Abstract Book

Society of Surgical Oncology
71st Annual Cancer Symposium

Chicago, Illinois
March 21-24, 2018

Electronic supplement to
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An Oncology Journal for Surgeons

71st ANNUAL
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SYMPOSIUM

Society of Surgical Oncology

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ABSTRACTS

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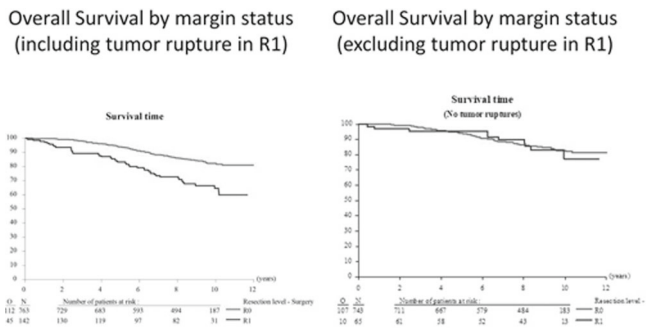
Microscopic Surgical Margins and Outcome in Localized GIST Treated within the Eortc Stbsg, Agitg, Unicancer, Fsg, Isg and Geis Randomized Trial On Adjuvant Imatinib A. Gronchi,[1]* S. Bonvalot,[2] A. Poveda,[3] D. Kotasek,[4] P. Rutkowski,[5] P. Hohenberger,[6] E. Fumagalli,[1] I.R. Judson,[7] A. Italiano,[8] H.J. Gelderblom,[9] F. van Coevorden,[10] N. Penel,[11] H. Kopp,[12] D. Goldstein,[13] J. Martin Broto,[14] E. Wardelmann,[15] S. Marreaud,[16] J.R. Zalcberg,[17] A. Le Cesne,[18] S. Litiere,[16] J. Blay,[19] P.G. Casali.[1] *1. Surgery, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy; 2. Institute Curie, Paris, France; 3. Fondacion Istituto Valenciano de Oncologia, Valencia, Spain; 4. Adelaide Cancer Centre, Kurralta Park, and Division of Medicine, University of Adelaide, Adelaide, SA, Australia; 5. Maria Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology, Warsaw, Poland; 6. Mannheim University Medical Center, Manheim, Germany; 7. Royal Marsden Hospital, London, United Kingdom; 8. Institut Bergonie, Bordeaux, France; 9. Leiden University Medical Center, Leiden, Netherlands; 10. Netherlands Cancer Institute, Amsterdam, Netherlands; 11. Centre Oscar Lambret, Lille, France; 12. Christian-Albrechts-University, Kiel, Germany; 13. Prince Of Wales Hospital, Sidney, NSW, Australia; 14. Hospital Universitario Viergen del Rocio, Sevilla, Spain; 15. University Hospital Münster, Munster, Germany; 16. EORTC Headquarters, Brussels, Belgium; 17. School of Public Health and Preventive Medicine, Monash University, Melbourne, VIC, Australia; 18. Institute Gustave Roussy, Villejuif, France; 19. Centre Leon Berard, Lyon, France.*

INTRODUCTION: The significance of R1 margins on the outcome of patients with primary gastrointestinal stromal tumors (GIST) is unclear. Available retrospective series contain small numbers of patients and have conflicting results. The only evaluation performed within 2 large prospective studies (ACOSOG Z9000 and Z9001) did not show any association between R1 and relapse free survival. The objective of this study was to assess the risk of death with and without imatinib (IM) according to resection margins as well as to the presence of tumor rupture in the largest randomized study on adjuvant imatinib. METHODS We reviewed operative and pathology reports for 908 patients undergoing resection of primary localized GIST from the European-Australasian randomized study run at 112 institutions in 12 countries, testing adjuvant IM for 2 years after resection of primary GIST. In the protocol tumor rupture was included per definition in the R1 category, but also analyzed separately. Patient, tumor, operative characteristics, factors associated with R1 resections, tumor rupture and disease status were analyzed. RESULTS: 142 (15.6%) patients had an R1 resection, 77 (54%) with tumor rupture). With a median follow-up of 9.1 years (IQR 8-10.1) there was a significant difference in overall survival (OS) for patients undergoing an R1 vs R0 resection of GIST with (hazard ratio [HR] = 2.58 95% CI (1.58, 4.23)) or without (HR = 2.26 95% CI (1.39, 3.69)) adjuvant IM. However, the risk of death in R1 patients was driven largely by the presence of tumor rupture. When tumor rupture was excluded this difference in OS between R1 and R0 resections disappeared (HR stratified by treatment 1.09 95% CI (0.57, 2.09)). CONCLUSIONS: Approximately 16% of 908 GIST patients had an R1 resection. The difference in OS with or without imatinib therapy in those undergoing an R1 vs R0 resection was not statistically significant at a median follow-up of 9 years, when tumor rupture was excluded. Quality of surgical margins over the organ of origin should not be considered an indication for surgical re-excision or adjuvant therapy.



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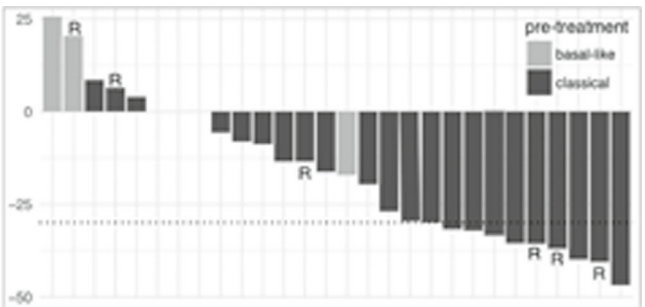
Molecular Subtypes Predict Therapy Response in Pancreatic Cancer J. Yeh,[1]* K. Collins,[1] B. Belt,[2] R. Moffitt,[3] R.Z. Panni,[4] T. Nywening,[4] A. Wang-Gillam,[4] D. Linehan.[2] *1. University of North Carolina at Chapel Hill, Chapel Hill, NC; 2. University of Rochester Medical Center, Rochester, NY; 3. Stony Brook Medicine, Stony Brook, NY; 4. Washington University in St. Louis, St. Louis, MO.*

Background: Recent molecular subtypes of pancreatic cancer have identified two tumor specific subtypes: classical and basal-like. Basal-like subtype tumors are similar to basal subtypes in breast cancer where differential response to therapies is seen. Retrospective analysis of a small number of patients with the basal-like tumors suggested that they may derive greater benefit from adjuvant therapy after surgery than patients with classical subtype tumors. Together these data suggest that molecular subtypes may be associated with differential therapy response. Methods: We examined basal-like and classical subtypes in patient samples from NCT01413022, a Phase Ib trial of a CCR2 inhibitor (PF-04136309) in combination with FOLFIRINOX in previously untreated patients with borderline resectable or locally advanced pancreatic cancer. Response was defined by RECIST 1.1. Baseline pancreatic protocol CT scans were obtained ≤28 days prior to initiating treatment. Molecular subtypes were defined by consensus clustering using previously published subtype specific genes. Patients receiving >2 cycles of treatment were evaluable for treatment response with repeat imaging obtained within 2–4 weeks of completing the last treatment cycle. Results: 28 patients had available RNA sequencing and response data. Patients with classical subtype tumors were significantly more likely to respond to the regimen (p=0.008). No patient (0/25) with a classical subtype tumor had progression of disease (PD) compared to 2 of 3 (66.7%) patients with basal-like tumors. Only patients with classical subtype tumors exhibited partial response (PR). Patients with basal-like tumors had a shorter overall survival with a median of 4 mos compared to 17 mos in classical subtype tumor patients (p=0.0002). Post-treatment samples were available for all patients. Only one patient (3.6%) had a molecular subtype that was different than pre-treatment, changing from classical to basal-like. Conclusion: Our results suggest that molecular tumor subtypes may be important in predicting response to therapies and may help determine first-line regimens in patients with pancreatic cancer. In addition, molecular subtypes appear to be stable after treatment.



Tumor response by molecular subtype in patients enrolled in the Phase Ib trial FOLFIRINOX and CCR2 inhibitor of patients with borderline resectable or LA pancreatic cancer. Waterfall plot showing tumor response, after treatment and prior to surgery, association with molecular subtype (blue – classical; orange – basal-like) determined through RNAseq. R - patients who went to resection.

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Influence of Timing of surgery on Perioperative Morbidity After Neoadjuvant Therapy for Locally Advanced Rectal Cancer C. Roxburgh,* P. Strombom, P. Lynn, P. Paty, J.G. Guillem, G.M. Nash, J. Smith, I. Wei, J. Garcia-Aguilar, M.R. Weiser. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Timing of surgery following completion of neoadjuvant therapy (NT) for locally advanced rectal cancer (LARC) has important implications for treatment response. However, it was recently reported in the GRECCAR 6 trial that delayed surgery beyond 8 weeks from completion of NT is associated with increased complications. Within a cohort of LARC patients treated with NT (CRT alone, Total NT (TNT) and chemotherapy alone) we examine perioperative complications based on time from NT to surgery. Methods: Pts with

Stage II/III LARC ≤15cm from the anal verge who received NT from 06/01/09 – 03/01/15 were identified and preoperative morbidity collected on those undergoing rectal resection. Pts were grouped according to time of surgery from completing NT (5-8 wks – early surgery / 8-12 wks – late surgery). Results: 798 pts were identified and 547 underwent rectal resection within 12 weeks of completing NT (440 LAR and 107 APR). Surgery was performed 5-8wks after NT in 252 pts and 8-12wks after NT in 246 pts. 204 pts (41%) had a post-op complication: 53 (10%) Grade 3-5 complication and 83 (17%) SSI. There were no statistically significant differences in rates of all complications (44% vs 38%), grade 3-5 complications (9% vs 11%), SSI (17% vs 17%), and LOS (median 6 days vs 6 days) between the early and late surgery groups. Similar results were obtained when evaluating subgroups by type of NT (CRT alone, chemo alone or TNT), surgical approach (open vs minimally invasive and sphincter preservation vs colostomy), post-treatment TNM stage and year of treatment (all NS). In addition, we did not observe differences in rates of downstaging responses: T downstaging (63% vs 64%), N downstaging (61% vs 54%), > 95% regression (34% vs 34%) or pCR rates (18% vs 18%) between the early and later surgery groups. Conclusions: In patients undergoing radical surgery for LARC post NT, we do not observe an effect of timing of surgery on surgical complications. Although timing of surgery is reported to influence response rates, we did not reproduce these findings, likely as a consequence of the high rate of deferral of surgery/ non-operative management in this cohort.

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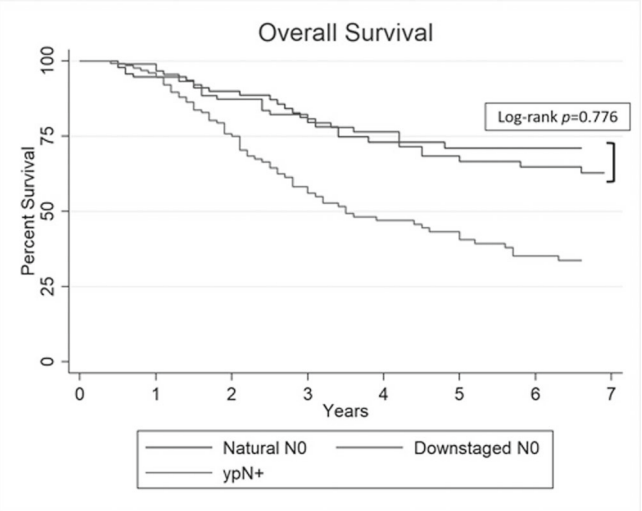
Nodal Downstaging in Gastric Cancer: Promising Survival if ypN0 Is Achieved N. Ikoma,* J. Estrella, W. Hofstetter, P. Das, J. Ajani, K. Fournier, P. Mansfield, B. Badgwell. *University of Texas MD Anderson Cancer Center, Houston, TX.*

Background The AJCC 8th edition introduced ypStage for patients with gastric cancer due to the increasing use of preoperative therapy. ypN0 patients have better survival than ypN+ patients; however, whether patients who had clinically positive nodal disease before preoperative therapy (cN+ ypN0) have similar survival to those who had natural N0 (cN0 ypN0) disease is unknown. Methods We reviewed an institutional database to identify patients with gastric adenocarcinoma who underwent potentially curative R0 resection after preoperative chemo- or chemoradiation therapy. Patients were categorized into 3 groups based on nodal status: natural N0 (cN0 ypN0), downstaged N0 (cN+ ypN0), and ypN+. Univariable and multivariable Cox regressions were performed to determine associations with overall survival (OS). Results We identified 316 patients who met study criteria, including 74 (23%) patients with GEJ tumors; 56% were white and 62% were male. Preoperative chemoradiation therapy was given to 239 (76%). Ninety-four (30%) had natural N0, 93 (29%) had downstaged N0, and 129 (41%) had ypN+ disease. Of all patients, 136 (43%) patients died during a median follow-up of 3.1 y. Median OS was 7.7 y, and 5-year OS was 60.3%. OS did not differ in patients with natural N0 disease (5-y OS, 72%) and those with downstaged N0 disease (5-y OS, 69%) (p=0.776, Figure), even though the downstaged N0 group had more advanced baseline cT disease than did the natural N0 group (p<0.001). On multivariable analysis adjusting for other factors, including ypT category, OS did not differ between natural N0 and downstaged N0 patients (hazard ratio [HR], 0.90; 95% confidence interval [CI], 0.54-1.48; p = 0.666), but it was shorter in ypN+ patients (HR, 1.82; 95% CI, 1.15-2.87; p=0.010). Sensitivity analyses also showed equivalent OS in the natural N0 and downstaged N0 groups within the ypT0-2 group (p=0.936) and the ypT3-4 group (p=0.608). Conclusion In patients with gastric cancer who underwent preoperative therapy, we found similar OS in patients with natural N0 and those with downstaged N0 disease. As ypN+ patients had poor OS, achieving ypN0 status is an important hallmark demonstrating the effectiveness of preoperative therapy.



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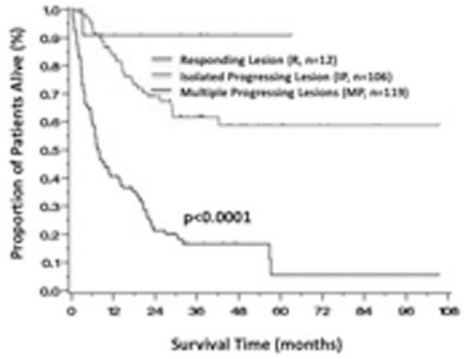
Outcomes of Patients with Metastatic Melanoma Selected for Surgery After Immunotherapy D.M. Bello,* K.S. Panageas, T.J. Hollmann, A.N. Shoushtari, P. Chapman, M.A. Postow, M.K. Callahan, J.D. Wolchok, M.S. Brady, D. Coit, C.E. Ariyan. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Immunotherapy has transformed the treatment of metastatic melanoma, with 3- year survival rates >50% for PD1 blockade alone or in combination with CTLA-4 blockade. However, the median progression free survival is 6.9 and 11.5 months, respectively. Many who progress have gone on to have surgery, yet the outcome of these patients has not been defined. This study analyzed the outcome of patients selected for surgery after immunotherapy. Methods: IRB approved review of a prospectively maintained institutional melanoma database from 2003 to 2017. 620 unresectable stage III and IV melanoma patients treated with checkpoint blockade, including CTLA-4, PD-1 and PDL1 blockade, followed by resection were identified. We eliminated procedures which did not involve tissue resection for a cohort of 237 patients. Overall survival (OS) was calculated from date of first surgery following immunotherapy. Response to immunotherapy was assessed at the time of surgery, and tumors were categorized as responding (R) n=12, an isolated progressing (IP) n=106, or multiple progressing (MP) lesions n=119. Results: Of 237 patients, 208 patients (88%) had stage IV and 29 (12%) had unresectable stage III disease. Median follow-up for the entire group was 23 months. The median interval from the start of immunotherapy to the first operation was 7 months. The majority of patients had only one operation (n=163, 69%). Median OS following immunotherapy and resection was 21 months. Resection to NED at the first operation (n=87, 37%), was associated with better survival over patients not resected to NED (n=150, 63%), with median OS that was not reached versus 10.8 months respectively (95% CI: 7.3,14.8; p<0.0001). Additionally, OS was associated with a response to immunotherapy R (median OS not reached) or IP (median OS not reached), compared with MP (median 7.8months, 95%CI: 6.2,11.2; p<0.0001) (Figure 1). Conclusion: In a highly selected population of patients with advanced melanoma treated with checkpoint blockade, surgical resection is associated with good outcomes. This is especially true in those who have demonstrated a measurable response to checkpoint blockade and can undergo complete resection.

Figure 1: OS for Stage III/IV melanoma patients stratified by disease response to immunotherapy.



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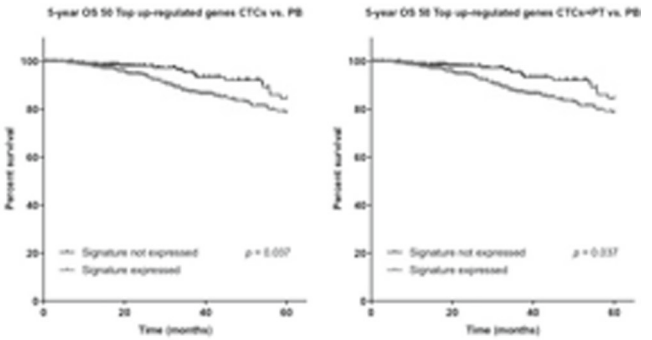
RNA Seq of Circulating Tumor Cells in Stage II-III Breast Cancer J.E. Lang,[1]* A. Ring,[1] T. Porras,[1] P. Kaur,[1] V. Forte,[1] D. Tripathy,[2] M. Press,[1] D. Campo.[1] *1. Surgery, University of Southern California, Los Angeles, CA; 2. MD Anderson, Houston, TX.*

INTRODUCTION: Circulating tumor cells (CTCs) are prognostic in breast cancer. The aim of our study was to characterize the whole transcriptome of CTCs in Stage II-III disease to evaluate for correlations with primary tumor biology. METHODS: We performed a prospective, observational study in which CTCs were isolated from 20 mL peripheral blood (PB) via immunomagnetic enrichment based on EpCAM and fluorescence-activated cell sorting (IE-FACS). CTCs, PB and fresh tumors were profiled with RNA Seq. Formalin-fixed, paraffin-embedded (FFPE) tumors were subjected to RNA Seq and NanoString PAM50 assays with Risk of Recurrence (ROR) scores. Data was analyzed with R and Ingenuity Pathway Analysis (IPA). RESULTS: CTCs were detected in 29/33 (88%) patients. We selected 21 cases to attempt RNA Seq (median number of CTCs=9). Of these, 16 CTC samples yielded results that passed quality control metrics. These samples had a median of 4,311,255 uniquely mapped reads, significantly less than PB or tumors. There were 8496 genes with significant differential expression (DE) between CTCs and PB. There were 2915 genes shared between CTCs and tumors with DE in PB. Intrinsic subtype predicted by comparing estrogen receptor (ER), progesterone receptor (PR) and HER2 versus NanoString PAM50 for FFPE tumors was 76.9% concordant. However, CTC RNA Seq subtype assessed by PAM50 or Sorlie classification was highly discordant both with the subtype predicted by ER/PR/HER2 as well as by NanoString PAM50. Two patients died of metastatic disease - both had high ROR scores and high CTC counts (n=39 and 65). We identified the top significant canonical pathways, upstream regulators and molecular interaction networks comparing CTCs by various clinical factors (i.e., ER positive versus negative, pathologic complete response versus no). We identified the 50 genes with highest expression in CTCs and in CTCs and tumors taken together as a group. Expression of either of these two signatures was prognostic in The Cancer Genome Atlas (n=817 patients), p=0.037. Single nucleotide variants in CTCs and tumors were also identified. CONCLUSION: It is feasible to use RNA Seq of CTCs in non-metastatic patients to discover novel tumor biology characteristics.

50 top up-regulated genes analyzed with The Cancer Genome Atlas (TCGA) gene expression data set (817 samples)



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FOLFIRINOX versus Gemcitabine/nab-Paclitaxel for Neoadjuvant Treatment of Resectable and Borderline Resectable Pancreatic Adenocarcinoma: A Propensity Matched Analysis M. Dhir,[1]* M.S. Zenati,[2] A. Hamad,[2] A.D. Singhi,[2] N. Bahary,[2] M. Hogg,[2] H. Zeh,[2] A. Zureikat.[2] *1. Surgery, SUNY Upstate Medical University, Syracuse, NY; 2. University of Pittsburgh Medical Center, Pittsburgh, PA.*

Background: Comparative effectiveness of FOLFIRINOX and Gemcitabine/nab-paclitaxel (G-nP) in the neoadjuvant treatment (NAT) of pancreatic ductal adenocarcinoma (PDA), remains unknown. The aim of this study was to perform a propensity matched analysis of neoadjuvant FOLFRINOX vs G-nP for resectable(R) and borderline resectable (BR) PDA. Methods: A single institution retrospective review of all R and BR PDA patients who underwent resection after NAT with FOLFIRINOX or G-nP was performed. Comparative effectiveness analysis was conducted using inverse-probability-weighted estimators. Primary endpoint was overall survival (OS) from the time of diagnosis. Results: A total of 193 patients (FOLFIRINOX=73, G-nP=120) who underwent resection from 01/11-03/17 were included. Median OS was 28.9 months (95% CI 26.1-39.7). Patients treated with FOLFIRINOX were younger (median age 63 v 69 y), had less comorbidities (median CCI 4 v 5), more frequent BR disease (79 v 59%), and larger tumors (median CT size 2.9 v 2.7 cm) compared to G-nP (all P<0.05). Duration of NAT was similar and both regimens were equally effective in achieving a 50% or 80% decline in CA19-9 (logistic regression, P 0.9). Rates of R0 resection were also similar (80%), but folfirnox was associated with a reduction in pN1 disease (56% v 72%, P=0.028). Receipt of adjuvant therapy was similar in both groups (74 v 75%, P=0.79). In a multivariable cox regression analysis utilizing only preoperative variables (FOLFIRINOX v G-nP, age, gender, CT tumor size, BR vs R, pre NAT CA19-9 and number of NAT cycles), only the number of neoadjuvant cycles was an independent predictor of survival (HR 0.49, 95% CI 0.34-0.71, P<0.001). In a propensity matched analysis of 166 patients using the same preoperative variables, the average treatment effect of FOLFIRINOX was to increase OS by 4.9 months above G-nP (P=0.012). Conclusions: FOLFIRINOX and Gem Abraxane are viable options for neoadjuvant treatment of PDA. In this study, FOLFIRINOX was associated with a 4.9 month improvement in OS when compared to G-nP in the neoadjuvant setting after adjusting for covariates.

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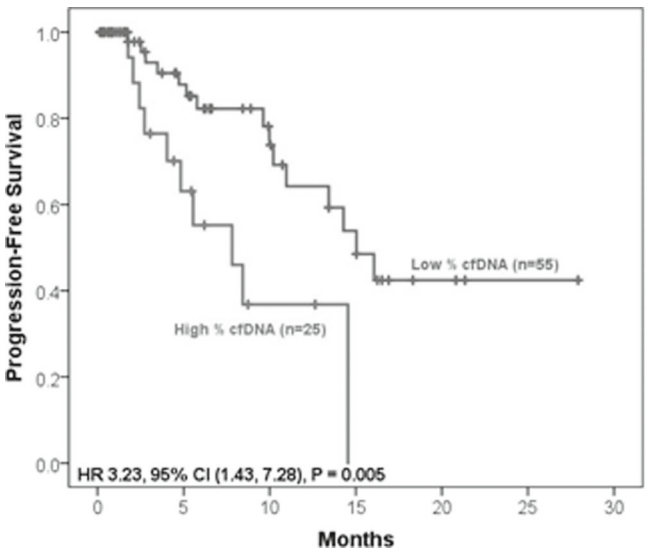
Preoperative Circulating Tumor DNA in Patients with Peritoneal Carcinomatosis Is an Independent Predictor of Progression-Free Survival J. Baumgartner,[1]* K. Banks,[2] R. Lanman,[2] L. Tran,[1] K.J. Kelly,[1] A. Lowy,[1] R. Kurzrock.[1] *1. UCSD, La Jolla, CA; 2. Guardant Health, Inc., Redwood City, CA.*

Background Next-generation sequencing (NGS) is a useful tool for detecting genomic alterations in circulating tumor DNA (ctDNA). To date, most ctDNA tests have been performed on patients with widely metastatic disease. Patients with peritoneal carcinomatosis present unique prognostic and therapeutic challenges. We therefore explored preoperative ctDNA in patients with peritoneal carcinomatosis undergoing surgery. Methods Patients referred for surgical resection of peritoneal carcinomatosis underwent preoperative

blood-derived ctDNA analysis (clinical-grade NGS, 70-73 genes). ctDNA was quantified as the percentage of altered circulating cell-free DNA (% cfDNA). Results Eighty patients had ctDNA testing: 46 (57.5%) women; median age, 55.5 years. The following diagnoses were included: 59 patients (73.8%), appendix cancer; 11 (13.8%), colorectal cancer; five (6.3%), peritoneal mesothelioma; two (2.5%), small bowel cancer; one (1.3%), each of cholangiocarcinoma, ovarian, and testicular cancer. Thirty-one patients (38.8%) had detectable preoperative ctDNA alterations, most frequently in the following genes: TP53 (25.8% of all alterations detected) and KRAS (11.3%). Among 15 patients with tissue DNA NGS, 33.3% also had ctDNA alterations (overall concordance = 97.2%). Patients with high ctDNA quantities (> 0.25% cfDNA) had a shorter progression-free survival than those with lower ctDNA quantities on univariate analysis (7.8 vs. 15.0 months; hazard ratio (95% confidence interval), 3.23 (1.43 to 7.28), P = 0.005), and when controlling for histologic grade and completeness of resection on multivariate analysis (hazard ratio 1.54 (1.01, 2.33), p = 0.044). Conclusions A significant proportion of patients with peritoneal carcinomatosis referred for surgical intervention have detectable ctDNA alterations preoperatively. Patients with high levels of ctDNA have a worse prognosis independent of histologic grade and completeness of resection.



Progression-Free Survival by % cfDNA (n=80 patients).

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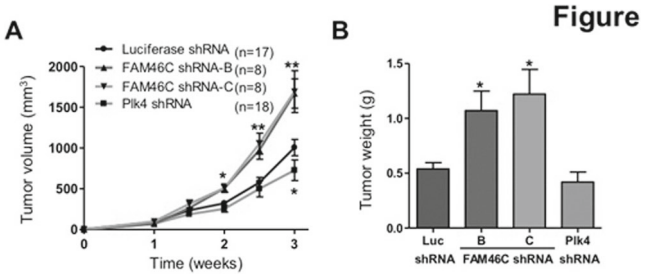
FAM46C Functions as a Novel Tumor Suppressor in Breast Cancer Cells and Xenografts K. Kazazian,[1]* Y. Haffani,[2] R. Xu,[3] J. Tan,[3] C.J. Swallow.[1] *1. Division of General Surgery, University of Toronto, Toronto, ON, Canada; 2. Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, ON, Canada; 3. University of Toronto, Toronto, ON, Canada.*

Increased expression of the polo-like kinase Plk4 predicts disease relapse and resistance to therapy in breast cancer patients, and a targeted anti-Plk4 agent is being assessed in phase I trials. We have shown that Plk4 overexpression drives not only centriole amplification, but also cancer cell invasion/metastasis (Cancer Res, 2017). We aim to understand the pathways that regulate Plk4's activity in order to therapeutically modulate its oncogenic effects. Based on physical interaction in Y2H screens and reciprocal co-immunoprecipitation, we identified FAM46C as a potential Plk4 functional interactor. Methods: We assessed the effect of FAM46C, a protein of previously unknown function, on Plk4 function using assays of in vitro kinase activity, centriole duplication (>100 cells, n=3 experiments), and tumor growth in a xenograft model. FAM46C knockdown in U2OS sarcoma and MDA MB-435 breast cancer cells was achieved by shRNA. Results: Kinase assays revealed that Plk4 autophosphorylation was markedly reduced in the presence of FAM46C. Deletion construct experiments showed that binding to FAM46C was dependent on Plk4's kinase domain. These results were consistent with inhibition of Plk4 kinase activity by FAM46C. FAM46C knockdown led to a Plk4-dependent increase in centriole number, while transfection with RFP-FAM46C caused a reduction in centriole number vs. control, further suggesting that FAM46C might function to restrain Plk4 activity. Using an aggressive human breast cancer xenograft model in nude mice to test for an interaction in vivo, we found that tumors formed by FAM46C-depleted cells progressed rapidly compared to controls (Fig, green lines/bars). As expected, tumors formed by Plk4-depleted cells displayed modestly reduced growth vs. control (Fig, blue lines/bars). Compound mutant cells with both Plk4 and FAM46C knockdown showed an intermediate phenotype, consistent with a functional interaction in vivo. Conclusion: FAM46C impairs Plk4 activity, restraining its promotion of centriole duplication in cells, and of tumor progression in a breast cancer xenograft model. These results implicate FAM46C as a potential tumor suppressor in breast cancer through its regulation of Plk4.



FAM46C suppresses MDA MB-435 xenograft tumor growth. Tumors were generated by injecting MDA MB-435 cells suspended in Matrigel subcutaneously into the right flank of nude mice. a) Tumor volume of xenografts at indicated times after injection, showing increased tumor size in FAM46C, and decreased tumor size in Plk4, vs. Luciferase shRNA after 2 weeks, *p<0.05, **p<0.01 vs. Luciferase. b) Corresponding tumor weights at sacrifice, showing increased weight of FAM46C shRNA xenografts, *p<0.05 vs. Luciferase shRNA.

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Changing Practice Patterns of Adjuvant Radiation Among Elderly Women with Early Stage Breast Cancer in the United States from 2004-2014 S.A. Reyes,[1]* A.D. Williams,[1] R.L. Arlow,[1] L.M. De La Cruz,[1] D.N. Anderson,[1] S. Ugras,[1] A.D. Brooks,[1] D. Sataloff,[1] G.M. Freedman,[2] J. Tchou.[1] *1. University of Pennsylvania, Perelman School of Medicine, Department of Surgery, Philadelphia, PA; 2. University of Pennsylvania, Perelman School of Medicine, Department of Radiation Oncology, Philadelphia, PA.*

Introduction Over the past decade phase III trials have challenged the need for breast radiation (RT) after breast conservation surgery (BCS) in all elderly women with early stage breast cancer by demonstrating only marginal improvement in local control and no survival benefit. The purpose of this study was to assess changing practice patterns in RT among women ages ≥70 in the United States and to examine factors associated with omission of RT. Methods Using the National Cancer Database, we identified women ≥70 years diagnosed with early stage invasive breast cancer that were treated with BCS between 2004-2014. Patients receiving palliative RT were excluded. Patients were divided into 4 groups: 1) no RT, 2) partial breast RT in 1-2wks(PBI), 3) hypofractionated in 3-5wks(HFx) and 4) conventional whole breast RT in 5-8wks(CRT). We compared patient demographics, year of diagnosis, tumor characteristics, hormone therapy, and facility type among the different treatment groups (Table 1). Results We identified 131,645 patients with a mean age of 76.2. Of those, 14,500 (11%) had PBI, 23,470 (18%) had Hfx, and 93,383 (71%) received CRT. Less than 1% of patients had RT omitted regardless of age, demographics, institution, or year of diagnosis. Of the 292 non-radiated pts, 83% had grade 2 or 3 tumors, 12% had lymphovascular invasion present, and 89% were not administered hormone therapy. Omission of RT increased marginally from 0.15% in 2004 to 0.26% in 2014. During this time, the use of Hfx increased from 3.95% to 40.10%, p<0.001 and conversely CRT decreased from 90% to 50%, p<0.001. When compared over two time periods, 2004-2009 and 2010-2014, academic centers showed a larger shift towards Hfx (6.0% to 23.2%) compared to community centers (2.8% to 16.6%). Conclusion Despite data suggesting marginal benefit, RT in women ≥70 years with early stage breast cancer has shifted to shorter treatment schedules rather than omission. The majority of patients omitting RT are not on hormone therapy and have intermediate or high grade tumors, suggesting that recurrence and survival rates from phase III trials may not be applicable in clinical practice.

Table 1: Patient Characteristics Among Four Radiation Treatment Groups

Characteristics	No Radiation (n=292)	Partial Breast Radiation (n=14,500)	Hypofractionated Radiation (n=23,470)	Conventional Whole Breast Radiation (n=93,383)	p-Value
Age at diagnosis (mean)	78.1±5.9	76.5±5.0	77.0±5.1	76.0±4.7	<0.001
70-74 yrs	108 (37.0%)	6,140 (42.3%)	9,168 (39.1%)	42,299 (45.3%)	
75-79 yrs	80 (27.4%)	4,500 (31.0%)	7,146 (30.4%)	30,058 (32.2%)	
>80 yrs	104 (35.6%)	3,860 (26.6%)	7,156 (30.5%)	21,026 (22.5%)	
Charlson Comorbidity Score					<0.001
0	173 (59.2%)	12,043 (83.1%)	19,042 (81.1%)	76,090 (81.5%)	
1	81 (27.7%)	2,069 (14.3%)	3,578 (15.2%)	14,338 (15.4%)	
2	38 (13.0%)	388 (2.7%)	850 (3.6%)	2,955 (3.2%)	
Grade					<0.001
1	43 (14.7%)	4,968 (34.3%)	7,270 (31.0%)	25,062 (26.8%)	
2	127 (43.5%)	6,745 (46.5%)	11,121 (47.4%)	43,379 (46.5%)	
3	116 (39.7%)	2,182 (15.0%)	3,876 (16.5%)	20,122 (21.5%)	
4	1 (0.3%)	21 (0.1%)	31 (0.1%)	202 (0.2%)	
unknown	5 (1.7%)	584 (4.0%)	1,172 (5.0%)	4,618 (4.9%)	
Hormone Therapy (HRT) - given	27 (9.3%)	9,489 (65.4%)	16,418 (70.0%)	65,869 (70.5%)	<0.001
HRT not given	261 (89.4%)	4,571 (31.5%)	6,429 (27.4%)	24,679 (26.4%)	
HRT unknown	4 (1.4%)	440 (3.0%)	623 (2.7%)	2,835 (3.0%)	
Year of Diagnosis					<0.001
2004 (n=9,833; 7.5%)	15 (0.15%)	595 (6.05%)	388 (3.95%)	8,835 (89.85%)	
2005 (n=9,954; 7.6%)	20 (0.20%)	844 (8.48%)	479 (4.81%)	8,611 (86.51%)	
2006 (n=10,713; 8.1%)	20 (0.19%)	1,156 (10.79%)	502 (4.69%)	9,035 (84.34%)	
2007 (n=10,866; 8.3%)	29 (0.27%)	1,448 (13.33%)	742 (6.83%)	8,647 (79.58%)	
2008 (n=11,437; 8.7%)	26 (0.23%)	1,516 (13.26%)	1,185 (10.36%)	8,710 (76.16%)	
2009 (n=11,875; 9.0%)	21 (0.18%)	1,506 (12.68%)	1,648 (13.88%)	8,700 (73.26%)	
2010 (n=12,112; 9.2%)	33 (0.27%)	1,432 (11.82%)	2,284 (18.86%)	8,363 (69.05%)	
2011 (n=13,343; 10.1%)	37 (0.28%)	1,782 (13.36%)	2,967 (22.24%)	8,557 (64.13%)	
2012 (n=13,332; 10.1%)	27 (0.20%)	1,407 (10.55%)	3,258 (24.44%)	8,640 (64.81%)	
2013 (n=13,997; 10.6%)	27 (0.19%)	1,496 (10.69%)	4,330 (30.94%)	8,144 (58.18%)	
2014 (n=14,183; 10.8%)	37 (0.26%)	1,318 (9.29%)	5,687 (40.10%)	7,141 (50.35%)	

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Chemoprevention Uptake for Breast Cancer Risk Reduction Varies by Risk Factors M. Flanagan,* E. Zabor, M. Stempel, D. Mangino, M. Morrow, M. Pilewskie. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction Randomized controlled trials have proven the efficacy of chemoprevention (CP) for breast cancer risk reduction among high-risk women; however, use of CP remains low. We sought to determine whether uptake of CP differed by risk factors and to identify reasons for refusal and termination. Methods Women seen in a high-risk clinic from 10/2014-6/2017 considered eligible for CP (CPE), defined as a history of LCIS, atypia, family history of breast/ovarian cancer, genetic mutation, or history of chest wall radiation, were retrospectively identified. Breast cancer risk factors were compared among those with and without CP uptake, and compliance noted. Results 1447 CPE women were identified, 24% with prior/current CP use. Forty percent had multiple high-risk factors. Women >50 years were more likely to use CP than women ≤50 (28% versus 12%, p<.001). CP uptake among women with established risk factors was: LCIS 29%, family history 29%, atypical ductal hyperplasia 19%, other atypia 13%, chest wall radiation 40% (2/5). Among 50 gene mutation carriers without history of prophylactic mastectomy, 20/50 (40%) had CP use. Having multiple risk factors did not increase CP uptake (Table). Forty-four percent (487/1099) of women with no prior CP use had documented discussions regarding CP at their most recent visit (3% accepted, 28% deferred the decision, 69% refused/reason not documented). The most common refusal reason was fear of side effects (54/157; 34%), followed by lack of interest, risk of thromboembolic disease, being of child bearing age or on hormone replacement therapy. Among current CP users, 31% were on tamoxifen and 67% raloxifene. Of the 165 women with prior CP use, the most common reason for termination was completion of ≥5 years of therapy (62%) followed by adverse side effects (32%). Conclusion Uptake of CP among women at increased risk for breast cancer remains low, with CP use ranging from 13% to 40% depending on risk factor. These data highlight the need for ongoing CP counseling among high-risk women as the majority who begin therapy complete 5 years of use. Given the generalized fear of CP side effects, ongoing study is needed to identify alternative risk-reducing strategies.

Comparison of risk factors among women with and without chemoprevention use

	Overall (n=1447)	Any current/prior use (n=348)	No current/prior use (n=1099)	p-value
Age at most recent visit				<001
≤ 50 years	342	42 (12.3%)	300 (87.7%)	
> 50 years	1105	306 (27.7%)	799 (72.3%)	
Women with any history of the following risk factors:				
Atypical ductal hyperplasia*				<001
Yes	597	113 (18.9%)	484 (81.2%)	
No	850	235 (27.6%)	615 (72.4%)	
Atypia other than ADH*				<001
Yes	180	23 (12.8%)	157 (87.2%)	
No	1267	325 (25.7%)	942 (74.3%)	
LCIS*				<001
Yes	634	184 (29.0%)	450 (71.0%)	
No	813	164 (20.2%)	649 (79.8%)	
Family history breast/ovarian cancer*				<001
Yes	596	175 (29.4%)	421 (70.6%)	
No	851	173 (20.3%)	678 (79.7%)	
History of chest wall irradiation*				0.599
Yes	5	2 (40.0%)	3 (60.0%)	
No	1442	346 (24.0%)	1096 (76.0%)	
Deleterious gene mutation*†				0.011
Yes	50	20 (40.0%)	30 (60.0%)	
No	1397	328 (23.5%)	1096 (76.0%)	
Multiple high-risk features				1
Yes	573	138 (24.1%)	435 (75.9%)	
No	874	210 (24.0%)	664 (76.0%)	

*Includes risk factor of interest in combination with any other risk factor present for each patient; total percentages add to more than 100%.
†Deleterious gene mutations included ATM (n=1), BRCA 1 (n=15), BRCA 2 (n=28), CDH-1 (n=1), CHEK2 (n=1), MSH2/MLN1 (n=1), PALB2 (n=1), MUTYH (n=1), Not specified (n=1)
ADH, atypical ductal hyperplasia; LCIS, lobular carcinoma in situ

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Black-White Breast Cancer Mortality Disparities in Atlanta: An Update (2004-2014) O. D'Angelo,[1]* S. Gabram-Mendola,[2] L. Collin,[3] A. Troeschel,[3] K. Ward,[3] L. McCullough.[3] *1. Emory University School of Medicine, Atlanta, GA; 2. Emory University School of Medicine, Department of Surgery, Atlanta, GA; 3. Rollins School of Public Health, Emory University, Atlanta, GA.*

Introduction: Racial disparities in breast cancer (BC) mortality among black women, compared to white women, are well-documented. Recently, Atlanta was reported to have the largest racial disparity in BC mortality among the largest 50 cities in the US. The purpose of this study was to examine how tumor characteristics may contribute to this disparity in metro-Atlanta. Methods: The study sample included non-Hispanic white (NHW) and non-Hispanic black (NHB) women with a first primary invasive BC diagnosed between 2004 and 2014 in the Surveillance, Epidemiology and End Results Program (SEER) Atlanta registry. Exclusion criteria were: patients <18 years, and patients diagnosed only via autopsy or death certificate. The final sample size included 17,825 women (10,654 NHW; 7,171 NHB) with data on age at diagnosis, SEER stage, estrogen receptor (ER) positivity, subtype (2010+), grade, and cause of death. We used Cox proportional hazards regression to estimate the age-adjusted HR and 95% CI between race and BC-specific mortality, overall and within strata of relevant covariates. Statistical analyses were performed using SASv.9.4. Results: NHB had a more than two-fold increased risk of death from BC when compared to NHW (HR=2.20; 95%CI=2.02-2.41). When we further stratified by relevant tumor characteristics (stage, grade, ER positivity, and subtype) we observed interactions with race on the multiplicative scale

(p<0.001). We found more than two-fold increased risk of death among NHB with localized disease (HR=2.49; 95%CI=2.05-3.02), low grade tumors (grade 1: HR=2.27; 95%CI=1.50-3.43), ER positivity (HR=2.26; 95%CI=2.00-2.55) (Table1). Conclusions: Our results demonstrate that traits typically associated with better prognosis (i.e., localized disease, hormone sensitive tumors) result in greater disparities among NHB than traits typically associated with worse prognosis (i.e., triple negative, high grade tumors) which were less pronounced. Taken together, these data suggest access to health care and treatment factors may be driving racial disparities in metro-Atlanta.

Table 1: Age-adjusted hazard ratios (HRs) and 95% confidence intervals (95% CIs) for death resulting from breast cancer overall and stratified by stage, grade, ER status, and intrinsic subtype. Effects are among non-Hispanic Blacks with non-Hispanic Whites as the reference.

	HR	*95% CI*
BC mortality	2.20	2.02-2.41
SEER Stage		
Localized	2.49	2.05-3.02
Regional	1.75	1.52-2.02
Distant	1.29	1.11-1.50
Interaction p-value	<.0001	
Grade		
1	2.27	1.50-3.43
2	2.12	1.78-2.52
3	1.62	1.43-1.84
Interaction p-value	<.0001	
ER status		
Positive	2.26	2.00-2.55
Negative	1.54	1.32-1.79
Interaction p-value	<.0001	
Subtype (2010+)		
Luminal A	2.58	2.00-3.33
Luminal B	2.65	1.58-4.45
HER2	2.86	1.43-5.71
Triple negative	1.53	1.07-2.17
Interaction p-value	<.0001	

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The Effect of Modifiable Risk Factors on Breast Cancer Aggressiveness Among Black and White Women B. Killelea,[3]* E. Gallagher,[1] S. Feldman,[2] E. Port,[1] S. Boolbol,[1] R. Franco,[1] K. Fei,[1] N. Bickell.[1] *1. Mount Sinai School of Medicine, New York, NY; 2. Montefiore Medical Center, New York, NY; 3. Yale University School of Medicine, New Haven, CT.*

Introduction: Although breast cancer incidence is higher among white women, blacks are more likely to have aggressive tumors with less favorable histology, and to have a worse prognosis. Obesity and alcohol consumption are two risk factors for breast cancer, while physical activity may offer protection. Little however is known about the association of these modifiable factors on the severity of breast cancer (as measured by Nottingham Prognostic Indicator (NPI)) and whether there are differences by race. Methods: Data collected as part of a large prospective study looking at insulin resistance and race among women with breast cancer was queried for patient characteristics, lifestyle factors and tumor characteristics. The association with NPI was assessed using univariate and multivariate linear regression. Results: Among 704 women in our cohort, 83% were white and 17% were black, mean age 58 years. The groups were well matched, and there was no racial difference in age or tumor size. Black patients were more likely to have high BMI (31.3 vs. 26.5, p<.001), larger waist circumference (106.4 vs 94.6 cm, p<.001), comorbidities (66% vs.53%, p=.01), self-reported poor diet (68% vs 43%, p<.0001), be sedentary (58% vs 46%, p=.03) and were less likely to consume alcohol (7% vs 31%, p<.0001). Overall, 18% of the patients had NPI > 4.4 which on bivariate analysis was significantly associated with younger age (55.6 vs 58.5 years, p=0.02), black race (25% vs 15%, p=0.005), triple negative cancer (14% vs 6%, p=0.005), and poor diet (55% vs 45%, p=0.04). On multivariate analysis, (model R2=0.12; p<0.001), younger age (β=-0.0105, p=0.002), healthy diet (β=-0.2089, p=0.02), and exercise (β=-0.004, p=0.03) were associated with lower NPI, while black race (β=0.2396, p=0.04) and triple negative cancer (β=0.8635, p<.0001) were associated with poor prognosis (higher NPI). Neither alcohol use nor BMI was significantly associated with NPI. Conclusion: Although modifiable risk factors including diet and exercise may have a small but significant impact on NPI, race and biologic subtype remain the most important determinants of prognosis.

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Radiation Therapy Associated Sarcoma After Breast Cancer Treatment: A Population-Based Study A.J.M. Rombouts,[1]* J. Huising,[1] N. Hugen,[1] S. Siesling,[2] H. de Wilt,[1] P.M.P. Poortmans,[4] I. Nagtegaal.[3] *1. Surgery, Radboudumc, Nijmegen, Netherlands; 2. comprehensive cancer organization the netherlands, Enschede, Netherlands; 3. Pathology, Radboudumc, Nijmegen, Netherlands; 4. Radiation Oncology, Radboudumc, Nijmegen, Netherlands.*

BACKGROUND: The aim of this study was to analyze the incidence and latency period of radiation-associated sarcoma (RAS) in patients who were previously treated with radiation therapy (RT) for breast cancer. In addition, different treatment regimens for RAS with corresponding survival outcomes were studied. METHODS: Data on all female breast cancer patients diagnosed between 1989 and 2014 and treated with a combination of surgery and RT were retrieved from the population-based Netherlands Cancer Registry. Patients who developed a sarcoma in the breast/chest wall as second primary were identified and expected to be induced by RT. Survival after RAS was analyzed using Kaplan-Meier curves and multivariable analysis was conducted by Cox regression. RESULTS: During the study period, 163,824 breast cancer patients were treated with surgery and RT. Median follow-up after diagnosis of primary breast cancer was 11.0 years (range 4.1-25.3). A total of 193 patients (1.2/1000) developed RAS. The median latency period between the diagnosis of breast cancer and the secondary sarcoma was 8 years (range 3-20). Median age at time of diagnosis of RAS was 73 (range 38-92). Additional data on non-irradiated patients will be presented at the meeting. Information on the treatment given for RAS was available in 176 patients (91.2%). Regardless of the type of treatment given for RAS, 5-year and 10-year survival rates were 38.6% (95% confidence interval [CI] 31.2-46.0), and 24.9% (95% CI 17.3-32.5%) respectively. In comparison with surgery alone (N=153), the addition of RT (N=15; HR 0.81, 95% CI 0.37-1.78) or chemotherapy (N=2; HR 1.63, 95% CI 0.35-7.70) to the treatment of RAS did not significantly improve overall survival (Table 1). DISCUSSION: RAS is rare and occurs in 1.2/1000 of patients treated with RT for breast cancer. With a median latency period of 8 years, most sarcomas develop after the standard follow-up time. Surgery is the treatment of choice for RAS; a beneficial effect of the addition of RT or chemotherapy to the treatment could not be assessed in this retrospective cohort.

Table 1 – Prognostic factors for overall survival after diagnosis secondary sarcoma

Factor	Univariable			Multivariable		
	N (%)	3-year survival	P-value	HR	95%CI	Adjusted P-value
BREAST CANCER						
Age <45 45-59 60-74 ≥75	9 (4.7) 57 (29.5) 94 (48.7) 33 (17.1)	76.2% 67.0% 46.6% 21.5%	<0.001*	0.30 0.50 1.00 1.67	0.07-1.30 0.31-0.80 - 1.04-2.66	<0.001* 0.107 0.004* - 0.032*
Surgical treatment Lumpectomy Mastectomy Surgery NOS	179 (92.7) 8 (4.1) 6 (3.1)	50.0% 37.5% 66.7%	0.662	NA	NA	NA
pTNMT pT1 pT2 pT3 pT4 pTx	161 (83.4) 30 (15.5) - 1 (0.5) 1 (0.5)	48.3% 56.2% 100% 100%	0.436	NA	NA	NA
pTNMN pN0 pN+ pNx	125 (64.8) 58 (30.1) 10 (5.2)	47.5% 49.8% 78.8%	0.231	NA	NA	NA
Morphology Ductal carcinoma Lobular carcinoma Ductal + lobular carcinoma Adenocarcinoma Cribiform carcinoma	143 (74.1) 22 (11.4) 8 (4.1) 19 (9.8) 1 (0.5)	53.7% 31.8% 62.5% 41.6% 0%	0.025*	1.00 1.69 0.48 1.53 0.48	- 1.00-2.86 0.14-1.64 0.80-2.94 0.05-4.60	0.121
Differentiation Well Moderate Poor Unknown	34 (17.6) 58 (30.1) 42 (21.8) 59 (30.6)	47% 49.4% 62.2% 44.1%	0.260	NA	NA	NA
SARCOMA						
Period of diagnosis 1989-1995 1996-2002 2003-2009 2010-2015	7 (3.6) 31 (16.1) 75 (38.9) 80 (41.5)	57.1% 41.9% 50.7% 52.3%	0.146	NA	NA	NA
Latency period 0-5 years 6-10 years 11-15 years 16-21 years	40 (20.7) 108 (56.0) 34 (17.6) 11 (5.7)	37.6% 53.0% 53.0% 60.6%	0.341	NA	NA	NA
Treatment regimen Surgery Surgery + RT Surgery + CT RT CT Unknown	153 (79.3) 15 (7.8) 2 (1.0) 4 (2.1) 2 (1.0) 17 (8.8)	52.6% 60.0% 50.0% 0% 0% 40.3%	<0.001*	1.00 0.81 1.63 5.97 4.02 2.46	- 0.37-1.78 0.35-7.70 1.75-20.40 0.95-16.97 1.11-5.46	0.009* - 0.596 0.537 0.004* 0.059 0.027*
Surgical treatment Total resection Partial resection Local excision Surgery NOS	83 (43.0) 9 (4.7) 30 (15.5) 48 (24.9)	52.9% 66.7% 59.8% 47.0%	0.002*	1.00 1.28 0.65 1.03	- 0.53-3.07 0.36-1.18 0.67-1.58	0.423

* Statistical significant. HR, hazard ratio; CI 95%, confidence interval 95%; NA, not applicable; RT, radiation therapy; CT chemotherapy; NOS not otherwise specified.

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Breast Cancers of Special Histologic Subtypes are Biologically Diverse A.B. Tadros,* H.Y. Wen, M. Morrow. *Breast Service, Memorial Sloan Kettering Cancer Center, New York, NY.*

Background: Cancers of tubular, papillary, mucinous, and cribriform histology are classified as "special histologic subtypes" and are felt to have a good prognosis. We used the 21-gene Oncotype DX Breast Recurrence Score® multigene assay, which quantifies the risk of distant recurrence and predicts the benefit of chemotherapy among ER+/HER2- patients, to examine prognostic variation within special histologic subtypes. We also examined the distribution of Recurrence Score® (RS) results among the more common ductal, not otherwise specified (IDC) and lobular (ILC) cancers. Methods: 610,350 tumor specimens examined in the Genomic Health clinical laboratory from 2/2004 to 8/2017 were included. Specimen histology was classified centrally using a single H&E slide and World Health Organization criteria. RS results based upon quantitative RT-PCR gene expression were calculated for each specimen. RS distribution (Low <18, Intermediate 18-30, and High ≥31) was compared among histologic subtypes. Results: The median patient age was 60 years (IQR 51-67) and 80% were node negative. Most patients had low RS results (59.2%) and only 9.5% had high RS results (Table). The lowest mean RS was seen in the papillary subtype (11), and the highest in the IDC group (18.4, Table). Mean RS for all special subtypes was significantly lower than the mean RS for IDC patients (p<0.001). Patients with tubular carcinoma (TC) were least likely to have high RS results (0.5%, 19/3,599). Even when the high RS threshold was decreased from 31 to 25, as used in the TAILORx and RxPONDER trials, only 3.2% (116/3,599) of patients with TC had a high RS. Patients with ILC had a lower mean RS result than patients with IDC, 16.5 vs 18.4. The mean RS result for classic ILC was 16.3, compared with 18.2 for ILC variants. Conclusion: There is substantial diversity in predicted prognosis among patients with cancers classified as special histologic subtypes with 12%-25% having intermediate RS results and 0.5%-9% having high RS results. Pending further definition of the role of chemotherapy for patients with intermediate RS results by the TAILORx and RxPONDER trials, the RS result may help to inform systemic therapy decisions in these patients.

