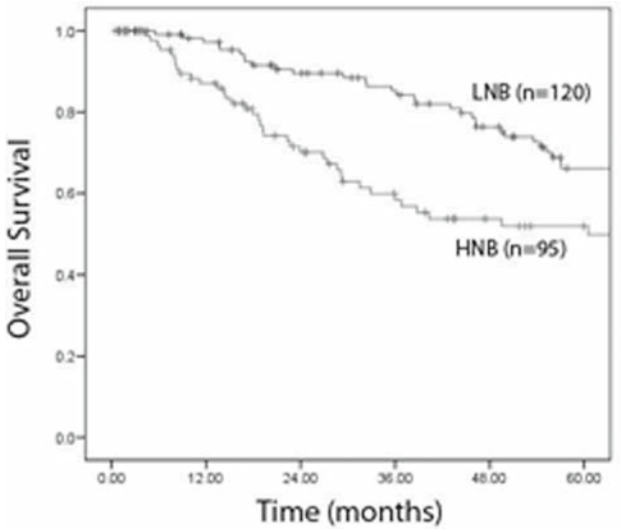
Clinical value of radiographic staging in patients diagnosed with AJCC stage III melanoma P.K. Pandalai,[1]* F.J. Dominguez,[3] J. Michaelson,[2] K.K. Tanabe.[1] *1. Division of Surgical Oncology; Department of Surgery, Massachusetts General Hospital, Boston, MA; 2. Division of Surgical Oncology; Department of Pathology, Massachusetts General Hospital, Boston, MA; 3. Surgical Oncology Department, School of Medicine, Pontificia Universidad Catolica de Chili, Santiago, Chile.*

Background: Patients (pts) with AJCC stage III melanoma represent a group of pts with a high risk of systemic relapse. The goal of this study is to evaluate the clinical usefulness of radiographic staging in this group at the time of diagnosis. Methods: Consecutive, asymptomatic pts who underwent standardized radiographic staging workup at our institution within 6 weeks of the diagnosis of AJCC stage III melanoma were reviewed. The true- and false-positive rates of staging radiographs and number of additional exams generated after a positive initial report were quantified. All suspicious findings in these reports were further studied by means of a biopsy, clinical, or radiologic assessment one year following the initial staging evaluation. Results: Fifty-eight pts underwent complete radiographic staging. Nineteen (33%) had ulcerated primary tumors. Forty-two (73%) patients presented with clinically negative lymph nodes that were proven to be positive on sentinel lymph node biopsy. Lymph node involvement was classified as N1a in 54%, N2a in 19%, N2b in 3% and N3 in 22% of patients. Among 204 staging exams in 58 pts, 52 (25%) were initially reported as positive. Three percent of these studies ultimately proved to be true-positives while 23% were false-positives. As analyzed per patient, in 37 of 58 pts (64%) at least one exam was initially reported as positive. However, only 3 pts (5%) had a true-positive report and 34 (59%) had at least one false-positive report. The positive reports of the staging scans generated 45 additional exams (0.78 per patient). Conclusion: Radiographic staging in asymptomatic pts with stage III melanoma detects a low but clinically important number of patients with unsuspected systemic disease. However the ratio of false to true positive is approximately 11:1 and the very large number of false-positives has both a financial cost and emotional impact for the patient. We contend that radiographic screening should only be considered in patients with high risk prognostic features, symptomatic complaints or in the context of clinical trials.

P247

Natural History of Patients with Stage III Melanoma of Unknown Primary G.C. Karakousis,[1]* S. Katz,[2] K. Panageas,[1] C. Ariyan,[1] M.S. Brady,[1] D. Coit.[1] *1. Memorial Sloan-Kettering Cancer Center, New York City, NY; 2. Roger Williams Medical Center, Providence, RI.*

Introduction: Several hypotheses have been postulated to explain melanoma of unknown primary (MUP), including an immune mediated regression of the primary lesion. Study of the clinical outcomes of these patients has been limited by their relative infrequency. We report our large experience of MUP with Stage III disease to describe their natural history and identify prognostic factors. Methods: The hospital and prospective melanoma databases were reviewed from 1984-2008 to identify patients with MUP presenting with stage III disease. Clinical and histopathologic variables were collected and correlated with outcomes. Overall survival (OS) was estimated by the Kaplan-Meier method and comparisons between groups were made using log-rank analysis. We performed multivariate analysis using a Cox regression model. Results: Of 215 patients with Stage III MUP undergoing lymph node dissection (LND), the majority were male (62%) with a median age of 56 years (range 11-91). The distribution of pathologic nodal basins was 48% axilla, 26% groin and 26% neck. With a median follow-up of 51 months, OS at 3 and 5 years was 74% and 60% respectively. Presence of high nodal burden (HNB, >1 node or matted nodes) upon lymph node dissection was associated with a poorer overall survival as compared to low nodal burden (LNB, 1 node) (p=0.003). The 5 yr overall survival in the LNB group was 66% versus 52% in the LNB group (figure 1). Age (< or≥ 60), gender and site of nodal disease were not significant predictors of overall survival. There were 105 patients who recurred, with a 28% 3 yr post-recurrence survival. Conclusions: This single center retrospective series corroborates previously reported findings that patients with MUP and stage III disease appear to demonstrate a relatively favorable overall survival. Nodal burden is predictive of overall survival in MUP patients. Patients with MUP who recur however demonstrate a relatively poor prognosis.



P248

Utility of pre-operative 18F-FDG PET/CT and brain MRI in melanoma patients with palpable lymph node metastases T.S. Aukema,* R.A. Valdés Olmos, M.W. Wouters, W.M. Klop, B.B. Kroon, W.V. Vogel, O.E. Nieweg. *Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands.*

Introduction: The aims of this prospective study were to assess the value of whole body hybrid 18F-fluorodeoxyglucose (FDG) PET/CT and brain MRI in melanoma patients with palpable lymph node metastases and to determine the impact on their management. Methods: An analysis was performed of 70 melanoma patients with palpable nodal lymph node metastases between October 2006 and March 2009. These patients were otherwise without evidence of dissemination and were scheduled to undergo regional node dissection with curative intent. Hypermetabolic PET/CT lesions were examined by histology or cytology, or were imaged further and followed if no pathology confirmation could be obtained. Follow-up findings within six months of the PET/CT and MRI were used to determine the diagnostic value of the preoperative scan. Results: PET/CT detected additional metastases in 26 patients (37%), was false positive in one patient (1%) and false negative in four (6%). This resulted in a sensitivity of 87% and a specificity of 98%. MRI revealed brain metastases in five patients (7%). PET/CT findings changed the intended regional node dissection in 26 patients (37%). Three patients received more extensive surgical treatment for additional regional node metastases and three patients received additional treatment for in-transit metastases. Instead of the node dissection, ten patients (14%) received palliative chemotherapy, two patients underwent palliative radiotherapy (3%) and eight patients (11%) received no further treatment. The overall survival of patients without additional lesions on PET/CT was 84% after two years, which was better than the 56% in patients with additional metastases ($p<0.001$). Conclusions: PET/CT has 87% sensitivity and 98% specificity for the detection of other metastases in melanoma patients with palpable lymph node metastases. PET/CT lead to a change in the planned regional node dissection in 37% of the patients in this study. MRI revealed brain metastases in five patients (7%). PET/CT findings are correlated with survival. Whole body PET/CT and MRI of the brain are recommended in patients with palpable lymph node metastases of melanoma.

P249

Synchronous pelvic disease in unselected sentinel-node positive melanoma patients treated with routine complete inguinopelvic lymphadenectomy C.K. Chu,* K.A. Delman, A. Hestley, G.W. Carlson, D.E. Murray. *Division of Surgical Oncology, Department of Surgery, Emory University School of Medicine, Atlanta, GA.*

INTRODUCTION True prevalence of synchronous pelvic metastases in the setting of a positive groin sentinel node (SN) is unknown. Role of pelvic dissection in the SN biopsy era remains controversial. Due to surgeon practice, we have an unselected group of SN-positive patients who underwent routine

inguinopelvic lymphadenectomy for microscopic disease. METHODS From 1994-2005, one surgeon routinely performed complete inguinopelvic lymphadenectomy for all melanoma patients after positive inguinal SN biopsy. All cases were identified from a prospectively-maintained database. Cases with and without non-SN pelvic disease were compared. RESULTS Forty unselected patients with positive inguinal SN underwent routine complete inguinopelvic lymphadenectomy; 2 patients underwent bilateral lymphadenectomy. Median age was 46.5y (range 25-79). Lower extremity primary sites were predominant (79%). Median Breslow depth was 2.3mm (range 1.0-10.0); %Clark's IV/V 98; %ulceration 26. Prevalence of synchronous pelvic disease upon completion lymphadenctomy was 5/42 (11.9%). Patients with and without non-SN pelvic disease were similar in age, sex, Breslow depth, Clark's level, ulceration, mitoses, and number of positive SN. All 5 cases with non-SN pelvic disease were extremity lesions (4 distal, 1 proximal); lymphoscintigraphy showed 1-channel drainage to ipsilateral inguinal basins only. Two of the 5 also had non-SN inguinal disease. Of the 5, 3 (60%) had ≥3 total involved inguinal nodes, compared to only 1 (2.7%) of the 37 cases without pelvic disease (p=0.003). Ratio of positive inguinal nodes to total retrieved (SN and non-SN) inguinal nodes was >0.20 in 80% of cases with pelvic disease and 8.6% of cases without (p=0.002). With 52m median follow-up, median time to 1st recurrence was 11m (2 local, 3 in-transit, 5 distant, 0 pelvic). Overall 5-year survival was 73%. CONCLUSIONS In this cohort of unselected, SN-positive patients with complete inguinopelvic lymphadenectomy, the risk of synchronous pelvic disease was 11.9%. Patients with ≥3 total involved inguinal nodes and inguinal lymph node ratio >0.2 may be more likely to harbor pelvic disease.

P250

Identification of Melanoma Sentinel Nodes with Lymphoseek: Phase III Clinical Trial Results at Moffitt Cancer Center V.K. Sondak,* S. Marzban, C.J. Rich, J.L. Messina, J.S. Zager. *Dept of Cutaneous Oncology, Moffitt Cancer Center, and University of South Florida College of Medicine, Tampa, FL.*

Background: Sentinel node biopsy (SNB) is widely used for staging node-negative melanoma. Most surgeons use both radiolabeled colloid and blue dye to identify the sentinel node. In the USA, however, there is no FDA-approved radiolabeled colloid for this purpose. Methods: Lymphoseek® (99mTc–diethylenetriamine pentaacetic acid–mannosyl–dextran) is a new tracer for the identification of sentinel nodes, designed to be rapidly transported from the injection site to the first draining node(s) and bind to moieties within the node, potentially providing greater selectivity in identifying the sentinel node. NEO3-05 is a non-randomized phase III trial designed to evaluate Lymphoseek compared to vital blue dye. The FDA accepted vital blue dye as a standard for sentinel node identification. Results: To date, 86 melanoma pts have been entered. Of these, Moffitt enrolled 25. 19 actually underwent SNB using Lymphoseek; 3 did not have SNB due to pathology change or comorbidities, 1 withdrew consent and 1 refused SNB. 1 pt was ineligible due to Breslow's thickness <0.76mm; 1 was subsequently found ineligible due to a prior melanoma. High-quality lymphoscintigrams were obtained from all 19 pts, and all successfully underwent identification and removal of the sentinel node. 41 blue nodes were removed from eligible patients, as well as an additional 15 non-blue hot nodes. Only 1 blue node did not meet study criteria for being hot, for 98% concordance with the lymphatic mapping reference standard 1% isosulfan blue. 3 pts had evidence of melanoma in the sentinel nodes; all nodes were hot and blue. All 3 node-positive pts underwent completion node dissection and no other involved nodes were found. There were no adverse events deemed related to the study drug, and to date there have been no recurrences in any pts. Conclusion: Lymphoseek effectively identifies sentinel nodes with a high degree of correlation to blue dye with an acceptable safety profile. In our experience, it travels to nodes relatively quickly and provides high counts in the sentinel node relative to background. The study design did not allow for a direct comparison of Lymphoseek to sulfur colloid.

P251

Effect of Body Mass Index on Overall Survival in Patients with Stage III Melanoma C.M. Shaw,[1]* F. Zhu,[2] S. Lessin,[3] E. Sigurdson.[1] *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Biostatistics, Fox Chase Cancer Center, Philadelphia, PA; 3. Dermatology, Fox Chase Cancer Center, Philadelphia, PA.*

Background: Obesity is associated with both the development of and mortality from several malignancies. Body mass index (BMI) is positively correlated with the incidence of melanoma. The objective of this study was to determine whether body mass index affects survival in patients with melanoma. Methods: A retrospective chart review was conducted using patients with Stage III melanoma who were treated at our institution from 2001-2007. Sixty-eight patients had complete medical records and were included. Data were analyzed using equality of survivor functions and Cox proportional hazards models. The Kaplan-Meier method was used to graphically examine data. Results: Median BMI was 28.2 (range 20.7-47.7). Median survival for all patients was not reached. On univariate analysis, overweight and obese individuals (BMI≥25) had a statistically significant increase in survival (p trend = .010, HR .284). A similar but weaker association was seen when evaluating obese patients (BMI≥30), (p trend = .026, HR .345). Age at diagnosis was negatively associated with outcome (p = .003, HR 1.043). On multivariate analysis, adjustment for age and BMI did not materially alter results. Adjustment for tumor depth resulted in a stronger association between both quantiles of BMI and increased survival. The association of BMI with overall survival did not vary by other factors including sex, primary tumor site, nodal status, year treatment began, or treatment with adjuvant therapy. Conclusion: Patients who are overweight have an increased survival in locoregionally advanced melanoma compared to normal weight and morbidly obese patients. Additional research including mechanistic studies and studies with larger populations are needed.

Univariate analysis of Survival using Cox Proportional Hazards Model and Associated Hazard Ratios

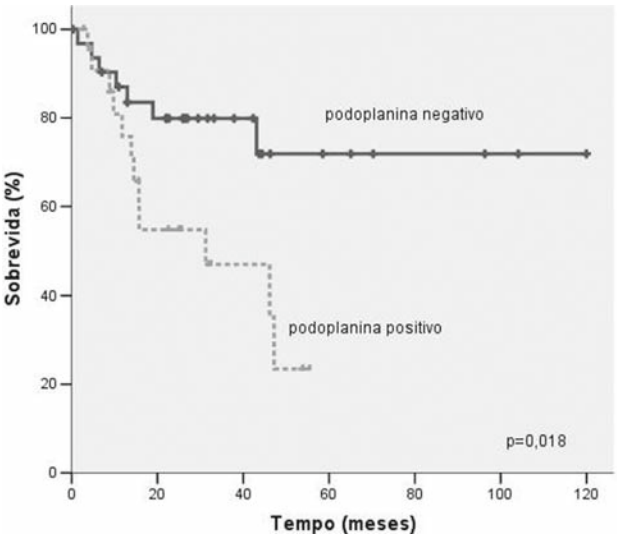
Characteristic	p value	Hazard ratio
Overweight (BMI≥25)	.010	.284
Obese (BMI≥30)	.026	.345
Age at diagnosis	.003	1.04
Sex	.777	ns
Year treatment began	.697	ns
Primary tumor site	.674	ns
Histology	.175	ns
Treatment with adjuvant therapy	.211	ns
Tumor size	.286	ns
Tumor depth	.384	ns
Nodal status	.703	ns

P252

Prognostic Factors in Patients with Locally Advanced Cutaneous Squamous Cell Carcinoma of Trunk and Extremities V.D. Vazquez,[1]* N.M. Perpetuo,[1] T. Sachetto,[1] C. Scapulatempo,[1] A.T. Oliveira,[1] J.G. Segalla,[2] A.L. Carvalho.[1] *1. Surgery, Hospital de Cancer de Barretos, Barretos-SP, São Paulo, Brazil; 2. Hospital Amaral Carvalho, Jaú, São Paulo, Brazil.*

Cutaneous squamous cell carcinoma of trunk and extremities (CSCCTE)is a local disease with low mortality, but can present local progression, regional and distant metastasis. Prognostic factors related to locally advanced disease are not well established. The aim of this study is to determine clinical, histopathological and molecular factors related to lymph node metastasis and prognosis in patients with locally advanced CSCCTE. Method: 63 patients with locally advanced CSCCTE retrospectively analyzed through medical records and tumor blocks, with construction of a Tissue Micro Array for immunohistochemical analysis of expression of HER family, E-cadherin and Podoplanin in primary tumors and lymph node metastasis. Results: Primary tumor: EGFR positive in 25,5%, HER-2 negative in all, HER-3 positive in 87,3% and HER-4 in 47,3%. E-cadherin positive in membrane in 47,3% and cytoplasm in 29,1%. Podoplanin positive in 29,1%. Lymph node metastasis: EGFR positive in 40,0%, HER-2 negative in all, HER-3 positive in 84,0%, HER-4 positive in 44,0%. E-cadherin positive in membrane in 28,0% and 3,6% in cytoplasm. Podoplanin positive in 40,0%. Intratumoral lymphocytic infiltrate was related to lymph node metastasis (53,3% versus 16,4%; p=0,046).Patients with T3 tumors presented higher cancer survival rate than T4 ones (62,5% versus 26,8%; p=0,012); Patients without lymph node metastasis presented higher cancer survival rate than those presenting (79,4% versus 30,6%; p=0,018); Patients with grade III tumors presented lower survival rate (23,8 % versus 82,2%; p=0,010), as well patients

with Podoplanin hyperexpression (23,5% versus 71,9%; p=0,018). Considering patients with lymph node metastasis, HER-4 hyperexpression determinate lower survival rate (37,5% versus 53,3%; p=0,038). Conclusions: Intratumoral lymphocytic infiltrate was related to lymph node metastasis; Patients with T3 tumors, low histological grade, N0 and negative primary tumor expression of Podoplanin presented higher survival rates. Metastatic patients to lymph nodes with metastasis positivity to HER-4 presented lower survival rate



Association Between Risk Factors and Lymphedema

	Reported Lymphedema (N=18)	No lymphedema (N=22)	p-value
Gender			0.3864
Female	72.2% (13/18)	59.1% (13/22)	
Male	27.8% (5/18)	40.9% (9/22)	
Age at Diagnosis			0.4751-W
Mean (std)	57.6 (15.3)	61.2 (16.6)	
Min/Med/ Max	35/60.5/ 84	26/64.5/ 85	
Location of Melanoma			0.0127
Above Knee	33.3% (6/18)	72.7% (16/22)	
Below Knee/Foot	66.7% (12/18)	27.3% (6/22)	
Surgical Margin			0.6038
10 mm	44.4% (8/18)	36.4% (8/22)	
20 mm	55.6% (10/18)	63.6% (14/22)	
Closure			0.4295
Primary	72.2% (13/18)	86.4% (19/22)	
Skin Graft	27.8% (5/18)	13.6% (3/22)	
BMI			0.2717-W
Mean (std)	28.2 (7.7)	25.2 (4.4)	
Min/Med/ Max	22.3/25.5/52.3	18.1/25.0/32.3	
Number of SNs			0.8241-F
1	16.7% (3/18)	13.6% (3/22)	
2-3	61.1% (11/18)	54.5% (12/22)	
4+	22.2% (4/18)	31.8% (7/22)	
Location of SNs			0.1396
Inguinal	50.0% (9/18)	72.7% (16/22)	
Inguinal + Iliac	50.0% (9/18)	27.3% (6/22)	
Surgeon			0.0064
A	83.3% (15/18)	40.9% (9/22)	
B	16.7% (3/18)	59.1% (13/22)	

p-values are calculated from chi-square test unless presented (F: Fisher's exact test; W: Wilcoxon's two-sample test)

P253

Risk of Lymphedema Following Sentinel Node Biopsy (SNB) for Lower Extremity Melanoma R.A. Graham,* P. Magoon, Y. Lee, J. Rothschild. *Tufts Medical Center, Boston, MA.*

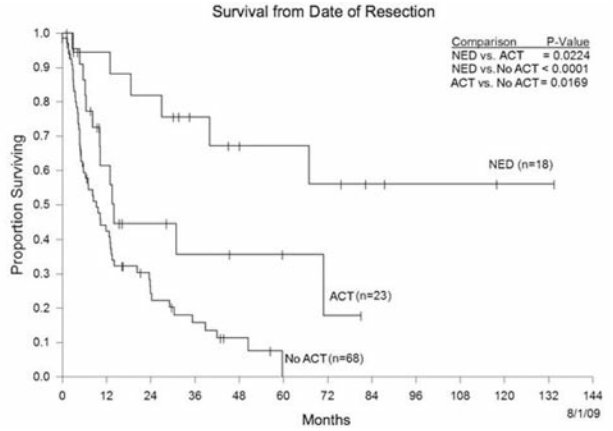
Introduction: The benefits of SNB for melanoma are well established, while the risks have received less attention. This study was undertaken to establish both the incidence of lower extremity (LE) lymphedema following SNB and the risk factors predictive for developing LE lymphedema. Methods: We conducted a retrospective chart review of all patients undergoing SNB at our institution between January 2000 and December 2007. Sixty-five patients were identified who had LE melanoma > 1 mm in depth who underwent inguinal SNB in the absence of a completion node dissection. After a minimum 1-year follow-up, questionnaires were mailed to each patient regarding their qualitative assessment of lymphedema. We then looked at specific risk factors for the development of lymphedema; comparisons were made using the Chi-square test, Fisher's exact test, and Wilcoxon's two-sample test. Results: Forty of 65 patients returned the questionnaire and are the subject of this study. All patients were operated on by 1 of 2 surgeons. Lymphedema was reported by 18 of 40 patients (45%) and was described as moderate/severe by 15 patients (38%). Lymphedema developed within 1 month in 12 patients ; in 1-3 months in 2 patients ; and after 3 months in 3 patients. Lymphedema persisted beyond 1 year in 9 patients (23%). Ten patients reported wearing a support stocking either occasionally (4 patients) or often/always (6 patients). Two patients reported that lymphedema limited their activities. Three of the 40 patients reported that they would not have the SNB again. Two risk factors were significantly associated with the development of lymphedema: surgeon and location of melanoma (above knee vs below knee/foot). Gender, age at diagnosis, BMI, surgical margins, type of primary wound closure, number of SNs removed, and concomitant removal of iliac nodes were not seen as significant risk factors (Table 1). Conclusions: Lymphedema following LE SNB is common. Choice of surgeon and location of melanoma appear to be significant risk factors. This suggests that surgical technique may play a major role in the development of lymphedema and should encourage all surgeons to assess their own practice.