		Recurrence Score (RS) Risk Group, n (%)		
Subtype	Mean RS	Low (<18)	Intermediate (18-30)	High (≥31)
Overall	18.0	361,574 (59.2)	190,749 (31.3)	58,027 (9.5)
Ductal, NOS	18.4	291,928 (57.9)	158,478 (31.4)	53,956 (10.7)
Lobular, classic	16.3	31,834 (63.9)	16,728 (33.6)	1,257 (2.5)
Lobular, other variants	18.2	2,738 (54.0)	1,905 (37.6)	426 (8.4)
Invasive, mixed	16.4	16,221 (64.0)	7,891 (31.2)	1,217 (4.8)
Mucinous	14.9	11,342 (70.4)	4,065 (25.2)	709 (4.4)
Papillary	11.0	3,308 (79.5)	485 (11.7)	366 (8.8)
Tubular	14.5	2,701 (75.1)	879 (24.4)	19 (0.5)
Cribriform	12.6	1,502 (79.2)	318 (16.8)	77 (4.1)

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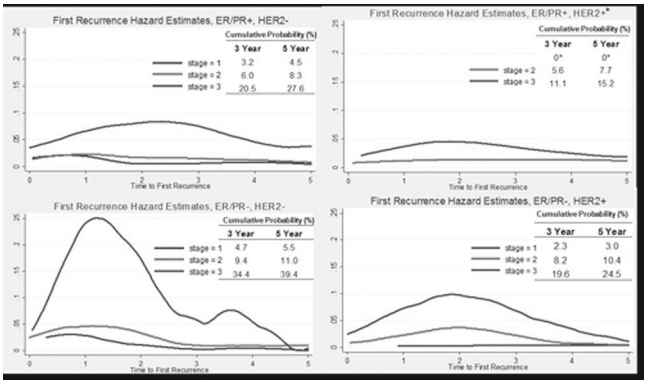
The Influence of Anatomic Stage and Receptor Status on First Recurrence for Breast Cancer within Five Years (AFT-01) H. Neuman,[1]* J.R. Schumacher,[1] B. Hanlon,[1] S. Edge,[2] K. Ruddy,[3] A. Partridge,[4] J. Le-Rademacher,[3] M. Yu,[1] D. Vanness,[1] D. Yang,[1] J. Havlena,[1] C. Greenberg.[1] *1. University of Wisconsin School of Medicine and Public Health, Madison, WI; 2. Roswell Park Cancer Center, Buffalo, NY; 3. Mayo Clinic, Rochester, MN; 4. Dana Farber Cancer Center, Boston, MA.*

Introduction: Receptor status is increasingly recognized as an important prognostic factor for breast cancer, prompting its incorporation into AJCC staging. Our objective was to assess the relationship of both anatomic stage and receptor status with first recurrence within 5 years. Methods: Data were included from 11 Alliance for Clinical Trials in Oncology legacy clinical trials that enrolled women diagnosed with stage I-III breast cancer. Women who had undergone surgery and modern era therapies, and had complete staging, receptor status, and recurrence information (n=10,357) were included. Smoothed estimates of hazards of recurrence were plotted at one-year intervals from the time of trial registration through the time of first recurrence. Patients were censored at the time of death, end of follow-up or at 5 years. Stratified Cox proportional-hazards regression models were used to produce 3- and 5-year cumulative probabilities of recurrence. A log-rank test was used to assess the difference in distribution of recurrence time by receptor status. Results: Annual hazards of first recurrence are presented (figure). Both anatomic stage (p<0.0001) and receptor status (p<0.0001) influenced likelihood of recurrence within 5 years. Timing of recurrence varied by receptor status (p<0.0001). 75% of recurrences occurred by 3.26 years for ER/PR+, Her2neu-; 1.94 years for ER/PR-, Her2neu-; 4.70 years for ER/PR+, Her2neu+; 2.87 years for ER/PR-, Her2neu+. Among stage 3 patients, ER/PR-, Her2neu- tumors recurred earlier and more often (3- and 5-year probability of recurrence was 34% and 39%) than ER/PR+, Her2neu+ tumors (3- and 5-year probability of recurrence was 11% and 15%), which were distributed over a longer time (see figure). Conclusion: Our study supports the importance of considering not only anatomic stage but also receptor status in staging, as these factors influence the likelihood of recurrence within 5 years. Given the predictable variation in the likelihood and timing of recurrence, these data also supports the need for a more personalized approach to follow-up than our current "one-size fits all" guidelines.



Annual Hazards and Cumulative Probability of First Recurrence by Receptor Status and Anatomic Stage within Five Years.

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Clinical Significance of Local Immune Cytolytic Activity in Breast Cancer T. Kawaguchi, Q. Qi, X. Peng, S. Narayanan, K. McDonald, S. Liu, L. Yan, K. Takabe.* *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Background: Recently it has been realized that not only intratumoral infiltration of CD8+ T-cells but also its cytolytic activity is critical to determine cancer biology. How interactions between cancer cells and the immune system in the tumor impact patient survival is less known. We hypothesized that intra-tumoral cytolytic activity is related to immune-mediated elimination which impacts survival in breast cancer patients. Patients and Methods: RNA-Sequence data with genomic and clinicopathological information from 1090 breast cancer patients were obtained from The Cancer Genome Atlas (TCGA). The immune Cytolytic Activity Score (CAS) was defined as the log average of GZMA (Granzyme) and PRF1 (Perforin) expression. Intra-tumoral immune cell composition was calculated using the CIBERSORT system Results: Breast cancer patients with high CAS showed better overall survival ($p=0.0031$), and had better survival in ER/PR+ or HER2+ patients (ER, $p=0.0059$; PR, $p=0.0085$; HER2, $p=0.011$). High CAS was also associated with improved survival in tumor infiltrating lymphocyte (TIL) positive breast cancer ($p=0.0023$). Multivariate analysis identified CAS as an independent prognostic marker independent of age, ER/PR status and stage. CAS also has a strongly positive association with expression of immune checkpoint genes: PD-1, PD-L1, and CTLA4 ($p<0.0001$) and regulatory T-cell (T-reg) markers; FOXP3 and CCR4 ($p<0.0001$). Significantly poorer survival was observed in patients with low PD-L1 expression and low CAS in their tumors ($p=0.0054$). CAS was associated with higher composition of immune-elimination cells: CD8+ T-cells, memory CD4+ T-cells, M1 macrophages, and memory B-cells ($p<0.0001$, $p<0.0001$, 0.00155, and $p<0.0001$, respectively). CAS was negatively associated with immune-suppression cells: M2 macrophages and T-reg cells ($p<0.0001$). Conclusions: Patients with high CAS breast cancers have improved survival, likely due to high intra-tumoral immunogenicity. CAS could also be used as a potential biomarker for immunologic response within tumors.

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Antibody Conjugation of Fluorescent Nanodiamonds for Targeted Innate Immune Cell Activation L.P. Suarez-Kelly,[1]* I.V. Rampersaud,[2] D. Albertson,[2] E. Morris,[2] T.C. Noel,[1] N.J. Buteyn,[1] J.P. Butchar,[1] L. Yu,[1] V.O. Yildiz,[1] N. Courtney,[1] C. Ren,[1] S. Tridandapani,[1] A.A. Rampersaud,[2] W.E. Carson III.[1] *1. The Ohio State University, Columbus, OH; 2. Columbus NanoWorks, Columbus, OH.*

Background: Fluorescent nanodiamonds (FNDs) are nontoxic, infinitely photostable, emit near infrared fluorescence and have a modifiable surface chemistry that allows for generation of protein-FND conjugates. Natural killer (NK) cells and monocytes detect and destroy cancerous cells through the process of neoplastic immunosurveillance. FND-mediated immune cell activation may serve as a strategy to enhance anti-tumor activity and promote immune cell visualization. Methods: Uncoated FNDs (u-FND) were fabricated and then conjugated with glycidol (a chemical linker, g-FND) or immunoglobulin G (IgG-FND). In vitro cellular FND uptake, viability, surface markers of activation and cytokine production in a breast cancer/NK/monocyte co-culture system were evaluated. Intratumoral FND delivery and fluorescence emission was evaluated in a breast cancer mouse model. Results: On flow cytometry, u-FND uptake was seen in both tumor cells (SKBR3 and EMT6) and immune cells, with monocytes having the highest uptake overall. There was increased uptake of IgG-FND compared to g-FND by monocytes ($p=0.004$) and NK cells ($p<0.001$). In co-culture, FNDs were preferentially taken up by monocytes compared to NK cells or SKBR3 cells ($p<0.001$). Confocal microscopy localized FND uptake to the cytoplasm. FND treatment did not affect immune cell viability. There was increased surface expression of CD69 and NKG2D activation markers in FND-treated NK cells compared to untreated ($p<0.001$ and $p=0.013$, respectively) or IgG-treated ($p<0.001$ and $p=0.016$, respectively) NK cells. In co-culture, IgG-FND treatment significantly enhanced monocyte TNF-α production and NK cell IFN-γ production compared to untreated ($p=0.015$ and $p=0.036$, respectively) or IgG-treated ($p=0.028$ and $p=0.011$, respectively) immune cells. In vivo, IgG-FNDs were visualized intratumorally for a longer duration compared to u-FNDs. Conclusion: FND conjugation with IgG enhanced FND uptake and immune cell activation with no effect on cell viability. FNDs were well-visualized following intratumoral injection. Antibody conjugated FNDs may serve as novel agents with "track and trace" capabilities for targeted activation of innate immune cells.

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Colon Cancer Quality Measure Adherence within Hospitals S.P. Shubeck,* A. Kanters, S. Regenbogen, H. Nathan. *University of Michigan, Ann Arbor, MI.*

Introduction: The Quality Integration Committee of the Commission on Cancer implemented guidelines for the treatment of colon cancer in 2008. These included (1) examination of ≥12 lymph nodes (12LN) at the time of resection and (2) adjuvant chemotherapy within 4 months of resection for patients with stage III disease (AC4). Previous analyses have considered the association between patient level factors and adherence to these quality measures; however, hospital-level factors are likely more relevant to benchmarking and quality improvement. Methods: Using the National Cancer Database from 2006-2013, we used a random effects logistic regression model to evaluate the impact of hospital-level variables on likelihood of patient receipt of guideline adherent care. We included cancer center type and each individual hospital's colon cancer population specific characteristics: volume, average income and education quintile of patients, and proportion of uninsured/Medicaid patients. We also accounted for patient level factors and year. Results: We identified 712,172 patients with lymph node data and 44,314 patients who met eligibility for AC4 at 1,283 hospitals. We found a trend toward guideline adherence for both measures from 2004-2013 (Table 1). Receiving care at high volume hospitals increases a likelihood of adherence to 12LN (OR 1.27 [1.17-1.40]), but not for AC4 (OR 1.11 [0.92-1.34]). Receiving care at hospitals serving a large proportion of low income patients did not impact 12LN adherence (OR 1.0 [0.93-1.11]), but did decrease a patient's likelihood of receiving care in accordance with AC4 (OR 0.71 [0.61-0.84]). Increased educational status a hospital's population improved guideline adherence for both measures evaluated. Conclusion: Rates of adherence to colon cancer treatment guidelines are increasing over time. We found that hospitals performing a high volume of colon cancer resections are more likely to deliver guideline concordant therapy, whereas those serving a large proportion of low income patients tend to be less compliant with adjuvant therapy recommendations. This suggests that targeting delivery of care based on the population a hospital serves could improve delivery of guideline concordant care.

Hospital Level Factors and Colon Cancer Guideline Adherence

		12LN (OR)	95% CI	AC4 (OR)	95% CI
Year	2005	1.18	(1.16-1.21)	1.02	(0.89-1.16)
(ref: 2004)	2006	1.48	(1.45-1.52)	0.98	(0.86-1.12)
	2007	2.09	(2.05-2.14)	1.04	(0.92-1.18)
	2008	2.36	(2.31-2.41)	1.10	(0.98-1.24)
	2009	2.62	(2.56-2.68)	1.09	(0.97-1.22)
	2010	2.69	(2.63-2.76)	1.10	(0.98-1.23)
	2011	2.71	(2.65-2.78)	1.12	(1.01-1.27)
	2012	2.77	(2.70-2.83)	1.11	(0.99-1.25)
	2013	2.92	(2.85-2.99)	1.14	(1.01-1.28)
Facility Type	Comprehensive	1.16	(1.10-1.23)	0.91	(0.80-1.04)
(ref: Community)	Academic	1.14	(1.06-1.22)	0.89	(0.76-1.04)
	Integrated	1.04	(0.95-1.14)	0.92	(0.72-1.18)
	Other	0.83	(0.66-1.04)	1.60	(0.75-3.40)
Volume	2	0.97	(0.90-1.05)	1.07	(0.92-1.25)
(Quintiles; ref:1)	3	0.94	(0.86-1.02)	1.01	(0.84-1.20)
	4	1.01	(0.91-1.10)	1.06	(0.89-1.28)
	5	1.28	(1.17-1.39)	1.11	(0.92-1.34)
Uninsured/Medicaid	2	1.01	(0.94-1.09)	0.96	(0.84-1.09)
(Quintiles; ref:1)	3	0.99	(0.91-1.06)	0.99	(0.87-1.13)
	4	0.99	(0.92-1.07)	1.02	(0.89-1.17)
	5	0.97	(0.89-1.05)	1.13	(0.97-1.31)
Income	2	1.01	(0.94-1.09)	0.98	(0.86-1.12)
(Quintiles; ref:1)	3	1.05	(0.97-1.14)	0.91	(0.79-1.05)
	4	1.06	(0.98-1.16)	0.79	(0.68-0.92)
	5	1.01	(0.93-1.11)	0.71	(0.61-0.84)
Education	2	1.06	(0.98-1.14)	1.05	(0.92-1.21)
(Quintiles; ref:1)	3	1.04	(0.96-1.13)	1.12	(0.97-1.29)
	4	1.16	(1.07-1.27)	1.26	(1.08-1.47)
	5	1.17	(1.07-1.29)	1.34	(1.13-1.58)

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Identifying and Characterizing Cancer Deserts in the United States A.N. Kothari,[1]* S.A. Brownlee,[1] A.N. Cobb,[1] E. Kirshenbaum,[1] P.C. Kuo,[2] G.J. Abood.[1] *1. Loyola University Medical Center, Maywood, IL; 2. USF Department of Surgery, Tampa, FL.*

Introduction: Geographic disparity in access to high-quality surgical cancer care is a modifiable risk factor. Our primary aim was to identify counties isolated from accredited cancer programs. Secondary aims included characterizing the travel burden and measuring outcomes for patients residing in these counties with gastrointestinal (GI) cancer undergoing surgical resection. Methods: The CDC NPCR and NCI SEER programs were used to measure United States county-level GI cancer incidences (colorectal, esophagus, liver, pancreas, and stomach). ACS Commission on Cancer (ACS COC) verified hospitals were identified using the AHA Annual Survey database. Counties and ACS COC hospitals were geomapped using QGIS software to calculate straight-line distances. "Cancer deserts" were defined as counties located in the top quartile of distance from an ACS COC hospital. Patient-level data were obtained from HCUP State Inpatient Databases. Risk-adjusted composite morbidity or mortality was calculated using mixed-effects logistic regression models. Results: A total of 2,925 counties were identified with at least 1 GI cancer case per 100,000 population/yr, representing a total study population of 248,396 patients. Of these, 585 counties were classified as "cancer deserts" with 13,658 patients (5.5%) residing in these counties (Figure). Using 4 geographically representative states (Florida, Iowa, New York, Washington), a total of 12,088 patients undergoing GI resection were identified. In this population, patients residing in "cancer deserts" traveled 382.1 km (SD 617.0) to receive care compared to 35.2 km (SD 42.3) for patients in "non-cancer deserts". Composite risk-adjusted morbidity or mortality was similar for both groups (17.3% [10.6 – 22.4%] vs. 19.6% [18.8 – 20.2%], P=.508). Conclusion: "Cancer deserts" in the United States are characterized by geographic isolation from accredited cancer centers. Though surgical morbidity and mortality appear similar for patients residing in these counties, a significant travel burden for quality care persists. These data can inform planning of future cancer networks and allocation of resources to maximize access for underserved populations.

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Detailed Outcomes Analysis of Over 1500 Patients Determines the Safety and Efficacy of Enhanced Recovery (ER) Protocols in Major Oncologic Surgery R.K. Marcus,* H.A. Lillemoe, B.J. Kim, R.W. Day, R.K. Voss, V.N.R. Gottumukkala, T. Aloia. *Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: ER protocols are increasingly being incorporated into surgical practice. Outside of colorectal surgery, their feasibility, safety and efficacy in major oncologic surgery has not been proven. This study assessed patient outcomes following multispecialty implementation of ER protocols at a large comprehensive cancer center. Methods: Surgical cases performed from 2011 to 2016 and captured by an institutional NSQIP database were reviewed. This database followed an "essentials" multispecialty model, capturing 14% of all cases. After excluding outpatient and emergent surgeries, 3256 cases (Colorectal 20.4%, Gynecology 19.5%, Hepatobiliary 8.9%, Thoracic 41.9%, Urology 9.3%) were included. Cases were stratified by presence or absence of ER compliance, which was defined by preoperative patient education and order set-driven narcotic-sparing anesthesia/analgesia, goal-directed fluid therapy and early postoperative diet advancement and ambulation. Results: 53.4% of patients were treated on traditional postoperative (TP) protocols and 46.6% on ER. Demographics including race/ethnicity, gender and age were equally distributed between cohorts. Pertinent preoperative comorbidities were compared between cohorts, and the only significant differences were fewer patients in the ER cohort with disseminated cancer (27.4 vs 23.8%) and taking anti-hypertensives (45.3 vs 40.4%). Treatment on an ER protocol was associated with decreased overall complication rates (33.9 vs 21.9%, $p<0.0001$), severe complication rates (11.7 vs 8.7%, $p=0.0048$), and median hospital length of stay (5 to 4 days, $p<0.0001$). A trend towards reduced NSQIP 30-day mortality (0.86 vs 0.4%, $p=0.097$) was also observed. No change in readmission rates occurred (TP vs ER, 8.9 vs 8.3%, $p=0.584$). Subspecialty analyses consistently demonstrated decreased complication rates, LOS, narcotic use and time to adjuvant therapy. Conclusions: Assessment of a large-scale ER implementation in multispecialty major oncologic surgery indicates its feasibility, safety and efficacy. Current efforts should be directed toward defining the oncologic benefits of these protocols.

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Combining Clinical Outcomes and Patient-Reported Experiences to Evaluate Hospital Cancer Surgery Quality J. Liu,[1]* A.L. Pusic,[2] B.L. Hall,[3] C.Y. Ko,[1] L.K. Temple.[4] *1. American College of Surgeons, Chicago, IL; 2. Memorial Sloan-Kettering Cancer Center, New York, NY; 3. Washington University in St Louis, St Louis, MO; 4. University of Rochester Medical Center, Rochester, NY.*

Introduction: Comprehensive assessments of quality should consider both clinician and patient perspectives in tandem. Focusing on patients undergoing major cancer surgery, we sought to characterize hospitals, and their patients, on both these axes of quality. Methods: Using the American College of Surgeons' National Surgical Quality Improvement Program registry, hospitals were profiled on a composite measure of death or serious morbidity (DSM) generated from a sample of patients who underwent colectomy, esophagectomy, hepatectomy, pancreatectomy, or proctectomy for cancer between January 1, 2015 and December 31, 2016. These hospitals were also profiled using a composite measure of seven clinically relevant Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) scales publicly reported on Hospital Compare. Hospitals performing in the top quartile on both the DSM

and HCAHPS composite measures (i.e., "best"), and their respective patients, were compared to hospitals performing in the lowest quartiles (i.e., "worst"). Results: Overall, 61,412 patients underwent their cancer operation at 536 hospitals. DSM occurred in 16.8%, and hospital performance on this metric varied significantly (p<0.001). When profiled by DSM and HCAHPS, there were 38 "best" and 46 "worst" performing hospitals (Figure). Compared to the worst performing hospitals, the best performing hospitals were more often NCI-designated cancer centers (29.0% vs. 2.2%, p<0.001) and cared for a lower proportion of Medicaid patients (13.6% vs. 22.6%, p<0.001). Patients who had their operation at the worst (vs. best) performing hospitals were more often black (20.3% vs. 8.4%, p<0.001), Hispanic (6.9% vs. 3.5%, p<0.001), functionally dependent (3.1% vs. 0.9%, p<0.001), and not admitted from home (4.3% vs. 2.4%, p<0.001). Conclusions: Quality improvement gaps can be identified with hospital quality metrics that incorporate both perioperative outcomes and patient experience. In this study, poor-performing hospitals appeared to be disproportionately serving disadvantaged and minority cancer patients.

ACS NSQIP hospitals profiled by a composite measure of death or serious morbidity (DSM) and a composite measure of seven HCAHPS scores (communication with doctors and nurses, responsiveness of hospital staff, discharge information, pain management, care transition, and willingness to recommend the hospital). Rho represents Spearman's rank correlation coefficient. Reference lines reflect means.

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Palliative Care Reduces Aggressive End of Life Care in Patients with Gastrointestinal Cancer S. Merchant,[1]* S. Brogly,[1] C. Goldie,[1] C. Booth,[1] S. Nanji,[1] S. Patel,[1] K. Lajkosz,[1] N. Baxter.[2] *1. Surgery, Queen's University, Kingston, ON, Canada; 2. University of Toronto, Toronto, ON, Canada.*

Introduction: Patients with cancer may receive aggressive end of life care (EOLC). We examined the delivery of palliative care (PC) services and its association with aggressive EOLC in patients with gastrointestinal (GI) cancer in Ontario, Canada. Methods: All patients with primary cause of death from esophageal, gastric, colon and anorectal cancer from January 2003–December 2013 were identified through the Ontario Cancer Registry. Information was obtained from administrative healthcare databases. PC services recorded within 2 years of death were identified using physician billing codes and were classified as: 1) any PC and 2) time PC initiated (≤7 days, 8-90 days, 91-180 days and 181-730 days before death). Aggressive EOLC was defined as any of chemotherapy, emergency department visits, hospital or intensive care unit (ICU) admissions (all ≤30 days of death), death in hospital and in ICU; these were combined as a composite outcome (any aggressive EOLC). We explored the association between PC and any aggressive EOLC using modified Poisson regression, adjusting for patient and clinical factors. Results: The cohort included 34,630 patients; 43% colon, 26% anorectal, 19% gastric and 12% esophageal cancers. Of these, 78% had at least one PC service. Patients who received PC were younger than those who did not receive PC (mean age at death 71.3 vs. 75.8 years). Timing of first PC service was variable: ≤7 days (12%), 8-90 days (43%), 91-180 days (16%), and 181-730 days (29%). Compared with patients not receiving PC, any PC was associated with a reduction in aggressive EOLC (RR 0.82, 95% CI 0.81-0.83), with the greatest reduction observed when PC began 91-180 days prior to death (RR 0.73, 95% CI 0.71-0.75). In contrast, the risk of aggressive EOLC was highest among patients who first received PC ≤7 days of death (RR 1.10, 95% CI 1.08-1.12) compared to those without PC. Conclusions: The majority of patients who die of GI cancer receive PC within 2 years of death. PC is associated with a lower risk of aggressive EOLC, with the lowest risk when first service is 91-180 days prior to death. In those who receive late PC, an earlier intervention may help to reduce aggressive EOLC.

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Breast Cancer Treatment Costs: Surgical Decisions and Preferences for Transparency R.A. Greenup,[1]* C.N. Rushing,[1] L.J. Fish,[1] B. Campbell,[1] T. Hyslop,[1] J.M. Peppercorn,[2] E.R. Myers,[1] Y. Zafar,[1] E.S. Hwang.[1] *1. Surgery, Duke University Medical Center, Durham, NC; 2. Massachusetts General Hospital, Boston, MA.*

INTRODUCTION: Cancer diagnoses are associated with an increased risk of bankruptcy, and financial distress predicts early mortality after cancer. Little is known about breast cancer treatment costs, their role in surgical decision-making, or patient preferences for cost transparency. METHODS: Women ≥18 years old with a history of breast cancer in the United States were recruited from the Army of Women and Sisters Network. An 88-item survey, based on previously validated questions, was distributed electronically and anonymously completed. RESULTS: 654 women completed surveys. Mean age was 58 years. Median time from diagnosis was 6.8 years. Stage at diagnosis was stage 0 (17%), I (37%), II (30%), III (10%), IV (1.5%), and unknown (3.5%). Most women had private insurance (69%) or Medicare (26%). 94% reported undergoing breast cancer surgery: 41% lumpectomy (BCS) (n=266), 24% mastectomy (n=155), 30% bilateral mastectomy (n=194), and 34% breast reconstruction (n=219). 43% reported considering costs in treatment decisions. 29% reported that costs were at least "somewhat" and 14% "extremely" important in surgical decision-making. Although "fear of recurrence" and "advice from the medical team" were prioritized in surgical decisions, treatment costs were considered as important as loss of sensation, need for surveillance, and avoiding radiation. Women with annual household income ≤$45K reported treatment costs were as important as appearance of and keeping the breast. Median reported out-of-pocket costs (OOP) differed by surgery type: $1,000 for mastectomy, $2,750 for BCS, $4,000 for mastectomy+reconstruction, and $6,000 for bilateral mastectomy+reconstruction. BCS was associated with significantly lower incurred debt (p<0.01 and p=0.03) and financial burden (p=0.03 and p<0.01) when compared to bilateral mastectomy +/- reconstruction. 79% preferred to know OOP costs prior to making treatment decisions. 78% reported never discussing costs with their cancer team. CONCLUSIONS: Health care costs are important to many women making breast cancer treatment decisions. Cost transparency may improve surgical decision-making, manage financial expectations, and reduce financial burden.

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Evolution of a Novel Robotic Training Curriculum in a Complex General Surgical Oncology Fellowship L.M. Knab,* M.S. Zenati, A. Khodakov, M. Rice, A. Al-abbas, D. Bartlett, A. Zureikat, H. Zeh, M. Hogg. *University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: Robotic surgery is being used for complex oncologic operations, although the learning curve required to become proficient has deterred many surgeons. Currently there is not a standardized robotic curriculum in place for surgical oncologists despite an increasing use of robotics. We describe the evolution of a proficiency-based robotic training program implemented for surgical oncology fellows and demonstrate outcomes of the program. Methods: A 5-step robotic curriculum began its integration in 7/2013. Fellows from 7/2013–8/2017 were included. An education portfolio was created for each fellow including: pre-fellowship experience (residency ACGME case logs, prior robotics, etc), fellowship experience with data from robotic curriculum and operative experience, and post-fellowship practice information. Results: Of the 30 fellows, 20% had completed a prior fellowship and 97% trained at an academic residency. Before fellowship, 57% had robotic training (median=5 hours) and 43% had performed robotic surgery (median=12 cases). In fellowship on average, fellows spent 5 hours on the virtual reality curriculum and performed 17 biotissue anastomoses (~12 hours). Procedure numbers can

be seen in Table 1. For total surgeries, fellows operating from the console increased over time (p=0.005). For pancreas, the average percentage of robotic whipple steps completed increased (p<0.01), as did the number of whipples in which the fellow completed the entire resection (p=0.013). Fellows also were 5x more likely to complete the entire distal than whipple from the console (p<0.01). Post-fellowship, 62% obtained an academic position, 21% mixed academic, and 17% community-based. In their jobs, 88% utilize robotics and 91% perform pancreatic surgery. Conclusions: With dedicated training, fellows can safely primarily perform complex gastrointestinal robotic surgeries, and take jobs after graduation incorporating this skill set. A pilot program at three additional fellowships is ongoing incorporating the same curriculum. In this era of scrutiny on cost and outcomes, specialized training programs offer a safe integration option for complex technical skills.

Median Procedure Volumes of Fellows

Procedure	Residency (median cases)	Fellowship (median cases)	
	Total [min, max]	Robotic [min, max]	Total [min, max]
Total Procedures*	521 [301, 1241]	33 [12, 80]	504 [216, 1154]
HPB (excluding cholecystectomy)	46 [0, 97]	22 [0, 54]	72 [46, 167]
Whipple	12 [2, 27]	10 [2, 23]	19 [7, 31]
Distal Pancreatectomy	7 [0, 14]	5 [1, 13]	9 [1, 16]
Other Pancreas	4 [0, 10]	2 [0, 12]	3 [0, 14]

*Note: total procedures for residency refers to total abdominal and thyroid cases, and for fellowship refers to total robotic cases and overall total cases performed during fellowship. HPB: hepatopancreaticobiliary

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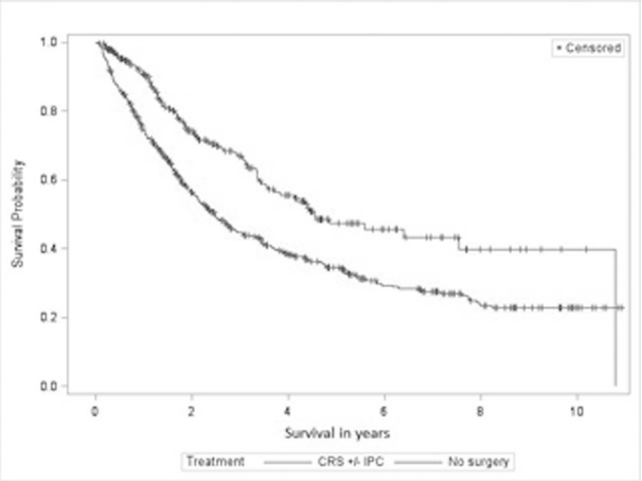
Appendiceal Carcinomatosis: The Burden of Suboptimal Treatment M.J. Selleck,[1]* L. Ji,[1] A. Kim,[1] R. Mehta,[1] S.S. Lum,[1] C.A. Garberoglio,[1] M.E. Reeves,[1] N. Solomon,[1] J.P. Namm,[1] C. Brown,[1] C. Dyke,[2] J.W. Morgan,[2] M. Senthil.[1] *1. Loma Linda University, Loma Linda, CA; 2. Surveillance Epidemiology and End Results (SEER) Cancer Registry, Cancer Registry of Greater California and California Cancer Registry, Sacramento, CA.*

Background: Cytoreductive surgery (CRS) with or without intraperitoneal chemotherapy (IPC) has been shown to improve survival in patients with appendiceal peritoneal carcinomatosis (PC). Despite this reported survival benefit, CRS has not been widely accepted which in turn could affect the type of treatment offered. Objective: To identify treatment trends and outcome differences in appendiceal PC in a large diverse population. Methods: Retrospective review of California SEER patient-level data (2004-2014) was performed to identify patients with appendiceal PC, type of treatment received, and nature and extent of surgical intervention (diagnostic vs. therapeutic). Propensity score weighted (age, sex, race/ethnicity, socioeconomic status) and covariate (grade, histology, surgery, node status, systemic chemo) adjusted Cox regression was used to assess mortality hazard ratios (HR). Results: A total of 723 patients with appendiceal PC were identified (292 males, 431 females). Median age was 56 years and median follow-up was 23.6 months. The majority were well and moderately differentiated (n=319; 54.2%) and mucinous adenocarcinomas (n=505; 69.8%). Four hundred forty-six patients (61.7%) received no surgical intervention and 31 (4.3%) underwent diagnostic surgery. CRS +/- IPC was performed in 246 (34%) patients. Median overall survival (OS) was 25, 33, and 67 months for diagnostic surgery, no surgical intervention, and CRS+/- IPC respectively (p<0.001). Systemic chemotherapy alone was given to 241(33.3%) of patients. Of those undergoing CRS +/- IPC, 119(48.4%) received systemic chemotherapy. Patients treated with CRS +/- IPC had significantly improved survival (HR=0.81;CI 0.68-0.98), compared to no surgery. Conclusion: In California, the majority of patients with appendiceal PC are treated without surgical intervention. Despite favorable biologic features, only 34% received CRS+/- IPC. To our knowledge, this is the first population-based study that has highlighted the problem of suboptimal treatment in patients with appendiceal PC. Significant effort is needed to educate physicians about this therapeutic option and facilitate referral of these patients to a peritoneal surface malignancy program.



Kaplan-Meier Survival Curve

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Defining Volume Thresholds for High-Risk Low-Volume Gastrointestinal and Thoracic Operations: A Pragmatic Approach to Regionalization A.A. Mokdad,[1]* J. Wang,[2] J. Mansour,[1] S. Wang,[1] M. Porembka,[1] M. Augustine,[1] P. Polanco,[1] R. Minter,[1] M.A. Choti,[1] J. Cao,[2] A. Yopp.[1] *1. Surgery, University of Texas Southwestern, Dallas, TX; 2. Southern Methodist University, Dallas, TX.*

Introduction: For high-risk low-volume operations, there is a rationale for implementing volume thresholds to improve patient outcomes. To guide regionalization, we quantified the impact of varying volume thresholds on mortality, travel burden, and access to surgical care. Methods: We identified patients undergoing pancreatic head, esophageal, liver, or major lung resections in the Texas Hospital Inpatient dataset, 2012–2015. We used a Bayesian mixed-effects regression model to estimate in-hospital postoperative morality over the range of available hospital volumes. We used geospatial software to quantify travel burden, defined as the change in the patients' actual driving times incurred at varying volume thresholds. County-level estimates of travel burden were estimated using spatial models. We also evaluated the distribution of qualified hospitals—those meeting the volume threshold. Results: We identified 2,659 pancreatic (pancreatic cancer, 53%), 1,586 esophageal (esophageal cancer, 32%, gastric cancer, 54%), 2,488 liver (liver cancer, 29%, metastasis, 61%), and 6,736 lung resections (lung cancer, 81%, metastasis, 10%). The range of annual hospital volumes were: pancreatic, 1-74, esophageal, 1-104, liver, 1-183, and lung resections, 1-208 cases. Higher volumes were associated with lower postoperative mortality: pancreatic (βvol=-0.37, 95% credibility intervals [CI], -0.57 to -0.16, Fig 1A), esophageal (β=-0.24, 95% CI, -0.42 to -0.06), liver (β=-0.25, 95% CI, -0.44 to 0.01), and lung resection (β=-1.87, 95% CI, -2.03 to -1.70). Travel burden increased with increasing volume thresholds (> 150 minutes of additional driving time were incurred with the highest volume threshold, Fig 1A). Counties distant from high volume hospitals incurred the largest increase in travel burden and reduction in available qualified hospitals (Fig 1B). Conclusion: For high-risk low-volume gastrointestinal and thoracic operations, regionalization, when guided by a comprehensive benefit-to-risk analysis, allows defining volume thresholds that help decrease mortality while maintaining a feasible travel burden and a non-restrictive access to surgical care.

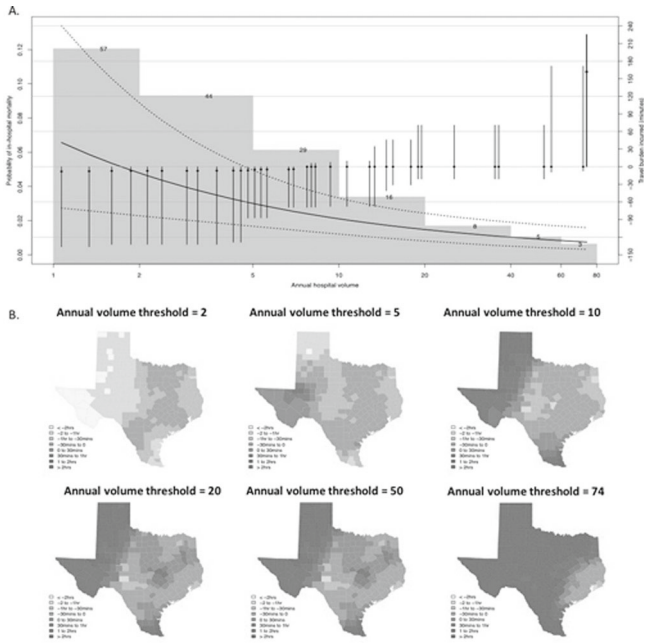

Figure 1. Pancreatic head resection. A) Postoperative mortality (mean and 95% credibility intervals), travel burden (vertical lines: median and interquartile range), and number of qualified hospitals (columns) at increasing volume thresholds. B) County-level estimates of travel burden at varying volume thresholds.

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Does a Gender Disparity Exist in the Bibliometrics and Professorial Ranks of Academic Surgical Oncologists in the U.S.? V. Nguyen,[1]* R.A. Marmor,[3] J. Sicklick.[2] *1. University of California, San Diego School of Medicine, La Jolla, CA; 2. University of California, San Diego, Division of Surgical Oncology, Department of Surgery, La Jolla, CA; 3. University of California, Department of Surgery, La Jolla, CA.*

Introduction An individual's h-index is defined as the number of h papers published, each with ≥ h citations. We hypothesized that male and female surgical oncologists had similar bibliometrics at each professorial rank. Methods We identified National Cancer Institute (NCI)-designated Comprehensive Cancer Centers (CCC) and used Doximity to identify the 50 highest-ranked general surgery residency programs with surgical oncology divisions. Data for academic surgical oncologists were collected from departmental websites, Grantome, and Web of Science. Results We identified 544 surgical oncologists (213 female, 331 male) from 64 programs with a mean h-index of 21±17. Compared to their female colleagues, male surgeons had higher median h-indices across all professorial ranks (Figure). The median h-indices were 5 vs. 10 for female and male assistant professors, 14 vs. 18 for associate professors, and 21 vs. 33 for full professors (all $p<0.01$). In addition, male academic surgical oncologists had higher total publication and citation counts than female surgeons across all professorial ranks. The median total publication counts were 18 vs. 32 for female and male assistant professors, 60 vs. 77 for associate professors, and 99 vs. 151 for full professors (all $p<0.01$). Similarly, the median total citation counts were 139 vs. 394 for female and male assistant professors, 788 vs. 1,242 for associate professors, and 1,763 vs. 3,961 for full professors (all $p<0.05$). Conclusions This is the first report to highlight a previously unappreciated gender disparity in the academic productivity amongst academic surgical oncologists in the U.S. When academic rank was accounted for, female surgical oncologists had lower h-indices, total publication counts and total citation counts compared to their male colleagues. Continued evaluation of the etiologies of this gender disparity is needed to address barriers to academic productivity faced by female surgical oncologists as they progress through their careers.

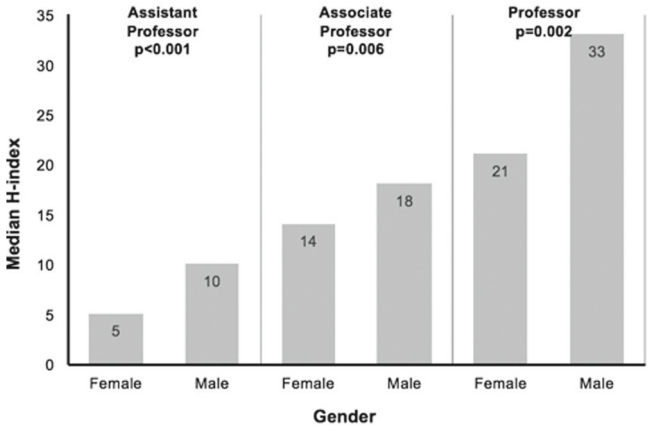

Figure. Gender disparity in academic productivity of U.S. surgical oncologists.

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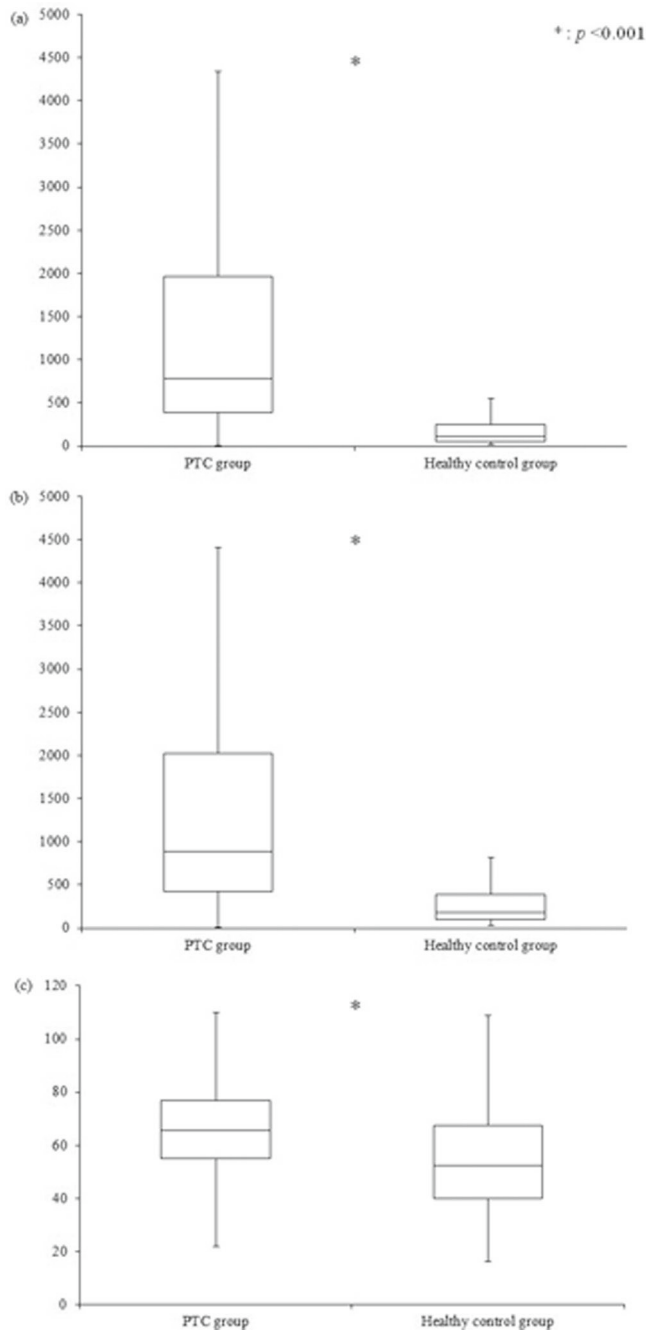
Case-Control Study of Papillary Thyroid Carcinoma on Urinary and Dietary Iodine Status in South Korea J. Lee.* *Surgery, Gil Medical Center, Incheon, Korea (the Republic of).*

Background Association between iodine levels and the risk of papillary thyroid cancer (PTC) has been suggested, but not definitively established. This study to compare the iodine status of a group of patients with PTC (with and without $BRAF^{V600E}$) with that of a healthy population cohort. Methods A cohort of patients scheduled for thyroidectomy was enrolled, along with a community-based health-screening cohort with no known history of thyroid disease. Median urinary iodine (UI) levels, creatinine-adjusted median UI levels, and food frequency questionnaire (FFQ) scores (mean ± standard deviation) were compared. In a subgroup analysis, these values were compared between $BRAF^{V600E}$-positive and $BRAF^{V600E}$-negative patients in the PTC group. Results The PTC group consisted of 210 patients, and the control group consisted of 90 healthy individuals. Among the 191 PTC patients whose $BRAF^{V600E}$ mutational status was reported, 169 (88.5%) were revealed positive for the mutation. The median UI levels were significantly higher in the PTC group (786.0 μg/l) than the control group (112.0 μg/l; $p<0.001$), as was the case with creatinine-adjusted median UI levels (884.6 μg/g creatinine versus 182.0 μg/g creatinine; $p<0.001$) and FFQ scores (66.2 ± 17.5, range: 13–114, versus 54.6 ± 21.5, range: 16–134; $p<0.001$). No significant differences were seen in the subgroup analysis between $BRAF^{V600E}$-positive and $BRAF^{V600E}$-negative patients. Conclusions Our results indicate that iodine status differs significantly between patients with PTC and healthy controls, suggesting that iodine may be involved in the occurrence of PTC, although the association between iodine levels and BRAF mutational status did not reach statistical significance.



Comparison of (a) median urinary iodine(p<0.001), (b) creatinine adjusted median urinary iodine (p<0.001), and (c) food frequency questionnaire scores (p<0.001) between the PTC group and the healthy control group

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Differences in the Impact of Age on Staging in Well Differentiated Thyroid Cancer H. Yan,* C. Wang, D.J. Winchester, R. Prinz, T. Moo-young. *Surgical Oncology, Northshore University Health System, Evanston, IL.*

INTRODUCTION: Well-differentiated thyroid cancer (WDTC) is unique in that patient age is part of staging. Several studies have shown a need to increase the age threshold in staging for WDTC, but the separate impact of age on prognosis for papillary and follicular carcinomas has not been examined. We hypothesize that age impacts survival differently for papillary and follicular carcinomas. METHODS: Patients with invasive papillary (PTC) and follicular thyroid cancer (FTC) were identified in the National Cancer Database 2004-2013. Overall survival (OS) was analyzed with univariate and multivariable Cox regression. Patients were stratified by histologic type. RESULTS: A total of 204,139 patients with well-differentiated thyroid cancer were identified; 188,393 (92.3%) had PTC while 15,746 (7.7%) had FTC. Average age was 48.4 years and OS for the entire group was 96.3% with a median follow-up of 52.7 months. When analyzing age in 5-year increments, overall mortality increased incrementally for the entire cohort and for PTC from age <35years to ≥70years without an optimal age threshold found. In FTC, however, mortality increased significantly once patients reached 45 years (table). When age was analyzed as discrete binary cut-offs, 45 was the optimal age threshold for FTC with highest hazard ratio for mortality: HR=4.81 (95% CI 3.43-6.74). CONCLUSIONS: Overall survival for PTC decreases incrementally with age, but OS for FTC decreases significantly in patients age 45 years and older. A higher age threshold may inappropriately downstage some high risk follicular cancer patients.

Mortality by Age Group

	Follicular			Papillary		
Age Group, years	Mortality	Hazard Ratio	p-value	Mortality	Hazard Ratio	p-value
<35	0.9%	Reference		0.5%	Reference	
35-39	1.3%	1.40 (0.75-2.61)	0.30	0.9%	1.54 (1.25-1.89)	<0.01
40-44	1.6%	1.71 (0.96-3.02)	0.07	1.1%	2.06 (1.71-2.48)	<0.01
45-49	4.1%	4.26 (2.66-6.83)	<0.01	1.7%	3.08 (2.59-3.64)	<0.01
50-54	4.9%	5.27 (3.33-8.33)	<0.01	2.2%	4.13 (3.50-4.87)	<0.01
55-59	6.3%	6.98 (4.45-10.94)	<0.01	3.2%	6.14 (5.22-7.21)	<0.01
60-64	7.7%	8.46 (5.40-13.26)	<0.01	4.3%	8.34 (7.09-9.79)	<0.01
65-69	12.6%	14.68 (9.49-22.72)	<0.01	6.5%	12.99 (11.08-15.22)	<0.01
≥70	27.0%	34.57 (22.81-52.39)	<0.01	17.9%	37.31 (32.23-43.19)	<0.01

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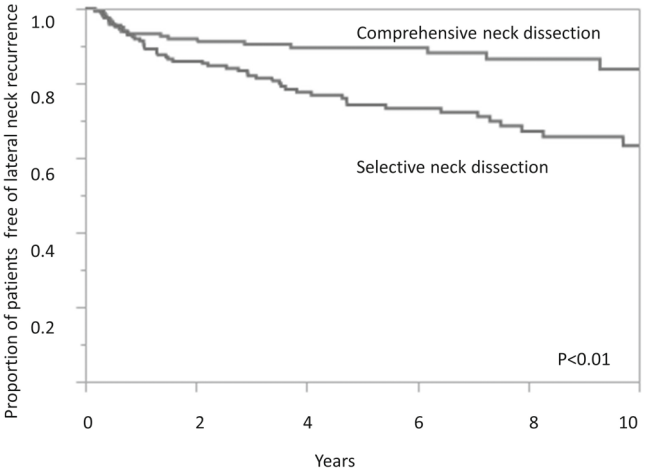
Comprehensive Lateral Neck Dissection in Papillary Thyroid Carcinoma May Reduce Lateral Neck Recurrence Rates V. Strajina,* Z. Al-Hilli, T.J. McKenzie, B.M. Dy, M. Ryder, D.R. Farley, G.B. Thompson, M.L. Lyden. *Surgery, Mayo Clinic, Rochester, MN, Rochester, MN.*

Introduction: The exact extent of the lateral neck dissection in patients with papillary thyroid carcinoma (PTC) has been controversial. We aimed to correlate the extent of the dissection with the incidence of recurrent disease in the lateral neck. Methods: A retrospective review of the operative, pathologic and postoperative surveillance data was performed for patients with PTC who underwent lateral neck lymphadenectomy from 2000 to 2015. Lateral neck recurrence-free interval was correlated with pathologic findings and the extent of surgery. The extent of surgery was recorded as either "comprehensive neck dissection" involving at least levels IIa-Vb (CND), or compartment-oriented dissection of lesser extent-"selective neck dissection" (SND). Kaplan-Meier curves were constructed; Wald and log rank tests were used to analyze survival time data. Results: 414 patients underwent 474 lateral neck dissections. Surveillance data were available for 323 patients who underwent 370 neck dissections (median follow up 5.3 years). CND was performed in 167 and SND in 203 patients. Lateral neck recurrence was detected in 68 patients (21%), and this occurred in levels 1 (n=2), 2 (n=28) 3 (n=26), 4 (n=29) and 5 (n=9). Multiple levels were involved in 25% of the recurrences, and 73% involved the levels included in the original dissection. Comparing CND to SND found that recurrence rates (13% vs. 26%), mean number of lymph nodes (LNs) retrieved (29 vs. 17), mean number of positive LNs (5.2 vs 4.0) and percentage of positive LNs (21% vs. 26%) were each significantly different between groups (p<.01). Lateral neck recurrence-free survival correlated with the percentage of positive LNs (p=0.03), total number of LNs harvested, the extent of neck dissection and younger patient age (p<.01). Estimated 5-year recurrence-free survival was better (88% vs. 77%) in patients with at least 23 LNs harvested (p<.01), and better (87% vs. 77%) in patients with less than 25% positive LNs (p=0.02). Conclusions: Younger patient age, more extensive dissection, total number of lymph nodes removed and a lower percentage of positive lymph nodes correlate with the lateral neck recurrence-free survival.



Lateral neck recurrence-free survival curves for patients undergoing selective (blue) and comprehensive lateral neck dissection (red).

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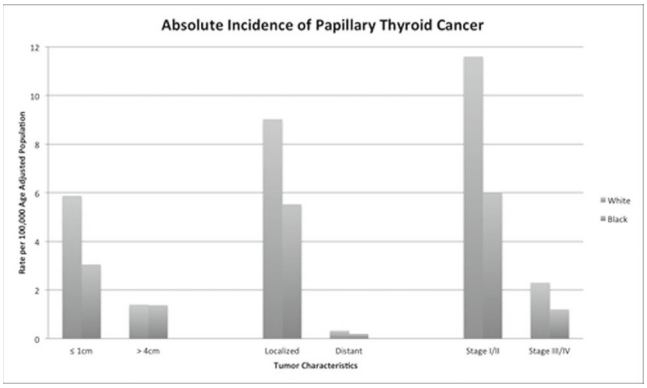
Racial Differences in Presentation and Survival with Papillary Thyroid Cancer (PTC) Result from Overdiagnosis of Small, Localized Tumors in White Patients A.R. Marcadis,[1]* J.L. Marti,[2] L.G. Morris.[1] *1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Weill Cornell Medical College, New York, NY.*

Introduction: Racial disparities in cancer are a significant problem. Prior analyses of PTC in the US suggest black patients present with more advanced disease and have poorer survival compared to white patients. This may be due to delayed diagnosis/treatment in black persons, excess diagnoses of small indolent PTCs in white persons, or both. Methods: This was a population-based analysis of 71,427 patients with PTC in the SEER 13 dataset, examining demographic and tumor characteristics at presentation, disease-specific survival, and incidence/mortality rates per 100,000 in white and black non-Hispanic persons (2010-2013). Results: In relative terms, more black compared to white patients presented with PTCs >4 cm (18 vs 10%;p<.01) and stage III/IV disease (16.3 vs 15.9%;p<.01). Black patients had poorer disease-specific 10yr survival (89 vs 92%;p<.01). In absolute terms, white persons had significantly higher incidence of small PTCs (rates ≤1cm 5.9 vs 3.1, 1.1-2cm 4.1 vs 1.8,p<.01) with no difference in PTCs >4cm (1.4 vs 1.4;p=.16). White patients had higher incidence of localized (9.0 vs 5.5;p<.01) and stage I/II (11.6 vs 6.0;p<.01) disease. Presentation with distant and stage III/IV disease, and disease-specific mortality, were not higher in black persons, and in fact slightly lower. Conclusion: In the US, there are more small, localized PTCs diagnosed in white compared to black persons with no difference in incidence of advanced PTCs. When evaluating differences in populations, absolute incidence should be used, rather than relative proportions, which can be misleading. When comparing cancer outcomes in populations, mortality rates should be used, rather than survival rates which are subject to lead- and length-time bias. Overdiagnosis refers to detection of cancers that would not have caused symptoms or death if undiscovered. Prior reports of racial disparity in PTC are likely due mainly to overdiagnosis of PTC in white persons. As we seek to eliminate racial disparity in healthcare, it is crucial to distinguish differences caused by inadequate access to care from those resulting from too much healthcare.



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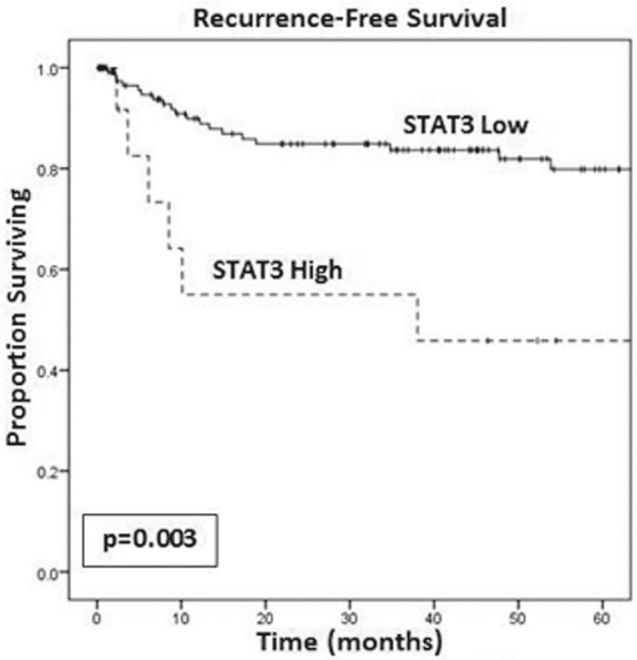
STAT3 Inhibition for Gastroenteropancreatic Neuroendocrine Tumors: Potential for a New Therapeutic Target? A.G. Lopez-Aguiar,[1]* L.M. Postlewait,[1] M.Y. Zaidi,[1] K. Zhelnin,[2] A. Krasinskas,[2] M.C. Russell,[1] D.A. Kooby,[1] K. Cardona,[1] B. El-Rayes,[3] S.K. Maithel.[1] *1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University Hospital, Atlanta, GA; 2. Department of Pathology, Winship Cancer Institute, Emory University Hospital, Atlanta, GA; 3. Department of Hematology Oncology, Winship Cancer Institute, Emory University Hospital, Atlanta, GA.*

BACKGROUND: Gastroenteropancreatic neuroendocrine tumors (GEP-NETs) are highly vascular tumors with similar treatments applied to all sites. The expression of pro-angiogenic factors (STAT3, VEGF, and HIF-1α) and their association with known adverse pathologic factors and disease recurrence after resection is not known. METHODS: All pts with non-metastatic primary GEP-NETs who underwent curative-intent resection at a single institution from 2000-2013 were included. Immunohistochemistry was performed for STAT3, VEGF, HIF-1α, Ki-67 index, and CD31 using tissue microarrays made in triplicate by a pathologist blinded to other clinicopathologic variables. STAT3, VEGF, and HIF-1α were categorized into high vs low expression; CD31 was dichotomized at the median value. Primary outcome was 3-yr recurrence-free survival (3-yrRFS); secondary outcomes were correlation of STAT3, VEGF, and HIF-1α expression with Ki-67 index, adverse pathologic factors, and CD31 expression, a marker of microvascular density. RESULTS: Of 265 GEP-NETs resected, 144 had tissue for analysis. STAT3 expression was high in 12(8%) and low in 132(92%). VEGF was high in 19(13%) and low in 125(87%), and HIF-1α was high in 1(1%) and low in 143(99%). High STAT3 expression was associated with worse 3-yrRFS compared to low expression(55%vs84%;p=0.003;Figure). High VEGF expression had a 3-yrRFS of 76% compared to 82% for low expression(p=0.098); HIF-1α expression was not associated with RFS. Ki-67≥3% was associated with worse 3-yrRFS(≥3%:51%vs<3%:84%;p<0.001), as was the presence of lymphovascular invasion(LVI:72%vs95%;p=0.001) and increased microvascular density per μm^2(CD31>median:75%vsCD31<median:86%;p=0.043). High STAT3 expressing tumors were more likely to have a Ki-67≥3%(42%vs7%;p<0.001). LVI was present in 82% of high STAT3 tumors compared to only 50% with low STAT3(p=0.058). CD31 overexpression was similar between groups(58%vs49%;p=0.5). CONCLUSION: In resected GEP-NETs, high STAT3 expression is associated with an increased Ki-67 index, presence of lymphovascular invasion, and worse 3-yr RFS. STAT3 inhibition may be a novel therapeutic option for patients undergoing resection of high-risk tumors.