P254

Thoracic Metastasectomy for Procurement of Tumor Infiltrating Lymphocytes in Melanoma Patients J.A. Klapper,* J.L. Davis, F.O. Smith, R.T. Ripley, A. Mathur, C.D. Kemp, D.M. Nguyen, K.F. Kwong, L. Mercedes, D.E. White, M.E. Dudley, J.R. Wunderlich, S.A. Rosenberg, D.S. Schrump. *Surgery Branch, National Cancer Institute, NIH, Bethesda, MD.*

Background: Metastatic melanoma is refractory to chemotherapy, but may respond to adoptive cell transfer (ACT). As novel treatments evolve, surgeons may be asked to perform metastasectomy not only for palliation or potential cure, but for isolation of tumor infiltrating lymphocytes (TIL) for ACT. This study was undertaken to examine outcome of melanoma patients undergoing thoracic metastasectomy in the context of investigational immunotherapy. Methods: Retrospective review of a prospectively collected database identified 109 patients who underwent 116 thoracic metastasectomy procedures from April 1998 to July 2009. Indications for surgery included procurement of TIL (71%), rendering patients NED (18%), symptom palliation (9%), and diagnosis (2%). Cytokine release assays were used to measure TIL reactivity in-vitro. RECIST criteria were used to assess response in patients undergoing ACT. Survivals following surgery were analyzed by Kaplan-Meier and log-rank methods. Results: Thoracotomy (57%) and VATS (38%) with non-anatomic resection (54%) and lobectomy (20%) were the most common procedures. Major complications included 1 mortality and 1 coagulopathy-induced hemorrhage. Nineteen patients were rendered NED. Virtually all patients with residual disease had tumor specimens cultured for TIL; approximately 65% of TIL cultures exhibited anti-tumor reactivity. Of the patients with residual disease, 26% (24/91) received TIL, with 7 objective responses (27% of patients receiving TIL; 8% based on intent to treat); rapid disease progression precluded ACT in most cases. Actual 1 and 3-year survival rates for patients rendered NED, receiving, or not receiving TIL were 94% & 76%, 61% & 36%, and 42% & 16%, respectively. Conclusion: Thoracic metastasectomy can be performed safely in melanoma patients. ACT

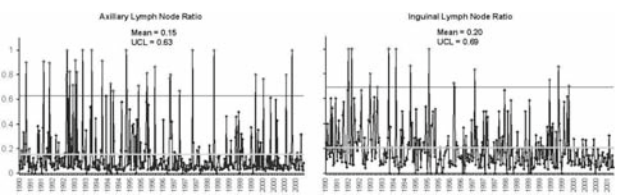
using TIL from thoracic metastases seems to improve survival of these individuals; yet, relatively few patients undergoing thoracic metastasectomy for TIL underwent ACT. Identification of prognostic factors correlating with response to ACT, as well as continued refinement of TIL expansion protocols may increase the number of melanoma patients benefiting from thoracic metastasectomy.



P255

Standards for lymph node ratio in dissections for melanoma patients: can they be achieved? N. Goel,[2]* R.L. Askew,[1] Y. Xing,[1] M.I. Ross,[1] J.E. Gershenwald,[1] J.E. Lee,[1] P.F. Mansfield,[1] A. Lucci,[1] R.E. Royal,[1] J.N. Cormier.[1] *1. surgery, UT M.D. Anderson Cancer Center, Houston, TX; 2. University of Illinois at Chicago, Chicago, IL.*

Introduction: Lymph node ratio (LNR), defined as the number of metastatic lymph nodes (LN) divided by the total number of LNs removed, has been shown to be an important prognostic factor for disease-specific survival in stage III melanoma patients. Optimal LNR thresholds have been reported as ≤0.13 and ≤0.18 for the axillary and inguino-femoral regions, respectively. The objective of this analysis was to determine whether these thresholds are achieved in clinical practice. Methods: A retrospective review of clinicopathologic data for 794 patients who underwent axillary or inguinal lymphadenectomy for node-positive melanoma was conducted (1990-2001). Patients were categorized according to nodal basin dissected. Pathology reports were used to determine LNR, and process control charts were constructed using STATA/SE9.2 and SPC-XL2000-4b statistical software packages to identify outliers beyond the upper confidence limits (UCL) over time. Results: 794 patients with a median age of 52 years underwent axillary (55%) or inguino-femoral (45%) LN dissection. Overall, LNR outliers were identified in 5.7% and 4.8% of patients who underwent axillary or inguino-femoral dissections, respectively. Prior to 1997, the percentage of outliers for axillary LNR was 8.1% compared to 3.1% after 1997 (61.8% decrease). Similarly, 6.9% of cases were identified as outliers for inguinofemoral LNR prior to 1997 compared to 2.6% after 1997 (62.5% decrease). Conclusion: In this cohort of node-positive melanoma patients, optimal LNR was achieved in the majority of operations, and fewer outliers were identified over time. Optimal LNR is an achievable goal in the vast majority of melanoma patients undergoing LN dissection.



P256

Prognostic significance of pelvic nodal drainage (PLND) at sentinel lymph node (SLN) mapping for patients with extremity melanoma G.C. Karakousis,[1]* N. Pandit-Taskar,[1] S. Atherton,[2] M. Hsu,[1] K. Panageas,[1] C. Ariyan,[1] M. Brady.[1] *1. Memorial Sloan-Kettering Cancer Center, New York City, NY; 2. University of Queensland, Brisbane, QLD, Australia.*

Introduction: A significant proportion of patients undergoing SLN mapping for lower extremity melanoma are found to have drainage to pelvic nodes (PLND) in addition to superficial inguinal nodes. The prognostic significance of this with regard to overall recurrence and pelvic nodal recurrence specifically is unknown. Moreover, factors predictive of PLND are understudied. Methods: Review of our prospective melanoma database identified 401 patients (1995-2008) who underwent SLN mapping for melanoma of the lower extremity or buttocks. Of these, 356 SLN procedures were performed for primary lesions with images available for re-review by a single nuclear medicine radiologist. Sixteen cases were excluded because of indeterminate PLND status. Clinical and pathologic factors were recorded and correlated with PLND in the remaining 340 cases. Results: Most cases were female (60%), and the median age was 57 years. The median Breslow thickness of primary lesions was 1.7 mm (range 0.3 to 19 mm). PLND was identified in 23% of cases. Of all factors examined, only thickness and age were associated with PLND by univariate analysis. No difference was found in SLN positivity in patients with and without PLND (p=0.76). By univariate analysis, PLND was marginally associated with a higher incidence of melanoma recurrence (p=0.06). By multivariate analysis, however, PLND was not associated with time to recurrence (TTR), while ulceration, SLN positivity, thickness, LVI and satellitosis were independently predictive of TTR. Among patients who recurred, the observed incidence of pelvic nodal recurrence did not differ by pelvic drainage pattern. Conclusions: PLND is marginally associated with a higher risk of overall recurrence in patients with lower extremity melanoma by univariate analysis but is not an independent predictor when other factors, including SLN status, are considered. Older patients and those with deeper primary tumors are more likely to demonstrate PLND by lymphoscintigraphy. No difference in pelvic nodal failure was observed in patients who recurred based on pelvic drainage pattern.

P257

Intraoperative Sentinel Lymph Node Analysis in Melanoma C. Pierce,* R. Broadwater, K. Westbrook, S. Korourian, D. Davis, K. Hiatt, J. Lee, S. Klimberg, B. Badgwell. *Surgical Oncology, University of Arkansas for Medical Sciences, Little Rock, AR.*

Background: The optimal technique and utilization of intraoperative evaluation of sentinel lymph nodes (SLN) for melanoma is controversial. The objective of this retrospective cohort study was to evaluate our experience with touch preparation cytology (TPC) and frozen section (FS) analysis in the intraoperative staging of melanoma. Methods: The study cohort was identified from all patients with clinically node negative melanoma undergoing a SLN biopsy using Technetium and/or blue dye mapping from 1/1998 to 10/2008. TPC and FS analysis was performed utilizing Diff-quick and compared to permanent section interpretation with H&E. Results: Of 271 patients undergoing SLN biopsy, 163 underwent intraoperative analysis of the sentinel node (125 underwent TPC alone, 15 underwent FS alone, 23 underwent both FS & TPC) and 108 underwent no intraoperative analysis. Thirty-three patients undergoing intraoperative analysis of the SLN were found to have positive nodes (20%) on permanent histology. There were no false positives identified (specificity = 100%). The overall sensitivity for all methods of intraoperative analysis was 61% (20/33). On a per patient basis, the sensitivity was 47% (9/19) for TPC alone, 75% (3/4) for FS alone, and 80% (8/10) for both TPC and FS. On a per lymph node basis, the sensitivity was 57% (13/23) for TPC alone, 60% (3/5) for FS alone, and 80% (8/10) for both TPC and FS. Conclusions: There were no false positives identified suggesting TPC and FS can be used safely to identify the majority of patients with SLN metastases from melanoma.

P258

The prognostic value of FDG-PET measured by Standardized Uptake Value in patients with melanoma stage III; evaluated in a prospective study E. Bastiaannet,[1]* O.S. Hoekstra,[2] J.R. De Jong,[1] A.H. Brouwers,[1] A.J. Suurmeijer,[1] H.J. Hoekstra.[1] *1. UMCG, Groningen, Netherlands; 2. VUMC, Amsterdam, Netherlands.*

Introduction. Melanomas are typically FDG-avid; combined with the fact that melanomas show an unpredictable pattern of spread, makes FDG-PET a

sensitive modality to detect melanoma metastases. Furthermore, FDG-PET is able to quantify FDG uptake, by standardized uptake value (SUV), which might be important for the prediction of survival. Therefore, aim of this study was to perform a prospective analysis to determine whether SUV is of prognostic value (DFS and DSS) for melanoma patients with palpable lymph node metastases (stage III). Methods. From July 2002-December 2007, all consecutive patients with palpable, histology or cytology proven lymph node metastases of melanoma referred for examination with FDG-PET were prospectively included. The SUVmean and SUVmax in the lymph node metastasis were calculated for patients who showed no distant metastases. Univariate and multivariable survival analysis was performed to determine whether SUV was associated with DFS and DSS (Cox Proportional Hazard analysis). Results. Overall, 87 patients were eligible. High SUV values were present in elderly patients (p=0.02), in patients with >15 nodes removed (p=0.05) and in patients with large tumor size ((>3.0 cm; p=<0.001). Patients with low SUVmean had a 3-years DFS of 68.5% compared to 40.9% for patients with a high SUVmean (HR 2.4;p=0.012). Also in multivariable analysis SUVmean was associated with DFS (HR 2.3; p=0.03). DSS for patients with a high SUV was decreased (79.4 versus 50.4) with a HR of 2.6 in multivariable analyses (p=0.04). Conclusion. The SUV in the lymph node metastasis is associated with Disease Free Survival and Disease Specific Survival for melanoma patients clinically stage III.

P259

Invasive Melanoma of the Face: Patterns of Local and Regional Disease in 261 Patients A.J. Chambers,* T. Murynka, J.P. Arlette, J.G. Mckinnon. *University of Calgary, Calgary, AB, Canada.*

Background: The face is a common site of melanoma occurence, and lesions in this location present specific management challenges. The purpose of this study was to examine outcomes associated with invasive melanoma of the face, with respect to local, regional and distant recurrence. Methods: Patients with invasive melanoma of the face managed from 1997-2008 were identified from a population-based tumor registry and retrospectively reviewed. Details of lesion histopathology, initial management, sentinel node biopsy (SNB), and local, regional or distant recurrences were recorded. Results: 261 patients were reviewed, mean age 68, median tumor thickness 0.87mm. Three patients (1.1%) had clinically involved nodes at presentation and underwent nodal dissection. Of 108 patients who were eligible for SNB (tumor thickness >1mm, Clark level ≥IV or ulceration) this was performed in only 29 (27%). SNB was successfully identified in 28 (97%). No facial nerve injuries occurred. A mean of 1.5 nodes were removed; from parotid region in 24, cervical chain in 12, submandibular in 5, submental in 1 and retroauricular in 1. SNB was positive in 3 (11%) who subsequently underwent neck dissection/parotidectomy. At mean follow-up of 37 months, local recurrence occurred in 13 (5%), in-transit recurrence in 4 (1.5%) and distant recurrence in 20 (7.7%). Regional nodal recurrence occurred in 10 (3.8%); after negative SNB in 1 (SNB failure rate 3.7%), after unsuccessful SNB in 1, following neck dissection for nodal disease at presentation in 1, and in 7 who did not undergo SNB (including 6 patients who were eligible). During the study period there were 60 deaths (crude mortality 23%); due to melanoma in 16, unrelated causes in 41, and indeterminate in 3. Conclusions: Facial melanoma is associated with low rates of regional recurrence despite a low rate of SNB for eligible lesions. Sentinel nodes were most commonly found in the parotid region and could be safely removed without nerve injury. Most regional recurrences occurred in patients eligible for SNB not undergoing this procedure. Due to the older age of patients with facial melanoma, most deaths occurring are from unrelated conditions.

P260

Elevated S-100B concentrations and levels of fluorodeoxyglucose uptake predict decreased overall and disease free survival in stage III melanoma patients S. Kruijff,* E. Bastiaanet, A. Brouwers, H. Hoekstra. *University medical centre Groningen, Groningen, Groningen, Netherlands.*

Introduction High values of S-100B and Standardized Uptake Value (SUV) measured preoperative in stage III melanoma patients could both be highly specific indicators of early recurrence and survival. Aim of this study was to assess the association between both markers and to study their influence on DFS and DSS. Methods All melanoma patients from february 2004 to august 2009 with palpable and cytology proven lymph node metastases, without distant metastases on FDG-PET and CT, were prospectively included in this study. Standardized Uptake Value (SUV) and S-100B preoperative were determined for each patient; S-100B values ≥0.15 μg/l were considered elevated, for SUV the median value of 6.4 was used as cut-off value. Correlation between SUV and S-100B was calculated as well as their association with Disease Free Survival (DFS) and Disease Specific Survival (DSS) by Cox Proportional Hazard Analysis. Results Overall, 59 patients (29 male and 30 females), median age 27 (range 25-93), were included in the study. A high S-100B was found in 28 patients (47.5%); a high SUV was measured in 31 patients (52.5%). There was a significant association between S-100B and SUV (p=0.03). DFS (3-years) was 44.1% for patients with a low S-100B and 23.8% for patients with a high S-100B (HR 1.96; p=0.045); DFS was 42.6% for patients with a low SUV and 23.4% for patients with a high SUV (HR 1.81; p=0.08). In multivariate analysis, an increased S-100B preoperative was associated with DFS (HR 1.81; p=0.045). DSS was statistically significant decreased in patients with a high S-100B (HR 2.67; p=0.012) and in patients with a high SUV (HR 2.69; p=0.014) in univariate analysis. Conclusion Preoperatively S-100B and SUV of FDG in stage III melanoma are correlated. Both parameters are associated, when elevated, with a reduced disease free and overall survival and can be an expression of early dissemination not detected by standard imaging tests. S-100B and SUV in true staged III melanoma could be used to stratify patients for adjuvant therapeutic trials.

Comparison between preoperative measured S-100B and SUV

N=59	Low	High		
S-100B SUV	52.5% 47.5%	47.5% 52.5%		p=0.03
DFS S-100B SUV	44.1% 42.6%	23.8% 23.4%	HR1.98 HR1.81	p=0.045 p=0.045
DSS S-100B SUV	65.0% 68.3%	38.3% 36.1%	HR2.67 HR2.69	p=0.012 p=0.014

P261

Increased serum S-100B level in melanoma patients during follow-up and utility of FDG PET/CT and brain MRI T.S. Aukema,* R.A. Valdés Olmos, T.M. Korse, B.B. Kroon, M.W. Wouters, W.V. Vogel, J.M. Bonfrer, O.E. Nieweg. *Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands.*

Introduction: The serum level of the S-100B protein is increasingly being used as a tumor marker in melanoma patients. The aims of this study were to assess the clinical relevance of an increased S-100B level during follow up of high-risk melanoma patients, and to determine the value of subsequent whole body PET/CT and brain MRI. Methods: Serum S-100B was monitored after the surgical treatment of regional or distant metastases, or because a patient was at increased risk due to primary tumor features. A retrospective analysis was performed of all 46 melanoma patients with a normal history and physical examination who were found to have an elevated serum S-100B level (≥0.10 μg/l) during routine follow-up between August 2006 and March 2009. Whole body hybrid PET/CT was performed in all patients and hypermetabolic lesions were biopsied for histological or cytological confirmation, or were imaged further and followed if no pathology confirmation could be obtained. Results: Half of the 46 patients with an elevated serum (≥0.10 μg/l) were found to have recurrent melanoma. There was no explanation for the false positive S-100B findings. PET/CT revealed suspicious lesions in 27 of the 46 patients (59%). PET/CT was never false negative as confirmed by median follow-up of one year, but was false positive in four patients. These findings result in a sensitivity of 100%, specificity of 83%, accuracy of 91%, positive predictive value of 85% and negative predictive value of 100%. MRI revealed brain metastases in one patient (2%). Six of the 23 patients (26%) with a true positive PET/CT scan received surgical treatment with a curative intent. Three of them were alive without recurrence after 11 months, 16 months and 19 months. The other 17 patients (74%) received palliative treatment or supportive care. The overall survival at two years was 52% in patients with a positive PET/CT compared to 100% in the patients with normal PET/CT findings (p=0.002). Conclusions: An elevated serum S-100B during follow-up of high-risk melanoma patients

has a modest 50% positive predictive value for recurrent disease. Subsequent PET/CT and MRI can identify patients with recurrent disease.

P262

Does increased experience with isolated limb infusion for advanced melanoma influence outcome? A comparison of two treatment periods at a single institution A.M. Huismans,[1]* H.M. Kroon,[1] P.C. Kam,[2] J.F. Thompson.[1] *1. Melanoma Institute Australia, Sydney, NSW, Australia; 2. Department of Anaesthetics, Royal Prince Alfred Hospital, Sydney, NSW, Australia.*

Introduction: Isolated limb infusion (ILI) with cytotoxic drugs is essentially a low-flow isolated limb perfusion performed via percutaneous catheters without oxygenation to treat advanced melanoma confined to a limb. In this study we evaluated our experience with ILI by analyzing outcome and toxicity from 'early' and 'late' treatment periods. Methods: We compared the results for 94 patients treated by ILI at one institution in the 'early' period (1992-1999) with results for 91 patients treated in the 'late' period (2000-2007). All patients had advanced limb melanoma and received a cytotoxic combination of melphalan and actinomycin-D. Results: The patient characteristics of the 'early' and 'late' groups were comparable except for a greater tumour load in the late group, expressed by a significantly larger median number of lesions (4 vs. 5; p=.02) and deeper tumour infiltration (p=.03). Drug circulation time and tourniquet time were longer in the late group; 22 vs. 31 minutes (p<.0001) and 45 vs. 65 minutes (p<.0001). In the late group higher initial and final limb temperatures were achieved. Complete response rates were 40% in the early group and 36% in the late group (p=.56). Partial response rates were 45% and 48% respectively (p=.61). The 'late' treatment group showed a trend towards less toxicity (p=.06). Conclusion: Response rates following ILI for advanced melanoma in our 'late' treatment period are comparable to those of our 'early' treatment period despite a greater tumour load in the late period. This could be attributed to our increased experience with the procedure, which is reflected in longer drug exposure times and higher limb temperatures, without increasing toxicity.