	Recurrence-Free Survival	
STAT3	1-yr	3-yr
Low	90%	84%
High	55%	55%

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Surgical Management of Appendiceal NETs: Does Size Matter? R. Thiagarajan,[1] J.P. Landry,[1]* B.A. Voros,[1] D.T. Beyer,[1] Y. Wang,[1] R.A. Ramirez,[2] J. Boudreaux,[1] E.A. Woltering.[1] *1. Surgery, LSU HSC New Orleans, Thibodaux, LA; 2. Ochsner Medical Center - Kenner, Kenner, LA.*

Background: NETs of the appendix are rare neoplasms most often discovered incidentally during appendectomy. Classically, tumor size has driven surgical management; however, recent guidelines show that tumor characteristics may have a greater effect on staging and outcomes. Methods: This is a retrospective review of patients diagnosed and treated with a primary appendiceal NET over a 19-year period at a single referral center. Patients who underwent appendectomy and/or right hemicolectomy were included. Patients diagnosed with goblet cell carcinoid or appendiceal adenocarcinoma, or those with inadequate data were excluded. Results: Sixty-three patients met inclusion criteria. The mean age at diagnosis was 39 ± 16.4 years; 22% (14/63) were males. 32% of patients (21/63) underwent appendectomy alone, while 67% (42/63) underwent additional right hemicolectomy. 26% of patients (17/63) had tumors <1 cm in size, 37% (23/63) had tumors between 1 and 2 cm, and 37% (23/63) had tumors >2 cm in size. Lymph nodes were positive in 41% of patients (26/63). 29%, 30%, and 61% of patients had positive lymph nodes in tumors <1 cm, 1- 2 cm, and >2 cm, respectively. 38% (24/63) had invasion of the mesoappendix. 17% of patients (11/63) had distant metastasis. Kaplan-Meier 5-, 10-, and 15-year overall survival was 94%, 91%, and 91%, respectively. Survival sorted by tumor size, lymph node involvement, and Ki-67 index was statistically significant ($p<0.05$). Tumors <1cm in size were associated with worse survival at all time points in this study compared to tumors >1cm. Conclusions: Patients with appendiceal NETs experience high 5, 10, and 15-year survival rates. Conventionally, tumor size is one of the main determinants of surgical management of appendiceal NET; however, our study shows tumors measuring <2cm have significant metastatic potential. Our study reports nodal positively and Ki-67 >3% were prognostic for worse survival in well-differentiated appendiceal NETs. In addition to tumor size, detailed examination of the surgical specimen with proper staining to evaluate critical tumor characteristics is necessary to adequately manage appendiceal carcinoid patients.

Tumor Characteristic	Tumor Size		
n positive / n assessed per tumor size	<1cm N=17	1cm-2cm N=23	>2cm N=23
Lymph Node Involvement (Appendectomy)	2 / 14	5 / 17	8 /14
Lymph Node Involvement (R Hemicolectomy)	4 / 7	6 / 14	14 / 22
Perineural Invasion (Appendectomy)	5 / 9	8 / 16	6 / 19
Lymphovascular Invasion (Appendectomy)	5 / 11	6 / 22	11 / 23
Proximal Margin	1 / 15	1 / 21	5 / 23
Distal Margin	0 / 15	3 / 12	5 / 16
Depth of Invasion			
Tumor invades the muscularis propria	2 / 12	1 / 31	2 / 22
Tumor invades the subserosa	5 / 12	2 / 31	1 / 22
Tumor invades the mesoappendix without involvement of the visceral peritoneum	5 / 12	10 / 31	13 / 22
Tumor perforates the visceral peritoneum (serosa)	2 / 12	8 / 31	16 / 23
Invasion of the Mesoappendix	6 / 14	14 / 23	16 / 23
Mitotic index			
<2 per 10 HPF	9 / 9	12 / 13	11 / 11
2-20 per 10 HPF	0 / 9	1 / 13	0 / 11
Ki-67 Proliferative Index			
Ki-67 <3%	9 / 12	16 / 19	14 / 15
Ki-67 3% to 20%	3 / 12	3 / 19	1 / 15

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Risk of Metastasis in Patients with Rectal Neuroendocrine Tumors I.W. Folkert,* A.J. Sinnamon, D.L. Fraker, B. Bennett, D. Metz, K. Stashek, R. Roses. *Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA.*

Introduction: Small (<2cm) and diminutive (<1 cm) rectal neuroendocrine tumors (RNET) are thought to have an indolent natural history provided they are completely resected. A large single center experience with rectal neuroendocrine tumors was reviewed to determine the incidence of metastasis in rectal neuroendocrine tumors stratified by size. Methods: All cases of rectal neuroendocrine tumor between 2010-2017 at a single institution were retrospectively reviewed. Rate of metastasis was determined and outcomes were stratified by tumor size. Univariate predictors of metastasis were identified and a classification and regression tree (CART) analysis was used to stratify risk of distant metastasis. Results: Ninety-nine patients were diagnosed with a rectal neuroendocrine tumor during the study period, with a median follow-up of 28 months. Seventy-eight patients had primary tumors less than 1.0 cm in size, 9 patients had tumors 1-2 cm, 11 patients had tumors ≥ 2.0 cm. Eighty-seven patients had Grade 1 (G1) tumors, 8 patients had Grade 2 (G2) tumors, and 4 patients had Grade 3 (G3) tumors. Twelve patients developed metastatic disease. Both size and grade were associated with distant metastasis on univariate analysis ($p<0.001$), however when stratified by grade, size was only predictive of metastasis in G1 tumors ($p<0.001$, Table 1). Of the 12 patients that developed metastatic disease, 3 (25%) had diminutive primary tumors smaller than 1.0 cm and 9 patients (75%) had primary tumors ≥2.0 cm. Of patients with metastatic disease, 3 (21%) had Grade 1 tumors, 7 (50%) patients had Grade 2 tumors, and 4 (31%) had Grade 3 tumors. Patients with diminutive tumors that developed metastatic disease all had intermediate-grade tumors (G2). Disease specific mortality for the entire cohort was 4%. Conclusion: Patients with diminutive and small rectal neuroendocrine tumors remain at risk for developing metastatic disease; tumor grade is a dominant predictor of dissemination. More aggressive initial management or closer surveillance may be warranted for patients with G2 tumors irrespective of size.

Incidence of Rectal Neuroendocrine Tumor Metastasis by Size and Grade

	No Metastasis	Metastasis	
	Grade 1 (n=87)		p value
<2.0 cm	85	0	p<0.001
≥2.0 cm	0	2	
	Grade 2 (n=8)		p=1.0
<2.0 cm	1	3	
≥2.0 cm	1	3	
	Grade 3 (n=4)		--
<2.0 cm	0	0	
≥2.0 cm	0	4	

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Role of Additional Organ Resection in Adrenocortical Carcinoma: Analysis of 167 patients from the US Adrenocortical Carcinoma Database P. Marincola Smith,[1]* C.M. Kiernan,[1] T.B. Tran,[3] L.M. Postlewait,[2] S.K. Maithel,[2] J. Prescott,[4] T. Pawlik,[4] T.S. Wang,[5] J. Glenn,[5] I. Hatzaras,[6] R. Shenoy,[6] J. Phay,[7] L. Shirley,[7] R. Fields,[8] L. Jin,[8] S. Weber,[9] A. Salem,[9] J. Sicklick,[10] S. Gad,[10] A. Yopp,[11] J. Mansour,[11] Q. Duh,[12] N. Seiser,[12] K. Votanopoulos,[13] E.A. Levine,[13] G. Poultsides,[3] C. Solorzano.[1] *1. Department of Surgery, Vanderbilt University Medical Center, Nashville, TN; 2. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 3. Stanford University School of Medicine, Stanford, CA; 4. The Johns Hopkins University School of Medicine, Baltimore, MD; 5. Medical College of Wisconsin, Milwaukee, WI; 6. New York University School of Medicine, New York, NY; 7. Department of Surgery, The Ohio State University, Columbus, OH; 8. Department of Surgery, Washington University School of Medicine, St Louis, MO; 9. Department of General Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 10. Department of Surgery, University of California San Diego, San Diego, CA; 11. Department of Surgery, University of Texas Southwestern Medical Center, Dallas, TX; 12. Department of Surgery, University of California San Francisco, San Francisco, CA; 13. Department of Surgery, Wake Forest School of Medicine, Winston-Salem, NC.*

BACKGROUND: Adrenocortical carcinoma (ACC) is a rare and aggressive cancer with a 5-year survival of 40% for those with resectable disease. Due in part to its low incidence, data on the benefit of many surgical factors is lacking. We describe the factors and outcomes associated with resection of extra-adrenal organs "en bloc" during index adrenalectomy. METHODS: Patients who underwent ACC resection from 1993-2014 at 13 participating institutions of the US ACC Group were included. Patients with metastatic disease were excluded. Factors associated with en bloc resection were assessed by uni- and multi-variate analysis. The primary endpoint was overall survival. RESULTS: 167 patients were included and categorized as "adrenalectomy with en bloc resection (AdEBR)" if they had extra-adrenal organs removed during their index operation or "adrenalectomy (Ad)" if they did not. Patient demographics were similar between AdEBR (68, 40.7%) and Ad groups, including age, gender, race, ASA Class, and BMI. The AdEBR group was more likely to have an open operation (98.5% vs 64.9%) and lymph node dissection (LND) (38.5% vs 12.9%). The most common organs removed were kidney (38, 55.9%), liver (19, 27.9%), and spleen (16, 23.5%). More than one extra-adrenal organ was removed in 26 patients (38.2%). On multivariate Cox regression adjusted for T/N stage, LND, margin, size, and hormone production, en bloc resection of extra-adrenal organs was not associated with a survival advantage (HR 1.49, 95%CI 0.74-3.01, p=0.262). For patients without extra-adrenal organ involvement on final pathology (T1-3 tumors) and negative surgical margins, removal of extra-adrenal organs was also not associated with any survival advantage (HR 1.21, 95%CI 0.72-2.01, p=0.471). CONCLUSION: This large multi-institutional analysis demonstrates that en bloc resection of extra-adrenal organs was believed necessary by the operating surgeon in over 40% of ACC patients. Additionally, when a margin negative resection can otherwise be achieved, removal of extra-adrenal organs en bloc does not provide additional survival benefit.

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Basal-Like Pancreatic Adenocarcinoma (PDAC) Subtypes Demonstrate Increased Expression of Immune Genes and a Signature of PD-1 Inhibition Resistance R. Joseph,[2] K. Collins,[1] D. Bortone,[1] B.G. Vincent,[1] J. Yeh,[1] A.J. McRee.[1]* *1. Lineberger Comprehensive Cancer Center, University of North Carolina, Chapel Hill, NC; 2. University of North Carolina, Chapel Hill, NC.*

Background: PDAC is a lethal disease with poor survival even when detected at an early stage. Recurrence rates after surgical resection remain high. Recently, two distinct molecular subtypes of PDAC (basal-like and classical) have been identified with basal-like tumors demonstrating inferior outcomes. We hypothesize that differences in tumor immunogenicity may contribute to this aggressive biology and predict response to immune checkpoint inhibitors. Methods: RNA sequencing was performed on formalin-fixed paraffin embedded samples of 60 resected PDAC patients. We evaluated previously published immune gene expression signatures comprised of 1400 genes and used a single sample classifier to determine molecular subtypes. Results: Table 1 summarizes patient characteristics in our cohort. There were 35 classical and 25 basal-like tumors. PFS was significantly shorter in patients with basal-like compared to classical subtypes (9 vs 15 mo, p = 0.006). In a multivariable model with molecular subtype, lymph node, and margin status, subtype was the only independent predictor of PFS (p = 0.028). Unsupervised clustering identified two distinct immune groups that were associated with molecular subtypes (p = 0.038) with higher expression of immune genes in basal-like tumors. Basal-like tumors were significantly associated with an immunosuppressive signature (p < 0.001) and a signature associated with non-response to PD-1 inhibition in melanoma (p = 0.001). Conclusions: This is the first study to show that basal-like pancreatic cancers are associated with increased immune gene expression and may help explain their inferior prognosis. We hypothesize that this reflects an increase in immunosuppressive cells in basal-like tumors that may predict decreased response to immune checkpoint inhibitors.

Table 1: Patient Characteristics

	Classical	Basal-like	P value
N	35	25	
Median age (Range)	65 (44-84)	70 (44-84)	0.380
Sex (%)			1
M	16 (45.7)	11 (44)	
F	19 (54.3)	14 (56)	
Nodal status (%)			0.054
N0	11 (31.4)	2 (8)	
N1	24 (68.6)	23 (92)	
Margins (%)			0.040*
R0	21 (60)	8 (32)	
R1	14 (40)	17 (68)	
Median PFS (months)	15	9	0.006*
Immune groups (%)			0.038*
Intermediate	18 (51.4)	6 (24)	
High	17 (48.6)	19 (76)	

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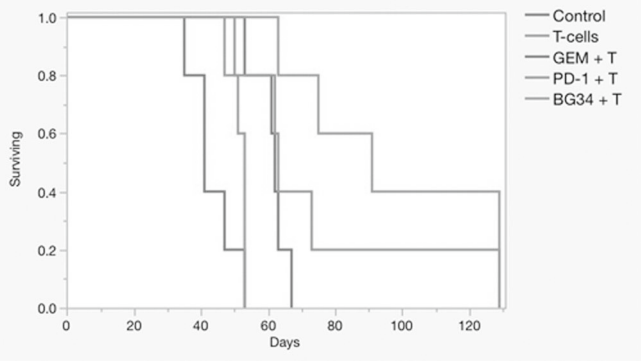
Improved Therapeutic Efficacy of T-Cells Derived from Human Pancreatic Cancer Draining Lymph Nodes in Combination with Immune Modulators in a Xenograft Model of Metastatic Human Pancreatic Cancer Z. Senders,[1]* M. Zhang,[2] H. Graor,[2] K. Choong,[1] J. Lyons,[1] V. Sandoval,[1] J. Hardacre,[1] J. Ammori,[1] J. Kim.[1] *1. Surgery, University Hospitals Cleveland Medical Center, Cleveland, OH; 2. Case Western Reserve University School of Medicine, Cleveland, OH.*

Introduction: Adoptive t-cell transfer has demonstrated responses in patients with melanoma, however its efficacy in treating pancreatic cancer (PC), a less immunogenic tumor, is unclear. The purpose of this study is to test the efficacy of t-cells derived from human pancreatic cancer draining lymph nodes (PDLN) in a mouse xenograft model of metastatic human PC, and to determine if efficacy is enhanced in combination with immune modulators. Methods: PDLN were obtained from patients undergoing pancreaticoduodenectomy for PC. SCID mice bearing a human PC cell line (AsPc1) were treated with ex vivo expanded PDLN-derived human t-cells. Mice were also treated with anti-PD1 antibody, Gemcitabine, or an immune modulator BG34 (beta glucan), alone or in combination with subtherapeutic doses of t-cells. The primary endpoint was overall survival. Results: Mice treated with t-cells exhibited a dose-dependent increase in survival compared to controls (p=.001). Anti-PD1 antibody in combination with a subtherapeutic dose of t-cells significantly improved survival compared to t-cells alone (p=.04) and untreated control (p=.01), although anti-PD1 alone did not (p=.86). BG34 alone did not significantly increase survival compared to control (p=.16), however combination therapy with BG34 and t-cells markedly increased survival (p=.002). Gemcitabine alone improved survival compared to control (p=.01) but this effect was not enhanced when combined with t-cells (p=.53). Flow cytometry revealed human t-cells persisting in tumor tissue, with a predominantly CD8+ phenotype. Immunohistochemistry confirmed the presence of tumor-infiltrating adoptively transferred human lymphocytes. Conclusions: T-cells derived from human PDLNs increase the survival of mice bearing human PC xenografts in a dose-dependent manner. The therapeutic efficacy of transferred PDLN cells is significantly enhanced when combined with certain classes of immune modulators. These findings support the use of immune modulators in adoptive immunotherapy treatment strategies.



Kaplan-Meier survival analysis of mice by treatment group, n=5.

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Preoperative Monocyte-to-Lymphocyte Ratio and Neutrophil-to-Lymphocyte Ratio are Associated with Overall Survival After Resection of Pancreatic Neuroendocrine Tumors R.Z. Panni,[1]* B.A. Krasnick,[1] J. Davidson,[1] M. McGilvray,[1] J. Rodriguez,[1] A.G. Lopez-Aguiar,[2] M. Dillhoff,[3] G. Poultsides,[4] E.R. Winslow,[5] F.G. Rocha,[6] K. Idrees,[7] C.S. Cho,[8] C. Hammill,[1] M.B. Doyle,[1] W. Chapman,[1] W. Hawkins,[1] S.M. Strasberg,[1] N. Trikalinos,[1] S.K. Maithel,[2] R. Fields.[1] *1. General Surgery, Washington University in Saint Louis, Saint Louis, MO; 2. Emory University Hospital, Atlanta, GA; 3. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 4. Stanford University School of Medicine, Stanford, CA; 5. University of Wisconsin Carbone Cancer Center, Madison, WI; 6. Virginia Mason Medical Center, Seattle, WA; 7. Vanderbilt University Medical Center, Nashville, TN; 8. University of Michigan, Ann Arbor, MI.*

Background: Neutrophil, monocyte and lymphocyte counts are important biomarkers of the tumor-induced systemic inflammatory response. A lower monocyte-to-lymphocyte ratio (MLR) and neutrophil-to-lymphocyte ratio (NLR) is associated with a favorable prognosis for certain tumors. However, this association has not yet been demonstrated in resected pancreatic neuroendocrine tumors (PNETs). The aim of this study was to investigate the prognostic significance of MLR and NLR in patients with resectable PNETs with regards to overall survival (OS). Methods: Eligible patients undergoing surgery between 2000 and 2016 were identified using a national multi-center cohort dataset. Their pre-operative neutrophil, monocyte and lymphocyte counts were imported and NLR and MLR were calculated. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut offs for NLR and MLR. Univariate analyses were used to compare patient factors and tumor characteristics in different groups. The difference in OS between high and low groups was explored with the use of Kaplan Meier curves and compared using log-rank tests. Results: A total of 635 patients were analyzed. Univariate analysis revealed that higher lymphocyte, low monocyte and low neutrophil counts were associated with improved OS (P = 0.0002, 0.014 and 0.011 respectively). TLower NLR (< 4) and lower MLR (< 0.25) were significantly associated with improved OS (p < 0.001 & p < 0.0001). Median survival was 141 months in the low NLR group (n = 474) and 119 months in the high NLR group (n = 161). The median survival in the high MLR group (n = 464) was 120 months and has not been reached in the low MLR group (n = 171). On multivariate analysis, low MLR was independent predictor of improved OS when controlling for age, race and comorbidities (p < 0.001). Conclusions: For resectable PNETs, low pre-operative NLR and MLR levels are significantly associated with improved survival. NLRs and MLRs may serve as valuable markers to stratify PNET patients for subsequent therapies and clinical trial enrollment.

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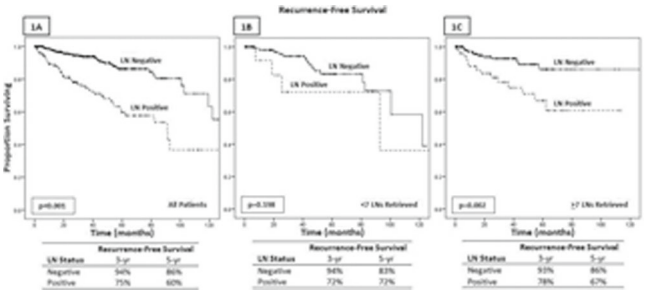
Defining the Role of Lymphadenectomy for Pancreatic Neuroendocrine Tumors: An Eight Institution Study of 695 Patients from the U.S. Neuroendocrine Tumor Study Group A.G. Lopez-Aguiar,[1]* M.Y. Zaidi,[1] M. Dillhoff,[2] E.W. Beal,[2] G. Poultsides,[3] E.A. Makris,[3] F.G. Rocha,[4] Z.S. Kanji,[4] K. Idrees,[5] P.M. Smith,[5] C.S. Cho,[6] M. Beems,[6] S. Weber,[7] A. Fisher,[7] R.C. Fields,[8] B.A. Krasnick,[8] K. Cardona,[1] S.K. Maithel.[1] *1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University Hospital, Atlanta, GA; 2. Division of Surgical Oncology, The Ohio State University Comprehensive Cancer Center, Columbus, OH; 3. Department of Surgery, Stanford University Medical Center, Stanford, CA; 4. Department of Surgery, Virginia Mason Medical Center, Seattle, WA; 5. Division of Surgical Oncology, Department of Surgery, Vanderbilt University Medical Center, Nashville, TN; 6. Division of Hepatopancreatobiliary and Advanced Gastrointestinal Surgery, Department of Surgery, University of Michigan, Ann Arbor, MI; 7. Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI; 8. Department of Surgery, Washington University School of Medicine, St. Louis, MO.*

BACKGROUND: Preoperative factors that reliably predict lymph node (LN) metastases in pancreatic neuroendocrine tumors (PanNETs) are unclear. The number of LNs needed to accurately stage PanNETs has not been defined. METHODS: Patients who underwent curative-intent resection of primary non-functional PanNETs at 8 institutions from 2000-2016 were analyzed. Tumors with poor differentiation and Ki-67>20% were excluded. Preoperative factors associated with LN metastases were identified. A procedure specific target for LN retrieval to accurately stage patients was determined. RESULTS: Of 2182 pts with GI NETs, 695 underwent resection of PanNETs. 33% of tumors were proximal (head/uncinate), and 67% were distal (neck/body/tail). 26% of pts (n=158) had LN+ disease, which was associated with worse 5-yr recurrence-free survival (RFS) (60%vs86%; p<0.001; Fig1A). Increasing number of +LNs was not associated with worse RFS. Preoperative factors associated with +LNs included tumor size ≥2 cm (OR6.6; p<0.001), proximal location (OR2.5; p<0.001), moderate vs well differentiation (OR2.1; p=0.006), and Ki-67≥3% (OR3.1; p<0.001). LN metastases were also present in tumors without these risk factors: <2cm (9%), distal location (19%), well differentiated (23%), and Ki-67<3% (16%). Median LN retrieval was 13 for pancreatoduodenectomy (PD), but only 9 for distal pancreatectomy (DP). Given that PD routinely includes a complete regional lymphadenectomy, a minimum number of LNs to accurately stage pts was not identified. For DP, however, removal of <7 LNs failed to discriminate 5-yr RFS between LN (+) and (-) pts (<7 LNs: 72%vs83%, p=0.198, Fig1B; ≥7 LNs: 67%vs86%, p=0.002; Fig1C). CONCLUSION: Tumor size ≥2 cm, proximal location, moderate differentiation, and Ki-67≥3% are preoperative factors that predict LN positivity in resected non-functional PanNETs. Given the 9-23% incidence of LN metastases in patients without such risk factors, routine regional lymphadenectomy should be considered. Pancreatoduodenectomy inherently includes sufficient LN retrieval, while distal pancreatectomy should aim to remove ≥7 LNs for accurate staging.



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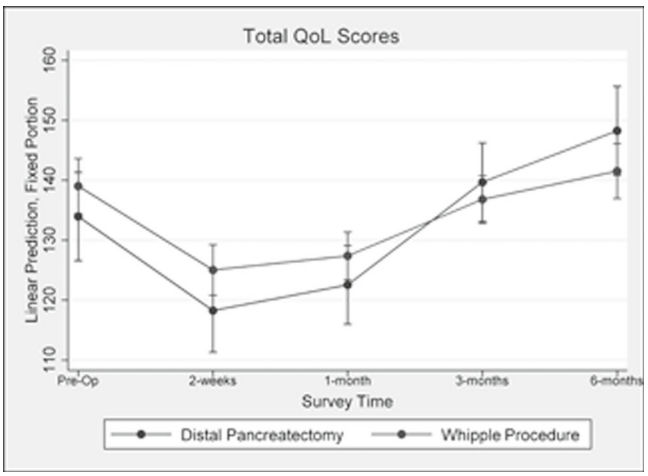
Quality of Life Following Major Laparoscopic or Open Pancreatic Resection R. Torphy,[1]* B. Chapman,[1] C. Friedman,[1] A. Paniccia,[1] C. Ryan,[2] C. Meguid,[1] C. Bartsch,[1] E. McIntyre,[1] M. McCarter,[1] R. Schulick,[1] B. Edil,[1] A. Gleisner.[1] *1. Univeristy of Colorado, Department of Surgery, Aurora, CO; 2. University of South Florida School of Medicine, Tampa, FL.*

Despite significant improvement in post-operative mortality following major pancreatic resection, morbidity remains high, and we lack an objective understanding of how major pancreatic resection affects quality of life (QoL). QoL was assessed with the Functional Assessment of Cancer Therapy-Hepatobiliary questionnaire in patients undergoing distal pancreatectomy (DP) or a Whipple procedure (WP). Surveys were completed pre-operatively, and 2 weeks, 1-, 3-, and 6-months post-operatively. Multilevel regression modeling was used to determine the variability in each domain using a linear spline to allow for different trajectories within the first 2 weeks (post-operative period) and thereafter (recovery period). Among 159 enrolled patients, 71.7% underwent a WP (32.5% lap), 28.3% underwent DP (57.8% lap). Patients completed a mean of 4.0 out of 5 surveys and reported a significant decrease in physical, functional, hepatobiliary, and total QoL over post-operative period followed by significant improvement in these domains in the recovery period. Patients who experienced a readmission within 90 days had a significantly greater drop in all QoL domains in the post-operative period compared to those not readmitted ($p<0.001$). Patients undergoing a DP vs WP had equivalent decreases in their total QoL scores in the post-operative periods, but those who underwent DP returned to their baseline total QoL faster than patients undergoing WP (1.0 vs 3.0 months, $p=0.002$). Patients undergoing laparoscopic surgery had a higher initial total QoL scores, but there was no significant impact of open vs laparoscopic surgery on change in QoL scores over the post-operative or recovery periods. Survey response rate did vary by surgical approach with a significant difference in mean response rate between patients undergoing laparoscopic WP (mean 4.4) and open WP (mean 3.67) ($p=0.001$). Major pancreatic resection results in a significant decrease in QoL post-operatively, and a larger decrease in QoL post-operatively is strongly associated with 90 day readmission. The decrease in post-operative QoL is similar between DP and WP; however, patients who undergo a DP return to their baseline total QoL at a faster rate.



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Interferons Induce Nucleotide Insufficiency and Sensitize Pancreatic Cancer Cells to Replication Stress A. Dann,* E. Abt, I.A. Elliott, S. Kim, T. Le, D.A. Tucker, C. Matsumura, J. Capri, W. Kim, S. Poddar, L. Li, N. Wu, M. Girgis, C. Radu, T. Donahue. *General Surgery, UCLA, Los Angeles, CA.*

Background Pancreatic ductal adenocarcinoma (PDAC) is characterized by an inflammatory tumor microenvironment with high baseline levels of interferons (IFNs) that can also be induced by immune-based therapies. In addition to the well-studied effects on immune cell function, we propose an important and novel role for IFNs in modulating tumor cell nucleotide metabolism and sensitizing them to inhibitors of the replication stress response (RSR) pathway. Methods Immunohistochemistry was performed on primary PDAC specimens. Where indicated PDAC cells were treated with 100U/mL IFNβ±500nM VE822, an established inhibitor of ATR, the key effector kinase of the RSR pathway. Labeled intracellular dNTPs generated from [^{13}C]glucose were quantified using liquid chromatography mass spectrometry (LC-MS). A SAMHD1 knock-out (KO) cell line was generated using CRISPR/Cas9. Immunoblots were performed on cell lysates. Growth curves were generated using tryptan blue exclusion. Results Moderate to strong STAT1 staining was observed in 68% (17/25) of patient tumors. In vitro, IFNβ exposure of PDAC cells increased expression of the dNTP hydrolase, SAMHD1 and significantly reduced in all four dNTP pools (Fig. 1a,b). This was accompanied by activation of the RSR pathway as indicated by the phosphorylation of CHEK1 and was generalizable to a larger panel of PDAC cell lines (Fig 1b). SAMHD1 KO abrogated the decrease of dCTP levels in response to IFNβ (Fig 1c), implicating it as the key mediator of IFN-induced dNTP pool depletion. Co-treatment of IFN-exposed cells with VE822 further decreased dCTP levels (Fig. 1d). Concordantly, the combination of IFNβ and VE822 robustly induced apoptosis, as indicated by cleavage of PARP and caspase 3 and 8 proteins, and yielded a synergistic cytotoxic effect (Fig. 1e,f). Conclusions Here we demonstrate that IFN exposure results in a critical depletion of dNTP pools in PDAC cells, thus sensitizing them to the RSR inhibitor, VE822. This work suggests future therapies combining immune-based therapies that stimulate IFN production with RSR inhibitors represent viable treatment strategies in a lethal disease notoriously resistant to traditional chemotherapies.

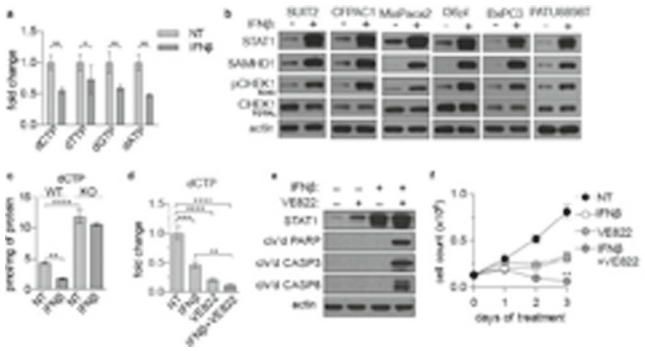

Figure 1: (a) LC-MS measurements of intracellular [^{13}C6]glucose-labeled dNTPs in SUIT2 cells (b) Immunoblot of PDAC cells treated with IFNβ. (c,d) LC-MS measurements of intracellular [^{13}C6]glucose-labeled dNTPs in (c) SUIT2 WT or SAMHD1 KO cells treated with IFNβ and (d) SUIT2 cells treated with IFNβ ± VE822. (e) Immunoblot and (f) growth curve of SUIT2 cells treated with IFNβ ± VE822. IFNβ: 100U/mL, VE822: 500nM. **p<0.01, ***p<0.001, ****p<0.0001.

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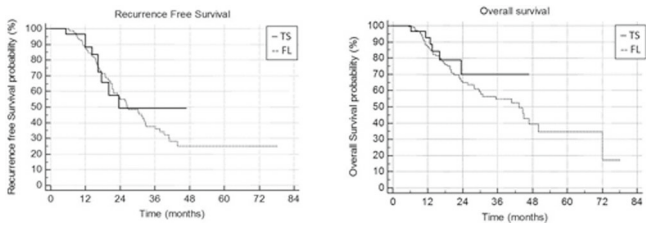
Chemotherapy Switch for Borderline/Locally Advanced Pancreatic Cancer is Not Detrimental and Allows Optimal Sequencing and Survival L. Yohanathan,* R.L. Smoot, M.H. Staebler, S.D. Guru, J.M. Wiisanen, J. Hubbard, T. Halfdanarson, C. Hallemeier, A. Grothey, R. McWilliams, H. Yoon, T.S. Bekaii-Saab, S.P. Cleary, M.L. Kendrick, D.M. Nagorney, M. Truty. *Hepatobiliary Surgery, Mayo Clinic, Rochester, MN.*

Background: Neoadjuvant chemotherapy (NAC) for borderline (BR)/locally advanced (LA) pancreatic ductal adenocarcinoma (PDAC) is recommended with modern combinatorial regimens. Optimal chemotherapeutic strategy is yet defined. We sought to evaluate incidence, indications, and outcomes of pts requiring systemic chemotherapy change and its effect on survival. Methods: Single site, retrospective review of BR/LA PDAC patients whom underwent NAC between 2013-2017. We identified a cohort receiving first line (FL) chemotherapy with FOLFIRINOX (FFX) or gemcitabine/nab-paclitaxel (GA) alone and a cohort requiring therapeutic switch (TS) to second line regimen. In patients deemed resectable after NAC in absence of metastatic disease, resection was performed. Results: 267 pts identified underwent NAC. In total 78 (29%) required TS from FL therapy; 87% switched from FFX to GA and 13% from GA to FFX. Indications for TS were non-metastatic progression/lack of objective response in 85% and toxicity/intolerance in 15%. 49 pts did not undergo curative resection after TS: 74% with progression/metastatic disease, 16% unresectable/unfit or refused surgery, and 10% awaiting surgery. The

median survival in these unresected pts after TS was 20.2 months. Of 218 pts undergoing resection, 189 (86%) received FL only, and 29 (14%) required TS. 77 (35%) pts developed recurrent disease with no differences between cohorts; 68 (36%) recurrences in FL only and 9 (32%) in TS (p = 0.68). The median RFS was 26.4 months with no difference between cohorts (p=0.69). 63 (29%) pts died at last follow-up with no differences between cohorts; 57 (30%) deaths in FL only and 6 (21%) in TS (p=0.33). The median OS was 44.6 months with no difference between cohorts (p=0.41). Conclusion: A significant proportion of PDAC patients undergoing NAC require chemotherapeutic switch with no apparent detriment to recurrence/survival outcomes. Changing NAC regimens should be considered if no objective responses are seen or for toxicities after FL therapy to ensure optimal systemic treatment and to improve postoperative oncologic outcomes in patients candidates for resection.



Recurrence Free Survival and Overall Survival comparison between TS and FL groups. Details in abstract.

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Effect of PET-CT on Disease Recurrence and Its Management in Patients with Potentially Resectable Colorectal Cancer Liver Metastases: The Long-term Results of a Randomized Controlled Trial P. Serrano,[1]* C. Gu,[1] M. Husien,[2] D. Jalink,[7] G. Martel,[3] M.E. Tsang,[4] J.L. Hallet,[5] S. Gallinger,[6] A. Ritter,[7] V. McAlister,[8] N. Sela,[8] H. Solomon,[4] K. Beyfuss,[9] C. Li,[1] E. Lee,[1] C. Moulton,[10] M.N. Levine.[1] *1. Surgery, McMaster University, Hamilton, ON, Canada; 2. Grand River Regional Cancer Centre, Kitchener, ON, Canada; 3. The Ottawa Hospital, Ottawa, ON, Canada; 4. University of Toronto, Toronto, ON, Canada; 5. Odette Cancer Centre, Toronto, ON, Canada; 6. Mount Sinai Hospital, Toronto, ON, Canada; 7. Queen's University, Kingston, ON, Canada; 8. University of Western, London, ON, Canada; 9. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 10. Toronto General Hospital, Toronto, ON, Canada.*

Background: PETCAM randomized trial evaluated the effect of PET-CT vs. no PET-CT on surgical management in patients with colorectal cancer liver metastases. 8% of patients had change in surgical management, including more major liver resections with PET-CT arm. Here, we compare groups for 5-year disease free (DFS) and overall survival (OS), evaluated their long-term clinical course, i.e. sites and management of recurrence. Methods: Recruitment occurred between 2005-2010, with last follow-up in 2013. Data on recurrence, management and mortality from 2013-2017 was collected from patient's charts. Recurrence according to site and management were described. Risk of recurrence/death were calculated using Cox proportional Hazard Model. OS was calculated with Kaplan-Meir and compared with log-rank test. Results: At 5 years, 157/404(39%) patients were alive and 19 were lost to follow-up. Median follow-up: 4.2 years. There were no differences in DFS (HR: 1.12, 95%CI: 0.88-1.42) or OS (HR: 0.97, 95%CI: 0.74-1.28). Median DFS for the 372 patients who had liver surgery was 17 months, 95%CI: 15-19. Recurrence risk factors were: extrahepatic disease, tumour size, and nodal stage. Median OS was 50 months, 95%CI: 44-64. Death risk factors also included age and prior chemotherapy. During follow-up, 287/404, 71% patients recurred (mostly liver and lung); 48% were treated with chemotherapy and 35% were treated with surgery with curative intent. Of these, the majority recurred (109/116, 94%). Median OS following first recurrence was 28 months, 95%CI: 23-30, longer for those who had surgery (53 months, 95%CI: 38-71). Death after recurrence risk factors included: number of recurrence sites and disease free duration since liver resection. Conclusions: PET-CT did not improve DFS or OS. Survival following liver resection is similar to previous reports, with most patients experiencing disease recurrence. A substantial proportion of patients who recur undergo surgery, however it is likely that they will recur again. Survival following surgery for recurrence is similar to survival following liver resection.

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Genomic Profiling of Intrahepatic Metastases Versus Localized Satellites in Intrahepatic Cholangiocarcinoma E. Simoneau,* Y. Chun, T. Karpinets, J. Zhan, X. Song, M. Javle, R. Shroff, A. Futreal, J. Vauthey, J. Estrella. *Surgery, MD Anderson Cancer Center, Houston, TX.*

Background: In multifocal intrahepatic cholangiocarcinoma (IHC), intrahepatic metastases (IM) represent a contraindication to resection, whereas localized satellites (LS) do not. No consensus criteria exist to distinguish IM from LS. The purpose of this study was to determine genetic alterations in multifocal IHC that would discriminate IM and LS. Methods: DNA from multiple resected tumors and adjacent normal liver from 6 patients undergoing hepatectomy was subjected to next-generation sequencing using a custom-designed targeted gene panel to detect copy number variation and somatic mutations in 201 cancer-associated genes. Proposed definitions in the literature were applied to categorize IM and LS lesions. Results: The median number of tumors per patient was 3 (2-47). Median sizes of the dominant and smaller tumors were 8.3(5.5-17.5) cm and 0.5(0.1-3.5) cm respectively. Seven IM lesions and 6 LS lesions were subjected to molecular analysis. Somatic mutations were identified in 5 patients, with 3 (range 1-5) mutations per tumor. For each of these 5 patients, potentially actionable driver mutations were ubiquitously present in all tumors. Mutations were concordant between the primary and smaller tumors in the chromatin remodeling genes BAP1 (Patients 1 and 2) and SMARCA4 (Patient 3). CHL1 which encodes a cell adhesion molecule, and MED12, which regulates DNA transcription, were shared among all tumors from Patients 4 and 5, respectively. In Patient 6, somatic mutations were not detected in any of the tumors sequenced. Copy number variation analysis demonstrated similar patterns among all tumors from an individual patient. Conclusion: In this cohort of multifocal IHC, genomic profiles were concordant among all tumors for each individual patient, suggesting a common progenitor cell origin, regardless of the location of tumors in the liver. Decision to perform surgery should not be based upon perceived biological differences between IM and LS, which both represent clones derived from the primary tumor. These results also imply that single tumor biopsy, to guide targeted therapy, should represent the molecular alterations present in all lesions.

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Resection is More Effective than Ablation for Early Hepatocellular Carcinoma: A Matched-Cohort Analysis A.D. Newton,* A.J. Sinnamon, M.K. Lee IV, D.L. Fraker, G. Karakousis, R. Roses. *University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA.*

Background: The optimal treatment strategy for AJCC stage I hepatocellular carcinoma (HCC) has not been established. Overall survival rates after radiofrequency ablation (RFA), resection, and transplant for clinical stage I HCC ≤ 5 cm were compared. Methods: Patients with clinical stage I HCC ≤ 5 cm treated with RFA, resection, or transplant were identified from the National Cancer Database (NCDB) (2004-2014). Predictors of treatment selection were identified with multinomial logistic regression. Overall survival (OS) was evaluated using Kaplan-Meier estimates stratified by tumor size. After excluding transplant, multivariable Cox regression identified covariates independently associated with worse OS, which were then used to match (1:1) patients undergoing resection versus RFA. Results: 10,197 patients with clinical stage 1 HCC ≤ 5 cm underwent RFA (n=4,768), resection (n=2,531), or transplant (n=2,988). RFA, resection, and transplant rates were 49.2, 16.7, and 34.1% for tumors ≤ 2.0 cm; 49.7, 20.9, and 29.4% for tumors 2.1-3.0 cm; and 38.3, 37.1, and 24.6% for tumors 3.1-5.0 cm, respectively. Predictors of selection of RFA rather than resection were white race, Charlson-Deyo comorbidity (CDC) = 2, grade 1, elevated AFP, higher bilirubin, higher INR, and size ≤ 2 cm. At a median 71.5 months follow-up, in all tumor size categories, median OS was better with transplant or resection compared to RFA (tumors ≤ 2.0 cm: 131.4 vs. 88.8 vs. 48.4 months; tumors 2.1-3.0 cm: not reached vs. 72.2 vs. 44.1 months; tumors 3.1-5.0 cm: 135.0 vs. 61.7 vs 32.1 months, P<0.0001, transplant vs. resection vs. RFA, respectively). Increasing age, CDC = 2, worsening grade, greater tumor size, higher bilirubin, higher INR, and RFA were independently associated with worse survival. Among 2362 patients who underwent RFA or resection matched 1:1 on these other covariates, resection was associated with better median OS for all tumor sizes (resection vs. RFA: 88.8 vs 40.8 months, ≤ 2.0 cm; 76.2 vs. 41.9 months, 2.1-3.0 cm; 69.1 vs. 31.9 months, 3.1-5.0 cm, P<0.0001). Conclusions: Overall survival is superior after resection compared to RFA in stage 1 HCC. Resection is likely underutilized.

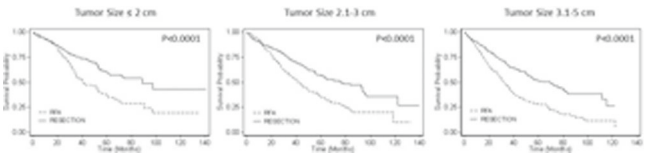

Figure 1: Overall survival with RFA vs. resection in the matched cohort stratified by tumor size.

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Is Low-Volume Disease in the Sentinel Node After Neoadjuvant Chemotherapy an Indication for Axillary Dissection? T. Moo,* M. Edelweiss, S. Hajiyeva, M. Stempel, M. Raiss, A.V. Barrio, M. Morrow. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction Frozen section (FS) evaluation of sentinel lymph nodes (SLNs) after neoadjuvant chemotherapy (NAC) has a higher false-negative (FN) rate than in the primary surgical setting, particularly for small tumor deposits. The additional tumor burden seen with isolated tumor cells (ITCs) and micrometastases in the primary surgical setting is low, but it is unknown whether the same is true after NAC. We examined the FN rate of FS after NAC and the association between size of SLN metastasis and residual axillary disease at axillary dissection (ALND). Methods Patients undergoing SLN biopsy after NAC were identified from a prospectively maintained institutional database. The association between size of SLN metastasis and residual axillary disease on ALND was examined using the Kruskal-Wallis test and Fisher's exact test. From July 2008-July 2017 702 patients (711 cancers) had SLN biopsy after NAC. On FS 181 had metastases, and 530 were negative; 33 negative cases were positive on final pathology (FN rate 6.2%). Among patients with a positive result on FS, 3 (2%) had ITCs and no further disease on ALND. 41 (23%) had micrometastases and 125 (69%) had macrometastases. 59% of those with micrometastases and 63% with macrometastases had ≥1 additional positive lymph node at ALND, and patients with macrometastases had greater numbers of additional positive nodes (Table)(p=0.03). Among those with a FN result, 10 (30%) had ITC, 15 (46%) micrometastases and 8 (24%) macrometastases. 17 had ALND and 59% had ≥1 additional positive lymph node. Overall, 1/6 (17%) patients with ITC and 22/44 (50%) with micrometastases had additional nodal metastases at ALND. Conclusion Low-volume disease in the SLN after NAC is not an indicator of a low risk of additional positive axillary nodes. These tumor cells are potentially drug resistant and are an indication for ALND, even when not detected on intraoperative frozen section.

Frequency of additional positive nodes at axillary dissection in patients with positive sentinel nodes after neoadjuvant chemotherapy

Additional positive ALN	Frozen Section: Positive			Frozen Section: False Negative		
	ITC (n=3)	Micromet (n=41)	Macromet (n=125)	ITC (n=10)	Micromet (n=15)	Macromet (n=8)
0	3 (100%)	15 (37%)	42 (34%)	2 (20%)	1 (7%)	4 (50%)
1	0	10 (24%)	21 (17%)	0	3 (20%)	1 (13%)
2	0	8 (20%)	13 (10%)	0	3 (20%)	2 (25%)
≥3	0	4 (10%)	38 (30%)	1 (10%)	0	0
Unknown	0	*4 (10%)	*11 (9%)	7 (70%)	8 (52%)	1 (13%)
P-value	0.03			0.2		

ALN, Axillary lymph node; ITC, isolated tumor cells. Unknown values represent patients who did not have axillary dissection. *Patients enrolled in Alliance A11202 trial and randomized to no-ALND arm

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Patients with HER2 Positive or Triple Negative Breast Cancer (TNBC) Treated with Neoadjuvant Chemotherapy Who Achieve a Breast Pathologic Complete Response have Low Rate of Nodal Positivity A.U. Barron,* T. Hoskin, C. Day, J.C. Boughey. *Surgery, Mayo Clinic, Rochester, MN.*

BACKGROUND Patients (pts) with breast cancer treated with neoadjuvant chemotherapy (NAC) have high rates of pathologic complete response (pCR). A recent single center study of 290 pts with clinically node negative TNBC or HER2+ reported that 100% of the 116 pts who achieved a breast pCR after NAC were pathologically node negative (pN0). The study's aim was to review the National Cancer Database (NCDB) and evaluate these rates in a multicenter database including academic and community settings. METHODS NCDB data from 2010-2014 was reviewed to identify pts with cT1-2, cN0-1 breast cancer treated with NAC followed by surgery. We compared pathologic nodal positivity (pN+) rates by breast pCR (vs residual disease in the breast) within each tumor subtype (HER2+; TNBC; HR+/HER2-) both in pts with cN0 and cN1 disease at presentation. Breast pCR was defined as ypT0 or ypTis on final pathology. RESULTS We identified 22695 pts with cT1-2 disease treated with NAC followed by surgery (12806 cN0, 9889 cN1). In cN0 HER2+ disease, 42.8% (1846/4313) achieved a breast pCR and of those, only 1.6% (95% CI:1.1-2.3%) were pN+. Similarly, in cN0 TNBC, 35.4% (1570/4440) achieved a breast pCR and only 1.7% (95% CI:1.2-2.5%) were pN+. Rates of pN+ were significantly higher (p<0.001) among cN0 patients without breast pCR (18.0% in HER2+ and 12.4% in TNBC). Among cN1 pts with HER2+ disease, 40.7% (1261/3100) achieved a breast pCR with 12.8% (162/1261) pN+, and in TNBC pts, 34.9% (899/2579) had a breast pCR with 14.3% (129/899) pN+. In HR+/HER2- disease, breast pCR rates were lower (11.7% in cN0 and 12.9% in cN1) and pN+ rates were 4.0% and 33.9% in cN0 versus 30.1% and 82.5% in cN1 pts with and without breast pCR, respectively. CONCLUSION Pts with HER2+ and those with TNBC treated with NAC have high rates of eradication of disease from the breast. In cN0 pts that achieve a breast pCR, axillary nodes were positive in <2% of HER2+ and TNBC cases, supporting that omission of axillary surgery could be considered in this subset of pts. Response rates in the breast in HR+/HER2- disease were significantly lower.

Table 1: Pathologic node status by breast pCR vs not, stratified by cT and cN category

	Breast – Path Complete Response			No Breast – Path Complete Response		
	Biologic Subtype	Pathologic Node Status		Biologic Subtype	Pathologic Node Status	
		pN0	pN+		pN0	pN+
cN0	HER2+			HER2+		
	cT1N0	517 (98.9%)	6 (1.1%)	cT1N0	586 (83.4%)	117 (16.6%)
	cT2N0	1,299 (98.2%)	24 (1.8%)	cT2N0	1,436 (81.4%)	328 (18.6%)
	HR-/HER2-			HR-/HER2-		
	cT1N0	371 (97.9%)	8 (2.1%)	cT1N0	566 (86.9%)	85 (13.1%)
	cT2N0	1,172 (98.4%)	19 (1.6%)	cT2N0	1,947 (87.7%)	272 (12.3%)
	HR+/HER2-			HR+/HER2-		
	cT1N0	101 (93.5%)	7 (6.5%)	cT1N0	436 (64.4%)	241 (35.6%)
	cT2N0	356 (96.7%)	12 (3.3%)	cT2N0	1,927 (66.4%)	973 (33.6%)
cN1	HER2+			HER2+		
	cT1N1	265 (86.3%)	42 (13.7%)	cT1N1	133 (34.9%)	248 (65.1%)
	cT2N1	834 (87.4%)	120 (12.6%)	cT2N1	568 (39.0%)	890 (61.0%)
	HR-/HER2-			HR-/HER2-		
	cT1N1	178 (79.1%)	47 (20.9%)	cT1N1	82 (26.9%)	223 (73.1%)
	cT2N1	592 (87.8%)	82 (12.2%)	cT2N1	495 (36.0%)	880 (64.0%)
	HR+/HER2-			HR+/HER2-		
	cT1N1	96 (64.0%)	54 (36.0%)	cT1N1	104 (14.3%)	621 (85.7%)
	cT2N1	284 (72.1%)	110 (27.9%)	cT2N1	536 (18.2%)	2405 (81.8%)

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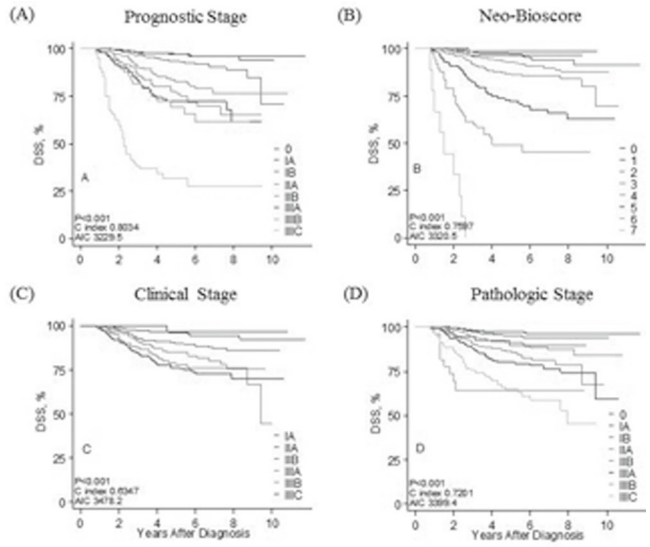
Staging for Breast Cancer Patients Receiving Neoadjuvant Chemotherapy: Utility of the 8th Edition AJCC Staging System M. Yi,* K. Hunt, I. Bedrosian, M. Chavez-MacGregor, E.A. Mittendorf. *Breast Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX.*

Background: The 8th edition AJCC staging manual defined a prognostic stage incorporating biologic factors to current standard clinical and pathologic T, N and M categories. This prognostic stage was developed using patients who underwent upfront surgery and its application in patients receiving neoadjuvant chemotherapy is not known. We had previously developed the Neo-Bioscore to improve prognostic stratification of patients receiving neoadjuvant chemotherapy. The Neo-Bioscore incorporates biologic factors with presenting clinical stage and final pathologic stage. This study was undertaken to compare the accuracy of these various staging models in predicting long term outcomes of patients receiving neoadjuvant chemotherapy. Methods: 2,363 patients treated with neoadjuvant chemotherapy from Jan 2005 - Dec 2012 at a single institution were identified and staged according to 4 systems: i) 8th edition clinical stage, ii) 8th edition pathologic stage, iii) 8th edition prognostic stage and iv) Neo-Bioscore. 5-year disease-specific survival (DSS) rates, Harrell's concordance index (C-index) and Akaike's information criterion (AIC) were compared. Results: Median follow-up was 4.2 years (range, 0.5-11.7 years). Five-year DSS was 89% (95%CI, 87%-90%). The models incorporating biologic factors including grade, ER, PR, and HER2 were the most precise (8th edition prognostic stage: C-index, 0.8034; AIC, 3229.5 [fig 1A]; Neo-Bioscore: C-index, 0.7597; AIC, 3320.5 [fig 1B] vs. 8th edition clinical stage: C-index, 0.6347; AIC, 3478.2 [fig 1C]; pathologic stage: C-in-

dex, 0.7201; AIC, 3399.4 [fig 1D]). The Neo-Bioscore provided the best separation of curves (fig 1B). Conclusion: These results confirm the importance of biologic factors in determining prognosis for breast cancer patients receiving neoadjuvant chemotherapy. The NeoBioscore, which incorporates clinical and pathologic stage, therefore reflects response to therapy, provided the greatest separation of curves suggesting it may have the most utility in counseling patients regarding prognosis. Ongoing analyses are being performed to validate these findings in a larger, population-based cohort.



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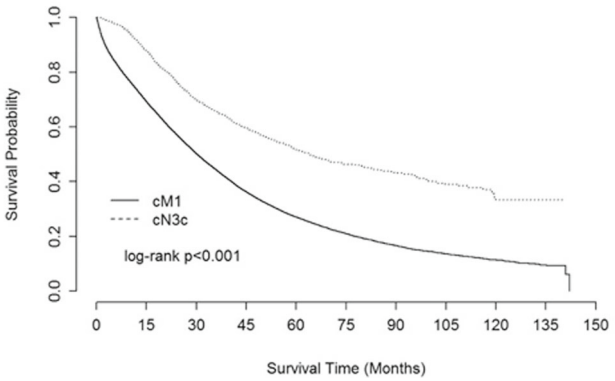
Treatment Patterns and Outcomes for Breast Cancer with Isolated Supraclavicular Metastases N. Tamirisa,* B. Campbell, Y. Ren, S.M. Thomas, O.M. Fayanju, J.K. Plichta, L.H. Rosenberger, J. Force, T. Hyslop, E.S. Hwang, R.A. Greenup. *Duke University Medical Center, Durham, NC.*

BACKGROUND: In 2002, breast cancer patients with supraclavicular nodal metastases were down-staged from stage IV to stage IIIc by the AJCC. Current NCCN treatment guidelines recommend neoadjuvant chemotherapy, lumpectomy or mastectomy with axillary lymph node dissection (ALND), and radiation therapy in these patients. We evaluated contemporary treatment patterns and outcomes among breast cancer patients with supraclavicular (N3c) nodal disease. METHODS: We used the National Cancer Data Base (2004-2014) to identify clinical stage T1-T4 breast cancer patients with SCN (cN3cM0) or metastatic disease (M1). Standard multimodal therapy was defined as receipt of chemotherapy, ALND (10+ lymph nodes removed), and radiation. Patient characteristics and treatment variables were compared between groups. Kaplan-Meier curves and the log-rank test were used to examine unadjusted overall survival (OS), and the Cox proportional hazards model was used to estimate the effect of diagnosis and treatment on OS after adjustment for known covariates. Robust sandwich covariance matrix estimates were used to account for within-hospital correlation of patient outcomes. RESULTS: In total, 2,147 patients with cN3cM0 disease were identified. 35%(N=751) received recommended multimodal therapy and 65%(1,396) did not (26% received chemotherapy only and 48% received chemotherapy and radiation without axillary surgery). Multimodal therapy was associated with improved 5-year OS compared to chemotherapy alone (62% vs. 38%, p<0.001). Guideline-concordant care increased over time from 2004 to 2013 (26% vs. 34%, p=0.04). Unadjusted 5-year survival was improved for all cN3cM0 patients when compared to M1 patients (52% vs. 27%, p<0.001, Figure 1). Worse outcome in M1 patients persisted even after adjustment for covariates (HR=1.73, 95% CI 1.59-1.88, p<0.001). CONCLUSION: Patients with cN3c breast cancer have improved OS when compared to stage IV patients. Multimodal therapy use in cN3c breast cancer is associated with improved OS when compared to chemotherapy alone, and should continue to be recommended as part of national guidelines.

Figure 1.

Unadjusted Survival for M1 vs cN3cM0 disease



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Risk of Regional Recurrence after Negative Repeat Sentinel Lymph Node Biopsy in Patients with Ipsilateral Breast Tumor Recurrence I. Poodt,[1]* G. Vugts,[1] A.J.G. Maaskant,[2] R. Schipper,[1] A.C. Voogd,[3] G.A.P. Nieuwenhuijzen.[1] *1. Catharina Hospital Eindhoven, Eindhoven, Netherlands; 2. Maxima Medisch Centrum, Veldhoven, Netherlands; 3. Maastricht University, Maastricht, Netherlands.*

Purpose:During last decade, repeat sentinel lymph node biopsy (rSLNB) in patients with an ipsilateral breast tumor recurrence (IBTR) emerged. Several studies showed a feasibility of approximately 62% and revealed the usefulness of this procedure in tailoring adjuvant treatment plans. Still, the safety in terms of regional disease control of this procedure remains unclear. This study evaluates the rate of regional recurrences as first event in patients with IBTR and a negative rSLNB, treated without additional lymph node dissection. Methods:Data were obtained from the Sentinel Node and Recurrent Breast Cancer (SNARB) study, a Dutch nationwide registration. In this study a total of 536 patients with IBTR underwent rSLNB and were treated with curative intent. In 202 patients, a tumor negative rSLNB was obtained. Results:Median age of patients at time of IBTR was 62.1 years (range, 37-87). After treatment of IBTR, 22.8% of patients underwent (re)radiation. Adjuvant hormonal therapy was administered in 56.9% of the patients and adjuvant chemotherapy in 17.3%. With a median follow-up time of 55.1 months (range, 9-152), regional recurrences (in any regional basin) occurred after a median time of 36.7 months in 5.0% (N=10) of patients as first event after IBTR and rSLNB. In 4 of these 10 patients the site of regional recurrence was in concordance with the drainage of rSLNB. Two of the 10 regional recurrences were reported in the ipsilateral axilla, resulting in an ipsilateral axillary regional recurrence rate of 1.0% in all patients. In the other 8 patients, the regional recurrences occurred ipsilateral supraclavicular (N=3), ipsilateral parasternal (N=1) and in the contralateral axilla (N=4). Univariable analysis showed that a triple negative secondary tumor was associated with developing regional recurrence as first event after a negative rSLNB (P 0.005). Conclusion:Regional recurrences as first event after IBTR occurred in 5.0% of patients with a negative rSLNB, and of which the ipsilateral axillary regional recurrence rate was 1.0%. These low relapse rates support the safety of rSLNB as primary staging in recurrent breast cancer.

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Predictive Modeling Demonstrates that Routine Axillary Ultrasound, with a Proposed Management Algorithm, Does Not Increase Rate of Axillary Lymph Node Dissection J.M. Wellington,[1]* A. Alden,[2] T. Sanders,[2] L. Stelle,[2] C. Harris,[2] M. Rosman,[2] C. Mylander,[2] L. Tafra,[2] R. Buras,[2] W. Liang,[2] R. Jackson.[2] *1. Walter Reed National Military Medical Center, Bethesda, MD; 2. Anne Arundel Medical Center, Annapolis, MD.*

Background We previously found that ~50% of patients with 1 suspicious node on axillary ultrasound (AUS) and metastasis on node needle biopsy (NNB) have N1 disease and are unlikely to need axillary lymph node dissection (ALND). 70% with ≥2 AUS-suspicious nodes and positive NNB have ≥3 positive nodes on ALND without neoadjuvant chemotherapy (NAC). We developed an algorithm using number of AUS-suspicious nodes and tumor biology to determine management (Figure); for ER+/HER2- breast cancer (BC) with a single AUS-suspicious node and positive NNB, sentinel lymph node biopsy (SNB) is performed with intraoperative x-ray documenting a retrieved clipped node. We hypothesized that routine AUS and this algorithm would decrease the number of ALND, compared to no preoperative AUS. Methods Decision tree analysis was used to assess the expected number of ALND in T1-2 BC with non-palpable nodes under two preoperative strategies (routine AUS vs. no AUS), using the proposed algorithm for routine AUS. Probabilities were drawn from literature review and an institutional database. We assumed nodal pathologic complete response rates as reported in the literature based on tumor biology. Results Using routine preoperative AUS, 29% of T1-2 BC with no palpable adenopathy would have suspicious AUS. Of those, 62% would have 1 suspicious node with 35% having a positive NNB. 38% would have > 1 suspicious node, with 45% having a positive NNB and proceeding to NAC. For a hypothetical strategy of no AUS, we assumed based on prior publications that with positive NNB, 50% of those with 1 AUS-suspicious node and 70% with ≥2 AUS-suspicious nodes would require ALND. Using the routine AUS and our algorithm, we predicted that 11% would undergo ALND, compared to 10% with a strategy of no AUS. At our institution, for every 100 T1-2 BC, 9 negative NNB and 8 positive NNB would be performed without resulting in decreased ALND rates. Discussion We were unable to demonstrate that routine AUS, with the proposed management algorithm could lead to lower ALND rates. These data argue against routine NNB of mildly suspicious, non-palpable nodes.

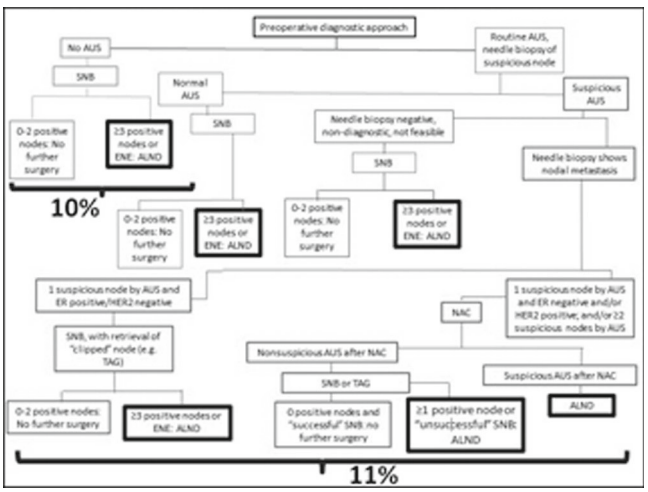

Figure. Decision tree for alternative preoperative diagnostic approaches, showing percent that would require ALND for each approach. For the approach of routine AUS, a management algorithm is employed by which patients with a single suspicious node and ER positive, HER2 negative disease still undergo SNB (including retrieval of the clipped node), e.g. a TAG procedure; other patients undergo neoadjuvant chemotherapy. A "successful" SNB after neoadjuvant chemotherapy is defined as use of dual tracer, retrieval of ≥3 lymph nodes, and retrieval of the clipped node. AUS, axillary ultrasound; SNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection; ENE, extranodal extension; ER, estrogen receptor; NAC, neoadjuvant chemotherapy; TAG, targeted axillary dissection (e.g. SNB and targeted retrieval of the clipped positive node).

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Surgical Risk Factors for the Delayed Initiation of Adjuvant Chemotherapy in Breast Cancer L.A. Riba,* A. Fleishman, T. James. *Surgery, Beth Israel Deaconess Medical Center, Boston, MA.*

Introduction: Timely administration of adjuvant therapy for breast cancer is associated with a survival benefit. Specific elements of surgical management may lead to delays initiating adjuvant chemotherapy, resulting in unfavorable outcomes. The purpose of this study was to determine the correlation between specific surgical factors and delayed adjuvant chemotherapy in patients treated for breast cancer. Methods: A retrospective analysis of the National Cancer Database was performed. The study population consisted of female patients with stage 1-3 breast cancer diagnosed between 2010 and 2014. Initiation of adjuvant chemotherapy greater than 90 days after surgery was defined as a delay in treatment. Multivariate logistic regression modeling was performed to establish associations between delayed chemotherapy and particular clinical and demographic factors of interest. Results: Of 139,071 women assessed, 4.19% had a delay in the initiation of adjuvant chemotherapy. Surgery-specific risk factors included unplanned readmission in the post-operative period (OR, 2.128; 95% CI, 1.819-2.489), lower surgical/facility volume (OR, 1.452; 95% CI, 1.308-1.613), mastectomy with immediate autologous reconstruction (OR, 1.345; 95% CI, 1.155-1.564), and positive surgical margins (OR, 1.344; 95% CI, 1.195-1.513). Conclusions: Risk factors for delayed initiation of chemotherapy specific to the surgical process were identified. Efforts should be made to address these surgical management issues and optimize the perioperative process in order to ensure timely patient treatment.

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Recurrence Score that Predicts Bone Recurrence and Worse Survival of Breast Cancer K. McDonald,* T. Kawaguchi, Q. Qi, X. Peng, S. Liu, L. Yan, K. Takabe. *Surgery, Roswell Park Cancer Insititute, Buffalo, NY.*

Introduction: Bone is the most frequent site for breast cancer metastasis which impacts quality of life and survival of the patients. Accurate risk stratification is critical to optimize patient outcomes. Traditionally, risk of metastasis is determined by clinical and pathologic variables. More recently, a genomic approach to prognostication has been adopted in malignancies such as colorectal cancer with liver metastasis. Here we sought to develop a multigene recurrence score that was both predictive and prognostic of bone metastasis in breast cancer patients (MRS-BM). Methods: mRNA-Sequence was performed on 20 fresh frozen tumor samples obtained at Roswell Park Cancer Institute. Ten patients that developed bone metastasis and ten matched patients without metastasis for more than 5 years served as the control. Two large datasets, TCGA and METABARIC, were used to evaluate the prognostic relevance of MRS-BM. Results: We found that three genes were significantly upregulated and another three genes were significantly down regulated in the bone metastasis group. We generated MRS-BM using the expression value of those six genes. A high MRS-BM was prognostic of decreased overall survival (OS) and disease free survival (DFS) in both the TCGA (n=193/893-High/Low, p=0.00005; n = 156/839-High/Low, p=0.011 respectively) and METABARIC cohorts (n=1242/662-High/Low, p<0.000001; n=1305/598-High/Low, p<0.000001 respectively). A high MRS-BM was associated with a worse OS in ER+ cancers in both the TCGA (n=134/668-High/Low, p<0.00013) and METABARIC cohorts (n= 901/558-High/Low, p<0.000001), as well as in HER2+ cancers (TCGA n=74/280-High/Low, p<0.00011; METABARIC n=1039/629-High/Low, p<0.000001). MRS-BM did not significantly associate with triple negative breast cancers. Conclusions: By utilizing a big dataset with sufficient statistical power, we found that a high MRS-BM was prognostic of survival in hormone positive breast cancer. The MRS-BM is an independent prognostic biomarker that can be used to predict bone metastasis.

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Impact of a Surgical Sealing Patch on Lymphatic Drainage After Axillary Dissection for Breast Cancer: Multicenter Randomized Phase III Swiss Group for Clinical Cancer Research (SAKK) 23/13 Trial W.P. Weber,[1]* C. Tausch,[2] S. Hayoz,[3] M. Fehr,[4] K. Ribi,[5] F. Chiesa,[6] K. Dedes,[7] G. Berclaz,[8] L. Lelièvre,[9] T. Hess,[10] U. Güth,[2] V. Pioch,[11] D. Sarlos,[12] C. Leo,[13] C. Canonica,[14] N. Gabriel,[15] E. Cassoly,[3] C. Andrieu,[3] P. Fehr,[16] M. Knauer.[6] *1. Surgery, University Hospital Basel, Basel, Switzerland; 2. Brustzentrum Zürich, Zürich, Switzerland; 3. SAKK Coordinating Center, Bern, Switzerland; 4. Kantonsspital Frauenfeld, Frauenfeld, Switzerland; 5. IBCSG Coordinating Center, Bern, Switzerland; 6. Kantonsspital St. Gallen, St. Gallen, Switzerland; 7. USZ Brustzentrum, Zürich, Switzerland; 8. Brustzentrum Bern der Lindenhofgruppe, Bern, Switzerland; 9. CHCVS Sion, Sion, Switzerland; 10. Kantonsspital Winterthur, Winterthur, Switzerland; 11. ZeTuP St. Gallen, St. Gallen, Switzerland; 12. 11Kantonsspital Aarau, Aarau, Switzerland; 13. Kantonsspital Baden, Baden, Switzerland; 14. IOSI Bellinzona, Bellinzona, Switzerland; 15. 14Stadtspital Triemli, Zürich, Switzerland; 16. Kantonsspital Graubünden, Chur, Switzerland.*

Introduction The human thrombin and fibrinogen patch TachoSil® has been suggested to reduce the lymphatic drainage after gynecologic and urologic lymphadenectomy procedures. We aimed at investigating the impact of TachoSil® on drainage after axillary dissection for breast cancer. Methods: In this phase 3 superiority trial, we randomized patients undergoing breast conserving surgery at 14 Swiss breast centers to receive vs. not receive 3 large TachoSil® patches in the dissected axilla. All patients received an axillary drain. Randomization was stratified by surgeon, levels of dissection, type of incision and use of neoadjuvant chemotherapy. Participants and the investigators assessing outcomes were masked to group assignment. The primary endpoint was total volume of axillary drainage. Results: Between March 2015 and December 2016, a total of 142 evaluable patients were randomized (72 in the TachoSil® group and 70 in the control group). The mean total volume of axillary drainage in the control group was 703ml (95% confidence interval [CI]: 512-895ml). The application of TachoSil® did not significantly reduce the total volume of axillary drainage (mean difference [MD] -110ml, 95%CI: -316-94, p=0.30). Similarly, there were no significant differences in the daily volume of drainage and duration until drain removal (MD -2ml, 95%CI: -10-7ml, p=0.71 and MD -0.4 days [d], 95%CI: -2.4-1.5, p=0.69, respectively). The length of hospital stay was longer in the TachoSil® group (MD 1d, 95%CI: 0.3-1.7, p=0.009). There were no differences regarding seroma, surgical site infection or lymphedema at 4 weeks after surgery, and the trend toward a faster decline of pain in the TachoSil® group was not significant (median time to clinically relevant reduction in pain severity 10d (95%CI: 3–27) without and 3d (95%CI: 1–5) with TachoSil®, p=0.17). All other secondary endpoints including quality of life were not significantly improved by the use of TachoSil®. Conclusions: The present trial did not show that TachoSil® significantly or relevantly reduced drainage after axillary dissection.

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A Phase 1B Study of Human Chorionic Gonadotropin: Induction of Apoptosis in Breast Cancer F. Delach,[1]* J. Sawicki,[2] E. Grujic,[1] W.B. Carter,[1] M. Truax.[1] *1. Breast Surgery, Bryn Mawr Hospital, Wyncote, PA; 2. Lankenau Hospital, Wynnewood, PA.*

BACKGROUND: Mechanisms that suppress apoptosis support the development of intrinsic or acquired resistance to chemotherapeutic agents. Thus, agents that promote apoptotic induction in breast cancer may potentially facilitate chemotherapeutic intervention and improve outcomes. Prior studies have identified that human chorionic gonadotropin (hCG) causes differentiation of glandular epithelium in normal breasts cells. Further, Luteinizing Hormone/Chorionic Gonadotropin receptor has been identified in breast cancer. We have prior identified that hCG induces apoptosis in human xenografts at 100 IU/mL by direct injection, but have not yet determined a therapeutic dose to induce apoptosis in human breast cancer. The aim of this study is to determine if hCG induces apoptosis in patients with breast cancer and to determine the therapeutic dose. METHODS: An IRB approved phase 1B trial of 9 post-menopausal patients was performed. Dose escalation was performed using 3 cohorts of 3 patients, with dosage cohorts of 100 IU/mL, 1000 IU/mL, and 10,000 IU/mL (the FDA approved dose for induction of ovulation). Core needle biopsies for each patient were assessed for hormone receptor status and Ki-67 (as a marker of proliferation). Apoptosis was determined using dUTP nick end labeling (TUNEL) assay. Each patient then received an US-directed intratumoral injection of hCG 48 hrs prior to surgery. Ki-67 and TUNEL were repeated on each surgical specimen post-injection. RESULTS: Of 9 patients, 6 were ER+/PR+, 1 was ER+/PR-, and 2 were ER-/PR-/HER2-. Apoptosis was significantly induced in all patients tested at 48 hrs. Apoptotic count increased by 8.24-fold at the lower dose, and 11.64-fold at the higher dose of hCG injection. There was no significant difference in Ki-67 expression before and after hCG injection. CONCLUSIONS: HCG induces apoptosis in human breast cancer via direct intratumoral injection. Tumor cell proliferation was not significantly altered by hCG as determined by Ki-67 testing. The study has been expanded into a pilot Phase II trial with 4 cohorts to evaluate efficacy in the major clinical breast cancer subtypes, using a dose of 10,000 IU/mL.

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Reprogramming Tumor Microenvironment to Improve Responses to Immunotherapy in Pancreatic Cancer R.Z. Panni,[1]* B. Knolhoff,[1] J. Herndon,[1] G. Hogg,[1] V. Gupta,[2] W. Hawkins,[1] R. Fields,[1] D.G. David.[1] *1. General Surgery, Washington University in Saint Louis, Saint Louis, MO; 2. Rush University Medical Center, Chicago, IL.*

Background: Survival in pancreatic cancer (PC) remains low and development of new and effective clinical approaches is critical. Modern strategies including immunotherapy have shown minimal efficacy in human PC. One way to improve response to immunotherapy is to reprogram the tumor microenvironment which includes desmoplastic stroma and abundant immunosuppressive myeloid cell infiltrate. Here we utilize a novel strategy of hyper-activating CD11b receptor using a small molecule agonist, ADH-503. ADH-503 binds to CD11b receptor, increasing its binding to ligand ICAM-1 which prevents leukocyte trans-endothelial migration. We hypothesize that hyper-activation of CD11b will reprogram myeloid cell response which will improve immunotherapeutic efficacy in PC. Methods: We utilized genetic (KPC, p48-Cre; LSL-KrasG12D; Trp53flox/flox) and orthotopic models of murine PC (KP2.0 & KrasINK) to evaluate the effect of ADH-503 on tumor growth and immune infiltrates. The tumors were analyzed using flow-cytometry and immunohistochemistry staining. Results: To determine the effect of CD11b hyper activation in murine PC, we treated orthotopic tumor bearing mice with ADH-503 for 10 days and observed a significant reduction in gross tumor weight (Fig1A&B). Analysis of myeloid cells showed that monocytes, granulocytes and macrophages were significantly reduced by ADH-503. Simultaneously there was a decrease in regulatory T cells and increase in $CD8^+$ T cell numbers, activation and proliferation. In addition, there was a significant increase in tumor infiltrating $CD103^+$ dendritic cells. We observed a significant change in gene expression profiles of tumor infiltrating macrophages after 48hrs of ADH-503 therapy, suggesting macrophage re-polarization (Fig1C). In orthotopic models of PC, which are extremely resistant to PD1 therapy, combination of ADH-503 with anti-PD1, showed significant regression of tumor growth, suggesting improved efficacy in combination with immunotherapy (Fig1D). Conclusions: Our data suggest that CD11b hyper-activation in combination with immunotherapy has the potential to overcome the barrier to T cell infiltration in PC and may be a useful strategy in the treatment of PC.

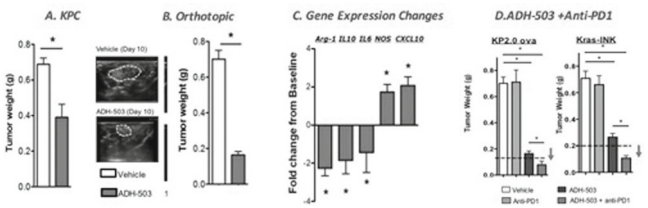

Figure 1: (A) KPC tumor weight (bar graph) and Ultrasound image after treatment with vehicle or ADH-503 for 10 days. (B) Tumor weights after 10day of treatment in orthotopic model, n=6-7/group (C) Fold expression change in macrophage gene expression after 48hrs of treatment. (D) Tumor weights in murine orthotopic modes of PC, KP2ova & KI treated with vehicle, ADH-503, +/- anti-PD1 IgGs. N=10/group, *p<0.05.

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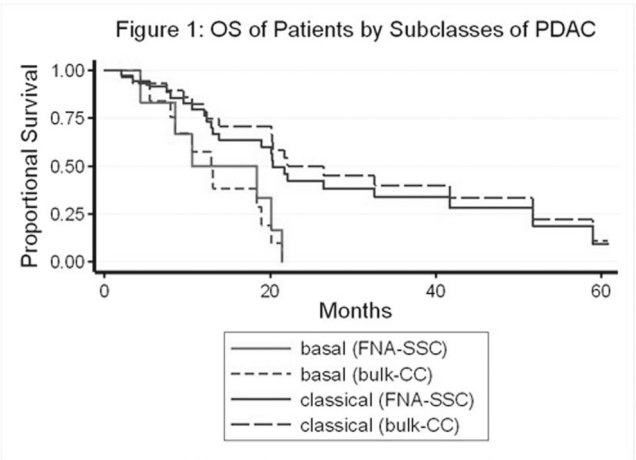
Clinically Usable Molecular Subtyping of Pancreatic Ductal Adenocarcinoma (PDAC) from Needle Biopsies B. Schmidt,[1]* R. Moffitt,[2] N. Rashid,[3] K. Voltzke,[3] G. Herrera Loeza,[1] K.E. Volmar,[3] K. Collins,[3] H. Kim,[1] J. Yeh.[1] *1. Surgical Oncology, University of North Carolina, Chapel Hill, NC; 2. Stony Brook School of Medicine, Stony Brook, NY; 3. University of North Carolina, Chapel Hill, NC.*

RNA based molecular subtypes of PDAC are emerging as predictors of tumor biology and response to therapy. Prior studies have been limited to bulk/resected tumors. Thus challenges to clinical implementation include the need to make subtype calls based on needle biopsies and to independently subtype a single sample. Using a newly developed single sample classifier (SSC) we evaluated molecular subtyping of fine needle aspiration (FNA) samples. Ex-vivo FNAs were performed using an 18 g needle x 3 passes on 43 patients undergoing surgery for PDAC. All patients had matched bulk tissue available. A SSC was developed for the subtyping of a single tumor sample. This was compared to hierarchical consensus clustering (CC) methodology previously developed. SSC results were compared between FNA and bulk samples and compared to CC calls. Overall survival (OS) was evaluated in both FNA and matched bulk samples. 29 patients had classical and 14 patients had basal-like subtype tumors by CC of bulk samples. Agreement between SSC and CC subtype calls of bulk samples was 90%. Agreement between FNA and bulk SSC subtype calls was 86% and 90% when 3 patients with indeterminate scores were excluded. Patients with basal-like subtype tumors classified with either CC or SSC had significantly shorter survival (p = 0.0004 CC-bulk; p = 0.0004 CC-FNA; p = 0.01 SSC-bulk; p = 0.02 SSC-FNA). Median survival of patients with basal-like tumors by SSC-FNA was 10.5 months compared to 12.9 months in basal-like patients called by CC of bulk samples. Median survival of patients with SSC-FNA classical tumors was 20.3 months compared to 22.1 months by CC of bulk samples. We have developed a clinically usable SSC with high accuracy for FNA samples that determines molecular subtypes in PDAC patients and continues to be prognostic. While further prospective validation is needed, this will be a promising approach for selecting patients for neoadjuvant therapy.



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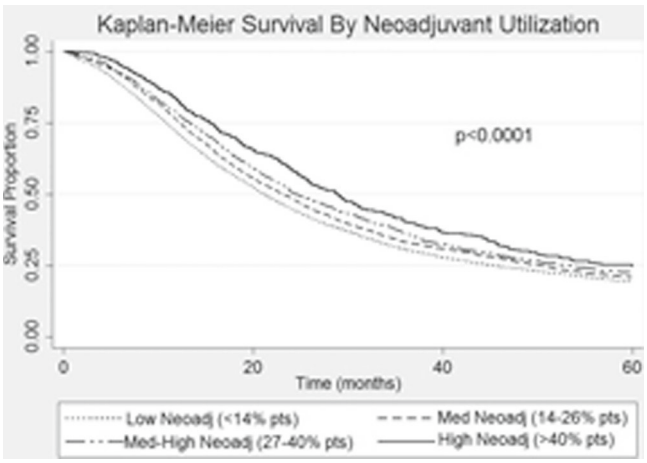
Neoadjuvant Therapy Utilization for Pancreatic Cancer Among High Volume Surgical Centers: Is It a Marker of Quality? A. Fisher,* D. Abbott, S. Campbell-Flohr, S. Ronnekleiv-Kelly, C. Greenberg, E.R. Winslow, S. Weber. *University of Wisconsin, Madison, WI.*

INTRO: Many surgeons advocate the use of neoadjuvant treatment for resectable pancreatic cancer, however little is known about variation in the utilization of neoadjuvant therapy at the hospital level. METHODS: The National Cancer Data Base was used to identify patients undergoing resection for pancreatic cancer between 2006-2014 at high volume centers performing >10 pancreatectomies annually. Hospitals were grouped by neoadjuvant therapy utilization using standard deviations (sd) from the mean as follows: high neoadjuvant utilizers (>2 sd above the mean, >40% of patients receiving neoadjuvant therapy), medium-high (1-2 sd, 27-40%), medium (0-1 sd, 14-26%), or low (-1.1-0 sd, <14%). Outcomes were compared across neoadjuvant utilization groups, and Cox proportional hazards modelling performed to identify predictors of overall survival (OS). RESULTS: Of 20,119 patients undergoing resection at 107 high volume centers, 2,952 (14.7%) received neoadjuvant therapy. The proportion of patients receiving neoadjuvant therapy varied widely among hospitals, ranging from 0% to 74.2%, with only five centers using neoadjuvant therapy in >40% of patients. These five hospitals had the longest median OS at 28.9 months, compared to 21.1 months for low neoadjuvant utilizers (p<0.0001). R0 resection occurred more frequently at high neoadjuvant centers (86% vs 77% at low neoadjuvant centers, p<0.0001). On multivariable analysis, high and medium-high neoadjuvant utilization predicted improved OS with HR 0.86 [0.77—0.95, p=0.003] and HR 0.89 [0.83—0.96, p=0.002] respectively, compared to low utilizers. After excluding patients who underwent neoadjuvant therapy, there remained an association of improved OS in high neoadjuvant utilization hospitals (25.3 months vs 20.7 months, p<0.0001). CONCLUSIONS: High volume hospitals that more commonly utilize neoadjuvant therapy demonstrate longer survival for all patients treated at those centers, whether or not they received neoadjuvant therapy. High neoadjuvant utilization may be a marker of institutional processes and/or structural factors that contribute to improved outcomes, but further studies are needed to define these factors.



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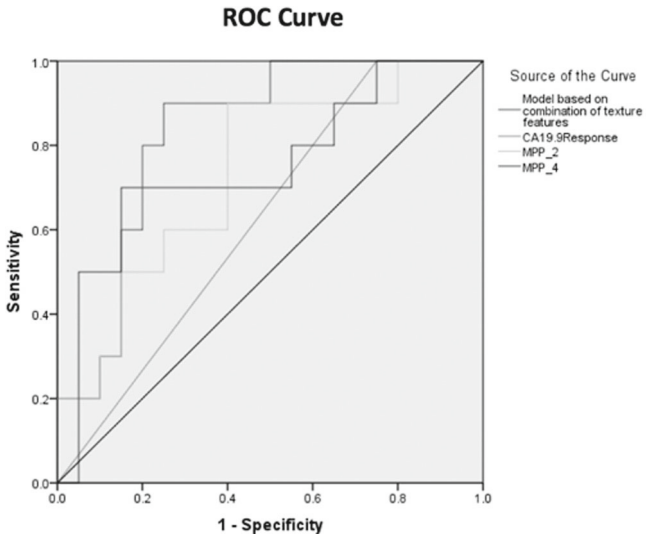
A Novel Imaging Biomarker for Assessment and Prediction of Response to Neoadjuvant Chemotherapy in Patients with Resectable Pancreatic Cancer: CT-Derived Texture Analysis N. Seiser,* M. Jennifer, R. Dewan, A. Furlan, M. Tublin, M. Hogg, A. Zureikat, H. Zeh, A. Borhani. *Surgical Oncology, UPMC, Pittsburgh, PA.*

BACKGROUND: Currently, there are no reliable imaging methods to assess treatment response to neoadjuvant therapy for pancreatic ductal adenocarcinoma(PDAC). Tumor spatial heterogeneity on CT scan is emerging as an important prognostic factor, and can be quantified with image texture analysis. We examined if CT-derived textural features correlated with histologic and biochemical treatment response in patients with PDAC. METHODS: The study included 39 patients with PDAC and a distinct mass >1cm, who underwent surgical resection. CT scans were performed before and after 2 cycles of neoadjuvant gemcitabine/nab-paclitaxel ± hydroxychloroquine. The region of interest was placed on the largest tumor cross section in late arterial phase images. CT textural features were extracted using TexRAD, which applies a 2-step filtration-histogram approach. Treatment response in surgical specimen was evaluated by Evans grade on histology. Biochemical response was defined as >50% drop in CA-19-9 level. Correlation between all parameters was assessed using Pearson and Mann-Whitney U tests. RESULTS: A statistically significant correlation was shown between kurtosis(flatness or histogram), skewness(asymmetry of histogram), SD(standard deviation of gray level distribution) and MPP(mean positive pixel) on initial CT scan and Evans grade. (r=-0.386, 0.428, -0.335 &0.312;p<0.05). Tumor heterogeneity parameters on initial CT scan were significantly different between responders and non-responders(Evans IIb-V&I/IIa). Tumor skewness and SD on post-treatment CT correlated with Evans grade(r=0.342 &0.360;p<0.05). Changes in kurtosis

and skewness correlated with biochemical response(p=0.014 &0.011). Texture parameters had better performance compared to CA-19-9 for predicting histological response based on ROC curve(0.830, 0.625;Figure). CONCLUSION: Quantitative parameters of tumor heterogeneity on baseline CT can predict response to neoadjuvant chemotherapy on histology, and outperform CA 19-9 in patients with resectable PDAC. Tumor heterogeneity is a potential imaging biomarker to predict the response to neoadjuvant chemotherapy.



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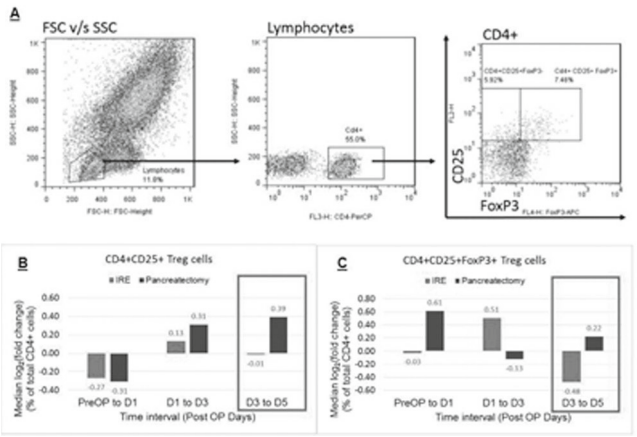
Evaluating Immunomodulation Effect of Irreversible Electroporation in Pancreatic Adenocarcinoma H. Pandit,* Y.K. Hong, Y. Li, J. Rostas III, Z. Pullium, S. Li, R.C.G. Martin. *Division of Surgical Oncology, Department of Surgery, University of Louisville, Louisville, KY.*

Introduction: Irreversible electroporation (IRE) has demonstrated an effective local modality for locally advanced (stage III) pancreatic adenocarcinoma. Immune regulatory cells (Tregs) induce immunosuppression of tumors by inhibiting patient's anti-tumor adaptive immune response. IRE creates a transient tumor lysis that may disturb Tregs post electroporation. The objective of this current study was to evaluate the immunomodulation effect of IRE with an aim to identify ideal time point for potential adjuvant immunotherapy. Methods: A prospective evaluation of an IRB approved study of patients undergoing either in situ IRE or pancreatectomy was performed. Patient blood samples were collected at different time points of PreOP, POD1, POD3, and POD5. Peripheral blood mononuclear cells were isolated and were evaluated for 3 different CD4+ Treg subsets (CD25+CD4+, CD4+CD25+FoxP3+, CD4+CD25+FoxP3-) by flowcytometry (Figure1.A). Results: Fifteen patients were analyzed with 11 in situ IRE and 4 pancreatectomy (PAN). Treg cells were calculated as a percentage of total CD4+ cells, and analyzed for median fold change between each two consecutive time points (MFC=$\log_2$(T2/T1)). CD25+CD4+ Treg cells decreased in both groups on POD1 followed by steady increase in pancreatectomy, while trend in the IRE group reversed between D3 to D5 (MFC: IRE(-0.01), PAN(+0.39); figure-1.B). CD4+CD25+FoxP3+ Treg subset showed most dramatic inverse effect for each time interval, with D3 to D5 showed most change (MFC: IRE(-0.18), PAN(+0.39); Figure1.C). CD4+CD25+FoxP3- Treg subset also showed inverse effect between D3 to D5 (MFC: IRE(-0.25), PAN(+0.49)). Altogether, an in situ IRE dramatically disturbed systemic Treg subsets compared with a pancreatectomy. Treg trend was inversely affected by IRE in situ procedure, with highest cumulative significant change for all 3 Treg subsets between D3 and D5 (MFC±SEM, IRE:-0.24±0.05, PAN: +0.37±0.02; p value= 0.016). Conclusions: Our data suggest in situ IRE procedure mediated Treg attenuation between POD3 and POD5 can provide a clinical window of opportunity to potentiate clinical efficacy in combination with immunotherapy.

Figure 1: (A) Identifying Treg subsets and analysis.Representative data showing flowcytometry workflow. FSC v/s SSC plot was gated for lymphocytes population. Next lymphocyte population was gated for CD4+ (T helper cells) and these CD4+ cells were further analyzed to identify double positive CD4+CD25+ Treg cells. Finally, FoxP3 expression was analyzed to define either (1) CD4+CD25+FoxP3+, or (2) CD4+CD25+FoxP3-(neg) Treg subsets. Comparing $\log_2$(fold change) difference between *in situ* IRE and pancreatectomy patients within **(B)** CD4+CD25+ Treg cells, and **(C)** CD4+CD25+FoxP3+ Treg cells. IRE procedure inversed Treg median fold change (MFC) between POD3 and POD5 time interval, and bring down Treg levels compared with pancreatectomy.



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COX-2 Inhibition Potentiates the Efficacy of VEGF Blockade and Promotes an Immune Stimulatory Microenvironment in Pancreatic Ductal Adenocarcinoma A. Kirane,[1]* Y. Zhang,[2] R. Brekken.[2] *1. UC Davis, Sacramento, CA; 2. UT Southwestern, Dallas, TX.*

Resistance to therapy remains a major challenge in treating pancreatic ductal adenocarcinoma (PDAC). Anti-VEGF therapy with r84 is shown to delay PDAC progression but resultant hypoxia induces a less differentiated mesenchymal-like tumor phenotype and eventual disease progression. This observation reinforces need for effective companion therapy to combat epithelial plasticity that results from anti-VEGF-induced hypoxia. Apricoxib, a novel inhibitor of COX-2, has been shown to promote tumor differentiation and improve therapeutic response in PDAC. We investigate the relationship between COX-2 activity and VEGF production in PDAC cells to evaluate the efficacy of COX-2 inhibition and VEGF blockade in preclinical models. In vitro, changes in VEGF production by PDAC cell lines following apricoxib administration were assessed. In vivo, the effect of r84, apricoxib, or the combination on tumor growth and metastases was determined in a genetically engineered mouse model of PDAC and SCID mice bearing established orthotopic pancreatic xenografts Given evidence that EMT contributes to immunosuppression in tumors, we examined the immune landscape of tumors in different treatment groups. In vitro, VEGF production occurred independently following COX-2 inhibition. Combination therapy of r84 and apricoxib had a more significant effect on reducing primary tumor size ($p<0.05$) and eliminating metastases ($p<0.01$) than single agent. Combination therapy also reversed anti-VEGF therapy-induced epithelial-mesenchymal transition and collagen deposition ($p<0.05$). and demonstrated that COX-2 inhibition combined with anti-VEGF therapy increased the level of tumor associated $CD8^+$ T cells and M1 macrophages ($p<0.001$) while reducing FasL expression on tumor endothelium ($p<0.01$). Together, these findings demonstrate that COX-2 inhibition enhances the efficacy of anti-VEGF therapy by reducing hypoxia-induced epithelial plasticity and promoting an immune landscape that supports immune activation. Targeting these molecular pathways may identify a potential strategy for improving response to emerging immunotherapies and chemotherapeutic regimens.

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Generation of Chemoresistant PDXs in the Era of Modern Neoadjuvant Therapy M. Hernandez,[1]* L. Yang,[1] J. Leiting,[1] J. Bergquist,[1] T. Ivanics,[2] M. Truty.[1] *1. Department of Hepatobiliary and Pancreas Surgery, Mayo Clinic, Rochester, MN; 2. Henry Ford, Detroit, MI.*

Background: Patient-derived xenografts (PDXs) allow for patient cancer tissue amplification and downstream in vivo research applications. A majority

of PDXs derive from treatment naïve (TN) tumors. We aimed to generate PDXs from surgically resected TN and neoadjuvant (NA) pancreatic (PDAC) cancers to compare engraftment outcomes and create modern agent chemoresistant models. Methods: We maintain a prospective GI cancer PDX program. With informed consent and IRB approval, resected PDAC tissue is implanted into immunocompromised mice. Tumor growth is monitored, viable tumor is passed into subsequent generations, and pathologists confirm PDX histopatholgy to original patient tumor. MatePair sequencing characterized generated PDXs. Outcomes include 1) ischemic time (IT - time from retrieval to implantation, and 2) engraftment (ER - % of successful engraftment). Patient clinical, pathologic, and follow-up data were abstracted. Grade III treatment response was considered chemoresistant. Results: During 1/2013-8/2017, 139 patients with histologically confirmed PDAC were implanted (48 naïve and 91 neoadjuvant) with successful PDX ER in 70 (51%) tumors that was higher for TN tumors. Mate-pair analysis demonstrated highly correlative genomic signatures to primary patient tumor and PDX. Median IT did not differ between treatment groups Table. In NA tumors successful PDX ER varied by therapy type: FOLFIRINOX (FFX) 51%, gemcitabine/nab-paclitaxel (GA) 62%, and combined FFX/GA 22%. Table compares clinicopathologic features and patient outcomes between therapy type and PDX ER. Patients with successful PDX ER had significantly worse clinical RFS and OS regardless of treatment status. In total, we generated 19 FFX, 6 GA, and 1 FFX/GA resistant PDX models for future work. Conclusion: PDX generation after NA therapy is feasible and allows for creation of chemoresistant models for future drug development. Engraftment is successful in patients with minimal treatment response. PDX growth correlates with outcomes and is a valuable translational model for any patient. These PDXs will accommodate and assess differential responses to current therapies and elucidate predictive markers of response or resistance.

	Treatment Naïve	Neoadjuvant	P value
Preoperative CA 19-9 (mg/dL)	131 [51-567]	30 [14-68]	0.006
+LN (#)	1 [0.2-4]	0 [0-1]	0.0004
% positive LN	75.6	32.6	0.0001
% +Margin status	18.3	5.6	0.02
Tumor size (cm)	3.3 [2.5-4.7]	2.7 [2.2-3.6]	0.01
% Perineual invasion	68	54	0.06
% Lymphovascular invasion	39	29	0.1
% Vascular Invasion	27	21	0.3
Ischemic time (min)	52	65	0.1
	PDX Engraftment	No PDX Engraftment	P value
% + LN	58.6	32.6	0.03
+ LN (#)	2 [1-4]	1 [0-2]	0.01
% Perineual invasion	83.3	53	0.01
% Lymphovascular invasion	50	20	0.04
% Grade III treatment response	47	19.4	0.04
% Specimen positive margin	9	0	0.03
Recurrence Free Survival (m)	14.7 [13.2-23.7]	32.7 [21-36.3]	0.0001
Overall Survival (m)	22.4 [16.5-28.4]	38.7 [29.6-38.7]	0.001

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Is Hepatectomy Justified for BRAF Mutant Colorectal Liver Metastases? J. Gagniere,[1]* S. Gholami,[1] A. Dupre,[2] D. Pezet,[3] P. Kingham,[1] P. Allen,[1] V. Balachandran,[1] R. DeMatteo,[1] J. Drebin,[1] N. Kemeny,[1] W. Jarnagin,[1] M. D'Angelica.[1] *1. Memorial Sloan Kettering Cancer Center, New York, NY; 2. Leon Berard Cancer Center, Lyon, France; 3. University Hospital of Clermont-Ferrand, Clermont-Ferrand, France.*

Introduction. Outcomes after hepatectomy for BRAF mutant resectable colorectal liver metastases (CRLM) have not been well studied. The aim of this study was to analyze clinical outcomes and prognostic variables of patients undergoing hepatic resection for BRAF mutant CRLM. Methods. All patients who underwent hepatectomy for CRLM with known BRAF status during 2001-2016 in 3 tertiary centers were analyzed. Results. Of the 4,132 patients who underwent hepatectomy for CRLM, 1,505 had complete gross resection and known BRAF status. Thirty-five (2%) patients had mutated BRAF, with a V600E mutation in 25 (71%) of 34 patients with known BRAF mutation type. Compared to BRAF wild-type patients, BRAF mutants more commonly presented with higher ASA scores (p=0.05), synchronous (77% vs 55%, p=0.01) and multiple CRLM (83% vs 54%, p<0.01), more CRLM (p<0.01), underwent more major hepatectomies (46% vs 30%, p<0.001) but had less extrahepatic disease (3% vs 10%, p<0.001). At a median follow-up for survivors of 60 and 57 months, respectively, median overall survival (OS) was 81 months for BRAF wild-type and 40 months for mutated patients (p<0.001). Of the 35 BRAF mutants, 17 (48%) and 6 (17%) were 3-year and 5-year survivors. Median recurrence-free survival (RFS) was 22 and 10 months for BRAF wild-type and mutated patients (p<0.001), respectively. The overall recurrence rate was significantly higher in BRAF mutants (91% vs 57%, p<0.001). Of the 35 BRAF mutants, there were 4 (11%) and 1 (3%) 3-year and 5-year recurrence-free survivors, respectively. For BRAF mutants, factors associated with worse OS were node-positive primary tumor, CEA level > 200 μg/L and clinical risk score ≥ 4. Factors associated with worse RFS were node-positive primary tumor and positive hepatic margin. A V600E BRAF mutation was not associated with worse OS or RFS. Conclusion. Patients with BRAF mutant CRLM are rare among patients selected for hepatic resection and more commonly present with multiple synchronous tumors. BRAF mutation is associated with a worse prognosis, however, long term survival among patients with BRAF mutant tumors is possible and associated with node negative primary tumors, low CEA levels and low clinical risk scores.

Clinicopathological and treatment features of patients who underwent complete gross resection of CRLM stratified by BRAF status*

Characteristics	BRAF wild-type (n=1470)	BRAF mutant (n=35)	p
Median age, years (range)	59 (19-91)	64 (41-85)	0.05
Sex Female Male	618 (43.1) 817 (56.9)	16 (45.7) 19 (54.3)	0.76
Median BMI, kg/m2, (range)	26 (11-49)	24 (19-41)	0.52
ASA score 1 2 3 4	57 (4.0) 635 (44.3) 439 (30.6) 19 (1.3)	0 (0) 14 (40) 21 (60) 0 (0)	0.05
Primary tumor site Colon Right Left Rectum	1051 (71.5) 488 (35.2) 563 (40.6) 336 (24.2)	28 (80.0) 19 (54.3) 9 (25.7) 7 (20.0)	0.06
Primary tumor nodal status Negative Positive	488 (34.0) 807 (56.2)	10 (28.6) 25 (71.4)	0.27
Synchronous presentation of CRLM	796 (55.5)	27 (77.1)	0.01
Median number of CRLM (range)	2 (1-15)	3 (1-8)	<0.01
Multiple lesions	781 (54.4)	29 (82.9)	<0.01
Median diameter of largest CRLM, cm (range)	3 (0-22)	2 (1-7)	0.05
Largest CRLM > 3 cm	504 (35.1)	9 (25.7)	0.22
Largest CRLM > 5 cm	329 (22.9)	5 (14.3)	0.22
Median CEA level, μg/L (range)	7 (1-19262)	4 (1-260)	0.61
CEA level > 200 μg/L No Yes	1194 (81.2) 60 (4)	33 (94.3) 2 (5.7)	0.83
CRS 0 1 2 3 4 5	36 (3.2) 193 (17.2) 337 (30.0) 452 (40.2) 88 (7.8) 19 (1.7)	1 (2.9) 3 (8.6) 10 (28.6) 15 (42.9) 6 (17.5) 0 (0)	0.33
Extrahepatic disease at presentation	138 (9.6)	1 (2.9)	<0.001
Perioperative chemotherapy No Yes Oxaliplatin-based Irinotecan-based Bevacizumab/Cetuximab	109 (5.2) 1361 (94.8) 894 (62.3) 642 (44.7) 316 (22.0)	1 (2.9) 34 (97.1) 25 (71.4) 17 (48.6) 12 (34.3)	0.76 0.34 0.48 0.19
Median number of resected segments (range)	2 (0-7)	2.5 (0-6)	0.06
Major hepatectomy	436 (30.4)	16 (45.7)	<0.001
Colorectal synchronous resection	227 (15.8)	5 (14.3)	0.46
Type of BRAF mutation V600E Non-V600E Unknown	- - -	25 (71.4) 9 (25.7) 1 (2.9)	-
Positive margin	109 (7.6)	2 (5.7)	0.68
Median margin, mm (range)	4 (0-70)	6 (0-30)	0.89

*Values in the table are numbers of patients (percentages) unless otherwise indicated

CRLM, Colorectal liver metastases; BMI, Body mass index; ASA, American score of anesthesiologists; CEA Carcinoembryonic antigen

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Tumor Differentiation Impacts Survival in Pancreatic Adenocarcinoma Patients Receiving Preoperative Therapy

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Background: The impact of tumor differentiation on survival for pancreatic ductal adenocarcinoma (PDAC) patients after preoperative therapy remains largely undefined. We hypothesized that tumor differentiation impacts survival for PDAC patients following preoperative therapy. Methods: A retrospective analysis of a prospectively maintained database was conducted of all patients who underwent pancreatectomy for PDAC from 1988-2015. Clinicopathologic characteristics, overall (OS) and recurrence-free survival (RFS) were compared between patients who received preoperative therapy (chemotherapy, radiation, or combination) versus upfront surgery. Treatment groups were further stratified by tumor differentiation (moderate or poor). Results: Among 909 pancreatectomy patients, 491(54%) had moderately differentiated (MD) tumors and 194 (21%) poorly differentiated (PD) tumors. Median OS and RFS were significantly higher for MD versus PD patients (OS 29 vs 22.6 months, p=0.01; RFS 15.1 vs 10.3 months, p=0.05). 378 (77%) patients with MD tumors and 159 (82%) patients with PD tumors received preoperative therapy. Patients with MD tumors treated with preoperative therapy had a longer median OS (32.6 vs 25.9 months, p=0.004) but no difference in RFS relative to MD patients treated with upfront surgery. No differences in OS or RFS were observed between PD patients stratified by treatment strategy. Receipt of preoperative therapy favored survival for MD patients on univariate analysis (HR 0.71, 95% CI 0.56-0.90, p=0.004). On multivariate analysis, factors associated with improved OS for patients with MD tumors included estimated blood loss <1 liter, R0 resection, lymph node ratio <0.2, and no perineural invasion, while neither receipt nor type of postoperative therapy was associated with improved OS. Conclusions: Following preoperative therapy, improved OS was observed in resectable PDAC patients with moderately differentiated tumors but not in patients with poorly differentiated tumors. Differentiation may be an important variable to consider when determining treatment sequencing plans and preoperative treatment intensity at diagnosis.

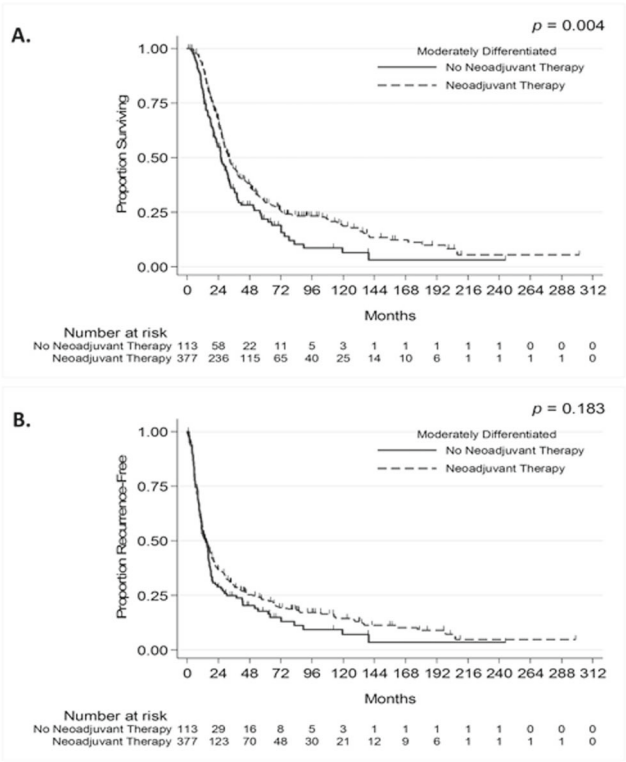

Figure 1: Overall (**A**) and recurrence-free (**B**) survival for all patients with moderately differentiated adenocarcinoma treated with surgical resection stratified by receipt of preoperative therapy.

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Lysosomal Inhibition Limits Amino Acids Availability for Nucleotide Synthesis and Sensitizes Kras-Driven Pancreatic Cancer to Replication Stress

I.A. Elliott,* A. Dann, S. Kim, W. Kim, S. Poddar, J. Williams, R. Ghukasyan, D.A. Tucker, C. Matsumura, N. Wu, L. Li, E. Abt, T. Le, M. Girgis, C. Radu, T. Donahue. *General Surgery, UCLA, Los Angeles, CA.*

INTRODUCTION Proteins degraded in lysosomes are a critical source of amino acids utilized to synthesize nucleotides and sustain the hyperproliferative state of Ras-driven cancer cells. We sought to determine if pharmacologic inhibition of lysosomal function would lead to a critical shortage of deoxyribonucleotide triphospahtes (dNTPs) in Ras-driven pancreatic ductal adenocarcinoma (PDAC) cells, thus sensitizing them to inhibitors of the replication stress response (RSR) pathway. METHODS Human and murine (KPC) PDAC cells were treated with inhibitors of lysosomal acidification, chloroquine (CQ) or NH_4Cl ± the ATR/RSR inhibitor, VE822. Labeled intracellular dNTPs generated from [^{13}C]glucose and their incorporation into DNA were quantified using liquid chromatography mass spectrometry (LC-MS). Immunoblots were performed on cell lysates. Cell viability was measured by Cell-Titer-Glo assay. KPC cells were injected SQ in the flanks of C57BL/6 mice. Mice were treated 3x/wk with CQ±VE822 (60mg/kg p.o.). Immunohistochemistry was performed on explanted KPC tumors after 3 days of CQ+VE822. RESULTS CQ treatment significantly decreased intracellular glucose-labeled dNTP pools and their incorporation into the DNA of proliferating PDAC cells (Fig.1a). This decrease was accompanied by activation of the RSR pathway as indicated by phosphorylation of CHEK1(Fig.1b). RSR induction with CQ or NH_4Cl was attenuated by supplementation with ribonucleosides or the amino acid, aspartate. Additionally, CQ-induced growth inhibition was reduced by aspartate supplementation (Fig.1c). Co-treatment with CQ+VE822 led to synergistic induction of DNA damage (via pH2A.X), and decreased cell viability in vitro (Fig.1d,e). Lastly, increased pH2A.X and impaired growth of KPC tumors were observed after CQ+VE822 treatment in vivo (Fig.1f). CONCLUSIONS We demonstrate that pharmacologic inhibition of lysosomes results in a shortage of aspartate required for de novo dNTP synthesis, leading to a critical

dNTP shortage and RSR activation. When combined with an RSR inhibitor, this leads to induction of DNA damage and synthetic lethality in PDAC cells in vitro and in vivo.