P263

Better understanding of cutaneous apocrine adenocarcinoma using national tumor registry K. Hollowell,* S. Agle, E. Zervos, T. Fitzgerald. *surgery, Brody School of Medicine, Greenville, NC.*

Introduction: Apocrine adenocarcinoma is a rare potentially aggressive adnexal neoplasm. Secondary to the low incidence of this tumor there is a paucity of data on demographics and survival with no clear consensus of optimal management. In order to better understand this rare neoplasm we analyzed data from a larger cohort of patients from a national tumor registry. Methods: Patients from ages 18-85 from 1973-2005 diagnosed with apocrine adenocarcinoma were identified in the SEER registry. Patients were excluded if neoplasm located in the breast or other non-cutaneous site. Data analyzed included basic demographics (age, sex, race, and gender), survival, surgical therapy, stage and postoperative radiotherapy. Results: A total of 186 patients with apocrine adenocarcinoma were identified. The mean age of diagnosis was 64.4, majority were white (76%) and there was an equal distribution of males and females. The most common primary site was trunk (likely axilla, 41%) followed by scalp/neck (14%), face (9.6%), eye lid (9.6%), upper extremity (6.9%), nipple (6.4%), scrotum (3%), lower extremity (2%), anus (1.6%), ear (1.6%) and NOS (2%). Cancer directed surgery was performed on most patients (93%), either simple excision (45%), wide excision (37%), mastectomy (6%), Mohs (5%) and miscellaneous (5%). In the remaining patients the diagnosis was made at autopsy (7%). At least one lymph node was analyzed in 12% patients. Only 18.6% had radiation. Overall survival was 45% at 5 years with a mean survival of 67 months. Presence of metastatic disease (p<0.001) was the most predictor of survival. However, race, gender, lymph node status and adjuvant radiation had no significant influence on 5-year survival. Conclusions: Cutaneous apocrine adenocarcinomas are a rare neoplasm occurring primarily on the trunk with a poor prognosis. Primary determinate of survival is presence of distant metastasis. In order to better understand the optimal treatment for this disease further evaluation of large cohorts with analysis of surgical and adjuvant therapy will be required.

P264

Long-term follow-up after sentinel lymph node biopsy in melanoma patients M. De Vries, M.J. Speijers,* R.J. Van Ginkel, J.T. Plukker, A.J. Suurmeijer, A.H. Brouwers, C. Lemstra, H.J. Hoekstra. *University Medical Center Groningen, Groningen, Netherlands.*

Introduction: Data with respect to long-term outcome of sentinel lymph node biopsy for melanoma are rare. Aim of the study was to assess the long-term outcome after sentinel lymph node biopsy (SLNB) in melanoma patients from a prospective collected database. Patients and methods: Between 1995-2009 443 melanoma patients underwent SLNB in a single center. Survival and prognostic factors were analyzed for all these patients. Results: Median age was 53 (range 11-84) years, 229 females (52 %) and 214 males (48 %), median Breslow tumor thickness was 2.5 (range 1-20) mm, 36% were ulcerated melanomas. The median follow-up was 64.6 (range 1-174) months. A tumour-positive SLNB was present in 137 patients (31%). Melanoma specific survival at 10 years was 77% for SLNB-negative patients compared with 60% for SLNB-positive patients (p<.001). Disease free survival at 10 years was 71% for SLNB-negative patients compared with 48% for SLNB-positive patients (p<.001). A total of 124 recurrences (28%) occurred during follow-up; 58 in the SLNB-positive group (58/137; 42%) and 66 in the SLNB-negative group (66/306; 22%; p<.001). In the SLNB-negative group 17 patients developed recurrence in the regional node field. The false-negative rate was 11%. Conclusions: This single-center study shows a remarkable high percentage of SLNB-positive patients (31%) related to the median 2.5 mm thickness of the primary melanoma. These long-term follow up data show that SLNB positive patients have a worse melanoma specific survival and disease free survival than SLNB-negative patients. The long-term false-negative rate is comparable with earlier reports.

P265

Prospective Evaluation of PET/CT as a Surveillance Tool to Define Response to Therapy and Identify New Recurrent Disease in Patients with Locally Advanced Melanoma Undergoing Regional Chemotherapy Treatment with Melphalan G.M. Beasley,* A. Selim, N.S. McMahon, A. Coleman, A.P. Abernethy, K. Nelson, S.K. Pruitt, H. Seigler, T. Wong, M. Onaitis, D.S. Tyler. *Duke University, Durham, NC.*

Background: While PET/CT has gained increasing acceptance as a staging test for patients with stage III melanoma, its clinical utility in defining response to therapy or surveillance after therapy remains to be determined. The goal of this study was to prospectively define the ability of PET/CT to determine response to isolated limb infusion with melphalan (ILI-M) as well as to define the surveillance value of PET/CT in patients with AJCC stage IIIB/C melanoma after regional therapy. Methods: We identified 47 patients who underwent ILI with melphalan who had whole body PET/CT scans performed before and every 3 months after treatment. Clinical response in the field of infusion was determined at 3 month intervals post treatment by RECIST. Results: The median time between scans was 110 days (range 50-365 days). The clinical in field response correlated with findings on PET/CT in 68% (32 of 47) patients. Interestingly, PET/CT was less accurate in identifying complete responders (7/14 (50%)) as compared to correctly classifying partial or progressive disease patients (25/33 (76%)). Over the year following regional infusion, PET/CT scans identified new disease outside the field of infusion in 22/47 patients (47%) that was not appreciated by clinical exam during the period of follow up. Of the 22 patients, 15/17 had pathologic confirmation and surgical resection of PET/CT identified local regional lymph node disease while 4/5 patients had surgical resection of their pulmonary metastatic disease. Conclusion: PET/CT does not appear to be as accurate as clinical/pathologic examination in determining response to regional melphalan. However, PET/CT does appear to be valuable in the surveillance of high risk stage IIIB and IIIC melanoma patients after regional therapy to help identify clinically undetectable but surgically resectable recurrent disease.

P266

Melanoma cells have phosphorylated c-Met through autocrine signaling by HGF, leading to downstream effects on Src and MAPK

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The metastatic phenotype of melanoma cells depends on their ability to survive and proliferate distant from the epidermal/dermal junction. Autocrine growth signaling is a critical mechanism for independent survival of cancer cells. Our preliminary data identified c-Met activation in human melanoma, but autocrine growth signaling has not been demonstrated formally. We hypothesized that metastatic melanoma uses HGF as an autocrine growth factor, acting through c-Met. Six human melanoma cell lines were assayed for c-Met and phosphorylated c-Met protein expression as well as HGF transcription and secretion. To test cell proliferation dependence on HGF, cells were treated with HGF antibody at 10ug/ml for 48 hours. Cells were analyzed after 6 and 12 hours for expression of phosphorylated c-Met(Y1234/1235) as well as downstream proteins Src, AKT and MAPK and phosphorylated Src, AKT and MAPK. All six cell lines expressed both c-Met and phosphorylated c-Met on Western blot. Each also had HGF transcription on qRT-PCR and HGF secretion on ELISA. HGF secretion was 60-360pg/mL, a 4 to 21-fold increase as compared to background. Treatment with an HGF antibody caused a 62-82% inhibition in proliferation of melanoma cells as compared to untreated cells. At 12 hours, HGF blockade resulted in complete suppression of phosphorylated c-Met expression. In addition, there was a 72-86% reduction in phospho-MAPK expression and a 67-82% reduction in phospho Src expression compared to untreated cells. There was no change in expression of Src, MAPK, AKT, or phosphorylated AKT. These results suggest an autocrine mechanism of HGF/c-Met signaling in melanoma. The complete suppression of c-Met phosphorylation after HGF blockade indicates the primary role of HGF in c-Met activation. It is not surprising that c-Met mediates downstream activation of Src, FAK and MAPK, but the degree of inhibition suggests a dominant role for autocrine c-Met activation. Autocrine signaling is an important method for melanoma to evade its microenvironment and metastasize widely. It is also an attractive target for therapy to reduce proliferation and metastasis of malignant melanoma.

P267

Human Acellular Cadaveric Dermis (AlloDerm®) As Definitive Reconstruction After Excision Of Skin And Soft Tissue Malignancies

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Introduction: Definitive reconstruction after excision of extensive skin and soft tissue malignancies (SSM) is often deferred awaiting permanent margin analysis. Surgeons are challenged to obtain suitable temporary coverage, which invariably necessitates reoperation. We describe the use of AlloDerm as an attractive temporary coverage with the potential for use as definitive reconstruction. Methods: We retrospectively reviewed 31 patients (pts) with SSM undergoing temporary or definitive reconstruction with AlloDerm from 2007-09. Demographic variables, preoperatively-stated intent of use (temporary or definitive), time to definitive reconstruction, and outcomes were analyzed. Results: The median age of the 31 pts was 76 yrs (range 33-92); 68% had melanoma. Most defects were on the lower extremity or scalp with a median defect size of 36 cm2 (2-272 cm2, Table1). In 27 pts (87%), AlloDerm was intended to be used as a temporary bridge to skin grafting, while in 4 (13%) the intent was for definitive reconstruction. All 4 pts had locally advanced disease and the procedures were either palliative (2) or in conjunction with limb infusions (2). Of the 27 pts planned to have skin grafts, 8 (30%) had no further intervention (ie, definitive reconstruction with AlloDerm) due to patient/physician preference and an acceptable early cosmetic outcome. Grafts were used in 19 pts (70%), of whom 8 (42%) required re-excision of margins. Median time to grafting was 10 days (6-24) and 15 of 19 pts (79%) had a healthy granulating bed at that time. Skin graft outcomes were consistent with our prior experience. Good cosmetic outcome after definitive AlloDerm reconstruction was noted in 11 of 12 pts (91%), while one pt had loss of the AlloDerm placed directly on calvarium and required flap reconstruction. Postoperative radiation was used in 3 pts in the AlloDerm group without compromise of cosmesis or wound breakdown. Conclusions: AlloDerm can be used either as a bridge to grafting or as definitive skin coverage in select pts with SSM. Good cosmetic outcomes were seen in 91% of pts with definitive reconstruction with AlloDerm, including after adjuvant radiation.

Table 1: Characteristics of patients undergoing temporary or permanent reconstruction with human acellular cadaveric dermis (AlloDerm) after excision of cutaneous malignancies.

Variable	N (%) (Total N=31)
Age >60 years	23 (74%)
Male Gender	21 (68%)
Disease	
Melanoma	21 (68%)
Undifferentiated/pleomorphic sarcoma	4 (13%)
Basal cell carcinoma	2 (6%)
Squamous cell carcinoma	2 (6%)
Merkel cell carcinoma	1 (3%)
DFSP	1 (3%)
Location	
Lower extremity	13 (42%)
Head and neck	12 (39%)
Upper extremity	4 (13%)
Trunk	2 (6%)
Definitive Reconstruction	
STSG with temporary AlloDerm	19 (61%)
Definitive AlloDerm	12 (39%)
Cosmetic Outcome	
STSG with temporary AlloDerm	
Well healed wound	13 (68%)
Partial loss of graft	2 (11%)
Complete loss of graft	3 (16%)
Digit amputation	1 (5%)
Definitive AlloDerm	
Well healed wound	9 (75%)
Partial loss of AlloDerm	2 (16%)
Complete loss/late reconstruction	1 (8%)

P268

Sun Protection Outreach Teaching by Students (SPOTS): Skin Cancer Education in the Adolescent Population

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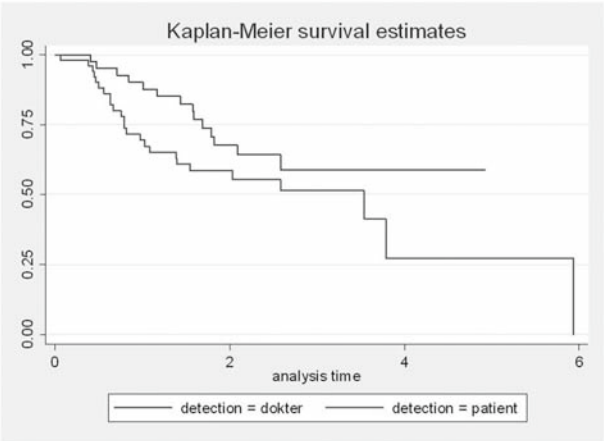
Background: Skin cancer, though largely preventable, remains a significant global health threat that is increasing in incidence. Exposure to ultraviolet radiation is a primary causative agent that can be reduced through efforts aimed at education and behavior modification. Unlike past sun protection education efforts that targeted elementary school children, the SPOTS program targets the teenage population. Methods: Medical and public health students received 5 hours of training and subsequently visited secondary schools to teach students visual recognition of skin cancers, risk factors, radiation dangers, sun protective measures, and tanning alternatives. Pre- and post-program surveys were administered to test program efficacy and make modifications. Complete program materials (training manual, video, lecture, lecture script, curriculum) are available free online (http://dermatology.slu.edu/spots, http://spots.wustl.edu). Results: Since 2006, 198 student teachers have been trained and over 9,200 (5783 middle school and 3500 high school) students at 23 public and private secondary schools in St. Louis, MO, have received the SPOTS program. Feedback from the teens and area schools has been overwhelmingly positive. Surveys are under review. Conclusion: The SPOTS program appears to be an effective educational tool that is welcomed by local schools. The program is easily implemented into existing secondary level health curricula and medical school student interest groups or elective curricula. Analysis is currently underway to quantify its efficacy in changing sun protective behaviors. Paper versions of our surveys will be distributed at the meeting. Program developers are seeking collaborators to create a SPOTS network to expand the program nationally. If you are interested, you may contact Stephanie Lickerman (636-458-4165; itineco@charter.net).

P269

Detection of nodal recurrence in melanoma by patient or doctor has no influence on Survival S. Kruijff,* E. Bastiaannet, A. Suurmeijer, H.J. Hoekstra. *University medical centre Groningen, Groningen, Netherlands.*

Introduction: Understanding the influence of the method of detection (detection by patient or a doctor) in nodal recurrence on prognosis in melanoma patients is essential for the coordination of a rational plan for follow up. The role of self-detected versus physician-detected palpable lymph nodes in stage III melanoma patients, who underwent therapeutic lymph node dissection, was evaluated. Methods: All melanoma patients with palpable lymph nodes, evaluated with PET and CT scan, were prospectively included (n=98) and the method of detection (by patient or by doctor) was recorded. Detection of lymph node metastases in association with pathological information of the lymph node dissection was assessed using multivariate logistic regression. Differences in Disease Free Survival (DFS) and Disease Specific Survival (DSS) were assessed by log-rank test (univariate analysis) and multivariable Cox proportional hazard analysis. Results: Overall 44.9 % of lymph node recurrences were detected by a doctor versus 55.1 % by patients. Age was significantly associated with method of detection. Patients ≤ 60 yrs detected in 68.9 % their lymph node metastases as opposed to 32.4 % of patients > 60 yrs (OR 0.3; p= 0.007). However, this was not associated with prognostic factors of the lymph node dissection (number of positive nodes, tumorsize or extranodal growth). Besides, nor the age (older or younger than 60 yrs) nor the method of detection was significantly associated with two years DFS or DSS. Conclusions: More than 55 % of lymph node recurrences in melanoma are detected by patients. Young patients detect there own lymph node metastases significantly more than older patients. However, there is no influence of the method of detection nor the age on two year DSS or DFS. Therefore the value of high frequency follow-up is stil being questioned.



P270

Determinants Of Resource Utilization In Pancreatoduodenectomy: A Multicenter Analysis Of 1467 Patients P.K. Gupta,[1]* K.K. Turaga,[2] H. Gupta,[1] W.J. Miller,[3] B.W. Loggie,[1] J.M. Foster.[1] *1. Creighton University, Omaha, NE; 2. H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL; 3. University of Virginia, Charlottesville, VA.*

Objective: Patient selection and outcomes for patients undergoing pancreatoduodenectomy (PD) have improved, but subsets of patients that significantly utilize more resources exist. Preoperative optimization may reduce this resource utilization. Our objective was to identify the modifiable preoperative variables that increase resource utilization in patients undergoing PD surgery. Methods: Patients undergoing PD for benign and malignant neoplasms were identified from the American College of Surgeons' 2007 NSQIP, a multicenter, prospective database. Resource variables were operative time (OT), hospital length of stay (LOS), RBC transfusion and occurrence of 17 postoperative complications. Demographic variables included functional status, obesity, neoadjuvant radiation and chemotherapy among others. Analysis was performed using multivariate regression modeling. Results: Of 1467 patients with a mean age of 64.8 (±12.4) years, 48% were males. The mean BMI of patients was 27.7 (±5.9) kg/m2. The mean and median OT were 375 and 359 (±119) minutes and the mean and median LOS were 14 and 10 (±12) days. Of the identified pre-operative variables, neoadjuvant radiation significantly increased OT (106.5 minutes, p<0.0001) but did not increase LOS (p=0.6). Neoadjuvant chemotherapy alone was not associated with either increased OT (p=0.96) or increased LOS (p=0.60). Higher BMI was significantly associated with increased OT (2.5 minutes increase / 1 kg/m2), as were male gender and DM. LOS was significantly extended in patients with CHF, COPD, and poor functional status. Increase in OT by 1 minute was associated with increased LOS by 0.013 days (p<0.001) (Table 1). No preoperative demographic or comorbidity variable had a statistically significant association with postoperative complications or RBC transfusion. Conclusions: Neoadjuvant radiation, obesity and diabetes increase OT after PD. Pre-existing conditions such as CHF, COPD and poor functional status are modifiable factors that increase LOS. Increase in OT increases LOS. Identification of these modifiable factors and optimization will be a critical first step in decreasing resource utilization.

Factors affecting Operating Time and Length of Stay (Table 1)

Determinant	Operative time increased in minutes	p value	Length of stay increased in days	p value
Age	-0.34	0.22	0.009	0.75
Chemotherapy within 30 days	-1.4	0.96	1.48	0.60
Congestive heart failure (CHF)	99.9	0.09	15.5	0.009
COPD	7.5	0.62	4	0.009
Decline in Functional status i.e., ability to do activities of daily living, from Independent to Partially dependent to Totally dependent	-34.5	0.11	9.5	<0.0001
Diabetes Mellitus	22.5	0.004	0.69	0.38
Male gender	17.8	0.004	0.19	0.76
Malignant tumor	32.4	0.002	0.92	0.38
Operative Time increase by 1 min	-	-	0.013	<0.0001
Race (African American)	-7.3	0.56	0.48	0.71
Radiotherapy within 90 days of surgery	106.5	<0.0001	-1.3	0.55
Rise in BMI by 1 kg/m2	2.5	<0.0001	-0.02	0.65

P271

Is Time to Delivery of Treatment a Reliable Measure of Quality of Care for Patients with Colorectal Adenocarcinoma? C.R. Roland,* R.E. Schwarz, L. Tong, C. Ahn, G.C. Balch, A.C. Yopp, T.A. Anthony, J.C. Mansour. *Surgical Oncology, University of Texas Southwestern, Dallas, TX.*

Introduction: Among patients with colorectal adenocarcinoma, patient race has been associated with survival differences. Ethnic survival disparities may be explained by differences in time to treatment, treating hospital, or other patient factors. In the present study, we analyzed whether differences in time between cancer diagnosis and definitive treatment affect outcomes of patients with colorectal cancer. Methods: We reviewed all patients with colorectal cancer treated between 2000 and 2008 at two affiliated hospitals with a shared faculty: a county hospital treating primarily indigent patients and a university-based hospital treating an insured population. Interval to treatment was calculated from date of diagnosis to first resection, chemotherapy or radiation treatment. Variables affecting the timing of initial cancer treatment based on patient, tumor, insurance, and hospital factors were assessed for their relationship to survival. Results: 1184 patients were treated for colorectal cancer at the county and university hospitals during the 8-year study period. For the 592 patients meeting inclusion criteria, no differences were found in cancer stage related to ethnicity, treating hospital or insurance status (Table 1). There were no differences in interval to treatment or median survival related to patient ethnicity or income with a median followup of 2.6 years. Patients treated at the county hospital had an increased interval to treatment compared to patients treated at the university hospital (29 vs 16 days; p<0.0001); yet, there was no difference in overall survival related to the treating hospital. When analyzed as a continuous variable or in quartiles, interval to treatment was not associated with worsened survival. Only tumor grade and tumor stage were associated with decreased survival. Conclusions: Though differences do exist related to the timing of definitive care for patients with colorectal adenocarcinoma, these differences do not translate to overall survival. Timing of treatment delivery is not a reliable indicator of the quality of care delivered to patients with colorectal cancer, as measured in survival outcomes.

Interval to Treatment and Median Survival

■■■■■■■■■■■■■■■■■		Interval to Treatment (days)	p-value	Median Survival (years)	p-value
Mean		24			
Median		16		4.9	
Range		0-190			
Gender	Male	24	0.59	5.1	0.62
	Female	26		4.3	
Hospital type	County	29	**<0.0001<b/>**	4.9	0.44
	University	16		5.0	
Ethnicity	African-American	25	0.99	4.3	0.35
	Hispanic	25		6.6	
	Caucasian	25		5.2	
	Others	23		2.7	
Insurance status	Insured	23	**0.04<b/>**	5.1	0.052
	Not insured	28		2.7	
AJCC Stage	I	29	0.14	NR	**<0.001<b/>**
	II	22		NR	
	III	25		6.6	
	IV	22		1.1	
Primary tumor site	Colon	20	**<0.001<b/>**	5.1	0.09
	Rectosigmoid	32		6.6	
	Rectum	40		3.1	
Interval to treatment (days)<b/>	<8 days	----	----	3.5	0.11
	8-16 days	----		5.2	
	17-34 days	----		4.6	
	>34 days	----		5.1	

P272

Timely Access and Quality of Care in Colorectal Cancer: A Population-Based Analysis G. Porter,[1]* R. Urquhart,[2] J. Bu,[2] Y. McConnell,[1] E. Grunfeld.[3] *1. Dalhousie University and QEII Health Sciences Centre, Halifax, NS, Canada; 2. Cancer Care Nova Scotia, Halifax, NS, Canada; 3. University of Toronto, Toronto, ON, Canada.*

Background: Both timely access and high-quality care are important to colorectal cancer (CRC) patients. This study examined the relationship between disease-specific quality indicators (QI) and time intervals (TI) in CRC patients. **Methods:** This population-based study included all patients undergoing non-emergent surgery for primary CRC in Nova Scotia, Canada from 1/1/2001 to 31/12/2005. The linkage of the provincial cancer registry with other databases (hospital discharge, physician billing, and national census data) provided clinicodemographic, diagnostic, and treatment event data. Associations between accepted and assessable QI and benchmarked TI for diagnosis, surgery, and adjuvant radiation therapy were examined using multivariate logistic regression. **Results:** Among the 2310 patients, the achievement of QI and TI benchmarks is presented in Table 1 below. On multivariate analysis, none of the QI were associated with the presentation to diagnosis TI, although both female patients (OR = 0.75; 95%CI 0.62-0.91; p = 0.004) and urban patients (OR = 0.80; 95%CI 0.66-0.98; p = 0.03) were less likely to achieve the benchmark. Patients who underwent preoperative colonoscopy (OR = 0.71; 95% CI 0.59-0.87; p = 0.0006) and those who had appropriate radiation consultation (OR = 0.4; 95% CI 0.29-0.56; p < 0.0001) were less likely to achieve the diagnosis to surgery TI benchmark controlling for other factors including age, stage, comorbidity, sex, rural/urban and perioperative mortality. No clinicodemographic factors or QI were associated with meeting the surgery to postoperative radiation TI benchmark (n=239). **Conclusions:** Although some staging and treatment-related QI may be associated with longer TI, the relationship between quality and timely access in CRC is neither simple nor consistent. Improved processes of care may optimize quality while not detrimentally impacting timeliness. Timely access should not be used as a surrogate measure for quality CRC care.

Table 1:Achievment of QI and TI Benchmarks (n=2310)

QI	%
Preoperative colonoscopy	57.8
Pathology report: margin status	94.5
Pathology report: number of lymph nodes (LN)	96.7
≥ 12 LN examined	31.8
In-hospital / 30-day mortality	2.7
Appropriate radiation consultation (rectal cancer)	73.2
TI Benchmark	
Presentation to diagnosis (≤ 4 weeks)	37.4
Diagnosis to surgery (≤ 4 weeks)	67.3
Surgery to postoperative radiation (≤ 8 weeks)	34.7

P273

Venous thromboembolism prophylaxis with Sequential compression devices, Early ambulation, and Dextran (SEED) is a safe, effective and easily reversible surgical prophylaxis intervention in peritoneal carcinomatosis management P.K. Gupta,* J.V. Blas, J.H. Carreau, T.E. Grotz, B.W. Loggie, J.M. Foster. *Surgery, Creighton University Medical Center, Omaha, NE.*

Introduction: Peritoneal malignancies (PM) represent one of the highest risk groups for perioperative venous thromboembolism (VTE). Without prophylaxis, this risk can approach 30-50% and with it, the incidence ranges from 10-20%. The extensive surgical dissection in cytoreductive surgery increases the risk of bleeding which may be exacerbated by DVT prophylaxis. For DVT prophylaxis after PM surgery at our institution,, we use sequential compression devices (SCD), early ambulation and dextran (SEED), the latter as its short half life is beneficial in the event of bleeding, as well as its value as a volume expander. Methods: Retrospective chart review was carried out on 155 patients who underwent cytroreductive surgery for pseudomyxoma peritonei, mesothelioma, ovarian cancer, and gastrointestinal neoplasms. Patient demographics, tumor and surgical characteristics as well as complications were recorded. All patients were started on dextran the morning of surgery, and it was continued for 72 hours. SCDs were used in all patients while in bed, and physical therapy assessed and ambulated all patients starting postoperative day 1. We determined the incidence of perioperative bleeding, and VTE rates in-hospital, 30days, and 90 days. Results: All 155 patients tolerated dextran and none (0%) developed a VTE or experienced post-operative bleeding complications in-hospital. Five patients developed VTEs (3.2%) between 30 and 90 days post-operatively, all out of hospital. Of these, there were 2 catheter related upper extremity DVTs, 2 lower extremity DVTs and 1 patient with DVT and PE who had a history of a previous DVT. There were no deaths due to VTE. Conclusion: These results demonstrate that SEED is a safe method of DVT prophylaxis in a high risk surgical group. Due to the low rates of VTE and bleeding complications, SEED is comparable and may be superior to other types of prophylaxis used in surgically treated PM patients. These results support a prospective trial in high risk abdominal surgeries comparing SEED to standard prophylaxis.

P274

Patient Surveillance after Curative-Intent Treatment for Ovarian Cancer G. Harmandayan,[1]* K.S. Virgo,[2] F. Gao,[3] D.G. Mutch,[3] F.E. Johnson.[4] *1. Surgery, Saint Louis University, St. Louis, MO; 2. American Cancer Society, Atlanta, GA; 3. Washington University, Saint Louis, MO; 4. Veterans Affairs Medical Center, Saint Louis, MO.*

Introduction: Surveillance of patients after initial treatment of ovarian carcinoma has important medical implications. The particular modalities used in surveillance by clinicians, and how frequently they are recommended, are unknown at present. We sought to determine the current surveillance patterns of credentialed experts. Methods: A custom-designed survey was created, featuring vignettes describing patients with ovarian carcinoma (FIGO stages I, II, III (with <1 cm residual disease), and III (with >1 cm residual disease)) and questions based on the vignettes. The survey was mailed to the 943 members of the Society of Gynecologic Oncologists (SGO). Those gynecologic oncologists who indicated that they performed ovarian cancer surgery and also participated in long-term follow-up were asked how often they requested 11 discrete surveillance modalities for their patients treated with curative intent in the first five and tenth post-operative years. Results: 323 gynecologic oncologists responded and 283 (88%) provided evaluable responses. The most frequently recommended modalities for each year in all 4 vignettes were office visit, pelvic examination, and serum CA-125 level. There was marked variability in the intensity of surveillance practice. For example, the number of pelvic examinations recommended in post-operative year 1 for patients with stage I ovarian cancer ranged from 1-12. Imaging studies were recommended sparingly. Gynecologic oncologists decreased the frequency of recommended testing with increasing post-operative years for all commonly used tests. For example, the mean number of times office visit was recommended for stage IV patients was 4.4 during year 1, decreasing to 1.1 by year 10. Conclusion: The details of the actual practice of routine surveillance testing for patients after primary treatment for ovarian cancer have not been documented. There is little agreement in the literature about the most appropriate surveillance methods and the optimal frequency of their use. This is the first data on this topic,

to our knowledge. There is marked variability in the intensity of surveillance among SGO members.

P275

High Resolution Intra-operative Two Dimensional Specimen Mammography and its Impact on Second Operation for Re-excision of Positive Margins at Final Pathology after Breast Conservation

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Aim:To assess the efficacy of high resolution two dimensional intra-operative specimen mammography in obtaining improved margin clearance on breast conservation specimens. Introduction:50-66% of women undergoing breast conservation surgery(BCS) undergo mastectomy due to residual cancer at the lumpectomy margin. This is despite the use of several intra-operative margin assessment techniques and is remarkable in view of the fact that the size of newly diagnosed breast cancer is less than 2cm. Methods:A retrospective review of 128 consecutive patients who underwent breast conservation procedures for early breast cancer (from August 2003 to January 2008) was performed using intra-operative specimen mammography without specimen compression. Specimen orientation was standardized. The goal for minimum distance for gross margin clearance was 1cm on specimen radiography. Results: A total of 131 procedures were performed. The average patient age was 58.6 years (range 36 to 89 years). Average tumor size was 1.6cm (range 0.3cm to 5.5cm). 23 specimens were found to have a positive margin and 18 had margin clearance of less than 1mm. Of these, 79.4% had invasive carcinoma and 20.6% had ductal carcinoma in situ (DCIS). 130 out of 131 (99.2%) lesions were successfully treated by BCS. Margins were clear at initial BCS in 86.3% of patients. 12.2% of patients required a subsequent re-excision for positive margins. Estimated median specimen volume was 120cc at first BCS. In those requiring an intra-operative re-excision, the median additional volume resected was 11.2cc. Intra-operative re-excision cleared the margin in 95.8% (23/24) of patients who would have otherwise required a subsequent re-excision. The sensitivity and specificity of the intra-operative margin assessment are 58.5% and 94.4% respectively. The positive predictive value is 82.7% and the negative predictive value of the study is 83.3% Conclusion:Intra-operative specimen mammography with standardized specimen orientation can decrease the rate of margin positivity and subsequent undesired mastectomies for positive margins.

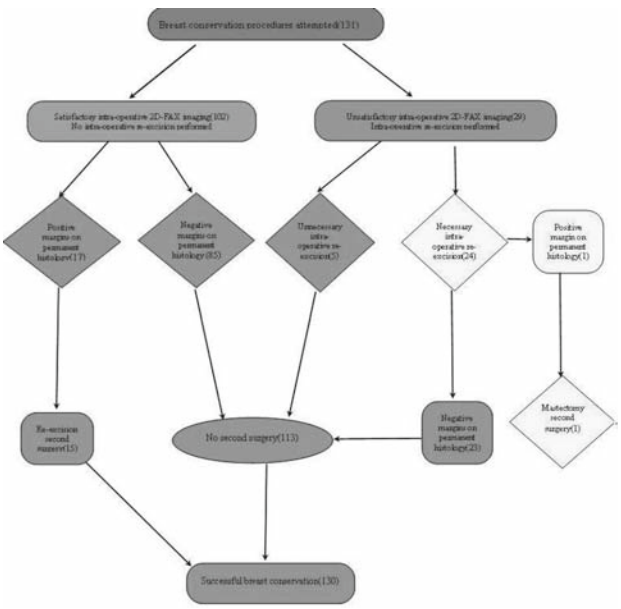

Figure: Treatment course of 131 excisions perfomed using 2D-FAX imaging for breast conservation surgery

P276

Predictors of Pulmonary and Cardiac Complications Following Pancreatoduodenectomy

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Introduction: Little is currently known about the epidemiology of and risk factors for perioperative pulmonary and cardiac complications in patients undergoing pancreatoduodenectomy (PD). Our objective was to identify preoperative factors associated with postoperative pneumonia (PP), respiratory failure (PRF) and myocardial infarction or cardiac arrest (MICA) within 30 days of PD surgery. Methods: Patients undergoing PD for benign and malignant neoplasms were identified from the American College of Surgeons' 2007 NSQIP, a multicenter, prospective database. Multivariate logistic regression analysis was performed on 1461 patients who underwent PD at 183 hospitals. PRF was defined as requiring mechanical ventilation >48 hours after surgery or reintubation and PP was defined as rales/dullness on percussion and sputum/blood culture or x-ray infiltrate and sputum/blood culture or positive serology. MICA was defined as myocardial infarction with new q waves or cardiac arrest requiring CPR. Results: PP was diagnosed in 92 patients (6.3%), PRF was found in 124 patients (8.5%) and MICA was seen in 23 patients (1.6%) undergoing PD for cancer. 30-day mortality was higher in patients who developed PP (18.95% vs 2.29%, p<0.0001), PRF (26.36% vs. 1.18%, p<0.0001) and MICA (79.17% vs. 2.11%, p<0.0001) compared to those who did not. 56 NSQIP preoperative variables analyzed by multivariate logistic regression modeling identified preoperative risk factors that were associated with PP, PRF, and MICA (Table 1). Conclusions: PP, PRF and MICA after PD are associated with increased 30-day mortality. They are predicted by modifiable and non-modifiable pre-operative risk factors. Through identifying risk factors, strategies to pre- and perioperatively optimize patients can be established to reduce complications. Additionally, these findings can help surgeons stratify individual patient risk and are useful for preoperative patient counseling and developing risk prediction/adjustment models to study and compare PD outcomes in the community and among individual centers.

Table 1

Risk Factors for Postoperative Pneumonia (PP)

Risk factor	Adjusted Odds Ratio	95% Confidence Interval
Esophageal varices within 6 months of surgery	21.8	1.3-363.5
Bleeding disorder	5.0	1.8-14.2
Radiotherapy within last 90 days	2.7	1.0-7.3
Dyspnea	2.3	1.4-3.8
Higher ASA class	1.7	1.1-2.6

Risk Factors for Postoperative Respiratory Failure (PRF)

Risk factor	Adjusted Odds Ratio	95% Confidence Interval
History of Peripheral vascular disease	4.8	1.6-14.1
Dyspnea	2.7	1.7-4.1
Decreasing functional status (Independent -> Partially dependent -> Totally dependent)	2.0	1.1-3.7
Days from surgical admission to operation	1.06	1.00-1.11

Risk Factors for Postoperative Myocardial Infarction or Cardiac Arrest (MICA)

Risk factor	Adjusted Odds Ratio	95% Confidence Interval
BMI >40 vs <25	5.8	1.4-24.4
ASA class	3.7	1.6-8.5

P277

The effect of surgeon volume on lymphedema development in older breast cancer women

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INTRODUCTION: Since axillary surgery results in the disruption and damage of lymphatic channels, it is likely that surgeon technique plays a role in the development of lymphedema (LE). We sought to determine the relative contribution of surgeon case volume (SV), as a surrogate for surgical technique, to the development of LE in a large, contemporary population of older breast cancer survivors. METHODS: Telephone surveys were conducted among

women (65-89 years) from 4 states (CA, FL, IL, NY) who had initial breast cancer surgery in 2003. The presence of self-reported LE, patient factors, pathology, treatment, SV and hospital case volume information were obtained from survey response, Medicare claims and state tumor registries. RESULTS: Of the 1,812 women operated on by 862 surgeons at 365 hospitals, 368 (20%) had self-reported LE at a median of 60 months postoperatively. Compared to low-volume surgeons (< 7 Medicare breast cancer operations/year), high-volume surgeons (> 14 cases/year) were more likely to perform a sentinel lymph node biopsy (71% vs. 43%; p < 0.001). Among high- and low-volume surgeons, there was no difference in the number of lymph nodes removed with an axillary node dissection (mean 7.8 vs. 9.4; p = 0.06) or a sentinel node biopsy (mean 2.7 vs. 2.7; p = 0.96). On univariate analysis, SV was not associated with LE (p = 0.31). On multivariate logistic regression analysis (Table), when controlling for patient age and SV, the independent predictors of LE were the removal of more than 5 lymph nodes, the presence of lymph node metastases, and type of breast surgery. CONCLUSIONS: Five years postoperatively, 20% of a contemporary, population-based cohort of elderly breast cancer survivors have self-reported LE. We show no relationship between SV and the development of LE. Although SV is one surrogate for surgical technique, we propose that other surgeon-specific characteristics (years in practice, percent of practice focused on breast cancer) might serve as more sensitive measures of surgeon technique and experience. We plan to further explore the relationship between these surgeon characteristics, including surgeon volume, and the development of LE.

Variables associated with lymphedema development in multivariate logistic regression analysis for breast cancer survivors (n = 1,812)*

Variable	Category	Odds Ratio	95% CI	P value
No. of lymph nodes removed				<0.0001
	None 1-5 6-10 11-15 16-25 >25	1.00 1.06 2.87 3.61 5.17 6.04	0.68-1.65 1.80-4.57 2.22-5.87 3.08-8.69 2.39-15.28	
Lymph node metastasis				<0.0001
	No Yes	1.00 2.10	1.56-2.82	
Type of breast surgery				0.04
	Lumpectomy Mastectomy	1.00 1.31	1.01-1.71	

*Controlled for patient age and surgeon case volume. The above relationships are unaffected with the addition of patient race, body mass index, hand dominance, tumor grade, tumor size, receipt of chemotherapy, receipt of radiation therapy, and hospital case volume.

P278

Prospective Identification of Vulnerability in Older Patients Undergoing a Pancreaticoduodenectomy: A Pilot Study K.K. Roggin,* J. Hemmerich, J. Wallace, C. Martens, E. Karr, A. Kamm, J.C. Baretto, J.B. Matthews, M.C. Posner, W. Dale. *Surgery, University of Chicago, Chicago, IL.*

Introduction: Older patients with pancreatic cancer are often not offered pancreaticoduodenectomy (PD) due to potentially high perioperative risk and prolonged post-operative recovery. We hypothesized that these patients may have undetected vulnerabilitities related to frailty and comorbidities that may adversely affect surgical outcomes. Methods: PD-eligible patient over 50 were enrolled onto this IRB-approved prospective outcomes study. Extensive perioperative clinical information as well as frailty, physical disability, and comorbidities on standardized instruments were collected. Specific assessments included: Vulnerable Elder Survey (VES-13), short physical performance battery (SPPB), and Fried's Criteria for frailty. Results: Fifty-two patients were enrolled: 34 had a PD (median age 71; range 57-85) and 18 were inoperable or declined PD. Vulnerability was identified in patients at baseline, including VES-13>3 in 27%; SPPB<10 in 32%; Fried's 10 lbs weight loss in 58%; Fried's exhaustion in 21%; and Fried's low grip strength in 67%. The perioperative morbidity rate was 62% (median grade of highest complication was IIIA); two patients died (6%). The most frequent complications were wound infections (44%) and intraabdominal abscess (24%). Approximately one-third of patients were admitted to the surgical intensive care unit (SICU) or initially monitored in the post-anesthesia care unit (PACU). The median length of hospital stay was 10 days (range 7-30). Only three required admission to an extended care facility. Fried's exhaustion (r=0.53, p<.01) and weakness (r=0.38, p<.05) predicted admission to the SICU; age predicted medical complications (r=0.34, p<.05) and days in the PACU (r=0.69, p<.001). None of the specific preoperative assessments correlated with complications or discharge to an extended care facility. Conclusions: We identified significant vulnerability in older patients undergoing PD. Early analyses suggest that age and elements of Fried's frailty correlate with complications and ICU stays. If sought for and identified, these issues could be managed expectantly, leading to more accurate preoperative counseling and in-hospital care.