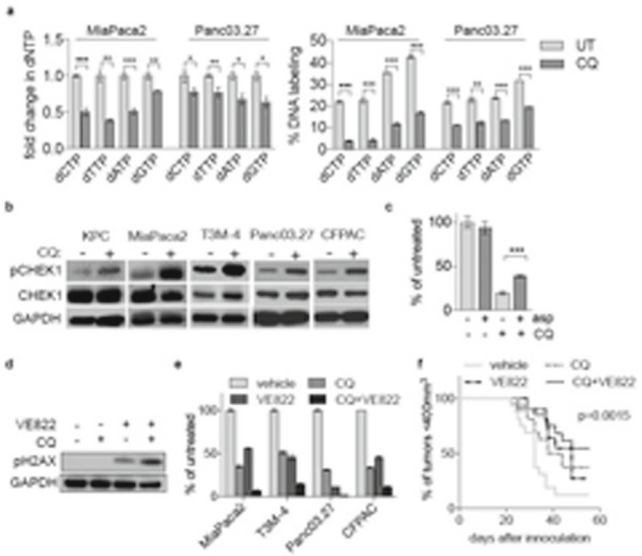

Figure 1: (a) LC-MS measurements of intracellular [^{13}C6]glucose-labeled dNTPs and [^{13}C6]glucose-labeled DNA. (b) Immunoblot of PDAC cell line panel treated with CQ (c) Viability of MiaPaca2 cells treated with CQ ± aspartate. (d) Immunoblot of MiaPaca2 cells treated with CQ ± VE822. (e) Viability of PDAC cells treated with CQ ± VE822 (f) Growth curves of mice treated with 60mg/kg CQ ± VE822. 20uM CQ, 10mM aspartate, 500nM VE822. *p<0.05, **p<0.01, ***p<0.001.

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Molecular Imaging of Colonic Neoplasms with Novel Receptor Targeted and NIR-Dye-Labeled Nanoparticles M. Jajja,[1]* H. Zhou,[1] W. Guy,[4] D. Martin,[4] D.A. Kooby,[1] A. Krasinskas,[2] H. Mao,[3] L. Yang.[1] *1. Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Pathology, Emory University, Atlanta, GA; 3. Department of Radiology and Imaging Sciences, Emory University, Atlanta, GA; 4. Cancer Animal Models Shared Resource, Emory University, Atlanta, GA.*

Introduction: Early colon cancer detection correlates with improved patient survival. Current screening modalities rely on white light visual inspection of mucosa, to identify and remove abnormal growths. Up to 10% of adenomas are missed with white light imaging. Adenomas transition to cancer through known genetic sequences. Adenomas share phenotypic features with their malignant counterparts, including genetic mutations and corresponding protein biomarker expression. We exploited the high expression of biomarkers (EGFR, IGFR, and uPAR) to detect adenomas using near infra-red (NIR)-dye labeled iron oxide nanoparticles in the APC$^{min+/-}$ transgenic mouse model of colorectal adenomas. Methods: NIR-830-malemide-dye (from our lab) was conjugated using free thiol or amine groups on targeting ligands. These were subsequently conjugated to 10nm magnetic iron oxide nanoparticles using surface carboxyl groups available on polymeric coating of nanoparticles. After a single administration of targeted dye labeled nanoparticles (300pm), mouse colons were imaged in-vivo and ex-vivo using an optical imaging system with an emission filter of 830nm. Immunohistochemistry was performed to evaluate receptor status, and an NIR imaging capable microscope was used to co-localize the targeted nanoparticles. Results: We demonstrated a significantly higher localization of targeted nanoparticles to the adenomatous regions of the colon compared to normal colonic mucosa, nearing 100% sensitivity. We also demonstrated improved targeting and delivery with EGFR coupled nanoparticles as compared with non-targeted, and other receptor (uPAR or IGFR) targeted nanoparticles. Higher expression of EGFR was observed in the adenomas compared to the other two biomarkers. This accounts for the better optical imaging results with EGFR targeted nanoparticles. Conclusion: This system has direct translational significance for colonoscopy procedures towards improved adenoma detection, where an NIR imaging capable colonoscope can be used for mucosal evaluation. Intraoperative margin status assessment during colon cancer surgery is another potential use.

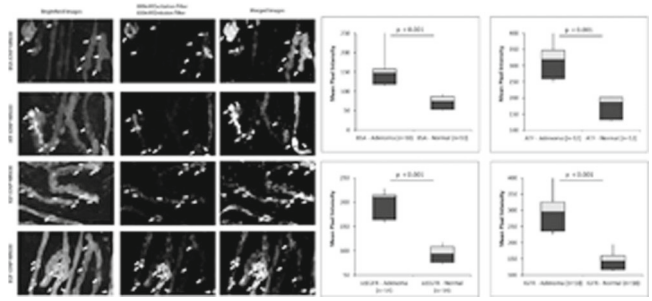

Figure 1 (a) Optical signal colocalization to adenomas with ex-vivo imaging after identification of neoplastic lesions on gross examination. (b) Significantly higher mean optical signal intensity in adenomas compared to adjacent normal mucosa for each targeted and non-targeted nanoparticle. The adenoma colocalization rate was >98% for EGFR targeted nanoparticles, 90-95% for ATF and IGFR targeting and 40% for non-targeted (BSA).

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Cytolytic Activity Score as a Marker for Intra-Tumoral Immunogenicity in Colorectal Cancer S. Narayanan,* T. Kawaguchi, L. Yan, X. Peng, Q. Qi, K. Takabe. *Roswell Park Cancer Institute, Buffalo, NY.*

Background: Increased levels of tumor infiltrating lymphocytes (TIL) often times in microsatellite instable colorectal cancer (CRC) tumor microenvironment is a known positive prognostic factor. This is likely due to direct interaction between cancer cells and cytotoxic T-cells which release cytolytic proteins including Perforin and pro-apoptotic Granzymes. We aimed to investigate this cellular interaction and correlate it with patient survival. Methods: Genomic expression and clinical data were obtained from 455 patients from The Cancer Genome Atlas (TCGA). The immune Cytolytic Activity Score (CAS) was defined using GZMA (Granzyme) and PRF1 (Perforin) expression, which was used to evaluate the association between CAS and overall (OS) and disease-free survival (DFS). We also used the CIBERSORT system to evaluate intra-tumoral immune cell composition. Results: Patients with high microsatellite instability (MSI-H) associated with high CAS. In agreement with previous reports, patients with high levels of TILs demonstrated better OS (p=0.066) and DFS (p=0.043). High CAS tumors associated significantly with high levels of activated memory CD4+ T cells (p<0.0001), gamma delta T-cells and M1 macrophages compared to the low CAS group. High CAS also directly associated with immune checkpoint molecules; PD-1 (Spearman corr.= 0.7, p<0.0001), PD-L1 (Spearman corr.= 0.675, p<0.0001), CTLA4 (Spearman corr. 0.637, p<0.0001) and regulatory T-cell markers FOXP3 (Spearman corr.= 0.517, p<0.0001) and CCR4 (Spearman corr.= 0.478, p<0.0001). CRC patients with high CAS had improved OS (p=0.019) and DFS (p=0.008) compared to low CAS patients. Multivariate analysis demonstrated that high CAS was a positive prognostic factor independent of age, lymphovascular invasion, colonic location and stage. Conclusions: High CAS within CRC tumors corresponded with improved survival likely due to increased immunogenicity and cytolytic activity of T-cells and M1 macrophages. High CAS also associated with high expression of immune checkpoint molecules and could potentially be used as a marker of the success of immune checkpoint blockade.

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Young Age-at-Onset Stage II/III Colon Cancer is Not Associated with Recurrence Risk Predicted by Tumor Gene Expression G. Chang,* Y. You. *Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: In recent decades, colorectal cancer (CRC) incidence and mortality among young adults in the US have been rising. Younger patients with CRC are more likely than older patients to receive postoperative systemic chemotherapy, despite lack of consensus on the prognostic value of patient age in this disease. Whether CRC diagnosed in younger patients is biologically different from that in older patients is not well understood. We examined

whether age-specific differences were measurable by tumor gene expression using the 12-gene Oncotype DX® Colon Recurrence Score™ (RS) test (Genomic Health, Inc. [GHI]; Redwood City, CA). The Colon RS test is validated to predict risk of recurrence in patients with stage II/III colon cancer. Methods: Among resected stage II/III (>90% stage II) colon cancers submitted for Colon RS testing by the GHI clinical laboratory, test reports from Jan 2010 to July 2017 were retrospectively identified. The Colon RS-defined recurrence risk was stratified by age at colon cancer diagnosis (age <40; 40-54; 55-64; and, ≥65). Colon cancers with known deficient DNA mismatch repair (dMMR) status were excluded. Results: A total of 21,925 Colon RS test reports have been delivered to date. Median age was 63 y; 50% were male. By age group, 3% were <40 y, 20% were 40-54 y, 27% were 55-64 y, and 50% were ≥65 y. Overall, 71% had low, 21% had intermediate, and 8% had high RS results. The overall Colon RS result distribution was similar across age groups (Table). Likewise, the expression of individual tumor genes measured in the Colon RS test were also not associated with age. Conclusions: The etiology for the increase in both incidence and mortality from CRC in persons <55 y is poorly understood. Most patients with stage II/III colon cancer, including younger patients (<55 y), have disease with low-risk for recurrence as predicted by tumor gene expression as demonstrated in this GHI clinical laboratory experience. Our findings suggest that the biology of colon cancer, as measured by the Colon RS test, is not different in younger patients and do not support the increased use of systemic chemotherapy among younger patients.

		All patients (N=21,925)	<40y (n=720)	40-54 y (n=4,482)	55-64 y (n=5,827)	≥65 y (n=10,896)
Sex,%	Male/Female	50/50	46/54	49/51	51/49	51/49
Recurrence Score result	% Low	71	72	73	72	70
	% Intermediate	21	19	19	19	19
	% High	8	8	8	8	8

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High-risk Stage II Colon Cancer: Not All Risks Are Created Equal B.D. Babcock,* M. Aljehani, B. Jabo, A. Choi, J.W. Morgan, M.J. Selleck, F. Luca, E. Raskin, M.E. Reeves, C.A. Garberoglio, S.S. Lum, M. Senthil. *Loma Linda University Medical Center, Loma Linda, CA.*

Introduction: National comprehensive cancer network (NCCN) guidelines recommend consideration of adjuvant chemotherapy in patients with stage II colon cancer with high-risk features (HRF). However, there is no quantification of the amount of risk conferred by each HRF or the overall survival (OS) benefit gained by chemotherapy based on each type of risk factor. Objective: To assess survival benefits associated with adjuvant chemotherapy among stage II colon cancer patients having one or more HRF (T4 tumors, <12 lymph nodes (LN) retrieved, positive margins, high grade tumor, perineural invasion (PNI), and lymphovascular invasion (LVI)). Methods: California Cancer Registry (CCR) data was used to identify patients diagnosed with stage II colon cancer between 2010-2013. Cox proportional regression models were used to calculate propensity score weighted all-cause mortality hazard ratios (HR) for combinations of HRF. Results: 5,160 stage II colon cancer patients were identified of which 2,374 had at least one HRF; 1,614(68%) had only one, 574(24%) had two, and 186(8%) had three or more HRF. Among the high-risk patients, 510 (21%) received adjuvant chemotherapy. Compared to patients with a single HRF, presence of any 2 or ≥3 HRF showed increasingly poorer survival (HR=1.42, C.I. 1.16-1.73 and HR=2.50, C.I. 1.96-3.20, respectively). Stratified analyses for single or two HRF showed that chemotherapy improved OS only among patients with T4 as the single HRF (HR=0.51, 95%CI=0.34-0.78) or combinations involving T4 as T4/<12 LN (HR=0.31, C.I. 0.11-0.90), T4/high grade (HR=0.26, C.I. 0.11-0.61), and T4/LVI (HR=0.16, C.I. 0.04-0.61). All other combinations of two HRF did not show survival benefits when treated with adjuvant chemotherapy. Especially, chemotherapy did not affect OS when <12 LN retrieved was the only HRF. Conclusions: Our study has clearly demonstrated that not all high-risk features have similar adverse effects on OS. Type and number of high-risk features should be taken into consideration when recommending adjuvant chemotherapy in stage II colon cancer.

Mortality Hazards for High Risk Features (HRF)

Risk factors	HR	95% CI
Categorized High Risk Features		
1 HRF vs no HRF	1.25	1.08-1.46
2 HRF vs No HRF	1.59	1.32-1.91
≥3 HRF vs no HRF	2.73	2.18-3.40
One Risk Factor		
T-stage = 4		
Chemotherapy (yes vs no)	0.51	0.33-0.78
<12 lymph nodes		
Chemotherapy (yes vs no)	0.76	0.49-1.18
Two risk factors		
T-stage = 4 and <12LN		
Chemotherapy (yes vs no)	0.31	0.10-0.89
T-stage = 4 and high grade		
Chemotherapy (yes vs no)	0.26	0.11-0.61
T-stage = 4 and LVI positive		
Chemotherapy (yes vs no)	0.15	0.04-0.61

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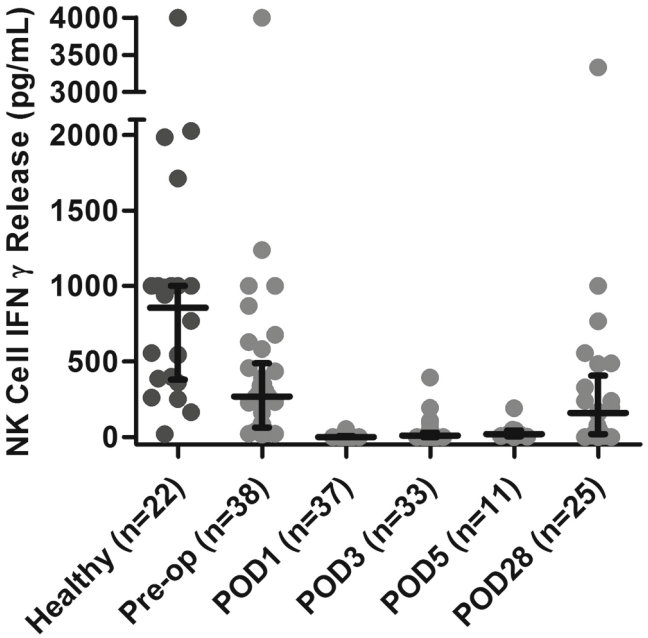
Surgical Stress Suppresses Natural Killer Cell IFNγ Release in Colorectal Cancer Patients L. Angka,[1] A.B. Martel,[1]* A. Jeong,[2] M. Sadiq,[2] M. Kilgour,[2] L. Baker,[1] C. Tanese de Souza,[2] M. Kennedy,[2] R. Auer.[1] *1. General Surgery, University of Ottawa, Ottawa, ON, Canada; 2. Ottawa Hospital Research Institute, Ottawa, ON, Canada.*

Background: Surgical stress results in profound immune suppression. Natural Killer (NK) cells play a central role in clearance of metastases and NK cell dysfunction, as measured by NK cell cytotoxicity (NKC), following surgery has been linked to cancer metastases in animal models. However, NK cell activity (NKA), as measured by secretion of interferon-γ (IFNγ), is a global measure of NK cell function since it measures activity from both the $CD56^{bright}$ and $CD56^{dim}$ subsets. NKA has been correlated with cancer prognosis in numerous clinical studies of varying cancer types. The effects of surgery on NKA have not been previously reported. Methods: A total of 22 healthy participants and 38 colorectal cancer (CRC) surgery patients were enrolled in an observational study (May 2016 to June 2017). For CRC patients, peripheral blood was collected preoperatively and on postoperative day (POD) 1, 3, 5, 28, and 56. NKC, measured by ^{51}Chromium assay; NKA, measured by production of IFNγ following cytokine stimulation and; immunophenotyping by flow cytometry were compared. Statistical analysis was performed using Mann-Whitney non-parametric testing. Results: NKC: NK cell cytotoxicity was reduced on POD1 to 65% of preoperative levels (p=0.0046, n=13). NKA (Figure 1): The median preoperative IFNγ levels for CRC patients (267 pg/mL) was significantly lower than that of healthy controls (855 pg/mL, p<0.001). However, surgical stress was associated with a complete loss of IFNγ secretion on POD1, with a median of 0 pg/mL (p<0.001, n=37). The impairment persisted until POD28 in 72% (n=18) of patients. Immune cell profiling did not reveal any differences in either the total NK cells ($CD56^{+}$ $CD3^{-}$) or the percentage of $CD56^{bright}$ and $CD56^{dim}$ subsets. Conclusion: Immediately following surgery there is significant decrease in NK cytotoxicity which is accompanied by a near complete loss of NK cell IFNγ production in all patients which persists for up to 1 month, and is not related to NK cell numbers. NKA is a more sensitive measure of postoperative NK cell dysfunction, as compared to NKC. Future work will study the effects of postoperative suppression of NKA on surgical outcomes and cancer recurrence.



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Treatment of Isolated Peritoneal Recurrences in Patients with Colorectal Peritoneal Metastases Previously Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy W.J. van Eden,[1]* F.M. Elekonawo,[2] B.J. Starremans,[2] N. Kok,[1] A.J. Bremers,[2] H. de Wilt,[2] a. aalbers.[1] *1. Surgical Oncology, The Netherlands Cancer Institute, Amsterdam, Netherlands; 2. Radboud University Medical Centre, Nijmegen, Netherlands.*

Background: Colorectal peritoneal carcinomatosis (PC) is preferably treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal intraperitoneal chemotherapy (HIPEC). Peritoneal recurrence of disease after treatment can occur without distant metastases, with a variety of treatment options. This study aimed to evaluate the management of isolated peritoneal recurrence after primary CRS-HIPEC. Methods: In two tertiary referral centers in The Netherlands, all patients who underwent CRS-HIPEC for colorectal PC between 2004 and 2015 and who developed isolated peritoneal recurrences were retrospectively evaluated. Location, treatment of peritoneal recurrences and curative or palliative treatment intent were reported. Univariable and multivariable Cox regression analysis and survival analyses were performed. Results: Of 414 patients treated with CRS-HIPEC for colorectal PC, 106 patients (26%) developed isolated peritoneal recurrence. Forty-three patients (41%) were treated with curative intent and 63 patients (59%) with palliative intent. Median overall survival in the patients treated with curative intent was 24.7 months (interquartile range (IQR) 12.1-61.7) compared to 7.6 months (IQR 2.5-15.9) in those treated with palliative intent (P<0.001). In the patients treated with curative cytoreductive surgery (n = 17) and curative second CRS-HIPEC (n = 15) median overall survival was 51.7 months (IQR 14.4-NA) and 29.0 months (IQR 18.1-63.0), respectively (P=0.620). Postoperative complications and hospital stay did not significantly differ between first and second CRS-HIPEC. Conclusion: After CRS-HIPEC for colorectal cancer approximately one out of four patients will develop isolated peritoneal recurrences. A substantial amount of these patients can be safely treated with curative intent yielding long term survival.

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Quality of Colon Cancer Surveillance Improves with the Implementation of a Personalized Surveillance Schedule B. Weixler,[1]* J. Rueff,[2] C.T. Viehl,[3] U. Guller,[4] W. Mingrone,[5] M. Zuber.[2] *1. Department of Surgery, Charite University Hospital Berlin, Campus Benjamin Franklin, Berlin, Germany; 2. Department of Surgery, Cantonal Hospital Olten, Olten, Switzerland; 3. Department of Surgery, Hospital Center Biel/Bienne, Biel/Bienne, Switzerland; 4. Division of Oncology and Hematology, Cantonal Hospital St. Gallen, St. Gallen, Switzerland; 5. Center for Oncology and Hematology, Cantonal Hospital Olten, Olten, Switzerland.*

Background Patients operated for colon cancer are at risk for disease recurrence. Structured surveillance is highly recommended as relapse detected early might be curable. We previously reported inadequate quality of surveillance among a multicentrtic Swiss cohort of patients with colon cancer (Ann Surg Oncol. 2010 Oct;17[10]:2663-9). The poor results lead to the introduction of a personalized surveillance schedule. The present study reassesses the quality of surveillance nine years after implementation of a personalized surveillance schedule and quantifies its efficacy. Patients and Methods Patients undergoing curative surgery for colon cancer between January 2009 and December 2014 were included in this prospective single center cohort study. All patients and involved physicians received a personalized surveillance schedule according to the national surveillance guidelines, recommending periodic measurement of carcinoembryonic antigen (CEA) levels, computed tomography (CT) and colonoscopy. All patients included gave written informed consent. Adherence to surveillance was compared with the national guidelines. Results A total of 93 patients were included in this study. Median follow-up was 46.9 months (IQR 25.3-59.7 months). Twenty patients (21.5%) had disease recurrence. Three-year overall and disease-free survival were 89.0% and 79.5%, respectively. Adherence to national guidelines was 76.1% for CEA measurements, 74.2% for CT-scan, and 71.8% for colonoscopy. Forty patients received adjuvant chemotherapy. No difference in compliance was detected between patients with and without adjuvant chemotherapy (p=0.185). In the above mentioned multicenter Swiss cohort study without a personalized surveillance schedule compliance with CEA measurements, CT-scan and colonoscopy was 32.8%, 31.7%, and 23.8%, respectively. Conclusion The implementation of a personalized surveillance schedule considerably increased the quality of surveillance after curative colon cancer resection. This study shows that a simple measure can raise the awareness of patients and health care professionals involved regarding the potential life-saving benefits from postoperative surveillance.

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Targeting Cellular Stiffness in the Prevention of Metastatic Disease D. Bryan,* M. Stack, A. Pearson, N. Khodarev, R. Rock, R. Weichselbaum, M. Posner. *University of Chicago, Chicago, IL.*

Introduction The majority of cancer deaths occur in patients who develop metastatic disease, therefore development of novel therapeutic approaches to limit the spread of cancer is paramount. Adhesion, invasion, and migration of malignant cells have been postulated to be necessary steps in the development of distant disease. Here, we report on the use of 4-hydroxyacetophenone (4HAP), a novel agent affecting cellular stiffness through activation of myosin II, therein limiting the ability of malignant cells to adhere, invade, and migrate. We additionally show the ability of 4HAP to limit metastatic tumor burden using an in vivo model for colorectal cancer (CRC) liver metastases. Methods In vitro adhesion, invasion, and migration assays were performed using HCT116 tumor cells with increasing concentrations of 4HAP. In vivo studies were done with athymic nude mice pretreated with intra-peritoneal injections of either control (PBS), or 4HAP, given every other day for two treatments, followed by intrasplenic injection of $1.5x10^6$ HCT116 cells double labeled with luciferase and TdTomato. Mice then continued to receive their respective treatments every other day for 4 weeks. Weekly bioluminescent imaging was conducted to track the development of tumor burden. Tumor size change was statistically modeled using mixed effect linear regression to account for repeated measures on each tumor. The tumor volume data was log transformed to account for exponential growth. Results Cell lines treated with low concentrations of 4HAP (1 uM) demonstrated a significant decrease in invasion (43.7%, p<0.01), and migration (83.6%, p<0.01). High concentrations of 4HAP (4 uM) resulted in a significant decrease in adhesion (60.5%, p<0.01). In vivo imaging demonstrated a statistically significant decrease in exponential

tumor growth rate in mice treated with 4HAP (p = 0.0129) figure 1. Addition of 4HAP increased the predicted fluorescence doubling time from 2.70 days to 4.57 days. Conclusions The data demonstrate that targeted therapy with cell migration inhibitors, specifically 4-hydroxyacetaphenone, has the ability to limit tumor cell metastatic properties in-vitro, and in-vivo.

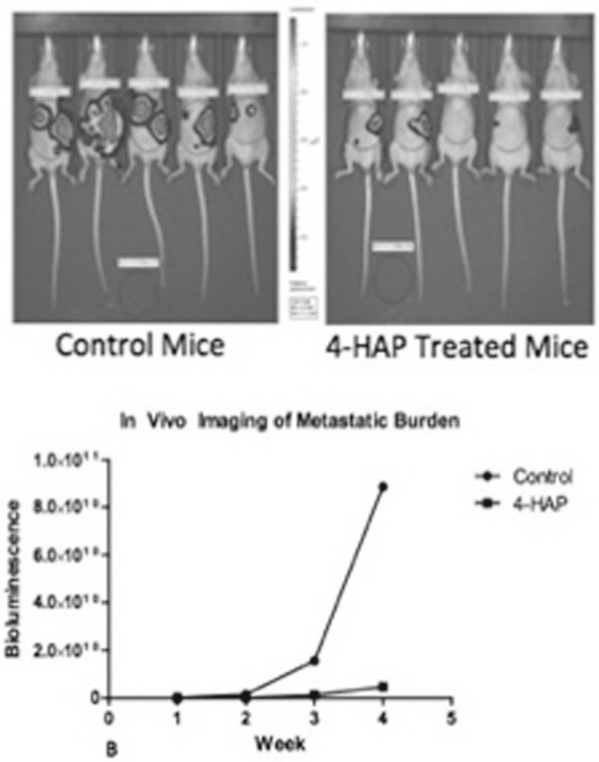

Figure 1. In vivo Liver Metastasis Model. Control mice (left panel) and 4HAP treated mice (right panel) at conclusion of 4 weeks. Lower panel shows absolute average difference in tumor-associated bioluminescence between control and 4HAP treated mice.

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Frequency of Unplanned Surgery in Patients with Stage IV Colorectal Cancer Receiving Palliative Chemotherapy with an Intact Primary: An Analysis of SEER-Medicare P.D. Lorimer,* B.M. Motz, R.C. Kirks, Y. Han, J.J. Hwang, J.C. Salo, J.S. Hill. *Surgical Oncology, Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC.*

Background Patients (pts) with stage IV colorectal cancer often begin palliative chemotherapy (PC) with the primary tumor in place. Low rates of unplanned surgical intervention secondary to intestinal obstruction or perforation undergoing this treatment strategy have been reported in single institution studies. We examined a large national dataset to determine the rate of unplanned surgical intervention in stage IV colorectal cancer pts on PC. Methods SEER-Medicare was queried for pts with metastatic colorectal cancer receiving PC (1998-2013). Pts who underwent procedures with curative intent (elective colorectal surgery, liver/pulmonary directed therapy) at any time were excluded. Thus, the analytic cohort was comprised of pts undergoing chemotherapy who never underwent planned surgery to the primary or metastases. The primary outcome measure was the need for non-elective surgery. Demographics, tumor characteristics and patient comorbidities were analyzed for effect. Time to surgery or death was measured. Conditional analyses were performed to determine the risk of surgical intervention at 6 months, 1 and 2 years post diagnosis. Results 13748 pts met inclusion criteria: 63% underwent upfront resection (excluded in further analyses), leaving 4692 pts receiving PC who served as the analytic cohort. In the analytic cohort: Median age=75; 53% male. White 79%, black 11% and other 10%. At 24 months, 80% of the pts had died. The overall unplanned intervention rate for those on PC was 12%. The conditional probability of requiring unplanned surgery between 6-12 months was 8.1%; 12-24 months=6.7%, and >24 months=5.3%. Males and those with right sided tumors were less likely to require surgery. Increasing age predicted a lower likelihood of surgery (Table 1). Conclusion This study utilizes a large series of pts with stage IV colorectal cancer receiving PC to determine the frequency of unplanned surgery. Pts treated with PC who are not resected upfront are unlikely to require unplanned surgery, and therefore prophylactic surgery to reduce the risk of perforation or obstruction may not be necessary.

Table 1: Multivariable logistic regression on likelihood of requiring unplanned surgery (n=4,692)

Variables	Odds Ratio (95% CI)	P value
Age (continuous)	0.978 (0.964, 0.994)	0.005*
Sex (ref=Female)		0.025*
Male	0.814 (0.679, 0.975)	
Tumor Site (ref=Right)		<0001*
Left	1.821 (1.434, 2.311)	
Transverse	2.069 (1.358, 3.151)	
Rectum	1.497 (1.168, 1.918)	
Unspecified	0.691 (0.453, 1.055)	
Tumor Differentiation (ref=Poorly diff.)		<0001*
Well/moderately diff.	0.880 (0.694, 1.116)	
Undifferentiated	1.114 (0.545, 2.278)	
Unknown	0.493 (0.373, 0.651)	
Charlson Comorbidity (ref=0)		0.038*
1	1.356 (1.090, 1.688)	
2	1.014 (0.725, 1.418)	
>=3	0.929 (0.651, 1.325)	

Multivariable results were adjusted for all covariates listed in the table above. Stepwise selection method was used to select the covariates in the model. The significance level of 0.1 was utilized for inclusion and exclusion from the model.

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DNA Demethylation Inhibits Colorectal Liver Metastases through Activation of an Epigenetically Controlled MicroRNA Cluster in the 14q32 Locus E.C. Poli,* G. Oshima, S. Pitroda, A. Uppal, M. Stack, N. Khodarev, M. Posner, R. Weichselbaum. *Surgery, University of Chicago, Chicago, IL.*

Background: Previously, we demonstrated that the expression of miRNAs (miRs) from a cluster encoded by the 14q32 locus can suppress metastases in liver and lungs. However, the ability to pharmacologically activate the expression of this cluster is unknown. In this study, we hypothesized that these oligometastatic miRs are regulated by DNA methylation and can be selectively activated by a demethylating agents to suppress liver metastases. Methods: Methods for this study include genomic mapping, bioinformatics analyses, cell culture with the HCT116 human colorectal cell line, use of a mouse model for liver metastasis, and CRISPR/Cas-9 genome editing. Results: Bioinformatic analysis revealed CpG islands near a unique transcription start site (TSS) encoding the 14q32 miRs and the long non-coding RNA genes in this region, including MEG3. The MEG3 differentially methylated region (DMR) coincides with the TSS. In colorectal tumors, levels of MEG3-DMR methylation is inversely correlated with expression of 14q32 miRs. Suppression of DNA methylation in tumor cells activated the 14q32 miRs and prevented their ability to form liver metastases in mice. HCT116 cells with genomic deletions of both DNMT1 and DNMT3b preferentially expressed miRs located in the 14q32 locus, and failed to produce liver metastases in a mouse model. Fine mapping of the MEG3-DMR locus detected 4 binding sites for CTCF, a transcriptional activator. Methyl-specific sequencing and CHIP-Seq demonstrated demethylation and binding of CTCF to these sites after treatment with Decitabine. CRISPR/Cas9-driven deletion of MEG3-DMR was found to provide advantages for peritoneal metastases as was evidenced from the clonal analysis of tumor cell populations in vitro and in vivo. Conclusions: Our data implicate 14q32 miRs as metastases suppressive agents, demonstrate that regulation of these miRNAs is controlled by DNA methylation and CTCF binding, and reveal the ability of a DNA demethylating chemotherapeutic to reactivate these miRs and suppress liver metastases.

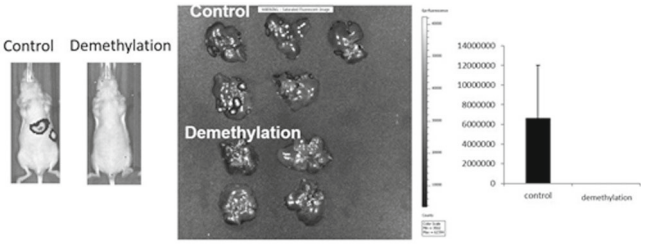

Figure A: Treatment with a demethylating agent abrogates the development of liver metastasis in mice.

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Clinical Importance and Surgical Management of Sentinel Lymph Nodes in the Popliteal Fossa of Melanoma Patients A.A.G. Nijhuis,[1]* I. Dunshee de Abranches Oliveira Santos,[2] R.F. Uren,[3] J.F. Thompson,[1] O.E. Nieweg.[1] *1. Melanoma Institute Australia, Sydney, NSW, Australia; 2. A.C. Camargo Cancer Center, São Paulo, Brazil; 3. Alfred Nuclear Medicine and Ultrasound, Sydney, NSW, Australia.*

Background: Patients with a primary melanoma below the knee may have a sentinel node (SN) in the popliteal fossa. Information on SNs in this nodal region is scarce. The purpose of this study was to describe the incidence, surgical management and clinical relevance of such SNs. Methods: Patients with a primary melanoma below the knee treated at Melanoma Institute Australia between 1992 and 2013 were identified. In those with a popliteal SN, data on lymphoscintigraphy, the SN biopsy, morbidity and follow-up were analyzed. Results: Lymphoscintigraphy showed drainage to the popliteal fossa in 176 of 3902 cases of melanoma below the knee (4.5%). In 96 of these patients (55%) popliteal SN biopsy was attempted. Reasons for not attempting the procedure were diverse and related to patient refusal, complex lymphatic drainage patterns, comorbidity, tumor characteristics and trial participation. SN biopsy was successful in 79 patients (82%), but failed to identify a node in 17 patients. Postoperative morbidity from the popliteal SN biopsy was reported in one patient (1.3%), who developed a wound infection. Lymphedema developed in 21 patients (27%) of whom 20 had undergone SN biopsy of the groin in addition to the popliteal fossa. The lymphedema was generally mild and transient. Thirteen patients (16%) had a positive popliteal node and in eight (10%) this was the only involved SN. Ten patients (13%) went to a higher AJCC-UICC tumor stage. A positive popliteal node was associated with a greater risk of recurrence at any site (69% vs 27%, p=0.007) and a diminished overall survival (56 months vs median not reached, p=0.011). Popliteal SN biopsy itself did not improve regional control or overall survival (p=0.52 and p=0.88, respectively; table 1). Completion popliteal fossa dissection was performed in four patients. Conclusion: Melanoma below the knee infrequently drains to SNs in the popliteal fossa and these are challenging to procure. Popliteal SN tumor status is predictive for recurrence and overall survival. A popliteal SN is tumor-positive in 16% of the patients, which may make the patient eligible for adjuvant systemic therapy and improve their prognosis.

Table 1: Follow-up and outcome.

IQR = Interquartile range

* In six patients, no follow-up data was available

	Total	No popliteal SN biopsy	Popliteal SN biopsy	Failed biopsy
Number of patients with follow-up*	170	78	75	17
Follow-up in months (IQR)	54 (27-99)	53 (27-80)	54 (22-101)	59 (44-146)
Recurrence	65 (38%)	31 (40%)	26 (35%)	8 (44%)
First recurrence primary site	14	7	4	3
First recurrence in-transit (lower leg)	20	9	6	5
First recurrence regional lymph node (groin)	16	10	6	-
First recurrence systemic	15	5	10	-
Months until recurrence (IQR)	23 (10-39)	20 (9-37)	22 (10-30)	43 (16-90)
Popliteal recurrence	6 (3.5%)	3 (3.8%)	3 (4.0%)	-
Groin recurrence	33 (19%)	19 (24%)	13 (17%)	1 (5.9%)
Systemic metastases	39 (23%)	20 (26%)	17 (23%)	2 (12%)
Alive last follow-up	128 (75%)	58 (74%)	56 (75%)	14 (82%)
Status last follow-up				
Alive without recurrence	107 (63%)	45 (57%)	50 (67%)	12 (71%)
Alive with disease	17 (10%)	11 (14%)	5 (6.7%)	1 (5.9%)
Alive, status unknown	4 (2.4%)	2 (2.6%)	1 (1.3%)	1 (5.9%)
Dead, melanoma	29 (17%)	14 (18%)	13 (17%)	2 (12%)
Dead, other cause	4 (2.4%)	2 (2.6%)	1 (1.3%)	1 (5.9%)
Dead, cause unknown	9 (5.3%)	4 (5.1%)	5 (6.7%)	-

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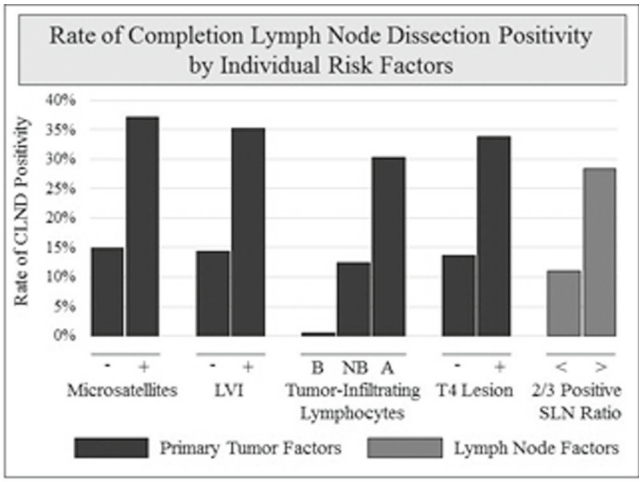
Prediction of Nodal Metastasis at Completion Lymph Node Dissection in Sentinel Lymph Node Positive Melanoma Patients A.J. Sinnamon,[1]* Y. Song,[1] C.E. Sharon,[1] Y. Yang,[2] D.E. Elder,[1] X. Xu,[1] R. Roses,[1] R.R. Kelz,[1] D.L. Fraker,[1] G. Karakousis.[1] *1. Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA; 2. University of Pennsylvania Center for Clinical Epidemiology and Biostatistics, Philadelphia, PA.*

Introduction While recent trial data have reported no survival benefit of immediate completion lymph node dissection (CLND) for sentinel lymph node (SLN) positive disease in melanoma, prediction of non-SLN disease can help inform clinicians in selectively recommending CLND at least for regional control or adjuvant therapy if nodal observation is pursued. While most prediction efforts have focused on the characteristics of the SLN, less study has evaluated clinical variables and features of the primary tumor. Methods A retrospective cohort of patients with positive SLNB who subsequently underwent CLND was identified (1996-2014). Clinical and pathologic factors associated with presence of any melanoma metastases identified at time of CLND were identified using univariate analyses and multivariable logistic regression. These factors were used to identify groups at low- and high-risk for additional lymph node disease. Results Overall, 299 SLN-positive patients were identified among whom 247 underwent planned CLND. Non-SLN positivity rate for those undergoing CLND was 19.4% (n=48). In multivariable analysis, in addition to >2/3 positive-to-total SLN ratio, primary tumor characteristics associated with CLND positivity were T4 stage, absent tumor infiltrating lymphocytes (TILs), lymphovascular invasion and microsatellitosis. Rates of CLND positivity with individual risk factors are shown in Figure. In patients with at least three of these risk factors (n=45, 18%), CLND positivity rate was 51%. Conversely, in patients with no risk factors (n=59, 24%), the non-SLN positivity rate was 6.8%. Patients with brisk TILs of the primary tumor (n=8) had no additional metastatic disease identified at time of CLND, whereas patients with absent TILs and one additional risk factor (n=59) had a CLND positivity rate of 39%. Conclusions In addition to characteristics of the SLNs, primary tumor features (thickness, LVI, microsatellites, and notably TIL) can help identify patients with appreciably high or low risk of non-SLN disease. These factors may help in the decision making for recommendations regarding CLND and/or consideration of adjuvant therapy.



LVI, lymphovascular invasion; B, brisk; NB, nonbrisk; A, absent

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The Prognostic Significance of Extracapsular Spread (ECS) in Sentinel Node Positive (SLN+) Patients for Cutaneous Melanoma

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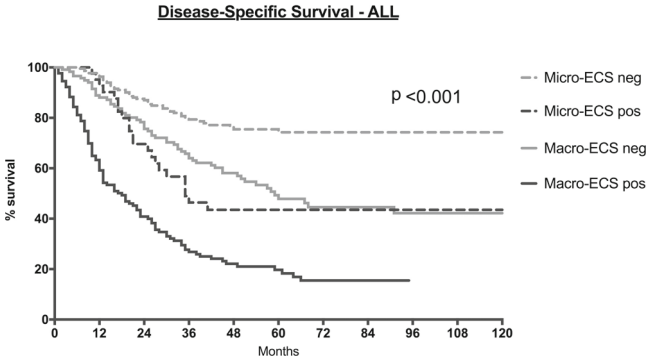
Objectives ECS, or extracapsular extension, is recognized to be a high risk factor in melanoma patients with macrometastatic (N+), palpable nodal disease. However, the risk of ECS in terms of patient outcomes in SLN+, micrometastatic stage III disease is less clear. The objective of this study was to examine ECS incidence and correlate this to patient prognosis (progression-free PFS, disease-specific DSS and overall survival OS). Methods A retrospective analysis of all patients undergoing nodal surgery with micro- or macrometastatic lymphadenopathy in two central University cancer centers between 2000 and 2017 was carried out. Patient demographics, tumor characteristics, nodal ECS status and patient outcomes were collected. Results 515 patients were identified with metastatic nodal disease. M:F ratio was 277:238; median age was 63 (17-94 years). There was an increased frequency of ECS disease in N+ compared to SLN+ disease (52.4% v 16.2%; P<0.0001). ECS was a significant DSS and OS prognostic indicator for both N+ and SLN+ nodal disease (Fig. 1). The absolute DSS difference for SLN+ patients was 30% at 5 years (72.6% v 32.4%; p<0.0001). The prognosis of SLN+/ECS+ patients was statistically similar to N+/ECS- patients. Multivariate analysis demonstrates ECS status, along with Breslow thickness and N-stage, was an independent prognostic indicator for PFS (HR=2.4; p<0.0001) and DSS (HR=2.3; p<0.0001) in patients with SLN+ disease. Median PFS in SLN+ and N+ disease was 20 and 10 months respectively. Discussion/Conclusion We present the outcomes of patients with ECS in stage III disease on a large combined dataset from 2 major cancer centers. We found that ECS is a significant PFS and OS indicator in both SLN+ and N+ disease. Our data suggests that recurrences occur rapidly following ECS diagnosis; surveillance scans should be focused to the initial 3-year period for both micro and macrometastatic disease. We demonstrated that ECS upstages stage III disease (Fig.1) in a similar fashion to ulceration in primary melanoma (stage I/II). We would advocate that ECS should be included in melanoma staging to better stratify treatment strategies in stage III.



Disease specific survival in ECS+/- micrometastatic and macrometastatic disease.

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Completion Lymph Node Dissection or Radiation Therapy for Sentinel Node Metastasis in Merkel Cell Carcinoma

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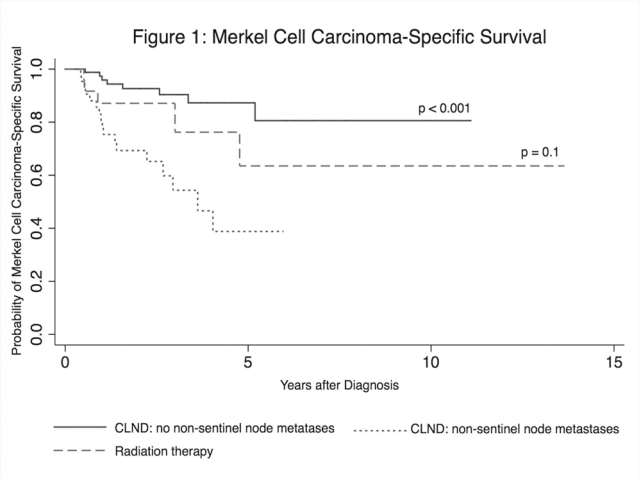
INTRODUCTION: Completion lymph node dissection (CLND) is often recommended for patients with sentinel lymph node (SLN) metastasis from Merkel cell carcinoma (MCC); however, the benefit of this treatment is unclear. In this study, we evaluated clinical outcomes of patients with SLN metastasis who underwent CLND or radiation therapy. METHODS: Using a prospective database, we identified patients with SLN metastasis from MCC. Our primary outcomes were MCC-specific survival, disease-free survival, and patterns of recurrence. Patients were stratified into two groups: CLND and radiation. Patients undergoing CLND were further stratified based on presence of non-sentinel lymph node (non-SLN) metastasis. Survival curves were computed using the Kaplan-Meier method and compared using the log-rank test. Logistic regression was used to identify predictors of non-SLN metastasis. RESULTS: From March 2006-February 2017, 163 patients were treated for SLN metastasis. Of these, 84% underwent CLND and 16% received radiation. Patients undergoing CLND had increased Breslow depth and were younger than those receiving radiation, but had no significant differences in lymphovascular invasion (LVI), ulceration, or SLN tumor burden. Of those undergoing CLND, 32% had non-SLN metastasis. Figure 1 shows MCC-specific survival for the cohort. Patients who underwent CLND and had non-SLN metastasis had significantly reduced MCC-specific (p<0.001) and disease-free survival (p=0.005) compared to those without non-SLN metastasis, but no significant differences in rates of nodal recurrence (p=0.9). The non-SLN metastasis group also had reduced MCC-specific and disease-free survival compared to the radiation therapy group, but these differences were not significant (p=0.1). They also had similar rates of nodal recurrence (p=0.3). Significant predictors of non-SLN metastasis were LVI (odds ratio 3.7, p=0.02) and SLN tumor burden greater than 10% (odds ratio 5.8, p=0.005). CONCLUSIONS: CLND provides important prognostic information, as non-sentinel node metastasis is associated with reduced MCC-specific and disease-free survival. This high-risk group should be considered in adjuvant therapy trials.



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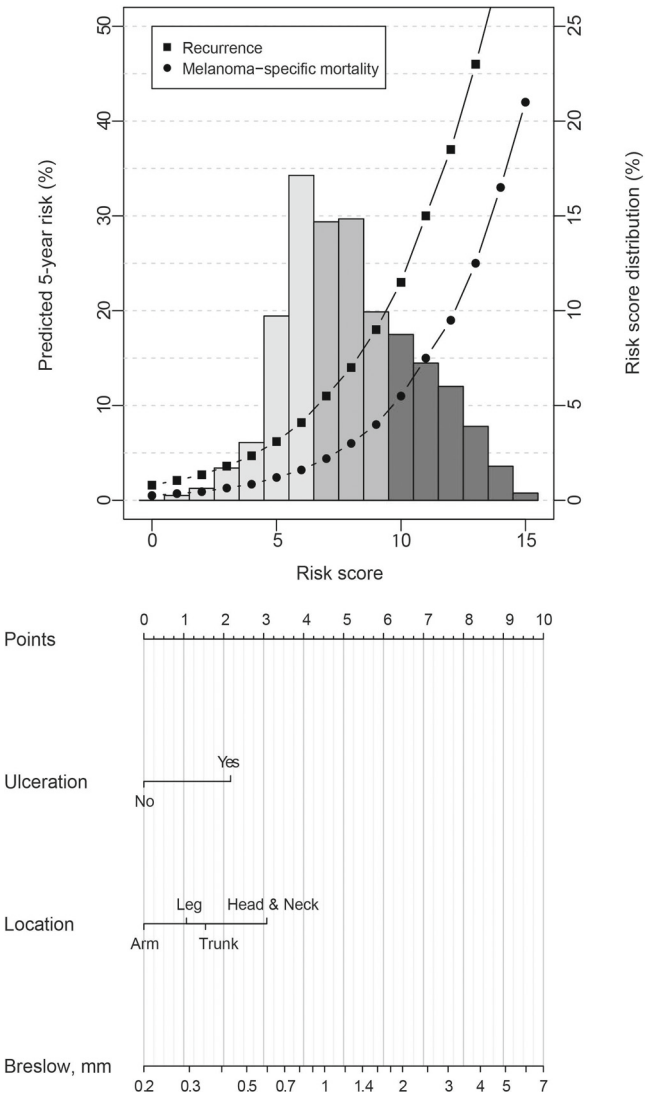
Development and Validation of a Nomogram for Recurrence and Melanoma-Specific Mortality in Sentinel Node Negative Melanoma Patients: a Retrospective Analysis D. Verver,[1]* D. van Klaveren,[2] A.C.J. van Akkooi,[3] P. Rutkowski,[4] U. Keilholz,[5] A.M.M. Eggermont,[6] D. Grünhagen,[1] C. Verhoef.[1] *1. Surgical Oncology, Erasmus MC Cancer Institute, Utrecht, Netherlands; 2. Leiden University Medical Center, Leiden, Netherlands; 3. Netherlands Cancer Institute - Antoni van Leeuwenhoek, Amsterdam, Netherlands; 4. Maria Sklodowska-Curie Institute – Oncology Center, Warsaw, Poland; 5. Charité - University of Medicine Berlin, Berlin, Germany; 6. Gustave Roussy Cancer Campus Grand Paris, Villejuif, France.*

BACKGROUND: The sentinel lymph node biopsy (SLNB) result, either positive or negative, is one of the most important prognostic indicators for recurrence and survival in melanoma patients. However, solely stratifying for sentinel node (SN) status does not provide a quantifiable risk for individual patients. A nomogram is a convenient tool for individualized outcome predictions since it combines several prognostic factors. Our objective was to construct and validate a nomogram for recurrence and melanoma-specific mortality in SN negative melanoma patients. METHODS: A previously collected and described cohort from four European Organization for Research and Treatment of Cancer (EORTC) Melanoma Group centers was used consisting of 4124 patients. We identified and incorporated significant prognostic factors for recurrence and melanoma-specific mortality to develop prediction models. Performance was assessed by discrimination (c-index) and calibration (plotting the predicted probability versus the actual probability) in cross-validation across four centres. The prediction models were graphically presented as nomogram for clinical use. RESULTS: A total of 3180 eligible patients were included for analysis. The multivariable prediction model for recurrence and melanoma-specific mortality included three independent prognostic factors: ulceration, anatomic location and Breslow thickness. A nomogram was developed based on these models for calculating the risk score. The c-index and calibration curves in cross-validation across four centres showed good model performance. Approximately one third of the negative SN patients had a recurrence probability of ~8.2% and ~6% had a recurrence probability of > 45% at 5-years. CONCLUSIONS: In conclusion, we constructed and validated a novel and easy-to-use nomogram for predicting recurrence and melanoma-specific mortality in negative SN melanoma patients. It provides personalized patient-specific estimates that can be useful for patient care, optimal tailoring of surveillance strategies (reduce or expand intensity), and selection of patients for adjuvant therapy (trials).



The risk curves refer to recurrence or melanoma-specific mortality at 5-years. Histogram refers to the risk score distribution in the cohort: light pink bars, the first tertile (low risk); medium pink bars, the second tertile (intermediate risk); and dark pink bars, the third tertile (high risk).

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Four Immune Modulating Genes in Primary Melanoma that Predict Metastatic Potential J. Erdrich,[1]* D. Kaufman,[2] N. Deng,[1] K. Gong,[2] R. Essner.[1] *1. Surgery, Cedars Sinai Medical Center, Los Angeles, CA; 2. David Geffen School of Medicine at UCLA, Los Angeles, CA.*

Introduction: Histologic characteristics cannot adequately predict which patients are at risk of developing metastatic disease after excision of a primary melanoma. The aim of this study was to identify which immunomodulatory genes in primary melanoma tumors are associated with development of distant metastases. Methods: Thirty-seven patients with primary melanoma and no metastases underwent surgical excision of the primary lesion and were followed prospectively for a median of 38 months (range 1-144 months). cDNA was generated from the primary tumor specimens and used for microarray analysis. Differential gene expression of 79 immunomodulatory genes was compared between patients who developed distant metastases and those who did not. Results: Of the 37 patients with primary cutaneous melanoma, 6 developed distant metastatic disease. There were no significant differences in age, gender, Breslow thickness, regression, ulceration, or mitotic index between the metastatic and non-metastatic groups. After multivariate analysis, four immunomodulatory genes were found to be overexpressed in the

group that eventually developed metastatic disease. CBL, a proto-oncogene relevant to ubiquitin pathways, was overexpressed in the metastatic group with differential expression fold change (DEFC) of 1.15, p=0.01. The CD276 gene, which activates T-cell immunity, was overexpressed with DEFC 1.16, p=0.04. CXCL1 and CXCL2, which encode chemokines regulating growth and inflammation, were overexpressed in the metastatic group with DEFC of 2.51 and 1.68 respectively, p<0.001 and p=0.01. CXCL1 showed a particularly strong area under the curve (AUC) of 0.80, demonstrating high predictive value. The patient 5-year survival for CXCL1 overexpression was 50% compared to 97% for those who underexpressed CXCL1. Conclusion: CXCL1, CXCL2, CBL, and CD276 are overexpressed immunomodulatory genes present in primary melanoma that are strongly associated with development of metastatic disease. Identification of their presence, particularly CXCL1, in the primary tumor could be used to predict who is at risk of future metastatic disease and thereby identify patients who might benefit from targeted immunotherapy.

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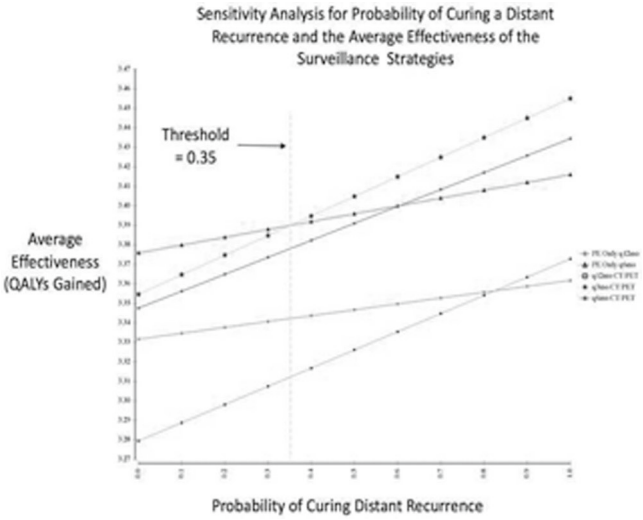
Cost-Effectiveness of Surveillance Strategies Following Resection of Stage III Melanoma R. Kang,[1]* M.V. Hill,[1] C.V. Angeles,[1] S. Tapp,[2] A.N. A. Tosteson,[2] S.L. Wong.[1] *1. Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, NH; 2. The Dartmouth Institute, Hanover, NH.*

Purpose: Standard surveillance strategies for resected stage III melanoma do not exist. Short-interval imaging may improve early detection, but is resource intensive. However, as more options for targeted therapy and immunotherapy become available, the likelihood of successfully treating distant disease increases and the value of routine imaging may also increase. Our objective was to evaluate the cost-effectiveness (CE) of surveillance strategies which employ routine imaging vs strategies which primarily rely on physical exams (PE). Methods: Published observational data was used to develop a Markov state transition model, replicating the natural history of stage III melanoma. The model was used to compare the CE of 5 surveillance strategies over a 5-year period. Strategies included routine CT/PET imaging at 3, 6, and 12 mos intervals, and PE with imaging limited to work-up of symptomatic complaints at 6 and 12 mos intervals. Cost data were obtained from the literature and the 2017 Medicare physician fee schedule. The primary outcome was cost per quality-adjusted life years gained (QALY). The base-case scenario was for a 50-year-old. One way sensitivity analyses were done on all variables and a Monte Carlo microsimulation was performed. Results: In the base case, PE every 6 mos with imaging for symptomatic complaints was the preferred strategy (3.38 QALYs & $7,755 per QALY gained). As the probability of curing distant disease increases (probability threshold of 0.35), CT/PET every 3 mos becomes the preferred strategy. A microsimulation of 10,000 patients in the base case shows annual PE is the most CE strategy with a mean cost of $6,634 per QALY gained. Repeat microsimulation at higher probabilities of cure for distant disease shows CT/PET every 3 months would have the highest mean effectiveness, but annual PE remains CE. Conclusion: An annual physician visit with PE and imaging studies to evaluate symptomatic complaints is a CE surveillance strategy. With newer therapies, the probability of curing distant disease is likely to increase. In these situations, routine imaging may yield higher effectiveness in terms of QALYs gained, but imaging remains a costly strategy.