P279

WITHDRAWN

P280

Outcomes after Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Surface Dissemination from Ovarian Neoplasms N. Parson,* P. Shen, G.B. Russell, S.S. Lentz, E.A. Levine, J.H. Stewart. *General Surgery, Wake Forest University School of Medicine, Winston-Salem, NC.*

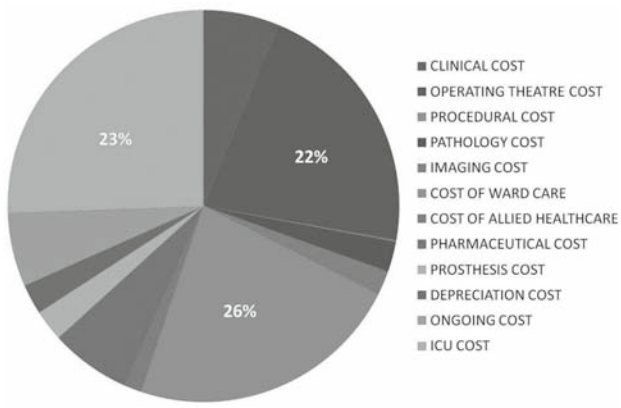
BACKGROUND: Although maximal tumor debulking is recommended for women with advanced ovarian cancer, little data exist on the clinical outcomes after cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for the treatment of patients with diffuse peritoneal surface dissemination (PSD) from ovarian cancer. We have reviewed our experience with cytoreductive surgery and HIPEC for PSD from ovarian neoplasms. METHODS: A total of 51 cases of PSD from proven ovarian neoplasms treated with HIPEC were identified from a prospectively managed database. All patients underwent aggressive tumor debulking followed by HIPEC with either mitomycin C (30-40 mg), carboplatin (400-1200 mg/m2), cisplatin (250mg/m2), or taxol (175 mg/m2). A retrospective review was performed with long-term survival as the primary outcome measure. RESULTS: A total of 59 HIPECS were performed on 51 patients for PSD from ovarian primary tumors between 1996 and 2009, with an average follow-up of 31.1 months. Eight of these patients underwent two cytoreductions followed by HIPEC. The median length of stay is 8.5 days. The median survival in this cohorts of patients was 28.5 months. The 1-, 3-, and 5-year survival rates for all cases were 73% +/- 6%, 48% +/- 7%, and 28% +/- 7%, respectively. When stratified by resection status, patients undergoing R0/R1 resections experienced a median survival of 47 months, while those undergoing R2a, R2b, and R2c resections experienced median survivals of 19, 6, and 11 months respectively (p=0.0002). Resection status (p=0.005) and estimated blood loss (p=0.025) were independently associated with survival. CONCLUSIONS: The data show that long-term survival is likely in patients who undergo complete cytoreduction followed by HIPEC for PSD from ovarian neoplasms. The findings presented herein underscore the importance of maximal cytoreduction followed by HIPEC in the treatment of these patients. In all, this work establishes a framework for the consideration of HIPEC in future trials for PSD from ovarian tumors.

P281

Evaluation of the Cost-Effectiveness of Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy (Peritonectomy) at the St George Hospital Peritoneal Surface Malignancy Program T.C. Chua,* S. Martin, A. Saxena, W. Liauw, T.D. Yan, J. Zhao, I. Lok, D.L. Morris. *UNSW Department of Surgery, St George Hospital, Sydney, NSW, Australia.*

Background Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a treatment approach for peritoneal carcinomatosis that has demonstrated improved survival outcomes with acceptable complication rates. This report aims to measure and describe the survival outcomes and health care cost associated with CRS and HIPEC for peritoneal surface malignancies at a centralized tertiary institution in Australia. Methods The expenditure of treatment for 136 consecutive patients who underwent 159 CRS and HIPEC from June 2002 to June 2008 were obtained. Together with their survival outcomes from treatment, a cost-effectiveness analysis was performed. Results The average cost of CRS and HIPEC per patient and per life year for appendix cancer is AUD$ 88,423 (range, AUD$ 23,933 to AUD$ 299,145) and AUD$ 37,737 / LY, for colorectal cancer is AUD$ 66,148 (range, AUD$ 26,079 to AUD$ 409,666) and AUD$ 29,757 / LY, for pseudomyxoma peritonei is

AUD$ 92,308 (range, AUD$ 11,562 to AUD$ 501,144) and AUD$ 29,559/LY, for peritoneal mesothelioma is AUD$ 55,062 (range, AUD$ 23,261 to AUD$ 94,104) and AUD $20,521 / LY, and for other peritoneal surface malignancies is AUD$ 44,668 (range, AUD$ 31,592 to AUD$ 70,026) and AUD$ 22,091 / LY. Conclusions This complex surgical treatment results in significant increment in medical costs but with a parallel increase in survival for a disease that has been poorly treated. Hence, it may be considered as cost-effective given the observed life years gained.



P282

The Effect of Splenectomy or Radiation Therapy on Survival for Patients with Hematologic Malignancies S. Misra,* N. Solomon, Y. Zhuge, L. Koniaris. *Surgical oncology, University of Miami, Miami, FL.*

Objective: Determine the effect of splenectomy or radiation therapy on outcomes for patients with hematologic malignancies. Methods: The SEER registry was accessed and patients diagnosed with hematologic malignancies were evaluated between the years 1973 to 2006. Common diagnoses examined were Hodgkins and Non-Hodgkins lymphoma (NHL), various leukemias and myelofibrosis. Treatment was stratified between surgery, radiation, combination of surgery and radiation and no therapy. Age, race, disease type, treatment type and survival rates were analyzed using univariate and multivariate analysis. Results: 82,375 patients were examined. 1642 (2%) patients underwent splenectomy. Patients undergoing splenectomy and or radiation fared better than those without any treatment p<.01. Median survival time for patients who had surgery alone was 89.6 months, those with radiation alone were 69.8 months and those who had both surgery and radiation were 96.8 months. Patients who had no forms of treatment fared the worst with a median survival of 58.4 months. 90% of the patients undergoing splenectomy had NHL. Overall patients with Hodgkin's lymphoma fared slightly better than NHL while all forms of leukemia had worse prognosis compared to NHL. Non-white races fared worse than whites. Patients greater than 30 years had decreased survival compared to those less than 30 years. Conclusions: Surgery and or radiation are associated with improved survival in hematologic malignancies. Prognosis for lymphoma is dependent on lymphoma type. Splenectomy for residual splenic disease or symptoms of hypersplenism appears to be a safe procedure.

P283

Is NCDB Data Valid For Estimating Completion Node Dissection Rate After Sentinel Node Biopsy In Melanoma? K.K. Turaga,* S.S. Marzbaan, E.L. Cox, V.K. Sondak, J.S. Zager. *H. Lee Moffitt Cancer Center and Research Institute, Tampa, FL.*

Introduction: Analysis of the National Cancer Database (NCDB) suggests that the rate of completion lymph node dissection (CLND) after positive sentinel lymph node biopsy (SLNB) for melanoma was only 64% at NCI cancer centers in 2004-05. We investigated whether this rate was representative of practices at our NCI center. **Methods:** We reviewed records of melanoma patients (pts) with a positive SLNB treated at Moffitt from 2004-05. These records were submitted for use in the NCDB. Validity of the records and data entry was verified and reasons for non-performance of CLND were investigated. **Results:** Of 77 melanoma pts with a positive SLNB, 83% (64/77) were recorded as having undergone a CLND. Median age was 61 yrs and 62% were male, which is similar to the NCDB data (59 yrs, 57% male, Table 1). Misclassification occurred in 1 pt who underwent a palliative lymph node excision for metastatic melanoma but was recorded as not having undergone CLND after positive SLNB. In the remaining pts, the CLND rate was much higher than in the NCDB (84% vs 64%). Reasons for no CLND were: refusal of recommended CLND in 6, interval development of a wound infection leading to recommendation for nodal observation in 2, and 1 each of the following: randomization to the observation arm of the MSLT-II trial, interval development of metastases, relocation to another state, and positive "in-transit" sentinel node with negative node basins, with recommendation for nodal observation. The head/neck and inguinal CLND rates (66% and 78%) were lower than other sites but much higher than the NCDB data. Of 12 pts older than 75 years of age, 75% underwent a CLND as opposed to NCDB's 43%. **Conclusions:** At our NCI designated center the CLND rate after positive SLNB was 84%. We discovered 1 misclassification, but otherwise found that the reasons for not performing CLND were clinically valid and did not suggest a high level of noncompliance with 'standard' guidelines. We also identified frequent reasons for not performing a CLND such as pt refusal or relocation and participation in randomized trials. We recommend large scale validation of the NCDB database before policy decisions are made.

Table 1: Comparison Of CLND Rate After A Positive SLNB At A NCI Designated Cancer Center And National Outcomes Reported From The NCDB

Variable	NCI Designated Center (n=77)	NCDB (n=2942)
Median Age	61 (IQR 46-70)	59(IQR 47-72)
Male sex	62%	57%
Completion Lymph Node Dissection		
Age		
<35 years	77.8%	57.4%
35-55 years	87.5%	50.1%
56-75 years	84.4%	50.5%
>75 years	75%	42.7%
Breslow Thickness		
<1.00mm	85.7%	40.2%
1.00-2.00mm	92%	53.0%
2.00-4.00mm	76.2%	53.9%
≥4.00mm	79.2%	55.7%
Location		
Upper Extremity	80.0%	51.1%
Head/Neck	66.7%	49.5%
Trunk	91.9%	57.6%
Lower Extremity	78.3%	39.0%

P284

Use Post-Mastectomy Breast Reconstruction in the Greater Sacramento Area: Disparities on the Rural to Urban Continuum W.H. Tseng,* R.J. Bold, R.J. Canter, S.L. Chen, V.P. Khatri, S.R. Martinez. *Surgery, UC Davis Cancer Center, Sacramento, CA.*

Background: Health care disparities have been documented in rural populations. We hypothesized that breast cancer (BCa) patients in urban Sacramento County would have higher rates of post-mastectomy breast reconstruction (BR) relative to patients in surrounding rural counties. Methods: We used the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute to identify patients diagnosed with BCa treated with mastectomy in the greater Sacramento area between 2000 and 2006. Patients diagnosed in Sacramento County composed the urban population, while patients from Amador, El Dorado, Placer, and Yolo Counties composed the rural population. Univariate models evaluated the relationship of rural or urban location with use of BR via the chi-square test. We used two multivariate logistic regression models to predict use of BR. The first model dichotomized counties into rural and urban areas, while the second assessed counties separately. Additional covariates included patient age, tumor size, nodal status, tumor grade, hormone receptor status, and use of radiation. Likelihood of undergoing BR was reported as odds ratios (OR) with 95% confidence intervals (CI); significance was set

at $p \leq 0.05$. Results: Among 2,400 BCa patients treated in Sacramento, California with complete information, 533 (22.2%) underwent BR. On univariate analysis, no differences in the rates of BR were noted in urban vs. rural areas ($p<0.18$) nor among the counties examined ($p<0.09$). On multivariate analysis rural status did not predict a decreased likelihood of undergoing BR (OR 0.88, CI 0.70-1.11, p=0.30). Relative to patients in Sacramento County, those from Amador County were less likely to receive BR (OR 0.32, CI 0.13-0.79, $p<0.02$). Conclusions: Overall, patients from rural areas as likely to receive BR following mastectomy for BCa as their urban counterparts. Patients from Amador County received lower rates of breast reconstruction which was unrelated to known tumor and treatment-related factors. Differences in use of breast reconstruction detected at a population level will need to be confirmed and addressed at the local level.

P285

Thromboprophylaxis Is Not Necessary In Patients Who Undergo Major Oncological Abdominal Surgery With Pre-Operative Epidural Analgesia F.F. Amersi,* T.K. Sibert, K. Sibert MD, E. Hemaya MD, A.W. Silberman MD, PhD. *Sugical Oncology, Cedar-Sinai Medical Center, Los Angeles, CA.*

INTRODUCTION: Patients with malignancies who undergo major abdominal surgery are at risk for venous thromboembolism. Thromboprophylaxis has been shown to decrease the risk of deep venous thrombosis (DVT). Epidural analgesia is commonly used to improve pain management in patients undergoing major abdominal surgery, however because of the concern of the sequelae of epidural hematomas, thromboprophylaxis is not co-administered. METHODS: We performed a retrospective review of a prospectively maintained database of all consecutive patients with malignancy who underwent major abdominal surgery who had epidural catheters placed pre-operatively for pain management between 1/04-5/09. Records of all patients were reviewed with particular attention to age, length of surgery, hospital length of stay, efficacy of analgesia, and clinical outcomes RESULTS: Of the 85 patients, 44% were female with a mean age of 63 years (range 36 – 87 years). All patients underwent major abdominal surgery for malignant disease. Average length of surgery was 6.12hrs (range 3.09-15.06 hrs). Of these pts, 52% were observed in the ICU for 24-48 hrs. Only one pt reported inadequate analgesia. Fifty four percent of pts were ambulating by POD #2. Nearly all pts (n=84) had their epidural infusion aborted between POD#3-4. Forty percent of pts were started on thromboprophylaxis after the epidural catheter was removed. Three pts developed soleus vein thromboses post-operatively, but had been in the hospital for one week pre-operatively without anti-coagulation No surgical complications were seen. CONCLUSIONS: Thromoboembolic complications after oncologic resections can be reduced with the use of epidural catheters. This maybe due to better analgesia resulting in early post-operative mobilization. In addition, epidural blockade may have an effect on venous hemodynamics in the lower extremities. These results also suggest that patients who have epidural analgesia, who undergo major oncological resections, and do not receive post-operative thromboprophylaxis, do not have an increased risk of thrombembolic events

P286

Patient Satisfaction with Timeliness of Care in Surgically-treated Gastric Cancer L. Donahoe,* K. Druhan, K. Inglis, G. Porter. *Dalhousie University, Halifax, NS, Canada.*

Introduction: Despite the current emphasis on access to cancer care, there exists no data examining timeliness of such care in gastric cancer. Moreover, patient satisfaction studies in gastric cancer have focused on treatment, not timeliness. The goal of this study was to (1) describe the timeliness of gastric cancer presentation, diagnosis, and treatment; and (2) examine the association between such timeliness and patient satisfaction. Methods: From 02/15/2002 – 02/14/2004, all patients undergoing resection for gastric cancer within a single health district were enrolled in a consecutive cohort study. Timeliness of care was determined via structured chart review and patient interview. A 5-item patient satisfaction tool, previously validated in colorectal cancer, was administered by telephone 1 week after hospital discharge. The association between satisfaction and timeliness was examined using linear regression. Results: Among the 28 patients in the study cohort, complete satisfaction data was available in 18. The median time for the interval from decision to see physician to first physician visit was 16 days (interquartile range (IQR) 1 – 31) and was not significantly associated with patient satisfaction ($r^2 = -0.27$; $p = 0.28$). The time from first physician visit to diagnosis was the longest of all intervals examined (median 80 days; IQR 27 - 229) but was not significantly associated with satisfaction ($r^2 = -0.03$; $p = 0.90$). Similarly, for the interval from diagnosis to surgery (median 21.5 days; IQR 18.5 – 30.5), satisfaction was not significantly associated with timeliness ($r^2 = 0.11$; $p = 0.65$). For the cumulative interval from patient decision to seek medical care to surgery (median 164 days, IQR 71 - 310), no association between timeliness and satisfaction was identified ($r^2 = -0.13$; $p = 0.60$). Conclusions: The timeliness of gastric cancer care has great variability, with the longest interval being from initial physician visit to diagnosis; this would appear to be the component of care most in need of optimization. Optimizing timeliness of care for the primary goal of increasing patient satisfaction is not supported by this study.

P287

Measuring the quality of sentinel lymph node biopsy (SLNB) for breast cancer in Ontario: A population based evaluation M. Quan,[1]* B.J. Wells,[2] R. Saskin,[3] N. Fraser,[2] F.C. Wright,[2] D.R. Urbach,[3] D.R. McCready.[4] *1. Department of Surgery, Foothills Medical Centre, Calgary, AB, Canada; 2. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 3. Institute for Clinical and Evaluative Sciences, Toronto, ON, Canada; 4. Princess Margaret Hospital, Toronto, ON, Canada.*

Background:Previous studies have identified variability in the training and implementation of sentinel lymph node biopsy (SLNB), however the quality of SLNB has never been evaluated in an era where the false negative rate is impractical to measure. We previously developed quality indicators for SLNB that were feasible to obtain. Therefore, the objective of this study was to measure the quality of SLNB in the province of Ontario using developed indicators. **Methods**:All patients diagnosed with breast cancer who had any axillary surgery between Jan 1, 2005 and Dec 31, 2005 were identified from the Ontario Cancer Registry. The cohort of patients who underwent a SLNB was then established using administrative datasets at the Institute for Clinical Evaluative Sciences (ICES) and primary chart abstraction. Data for measurement of the 8 quality indicators was then abstracted. The influence of patient, provider and institutional level characteristics on each indicator was determined using generalized estimating equations (GEEs) to account for clustering of patients within centres. **Results**:We identified 5134 patients with breast cancer during the study period, of which 2323 were confirmed to have underwent a SLNB. Quality indicators for the entire cohort were calculated (Table 1). Both the proper identification of the SLNB and performance of SLNB concurrently with primary breast surgery were high, exceeding 90%. As expected, the rate of completion axillary node dissection for positive SLN increased with the size of metatases and decreased with age. The proportions of cases having appropriate pathology evaluation and reporting were modest. Hospital volume of breast cases, urban/rural and academic/community status were not significant predictors for any of the indicators. Younger patient age was a significant predictor of node positivity ($p = .002$) and number of nodes removed >1 ($p = .008$) which may reflect individual provider influence. **Summary**:The overall measure of quality in SLNB practice was high in the province. Further evaluation is required, particularly in determining how to improve appropriate pathologic evaluation and reporting.

Table 1. Quality indicators for sentinel lymph node biopsy in breast cancer

Quality Indicator	Description	
Axillary node positivity rate	Proportion of patients undergoing SLNB in whom SLNB was identified and found to be positive	28.1%
Proper identification of SLN	Proportion of patients in whom sentinel lymph node(s) (SLNs) were identified as "hot" and/or "blue" and/or "clinically suspicious" in the chart or operative note	94.6%
Number of nodes removed (>1)	Proportion of patient who underwent SLNB in whom the number of nodes removed is greater than 1	63.7%
Pathologic evaluation protocol	Proportion of patients in whom the SLNs were examined using a recognized serial-sectioning protocol	59.1%
Pathologic reporting by AJCC guidelines	Proportion of SLNB final pathology reports that report the category of metastases identified and the patterns of tumour present according to AJCC criteria	37.8%
SLNB concurrent with lumpectomy/ mastectomy	Proportion of patients who underwent SLNB and primary breast surgery (lumpectomy/mastectomy) concurrently	94.4%
Completion ALND for positive SLNB	Proportion of patients with a positive SLNB (as defined by micrometastases greater than 0.2mm) who received a completion axillary lymph node dissection (ALND)	macromet 91% micromet 65% ITCs 54%
SLNB performance in ineligible patients	Proportion of patients who undergo SLNB as a stand-alone axillary procedure who are "ineligible" based on preoperative disease characteristics (i.e. inflammatory breast cancer, etc.)	1.9%

P288

Extra Pulmonary Small Cell Cancers: A Population Based Study Comparing Epidemiology and Survival Rates with Pulmonary Small Cell Cancers S. Misra,* N. Solomon, Y. Zhuge, L. Koniaris. *Surgical oncology, University of Miami, Miami, FL.*

Objective: Extra Pulmonary Small Cell Cancers (EPSCC) are rare tumors and this population based study evaluates the distribution, pathological characteristics and survival outcomes for various forms of EPSCC while comparing the same for Pulmonary Small Cell Cancers (PSCC). Method: The SEER registry was accessed and patients diagnosed with small cell cancers were evaluated between the years 1973 to 2004. Age, race, disease specific sites, pathologic grade, stage, treatment type and survival rates were analyzed using uni and multi-variate analysis. Results: 105,903 patients were examined. 99,597 (94.1%) and 6,306 (5.9%) patients had PSCC and EPSCC respectively. Mean age of the sample was 66.5 years. 55.2% were males and 44.8% were females. There were 88.3% whites, 7.8% blacks, and 3.9% other races. Patients with small cell cancer of the breast had better survival than PSCC while patients with small cell cancers of the gastrointestinal, genito-urinary and miscellaneous sites had worse survival, $p<0.05$. Small cell cancers of the head and neck also had worse outcomes but this was not statistically significant. Oat cell cancers patients performed poorly compared to other variants of small cell cancers. Grade of the tumor had no effect on survival. Patients who were treated with surgery and or radiation fared better than those without treatment. People of non-white racial origin had slightly worse outcomes. Conclusion: EPSCC continue to have poor survival with the exception of small cell cancer of the breast. Treatment with surgery and radiation in selected cases seemed to improve survival.