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The MELFO-Study: A Multi-Center Prospective Randomized Clinical Trial on the Effects of a Reduced Stage-Adjusted Follow-up Schedule on Cutaneous Melanoma IB-IIC Patients: Results After 3-Years E. Deckers,[1]* J. Hoekstra-Weebers,[1] S. Damude,[1] A. Francken,[2] S. ter Meulen,[3] E. Bastiaannet,[4] H. Hoekstra.[1] *1. Surgical oncology, UMCG, Groningen, Netherlands; 2. Isala, Zwolle, Netherlands; 3. Antoni van Leeuwenhoek, Amsterdam, Netherlands; 4. LUMC, Leiden, Netherlands.*

Introduction: The lack of an evidence-based guideline on the follow-up of cutaneous melanoma initiated the melanoma follow-up study (MELFO). Preliminary one-year results showed that the stage-adjusted, reduced follow-up schedule did not adversely affect patients' well-being, the number of recurrences and melanoma deaths compared with the conventional follow-up schedule. Current analyses were performed after three years, since the majority of recurrences are detected within three years. Methods: One-hundred-eighty eligible patients, 87 males and 93 females, with a median age of 57 years (20-85), entered the study (response=85%). Patients were randomized into a conventional (CSG; n=93) or experimental follow-up group (ESG; n=87). Participants completed the State-Trait Anxiety Inventory (STAI), Cancer Worry Scale (CWS), Impact of Event Scale (IES), and Mental and Physical Component scales (PCS/MCS) of the RAND-36 at study entry (T1) and at three years (T3). Clinicians registered the assigned follow-up schedule in terms of clinicopathologic features. 110 patients (CSG; n=56, ESG; n=54) completed T1 and T3 quality of life questionnaires. Seventy patients were off study: 24 patients with recurrent disease (of whom 12 died); three patients died of other causes; 43 declined T3 participation. Results: A significant group effect was found on the IES and PCS RAND-36 in favor of the ESG; p= 0.001 and p= 0.02 respectively. Twenty-four patients, 15/93 (16%) CSG and 9/87 (10%) ESG (p=0.254), developed a recurrence within three years after a median follow-up of 369 (203-1040) and 406 days (179-741) respectively (p= 0.835). Twelve patients died of their melanoma, 6/93 (6%) GSC and 6/87 (6%) ESG (p=0.905), with a median follow-up of 513 (203-1007) and 389 days (179-665) respectively (p= 0.262). Conclusion: These three-years follow-up results, support the notion that an abbreviated stage-adjusted schedule forms an appropriate and safe alternative to the follow-up regime as currently advised in the Dutch Melanoma guidelines.

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The Impact of Effective Systemic Therapies on Surgery for Stage IV Metastatic Melanoma H.G. Smith,* K. Joshi, D.C. Strauss, A.J. Hayes, J. Larkin, M.J. Smith. *Sarcoma/Melanoma Unit, The Royal Marsden Hospital, Ashford, United Kingdom.*

Introduction The outcomes of patients with metastatic melanoma has significantly improved in recent years with the evolution of effective systemic therapies (EST). The impact of EST on the role of surgery in Stage IV melanoma is yet to be defined. We sought to characterise the patterns and outcomes of surgery in patients with Stage IV melanoma before and after the introduction of EST. Methods A retrospective review of patient records was performed to identify patients treated with surgical resection for Stage IV melanoma at a single institution. Patients were grouped into those treated before-EST (2003-2007) and after-EST (2011-2015). Outcomes and indications for surgical intervention were retrieved from electronic patient records. Results A total of 138 patients underwent surgery for Stage IV melanoma during the study period, with 69 patients in the before-EST and after-EST cohorts. No significant difference was found in the ratio of operations/patient performed between cohorts. However, the pattern of operations was different, with a significant decrease in the excision of in-transit deposits (0.9% vs 19.4%, $p < 0.001$) and an increase in abdominal metastasectomies (21.1% vs 4.2%, $p < 0.001$) after-EST. Novel indications for surgical intervention were noted after-EST, with a significant increase in potentially curative metastasectomy (15.9% vs 4.3%, $p = 0.045$). Survival following surgery was prolonged in the after-EST cohort (median survival 16 months vs 6 months, $p < 0.001$), with stage at initial metastasectomy (Stage 4a, HR 0.45 (0.28-0.73), $p = 0.001$) and treatment with immune checkpoint inhibitors (HR 0.38 (0.25-0.60), $p < 0.001$) found to be associated with prolonged survival. Conclusions Surgery for Stage IV melanoma remains an important treatment modality in the era of EST, with evolving indications and patterns of intervention. Surgery for abdominal metastases is increasingly common, emphasising the importance of the inclusion of surgical oncologists with competence in visceral resection in the multidisciplinary management of an increasingly complex population of patients.

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Neutrophil to Lymphocyte Ratio (NLR) is Associated with Survival But Varies with Disease Burden in Melanoma Patients Treated with PD-1 Inhibitor Monotherapy E. Bartlett,* R.A. Ferraro, J.M. Stacruz, M.A. Postow, D. Coit, C.E. Ariyan. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Elevated NLR has been associated with poor survival in cancer patients. Data suggest it may have prognostic value in the setting of treatment with CTLA-4 blockade, but its relationship to outcome in the setting of PD-1 blockade remains inadequately defined. We sought to investigate the relationship between NLR and survival in melanoma patients treated with PD-1 inhibition with correlation to tumor burden. Methods: This was an IRB approved retrospective analysis of a prospectively maintained database. Patients undergoing initial treatment with PD-1 inhibitor monotherapy for stage IV melanoma at a single center from 2012-2015 were included. Clinical parameters were examined and tumor burden was classified by number of sites of disease (1-4+). NLR was determined pretreatment. An NLR cut-point at 5 was utilized to be consistent with prior studies. Kaplan Meier and Cox regression analyses identified factors associated with disease-specific survival (DSS). Results: Of the 230 patients, 64% were male, the median age was 66, and 50% of patients had an ECOG performance status of 0. Forty-seven patients were treated with nivolumab and 183 with pembrolizumab. NLR≥5 was associated with a poor survival in univariate analysis (39% vs. 66% 2-yr DSS, p=0.004). In a multivariate analysis, site of the primary melanoma, number of metastatic sites, and NLR≥5 were all associated with poor DSS (Table 1). 9% of patients with a single metastatic site had NLR≥5, compared to 28% of those with 2-3 metastatic sites, and 39% of those with 4+ metastatic sites (p<0.001). In patients with NLR<5 and 1 metastatic site (n=49), the 2-yr DSS was 69% compared to 25% in patients with 4+ metastatic sites and NLR≥5 (n=23, p=0.002). Discussion: Pretreatment NLR≥5 is independently associated with worse DSS confirming its prognostic role in the setting of PD-1 inhibition for melanoma. Moreover, NLR≥5 is significantly associated with disease burden. Taken together, NLR and the number of metastatic sites can widely risk-stratify patients for death from disease.

Table 1. Factors associated with DSS in Melanoma Patients Treated with PD-1 Inhibition

				Univariate*	Multivariate		
		Number	2-yr DSS	p-value	HR	95% CI	p-value
Pretreatment NLR	<5	169	61%	0.001	ref	ref	ref
	≥5	61	39%		1.94	1.27-2.94	0.002
Primary Site	Cutaneous	155	58%	<0.001	ref	ref	ref
	Mucosal	25	32%		2.39	1.41-4.04	0.001
	Ocular	17	31%		3.48	1.78-6.80	<0.001
	Unknown	33	72%		0.60	0.32-1.13	0.11
Number of Metastatic Sites	1	54	76%	0.001	ref	ref	ref
	2-3	117	54%		1.43	0.83-2.45	0.19
	4+	59	42%		1.98	1.10-3.57	0.023

*Variables included in univariate analysis but not found to be significant were: sex, age, ECOG performance status, prior immune therapy within 90 days, drug, M Stage (M1a, M1b, M1c: was significant but interacted with number of metastatic sites thus was excluded from MV analysis)

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Impact of a Culturally-Tailored Institutional Patient-Navigation Program for Colonoscopy Completion J.C. Hardaway,* A. Allard-Picou, J. Espat, A. Saied-Calvino. *Surgical Oncology, Roger Williams Cancer Center, Providence, RI.*

Introduction Incidence and mortality rates of colorectal cancer (CRC) have decreased with utilization of screening tests; yet CRC remains the second leading cause of cancer related mortality among Hispanics in the U.S., with males in this demographic having the lowest reported colonoscopy completion rates (CCR). Two-thirds of Hispanics are more likely to have advanced stage disease at diagnosis, which may account for the substantially worse outcomes as compared to Caucasians. A general consensus exists that several factors affect this observation, such as: healthcare access, cultural and language barriers. The objective of this study was to evaluate the impact of a culturally tailored patient-navigation program (CTPNP) on CCR. Methods A CTPNP was implemented to overcome barriers for CCR among Hispanics. Hispanic patients referred to the CTPNP received an introductory letter/phone call from our culturally competent, Spanish-speaking navigator. The navigator was trained to educate the patient on the importance of the test and to ameliorate cultural barriers through tailored interventions that include bowel preparation education, scheduling, transportation assistance, and work letters. All patients were directly scheduled for colonoscopy without a pre-procedure visit. Results Over a 9-month period, 149 patients (78 F, 71 M) were enrolled with a CCR of 93% (n=139) and a 7% 'no-show' rate (n =10). Female CCR was 94% (n=73) and 93% (n=66) for males. 'No shows' were 5 male and 5 females. Reasons for 'no-shows' included work-related constraints and \ fear of the procedure not previously expressed to the navigator. Within the CCR group, 56 patients (42%) required polypectomy and 2 patients underwent colectomy for CRC. Adequate bowel preparation was reported in 82% (n=114). Post-colonoscopy survey was uniformly positive across all participants and 76% (n=105) replied that they would not have completed colonoscopy without the CTPNP. Conclusion CTPNP is an effective care model to achieve high CCR among Hispanic patients; with >90% CCR in the cohort. Most notably, males and females achieved an equivalent CCR, offering support that CTPNP may abolish the CCR gender disparity.

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Facilities that Service Higher-Income Areas Are More Likely to Perform Metastasectomy for Patients with Colorectal Liver Metastases A. Uppal,* F. Smieliauskas, B. Polite, M. Posner, K. Turaga. *Surgery, University of Chicago, Santa Monica, CA.*

Introduction: Metastasectomy of isolated colorectal liver metastases (CRLM) is the gold standard for patients with resectable colorectal cancer. We hypothesize that disparities in advanced colorectal cancer care occurs based on facility characteristics; specifically that hospitals which treat a greater percentage of patients from higher-income catchment areas (High-Income Hospitals, HH) are more likely to perform metastasectomies. Methods: Using NCDB data (2010-2013) we identified patients with liver-only metastases from colorectal adenocarcinoma. We stratified facilities into quartiles based on proportion of patients from highest-income ZIP codes (Q1 <2.1%, Q2 2.2-15.6%, Q3 15.7-40.2%,Q4 >40.3%). Multi-variate logistic regression, adjusting for factors

including patient characteristics (distance traveled, socio-economic status), tumor characteristics and facility characteristics (academic and high volume) was performed to identify associations with metastasectomy. Results: We identified 15,386 out of 712,172 patients with isolated liver metastases, of whom 2,335 (15%) underwent metastasectomy. Patients with Stage IV colorectal cancer were more likely to undergo metastasectomy (11% Q1, 14% Q2, 16% Q3, 18% Q4, p=0.001) and systemic chemotherapy (75, 74, 84, 83%, p=0.05) at HHs. This trend was not observed in Stage I-III cancers (resection rates of 93, 90, 94, 95%, p=0.94). After adjusting for insurance status and other socio-economic proxies, patients treated at HHs were more likely to undergo metastasectomy (OR 1.35, [1.11-1.63], p=0.002). This disparity was most pronounced at academic facilities (33.1% at Q4 vs. 16.5% at Q1 facilities, p=0.001). Conclusion: Metastasectomy for CRLM is more likely to occur at facilities that serve a greater percentage of patients from high-income catchment areas, regardless of individual patient characteristics. This disparity uniquely affects patients with advanced cancers and is most evident at academic facilities. We propose further investigation of the underlying causes for this disparity, such as referral patterns or systematic obstacles to healthcare access in lower-income areas.

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Race and Health Disparities in Patient Refusal of Surgery for Early-stage Pancreatic Cancer: An NCDB Cohort Study

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Introduction: Despite continued improvement in outcomes, a considerable proportion of patients never receive curative-intent surgery for resectable early pancreatic cancer. Earlier studies ten years ago show that up to four percent of patients refuse surgery. Several socioeconomic factors have been linked to the likelihood of a patient refusing surgery for resectable cancer. The purpose of this study was to identify the incidence, trends, risk factors, and eventual survival outcomes associated with refusal of surgery for early stage pancreatic cancer on a national scale. Methods: Using the National Cancer Data Base (2003-2012), 12,682 patients were identified with potentially resectable tumors (pretreatment clinical Stage I: T1 or T2 N0M0). Multivariate models were employed to identify factors predicting failure to undergo surgery and assess the impact on survival. Results: Of Stage I patients, 8.4% (1,064/12,682) refused surgery for resectable early stage pancreatic cancer. An increasing trend was observed from 2003 to 2012. On multivariable analysis, patients were more likely to refuse surgery if they were older (OR=1.18; 95%CI 1.16-1.19), females (OR=1.52; 95%CI,1.33-1.73), African-American (vs White, OR=1.79; 95% CI, 1.37-2.34), on Medicare/Medicaid (vs private, OR=2.75; 95% CI, 1.54-4.92) or had a Charlson-Deyo score of 2 (vs 0, OR=1.33, 95% CI 1.03-1.72). Patients were significantly more likely to refuse surgery if they were seen at a center that is not an Academic/Research program (OR 1.9, 95% CI 1.6-2.27). Patients who were offered surgery but refused had significantly worse survival than those with Stage I who received surgery (Median Survival 6.8 vs. 24 months, P<0.001) Conclusion: The percentage of patients refusing surgery for operable early stage pancreatic cancer has doubled in the last decade which significantly affects survival. Disparities in the refusal of surgery are independently associated with several socioeconomic variables including gender, race and insurance. To mitigate national disparities in surgical care, future studies should focus on exploring potential reasons for refusal and developing communication interventions.

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Intraoperative Radiotherapy for Early-Stage Breast Cancer in a Predominantly African-American Patient Population

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Background: Intraoperative Radiotherapy (IORT) offers exceptional convenience compared to external beam radiotherapy (EBRT) following breast-conserving surgery. IORT studies are limited by short-term follow-up, but this treatment is very attractive for poorly complaint patients. This study describes the implementation of a high-volume IORT program at a large academic cancer center, serving mainly African Americans. Methods: We conducted a retrospective review of outcomes of early-stage breast cancer patients treated with IORT consisting of 20 Gy of low-energy x-rays delivered to the partial mastectomy cavity via spherical applicator. All patients met the following criteria pre-operatively: DCIS or invasive cancer ≤ 3.0 cm; negative axillary exam; hormone-receptor positive; Her-2 negative for invasive disease. Results: Our cohort included 103 consecutive patients, 67.0% African-American with median age 68 years (49 – 89). Median Body mass index was 30.1. Histologically, 70 patients had invasive ductal carcinoma and 33 had DCIS. IORT was delivered after completion of partial mastectomy (+/- sentinel node biopsy) in 96 cases (93.2%), with the remaining 7 cases (6.8%) treated during a dedicated second procedure or at the time of a re-excision. Delivery time ranged from 15.6 – 46.2 minutes. Median operative time was 128 minutes (48 – 216). Outcomes are summarized in the table. Seventy-six patients (73.8%) had no indication for supplemental surgery or radiation therapy. Fourteen patients (13.5%) were recommended for supplemental EBRT. Five patients (4.9%) received chemotherapy. All patients was recommended hormonotherapy. Wound-healing complications were seen in 11 patients (10.7%). There was one ipsilateral breast recurrence that was diagnosed and treated within one year of IORT. Conclusions: IORT is a highly desirable and convenient alternative to EBRT for early-stage breast cancer. With careful selection criteria, it can be offered successfully with very acceptable operative times and low complications. This treatment is also very attractive for poorly complaint patients and does not preclude EBRT if necessary based upon the final pathologic report.

Outcomes of 103 patients

76 (78.3%)	Surgery + IORT
27 (21.7%) needs additional radiation therapy or surgery	14 were recommended EBRT because of: - LVI -Intermediate or High grade Oncotype -Unwillingness to take endocrine therapy
	13 had positive margins defined as tumor at the ink for invasive cancer and < 2 mm margins for DCIS - 4 underwent mastectomy - 6 postmenopausal with DCIS < 2mm were offered endocrine therapy only -2 with < 2 mm margins for DCIS had many comorbidities to offer additional surgery -1 patient with close margins declined additional surgery

IORT= Intraoperative Radiation Therapy; EBRT= External Beam Radiation Therapy; LVI= Lymphovascular invasion

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Does Race Predict Survival for Women with Invasive Breast Cancer?

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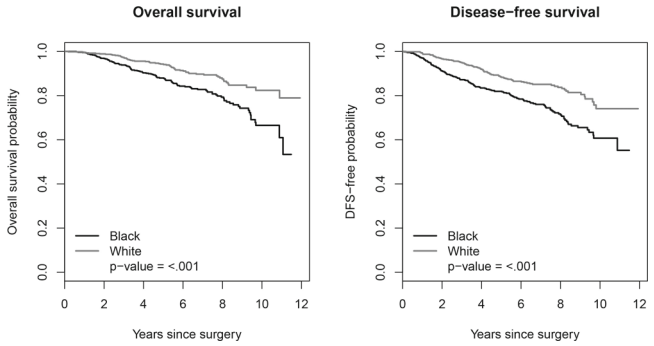
Introduction Despite recent treatment and prognosis advances, the racial gap in breast cancer death rates has widened, with consistently lower overall survival (OS) and disease-free survival (DFS) in black women. Here we examine treatment and survival outcomes in black women with invasive breast cancer versus white, in a single institution with a standardized approach to care. Methods An institutional, retrospective review of black women treated for invasive breast cancer between 2005 and 2010 was performed. This group was compared with a group of white women matched by age and year of surgery. OS and DFS were analyzed using Cox regression models stratified by match set. Results Our study consisted of 1332 women, half of whom were black. The median age at surgery was 55 (range: 24-94 yrs). Black women were found to have larger median tumors (1.6 versus 1.3 cm, p<0.001), more ER negative breast cancer (32.9% versus 15%, p<0.001), high-grade tumors (43.5% vs 31.1%, p<0.001) and more node-positive disease (41.1% vs 32%, p<0.001). Triple negative subtype was more frequently seen in black women (24% vs 8.9%, p<0.001). Black women had significantly worse OS and DFS on univariable analysis (Figure). On univariable analysis, increased tumor size, more advanced stage, positive lymph nodes, and triple negative tumor subtype were all significantly associated with worse OS and DFS. On multivariable analysis only triple negative tumor subtype remained associated with worse OS and DFS. Race was not significantly associated with OS (p = 0.456) or DFS (p = 0.302) in multivariable analysis. Conclusions Black women were found to have more advanced disease and adverse prognostic indicators at diagnosis, including more triple negative breast cancer. However, race was not an independent predictor of OS or DFS, after adjusting for tumor subtype and other prognostic factors. Further research is necessary on factors associated with advanced disease at presentation for black women.



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Challenging the Homogeneity of Clinical Trials to Include Women of Diverse Races/Ethnicities L. Kruper,[1]* T. Chavez,[1] V. Jones,[1] C. Vito,[1] S. Clancy,[1] A. Polverini,[1] C. Thai,[1] A. Sanchez,[1] M. Robles,[1] N. Chavez,[1] O. Idassi,[1] K. Kennedy,[1] A. Nunez,[1] J. Lopez,[1] S. Shalabi,[1] C. Kalu,[1] J.A. Alva-ornelas,[1] J. Tomsic,[1] E. Rippberger,[1] T. Hyslop,[2] C. Zalles,[3] P. Chu,[1] L. Yee,[1] C. Kupperwasser,[4] D. Schmolze,[1] C. Sistrunk,[1] V. Seewaldt.[1] *1. City of Hope, Los Angeles, CA; 2. Duke University, Durham, NC; 3. JFK Medical Center, Atlantis, FL; 4. Tufts University School of Medicine, Boston, MA.*

BACKGROUND: Blacks, Latinas, Native Americans, Asians have poorer breast cancer (BC) outcomes and higher mortality rates compared to Northern-European Whites (NE/W) or non-Hispanic Whites (NHW). Participation in clinical trials (CTs) could improve these health disparities; however, the majority of CTs disproportionately enroll NE/W or NHW (e.g. over 96% of women enrolled in the BC Prevention Trial (P1) and STAR trial were of NE/W descent). Here we describe a successful recruitment strategy for inclusion of women of diverse races/ethnicities to a BC trial. METHODS: Focus groups emphasized the community's role in the process of mentoring future medical providers. Thus, we recruited 4 bicultural, bilingual clinical research assistants (CRAs) representing the diversity of our Los Angeles catchment area. At City of Hope (CoH), Our CRAs along with 5 breast surgeons, screened and consented all eligible patients. RESULTS: The CRAs were 1) first generation American representing diverse races/ethnicities, 2) raised and attended college in Southern California, and 3) pre-med/nursing. The CoH clinic population is 48% NHW, 23% Latina, 12% Asians/Pacific Islanders (A/P), 7% Black, and 0.1% Native American (NA). A total of 1,129 patients were screened: 139 women were eligible, 119 consented and 20 declined. Of the consenting population, 31% were NHW, 43% Latina, 16% A/P, 8% Black, and 2% NA. Primary languages included 86% English, 9% Spanish, 4% Chinese, and 1% Armenian. Of the consenting NHW, 92% descended from Northern Europe, while 8% were from the Middle East/North Africa. Recruitment exceeded CoH interventional CT accrual of 55% NHW, 21% Latina, 10% A/P, 4% Black, and 0.1% NA. CONCLUSION: We have demonstrated that Black, Latina, NA and A/P women are equally as likely to participate in CTs when approached by a culturally competent CRA. Our ability to recruit diverse populations to CTs lies in the 1) simplistic act of approaching all those eligible, 2) racial diversity and cultural competency of our CRAs and 3) willingness of women representing diverse races/ethnicities to participate in CTs.

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The Impact of American Indian and Alaska Native Ethnicity on the Presentation and Surgical Treatment of Gastric Cancer: An NCDB Analysis from 2004-2014 B. Vuong,[2]* S.J. Klempner,[4] T. Nguyen,[2] S. Young,[1] A. Dehal,[2] A.N. Graff-Baker,[2] s. chang,[3] A. Bilchik,[2] M. Goldfarb,[2] T. Fischer.[2] *1. General Surgery, Kaiser Permanente Los Angeles Medical Center, Los Angeles, CA; 2. John Wayne Cancer Institute at Providence Saint John's Health Center, Santa Monica, CA; 3. Providence Health and Services, Portland, OR; 4. The Angeles Clinic and Research Institute, Los Angeles, CA.*

Background: American Indian/Alaska Natives (AI/ANs) with gastric adenocarcinoma (GC) have an incidence and mortality nearly double that of matched Non-Hispanic Whites (NHW) in historical data sets. However, the impact of AI/AN ethnicity on disease presentation and treatment is underrepresented in gastric cancer epidemiologic studies and has not been evaluated in a contemporary population. Methods: The National Cancer Data Base (NCDB) was queried from 2004-2014 to identify patients with gastric cancer who identify as AI/AN or NHW. Patient demographics, tumor characteristics, and treatment details, including surgical quality metrics, were compared using Chi-square and Student's t-tests. Results: There were 22,286 NHW and 115 AI/AN GC patients with complete staging information. Compared to NHW, AI/ANs were younger (age ≤65) at diagnosis ($p < 0.001$), which translated to a younger mean age at death (NHW:70.4 years, AI/ANs:60.2 years, $p < 0.001$). AI/ANs more often lived over 100 miles from their treatment facility ($p < 0.001$) in non-metropolitan cities ($p < 0.001$). Stage distribution was not different for the AI/AN population when compared to the NHW population: 37% vs. 35% Stage I; 33% vs. 37% Stage II; 10% vs. 11% Stage III; and 19% vs. 16% Stage IV (p = NS). However, AI/ANs had a higher rate of signet ring cell histology and linitis plastica (26% vs. 15%, $p = 0.002$) compared to NHWs. More AI/AN patients compared to NHW patients had delays over eight weeks to initiation of treatment, 19% vs. 11% ($p = 0.008$). There were no statistically significant differences for surgical quality metrics, including type of surgery, rate of ≥15 lymph nodes retrieved, margin positivity, or 30-day mortality (p = NS). Conclusions: Both biological and social disparities are evident for AI/ANs with gastric cancer. AI/ANs develop and die from gastric cancer at younger ages compared to NHWs and present with higher rates of aggressive histology. They also travel longer distances for treatment and experience greater treatment delays. These features may partly underlie the higher mortality rates previously described.

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Impact of National Comprehensive Cancer Network (NCCN) Genetic Testing Guidelines on Genetic Counseling Referral Patterns for Triple Negative Breast Cancer (TNBC) Patients I. Rakitin,* M. Quigg, M. Nyhuis, L. Petersen, D. Nathanson, M. Davis, L. Susick, E. Proctor, J. Bensenhaver, L. Newman. *Breast Surgery, Henry Ford Health System, West Bloomfield, MI.*

Introduction: In 2011 the NCCN revised the clinical practice guideline regarding identification of breast cancer pts that should be referred for genetic counseling/testing, to include any woman diagnosed with triple negative breast cancer (TNBC) ≤60 years, regardless of family history. Little is known regarding the impact of this revision on referral patterns and testing results among African American (AA) women, who face an increased risk of TNBC compared to White Americans (WAs). Methods: We queried a prospectively-maintained, IRB-approved breast cancer database linked to a genetic counseling program in a diverse metropolitan multi-hospital health system. Genetic counseling referrals prior to 2011 versus after 2011 were evaluated and stratified by AA versus WA. Results: Of 2984 pts with invasive breast cancer (57% WA; 32% AA) seen 05/1997 to 01/2017, 12% had TNBC. Frequency of TNBC was 16% for AA and 10% for WA pts ($p<0.05$). Median age was 62 years for WA versus 60 for AA TNBC pts. Of the 1288 pts ages ≤60 years, 495 (38%) were AA. Prior to 2011, 52% of WA pts were referred for genetic counseling and 54% of the 24 pts that completed testing were found to harbor a genetic mutation; 26% of the AA pts were referred for genetic counseling and 0% of the 4 pts that completed testing were found to harbor a genetic mutation. From 2011 onward, 53% of the WA pts ≤60 were referred for genetic counseling and 15% of the 13 pts that completed testing were found to harbor a genetic mutation; 50% of the AA pts were referred for genetic counseling and 17% of the 12 pts that completed testing were found to harbor a genetic mutation. The increase in genetic counseling referrals for AA TNBC pts <60yrs pre-2011 versus 2011 and later was statistically significant ($p<0.05$). Conclusion: The NCCN guidelines resulted in modest increases in genetic counseling referrals among WA TNBC cases but significant increases for AA pts. The revised guidelines will likely result in improved knowledge about hereditary susceptibility for breast cancer among AA women.

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Surgical Outcomes After Neoadjuvant Chemoradiation Followed by Curative Surgery in Patients with Esophageal Cancer: An Intergroup Phase-lll Trial of the Swiss Group for Clinical Cancer Research (SAKK 75/08) U. von Holzen,[1]* S. Sven,[3] S. Hayoz,[4] T. Steffen,[5] F. Grieder,[6] D. Bartsch,[7] A. Schnider,[8] W. Knoefel,[9] T. Schmid,[10] G. Piessen,[11] C. Kettelhack,[2] W.R. Marti,[12] M. Schafer,[13] R. Fugger,[14] A. Konigsreiner,[15] B. Gloor,[16] M. Furrer,[17] M. Gerard,[4] M.K. Walz,[18] P. Alesina,[18] T. Ruhstaller.[5] *1. Goshen Center for Cancer Care, Goshen, IN; 2. University Hospital Basel, Basel, Switzerland; 3. Klinikum Ernst von Bergmann, Potsdam, Germany; 4. SAKK Coordinating Center, Bern, Switzerland; 5. Kantonsspital St. Gallen, St. Gallen, Switzerland; 6. Kantonsspital Winterthur, Winterthur, Switzerland; 7. Universitätsklinikum Giessen und Marburg, Marburg, Germany; 8. Stadtspital Triemli, Zurich, Switzerland; 9. University Hospital Düsseldorf, Dusseldorf, Germany; 10. Medizinische Universität Innsbruck, Innsbruck, Austria; 11. Centre Hospitalier Régional Universitaire de Lille, Lille, France; 12. chirurgieaarau, Aarau, Switzerland; 13. Lausanne University Hospital, Lausanne, Switzerland; 14. Krankenhaus der Elisabethinen Linz, Linz, Austria; 15. Eberhard Karls University Tübingen, Tubingen, Germany; 16. Inselspital Bern, Bern, Switzerland; 17. Kantonsspital Graubünden, Chur, Switzerland; 18. Kliniken Essen-Mitte, Essen, Germany.*

Background In this multicenter phase III trial (NCT01107639) induction chemotherapy followed by chemoradiation and surgery in patients with locally advanced esophageal cancer was investigated. Methods Patients in the control arm received induction chemotherapy consisting of cisplatin and docetaxel, followed by concomitant chemoradiation therapy with cisplatin, docetaxel and 45Gy. In the experimental arm, the same regimen was used with addition of cetuximab. After completion of neoadjuvant treatment, patients proceeded to esophagectomy. Results 300 patients were enrolled in 4 European countries, of which 259 underwent esophagectomy. Median follow up was 4 years. 63% of patients had adenocarcinoma, and 37% had squamous cell carcinoma. In 95% the tumor was located in the distal esophagus or at the GE junction. Median progression-free survival was 2.9 years in the investigational group vs. 2.0 years in the control group (p=0.13). 96% had R0 resections. Transthoracic resection was performed in 75% and transhiatal resection in 24%. Cervical anastomosis was performed in 32%, and thoracal anastomosis was performed in 68%. Overall complication rate was 56% and reoperation rate was 15%. There was no difference in complication rates for transthoracic vs. transhiatal resections (56% vs. 54%, p=0.77), nor in complications for VATS vs. open transthoracic resections (67% vs. 55%, p=0.32). We observed a trend to higher overall complications for cervical vs. thoracal anastomosis (63% vs. 53%, p=0.11). There was no difference in complications for two stage reconstruction (67% vs. 55%, p=0.31), but a trend to increased reoperation rates (31% vs. 14%, p=0.081). Major complications were pneumonia in 23% and anastomotic leak in 17%. 30 day postop mortality rate was overall 3.1%, and in-hospital mortality rate was 4.6%. Conclusion This trial showed an overall low post-operative mortality rate, no evidence for a difference in surgical complication rates between transthoracic and transhiatal esophageal resections, but weak evidence for more complications with cervical anastomosis.

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Preoperative Therapy for Gastric Adenocarcinoma is Protective for Poor Oncologic Outcomes in Patients with Complications After Gastrectomy D. Vicente,* N. Ikoma, Y. Chiang, K. Fournier, P. Mansfield, J. Ajani, B. Badgwell. *University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Postoperative complications (POC) are associated with poor oncologic outcomes in gastric cancer, however, it is unknown if preoperative therapy has any impact on this association. We sought to evaluate the impact of POC on survival in patients with gastric cancer treated with upfront surgery versus those treated with preoperative therapy. Methods: We analyzed a prospectively maintained database of patients who had undergone resection of their gastric cancer between 1995 and 2015. Patients with T1N0 or M1 lesions, recurrent disease, mortality within 90 days, and GEJ tumors were excluded. Cox regression analyses were used to examine factors associated with overall survival (OS) and disease free survival (DFS). Interaction terms between complications and preoperative therapy were used in the multivariate model to determine their impact on OS and DFS. Results: 421 patients underwent resection of gastric cancer: 30% underwent upfront surgery, and 51% had a POC. Variables associated with POCs included total gastrectomy (p=0.02) and additional organ resection (p=0.05). Among patients who had POCs, 71% were infectious, 41% experienced multiple complications, and 55% were classified as Clavien-Dindo grade III or IV. On multivariable analysis, the presence of a POC had the strongest association with diminished OS (HR 3.5, 95% CI 1.9-6.5). Among patients who underwent upfront surgery, patient with a POC had shorter OS (5-year, 47% vs. 85%; p<0.001) and DFS (5-year, 46% vs. 76%; p<0.001) than those without a POC. In contrast, there was no difference in OS (5-year, 57% vs. 63%; p=0.77) and DFS (5-year, 52% vs. 52%; p=0.52) between patients with and without POC who received preoperative therapy. Interaction terms between preoperative therapy and complication in the multivariable Cox regression model were significant on OS (3.53 [95%CI: 1.92-6.52]) and DFS (2.84 [95%CI: 1.59-5.08]), which indicated that the negative impact of complications were reduced if patients received preoperative therapy. Conclusion: The use of preoperative therapy negated the impact of POCs on OS and DFS in patients undergoing resection for gastric cancer.

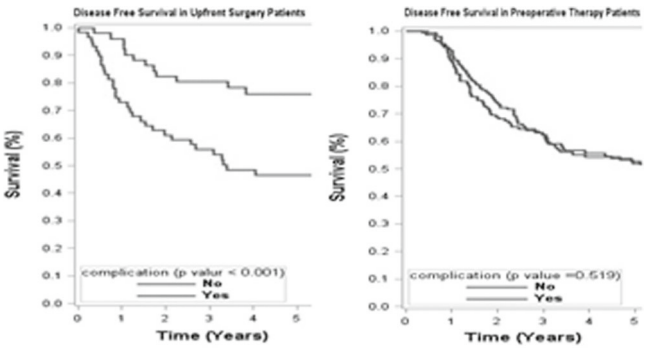

Figure 1: Patients undergoing gastric cancer resection with a post-operative complication had significantly shorter disease free survival disease free survival than patients without complications (5-year, 46% vs. 76%; p<0.001). While the disease free survival in patients who received pre-operative treatment was not significantly affected by post-operative complication (5-year, 52% vs. 52%; p=0.52) .

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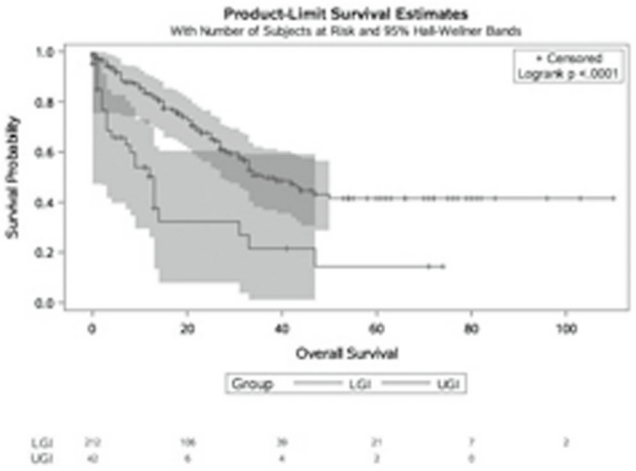
Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy in Upper Gastrointestinal Malignancies: A Cautionary Tale N.L. Leigh,* D. Solomon, D. Feingold, D.M. Labow, D.R. Magge, U. Sarpel, B.J. Golas. *Icahn School of Medicine Mt. Sinai, New York, NY.*

Objective: Select patients with peritoneal carcinomatosis (PC) secondary to lower gastrointestinal (LGI) malignancies derive benefit from cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) particularly in colorectal primaries. However, the role of CRS/HIPEC in upper gastrointestinal (UGI) malignancies with PC remains unclear. Methods: We retrospectively analyzed all patients who underwent attempted CRS/HIPEC for GI malignancies with PC at our institution from 2007 to 2017. We compared clinicopathologic, perioperative, and oncologic outcomes of UGI and LGI malignancies. Results: Of 441 total patients, CRS/HIPEC was attempted in 254 patients with PC from GI malignancies; 42 with UGI (34 gastric, 8 small bowel) and 212 with LGI (119 colon, 91 appendiceal, 2 rectal). For UGI and LGI respectively, EBL (200 vs. 200 ccs, p=0.6044), operative time (296 vs. 292 mins, p=0.6205), PCI (14 vs. 12, p=0.3619), completeness of cytoreduction (CC-0/CC-1 67% vs. 73%, p=0.4267) and aborted procedures (24% vs. 18%, p=0.3735) were similar. Though 30-day mortality was comparable (0% vs. 1%, p=0.5264), LOS (10 vs. 6 days, p=0.0351) and major postoperative morbidity (Clavien III-V, 36% vs. 18%, p=0.0078) were both higher in the UGI cohort. Rates of adjuvant chemotherapy were equivalent (76% vs. 88%, p=0.05). Median follow-up for all patients was 15 months. Median PFS (8 vs. 12 months, p=0.0105), 1-year OS (50% vs. 83%) and 3-year OS (22% vs. 50%, p<0.0001) were all significantly shorter in the UGI cohort. On multivariate analysis, higher PCI and tumor recurrence were significant predictors of poor OS (p<0.05). Conclusions: Our extensive experience with CRS/HIPEC in GI malignancies suggests that primary tumor origin within the GI tract is highly relevant in patient selection. Due to a significant complication profile coupled with poor outcomes, CRS/HIPEC should be used with extreme caution

in patients with PC secondary to UGI malignancies. However, CRS/HIPEC remains a viable treatment modality for select patients with LGI malignancies.



Kaplan-Meier curves of overall survival for UGI and LGI cohorts

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Personalized Medicine Applications for Endoscopic Derived Gastric Cancer Organoids M. Lin,* K. Hirai, D. Tzimas, L. D'Souza, J. Bucobo, J.M. Buscaglia, S. Powers, M. Rao, M. Choi, G.V. Georgakis, A. Sasson, M. Talamini, M. Gao, J. Kim. *Stony Brook Medical Center, Nesconset, NY.*

Background: Patient-derived 3-D in vitro cancer models, aka organoids, accurately portray human cancer genotype and phenotype. Our primary objective was to assess if endoscopic-derived gastric cancer organoids could be used in drug sensitivity testing for personalized medicine. Methods: Informed consent was obtained from patients undergoing endoscopy for suspected gastric cancer to obtain additional forceps biopsy tissues. These endoscopic tissues were used to create gastric cancer organoids. Paired gastrectomy cancer tissues were also collected to create organoids and to perform next generation sequencing (NGS). Gastric cancer origin of organoids was assessed by immunofluorescent (IF) staining. For drug screening, we administered current standard of care drugs to organoids and measured cytotoxic responses. Results: Gastric cancer organoids were created from endoscopic biopsies (n=5 patients) and paired gastrectomy tissues (n=2 patients). Gastric epithelial origin of organoids was confirmed by IF positivity for Lgr5 and Troy. In 1 patient, 3 sets of organoids were created from 3 different endoscopic biopsy locations of the primary tumor. This tumor was subsequently removed by gastrectomy and whole tumor lysates underwent NGS, which categorized the primary tumor as genomically stable and revealed that all 3 sets of endoscopic-derived organoids were genomically identical to the primary tumor. Finally, endoscopic-derived organoids were treated with clinical monoclonal antibodies and cytotoxic chemotherapies. Treatment with trastuzumab showed low cytostatic effects consistent with Her2 negativity in the paired primary tumor. Ramucirumab showed similar low cytostatic effects, predicting low clinical response. Cytotoxic response curves with oxaliplatin, cisplatin, and irinotecan revealed that cisplatin was most effective in killing gastric cancer organoids. Conclusions: Gastric cancer organoids are quick-to-develop accurate models of human gastric cancer. We report the first successful creation of organoids from endoscopic biopsies of human gastric adenocarcinoma. These organoids show tremendous potential for personalized medicine as ex vivo predictors of in vivo drug response.

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Omental Exosomes Promote Gastric Cancer Aggressiveness: A Potential Novel Mechanism of Gastric Cancer Peritoneal Metastasis S. Loewenstein, F.M. Johnston, N. Lubezky, E. Nizri, J.M. Klausner, G. Lahat.* *Surgery, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel.*

Background: Malignant progression results from a dynamic cross-talk between stromal and cancer cells. Data suggest that this cross-talk is mediated to a significant extent by exosomes, nanovesicles secreted by various cell types and which allow the transfer numerous molecules between cells. We investigated the potential role of omental exosomes in gastric cancer peritoneal metastasis. Methods: Gastric cancer cell lines were used for all in vitro experiments. Omental fat exosomes were produced from fresh human omental tissues. Proliferation, migration, invasion and chemoresistance were used to evaluate the phenotypic behavior of omental- exosomes treated cancer cells. Using mass spectrometry we identified the proteome of omental exosomes. RNA array identified exosomal- induced cancer cell genetic deregulations. Results: Initially, we demonstrate a robust uptake of omental exosomes by gastric cancer cells; these exosomes enhance gastric cancer cell proliferation, migration and invasion. We also revealed that the number of exosomes is directly related to their effect on gastric cancer cells. We further show that omental exosomes induce gastric cancer cellular chemoresistance to platinum-based therapy, and that omental exosomes augment gastric cancer xenograft tumor growth and resistance to chemotherapy in- vivo. We characterized the proteome of omental exosomes and several established oncomiRs implicated in cellular adhesion and chemotaxis, tumor growth and motility as well as chemoresistance; some of these molecules have been reported as pro-tumorigenic factors in gastric cancer. Finally, we demonstrate that omental- exosomes increase the expression of transcription factors, mRNA of extracellular matrix proteins, and adhesion molecules within gastric cancer cells. Conclusions: These observations demonstrate for the first time uptake of omental exosomes by cancer cells; these vesicles carry different molecules which promote gastric cancer cellular aggressiveness in vitro and in vivo. Taken together, our data imply that omental exosomes might play a role in gastric cancer peritoneal spread.

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Intercellular Adhesion Molecule-1 as a Potential Therapeutic Target in Gastric Cancer K.D. Gray,[1]* O. Kalloo,[2] Y. Vedvyas,[2] T.M. Ullmann,[1] R.K. Yantiss,[1] M.M. Jin,[2] T.J. Fahey,[1] I.M. Min,[2] R. Zarnegar.[1] *1. New York Presbyterian-Cornell, New York, NY; 2. Weill Cornell Medicine, New York, NY.*

Introduction: Intercellular adhesion molecule-1 (ICAM1) is a cell surface molecule that is overexpressed in many solid tumors and is a known marker for aggressive tumor behavior. We aim to evaluate whether ICAM1 is highly expressed in gastric adenocarcinoma and to determine if it is a potential therapeutic target for T cell immunotherapy. Methods: Gastric adenocarcinoma cell lines (NCI-N87, KATOIII, and MKN45) and formalin-fixed, paraffin-embedded (FFPE) tissue blocks of gastric and gastro-esophageal junction adenocarcinoma from a tertiary referral center were evaluated. Flow cytometry was performed with anti-human FITC-conjugated ICAM1 (monoclonal antibody R6.5) for cell line analysis, and FFPE blocks underwent immunohistochemistry staining with anti-ICAM1 monoclonal antibody clone G-5. Effector:target assays were constructed using a previously established chimeric antigen receptor (CAR) T construct developed to target ICAM1. Results: All three cell lines tested were positive for ICAM1, with poorly differentiated cell lines (KATO III and MKN45) showing high percentages of R6.5 binding (95.2% and 82.4%, respectively) and NCI-N87, a well-differentiated gastric adenocarcinoma, showing moderate R6.5 binding (60.7%). A cohort of eighteen FFPE patient blocks from primary tumors showed that 11/18 (61%) samples were positive for ICAM1. There was a higher percentage of ICAM1-positivity in primary tumors with known distant metastases (5/6, 83.3%) than in tumors that were localized or metastatic to lymph nodes only (6/12, 50%), although this did not reach statistical significance ($p = 0.17$). Additional matched samples of lymph nodes containing metastatic foci (n=3) and biopsies of liver metastases (n=2) showed concordant ICAM1 staining to the primary tumor in all cases. Finally, an effector:target assay was performed using ICAM-1 specific CAR T cells with effective killing of ICAM1-positive tumor cells and sparing of

ICAM1-negative cells (Figure 1a-b). Conclusions: Gastric adenocarcinomas demonstrate high ICAM1 expression, which was retained in metastatic foci. In vitro data indicates that ICAM1 can be used as a potential therapeutic target for T cell immunotherapy in gastric cancer.

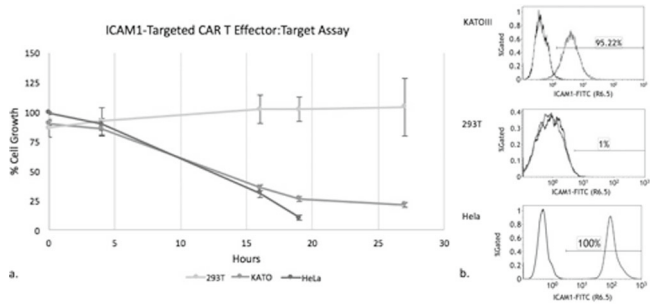

Figure 1. a. in vitro effector:target assay showing rapid KATO III tumor killing with ICAM1-targeted CAR T therapy. b. flow cytometric staining for KATO III, 293T (ICAM1-negative control: immortalized embryonic kidney cell line), and HeLa (ICAM1-positive control: cervical cancer cell line).

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Intratumoral Immune Response to Gastric Cancer Varies by Molecular and Histologic Subtype T. Kim,[1]* E.M. Da Silva,[2] D. Coit,[2] L.H. Tang.[2] *1. Surgery, University of Washington, Seattle, WA; 2. Memorial Sloan Kettering Cancer Center, New York, NY.*

INTRODUCTION: Recent trials have demonstrated an effect of PD-1 blockade in a subset of patients with advanced gastric cancer. Genomic profiling has revealed the molecular heterogeneity of gastric adenocarcinomas. However, the gastric cancer immune microenvironment, as well as the predictors of response to checkpoint blockade, remain poorly understood. We aimed to better characterize the immune response to gastric cancer. METHODS: Retrospective review of an institutional database was performed to identify patients who underwent curative intent resection of gastric adenocarcinoma from 2007-2016. Tumors were classified according to modified TCGA subtype: (1) Epstein-Barr virus-associated (EBV), (2) microsatellite instability-high (MSI); (3) intestinal, as a surrogate for chromosomal instability (CIN); (4) diffuse/signet-ring cell, as a surrogate for genomically stable (GS). Tumor infiltrating leukocytes (TIL) were measured using immunohistochemistry and digital image analysis. RESULTS: Forty-three patients were identified, including 6 EBV, 11 MSI, 14 intestinal, and 12 diffuse. The most prevalent TIL were $CD8^+$ T lymphocytes and $CD68^+$ macrophages, which comprised 16% and 13% of all tumor cells, respectively (Fig. 1). EBV and MSI tumors harbored the most immune infiltrate, with 30-50% of all tumor cells consisting of T cells, and 20% of cells consisting of macrophages. Intestinal tumors contained fewer T cells, and were most infiltrated by macrophages (mean frequency, 14%). Diffuse tumors were the least infiltrated, but did consist of 15% T cells and 2% macrophages. Expression of the checkpoint receptor programmed cell death protein 1 (PD-1) was most frequent in intestinal tumors (mean frequency, 10%), whereas intestinal, EBV, and MSI subtypes all had a similar frequency of programmed death-ligand 1 (PD-L1) expressing cells (4-7%). CONCLUSIONS: Gastric adenocarcinoma generates a heterogeneous immune response that varies by tumor subtype and has implications for future immunotherapy trials. Checkpoint blockade is unlikely to be effective single agent therapy in patients with intestinal and diffuse type tumors lacking a prominent T cell infiltrate.

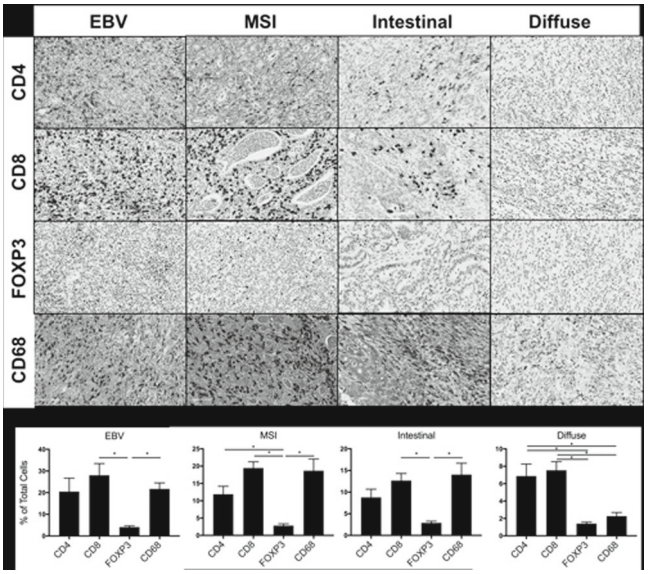

Figure 1. Representative immunohistochemistry depicting the most prevalent immune cell types infiltrating gastric adenocarcinoma. Staining is quantified below (n = 6 EBV, 11 MSI, 14 intestinal, 12 diffuse). Bars, mean +/- SEM. *, $p < 0.05$.

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Viral ILP combines with PD-1 Blockade to Improve Local and Distant Disease Control in Extremity Soft Tissue Sarcoma (ESTS) H.G. Smith,[1]* M. Wilkinson,[1] J. Kyula-Currie,[2] V. Roulstone,[2] D. Mansfield,[2] M. McLaughlin,[2] K. Harrington,[2] A.J. Hayes.[1] *1. The Royal Marsden Hospital, London, United Kingdom; 2. The Institute of Cancer Research, London, United Kingdom.*

Introduction: Isolated limb perfusion (ILP) is a crucial part of the multimodal management of locally advanced ESTS, being used either for limb salvage or as an induction therapy to facilitate function-preserving resections. Current limitations to ILP include a short duration of response and an inability to prevent progression outside of the perfusion field. We sought to determine whether combining ILP with oncolytic virotherapy and PD-1 inhibitors could address these limitations. Methods: An immune-competent model of ILP was developed using Brown Norway rats and the BN175 sarcoma cell line. A vaccinia virus (GLV-1h68) and PD-1 inhibitor (J43) were combined with melphalan and TNFα. Therapeutics were given as a single treatment (palliative ILP model) or prior to surgery and radiotherapy (induction ILP model). Results: The addition of GLV-1h68 to melphalan and TNFα (viral ILP) in a palliative ILP model significantly delayed tumour growth and prolonged survival compared with standard ILP (median 35 vs 23 days, $p<0.001$). However, local control was not achieved. Tumour growth was delayed further with the addition of PD-1 inhibitors to viral ILP ($p<0.001$), resulting in complete regression in 1/3 of animals. However, treatment resistance rapidly developed and survival was not improved. PD-1 inhibitors were unable to induce tumour regression as a monotherapy, indicative of a sensitising effect of viral ILP to these agents. In an induction model, ILP with GLV-1h68, melphalan and TNFα cured local disease in 1/3 of subjects but was insufficient to prevent systemic relapse. The addition of PD-1 inhibitors to this induction protocol cured local disease in all animals and improved systemic control. In vitro, melphalan and GLV-1h68 induce markers of immunogenic cell death. Ex vivo, viral ILP increases intra-tumoural PD-1 expression compared with standard ILP, suggestive of immune cell activation. Conclusion: Viral ILP augments the efficacy of PD-1 blockade and combines to improve both local and distant disease control. This novel combination immunotherapy has the potential to improve outcomes from ILP in both palliative and potentially curative settings.

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Rb-deficient Myxofibrosarcoma and Undifferentiated Pleomorphic Sarcoma have Oncogene Addiction to Skp2 and Show High Sensitivity to Skp2 Inhibitors G. Li,* X. Xu, N. Agaram, N. Socci, S. Singer. *Surgery, Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Myxofibrosarcoma and undifferentiated pleomorphic sarcoma (MFS/UPS) are the most common truncal/extremity soft tissue sarcomas, but there is no effective systemic therapy for the 50% of patients who develop metastases. Up to 70% of MFS/UPS have loss of Rb tumor suppressor function. In retinoblastoma, loss of the Skp2 oncogene is synthetically lethal with Rb loss, so we explored whether Skp2 is required for MFS/UPS tumorigenesis. Methods: Agilent CGH microarrays were used to assess DNA copy number changes in 94 specimens of untreated primary MFS/UPS. In vitro experiments were performed on the Rb-deficient cell line MFS8000S and, for comparison, on the RB-wild type MFS2734 line. MFS8000S was used to generate subcutaneous xenografts in mice. Skp2 was inhibited genetically via lentiviral shRNA knockdown or pharmacologically via pevonedistat, a neddylation inhibitor that blocks Skp2 activity. Proliferation was measured using the CyQUANT assay, and apoptosis was measured using annexin V staining. Results: Of the 94 tumors, 68% had shallow or deep deletion of RB1, 40% had gain or amplification of SKP2, and 31% had both. In Rb-deficient MFS8000S, Skp2 knockdown increased protein levels of the p27 cell cycle inhibitor, decreased proliferation (Fig 1A; $p<0.0001$), and increased apoptosis (40% vs. 6.7% in control cells, $p<0.001$). Pevonedistat treatment of MFS8000S also increased p27, decreased proliferation with an IC50 of 62 nM (Fig 1B), and increased apoptosis (64% vs. 8.8% in control cells, $p<0.001$). The Rb-WT MFS2734 were less sensitive than MFS8000S to pevonedistat (Fig 1B) and Skp2 knockdown. Treatment of MFS8000S-derived xenografts with pevonedistat significantly decreased tumor growth (Fig 1C; $p<0.0001$). Conclusions: Rb loss coexists with SKP2 amplification in 31% of MFS/UPS. Skp2 inhibition decreases proliferation and tumor growth and increases apoptosis in Rb-deficient MFS/UPS cells and xenografts via induction of p27. These results suggest that Skp2 is an oncogenic driver in Rb-deficient MFS/UPS and support the design of a phase I/II clinical trial of pevonedistat for patients with Rb-deficient tumors.

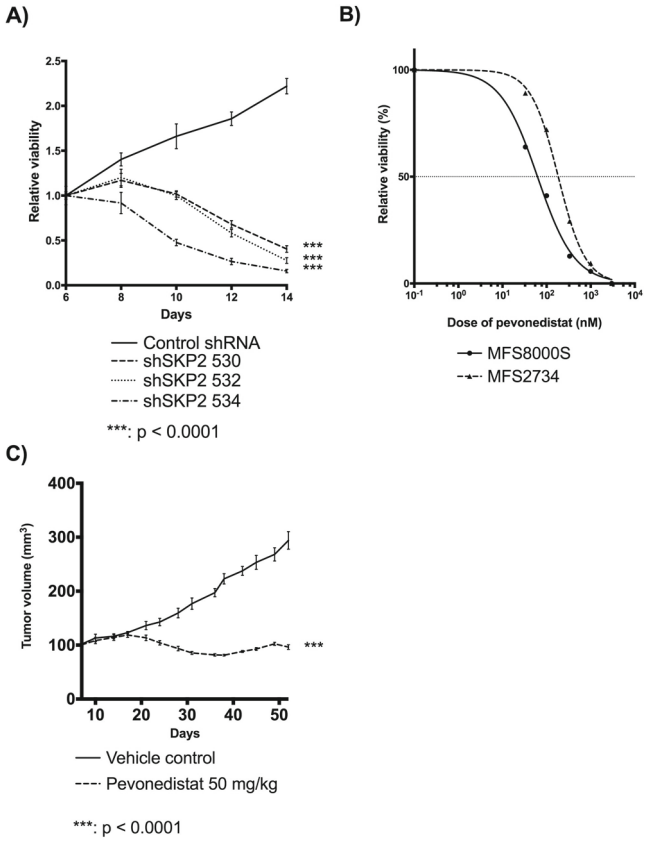

Figure 1. A) MFS8000S cells were treated with control shRNA or 3 different anti-SKP2 shRNAs, and proliferation was measured with CyQUANT. P values are relative to control shRNA, and error bars indicate standard deviation. B) MFS8000S and MFS2734 cells were treated with varying doses of pevonedistat for 4 days, and proliferation was measured with CyQUANT. C) MFS8000S xenografts were treated with vehicle control or pevonedistat 50 mg/kg, and tumor volume was determined using caliper measurements. Error bars indicate standard deviation.

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Management of Recurrent Retroperitoneal Liposarcoma Favors Surgical Resection for First but Not Subsequent Recurrences L.P. Suarez-Kelly,[1]* E.W. Beal,[1] R.D. Shelby,[1] P.Y. Yu,[1] T. Hughes,[1] M. Palettas,[1] C.G. Ethun,[2] T.B. Tran,[3] G. Poultsides,[3] J. Tseng,[4] K.K. Roggin,[4] K. Chouliaras,[5] K. Votanopoulos,[5] B.A. Krasnick,[6] R. Fields,[6] H. Mogal,[7] C.N. Clarke,[7] T.C. Gamblin,[7] A. Salem,[8] S. Weber,[8] R. Pollock,[1] J. Howard,[1] K. Cardona,[2] V.P. Grignol.[1] *1. The Ohio State University, Columbus, OH; 2. Emory University, Atlanta, GA; 3. Stanford University, Palo Alto, CA; 4. University of Chicago Medicine, Chicago, IL; 5. Wake Forest University, Winston-Salem, NC; 6. Washington University School of Medicine, St. Louis, MO; 7. Medical College of Wisconsin, Milwaukee, WI; 8. University of Wisconsin, Madison, WI.*

Background: Surgery is the mainstay of therapy for retroperitoneal liposarcomas (RLS). However, even with complete resection local recurrence is common. The aim of this study was to evaluate survival based on management strategy of recurrent disease. Methods: A retrospective review of all adult patients with RLS who underwent surgical resection and presented with or developed n≥1 recurrences at 8 U.S institutions from 2000-2016 was performed. Due to low numbers, patients with ≥4 recurrences were grouped together. Median OS was calculated and Kaplan–Meier curves were generated. Recurrence free survival (RFS) and overall survival (OS) were calculated using Cox proportional hazard regression models for tumor histology. Results: 181 of 317 (57%) patients with surgically treated RLS developed n≥1

recurrence. The most common histology at presentation was well-differentiated liposarcoma. The most common histology at recurrence was de-differentiated liposarcoma. Number of recurrences ranged from 1-9 (n=119, 1 recurrence; n=63, 2 recurrences; n=30, 3 recurrences; n=25, 4-9 recurrences). For each recurrence patients were grouped according to management: resection, observation, non-operative therapy (chemotherapy, radiation, and/or ablation) or resection and non-operative therapy (Table 1). Median OS favored treatment with resection and resection plus non-operative therapy for the 1st recurrence [median OS 26.45 (15.37, 45.11) and 18.73 (13.10, 51.61)] vs observation or non-operative therapy [median OS 1.90 (0.69, 6.70) and 5.91 (0.92, 7.85)]. For subsequent recurrences no treatment strategy was favored over another for prolonging OS. RFS and OS was worse for de-differentiated vs mixed-type or well-differentiated RLS. Conclusion: This multi-institutional study demonstrated OS is prolonged for recurrent RLS when treated with surgery at initial recurrence. However, for subsequent recurrences no treatment strategy improves OS over another. These data should be interpreted with caution due to inherent selection bias and inequity in number of patients per treatment group.

Table 1. Treatment and Overall Survival of Recurrent Retroperitoneal Liposarcoma

	Resection		Observation		Non-operative Therapy		Resection + Non-operative Therapy	
Recurrence	N	Median OS (IQR)	N	Median OS (IQR)	N	Median OS (IQR)	N	Median OS (IQR)
1	68	26.45 (15.37, 45.11)	23	1.90 (0.69, 6.7)	15	5.91 (0.92, 7.85)	13	18.73 (13.10, 51.61)
2	34	27.66 (13.24, 35.91)	8	7.47 (3.17, 16.26)	16	6.63 (3.28, 24.08)	6	38.35 (10.45, 33.41)
3	11	10.67 (7.79, 44.41)	8	12.56 (5.19, 20.89)	7	8.34 (3.02, 26.21)	4	24.54 (12.91, 43.86)
≥ 4	16	44.41 (23.49, 47.63)	3	22.24 (n/a)	4	23.32 (1.71, 29.86)	2	43.86 (n/a)

N, number; OS, overall survival; IQR, interquartile range

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The Effect of Margin Status on Multivisceral Resection of Retroperitoneal Sarcoma: Results from a 598 Patient Cohort from the U.S. Sarcoma Collaborative L. Hoefer,[1]* C.G. Ethun,[2] V.P. Grignol,[3] J.H. Howard,[3] H. Mogal,[4] T.C. Gamblin,[4] T.B. Tran,[5] G. Poultsides,[5] K. Chouliaras,[6] K. Votanopoulos,[6] B.A. Krasnick,[7] R.C. Fields,[7] S. Ronnekleiv-Kelly,[8] S. Weber,[8] K.K. Roggin,[1] K. Cardona,[2] J. Tseng.[1] *1. University of Chicago Medicine, Chicago, IL; 2. Winship Cancer Institute, Emory University, Atlanta, GA; 3. Arthur G. James Comprehensive Cancer Center, The Ohio State University, Colombus, OH; 4. Medical College of Wisconsin, Milwaukee, WI; 5. Stanford University, Palo Alto, CA; 6. Wake Forest University, Winston-Salem, NC; 7. Washington University, St. Louis, MO; 8. University of Wisconsin, Madison, WI.*

Objective: Achieving negative margins during surgery for patients with retroperitoneal sarcoma (RPS) often requires resection of multiple organs. The objective of this study was to determine the impact of multivisceral resection on recurrence-free (RFS) and overall survival (OS) in patients undergoing resection of RPS. Methods: 598 patients undergoing surgery for RPS with one or more organs resected between 2000 and 2016 were identified from a database of patients from eight U.S. institutions. RFS and OS were estimated by the Kaplan-Meier method. Multivariate Cox proportional hazards models were constructed to determine factors affecting RFS and OS. Results: Patient median age was 58 years (range: 18-88 years). The most common histopathologic tumor types were liposarcoma (36.5%) and leiomyosarcoma (28.8%). Amongst all patients undergoing resection for RPS, R0 resection improved RFS (HR 0.61, p=0.038, 95% CI 0.39-0.97) and OS (HR 0.41, p=0.025, 95% CI 0.19-0.90) in multivariate analyses. For patients undergoing curative intent surgery (n=550), patients with R0 and R1 resections had similar improved OS compared to R2 resection (HR 0.57, p=0.009, 95% CI 0.38-0.87). For the 48 patients who underwent resection for palliative intent, multivisceral resection was associated with increased OS (HR 0.36, p=0.020, 95% CI 0.15-0.85) regardless of margin status (Figure 1). Resection of the duodenum was associated with decreased OS in patients undergoing multivisceral resection for curative (HR 4.27, p=0.002, 95% CI 1.70-10.26) and palliative (HR 9.38, p=0.008, 95% CI 1.77-49.58) intent. Conclusions: R0 multivisceral resection improves RFS and OS in all patients undergoing resection for RPS. For patients undergoing surgery for curative intent, attempts should be made to remove all gross disease, as this was associated with improved OS. Multivisceral resection should be considered for patients undergoing palliative surgery, as this may prolong survival. Duodenal resection should be approached with caution for the resection of RPS, as it is associated with worse survival outcomes.

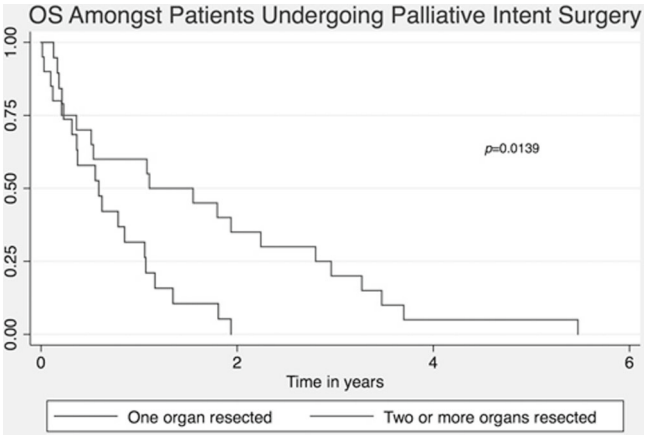

Figure 1: Kaplan Meier estimates of OS amongst patients undergoing palliative intent resection of RPS by multivisceral resection status

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Outcome After Surgical Resection of Dermatofibrosarcoma Protuberans (DFSP): A Multicenter Study E.A. Huis in 't Veld,[1]* F. van Coevorden,[2] D. Grünhagen,[3] M.J. Smith,[1] A.J. Hayes,[1] C. Verhoef,[3] D.C. Strauss,[1] W.J. van Houdt.[1] *1. Royal Marsden Hospital, London, United Kingdom; 2. Dermatology, Antoni van Leeuwenhoek, Amsterdam, Netherlands; 3. Erasmus MC, Rotterdam, Netherlands.*

Background: Dermatofibrosarcoma protuberans(DFSP) is a rare, soft tissue sarcoma. After surgical resection, follow-up with clinical examination is recommended up to 10 years. This study aims to identify prognostic factors for local and distant recurrence, and evaluate the utility of follow-up schedules after treatment. Methods: Patients with DFSP treated between 1991-2016 at 3 tertiary centers were assessed. Patients were clinically examined every 4-12 months for a period of at least 3 years. Cox regression analyses were used to identify variables associated with the primary endpoints; local recurrences and metastases. Results: A total of 357 patients were included, median age 38 and median follow-up of 58 months. Before referral, 278 were initially treated at other hospitals, while only 79 patients were referred to the tertiary center for primary treatment. Of all, 82 developed a local recurrence(22.9%), with median time to recurrence of 55.5(2-348)months. Of these, 47(57.3%) were identified by patient self-examination, whilst in 3(3.7%)cases recurrence was found at clinical surveillance. The remaining 32 presented at other institutions, and there was no data on how these were found. Fibrosarcomatous(FS) change(Hazard Ratio[HR]7,74;p<0.001), number of excisions for primary DFSP(HR 0,29;p=0.006), and R1 resection(HR11;p<0.001), were independent prognostic factors for local recurrence. The 2-and 5-year recurrence free survival was 94% and 82% respectively. Distant metastases occurred in 4 patients(1.1%). FS changes were observed in 3, while in 1 patient the presence of FS change was unknown. All patients were identified by imaging after presenting with symptomatic metastases. Metastases were more likely in patients with FS change(p<0.001)and tumours >5cm(p=0.014). Conclusion:Recurrence after resection of DFSP remains a significant issue, while metastases are rare. Recurrences may occur years after primary resection, with the majority being identified by patient self-examination. Consideration should be given to individualised follow-up regimes based on risk factors of the primary tumour, with robust access to services for patients identifying signs suspicious for recurrence.

Patients, tumor and treatment characteristics

	N (%)	Median (range)
Gender		
Male	178 (49,9)	
Female	179 (50,1)	
Age (years)		38 (2-87)
Follow-up in months		58 (0-590)
Follow up schemes		
Clinical examination only	128 (35,9)	
Clinical examination + Chest x-ray	144 (40,3)	
Clinical examination + other imaging	14 (3,9)	
Other hospital / unknown	71 (19,9)	
Size <5cm	134 (35,5)	
Size >5cm	49 (13,8)	
unknown	174 (48,7)	
Site		
Head and Neck	38 (10,6)	
Shoulder	51 (14,3)	
Arm	24 (6,8)	
Torso	103 (28,8)	
Hip/groin	34 (9,6)	
Leg	44 (12,3)	
Resection margin		
R0	234 (65,6)	
R1	40 (11,2)	
Unknown	83 (23,2)	
Fibrosarcomatous changes		
Yes	28 (7,8)	
Incipient	12 (3,4)	
No	306 (85,7)	
Unknown	11 (3,1)	

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The Approach to Solitary Fibrous Tumours(SFT): Are Clinicopathological Features and Nomograms Accurate in the Prediction of Prognosis? D. Ng,* D. zhao, G. Tan, N. Shannon, W. Loh, C. Chia, K. Soo, M. Teo. *National Cancer Centre, Singapore, Singapore.*

Introduction: Solitary fibrous tumors (SFTs) are rare mesenchymal neoplasms. Currently, factors such as size, mitotic rate and degree of necrosis have been shown to influence survival and prognosticate SFTs. However, there remains no consensus regarding the associations between tumor characteristics and the malignant nature of these tumors. The aim of this paper was to identify factors that would help in prognosticating SFTs into benign or malignant and validate the MD Anderson Cancer Centre (MDACC) SFT nomogram in the largest known series of SFTs treated in an Asian population. Methods: A retrospective review of all patients with a diagnosis of SFT treated surgically in our institution between 2005-2015 was carried out. Basic demographics, clinicopathological and surgical factors were recorded, and the association with clinical outcomes (recurrence and death) were performed. Factors that predicted for poor survival were considered to be associated with malignant SFT. The MDACC nomogram was validated by assessing the extent of discrimination, defined as the ability to separate patients with different outcomes, and quantified using Harrell's c-index. Results: Patients who did not undergo surgical resection or had missing data were excluded- 59 patients remained for analysis. The median length of follow-up was41 months (6-134), median disease-free interval (DFI) was 11 months (3 -54) and median overall survival (OS) was not reached as there were only 3 deaths. Significant univariate associations for DFI were found for mitotic rate (p=0.005) and presence of necrosis (p=0.001). Significant univariate associations for overall survival were found for age (p=0.055), presence of recurrence (p=0.035), presence of necrosis (p=0.072) and mitotic rate (p=0.033). The C-index associated with the nomogram was 0.75. Conclusion: There is a negative association for DFI and OS, with the mitotic rate and presence of necrosis. We propose that SFTs with these features should be regarded as malignant. In addition, the MDACC nomogram was found to be accurate and generally predicts well for patients in an Asian population.

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Cytoreductive Surgery (CS) for Patients with Metastatic Gastrointestinal Stromal Tumor (GIST) on Tyrosine Kinase Inhibitor (TKI) Therapy: Is There a Role for R2 Resection? M. Fairweather,* G. Li, M. Bertagnolli, C. Raut. *Brigham and Women's Hospital, Boston, MA.*

Introduction: Patients (pts) with metastatic GIST may be candidates for CS, particularly if their disease remains responsive to or stable on TKI therapy at the time of surgery. Surgeons may be asked to consider a macroscopically incomplete (R2) resection for some pts with progressive disease. We report the natural history of pts undergoing R2 CS for GIST to describe the clinical significance of residual disease. Methods: We reviewed all GIST patients treated with any TKI and R2 CS between 2001-2014 at our institution. Clinicopathologic and operative variables were analyzed. Survival outcomes including progression-free survival (PFS) and overall survival (OS) were assessed. Results: R2 resections were performed in 75 of 158 GIST pts undergoing CS. Overall, 37 pts (49%) had symptomatic disease, of which 10 (13%) required urgent surgery. Common symptoms included pain (n=12), infection (10), and bleeding (8). Symptoms were successfully palliated in 33 pts (89%). The most common reasons for elective R2 resection were planned resection of progressing disease only (12, 18%) and unresectable disease (40, 62%) secondary to sarcomatosis (18, 28%), bilobar liver disease (12, 18%), or involvement of critical structures (10, 15%). Postoperatively, residual disease remained in liver only (22, 34%), peritoneum only (15, 23%), or both (28, 20%). Residual progressive disease was present in 18 pts (28%); 24 pts (37%) underwent additional surgery for residual disease. Significant postoperative complications (Clavien-Dindo grade ≥3) occurred in 9 pts (14%). With a median follow-up of 29 months (m), median PFS was only 5m, and median OS was 49m. There were no differences in PFS or OS between pts with all progressive disease removed and those with residual progressive disease. Conclusions: R2 resections for metastatic GIST have short PFS regardless of whether or not all progressive disease is removed. While symptom control may be a reasonable justification for R2 CS, this hypothetical benefit needs to be confirmed with prospectively gathered patient reported outcomes.

Table 1. Clinicopathologic and operative characteristics for patients (n=65) with metastatic GIST treated with TKI followed by elective incomplete (R2) resection.

Clinicopathologic/operative characteristics	Number of patients
Median tumor size, cm (interquartile range (IQR))	
Primary tumor	12 (8-17)
Metastatic disease*	15 (8-27)
Location of primary tumor	
Gastric	14 (22%)
Small bowel	38 (58%)
Duodenum	2 (3%)
Other	11 (17%)
Metastatic mitotic index (n=54)	
<5 per HPF	4 (7%)
≥5 per HPF	50 (93%)
Location of metastasis	
Liver only	3 (5%)
Peritoneum only	27 (42%)
Both	35 (54%)
TKI at time of surgery	
Imatinib	21 (32%)
Sunitinib	25 (38%)
Other	19 (29%)
Median duration pre-op TKI, mos (IQR)	
Overall	18 (8-39)
Imatinib	8 (5-22)
Sunitinib	26 (11-47)
Other	28 (12-43)
Radiographic response at time of surgery	
Responsive	5 (8%)
Stable	16 (25%)
Unifocal progression	21 (32%)
Multifocal progression	23 (35%)
Residual disease status	
Non-progressing	47 (72%)
Progressing	18 (28%)
Symptomatic at time of surgery	
Yes	27 (42%)
No	38 (58%)
Sarcomatosis	
Yes	28 (43%)
No	37 (57%)
Reason for R2 resection	
Unresectable	40 (62%)
Sarcomatosis	18 (28%)
Involvement of critical structures	10 (15%)
Bilobar liver disease	12 (18%)
Only progressing disease removed	12 (18%)
Other#	13 (20%)
Location of residual disease	
Liver only	22 (34%)
Peritoneum only	15 (23%)
Both	28 (20%)
Median size of largest residual mass, cm (IQR)	2.4 (1-5.6)
Postoperative complications	
Total	18 (28%)
Grade ≥3	9 (14%)
Further surgery for residual disease	
Yes	24 (37%)
No	41 (63%)

Abbreviations: TKI, tyrosine kinase inhibitor; IQR, interquartile range.
*Aggregate size of metastatic lesions resected
#Includes combination

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Desmoplastic Small Round Cell Tumor: A Nationwide Study of a Rare Sarcoma Z.E. Stiles,[1]* P. Dickson,[1] E.S. Glazer,[1] A.J. Murphy,[2] A.M. Davidoff,[2] M.G. Martin,[1] J.L. Deneve.[1] *1. University of Tennessee Health Science Center, Memphis, TN; 2. St. Jude Children's Research Hospital, Memphis, TN.*

Background: Desmoplastic small round cell tumor (DSRCT) is a rare peritoneal surface malignancy. Currently, research is limited by the scarcity of this aggressive disease. Methods: The 2004–2014 NCDB was queried for patients with intra-abdominal DSRCT. Factors affecting overall survival (OS) after surgery were assessed with the log-rank test and Cox multiple regression. Separately, we examined trends in treatment and outcomes based on the volume of cases treated at individual facilities. Results: 125 patients were identified. Patients were predominantly male (80.8%) with a median age of 21 years (IQR 15–27). Six patients were noted to have extra-abdominal disease and 15 (12%) had liver involvement. Median OS was 28 months, with 1, 3, and 5-year survival rates of 85%, 29%, and 13%, respectively. 74 patients underwent surgical resection with therapeutic intent and demonstrated a trend toward improved OS compared to those who did not (31.3 vs. 18.3 months, p = 0.095). The absence of liver involvement and receipt of postoperative systemic therapy were associated with significantly improved OS on univariate analysis (31.8 vs 23.1 months, p = 0.027 and 45.8 vs 31.3 months, p = 0.026, respectively). While no variable was independently associated with OS on multivariable analysis, two factors approached significance: the use of adjuvant chemotherapy was associated with reduced the risk of mortality (HR 0.3, p=0.073) and the presence of residual macroscopic disease after resection correlated with increased risk of mortality (HR 5.3, p=0.071). Patients treated in high-volume facilities (≥5 DSRCT cases/study period) were found to experience improved OS (median 59.1 vs 28.8 months), albeit not significantly (p=0.262) compared to patients treated in low-volume centers. Conclusion: DSRCT is an extremely rare disease with dismal outcomes. Aggressive surgical resection and post-operative chemotherapy appear to improve survival. Facilities with experience treating this uncommon disease may offer superior outcomes.

ABSTRACTS

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Carbon Suspension Tattooing of Biopsied Axillary Lymph Nodes with Ultrasound Guidance in Breast Cancer Patients Undergoing Neoadjuvant Chemotherapy, and Identification of Tattooed Nodes at the Time of Surgery T.M. Allweis,[1]* H. Cernik,[2] I. Fainarov,[2] I. Bokov,[2] M. Damari,[3] J. Diment,[4] N. Ben Baruch,[5] E. Mavor.[6] *1. Dept of Surgery and Breast Health Center, Kaplan Medical Center, Rehovot, Israel; 2. Dept of Radiology and Breast Health Center, Kaplan Medical Center, Rehovot, Israel; 3. Breast Health center, Kaplan Medical Center, Rehovot, Israel; 4. Dept of Pathology, Kaplan Medical Center, Rehovot, Israel; 5. Dept if Oncology, Kaplan Medical Center, Rehovot, Israel; 6. Dept of Surgery, Kaplan Medical Center, Rehovot, Israel.*

Background: Breast cancer patients with lymph node (LN) metastases at diagnosis often undergo neoadjuvant chemotherapy (NAC). Identification of a LN which regressed after NAC remains a challenge, and the available tools for marking the LN are technically cumbersome. The current study examined a technique, previuosly reported by others, of tattooing the LN by injecting a small amount of carbon suspension (spot^{tm}), a commercially available product originally intended for marking lesions in the intestinal tract at endoscopy. The aim of this study was to evaluate the feasibility of marking suspicious / biopsied nodes and later identifying the tattooed nodes at the time of surgery,. Methods: A small amount (0.2-0.5ml) of carbon suspension was injected into one or two axillary LNs using a 21g needle, under ultrasound guidance, either at the time of LN biopsy, or before or shortly after starting NAC. During surgery an attempt was made to identify the tattooed LN, which was removed and sent for pathological evaluation as a separate specimen. All patients underwent a sentinel lymph node biopsy and/or axillary lymph node dissection as mandated by their clinical status. Results: Thirty patients underwent tattooing of axillary LNs as described, with no complications or adverse events. To date, 22 patients underwent surgery (the other 8 have not completed NAC). In 21 patients the tattooed LN was easily identified at the time of surgery. The tattooed LN was also a sentinel LN in 20/21 patients. Discussion: These preliminary results confirm that marking axillary LNs with carbon suspension is safe and easily performed. The tattooing was helpful in identifying the marked LN in the majority of cases. Conclusions: Ultrasound guided tattooing of axillary LNs with carbon suspension appears to be a convenient, safe and effective method of marking LNs which need to be excised after NAC. Further study is needed to establish the correlation between a tattooed node and the sentinel lymph node(s), and the appropriate management of an involved axilla after NAC. The study is ongoing.

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Downregulation of Antigen Processing is Associated with High Neoepitope Burden in Triple Negative Breast Cancer M. Chen,[1] P. Narang,[2] A. Sharma,[1] M. Wilson Sayres,[2] B.A. Pockaj,[3] K. Anderson.[1]* *1. Biodesign Institute, Tempe, AZ; 2. School of Life Sciences, Arizona State University, Tempe, AZ; 3. Mayo Clinic Arizona, Phoenix, AZ.*

Introduction: Tumors with high mutational burden have improved response rates to checkpoint blockade, and mutations of antigen processing machinery (APM) are associated with resistance to immunotherapy. Somatic mutations can generate novel HLA-binding epitopes (neo-epitopes), which potentially elicit tumor specific CD8+ T cells. We developed a bioinformatics pipeline to predict neo-epitopes in breast cancer. We evaluated the frequency of neoepitopes of triple negative breast cancers (TNBC) from the TCGA dataset and determined the correlation with RNA expression of APMs. Methods: We analyzed 98 TNBC and matched normal (germline) breast tissue exome sequencing datasets from TCGA to identify cancer specific mutations. For each non-synonymous mutation, we identified possible neo-epitopes. HLA typing of A, B and C MHC class I genes of each patient was determined using the Polysolver algorithm. We selected high affinity binding epitopes using the IEDB prediction algorithm of patient-specific HLA alleles (IEDB score < 500). We then filtered the epitopes based on tumor transcript abundance using RNAseq expression. We analyzed RNAseq data to determine the expression of APM signature. Results: TNBC tumors had a median of 53 nonsynonymous mutations with a range of 2-1162. Approximately 15% of the mutations led to the generation of high affinity neo-epitopes. The majority of patients (n= 79/97, 81%) had at least one neo-epitope. In RNAseq analysis, an antigen processing machinery signature (including HLA-A, B, C, B2M, TAP1, TAP2, and TAPBP) was lower in the subset of patients with high mutational burden. In addition, of 24 patients with high mutational burden, 9 (37.5%) had at least one mutated gene involved in the antigen rpocessing machinery genes, compared to 3 of 24 (12.5%) within the subset of tumors with low mutational burden. Conclusions: Eighty-one percent of TNBC tumors have at least one expressed neo-epitope, which may serve as candidates for targeted immunotherapy. Those tumors have evidence of immune escape by altering antigen processing.

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A Novel Chimeric Antigen Receptor T Cell (CAR T) Therapy Target for Breast Cancer A.D. Williams,* A. Posey, J. Tchou. *University of Pennsylvania, Philadelphia, PA.*

Introduction: Immunotherapy for breast cancer (BC) has lagged behind its use for tumors such as melanoma and lung cancer. One barrier is the lack of tumor-specific antigens (TSA) to serve as targets for immunotherapy strategies such as chimeric antigen receptor T cell (CAR T) therapy. Most tumor antigens being targeted are peptide-based, but other cell surface molecules such as the sugar moiety of glycosylated proteins may serve as potential targets. We investigated an aberrantly-glycosylated mucin, Tn-MUC1, as an appealing TSA for effective CAR T immunotherapy against BC in breast cancer. Methods: Gene expression analyses of MUC1 and several enzymes involved in Core 1 and Core 3 O-glycosylation (C1GalT1, C1GalT1C1, ST6GalNAc1 and B3GNT6) were performed using data from the 955-patient BC cohort of The Cancer Genome Atlas (TCGA) to confirm expression of Tn-MUC1. Tn-MUC1 expression was further validated by immunohistochemistry (IHC) analysis of 52 breast tumors (validation cohort). A CAR construct directed against Tn-MUC1 was assembled. Cytotoxicity assays to evaluate CAR T directed against Tn-MUC1 activity against several BC cell lines were then performed. Results: Analysis of TCGA data revealed a significant difference in MUC1 expression when patients are stratified by tumor stage and molecular subtype ($p<0.001$). Hormone receptor (HR)-, HER2+ cancers exhibited higher expression of ST6GalNAc1 and B3GNT6 when compared to all other subtypes (both $p<0.001$). We confirmed Tn-MUC1 expression by IHC in 67.3% of our validation cohort. Tn-MUC1 expression was not associated with prognostic variables such as tumor size or nodal status in this cohort, but significant expression of Tn-MUC1 in DCIS correlated with decreased survival and progression-free survival. Tn-MUC1-specific CAR T cells were effective in lysing triple-negative BC cell lines BT20, MDA-MB-231, and TB129, a primary breast cancer cell line and in MCF7, a HR+ cell line. Conclusion: Tn-MUC1 is a novel TSA in breast cancer. CAR T directed against Tn-MUC1 have potent cytolytic activity against breast cancer cell lines in vitro suggesting that CAR T against Tn-MUC1 may be effective in in vivo tumor models and in the clinic.

ABSTRACTS

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QS1

Identification of DNA Repair Genes That Attract Tumor Infiltrating Immune Cells and are Associated with Better Survival in Breast Cancer T. Kawaguchi, X. Peng, Q. Qi, J. Young, S. Liu, L. Yan, K. Takabe.* *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Backgrounds: Evading the immune system is one of the Hallmarks of Cancer. Indeed, tumor infiltrating immune cells has been shown to play critical roles in suppression of cancer progression. Genetic aberration of DNA repair genes is known to increase immunogenicity in breast cancer. However, the clinical significance of tumor microenvironment including tumor infiltrating immune cells in regard to DNA repair genes has not yet elucidated in breast cancer patients. We hypothesized that DNA repair gene deficiency is related to increased global genomic instability that leads to increased mutation burden, which recruits infiltrating immune cells to tumor microenvironment that result in better prognosis of breast cancer. Patients and Methods: Integrated and unbiased transcriptomics approach was conducted on genomic and clinicopathological information of 3614 breast cancer patients, using TCGA and METABRIC, to evaluate the association between the aberration of DNA repair genes and tumor infiltrating immune cell composition in breast cancer tumors, as well as its significant clinical relevance. Results: First, we investigated survival relevance of 10 DNA repair genes; BRCA1, BRCA2, BLM, WRN, RECQL4, RECQL5, TOP2A, PRKDC, and XRCC5/6. BRCA1, PRKDC, and RECQL4 showed consistent result in both TCGA and METABRIC cohorts; low expression level of BRCA1, PRKDC, and RECQL4 demonstrated significantly better prognosis in TCGA and METABRIC cohort ($p=0.018$ and $p=0.021$, $p=0.036$ and $p<0.001$, $p<0.001$ and $p<0.001$, respectively). Of the 3 genes, low expression of BRCA1 significantly associated with high levels of CD8 positive cell composition in both cohorts (TCGA, $p<0.001$; METABRIC, $p<0.005$) utilizing CIBERSORT system that estimate the fraction of 22 immune cell types in each tumor, which implicate that tumor infiltrating lymphocytes are attracted to BRCA1 low expressing tumors. Conclusions: We conclude that our immunogenomics approach identify the interplay between DNA repair genes, especially gene expression of BRCA1, and tumor infiltrating immune cells, which translate into significantly better prognosis in breast cancer.

QS2

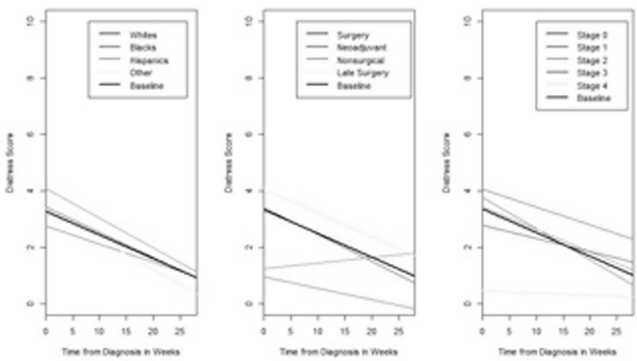
What is the Utility of Routine Complete Blood Count, Liver Function Tests, and Chest X-ray in the Evaluation of Patients with Clinically Node-Negative Breast Cancer? A.Y. Merrill,* M.M. Garland, M. Isnassuos, K.C. Perry, M. Howard-McNatt, E.A. Levine. *Wake Forest School of Medicine, Winston-Salem, NC.*

Background: Current National Comprehensive Cancer Network (NCCN) Guidelines suggest a selective approach to the workup of early-stage (I/II) breast cancer with complete blood count (CBC) and liver function tests (LFTs) and no longer recommend chest x-ray (CXR) to screen for occult metastasis. This study evaluated the utility of these tests when performed routinely on patients with clinically node-negative breast cancer and reevaluated institutional practices. Methods: We identified patients treated for clinically node-negative breast cancer at Wake Forest Baptist Health from October 1998 through December 2015. We evaluated the frequency of screening CBC, LFTs, and CXR obtained upon presentation and calculated the yield that a preoperative screening test led to the discovery of metastasis. Results: 1,611 patients were identified (median age, 60 [range, 23-91]). 94.4% of patients underwent at least one preoperative screening test: 90.8% had a CBC, 89.4% had LFTs, and 63.6% had a CXR. 20.0% of tests were abnormal with CBC being abnormal in 32.7%, LFTs in 11.7%, and CXR in 4.2% of patients. The most common abnormality on each test was anemia on CBC (18.8%), elevated alkaline phosphatase on LFTs (6.0%), and a lung nodule on CXR (2.6%). Abnormal screening tests led to 17 computed tomography (CT) scans, of which only one led to a preoperative diagnosis of metastatic breast cancer. Of the 11 patients discovered to have metastatic disease postoperatively through CT, PET/CT, MRI, or bone scan, only half had any abnormality present on a preoperative screening test. The positive predictive values of preoperative CBC, LFTs, and CXR for the detection of occult metastasis are 1.3%, 1.1%, and 1.5%, respectively. Conclusion: Routine preoperative evaluation with CBC, LFTs, and CXR in clinically node-negative breast cancer is low-yield. Even when abnormalities are found, metastatic disease is present in less than 1% of cases, and a normal study does not rule out metastasis. Routine preoperative determination is not warranted, and staging studies should be limited to patients with significant symptoms or complaints.

QS3

Race, Marital Status and Stage are Associated with Patient-Reported Distress After Breast Cancer Diagnosis: A Review of >5000 Patient Visits O.M. Fayanju,* K. Yenokyan, B.A. Goldstein, I. Stashko, S. Power, E.S. Hwang. *Duke University, Durham, NC.*

INTRODUCTION The NCCN Distress Thermometer (DT) is a validated patient-reported outcome instrument that uses a 10-point scale to screen for distress in cancer patients (0=none,10=extreme). Using data from our electronic health record (implemented in 2013), we examined factors associated with elevated distress in newly diagnosed breast cancer patients at first visit and over time. METHODS Prospective data from women≥18 with Stage 0-IV breast cancer diagnosed at our institution from 1/2014-7/2016 were included. DT scores were abstracted for up to 26 weeks from date of diagnosis. Kruskal Wallis and chi square tests were used to compare patients with high (≥7) and low (≤6) DT scores. Linear regression was used to estimate associations between initial DT score and race, marital status, stage, and treatment sequence. Linear mixed effect models were used to estimate the effect of time from diagnosis on distress level. We report proportions and risk differences (RD) with two-tailed $p<0.05$ as significant. RESULTS We analyzed 5687 visits for 972 unique patients (median age=59). At first visit, median DT score=3 (IQR 0-6); patients who were black (RD -0.58), older (RD -0.30/10y), and had DCIS (i.e., Stage 0, RD -0.97) had lower DT scores vs patients who were white, younger, and had Stage I disease, respectively (all $p<0.01$). Over time (i.e., decline in DT score/week), distress levels improved across all groups except Stage IV patients. Patients who were black (vs white, 0.06 vs 0.09), received neoadjuvant therapy (vs surgery 1st, 0.04 vs 0.10), and had DCIS (vs Stage I disease, 0.05 vs 0.11) had the least longitudinal improvement in DT scores (all $p<0.01$, Figure 1). 4.2% of patients had DT scores persistently ≥7, and nearly 2x as many of these patients were unmarried as those with DT scores≤6 (63.5% vs 33.6%, $p<0.001$). CONCLUSIONS Over time, DT scores did not decline in Stage IV patients and improved significantly less for blacks. Being unmarried was associated with persistently high DT scores. The NCCN DT can provide valuable longitudinal distress data for breast cancer patients and potentially enable targeted support during treatment.



NCCN Distress Thermometer: Change in DT Score over Time by Race/Ethnicity, Treatment Sequence, and Stage

QS4

Impact of the 70-Gene Signature on Chemotherapy Administration in Dutch Early Stage Breast Cancer Patients J. van Steenhoven,[1]* A. Kuijer,[1] K. Schreuder,[3] A. van Bommel,[1] S. Elias,[4] C. Smorenburg,[2] S. Linn,[2] E. Rutgers,[2] S. Siesling,[3] T. van Dalen.[1] *1. Surgery, Diakonessenhuis Utrecht, Amsterdam, Netherlands; 2. Antoni van Leeuwenhoek ziekenhuis, Amsterdam, Netherlands; 3. Integraal Kankercentrum Nederland, Utrecht, Netherlands; 4. UMC Julius Centrum, Utrecht, Netherlands.*

Background and aim: Gene expression profiles (GEPs) are advocated to optimize chemotherapy (CT) decisions for early-stage breast cancer patients with hormone receptor positive (ER+) cancers. In the present study, we assessed the use and clinical implications of 70-GS use on CT administration in patients eligible for GEP deployment. Patients and methods: Patients with an indication for GEP use according to national breast cancer guidelines, surgically treated between January 1, 2013, and December 31, 2015, were selected from the Netherlands Cancer Registry (NCR). The use and impact

of the 70-GS was evaluated within four national guideline directed subgroups of ER+ patients delineated by grade, size and the presence of lymph node metastases: group A (pN0; BR I; >2cm), group B (pN0; BR II; >1cm), group C (pNmi, BR I/II) and group D (pN1a, BR I/II). Results: A total of 5.091 patients treated for ER +/HER2- invasive ductal breast cancer and eligible for GEP-use were selected from the NCR and 1.537 received the 70-GS (30%). The 70-GS was most commonly deployed (44%) in patients with group B (pN0; BRII) and rarely in group D (N1a; n=101, 7%) (Table 1). Overall, adherence to the 70-GS test result was 90%, adherence to the 70-GS was significantly lower in group D (78%). In all patients eligible for GEP deployment, 70-GS use was associated with a 21% reduction of patients receiving CT (P < 0.001) (Table 1). In patients with micro- or macro-metastatic axillary lymph node involvement (N1mi/N1a) the impact of 70-GS was most apparent: a 16% and 34% decrease, respectively (P < 0.001) (Table 1). Conclusion: In patients with an indication for GEP use according to Dutch guidelines, the 70-GS is associated with a significant decrease of CT administration, especially in patients with axillary lymph node involvement. In the latter category 70-GS deployment was still rare.

Table 1 The uptake and impact of 70-GS use on adjuvant CT administration in the total study population (n=5091) and guideline directed subgroups of patients with an indication for GEP use according to national breast cancer guidelines (all younger than 70 years of age, ER+/HER2-, invasive ductal carcinoma

	N	70-GS use (%)	Chemotherapy use (%)		P-value
			70-GS used	70-GS not used	
All patients (A, B, C, D)	5091	30	31	52	<0.001
Group A N0, BR I, >2cm	215	34	16	23	0.38
Group B N0, BR II, >1cm	2652	44	31	33	0.17
Group C pNmi, BR I/II	780	24	30	46	<0.001
Group D N1a, BR I/II	1444	7	43	77	<0.001

GEP; gene expression profile, 70-GS; 70-gene signature, BR; Bloom-Richardson grade, N0; no axillary lymph node involvement, Nmi; micro-metastasis, N1a: 1-3 ipsilateral positive axillary lymph nodes (at least one >2mm)

QS5

Breast Density in a Contemporary Cohort of Women with Ductal Carcinoma in Situ J.C. Gooch,* J. Chun, S. Raymond, J. Lee, A. Yakes, T. Jubas, E. Kurz, A. Guth, F. Schnabel. *NYU Langone Health, New York, NY.*

Introduction Mammographic breast density (MBD) is an independent risk factor for breast cancer. However, the relationship of MBD and tumor characteristics in women with ductal carcinoma in situ (DCIS) is lacking. The purpose of this study was to examine the clinicopathologic characteristics of DCIS in women stratified by their mammographic breast density. Methods A retrospective review of a prospectively maintained single institution database was performed to identify women diagnosed with pure DCIS who underwent pre-operative mammography between 2010-2017. Clinicopathologic and demographic data were collected. MBD was grouped into "non-dense" (BI-RADS density categories A, B) and "dense" (BI-RADS C, D) as gleaned from clinical radiology reports prior to or at time of diagnosis. Pearson's Chi-Square and Wilcoxon rank-sum tests were performed. Results Out of 2816 women with a cancer diagnosis at our institution, 21% had pure DCIS with a median follow up of 4.7 years (range: 0.4-7.8 years). Of these, 41% had non-dense breasts and 59% had dense breasts. The majority of lesions were non-palpable (92%) and detected by mammography (83%). Of those with palpable findings, women with dense breasts were significantly younger (median age 45 years) compared to those with non-dense breasts (median age 65 years) (p=0.002). Patients with dense breasts were significantly younger at the time of diagnosis (p<0.001) and had a lower BMI (p<0.001) (Table 1). Family history, BRCA mutation status and parity were not significantly different between the MBD groups. There were also no differences in hormone receptor status, tumor histology, size or site of first recurrence between the two groups. Higher grade disease is associated with dense breasts (p=0.014) (Table 1). Conclusions Our study found that women with pure DCIS and higher MBD are younger at time of diagnosis and significantly more likely to present with a palpable lesion. This suggests the importance of physical exams and the utility of additional imaging modalities in this population. Those with dense breasts were more likely to have high grade DCIS. Further research on the relationship of age, MBD and tumor biology in DCIS is warranted.

Clinical and Tumor Characteristics by Mammographic Breast Density (BI-RADS density A-D)

VARIABLES	NON-DENSE (A,B) N=241 (41%)	DENSE (C,D) N=340 (59%)	P-VALUE*
AGE AT DIAGNOSIS (median years, range)**	64 (34-88)	52 (29-89)	<0.001
FIRST DEGREE FAMILY HISTORY OF BREAST CANCER			0.395
Positive	82 (34%)	104 (31%)	
Negative	159 (66%)	235 (69%)	
BRCA 1/2 MUTATIONS			0.235
Positive	8 (12%)	9 (7%)	
Negative	57 (88%)	117 (93%)	
BODY MASS INDEX (BMI) (median, range)**	28 (17-46)	24 (16-41)	<0.001
PARITY			0.320
Nulliparous	73 (30%)	116 (34%)	
≥1 Live Birth	168 (70%)	223 (66%)	
PALPABILITY			0.015
Palpable	12 (5%)	36 (11%)	
Non-Palpable	229 (95%)	304 (89%)	
HORMONE RECEPTOR			0.838
Positive	195 (83%)	274 (83%)	
Negative	41 (17%)	55 (17%)	
HISTOLOGIC GRADE			0.014
Low	20 (8%)	14 (4%)	
Intermediate	114 (47%)	136 (41%)	
High	107 (44%)	184 (55%)	
TUMOR SIZE (median cm, range)**	0.9 (0-10)	1.0 (0-8.6)	0.422
HISTOLOGY			0.878
Comedo	73 (31%)	102 (32%)	
Non-Comedo	162 (69%)	220 (68%)	
RECURRENCE			0.549
Present	7 (3%)	13 (4%)	
Absent	234 (97%)	327 (96%)	

*Pearson's Chi-Square Test
** Wilcoxon Rank-Sum Test

QS6

H2AX is a Novel Prognostic Marker of Breast Cancer E. Katsuta,* M. Ouchi, T. Ouchi, K. Takabe. *Roswell Park Cancer Institute, Buffalo, NY.*

INTRODUCTION: H2AX is a histone and localized in DNA lesion, plays a key role in DNA damage repair. High expression of H2AX was observed in various types of cancer compare to normal tissue. Previously we found that H2AX determines clonogenic cell survival under metabolic oxidative stress and cellular levels of Reactive Oxygen Species (ROS). In this study, we investigated the impact of H2AX expression on breast cancer patients' survival, as well as underlying mechanisms. METHODS: Breast cancer patients in the Cancer Genome Atlas dataset were classified as either high or low expression of H2AX. Overall Survival (OS) and Disease-Free Survival (DFS) as well as Gene Set Enrichment were compared between these two groups. Gene expression of each cell lines were analyzed by RNA-seq. Radiation sensitivity was quantified using cells from Patients derived xenograft. RESULTS: H2AX high expression tumor showed significantly worse OS (p=0.007) as well as DFS (p=0.001). The proportion of H2AX high tumor patients was higher in advanced Stage (Stage I: 2.8%, Stage II: 5.5%, Stage III/IV 7.4%). OS was significantly worse in H2AX high group only in Stage III/IV patients (p=0.008), but not in Stage I/II patients (p=0.366). In agreement, breast cancer cell line clones that develop metastasis expressed higher H2AX compared from their parental cells (4T1 vs 4T1.2; p<0.001, MDA-MB-231 vs LM2-4; p=0.042). Gene Set Enrichment Analysis (GSEA) demonstrated that not only DNA repair (p<0.001) and ROS related gene set (p=0.011), but also Myc target related gene sets (p=0.002) as well as UV response related gene set (p<0.001) were significantly enriched in H2AX high patients. Furthermore, H2AX high expressing cells showed significantly higher sensitivity to radiotherapy due to ROS production. CONCLUSIONS: H2AX high expression tumors in advanced Stage breast cancer patients had worse OS and DFS, but showed higher sensitivity to radiation. H2AX might be a predictive biomarker to identify the patients who have worse prognosis but are sensitive to radiation therapy.

QS7

Quantitative Radiomics Analysis for Assessment of Breast Cancer Risk I. Bedrosian,[1]* N. Tayob,[1] L. King,[1] R. El-Zein,[3] K. Mendel,[2] M. Giger.[2] *1. Breast Surgical Oncology, MD Anderson Cancer Center, Houston, TX; 2. University of Chicago, Chicago, IL; 3. Houston Methodist Research Institute, Houston, TX.*

Background: Mammography remains the mainstay for early detection of breast cancer. Recently, there has been significant controversy over utility of annual screening. Although changes to standard annual mammography are meant to be tailored to a woman's risk, low risk women represent the majority of breast cancer events and reduced screening in this population may potentially delay diagnosis. Limitations in current risk assessment tools thus represent a barrier to appropriate tailoring of screening exams. We hypothesized that density and texture analysis of the mammographic image may provide a novel approach to risk assessment. Methods: Breast cancer patients (pts) and cancer free controls were prospectively accrued as part of an institutional protocol for development of risk biomarkers. Digital mammographic images obtained at time of enrollment were analyzed. Quantitative radiomic analysis was performed to capture texture and density features from a standard region of interest behind the nipple. For cancer pts the contralateral breast was examined. Data was acquired by 2 independent observers. Inter-observer variability was assessed using a random effects model. The partial AUC (pAUC) at high specificity was used to evaluate individual discriminatory features. A permutation based procedure was used to select statistically significant features. Results: Images from 152 cancer pts and 131 control pts were analyzed. 101 pts had hormone receptor (HR) +, 25 HER2+ and 26 had HR-, HER2- cancer. 42 of 47 features had low inter-observer variability (ICC ≤0.05). Of these, 23 features were identified that were highly correlated and removed from further analysis. The remaining 19 features were evaluated for discrimination between cancers and controls in 4 settings: all cancers vs all controls, as well as by each of the subtypes vs controls. Several texture based features were identified that discriminated between cancers, by subtype, and controls with pAUC between 0.011-0.029. Conclusion: Mammographic features appear to discriminate between cancers and controls in subtype specific fashion. These data suggest opportunity to develop mammographic signatures of risk to guide screening.

QS8

The Spatio-Temporal Evolution of Lymph Node Spread in Early Breast Cancer: A Pilot Study P.A. Barry,[1]* A. Vatsiou,[2] I. Spiteri,[2] A. Acar,[2] N. Trahearn,[2] M. Punta,[2] K. Chkhaidze,[2] D. Nichol,[2] S. Hrebien,[2] I. Garcia-Murillas,[2] L. Ermini,[2] I. Huntingford,[3] F. MacNeill,[1] J. Rusby,[1] F. Muscara,[1] C. Maley,[4] S. Lise,[2] Y. Yuan,[2] N. Turner,[2] G. Schiavon,[5] A. Sottoriva.[2] *1. Surgery, Royal Marsden Hospital, Sutton, United Kingdom; 2. Institute of Cancer Research, London, United Kingdom; 3. Mater Dei Hospital, Malta, Malta; 4. Biodesign Institute, Tempe, AZ; 5. Oncology IMED, AstraZeneca, Cambridge, United Kingdom.*

The most significant prognostic factor in early breast cancer is lymph node involvement. This stage between localised and systemic disease is key to understanding breast cancer progression, however our knowledge of the evolution of lymph node malignant invasion remains limited, as most currently available data derives solely from primary tumours. In 11 treatment-naïve node positive early breast cancer patients without clinical evidence of distant metastasis, we investigated lymph node evolution using spatial multi-region sequencing of primary and lymph node deposits and genomic profiling of matched longitudinal circulating tumour DNA (ctDNA). Sequential evolution[PB1] from primary to lymph node was rare (1/11); the majority of cases displaying either early divergence between primary and nodes (4/11), or an intrinsically metastatic evolutionary trajectory (6/11) where both primary and nodal cells belonged to a single recent expansion of a metastatic clone. Divergence of metastatic clones was driven in part by APOBEC. Longitudinal ctDNA from 2 subjects taken peri-operatively reflected the evolutionary patterns of the two major groups and demonstrates, even in this early disease cohort, the principle of detection of private mutations from an early metastatic nodal deposit. This study sheds new light on a crucial evolutionary step in the natural history of breast cancer.

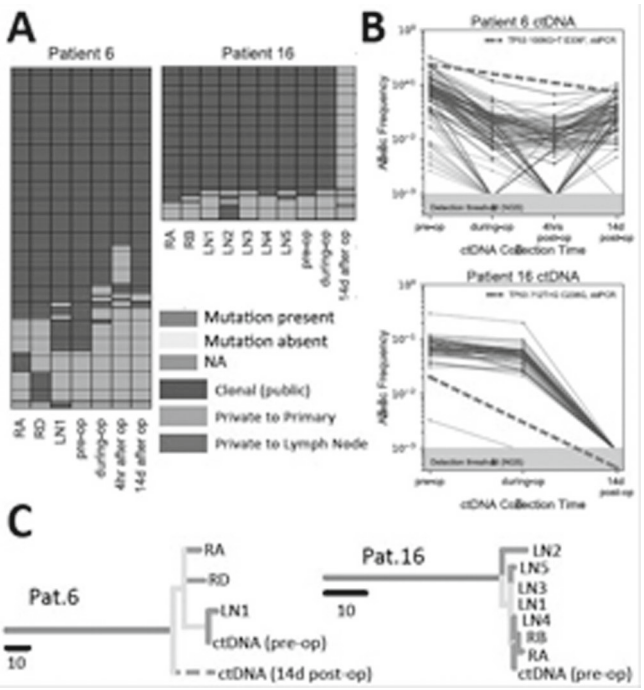


Figure 1. Longitudinal ctDNA analysis recapitulates tissue evolution. (A) The cohort-specific targeted panel was applied to ctDNA for two patients, heatmaps show presence (blue) and absence (yellow) of variants at four time points (pre-operation, immediately post-resection, 4 hours after operation and 14 days after operation) compared to the corresponding primary and lymph node samples per patient. (B) Variant allele frequency (VAF) changes of all mutations at different time points. (C) Phylogenetic trees reconstructed with both solid and liquid genomic data confirm these patterns.

QS9

Simple Reapproximation of Surgically Disrupted Lymphatics Reestablishes Lymphatic Flow via Lymphangiogenesis J. Barreto-Andrade,[1]* Y. Kaufmann,[1] C. Fan,[1] E. Siegel,[1] J.H. Aronson,[1] V.S. Klimberg.[2] *1. Surgery, University of Arkansas for Medical Sciences, Little Rock, AR; 2. University of Texas Medical Branch, Galveston, TX.*

INTRODUCTION. Surgical lymphedema (LE) affects millions worldwide, is caused by lymphatic disruption at the time of lymphadenectomy, and is the most feared complication of the surgical treatment of several types of cancer. Sentinel lymph node biopsy has greatly lessened LE but not prevented it. Based on our clinical data, we sought proof of concept of a simple technique (reapproximation of afferent and efferent lymphatic channels) to induce spontaneous restoration of lymphatic flow. METHODS. The experimental model used transection of the tail lymphatics in male Sprague-Dawley rats followed by lympho-lymphatic reapproximation. Isosulfan blue dye was used to visualize the bilateral tail lymphatic channels. After transecting the tail lymphatics on one side, the lymphatics were reapproximated (tied together) with absorbable suture (Fig 1a), while the ends on the contralateral control side were divided without reapproximation. The tail lymphatics were reexplored at different time points. Lymphatic flow restoration was examined using isosulfan blue dye. Histopathology of the excised anastomosis site was examined for lymphangiogenesis by evaluating the expression of podoplanin (D2-40), an immunohistochemical marker for lymphatic endothelium. RESULTS. Forty-four lymphatics in 22 animals were studied. Initial assessment of lymphatic recanalization at earlier time points (less than 5 weeks) showed inconsistent recanalization in only 50% of cases. At 6 weeks and 9 weeks, the combination of lymphatic flow assessment and immunohistochemistry showed a successful rate of lymphatic recanalization in 90% of the reapproximated lymphatics. None of the non-reapproximated lymphatics showed flow restoration. There was positive expression of D2-40 at the anastomotic site in the recanalized lymphatic tissue (Fig 1b). CONCLUSIONS. Our results indicate that simple

reapproximation of lymphatic channels after surgical transection has the ability to induce recanalization via lymphangiogenesis. This study provides proof of concept that simple reapproximation of lymphatics, as our clinical practice suggests, can prevent lymphedema by lymphangiogenesis-induced recanalization.