P289

An Acuity Adaptable Patient Care Unit Does Not Change Surgical Outcomes in Patients Undergoing Esophagectomy A. Kothari,[1]* M. Hennon,[2] T. Bretl,[2] A. Munoz-del-Rio,[3] T. Weigel.[2] *1. Department of Surgery, Division of Cardiothoracic Surgery, University of Wisconsin, Madison, WI; 2. University of Wisconsin Department of Surgery, Division of Cardiothoracic Surgery, Madison, WI; 3. University of Wisconsin Department of Surgery, Division of Biostatistics, Madison, WI.*

Background: Several academic and community medical centers have adapted an Acuity Adaptable Care Unit (AACU) in an attempt to streamline post-operative care processes and lower patient stay costs. The AACU patient care model appears to reduce medication errors, patient transfers, and improve patient satisfaction, yet few data exist on the impact of an AACU on surgical outcomes. We examined the effects of implementing an Acuity Adaptable Care Unit (AACU) and compared it to our former intensive/general care model with respect to surgical outcomes for patients with esophageal cancer undergoing esophagectomy. Methods: We reviewed data from an IRB-approved, prospectively maintained thoracic surgery database for patients undergoing esophagectomy during the three year periods pre- and post-adoption of an AACU model. As surrogate endpoints to quality and cost, we measured length of stay (mean values, medians, and a Kruskal-Wallis test to assess differences across eras), readmission rate, 30 day mortality, and incidence of post-operative complications in patients undergoing esophagectomy for primary cancers during these two time periods. Results: 234 patients had an esophagectomy in this 6 year time period, with 115 (49%) in the ICU era and 119 (51%) in the AACU era. Hospital mortality of the patient series was .02% (5/234). There were no differences in 30 day hospital mortality (0% ICU vs. 1.6% AACU; p=(0.50), length of stay (LOS: median=9d IQR=7-13d ICU vs. median=8d IQR=7-12d AACU; P=0.21), 30 day readmission rate (11.3% ICU vs. 9.2% AACU; p=0.67) or post-operative events (58.3% ICU vs. 51.3% AACU; p=0.30). Conclusions: An Acuity Adaptable Care Unit is a viable post-operative care model for patients undergoing esophagectomy. The AACU may improve patient satisfaction, reduce medication error and patient transfers, and our results suggest the model does not appear to negatively impact surgical outcomes. These data may guide surgeons, nursing and hospital administrators in their mutual goal of maximizing quality, patient satisfaction and cost-effective post-operative surgical care.

P290

Peritoneal Carcinomatosis in the Geriatric Patient: Outcomes with Cytoreductive Surgery and HIPEC H.A. Thieme,* V. Gushchin, A. Sardi, N. Athas. *Dept of Surgical Oncology, Mercy Medical Center, Baltimore, MD.*

Introduction: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CS/HIPEC)is the treatment of choice for peritoneal carcinomatosis, but for patients over 65, the risks of surgery are more pronounced. We evaluated our patients over the age of 65 who underwent CS/HIPEC. Methods: A retrospective review was performed on patients over the age of 65 treated with CS/HIPEC over 10 years by a single surgeon. Results: From 1999 to 2009, 29 patients over 65 years were treated with CS/HIPEC, average 69.8 years (range 65-80). Nineteen patients had significant co-morbidities: hypertension (10); obesity (3), COPD (3), asthma (3), diabetes (2), gastric ulcer (3), prostate cancer with metastasis (1), ulcerative colitis (1), thrombocytopenia (1), bipolar disorder (1), and CVA (1). Complications included renal failure (2), enterocutaneous fistulae (2), myocardial infarction (2, one death), arrhythmias (2) emergent reoperation for an acute bleed (one, with subsequent death), respiratory failure leading to tracheostomy (1). Readmissions occurred for severe vomiting (2) and UTI (1). Patients spent an average of 18.7 days in the hospital (range 9 to 84, median 12 days). Ten patients have died since their surgery, two of perioperative complications. None of our patients under the age of 65 have died in the perioperative period. Five patients died of disease, living an average of 54 weeks after their surgery (range 26-104). Other causes were an MI (32 weeks postoperative), enterocutaneous fistulae complications (32 weeks), and failure to thrive (21 weeks). Currently 14 patients have no evidence of disease, and four are alive with disease. Follow-up ranges from 26 to 518 weeks (average 146 weeks). One patient with recurrent disease underwent a second CS/HIPEC surgery five years later. Conclusions: The morbidity and mortality of cytoreductive/HIPEC surgery is a significant concern in geriatrics; however, the majority recovered without significant complications and returned to their baseline activities. CS/HIPEC can therefore have a significant positive effect on length and quality of life.

P291

Esophagectomy in the State of Florida: Is Regionalization of Care Warranted? K. Ben-David, D. Ang, S.R. Grobmyer, T. Kim, S. Hochwald.* *Surgery, University of Florida College of Medicine, Gainesville, FL.*

BACKGROUND:Centralization of cancer care has been initiated in some states with the goals of improving outcomes and reducing costs. Decisions regarding regionalization of care should be based on evidence that regionalization will improve outcomes in a given region. Hence, we sought to determine variations in outcome across the state of Florida for a single high-risk cancer operation, esophagectomy. METHODS: We analyzed outcomes for esophagectomy, performed in Florida (1997-2006) using the Agency for Health Care Administration database. We calculated the frequency of esophagectomy performed between 1997-2001 and 2002-2006. Three regions within Florida were classified as high volume (HV), defined as performing > 11 cases per year. We determined the risk-adjusted mortality rate for the procedure in low volume (LV) and HV regions with adjustment for age, race, gender, principle payer, DRG and comorbidities. Statistical analysis performed via Chi square, t-test and multiple variable logistic regression. RESULTS: Over the 10 year time period of the study 991 esophagectomies were performed in Florida. The incidence of esophagectomy significantly increased in Florida from 1997-2001 vs 2002-2006 and the postoperative mortality significantly decreased in the latter time period (OR 1.87, CI 1.16, 3.03). The three HV regions for esophagectomy in the State accounted for 55% of the cases. The risk adjusted post operative mortality was significantly lower (OR 0.54, CI 0.32, 0.92) in HV regions (5.1% vs 10.4%, HV vs LV regions, respectively). However, this was not explained by a difference in anastomotic leak rates which were 8.2% in both HV and LV regions. LOS was shorter in HV regions (16.3 vs 18.0 days, p=0.06). Total charges were similar in both HV and LV regions (p=0.33, $105,630 vs $109,848, respectively). CONCLUSIONS: In the largest population based study to date for esophagectomy in Florida, outcomes are better in HV regions. This data supports the regionalization of esophagectomy to such HV locations in Florida to reduce procedure related mortality. Expertise and resourses available for managing life threatening complications may account for observed differences in outcome.

P292

Analysis of Receptor Tyrosine Kinase Activation in Peritoneal Mesothelioma Treated by Cytoreduction and Hyperthermic Intraperitoneal Chemotherapy M. Deraco,* F. Perrone, A.D. Cabras, D. Baratti, N. Zaffaroni, G. Jocollè, S. Kusamura, S. Pilotti. *Fondazione IRCCS Istituto Nazionale Tumori, Milan, Italy.*

Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) have been suggested as the treatment of choice for selected patients with diffuse malignant peritoneal mesothelioma (DMPM). DMPM biology is still poorly known and no information is available on receptor tyrosine kinase (TK) activation in this tumor. METHODS A prospective database of 91 patients with DMPM undergoing CRS and close-abdomen HIPEC with cisplatin and doxorubicin was reviewed. Prognostic factors were analyzed by Cox regression. In 20 patients, endothelial growth factor receptor (EGFR), platelet-derived growth factor receptor (PDGFR) A and PDGFRB expression and phosphorylation were immunohistochemically and biochemically analysed. The TK domain of EGFR gene, the extracellular, juxtamembrane and TK domain of PDGFRA and PDGFRB were automatically sequenced. Cognate ligand expression was investigated by real time PCR. Downstream pathway was explored by mutational and biochemical analysis of PI3KCA gene/PTEN/AKT, ERK, mTOR and S6. RESULTS Median follow-up and overall survival were 58 (range 1-141) and 62 months, respectively. Operative death and morbidity were 2.2% and 26.4%. Increased survival correlated with completeness of CRS (hazard ratio (HR) 1.6; 95% confidence interval (CI) 1.1-2.4; P.040), epithelial histology (HR 2.8; CI 1.2-66; P.016), negative nodes (HR 4.5; CI 1.6-12.9; P.005), mitotic count <4/50HPF (HR 3.8; CI 1.6-9.1; P.002). Immunohistochemical and western blot analyses showed EGFR, PDGFRA and PDGFRB expression and activation in the most of the cases. EGFR and PDGFRA were more frequently phosphorylated than PDGFRB. Autocrine loop activation was suggested in all cases by the expression of the related cognate ligands TGF-α, PDGFA and PDGFB, in absence of receptor gain of function mutations. No PI3KCA mutation was found. All cases showed expression/activation of PTEN, AKT, ERK, mTOR and S6. CONCLUSION CRS and HIPEC result in improved outcome. EGFR, PDGFRA and PDGFRB may be potential targets for molecular therapy. The strong activation of the downstream signalling suggests a role of mTOR inhibitor in DMPM treatment.

P293

Complications Following Elective Hepatic Resection for Malignancy: Are They Associated with Institutional Volume? G.D. Young,[1]* C.J. Gannon,[1] V. Dombrovskiy,[2] D.R. Carpizo,[1] T.R. Vogel.[2] *1. Cancer Institute of New Jersey, New Brunswick, NJ; 2. Surgical Outcomes Research Group, Robert Wood Johnson Medical School, New Brunswick, NJ.*

Background: Retrospective analyses of state and national databases have consistently documented institutional volume related mortality rates for hepatic resection at low-volume hospitals (LV). However, a causal relationship has not been definitively determined to account for this higher postoperative mortality rate. Hypothesis: Postoperative complications after elective hepatic resection at LV are more frequent than at high-volume hospitals (HV). Methods: The Nationwide Inpatient Sample (NIS) database was queried from 1998-2007 for patients older than 18 years of age undergoing elective hepatic resection for neoplastic diagnosis. A threshold of twenty hepatic resections annually was utilized in each hospital to separate LV from HV. Postoperative complications analyzed included hemorrhagic, hepatobiliary, pulmonary, cardiac, renal, liver failure, and sepsis. Differences between parameters were examined by chi-square statistics followed by multivariable logistic regression analysis with patient's sociodemographic characteristics (age, gender, race) and comorbidities, indications for procedure, and hospital volume as independent variables. Odds ratio (OR) and 95% confidence interval (CI) were computed and compared. Results: 9,289 cases were included in the analysis. Patients at LV experienced at least one of the analyzed postoperative complications more often than at HV (Table). Hemorrhagic, septic, and pulmonary complications were also more likely to occur at LV; however, hepatobiliary complications occurred less frequently at LV. Patients with complications were 6.6 times as likely to die (CI = 4.54- 9.69). Multivariate analysis revealed that, overall, patients after elective hepatic resection at LV are 1.4 times (CI = 1.02-1.93) as likely to die as patients at HV. Conclusion: Following hepatic resection, patients at LV centers were more likely to develop postoperative complications and LV centers had higher overall mortality after adjustment. Hepatic complications were significantly associated with mortality in all center types. Further analysis of LV institutions and prevention of complications may improve future patient outcomes.

Significant post-operative complications and mortality after elective hepatic resection

Parameters	LV (%)	HV (%)	OR (adjusted)	95% CI
Complications:				
Any	31.4	27.8	1.14	1.02-1.27
hemorrhagic	11.99	8.03	1.48	1.25-1.75
pulmonary	9.46	6.99	1.37	1.14-1.65
sepsis	2.88	1.72	1.63	1.15-2.30
hepatobiliary	0.83	2.25	0.41	0.26-0.66
Hospital Mortality	3.62	2.36	1.40	1.02-1.93

P294

Schizophrenic patients with breast cancer: poor compliance with adjuvant chemotherapy M. Hwang,[1]* M. Farasatpour,[1] C. Williams,[1] J.A. Margenthaler,[2] K.S. Virgo,[3] F.E. Johnson.[1] *1. Surgery, Saint Louis University, Saint Louis, MO; 2. Washington University, Saint Louis, MO; 3. American Cancer Society, Atlanta, GA.*

Introduction: Schizophrenia affects >1% of the adult U.S. population. It alters the outcomes of other disorders. We sought to quantify the clinical course of schizophrenic breast cancer patients offered adjuvant chemotherapy. Methods: We searched the Patient Treatment File (PTF), the national inpatient computer database of the Department of Veterans Affairs (DVA) to identify patients with schizophrenia who later developed breast cancer and were treated in DVA Medical Centers (DVAMCs). PTF data was supplemented via chart-based clinical indicators from DVAMCs nationwide. Results: Of the 126 patients identified by computer, 56 appeared to be appropriate candidates for adjuvant systemic therapy and were deemed evaluable. 28 (50%) were Caucasian, 19 (35%) were African-American, 3 (6%) were Hispanic, and 5 (9%) were of other ethnicities. There were 18 men (32%) and 38 women (68%). Before breast cancer treatment, 17 of the 56 (28%) had documented suicidal ideation; 12 patients (21%) had attempted suicide. At least 10 of the 56 patients (18%) had verbally abused healthcare workers; 7 (13%) had physically assaulted caregivers; 5 (8%) had documented homicidal ideation. 14 of the 35 patients (40%) for whom staging data were available had TNM stages III-IV; at least 5 of these 14 had ignored obvious signs of breast cancer (mass and/or ulceration noted by patient) for 6 months to 9 years; 4 other patients with biopsy-proven cancer delayed treatment for >3 months. In the 25 patients for whom tumor size was recorded, 17 (65%) were > 2 cm (mean = 5.8 cm). Among the 56 patients who appeared to be candidates for adjuvant cytotoxic therapy, there were 46 for whom adequate data about this option were available; 39/46 (85%) were offered postoperative cytotoxic chemotherapy; 12 of these 39 (31%) refused or were noncompliant. Conclusions: Schizophrenic patients often do not understand their health problems. They often have advanced-stage cancer at diagnosis, delay diagnosis, refuse therapy and/or are non-compliant. Initial radical surgery may be preferable to breast-preserving treatment plans that require adjuvant chemotherapy.

P295

Cytoreductive Surgery and Intraperitoneal Chemotherapy Improve survival in Patients with Peritoneal Carcinomatosis from Colorectal Cancer J. Ojo,* S. McKenzie, R. Morgan, B. Paz, L. Leong, J. Ellenhorn, J. Garcia-Aguilar, L. Lai. *Surgery, City of Hope Hospital, Duarte, CA.*

Introduction: The natural history of peritoneal carcinomatosis(PC) from colorectal cancer(CRC) remains poorly understood and effective therapy is an area of active investigation. We sought to determine the incidence, presentation, clinical treatment, and outcome of patients diagnosed with PC at a single institution. M&M:Clinicopathologic data was obtained by a retrospective chart review of patients diagnosed with PC from CRC between 1995 and 2008.Survival was calculated with Kaplan Meier analysis and differences in survival were determined using the Log-rank test.Predictive factors were determined through Cox regression analysis. Results:Of 411 patients who presented with CRC metastases during the study period,45(11%)of the patients had metastasis to the peritoneum.The primary site of disease included the right colon in

17 patients; sigmoid colon 14; appendix 9; rectum 3, and caecum in 2 patients. All patients underwent surgery during the course of their treatment. Thirteen patients underwent cytoreductive surgery while the remaining 32 patients were treated with colectomy only.34 patients had intravenous chemotherapy (CT), 12 patients received intraperitoneal (IP) chemotherapy alone, and 2 patients received both forms of (IP+IV), CT after surgical resection. Overall 1 and 4 year survivals are 88% and 9%, with a median survival (MS) of 26months.. When compared with IV CT, patients receiving IP CT had improved MS (21 months. 36 months, respectively, p = 0.0171). Patients who had undergone cytoreductive surgery had a trend towards a favorable survival (28months, n=13) compared to patients who had undergone colectomy alone (21months, n=22) (p= 0.057). By multivariate analysis,no independent clinical factor was associated with improved survival. Conclusion: PC alone represents 11% of all CRC metastases and the prognosis remains poor.Our study confirms that aggressive treatment with cytoreductive surgery and IP CT can improve survival in this patient population.Further studies are necessary to determine optimal patient selection for this aggressive multimodal approach.(CA33572)

P296

Malignancies after renal transplantation E. Bastiaannet,[2]* J.J. Homan-van der Heide,[1] R.J. Ploeg,[1] H.J. Hoekstra.[1] *1. UMCG, Groningen, Netherlands; 2. CCCNE, Groningen, Netherlands.*

Introduction. Renal transplant patients who receive immunosuppression therapy are at an increased risk to develop a malignancy during the follow-up. Aim of this study was to assess the risk of malignancies in a regional renal transplantation population. Methods. Data from the renal transplant centre (1989-2003) was linked to data from the regional cancer registry (1989-2007). The risk to develop a malignancy was calculated using the Standardized Incidence Ratio (SIR). Results. Overall, 1123 patients (650 (58%) male and 473 (42%) female) who received a renal transplantation were included. Linkage with the regional cancer registry showed 229 (19.3%) malignancies in the follow-up and an increased SIR for the most prevalent tumours in the Netherlands (prostate, lung, colorectal, non-melanoma skin, Non-Hodgkin & Hodgkin lymphoma, head & neck and bladder cancer). However, we found no increased risk for melanoma, breast and cervical cancer. Male transplant patients had a higher SIR (12.3) than females (7.5). Besides, the SIR for malignancies in the first 5 years after transplantation was higher in the last years of transplantation (2.7 for 1989-1993; 1.9 for 1994-1998 and 2.9 for 1999-2003). Conclusion. Renal transplantation patients in this study have an increased risk for malignancies in the follow-up. The SIR after transplantation is low compared to other countries. An increased SIR was not found for all tumors; immunosuppression, conventional, endocrine or genetic risk factors could contribute to this.

P297

Quality of care for colorectal cancer patients in Japan –an Analysis of the Japanese Colorectal Cancer Registry M. Ishiguro,[1]* T. Higashi,[2] K. Sugihara,[1] T. Sobue.[3] *1. Department of Surgical Oncology, Tokyo Medical and Dental University, Tokyo, Tokyo, Japan; 2. The University of Tokyo, Graduate School of Medicine, Department of Public Health / Health Policy, Tokyo, Japan; 3. Center for Cancer Control and Information Services, National Cancer Center, Tokyo, Japan.*

Introduction: In Japan, colorectal cancer patients are treated in not only in specialized facilities but also in general hospitals. Although great efforts, including making clinical practice guidelines, have been made to standardize the care for colorectal cancer,actual quality of care for colorectal cancer in Japan has not been systematically evaluated. The aim of this study is to develop a set of process-of-care quality indicators (QIs) for colorectal cancer, and to evaluate the current status of colorectal cancer care in Japan. Methods: We identified 47 candidate QIs based on the current clinical practice guidelines and the review of literature. A multi-disciplinary panel of 11 experts examined the candidate QIs and determined a final set of QIs through modified-Delphi process. Each QI describes standards in a particular aspect of care, and the score is calculated as the percentage of applicable patients who received the recommended care (adherence score). We applied the final QIs to the data in the Japanese colorectal Cancer Registry, which covers about 10% of all Japanese colorectal cancer patients. Results: The 45 QIs were finally agreed by the panel, covering the continuum of colorectal cancer care from initial evaluation to follow-up. Of the 45 QIs, 9 could be scored using data in the Japanese Colorectal Cancer Registry. The study population included 6242 patients registered by 95 facilities throughout Japan in 1998. Overall, patients received 81% of recommended care, but substantial variation in adherence scores was seen across QIs (56-99%). Adherence score was less than 80% in 5 of 9 QIs. Wide variation across facilities was observed in 4 QIs. Conclusions: We developed a set of QIs to assess the care of colorectal cancer patients in Japan. Japanese Colorectal Cancer Registry enabled us to score 9 QIs, revealing substantial variation in adherence scores was seen across QIs and facilities. Japanese cancer registry provided a unique opportunity for us to implement the subset of our QI set. Future research could expand our activity to measure and improve the quality of colorectal cancer care in Japan.

P298

Perioperative Morbidity and Mortality for Extremity and Truncal Soft Tissue Sarcomas: Insight from the NSQIP Database M. Raoof,[1]* W.H. Tseng,[2] R.M. Tamurian,[2] R.J. Canter.[2] *1. University of Arizona, Tucson, AZ; 2. Surgery/Surgical Oncology, UC Davis Medical Center, Sacramento, CA.*

Background: The incidence of overall postoperative complications following resection of extremity and truncal soft tissue sarcoma (STS) is largely unknown, particularly in the setting of preoperative radiotherapy (RT). We sought to examine the overall perioperative morbidity and mortality rates following resection of STS in a nationwide database. Methods: Utilizing data from 2005 to 2007 from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP), we identified cases of soft tissue tumor resection by CPT code and stratified by ICD-9 codes for primary malignant neoplasm of connective and soft tissue. Benign, uncertain, and secondary malignant neoplasms were excluded. Univariate analyses were performed using all preoperative NSQIP variables for likelihood of postoperative complications. Multivariate analysis was performed using a logistic regression likelihood model, adjusting for body mass index, albumin, hematocrit, pre-existing wound infection, tumor location, ASA class, wound classification, and delivery of RT. Results: Entry criteria were met by 215 patients. Tumor distribution was lower extremity (67%), upper extremity (29%) and body wall (8%). Overall morbidity and mortality rates were 14% and 0.9%, respectively. RT was administered to 20 (9.3%) patients. Complications included reoperation=18, pulmonary=2, neurological=2, infectious=3, thrombotic=1, and any wound=14. Univariate analysis demonstrated pre-existing wound infection (p=0.01) and ASA class (p=0.02) as significant predictors of perioperative complications. Multivariate analysis revealed ASA class as the only significant predictor of perioperative complications (p= 0.01, see Table 1). RT was not independently associated with perioperative complications (p=0.80). Conclusion: NSQIP data demonstrate low rates of perioperative morbidity and mortality following resection of extremity and truncal STS. Although limited to 30 days of follow up, these data suggest that STS resections can be performed safely with low complication rates, even following preoperative RT.

Multivariate Analysis of Predictors of Complications Following Resection of Extremity and Truncal Soft Tissue Sarcomas (N=215)

Variable	Odds Ratio	95% CI	P value
Body Mass Index	0.92	0.82 - 1.03	0.13
Hematocrit	1.07	0.92 - 1.26	0.38
Albumin	1.79	0.45 - 7.14	0.41
ASA Class 2 3 4	1.00 (referent) 11.58 54.89	 1.90 - 70.46 1.02 - 2948.03	 0.01 0.05
Pre-existing Wound Infection No Yes	1.00 (referent) 3.72	 0.39 - 35.86	 0.26
Wound Class 1 2 - 3 4	1.00 (referent) 2.42 - 1.05	 0.27 - 21.83 - 0.01 - 79.8	 0.43 - 0.98
Tumor Location Lower Upper Trunk	1.00 (referent) 0.99 -	 0.21 - 4.83 -	 0.99 -
Radiation Therapy No Yes	1.00 (referent) 1.48	 0.07 - 32.8	 0.80

P299

Alveolar Soft Part Sarcoma: clinical features, treatment and outcome in a series of 33 cases E. Pennacchioli,* M. Fiore, P. Collini, S. Stacchiotti, P. Dileo, A. Gronchi. *surgery, national cancer institute of milan, Milan, Italy.*

PURPOSE: Alveolar soft part sarcoma (ASPS) is a rare soft tissue neoplasm that usually affect young patients. The authors performed a comprehensive retrospective review of the clinical presentation, treatment, outcome, and patterns of failure in a consecutive series of patients with localized or metastatic ASPS between 1975 and 2006. METHODS: After institutional review board approval, we examined the records of all patients who received treatment for ASPS in the past 30 years. Demographics, tumor sizes, sites and extent of disease, treatments used, progression-free survival, and overall survival were evaluated. RESULTS: Each of the 33 patients presented with a mass, in 4 cases associated to pain. Primary disease sites were thigh (n =15), arm (n= 4), leg (n=3), forearm (n= 3), buttock (gluteus n= 2), abdominal wall (n= 1), pelvis (n=3), pharynx (n=1), cervical paravertebral region (n=1). The mean diameter of the mass was 7.15 cm (range 2 to 15 cm). In patients with a soft tissue tumor, the mass was deeply located in 26 cases, while it was subcutaneous in 7 cases. 10 patients presented distant metastases at time of diagnosis. A wide R0 resection was obtained in 27 cases. Complementary treatments were used as follow: adjuvant radiotherapy in 12 cases, in 6 cases associated to chemotherapy; in 2 patients CT/RT was the only treatment; pre-operative systemic chemotherapy in 4 cases, while in the adjuvant setting in 3 cases. 10 patients (30.3%) didn't receive any complementary treatment after adequate surgery. 21 (63.6%) of 33 patients exhibited metastases either at presentation (10 patients) or later. Median overall follow-up was 71.6 months. CONCLUSIONS: Achievement of complete microscopic resection is critical in localized alveolar soft part sarcoma. Despite the occurrence of metastases in 63 % of patients, 5-year overall survival was 68.7 %, and 10 yrs OS was 53.4%. We found an association between smaller tumor size and longer time to progression, and a benefit on long term outcome after adequate surgery. Metastasectomies have been performed in multiple long-term survivors.

P300

Desmoid Tumors: Differences in Behavior Based on Site of Disease A.J. Russ,* J. Yang, C.P. Heise, C.S. Cho, S.M. Weber. *Surgery, University of Wisconsin Hospitals and Clinics, Madison, WI.*

Background: Desmoid tumors, also known as aggressive fibromatosis, consist of mature fibroblasts that proliferate from musculoaponeurotic structures. No treatment regimen has proven to be particularly effective, and reported recurrence rates are as high as 90%. The purpose of this study was to examine differences in biological behavior of desmoids based on the site of disease. Methods: Patients with the diagnosis of fibromatosis or desmoid tumor from 1990-2005 were identified from hospital records and a retrospective chart review was performed. Demographic data, tumor location, and outcomes were analyzed. Patients were classified into groups based on site of disease (intra-abdominal vs extremity/trunk). Complications were graded from 1-5, according to previously defined criteria. Recurrence was defined as tumor detected on physical exam, imaging, or biopsy, occurring in patients after R0 or R1 resection. Analysis was undertaken using Fisher's exact test. All t-tests were two-tailed and significance was determined at $p < 0.05$. Results: A total of 59 patients were identified, including 21 with intra-abdominal disease (36%) and 38 with extremity or trunk tumors (64%). Eleven patients (19%) had multiple sites of disease. Surgical resection was performed in 52 (88%) patients. Postoperative mortality was 3.4%, all in patients with intra-abdominal desmoids, and was directly attributable to their disease. There were no differences in overall postoperative complications between groups ($p = 0.77$), although there were significantly more major complications (grade ≥3) in patients with intra-abdominal tumors. Outcome differences between patients with intra-abdominal vs. extremity/trunk desmoids are seen in Table 1. Adjunctive treatment regimens did not differ between groups. Conclusions: Patients with intra-abdominal desmoids are more likely to be incompletely resected, and have an increased complication severity post-operatively. These differences are likely explained by the anatomical constraints associated with resection of intra-abdominal desmoids. Further development of novel therapeutic strategies is needed to improve local disease control and patient outcomes.

Variable	Intra-abdominal	Extremity/Trunk	p-value
Resection status			
R0	15/24 (62.5%)	39/47 (83%)	0.0784
R1	1/24 (4.2%)	6/47 (12.8%)	0.4102
R2	8/24 (33%)	2/47 (4.3%)	0.0019*
Recurrence			
Yes	7/16 (43.8%)	30/45(66.7%)	
No	9/16(56.3%)	15/45 (33.3%)	0.1402
Complication grade			
none/minor (0-2)	19/25 (76%)	52/54 (96.3%)	
major (≥3)	6/25 (24%)	2/54 (3.7%)	0.0108*

P301

Activation of Peptidergic Neurons by Two Sarcoma Cell Lines M.A. Lautner,* T.E. Stewart, J.C. Fehrenbacher, P.E. Scotland, C.B. Gonzales, A.M. Patwardhan, K.M. Hargreaves. *Surgery, UTHSCSA, San Antonio, TX.*

Due to improved early detection and screening, those patients diagnosed with a malignancy are living longer; however, many will experience severe to moderate pain during the extended course of their disease (Mantyh 2006). In addition, the exact etiology of cancer pain is not well understood. Three well studied proposals consist of neural invasion by tumor growth, tumor-evoked local inflammation and soluble factors released by tumors themselves that activate and/or sensitize nearby nociceptor terminals. Our hypothesis focuses on the last mechanism, namely that sarcoma cells release a soluble factor that activates peptidergic neurons thereby causing cancer pain. We examined the effects of conditioned media from several different sarcoma cell lines on rat trigeminal ganglia (TG) peptidergic neurons. Sarcoma cells were purchased from ATCC and grown in the recommended culture media until confluency. Serum-free media was placed on the tumor cells and the conditioned media (CM) was collected after 6,8,12,24,30 and 48 hours of incubation with tumor cells. Concurrently, 6 TG were harvested from adult male rats and placed into primary culture for 5-7 days. CM was then applied to TG neurons for 15 minutes and the supernatant collected. Immunoreactive calcitonin gene related peptide (iCGRP) release from the neurons was measured by radioimmunoassay (RIA) and data were analyzed by ANOVA/Dunnett test. CM collected at 6, 8, 24, and 30hrs of exposure to fibrosarcoma cells (ATCC designation HT-1080) significantly ($p<0.05$) increased CGRP release from cultured TG neurons as compared to control. This significant increase ($p<0.05$) was also seen after the application of CM collected at 6, 8 and 12hrs of exposure to rhabdomyosarcoma cells (ATCC no. CRL-1598). Conversely, there was no increase of CGRP release from peptidergic neurons after exposure to two other (CRL-7062 and CCL-136) sarcoma cell lines. These data indicate that certain types of sarcoma cell lines release a soluble factor that activates peptidergic neurons. This difference in activation may play a key role in understanding the etiology of some types cancer pain and subsequently facilitate the development of tumor specific analgesic therapies.

P302

Peritoneal sarcomatosis: is there a subset of patients who may benefit of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy? D. Baratti,* E. Pennacchioli, A. Gronchi, P.G. Casali, M.R. Balestra, S. Kusamura, C. Colombo, M. Fiore, M. Deraco. *Fondazione IRCCS Istituto Nazionale Tumori, Milano, Italy.*

Peritoneal sarcomatosis (PS) is a rare condition often related to end-stage retroperitoneal or visceral sarcoma. Unlike novel molecular-targeted therapies for metastatic gastro-intestinal stromal tumors (GIST), conventional treatment options are mostly ineffective, with median survival of 13-29 months for PS from non-GIST sarcoma (<18 months for uterine leiomyosarcoma [UL]). As with carcinomatosis of epithelial origin, aggressive loco-regional treatment is supported by a rational basis, but the use of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in this setting is still controversial. METHODS A prospective database of 37 patients undergoing CRS and close-abdomen HIPEC with cisplatin + doxorubicin (n=25) or cisplatin + mitomycin-C (n=12) from February 1996 to May 2006was reviewed. Outcome and clinico-pathological prognostic factors were assessed. RESULTS PS originated from GIST (pre-imatinib era) in 8 patients, UL in 11, retroperitoneal liposarcoma (RPL) in 13, other sarcoma in 5; 15 patients had prior systemic chemotherapy. CRS was macroscopically complete in 28 patients (75.7%)

and near complete (residual nodules ≤2.5mm) in 3 (8.1%). Operative mortality was 3.7% and morbidity 21.6%. After a median follow-up of 104 months (range 1-131), peritoneal disease progression occurred in 16 patients, distant metastases in 5 and both in 11 (see table). For all patients, overall survival was 26.2 months; 7 patients (4 with UL, 2 with RPL, 1 with GIST) were alive at 46-130 months. RPL had the best survival but 100% peritoneal relapse, GIST the lowest overall, local-free and distant-free survival, UL the highest proportion of long survivors and local-free survival. Increased survival correlated to complete CRS (P.040), no prior chemotherapy (P.039) and, with weaker significance, use of doxorubicin for HIPEC (P.058). CONCLUSION Overall, results of CRS and HIPEC did not compare favourably to those of conventional therapy. In a subgroup analysis, the natural history of GIST and RPL was not changed by combined treatment, while the interesting results with UL may warrant further investigations.

	Overall series	Uterine leiomyosarcoma	Retroperitoneal liposarcoma	GIST	Other sarcoma
Dead of disease	29/37	6/10	11/13	7/8	5/5*
Median survival (mos.)	26.2	29.5	34.0	18.2	19.7
Local progression	27/37	6/10	13/13	7/8	1/5*
Local-free survival (mos.)	12.1	15.0	12.1	5.9	6.7
Distant metastases	16/37	3/10	4/13	5/8	4/5
Distant-free survival (mos.)	80.0	NR	NR	5.5	9.3

NR: not reached; *operative death occurred in one patient

P303

Sphincter preservation for perirectal gastrointestinal stromal tumors – A "radical" departure from surgical management in the past J. Nitzkorski,[1]* M. Von Mehren,[2] J.C. Watson.[1] *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Fox Chase Cancer Center - Medical Oncology, Philadelphia, PA.*

Introduction: The management of gastrointestinal stromal tumors (GIST) has evolved since the discovery and application of imatinib. Historically, exenterative resections have been necessary for local control of those that occur in association with the rectum. Because imatinib therapy has been quite effective in treating high-risk GIST, we sought to examine our institutional experience with perirectal GIST, both before and after the imatinib era. Methods: A retrospective chart review of seven patients diagnosed with a perirectal GIST since 1993 was performed to obtain clinicopathologic data. Results: Three patients were treated prior to the availability of imatinib initially with exenterative surgery ± radiation ± non-imatinib chemotherapy, and all experienced recurrence after a median of 72 months (12-108) which was ultimately treated with imatinib ± surgical resection. Two of these patients remain alive with unresectable metastatic disease. Subsequent to the imatinib era, the remaining four patients were treated from the outset with goal of sphincter preservation through the incorporation of adjuvant ± neoadjuvant imatinib administration relative to sphincter preserving surgery. No patients undergoing sphincter preserving surgery have demonstrated recurrence after a median of 25 months (2-77). Conclusions: Sphincter preserving surgery for perirectal GIST in the era of imatinib is feasible. Although long term oncologic outcomes await further study, short-term outcomes and patient satisfaction support consideration of early imatinib treatment of perirectal GIST as an alternative to exenterative surgery, in order to achieve sphincter preservation.

P304

Impact of Local Recurrence on Extremity and Pelvic Soft Tissue Sarcoma Survival P.F. Hwang,[1]* C.B. Hampton,[1] B.K. Potter,[2] R.G. Shoemaker,[1] J.C. Graybill,[1] J.A. Forsberg,[1] R.A. Schaefer,[2] G.E. Peoples,[3] A. Stojadinovic.[2] *1. Walter Reed Army Medical Center, Washington, DC; 2. Walter Reed Army Medical Center, Uniformed Services University, United States Military Cancer Institute, Washington, DC; 3. Brooke Army Medical Center, Uniformed Services University, United States Military Cancer Institute, Fort Sam Houston, TX.*

Introduction: Despite surgical resection with curative intent, patients with extremity and trunk soft tissue sarcomas (STS) experience local recurrence at a rate of 8-20%. The impact of local recurrence on survival remains controversial. Purpose: To identify risk factors for local recurrence (LR) and analyze the impact of local recurrence on disease-specific (DSS) and overall (OS) survival. Methods: This study is a retrospective review of a prospectively enrolled cohort of 402 patients with extremity and pelvic soft tissue sarcomas between 1988-2007. DSS and OS were characterized by Kaplan-Meier curves and the impact of LR determined by log rank test and Cox regression analysis. Results: Seventy-two of 402 patients (18%) developed LR, and 101 (25%) died of disease. The mean time to LR was 21 months, and mean time to sarcoma-related death was 33 months. The mean duration of follow-up for surviving patients was 103 months (range, 60-228). Multivariate analysis for LR demonstrated that positive resection margins and size > 10cm were independently associated with LR. Multivariate analysis for DSS and OS demonstrated that tumor size > 10cm, positive resection margin, history of metastasis, chemotherapy, synovial histological sub-type, and radiation therapy (DSS only) were adverse prognostic factors. Local recurrence was not independently associated with either DSS or OS on multivariate analysis. Conclusion: Tumor size and positive resection margins were the most significant factors associated with locally recurrent STS of the extremities and pelvis. Local recurrence did not demonstrate an adverse effect on DSS or OS.

P305

Histology, not lymph node involvement predicts long-term survival in bronchopulmonary carcinoids R.J. Johnson,[1]* S. Trocha,[1] M. McLawhorn,[4] M. Worley,[3] G. Wheeler,[4] L. Thompson,[2] N. Schisler,[2] D. Schammel,[1] C. Schammel,[2] J. Stephenson,[1] W. Bolton.[1] *1. Greenville Hospital System, Greenville, SC; 2. Furman University, Greenville, SC; 3. Wofford College, Spartanburg, SC; 4. Medical University of South Carolina, Charleston, SC.*

Background: Over the last 30 years, the incidence of bronchopulmonary carcinoid has increased approximately six percent per year. Over the same interval, survival associated with both typical and atypical subtypes has declined. We reviewed our experience with bronchopulmonary carcinoid to identify prognostic factors associated with long-term survival. Methods: We retrospectively reviewed the cancer registry from January 1985 to May 2009 for all patients undergoing surgical resection for bronchopulmonary carcinoid. Patients with tumor-lets, or concurrent primary lung cancers were excluded. Cox regression analysis was utilized to evaluate univariate and multivariate prognostic factors. Results: Fifty two patients met criteria for inclusion in this review. Forty-three patients (82%) presented with typical histology; these patients were younger (p=0.013) and more frequently female (p=0.002) than those presenting with atypical histology. The patients underwent lobectomy in 52% of cases, wedge/segmental resection in 29% of cases, and more advanced resection was required in 19% of cases. There were no local or distant recurrences. The likelihood of lymph node metastasis was similar for patients with typical histology (8/43, 19%) when compared with patients who had atypical histology (2/9, 22%). For patients with typical histology, the five-year survival rates for patients with and without lymph node metastases were 100% and 97% respectively (p=0.420). The survival rate for patients with typical histology (97% at 5 years; 72% at 10 years) was significantly better than for patients with atypical histology (35% at 5 years, 0% at 10 years) (p<0.001). Univariate and multivariate analyses demonstrated that long-term survival was associated with histology but not lymph node involvement (HR=14.6, 95% CI: 1.7, 125.2). Conclusion: Lymph node metastases were more commonly encountered than expected in patients with typical carcinoid tumors. However, our data suggests that long-term survival is associated with histology, not lymph node involvement. We found tumor histology to be the strongest predictor of long-term survival in patients with pulmonary carcinoid tumors.

Table 1: Univariate and Multivariate Predictors of Survival in Bronchopulmonary Carcinoid Patients

	Univariate p-value	HR (95% CI)	Multivariate p-value	HR (95% CI)
Sex (Male vs. Female)	0.026	4.10 (1.07, 15.65)	0.209	3.44 (0.50, 23.60)
Type (Atypical vs. Typical)	<0.001	11.26 (2.67, 47.60)	0.014	14.64 (1.71, 125.15)
Region (Central vs. Peripheral)	0.331	0.51 (0.13, 2.01)	0.995	0.99 (0.19, 5.10)
Lymph Node Involvement (Yes vs. No)	0.804	1.22 (0.25, 5.90)	0.129	0.17 (0.02, 1.68)
Tumor Size (≥2 cm vs. <2 cm)	0.694	1.38 (0.28, 6.85)	0.533	0.53 (0.07, 3.95)

P306

Minimally Invasive Esophagectomy (MIE) is Safe and Effective Following Neoadjuvant Chemoradiation (NACR) Therapy K. Ben-David, N.A. Kissane, G. Rossidis, S.R. Grobmyer, J.C. Cendan, G.A. Sarosi, S. Hochwald.* *Surgery, University of Florida College of Medicine, Gainesville, FL.*

Background: MIE is a technically demanding procedure requiring expertise in advanced laparoscopy and esophageal surgery. Implementation has been hindered by high complication rates and the inability to rapidly demonstrate improved outcomes. Despite widespread concern about the successful performance of this procedure following NACR treatment, we hypothesized that safe and effective MIE could be performed in this setting. Methods: From 3/08-9/09, all patients being considered for esophagectomy were offered a MIE. Treatment recommendations were obtained from a multidisciplinary tumor board and a standardized post-op clinical pathway was implemented. We reviewed our prospective database of patients undergoing MIE at our university hospital during this time period. We analyzed the association of NACR on perioperative outcomes and compared the LOS of those patients undergoing NACR and MIE or NACR and an open esophagectomy in the preceding 2 years. Statistics was via Chi Square analysis. Results: 42 consecutive patients underwent a planned MIE. A completely MIE or hybrid procedure was performed in 41 patients (97%) while 1 patient was unresectable. Median age was 67 (range 38-85). NACR was utilized in 35 patients. Anastomoses were performed in the cervical region in 30 patients (85%), 3 patients had a right thoracoscopic anastomosis and 2 underwent a mini-thoracotomy. None of the patients had a pyloroplasty. Complications included: 1 gastric conduit (3%) and 2 cervical anastomotic leaks (6%), 1 thoracic duct leak, 6 pneumonias (17%), 3 atrial fibrillations (9%), 3 delayed gastric emptying, and 5 transient recurrent laryngeal nerve injuries (14%). There was no difference in complications in patients undergoing NACR with MIE vs MIE without NACR (p=0.41). In-hospital mortality was 0%. Median EBL was 150 mL. Negative pathologic margins were achieved in all patients. Median number of lymph nodes excised was 13. Median postop LOS in those undergoing MIE was 10 days compared to our open era of 17 days ($p<0.05$). Conclusion: MIE is safe following neoadjuvant therapy. Excellent results can be achieved with this operation through interdisciplinary collaboration.

P307

The Roles of Neoadjuvant Radiotherapy and Lymphadenectomy in the Treatment of Esophageal Adenocarcinoma N.L. Solomon,* Y. Zhuge, M. Cheung, D. Franceschi, L. Koniaris. *Surgical Oncology, University of Miami, Miami, FL.*

Objective: Using a population-based registry, we evaluate the impact of neoadjuvant radiotherapy and lymphadenectomy on survival of patients undergoing curative intent surgery for esophageal adenocarcinoma (EAC). Methods: SEER data for patients with esophageal adenocarcinoma from 1988-2005 were queried. Patients undergoing curative operations were included. Treatment was stratified between no radiotherapy, neoadjuvant versus adjuvant radiotherapy, and adequate (≥18 lymph nodes) versus inadequate (<18 lymph nodes) lymphadenectomy. Univariate and multivariate analysis were performed to determine median survival (MST) and cause-specific survival (CSS). Results: Overall, 4,224 patients underwent surgical extirpation with curative intent for EAC in the study period. MST and CSS for the entire cohort were 25 and 31 months, respectively. Multivariate analysis showed age < 65 years, well-differentiated tumors, local disease, negative lymph node status, adequate lymphadenectomy, and neoadjuvant radiotherapy to be independent predictors of improved survival. In node-positive patients, the greatest survival benefit was seen in patients who received both neoadjuvant radiotherapy and adequate lymphadenectomy (MST=32 months, CSS=34 months). The lymph node ratio (LNR) for adequately dissected patients treated with neoadjuvant radiotherapy was 0.17, which is <0.2, the established LNR cutoff that is an independent predictor of improved survival. The survival benefit of neoadjuvant treatment is additive to that of adequate lymphadenectomy. Conclusion: There is survival benefit for neoadjuvant radiation and adequate lymphadenectomy in patients with node-positive EAC. Both are independent predictors of improved survival. Patients who have clinically node-positive disease should undergo both neoadjuvant radiation and adequate lymphadenectomy to ensure optimal outcome.

P308

An Abbreviated Thoracic Onco Geriatric Assessment (TOGA) and Its Components Predict Outcomes of Esophagectomies T. Weigel,[2]* A. Kothari,[1] T. Bretl,[2] K. Block,[2] N.K. LoConte.[3] *1. Department of Surgery, Division of Cardiothoracic Surgery, University of Wisconsin, Madison, WI; 2. University of Wisconsin Department of Surgery, Division of Cardiothoracic Surgery, Madison, WI; 3. University of Wisconsin Department of Medicine, Division of Hematology/Oncology, Madison, WI.*

Surgical resection is a high risk, potentially curative, therapeutic approach used to treat esophageal cancer. At present, no tool currently exists to easily allow surgeons to objectively quantify surgical risk in geriatric patients undergoing major thoracic surgeries. The goal of our study is to develop a pre-operative thoracic onco-geriatric assessment (TOGA) which is patient and physician-friendly, and successfully estimates surgical risk in geriatric patients presenting with primary esophageal carcinoma. Patients ≥70 years old were recruited to participate in a prospective, IRB-approved study that involves the preoperative administration of a panel of validated functional and cognitive screening tests including: Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL), Geriatric Depression Screen (GDS), Brief Fatigue Inventory (BFI), Eastern Cooperative Oncology Group Performance Status (ECOG PS), Mini Mental State Exam (MMSE), and a Mini Nutritional Assessment (MNA). Interim analysis was performed on 19 patients over the age of 70, who had an esophagectomy between August, 2007 and February, 2009. The overall and thirty day mortality was 0% (0/19) and 0% (0/19), respectively. ECOG PS score predicted patient discharge to a nursing home (CC* = .51 p = .02). Both the MNA score (CC = .44 p=.06) and BFI score (CC = .43 p =.06) correlated with post-operative complications. The MNA score was also marginally predictive of the odds of an extended length of stay (OR* = 11.19 p = .10). *CC = correlation coefficient, OR = odds ratio. Our initial data suggest that an abbreviated TOGA including three simple screening tests: MNA, BFI, and ECOG PS could be used as a pre-operative risk stratification tool for geriatric patients with esophageal cancers undergoing esophagectomy. Ongoing study may validate these preliminary results and will hopefully yield an abbreviated TOGA assessment to improve utility. These outcome data may enable geriatric patients and their physicians to make more informed treatment choices. These outcome data may enable geriatric patients and their physicians to make more informed treatment choices.

P309

Is FDG PET/CT useful for the early prediction of histopathologic response to neoadjuvant erlotinib in patients with NSCLC? T.S. Aukema,[1]* I. Kappers,[1] R.A. Valdés Olmos,[1] H.E. Codrington,[2] H. Van Tinteren,[1] R. Van Pel,[1] H.M. Klomp.[1] *1. Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands; 2. Haga Hospital, The Hague, Netherlands.*

Introduction: Early prediction of treatment response is of great value to avoid unnecessary toxicity of ineffective treatment. The objective was to prospectively evaluate the role of integrated 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) as a tool for early identification of response to neoadjuvant erlotinib, an epidermal growth factor receptor -tyrosine kinase inhibitor (EGFR-TKI). Methods: From October 2006 to March 2009, 23 patients with non-small cell lung cancer (NSCLC) eligible for surgical resection, participated in this study. Patients received preoperative erlotinib 150 mg once daily for 3 weeks. FDG PET/CT before (baseline) and within 1 week of initiation of erlotinib treatment was performed. Tumor FDG uptake and changes were measured by standardized uptake values (SUV) and assessed prospectively according to the European Organization for Research and Treatment of Cancer (EORTC) criteria. Patients with a decrease in SUV of ≥25% were classified as metabolic responders. Histopathologic examination of the resected specimen provided a pathologic response, ≥50% of necrosis was classified as a response.The metabolic response was compared to the. histopathological response Results: According to the EORTC criteria, there were six patients with a partial remission (26%) within one week, 16 patients with stable disease (70%) and one patient with progressive disease (4%). The median percentage of necrosis in the early metabolic responder group was 70% (SD37), the median percentage necrosis in the non responders group was 40% (SD 21) (p=0.09). The kappa agreement between the metabolic and the pathologic responders was 0.55 (p=0.008). Conclusion: This study suggests

that early during the course of EGFR TKI therapy, FDG PET/CT may be able to predict response to this treatment in patients with NSCLC.

P310

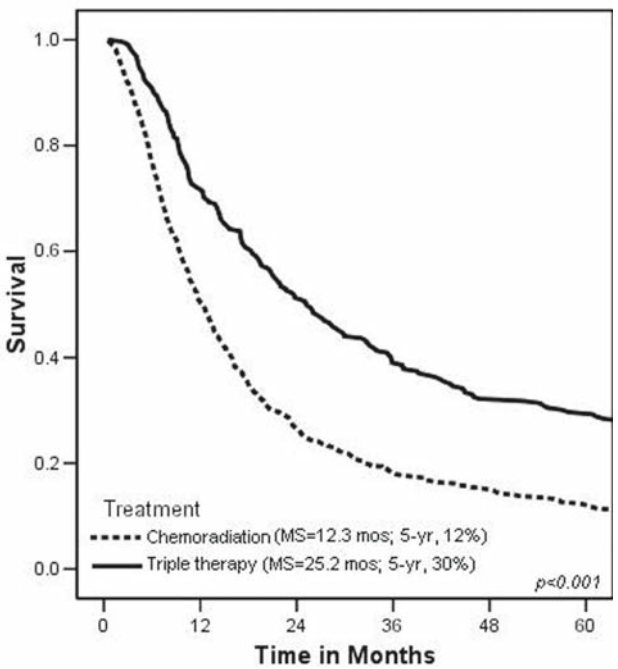
Gender Disparities and Outcomes in the Surgical Management of Lung Cancer. Analysis of the NIS: 2005-2007 H. Dao,* P. Lee, J. Lee, F. Cotopassi, M.J. Lopez. *St.Elizabeth's Medical Center, Boston, MA.*

Introduction: To determine the presence of gender disparities and outcomes in the surgical management of lung cancer. Methods: A retrospective analysis of the Nationwide Inpatient Sample (NIS) from the Healthcare Cost and Utilization Project (HCUP) for the years 2005 to 2007 was performed. This is a cross-sectional administrative database that incorporates a 20% sample of all annual US hospital discharges. ICD9 codes were used to identify principal and secondary diagnosis and procedures. Primary outcomes were the identification of likelihood of procedure utilization depending on gender and in-hospital mortality. Patient demographics, type of procedures, principal payer and in-hospital mortality were included as independent variables. Results: The mean age of the group was 67 ±10 years (52% male). A total of 23,025 surgical interventions were performed for lung cancer, of these 18,832 (82%) were open procedures and 4893 (18%) were video assisted thoracoscopic surgeries (VATS). There were no differences among the rate of utilization of open procedures versus VATS in white patients and non-whites (p=0.8799, OR 1.010, 95% CI 0.9047- 1.128). Male patients were more likely to undergo VATS than females (p<0.0001, odds ratio [OR] 1.173, 95% confidence interval [CI] 1.100 -1.249). Overall in-hospital mortality rate was 2.5% Females were more likely to die during admission than males (p< 0.0001, OR 1.753, 95% CI 1.480-2.077). In-hospital mortality was no statistically significantly different among white patients and non-whites (p=0.137, OR 07.802, 95% CI 0.572-1.063). Conclusions: Females patients undergo statistically significantly less VATS procedures for lung cancer than males. In-hospital mortality rate seems to be higher among females than males. There were no statistically significant differences between whites and non-white patients in overall procedure utilization and mortality.

P311

The benefit of surgical resection in the multimodality management of esophageal cancer S. McKenzie,[1]* A. Artinyan,[2] B. Mailey,[1] M. Metchikian,[1] K. Kernstine,[1] J. Kim.[1] *1. city of hope national medical center, Duarte, CA; 2. baylor university medical center, Houston, TX.*

Introduction: Recent trials have questioned the role of surgical resection with primary chemoradiotherapy in patients with esophageal cancer. Our objective was to determine the benefit of curative esophageal resection in the multimodality management of esophageal cancer. Methods: Using the Los Angeles County Cancer Surveillance Program (CSP), we identified all patients, ages 18-80, with locoregional (ie.AJCC Stages I-III) esophageal cancer during the years 1988-2006. Overall survival was assessed by the Kaplan-Meier method and multivariate Cox-regression analysis was performed. Results: From CSP, 2233 patients with esophageal cancer were identified. Median survival (MS) of the entire cohort was 13.1 months. Of the entire cohort, 645 (29%) patients received chemoradiation as primary therapy and 286 (13%) patients received trimodality therapy. When these two groups were compared, trimodality patients were younger and more likely to have lower esophageal lesions, regional disease, and lymph node positivity. Patients receiving trimodality therapy had significantly improved survival over primary chemoradiation (MS 25.2 vs. 12.3 months, respectively; p<0.001) (5-year survival 30% vs. 12%, respectively). Multivariate analysis identified curative-intent surgical resection as an independent predictor of survival (HR 0.47, CI 0.41-0.53, p<0.001). On subset analysis of the trimodality therapy cohort, neoadjuvant radiation sequence and lymph node retrieval >15 were associated with improved survival. Age, race, stage, histology, and tumor site did not impact survival. Conclusion: Surgical resection remains a critically important component of multimodality management of esophageal cancer. Future studies should focus on optimal timing and sequence of trimodality therapy.



Survival analysis of all patients in CSP diagnosed with stage I-III esophageal cancer treated with either chemoradiation or trimodality therapy

P312

SIGNIFICANT IMPACT OF PHASE TRANSITIONS AND CELL RATIO FACTORS FOR 5-YEAR SURVIVAL OF CARDIOESOPHAGEAL CANCER PATIENTS AFTER SURGERY O. Kshivets.* *thoracic surgery, Klaipeda University Hospital, Siauliai, Lithuania.*

OBJECTIVE: We examined factors associated with low/high-risk of generalization of cardioesophageal cancer (CEC) (T1-4N0-2M0) after complete (R0) left thoracoabdominal esophagogastrectomies (EG). METHODS: We analyzed data of 175 consecutive CEC patients (CECP) (age=55.3±8.7 years; tumor size=6.9±3.3 cm) radically operated and monitored in 1975-2008 (m=132, f=43; combined EG with resection of pancreas, liver, diaphragm, colon transversum, lung, trachea, pericardium, splenectomy=71; adenocarcinoma=112, squamous=58, mix=5; T1=24, T2=38, T3=66, T4=47; N0=70, N1=22, N2=83. Multivariate Cox modeling, clustering, SEPATH, Monte Carlo, bootstrap and neural networks computing were used to determine any significant dependence. RESULTS: Overall life span (LS) was 1381.6±1486.7 days and cumulative 5YS reached 36.1%, 10 years – 26.6%. 53 CECP lived more than 5 years without CEC. 104 CECP died because of CEC. Cox modeling displayed that 5YS of CECP significantly depended on: phase transition (PT) early-invasive CEC, PT N0-N12, age, T, tumor growth, Rh-factor, blood cell subpopulations, cell ratio factors (CRF) (ratio between cancer cells – CC and blood cells subpopulations) (P=0.000-0.047). Neural networks, genetic algorithm selection and bootstrap simulation revealed relationships between 5YS and early-invasive CEC (rank=1), PT N0-N12, thrombocytes/cancer cells (CC), healthy cells/CC, stab neutrophils/CC, lymphocytes/CC, eosinophils/CC, monocytes/CC, leucocytes/CC, erythrocytes/CC, segmented neutrophils/CC. Correct prediction of 5YS was 100% by neural networks computing. CONCLUSIONS: 5YS of CECP after radical procedures significantly depended on: 1) PT "early-invasive CEC"; 2) PT N0-N12; 3) CRF.

P313

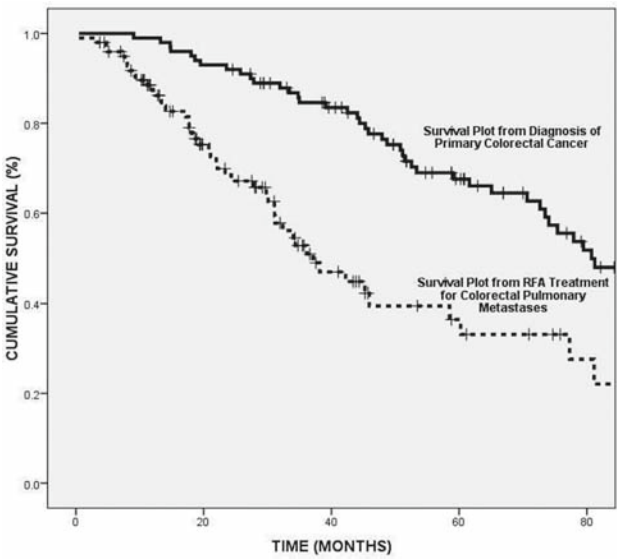
SCCRO-3 (DCUN1D3) is Underexpressed in Human Lung Cancer and is a Novel Tumor Suppressor Gene C.T. Stock,[1]* C. Bommelje,[2] G. Huang,[3] R. Ryan,[4] S. Bains,[5] Y. Ramanathan,[6] B. Singh.[7] *1. Surgery, New York Presbyterian Hospital Weill Cornell, New York, NY; 2. Memorial Sloan Kettering Cancer Center, New York, NY; 3. Memorial Sloan Kettering Cancer Center, New York, NY; 4. Memorial Sloan Kettering Cancer Center, New York, NY; 5. Memorial Sloan Kettering Cancer Center, New York, NY; 6. Memorial Sloan Kettering Cancer Center, New York, NY; 7. Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: SCCRO (DCUN1D1) is overexpressed in many types of human cancers and is thought to function as an oncogene through the augmentation of cullin neddylation. SCCRO-3 (DCUN1D3) is a member of the SCCRO family of genes, is membrane bound in vivo, and contains a conserved cullin binding domain. Recent studies have found that SCCRO-3 may play a role in cullin neddylation, but its expression in lung cancer has not been investigated. We sought to characterize the expression and function of SCCRO-3 in human lung cancer. Methods: Human tumors along with matched control tissue from our database were sequenced using RT-PCR. Soft agar assays and migration assays were performed using either wild type H1299 cells as controls or SCCRO-3 transfected cells. For morphological studies wild type H1299 or SCCRO-3 transfected cells were stained for actin using Alexa Fluor 488 phalloidin stain (Invitrogen). In vivo SCCRO-3 cullin neddylation assays were carried out using HeLa cells co-transfected with either SCCRO or SCCRO-3 and quantified by western blot. Results: Using RT PCR we found that SCCRO-3 was underexpressed in 57% of lung squamous cell carcinoma, 48% of lung adenocarcinoma, and 85% of lung neuroendocrine tumors. When SCCRO-3 was transfected into the lung adenocarcinoma cell line H1299 found underexpress SCCRO-3, these cells became less mesenchymal and more epithelial in their appearance. H1299 cells transfected with SCCRO-3 formed fewer colonies in soft agar than wild-type cells. Furthermore, H1299 cells transfected with SCCRO-3 migrated less in a scratch assay than wild-type H1299 cells. SCCRO-3 was required to be membrane bound and have the ability to bind cullin to have this effect on H1299 cells. In an in vivo neddylation reaction, SCCRO-3 was able to inhibit SCCRO mediated cullin neddylation. Mutants of SCCRO-3 that were unable to bind either to the membrane or cullin were unable to inhibit SCCRO mediated cullin neddylation. Conclusions: SCCRO-3 is underexpressed in a number of histologic types of lung cancer and likely functions as a novel tumor suppressor gene through the inhibition of SCCRO.

P314

Radiofrequency Ablation as an Adjunct to Systemic Chemotherapy for Colorectal Pulmonary Metastases T.C. Chua,* K. Thornbury, A. Saxena, W. Liauw, D. Glenn, J. Zhao, D.L. Morris. *UNSW Department of Surgery, St George Hospital, Sydney, NSW, Australia.*

Background Radiofrequency ablation (RFA) is an alternative to local treatment for pulmonary metastases in patients who are non surgical candidates. Based on previously documented efficacy of this treatment, we retrospectively studied the prognostic factors for long-term survival through a large single institution experience of this treatment with a focus on the use of systemic chemotherapy together with RFA. Methods One hundred patients with unresectable colorectal pulmonary metastases underwent percutaneous RFA. Clinical and treatment variables were collected and evaluated using univariate and multivariate analyses with overall survival as the primary endpoint. Results At a median follow-up period of 23 (range, 1 to 96) months from the time of RFA treatment, 49 patients have died. The median overall survival after RFA treatment was 36 months and 5-year overall survival rates of 30%. Univariate analyses demonstrated that histopathological grade ($p<0.001$), time to RFA treatment ($p=0.024$), response to treatment ($p<0.001$). repeat RFA treatments ($p=0.001$), presence of extrapulmonary metastases ($p=0.003$), presence of mediastinal lymphadenopathy ($p=0.005$), and adjunct systemic chemotherapy ($p<0.001$) were associated with overall survival. Multivariate analyses demonstrated that response to RFA treatment ($p<0.001$), repeat RFA treatment ($p=0.002$), presence of extrapulmonary metastases ($p=0.007$), and use of adjunct systemic chemotherapy ($p=0.025$) were independent predictors for survival. Conclusion Radiofrequency ablation for colorectal pulmonary metastases represents a step forward towards a non surgical option of combining systemic and local treatment for metastatic disease and is a safe treatment with a low risk profile.



Kaplan-Meier Survival Plots of Patients with Colorectal Pulmonary Metastases from time of RFA treatment (dotted line) and from initial diagnosis of primary colorectal cancer (solid line).

P315

Increased Colorectal Cancer Risk after Radiation Therapy for Prostate Cancer A.M. Leung,* H.N. Vu. *Medical College of Virginia Virginia Commonwealth University, Richmond, VA.*

Introduction: Radiotherapy is a standard therapeutic option for patients with prostate cancer, however, it has been implicated in the induction of second primary neoplasms. The purpose of this study was to assess the risk of developing a second primary colorectal cancer following prostate irradiation for prostate cancer. Methods: A retrospective chart review was performed of all patients from our tumor registry at the VA hospital over sixteen years (1993-2008). The incidence of subsequent colorectal cancer was compared between patient with prostate cancer treated with radiation therapy and those not irradiated. Results: There were 3,481 total prostate cancer cases. 752 (21%) of these cases were treated with radiation while 2729 (89%) were not treated with radiation. 59 (0.016%) patients with prostate cancer developed subsequent colorectal cancer. 27 (46%) of these patients had not received prostatic radiation for an incidence of 0.00968%. 32 (54%) patients who had radiation for their prostate cancer developed subsequent colorectal cancer for an incidence of 0.0426%. The calculated relative risk of radiation for prostate cancer on subsequent primary colorectal cancer was 4.301 ($P<0.0001$ by Fisher's exact test). Conclusions: Radiation for prostate cancer appears to be associated with a higher incidence of subsequent colorectal cancer. Further work needs to be done to validate these results.

AUTHOR INDEX

63rd Annual Cancer Symposium
Society of Surgical Oncology
March 3-7, 2010
St. Louis, Missouri

D

E

F

K

L

Q

R

S

T

U

V

W

X

Y

Z