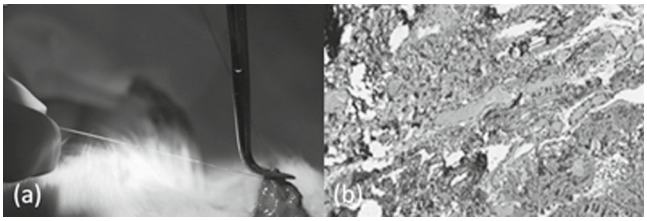


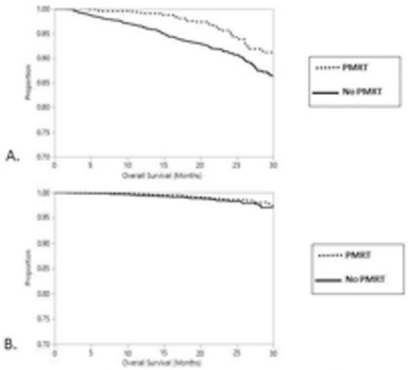
Figure 1. (a) Transection and reapproximation of lymphatics (b) Podoplanin (D2-40) expression in recanalized lymphatic tissues (20X).

QS10

Identifying Factors Impacting Efficacy of Postmastectomy Radiotherapy in Women with T1-2 Breast Cancer and One to Two Positive Lymph Nodes N. Bhutiani,[1]* M. Egger,[1] A.J. Stromberg,[2] N. Ajkay,[1] K.M. McMasters.[1] *1. Surgery, University of Louisville, Louisville, KY; 2. University of Kentucky, Lexington, KY.*

Introduction: The ASCO-ASTRO-SSO guidelines regarding postmastectomy radiotherapy (PMRT) supports its use in women with T1-2 breast cancer and 1-3 positive axillary lymph nodes (LN) to decrease locoregional recurrence. However, in patients at low risk for recurrence, PMRT's benefit may not outweigh its toxicity. This study sought to identify factors associated with efficacy of PMRT in such patients to guide PMRT administration. Methods: The National Cancer Database was queried for women with T1-2 breast cancer undergoing mastectomy with 1-2 positive LN identified on axillary lymphadenectomy. Women receiving neoadjuvant therapy were excluded. Patients were grouped by number of positive LN and compared across demographic and tumor variables. Differences in overall survival (OS) in patients who did and did not receive PMRT were evaluated using Cox proportional hazards models and Kaplan-Meier (KM) curves with Log-Rank tests. Results:Of 13,359 patients, 8,888 had 1 positive LN and 4,471 had 2 positive LN. Use of PMRT was higher in patients with 2 positive LN compared to 1 positive LN (44% vs. 27%, $p<0.001$). Within each nodal group (1 or 2 positive LN), younger patients and those with higher grade and larger tumors were more likely to receive PMRT. Patients with T2 tumors were more likely to receive PMRT regardless of number of positive LN. Multivariate modeling demonstrated an interaction effect of age on the efficacy of PMRT. In patients ≥60, PMRT significantly improved OS when adjusted for age, tumor grade, and number of positive LN (HR=0.56, 95% confidence interval=0.38-0.81, $p=0.002$). In patients <60, tumor size and grade but not PMRT were associated with improved OS. KM curves demonstrated improved OS in patients ≥60 who received PMRT but not in patients <60 (Figure). Conclusion:For women with T1-2 breast cancer and 1-2 positive LN, the association of PMRT with OS is influenced by age, tumor grade, and number of positive LN. PMRT appears to be associated with improvements in OS in older patients (age ≥60) regardless of tumor size or nodal status. In younger patients (<60 years old), PMRT is not associated with improvement in survival.

Figure: Kaplan-Meier Curves Evaluating the Effect of Postmastectomy Radiotherapy on Overall Survival in Patients with T1-2 Breast Cancer and 1-2 Positive Lymph Nodes Stratified by Age



(A) demonstrates improved overall survival in older patients (≥60) with either 1 or 2 positive LN receiving PMRT ($p<0.001$) while (B) demonstrates no difference in overall survival in younger patients (<60) with either 1 or 2 positive LN receiving PMRT ($p=0.37$). In both cases, dashed lines represent patients receiving PMRT and solid lines represent those receiving no PMRT.

QS11

Variation in the Use of Adjuvant Chemotherapy Following Neoadjuvant Radiotherapy and Surgery for Rectal Cancer in a Publicly-Insured Healthcare System L.D. Bubis,[1]* A. Mahar,[2] V. Gupta,[1] Y. Jeong,[1] L. Davis,[2] Q. Li,[3] P. Karanicolas,[4] N. Coburn.[4] *1. Surgery, University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Research Institute, Toronto, ON, Canada; 3. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada; 4. Sunnybrook Health Sciences Centre, Toronto, ON, Canada.*

BACKGROUND: The efficacy of routine administration of adjuvant chemotherapy following sequential neoadjuvant chemoradiotherapy and surgery for rectal cancer is uncertain. This uncertainty may lead to practice pattern variations, with significant downstream discrepancies in oncological outcomes, patient-centered outcomes, and healthcare costs. The objective of this study, therefore, was to evaluate patient, disease, and health system factors associated with receipt of adjuvant chemotherapy following neoadjuvant radiotherapy and proctectomy. METHODS: A retrospective cohort study of patients diagnosed with rectal cancer undergoing preoperative radiotherapy prior to proctectomy from January 1, 2010 to December 31, 2014 was performed using linked administrative healthcare databases. We compared the rate of chemotherapy administration (≥ 1 billing record) within 180 days of index rectal resection by healthcare administrative region in Ontario, Canada (2014 population: 13.4 million). Multivariable logistic regression models were constructed to assess patient, disease, and health system factors associated with differences in receipt of adjuvant chemotherapy. RESULTS: We studied 1668 patients treated with preoperative radiotherapy and proctectomy, of whom 67% received chemotherapy within 180 days after surgery. The rate of adjuvant chemotherapy administration varied among health regions from 54% to 93%. On multivariable analysis, health region of residence, younger patient age, lower baseline comorbidity burden, and pathological nodal involvement were significant predictors of receipt of adjuvant chemotherapy. CONCLUSIONS: There is significant variation in receipt of adjuvant chemotherapy for patients receiving preoperative radiotherapy followed by proctectomy in Ontario. This variability is associated with patient, disease, and health system-related factors. Identifying the drivers of variability in cancer care practice may help to provide a basis for understanding and potentially addressing discrepancies in clinical, patient-centered, and economic outcomes in healthcare systems.

QS12

Preoperative Tranexamic Acid Does Not Reduce Transfusion Rates in Major Oncologic Surgery: Results of a Randomized, Double-Blind, Placebo-Controlled Trial G. Wright,[1]* A.M. Wolf,[1] E.D. Laney,[2] B.R. Lane,[1] m. chung.[1] *1. Spectrum Health/Michigan State University CHM, Grand Rapids, MI; 2. Spectrum Health, Grand Rapids, MI.*

Introduction: Allogeneic blood transfusions have been associated with poorer postoperative outcomes, particularly in patients undergoing major

oncologic surgery. The aim of this study was to introduce a simple preoperative intervention to reduce transfusion rates in this population. Methods: Adult patients undergoing major oncologic surgery in six categories (hepatectomy, pancreatectomy, esophagectomy, cytoreductive surgery +/- intraperitoneal chemotherapy, cystectomy, and prostatectomy) with similar historical transfusion rates were recruited for enrollment. Exclusion criteria included: history of hypercoagulopathy or thromboembolic event, creatinine >2.83 mg/dL, and known hypersensitivity to tranexamic acid. Patients received a single preoperative intravenous dose of placebo or tranexamic acid (1000 mg). Transfusion was performed intraoperatively at the discretion of the anesthesiologist and surgeon and postoperative transfusion criteria were standardized. The primary outcome measure was transfusion rate (intra- or post-operative). Secondary outcome measures included estimated blood loss, thromboembolic events, morbidity, hospital length of stay, and readmission rate. The study was halted early due to conditional power of <10% at interim analysis. Results: Seventy-six patient were enrolled and included for analysis, 39 patients in the tranexamic acid group and 37 in the placebo group. Demographics and surgery type were equivalent between groups. The transfusion rates were 8/39 (20.5%) in the tranexamic acid group and 5/37 (13.5%) in the placebo group, respectively (p=0.418). Median estimated blood loss was 400 mL (IQR=150-600) in the tranexamic acid group compared with 300 mL (IQR=150-800) in the placebo group (p=0.983). There was one pulmonary embolism in each arm and no deep venous thrombosis (p>0.999). There was no difference in postoperative morbidity, length of stay, or readmission rate between groups. Conclusion: Preoperative administration of tranexamic acid at a 1000 mg intravenous dose does not decrease transfusion rates or estimated blood loss in patients undergoing major oncologic surgery.

QS13

Examining the Incidence of GI Malignancy Among Solid Organ Transplant Recipients H. Khadra,* J. Crowther, A.S. Paramesh, J.F. Buell, E. Kandil, H. Jeon, C. DuCoin, M.T. Killackey, J. Hamner. *Department of Surgery, Tulane University School of Medicine, New Orleans, LA.*

Background Chronic immunosuppression required to prevent rejection in solid organ transplantation recipient has long been established as a risk for the development of malignancy. The true incidence of malignancy has yet to be established with an incidence varying from 20 to 80% after two decades of chronic immunosuppression and representing the third leading cause of post-transplant mortality. Methods We examined the incidence of gastro-intestinal (GI) malignancies among all solid organ transplant recipients from 1989-2015 using the United Network for Organ Sharing (UNOS) registry. The types of transplants included: intestinal, kidney, pancreatic, kidney + pancreatic, liver, heart, lung, and heart + lung. Results There were 624,985 patients who underwent solid organ transplants with a median follow up of 5.5 years that were included in our analysis. There were 7,979 patients who subsequently developed GI malignancies, with 2335 of these being recurrence of a pre-transplant malignancy, and 5644 being a de novo malignancy developed post-transplant. Overall, there was a significant difference in the rate of development of de novo GI malignancies across transplant types (chi^2 (7) = 1071, $p < 0.001$), with pancreatic having a relatively low overall incidence (195 in 100,000) of GI malignancy whereas liver and thoracic organ transplants had relatively high incidences (1101-1465 in 100,000) of GI malignancies. There was also a significant difference in the rate of recurrence of pre-transplant malignancies (chi^2 (7) = 8000, $p < 0.001$), with the liver transplant being associated with a much higher rate of recurrent liver cancer as compared to other types of transplants. Conclusion The current registry study demonstrates that extra renal solid organ transplant recipients are at an increased risk of developing GI malignancies. This strongly correlates with the intensity of chronic immunosuppression required in maintenance therapy. This increased risk suggests more intense screening should be considered for GI cancers in the post-transplant setting. Recurrent cancer in this data also suggests careful selection should be employed in renal and liver transplants performed for cancer related failure.

Incidence (per 100,000 patients) of development of de novo malignancies following transplant type (absolute number of patients)

Transplant Type	Esophageal Cancer	Gastric Cancer	Small Bowel Cancer	Pancreatic Cancer	Colorectal Cancer	Hepatocellular Cancer
Intestinal	0 (0)	43 (1)	86 (2)	43 (1)	216 (5)	130 (3)
Kidney	63 (238)	66 (247)	27 (100)	121 (454)	253 (952)	154 (579)
Pancreas	19 (3)	25 (4)	6 (1)	31 (5)	57 (9)	57 (9)
Kidney-Pancreas	69 (13)	42 (8)	42 (8)	64 (12)	286 (54)	48 (9)
Liver	120 (152)	85 (108)	39 (49)	196 (248)	413 (522)	612 (773)
Heart	152 (85)	152 (85)	102 (57)	41 (23)	165 (92)	287 (160)
Lung	135 (39)	97 (28)	55 (16)	159 (46)	595 (172)	325 (94)
Heart+Lung	0 (0)	275 (2)	138 (1)	0 (0)	550 (4)	138 (1)

QS14

The Drivers of Cost of Pancreatic Surgery: It's Not All About Volume J. Olson,* S. Bateni, D. Burgess, S. Gholami, R. Canter, R.J. Bold. *University of California, Davis, Sacramento, CA.*

Introduction Pancreatic resection has been studied extensively to identify predictors of outcome due to the high risk of morbidity and mortality; high-volume centers have been demonstrated to have superior outcomes compared to low-volume centers. Ongoing investigation into surgical outcomes are now including the cost of care delivery given the national focus on restraint in US health care costs. Presumably efforts to decrease cost (such as decreasing length of stay [LOS]) should not negatively impact postoperative outcomes. Therefore, we sought to evaluate the relationship between operative costs of pancreatic surgery with postoperative outcomes. Methods Using the Vizient database, we analyzed patients who underwent pancreatic resection between 10/2013 and 6/2017. Costs were calculated from charges using a cost-charge ratio adjusted for geographic variation. Vizient data includes a risk-adjustment based on patient characteristics for cost, LOS, mortality, complication and readmission rate. We performed robust linear regression analysis of the actual and risk-adjusted data to evaluation the relationship between cost and LOS, severe complication rate, in-hospital mortality rate, readmission rate and hospital volume. Data 15994 patients who underwent pancreaticoduodenectomy or distal pancreatectomy at 167 hospitals were identified. Median cost per hospitalization was $13,648 (interquartile ratio $11,761 to $17,454). Median LOS was 6 days which positively correlated with median costs (P=<0.001). 30-day severe complication rate was 7.5% and also associated with hospitalization costs (P=<0.001). Interestingly, hospitalization costs were not associated with readmission rate (P=0.76), in-hospital mortality (p=0.58), or annual pancreatectomy volume (P=0.77). Conclusion Cost of pancreatic surgery can be primarily impacted by efforts at reducing LOS and complication rate. While high volume hospitals tend to have lower LOS and complication rate, pancreatic surgical volume is not an indicator in itself of improved healthcare efficiency reflected by lower costs. Additionally, efforts to reduce LOS do not appear to have an adverse impact on readmission rate.

QS15

Modifiable Preoperative Risk Factors in Pancreatic Cancer: The Impact of Obesity on Gastric Emptying and Survival After Pancreaticoduodenectomy A. Khader,* S. Ruff, C. Conte, A. Kadison, J. Sullivan, J. Wang, R. Zaidi, G. Deutsch. *Surgery, Hofstra Northwell School of Medicine, Manhasset, NY.*

INTRODUCTION: Delayed gastric emptying (DGE) is a significant cause of morbidity and increased length of stay after pancreaticoduodenectomy (PD). The current literature, consisting of mainly single institutional studies, is often contradictory in identifying modifiable preoperative risk factors for DGE. METHODS: All patients from the ACS-NSQIP pancreas-specific database who underwent PD between 2014 and 2015 were selected. Preoperative variables were assessed for prediction of DGE, which was defined as no oral nutrition and/or nasogastric tube placement in the first two post-operative weeks. RESULTS: The analysis included 6409 patients with an average age of 64.2 ± 11.7 years, 53.9% were males, 30.4% were obese (BMI>30), and the rate of DGE and 30-day mortality were 17.5% and 1.8%, respectively. Pre-operative factors were selected for univariable and multivariable analysis based on clinical and statistical criteria (Table 1). Older age (HR 1.01; p=0.03), male sex (HR 1.46; p<0.01), end-stage renal disease on dialysis (HR 3.45; p=0.04), and severe chronic obstructive lung disease (HR 1.52; p<0.01) were all associated with an increased likelihood of DGE. Obesity (BMI > 30) was the only modifiable preoperative risk factors significantly associated with

DGE [HR 1.26 to 1.58; p<0.05]. Diabetes was not associated with DGE after PD. Paradoxically, preoperative obstructive jaundice (HR 0.84; p=0.01) and receipt of neoadjuvant chemotherapy (HR 0.81; p=0.03) were associated with a lower incidence of DGE. Obesity (BMI>30) was also associated with an increased 30-day mortality after PD (HR 1.53; p=0.02). Subgroup analysis of the obese population for intraoperative factors did not show any effects of anesthetic or operative techniques on DGE. CONCLUSIONS: To our knowledge, this is the first population study to identify obesity as a risk factor for DGE and 30-day mortality in patients undergoing PD. Further research is needed to determine whether obese patients with BMI > 30 may benefit from early intervention strategies, such as gastrointestinal motility agents and rigorous exercise regimens.

Effect of Preoperative Factors on Delayed Gastric Emptying after Pancreaticoduodenectomy

Preoperative Factors		Univariable Analysis		Multivariable Analysis	
		p value	HR	p value	HR
Age		0.01	1.01	0.03	1.01
Gender		<0.01	1.44	<0.01	1.46
BMI (Normal 18.5-24.9)	Underweight (<18.5)	0.86	0.96	0.91	1.03
	Overweight (25-29.9)	0.06	1.17	0.99	1.12
	Obese (30-34.9)	<0.01	1.32	0.02	1.26
	Severely obese (35-39.9)	<0.01	1.59	<0.01	1.58
	Morbidly obese (>40)	0.07	1.37	0.04	1.44
Diabetes	Non-insulin dependent	0.11	1.17	0.55	1.06
	Insulin dependent	0.51	0.93	0.18	0.87
End stage renal disease on dialysis		0.04	3.38	0.04	3.45
History of severe COPD		<0.01	1.51	<0.01	1.52
Preoperative obstructive jaundice		0.05	0.88	0.67	1.16
Chemotherapy within 90 days		0.01	0.78	0.03	0.81
Current smoker within 1 year		0.04	0.84	0.08	0.85
Steroid use for chronic conditions		0.11	1.37		
More than 10% weight loss in 6 months		0.32	0.92		

QS16

Implementation of a Standardized Frailty Assessment Identifies Patients at Risk for Prolonged Length of Stay and Discharge to an Extended Care Facility P.R. Varley,[1]* D. Hall,[1] S. Ahrendt,[2] M.E. Brozovich,[1] J. Celebrezze,[1] H. Choudry,[1] S. Evans,[1] M. Hogg,[1] J. Holder-Murray,[1] M. holtzman,[1] K.K. Lee,[1] J.W. Marsh,[3] J. Salgado,[1] J. Rubin,[1] A. Tsung,[1] A. Zureikat,[1] D.S. Medich,[1] D.A. Geller,[1] D. Bartlett,[1] J. Pingpank.[1] *1. General Surgery, UPMC, Pittsburgh, PA; 2. University of Colorado Hospital, Denver, CO; 3. WVU School of Medicine, Morgantown, WV.*

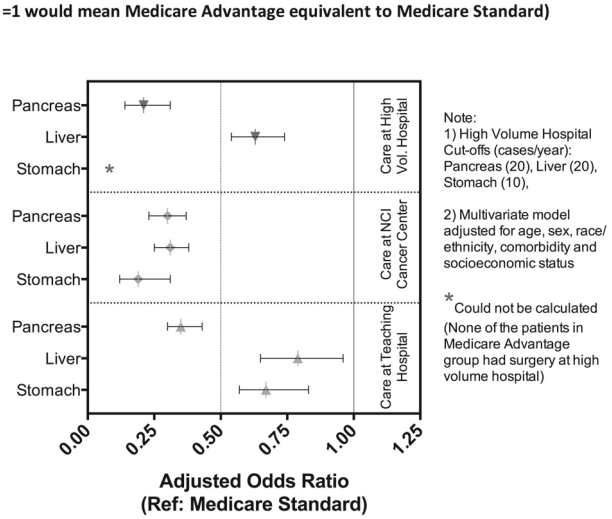
Background: Though a number of frailty instruments have been described and applied, there is no consensus regarding the most appropriate tool for use within surgical oncology practices. The goal of this project was to implement a prospective, standardized frailty screening protocol in the surgical oncology practices of at a quaternary academic medical center. Methods: All new patients seen for both malignant and benign indications within the Department of Surgical Oncology at a large, academic medical center were assessed using the Risk Analysis Index (RAI). Patient RAI data was linked to institutional National Surgical Quality Improvement Project (NSQIP) data to obtain standardized surgical outcome information. Logistic and linear regression was used to identify associations between RAI score and postoperative morbidity/mortality, discharge disposition, and hospital length of stay. Results: From February-December 2016, 2829 new patients were evaluated with an RAI score and 522 had available data abstracted for NSQIP reporting. Of this cohort, 53.0% were female and the mean age was 64.3±14.0 years. The median RAI score was 7 (range 0-48, IQR 3-11.5). Cases were divided among pancreas (12.1%), hepatobiliary (17.3%), colorectal (31.8%), skin, soft tissue and breast (11.8%), upper GI (3.5%) and other abdominal cases (23.5%). Interestingly we noted that 12.3% (n=64) noted impairment in at least one ADL domain, while only 1.7% (n=7) were rated as partially or totally dependent by NSQIP abstractors. With regard to outcome, the rate of death or major morbidity (DMM) was 11.3% (n=59). When controlling for procedure group, RAI score was not significantly associated with DMM (p= 0.199). RAI was however significantly associated with both length of stay (coefficient 0.06, p=0.014) and discharge to a facility other than home (OR 1.12, p < 0.001). Conclusions: Implementation of a standardized frailty assessment within a surgical oncology group at a quaternary academic medical center is not only feasible, but may help identify patients at risk for prolonged length of stay and discharge to a facility other than home.

QS17

Medicare Advantage: A Disadvantage for Complex Cancer Surgery Patients M. Raoof,* P. ituarte, O.S. Eng, Y. Fong. *Surgery, City of Hope Cancer Center, Duarte, CA.*

Background: To enhance health care efficiency, managed care plans (such as Medicare Advantage) typically restrict access to certain in-network specialists. Whether or not, this is a barrier to centralization of complex cancer surgery is unknown. Methods: We compared access to optimal surgical cancer care for Medicare Standard (MS) vs. Medicare Advantage (MA) beneficiaries in the state of California, undergoing gastric, hepatic, pancreatic resections. Optimal care was defined as access to; 1) high volume hospital (HVH), 2) National Cancer Institute (NCI) Designated Cancer Center, or 3) teaching hospital. Data were abstracted from the Office of Statewide Health Planning Inpatient Database and linked to California Cancer Registry from 2000-2012. Multiple logistic regression analyses were performed to adjust for covariates. Results: There were 3,580 primary gastric cancer, 3,311 hepatic (primary or metastatic cancer), and 2,281 pancreatic cancer resections that met inclusion criteria. Approximately one-third of the patients were MA beneficiaries. In comparison to MS, enrollment in MA plans was associated with a lower likelihood of care at HVH for gastric (5% vs. 0%), hepatic (43% vs. 32 %) and pancreatic resections (15% vs. 3%); [All P<0.001]. For all surgical resections, MA was associated with significantly lower likelihood of care at NCI designated cancer center or a teaching hospital (P<0.001). These findings persisted after adjusting for age, sex, comorbidities, race/ethnicity and socioeconomic status Figure 1. In comparison to MS, enrollment in MA plans was associated with a higher likelihood of 30-day post-operative mortality for gastric [4.7% vs. 6.9%; Adjusted OR: 1.37, 95%CI (1.01-1.90); p=0.043], hepatic [4.5% vs. 6.6%; Adjusted OR: 1.62, 95%CI (1.15-2.26); p=0.005] and pancreatic resections [4.7% vs. 6.9%; Adjusted OR: 1.52, 95%CI (1.03-2.25)] Conclusions: MA beneficiaries have higher post-operative mortality which is attributable to significantly lower odds of surgical cancer care at HVH, NCI-designated cancer centers and teaching hospitals.

Figure 1. Lack of Access to Optimal Surgical Cancer Care for Medicare Advantage beneficiaries



QS18

A Critical Evaluation of Quality Assessment in Surgical Oncology Operations Performed with Palliative Intent E.A. Fallon,[1]* A.M. Blakely,[2] K.P. Charpentier,[1] W.G. Cioffi,[1] T.J. Miner.[1] *1. General Surgery, Brown University / Rhode Island Hospital, Providence, RI; 2. City of Hope Medical Center, Duarte, CA.*

INTRODUCTION: Quality analysis (QA) following palliative operations (PO) remains challenging as the influence of both surgical and palliative care (PC) metrics must be considered. Information to effectively evaluate PO is often unavailable from regularly utilized administrative data. METHODS: Patients undergoing PO for advanced cancer were identified from the PC surgery database. Data include complications, factors leading to death, symp-

tom improvement, and established core components of PC. All were followed for ≥90 days or until death. RESULTS: From 2003-2015, 187 patients had palliative-intent surgery. Median survival was 277 days. Ten (5.3%) died within 30 days; 24 (14%) died within 90 days. Cause of death (30 vs. 90 days) was predominantly from postoperative complications (n=1, 10% vs. n=3, 12%), disease progression (n=1, 10% vs. n=17, 71%; p=0.014), or decisions made by patient/family/surgeon to cease active treatment (n=8, 80% vs. n=4, 17.0%; p=0.003). Symptom improvement was seen in 149/187 (80%); 17% developed new (n=31, median 174 days) and 13% had recurrent symptoms n=25, median 221 days). PC core components were addressed more frequently in the relationship/rapport building (96%), symptom management (93%), establishing illness understanding (92%), discussion of care options (98%), and involving family (93%) domains than in the addressing coping (66%) and end-of-life planning (47%) areas (p<0.001). Direct hospice referrals were made in 21% (40/187), but were less common in patients dying within 30 (20% (2/10)) vs. 90 days (75% (18/24), p=0.003). In most early mortality cases, end-of-life care often was managed by the surgical oncology team and referrals were not made. DISCUSSION: Traditional QA provides an incomplete assessment of PO. Although patients often improve, continued PC is essential to manage new and recurrent symptoms. Perioperative complications and disease progression have distinct effects on 30 and 90-day mortality. Although surgeons frequently provide high-quality primary PC, referral patterns to PC specialists challenge the validity of hospice or PC referral as an independent quality measure for this patient population.

QS19

Evaluating Faculty Mentorship and Onboarding through Assessment of Patient Outcomes by Surgeon Seniority C.H. Davis,* C. Roland, M. Katz, N.D. Perrier, G. Chang, J. Vauthey, P. Mansfield, M.I. Ross, K. Hunt, J. Skibber, J.E. Lee, T. Aloia. *The University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: As more surgical residents seek fellowship training, the impact of new faculty onboarding and mentorship on historical relationships between surgeon experience and patient outcomes is being revisited. Methods: Rates of serious morbidity (SM) and mortality in the Department of Surgical Oncology (DSO) from 2011-2016 were extracted from a single-center ACS-NSQIP database and compared across 4 levels of surgeon time in service (TIS) and 8 disease groups. All faculty were fellowship trained and were exposed to a general onboarding program. In addition, Breast and Colorectal (CRS) surgery had a formalized surgical mentorship program. Results: 5,452 elective procedures were analyzed. Full professors accounted for 55% of all faculty and performed 47.6% of all cases (associate 20.7%, assistant>24 months TIS 23.2%, and assistant<24 months TIS 8.4%). Based on RVU values, case magnitude was similar across TIS cohorts, however, reoperative and multiteam cases were more prevalent in the full professor cohort, reflecting a bias toward higher complexity. Assistants<24 months operated on more ASA Class 3&4 patients than surgeons with longer TIS (p=0.047). While 30-day mortality rates were low and comparable regardless of TIS (0.1% overall, p=0.460), complication rates were lower for both assistant professor sub-groups, compared to associate and full professors (4.8%, 5.1%, 8.8%, 7.2%, p=0.001). After adjustments for demographic and comorbidity factors the odds of SM were higher for associates (OR:1.9) and full professors (OR:1.6), compared to assistant professors (p=0.003). Within each disease area, outcomes were similar across levels of experience with the exception of CRS, which demonstrated lower odds of SM in assistant compared to associate/full professors (p=0.031). Conclusions: Despite the influence of unaccounted for case/cancer complexity, the combination of fellowship training and programmatic onboarding appears to blunt the traditionally expected new faculty learning curve across multiple procedures. Superior outcomes for new faculty exposed to a dedicated mentorship program, as seen here for CRS, suggest that additional improvement can be achieved.

Table: Patient Characteristics and Outcomes by Surgeon Time in Service

	Surgeon Time in Service					
Patient Features	Assist<24mo	Assist>24mo	Associate	Professor	All combined	p=value
N	460	1266	1131	2595	5452	
Male (%)	31.1	30.0	32.4	37.7	34.4	<0.001
Age (median)	58.77	57.25	58.46	58.71	58.31	0.021
BMI (median)	28.65	28.15	27.64	27.69	27.84	0.069
RVU (median)	18	17	17	18	17	0.261
ASA Class						0.047
ASA1	0.0	0.5	0.2	0.3	0.3	
ASA2	14.3	19.8	16.4	18.8	18.2	
ASA3	83.3	78.6	81.7	79.2	79.9	
ASA4	2.4	1.1	1.8	1.7	1.6	
Serious Morbidity (%)	4.8	5.1	8.8	7.2	6.9	0.001
Mortality (%)	0.0	0.1	0.0	0.2	0.1	0.460
Adjusted OR, Serious Morbidity	1.0 (ref)	1.108	1.925	1.495		0.003

BMI: body mass index; RVU: relative value unit; ASA Class: American Society of Anesthesiologist's Classification; OR: odds ratio

QS20

Academic Productivity in 2017: Where is the Bar Set for Surgical Oncologists Training the Next Generation? C.J. LaRocca,* P. Wong, O.S. Eng, M. Raoof, S. Warner, L.G. Melstrom. *City of Hope National Medical Center, Duarte, CA.*

Background: Promotion to a higher rank is an important milestone in the career of an academic surgical oncologist, and the impact of one's academic achievements is an integral component of this process. The aim of this study was to analyze academic productivity as a function of rank among academic surgical oncologists. Methods: Faculty were identified from the Accreditation Council for Graduate Medical Education (ACGME) surgical oncology fellowships in the United States. Scopus was used to obtain the number of publications/citations and h-index values. The h-index reflects both the total number of publications and the number of citations per publication. The National Institutes of Health (NIH) RePORT website was used to identify faculty members with previous or current NIH funding. Results: Of the 319 surgeons identified, complete rank information was obtained for 311. Males were 70% of the total. There were 106 (34 %) assistant, 83 (27 %) associate, and 122 (39 %) full professors. Of the full professors, only 14 (11%) were female. Only 10% of all faculty had MD PhD's. The median number of publications for assistant, associate, and full professor was 16, 49, and 162 respectively. The median number of citations in the respective ranks was 220, 1229, and 6033. Similarly, the median h-index values were 7, 17, and 39. A total of 28% of surgical oncologists have been the primary investigator on an NIH grant at some point during their career, while only 12% are currently funded. A multivariate analysis demonstrated that only years in practice, h-index, and a history of NIH funding significantly affected a surgeon's academic rank (p<0.05). Despite the vast difference in gender distribution with increasing rank level (Table), gender and type of degree did not have a significant correlation with academic rank. Conclusion: Objective benchmarks such as the median h-index and NIH funding may be useful metrics to provide insight for both junior faculty and leadership into the productivity needed to attain promotion to the next academic rank. Additional work is needed to further evaluate factors that may correlate with productivity and rank.

Surgical Oncologist Productivity as a Function of Academic Rank

	Assistant		Associate		Professor	
	Median	Range	Median	Range	Median	Range
Years In Practice	6	1-28	12	4-38	25	10-60
Gender						
Male (%)	54		63		89	
	Median	Range	Median	Range	Median	Range
Number of Publications	16	1-124	49	6-225	162	12-1014
	Median	Range	Median	Range	Median	Range
Number of Citations	220	1-3385	1229	57-12899	6033	166-73459
	Median	Range	Median	Range	Median	Range
h-index	7	1-30	17	3-44	39	6-138
History of NIH Funding (%)	5		25		51	
Current NIH Funding (%)	2		16		20	

QS21

Novel Endoscopic Criteria Using Magnified Chromoendoscopy for Evaluating Complete Response to Neoadjuvant Chemoradiotherapy in Rectal Cancer T. Konishi,* A. Chino, A. Ogura, H. Kawachi, H. Osumi, S. Saito, T. Akiyoshi, Y. Fukunaga, M. Ueno. *Department of Gastroenterological Sugery, Cancer Institute Hospital of the Japanese Foundation for Cancer Research, Tokyo, Japan.*

Background and Aims: Precise endoscopic assessment of complete response to neoadjuvant chemoradiotherapy is important for optimizing surgical and non- surgical treatments in rectal cancer. We created new endoscopic criteria to define endoscopic complete response using magnifying chromoendoscopy, hypothesizing that magnifying chromoendoscopy would detect minor residual cancer nests and increase diagnostic accuracy. This study aimed to prospectively evaluate diagnostic accuracy of the new criteria to identify pathological complete response, and to compare it with the conventional Habr-Gama's criteria. Methods: The new criteria were composed of 5 notable endoscopic findings, including shape of the scar, state of the ulcer, presence of residual protruded nodules, flexibility of rectal wall, and presence of neoplastic pit-patterns under magnifying chromoendoscopy. Forty-seven patients with stage II-III low rectal cancer who received conventional neoadjuvant chemoradiotherapy were prospectively evaluated by 3 endoscopists within 3 days before surgery. Evaluation was also performed using the Habr-Gama's criteria, and diagnostic accuracy to identify pathological complete response was compared between the 2 criteria. Results: Pathological complete response was obtained in 8 patients (17%). Diagnostic accuracy of the new criteria was 87%, with a sensitivity of 50%, specificity of 95%, positive predictive value (PPV) of 67% and negative predictive value (NPV) of 90%. In the Habr-Gama criteria, the values were 79%, 50%, 85%, 40% and 89%, respectively (Table). Conclusion: The new endoscopic criteria using magnifying chromoendoscopy had better diagnostic accuracy to identify pathological complete response with improved specificity and PPV but similar sensitivity and NPV compared to the Habr-Gama's criteria. Magnifying chromoendoscopy may decrease false-positive and provide more precise selection for non-surgical management compared to the conventional endoscopic assessment.

Comparison of the two endoscopic criteria to identify complete response

	New criteria using magnifying chromoendoscopy			Habr-Gama's criteria		
	Pathological complete response	Pathological incomplete response	Total	Pathological complete response	Pathological incomplete response	Total
Endoscopic complete response	4	2	6	4	6	10
Endoscopic incomplete response	4	37	41	4	33	37
Total	8	39	47	8	39	47
	Accuracy, 87%; Sensitivity, 50%; Specificity, 95%; PPV, 67%; NPV, 90%			Accuracy, 79%; Sensitivity, 50%; Specificity, 85%; PPV, 40%; NPV, 89%		

QS22

Improvements in Outcomes after Robotic Colorectal Resection for Cancer in New York State M. Symer,* A. Sedrakyan, H. Yeo. *Surgery, Weill Cornell Medical College, New York, NY.*

Introduction: Robotic surgery for colorectal cancer offers many potential benefits, but early data suggest a high rate of iatrogenic complications. We sought to identify trends in the uptake of robotic resection and to describe outcomes as the volume of robotic resections increases. Methods: The New York Statewide Planning and Research Cooperative database was used to identify all adults undergoing colon or rectal resection for cancer from 2009 through 2014. Those undergoing flap reconstruction or pelvic exenteration were excluded. Patient characteristics and hospital volume tertile were identified. Primary outcome was in-hospital major events (myocardial infarction, pulmonary embolism, shock, and death). Secondary outcomes were iatrogenic complications (wound infection, hematoma formation) and anastomotic leak. Multivariable logistic regression was used to compare outcomes of procedures occurring from 2009-11 to those occurring from 2012-14. Results: 1,705 robotic procedures were identified, with volume increasing from 43 cases in 2009, to 652 in 2014. Most patients were under 65 years old (57.1%), White (77.2%), and had commercial insurance (61.6%). Rectal resection was most common (61.6%). 32.7% of resections occurred at hospitals performing <10 robotic colorectal resections. Comparing outcomes from 2009-11 to 2012-14, major complications (OR 1.18 95%CI 0.55-2.53; p=0.67) and iatrogenic complications did not change (OR 1.10 95%CI 0.37-3.21; p=0.87), but anastomotic leak decreased significantly (OR 0.13 95%CI 0.07-0.26; p<0.01). Length of stay remained the same (median 5 days). In adjusted analysis, major events and iatrogenic complications did not change, but anastomotic leak decreased in the latter half of the study period (OR 0.13 95%CI 0.06-0.27; p<0.01). Throughout this time there was a nonsignificant trend toward improved outcomes at higher volume hospitals compared to low volume (OR 0.40 95%CI 0.15-1.08; p=0.07). Conclusion: Robotic colorectal resection has been rapidly adopted in New York State in recent years and outcomes related to anastomotic leak have improved. The effects of patient selection and surgeon experience on these outcomes should be explored further.

QS23

Accuracy of Nodal Staging is Influenced by Sidedness in Colon Cancer: Results of a Multicenter Prospective Trial A. Dehal,[1]* a. Graff-Baker,[1] B. Vuong,[1] s. chang,[2] M. Goldfarb,[1] A. Bilchik.[1] *1. Department of Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA; 2. Medical Data Research Center, Providence Health & Services, Portland, OR.*

Background: National guidelines define adequate lymph node (LN) sampling in colon cancer (CC) as ≥ 12 LNs. Recent data suggests that sidedness impacts survival in CC. The difference in LN number to accurately stage T3N0 disease in right vs left CC has not been previously evaluated in a prospective trial. Methods: Patients with pathologic T3 CC who had at least one LN examined were identified from a randomized, multicenter, international trial of ultrastaging in CC (ID: NCT00949312). The probability of true nodal negativity based on the number of LNs examined was calculated for left and right CC. These results were then validated in a cohort of patients with similar inclusion criteria selected from the National Cancer Database (NCDB) between 2006 and 2014. Results: 370 patients met the inclusion criteria in the trial cohort; 48% were LN-negative. Of 153,945 patients in the NCDB with similar inclusion criteria, 57% were LN-negative. The probability of true nodal negativity when 12 LNs were examined was 64% for left and 68% for right CC in the trial cohort and 72% and 77% in the NCDB. The probability (80-95%) of true nodal negativity comparing left to right CC was significantly different in both the trial (p <0.001) and the NCDB (p <0.001) (Table 1). Conclusions: In both a prospective multicenter trial and the NCDB, sidedness influences the total number of LNs needed to predict nodal negativity in CC. Current guidelines regarding the minimum number of LNs needed to accurately stage patients with T3N0 CC may need to be re-evaluated since the decision to treat patients with adjuvant chemotherapy is largely determined by LN status.

Table 1.

Probability of true nodal negativity	Number of lymph nodes			
	Clinical Trial		NCDB	
	Left CC	Right CC	Left CC	Right CC
80%	26	22	19	15
85%	31	27	25	20
90%	36	32	31	27

QS24

Deciphering Tumour Biology in Colorectal Peritoneal Carcinomatosis: The March from Conventional Chemotherapeutics to Targeted Therapy J. Hendrikson,* Q. Tan, W. Ng, N. Shannon, H. Lim, J.W. Tan, C. Chia Shulyn, G. Tan, O. Kon, J. Ong, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction Peritoneal carcinomatosis (PC) is a form of metastasis confined to the abdominal cavity in 15% of colorectal cancer patients. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) has improved patient outcomes but use of conventional chemotherapeutic agents in HIPEC relies on cytotoxic effects without considering tumour biology. This study aimed to identify novel small molecule inhibitors that can be added to the HIPEC regimen to reduce locoregional recurrence and improve patient outcome. Methods Matched samples of primary colorectal tumour, metastases and normal colonic mucosa were collected from patients who underwent CRS (n=15). Epithelial and stromal components were isolated using laser capture

microdissection (LCM) and subesequently profiled using RNA sequencing. Small molecule inhibitors targeting peritoneal metastasis were identified by connectivity map analysis and downstream validation performed with immunohistochemistry and an in-vitro drug screen. Results LCM of samples coupled with RNA sequencing identified multiple signalling cascades specific to peritoneal metastasis with high fidelity. Connectivity map analysis identified multiple drugs that target peritoneal metastasis. PI3K inhibitors, such as LY294002 and quinostatin, showed strong antagonistic gene expression profiles to epithelial and stromal metastatic tumour signatures (connectivity score -0.221 ($p<0.0001$) and -0.826 ($p<0.001$), respectively). Immunohistochemistry confirmed raised PI3K pathway activity in peritoneal metastases compared with primary tumours. 5 inhibitors specifically targeting PI3K signalling were tested against 2 metastatic colorectal cancer cell lines with varying sensitivity towards mitomycin (conventional chemotherapeutic agent in HIPEC). BEZ235, a dual PI3K and mTOR inhibitor, was most effective in inhibiting cellular proliferation (IC50:0.39–0.49 uM). Conclusion We have identified and validated PI3K signalling as the predominant signalling pathway in metastatic tumours of colorectal PC. Treatment with dual PI3K/mTOR inhibitor provides a putative efficacious adjunct to HIPEC in colorectal PC.

QS25

Nanoparticle Delivery of Oligometastastic-Associated microRNA Inhibits Growth of Colorectal Metastases L. Xue,* G. Oshima, N. Guo, C. He, M. Stack, W. Li, R. Weichselbaum, N. Khodarev, M. Posner. *University of Chicago, Chicago, IL.*

Introduction: Patients with oligometastatic CRC, present with hepatic metastases that are limited in number that can respond favorably to local therapeutic strategies. We previously found that several microRNA clustered on 14q32 are upregulated in oligometastases as compared to polymetastases. These miRNAs supress cellular pathways of adhesion, invasion and motility. In this study, we use nanoparticles to deliver oligometastasis-associated 14q32-encoded miRNA miR655 into liver metastases and show this strategy can effectively inhibit liver metastases progression in a murine xenogenic model of CRC. Methods: Splenic injection of the luciferase/tdTomato dual-labelled HCT116 cells were performed on athymic nude mice to generate liver metastases. Mice were treated with nanoparticles labelled with Alexa647 and carrying miR655 twice weekly for 4 weeks. Tumor burden was quantified by in vivo luminescent and ex vivo fluorescent imaging. qPCR was used to measure gene expressions of TGFBRS and ICK, two known targets of miR655. Results: We treated 2 groups of metastases bearing mice with nanoparticle carrying non-targeting microRNA or miR655. Highly selective co-localization of tdTomato and Alexa647 occurred post-injection. The fluorescence from HCT116 tumors were 4.3-fold lower in the miR655 group at 4wks (Figure 1). The number of tumor colonies in miR-655 group are decreased at 4wks. TGFBR2 and ICK expression is decreased by 63% and 73% respectively, in the miR655 group. Conclusion: Nanoparticle delivery of oligometastases-associated microRNAs is targeted and effective in the suppression of liver metastases. Our model of liver metastasis is a robust platform to test potential novel adjuvant therapy approaches for CRC hepatic metastatic disease.

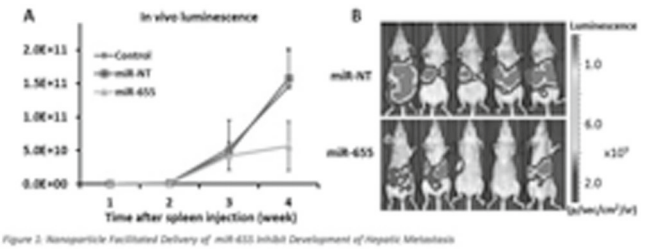


Figure 1: Nanoparticle Facilitated Delivery of miR-655 Inhibit Development of Hepatic Metastasis

QS26

A Novel 3-Dimensional (3D) Micro-Fluidics Device to Model the Tumor Microenvironment (TME) Y. Bi,[1] B.A. Krasnick,[1]* G. Maddy,[1] S.P. Goedegebuure,[1] V. Shirure,[2] S. George,[2] R. Fields.[1]
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2. University of California Davis, Davis, CA.

Introduction: In vitro models of cancer have led to significant therapeutic advances. Despite the widespread use of in vitro tissue culture, the ability to directly evaluate human biology is limited by the inability to model the complex, 3D nature of the TME. We introduce a novel, microfluidic-based system of 3D human micro-tumors perfused with a network of human micro-vessels which could overcome the shortcomings of current in vitro systems. Methods: The micro-device was created by casting polydimethylsiloxane (PDMS) onto master molds, which are then bonded to a flat PDMS sheet using air plasma. Normal human lung fibroblasts (NHLF) and GFP labelled endothelial colony forming cell derived endothelial cells (EC-FCECs) were loaded in a fibrin gel into the central tissue chamber. Media was introduced through the microfluidic lines. The vascular network was developed with complete EGM2 media under nominal interstitial flow. Colorectal tumor cell lines labelled with mCherry were loaded to the side chambers on the 7th day after NHLF and EC loading. Bevacizumab or TGF- β were added on the 2nd day after tumor cell loading. Results: Micro-vessels formed in the central chamber in 5-7 days after loading. The vessels were perfused with 70KDa fluorescent (red) dextran, and displayed intact vessel wall barrier. A suspension of a colorectal tumor cell line was loaded into the device side chambers, next to a fully developed vasculature. The tumor cells drove angiogenesis into the side chambers, and at the same time tumor began to migrate into the central chamber and within the vessel lumen. The angiogenesis induced by tumor cells can be pharmacologically inhibited, and the migration/ intravasation of tumor cells can be stimulated by TGF-β. Conclusions: Our novel micro-device system can be used as a functional in vitro system that can model the tumor micro-environment. This system has the advantage over current in vitro and in vivo systems in that it is high-throughput, rapid, cost-effective, and re-creates many features of the 3D TME. We are currently: (1) expanding the platform to incorporate immune cells and (2) designing a completely autologous system to test cancer immunotherapeutics.

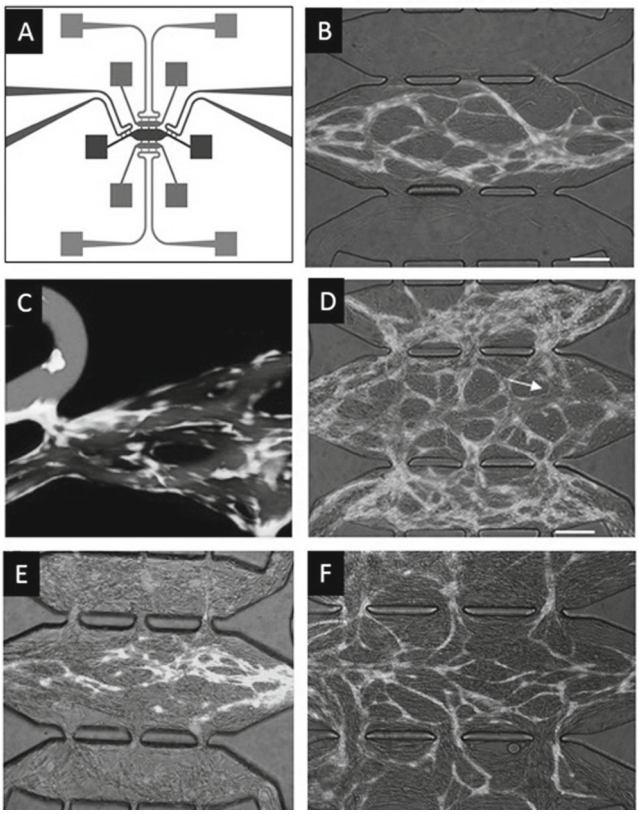

Figure: (A) Actual micro-device design, where microporous walls separate the tissue chambers (2 green, 1 red). Vasculature develops in the central chamber (red) fed via fluidic lines (blue) connected to media reservoirs that are varied to control interstitial flow. (B) represents GFP labelled microvessels within the central chamber of micro-device, (C) represents intact vasculature with red dextran in the intraluminal space, (D) mCherry labelled tumor cell migration into the central chamber and vessel lumen, (E) represents the addition of the VEGF inhibitor Bevacizumab to the system with resultant decreased vascular networks present, and (F) demonstrates increased mCherry labelled tumor cell invasion into the central chamber with the addition of TGF- β to the system.

QS27

Tumor Infiltrating Lymphocytes and Macrophages Improve Survival in Microsatellite Unstable Colorectal Cancer

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Introduction: Due to the loss of DNA repair mechanisms in colorectal cancer (CRC) with microsatellite instability (MSI), somatic mutations accumulate within DNA. This genomic instability can make them more prone to attack by tumor infiltrating lymphocytes (TIL) and macrophages. We hypothesize that MSI-High (MSI-H) patients have favorable overall survival (OS) due to increased tumor immunogenicity and attraction of TILs. Methods: The Cancer Genome Atlas (TCGA) was used to evaluate gene expression from 283 patients with CRC, comparing MSI-H and microsatellite stable (MSS) patients. The CIBERSORT algorithm was used to estimate the fraction of immune cell types in a mixed cell population of each tumor obtained from TCGA sequencing. Results: We found that low expression of several DNA repair genes correlated with MSI-H including: MLH1 ($p< 0.0001$), PMS1 ($p= 0.002$), PMS2 ($p < 0.0001$) and MLH3 ($p =0.036$) as well as non-mismatch repair genes- ATM, PRKDC, ATR ($p < 0.0001$) and BRCA2 ($p= 0.0081$). Improved OS was seen in patients with low ATM ($p= 0.004$), PMS2 ($p= 0.003$) and MLH 3 ($p= 0.0097$). TIL expression was higher in the MSI-H group vs. MSS in the helper T-cell population (0.058 vs. 0.047, $p= 0.034$). This trend was seen in CD8+ T-cells (0.031 vs. 0.021, $p = 0.13$) and memory T-cells (0.091 vs. 0.081, $p= 0.26$). MSI-H patients had more M1 macrophages than MSS (0.059 vs. 0.028, $p<0.0001$). MSI- H and MSS tumors were also assessed for expression of immune checkpoint molecules including PD-1, PD-L1, CTLA4, LAG3 and TIM3, all of which had higher expression in the MSI-H group than MSS ($p< 0.0001$). OS was worse for MSS patients with elevated PD-L1 ($p= 0.01$) and LAG3 ($p= 0.021$). Conclusions: In this cohort of CRC patients, we found that decreased expression of certain DNA repair genes associated with elevated MSI. MSI-H patients had improved OS compared to MSS patients, likely due to higher composition of TIL and M1 macrophages and their cytotoxic/pro-inflammatory role within the tumor micro-environment. MSI status also associates with expression of immune checkpoint molecules which can be important for prognostication as well as further development of therapeutic targets.

QS28

National Post-operative and Oncologic Outcomes after Pelvic Exenteration for Primary Rectal Cancer I. Konstantinidis,* B. Lee, V. Trisal, K. Melstrom, S. Sentovich, L. Lai, M. Raoof. *Surgery, City of Hope Cancer Center, Duarte, CA.*

Background: Data on outcomes after pelvic exenteration are limited to single-institutional series. The purpose of this study was to evaluate early post-operative and oncologic outcomes after pelvic exenteration for primary rectal and rectosigmoid cancers in a national multi-institutional cohort Methods: Using the National Cancer Database (NCDB) - that captures data from Commission on Cancer (CoC) – accredited hospitals, we analyzed patients undergoing pelvic exenteration for primary rectal or rectosigmoid adenocarcinoma over a ten-year period (2004-2013). Patients with metastatic disease were excluded. Factors predictive of 90-day mortality were evaluated using logistic regression. Primary outcome was overall survival (OS) and factors associated with survival were analyzed using Cox proportional hazards model. Results: There were 3,235 pelvic exenterations performed in 743 hospitals. Median age was 61 (IQR: 51-71) years and majority (n=1,935 ;60%) were female. Median length of stay was 8 days (IQR 6-11). Following exenteration, 30-day mortality rate, 90-day mortality rate and readmission rate was 1.8%, 4.0% and 6.9%, respectively. Age ≥60 years and higher Charlson-Deyo comorbidity index were independently associated with increased 90-day mortality (both $p<0.001$). Receipt of neoadjuvant chemoradiation was associated with decreased 90-day mortality (OR 0.50, 95% CI 0.30-0.84; $p=0.009$). Median OS was 70 months (IQR 27 – 138). After adjustment of significant covariates, (age, sex, Charlson-Deyo comorbidity index, grade, pT- and pN-stage), negative margin status (adjusted HR 0.53, 95% CI 0.46 – 0.62, $p<0.001$) and receipt of perioperative radiation (adjusted HR 0.71, 95% CI 0.62 – 0.81, $p<0.001$) were significantly associated with decreased risk of death although margin positive rate was 17.2% and 64% of patients received perioperative radiation. Conclusions: Pelvic exenterations are performed safely in CoC-accredited hospitals. However, many patients have suboptimal resections or are subject to underutilization of perioperative radiation therapy. Both factors are critical for long-term survival and attention to these factors may improve outcomes.

QS29

Does Medicare Severity-Diagnosis Related Group Payment Methodology Accurately Reflect Cost Structures of Benign and Oncologic Resection in Medicare Patients? B.D. Hughes,* H.B. Mehta, Y. Shan, A.J. Senagore. *Surgery, University of Texas Medical Branch, Galveston, TX.*

Introduction Reimbursement for colonic pathology by the Centers for Medicare and Medicaid Services (CMS) are grouped in the Medicare Severity-Diagnosis Related Groups (MS-DRG). While this system is meant to reflect resource consumption for these procedures, there is little data comparing the relative impact of the MS-DRG system on cost and reimbursement for oncologic versus benign colon resection. Methods This retrospective cohort study used 5% national Medicare data from 2011 to 2014 and included elderly patients undergoing colonic procedures with or without comorbidity/complications (DRG 330 and 331). Based on the primary diagnosis, patients were classified as having benign disease or cancer. Descriptive statistics were used to evaluate the surgical approach and health resource utilization. Results The study included 10,928 patients (33% benign vs. % 67% cancer), with the majority of being non-Hispanic white women. Mean age was 70.9 ± (9.7) and 76.6± (8.7) in the benign and cancer cohort cohorts ($p<0.001$), respectively. Open colectomy was performed more commonly for both oncologic and benign resection (open: 63% vs. 60%, $p<0.001$; laparoscopic: 40% vs. 36.8%, $p <0.001$,). Benign colectomy was associated with higher total charges

($66,033 vs. $60,581, p<0.001), and a longer length [days] of stay (7.25 vs. 6.92, p=.0002) when compared to the oncologic group. Inpatient mortality was higher in the cancer group as well (15 patients vs. 27 patients; p<0.001). Interestingly, payments were not significantly different between the cohorts (benign- $10,358 vs. oncologic- $10,483, p=0.434). However, cancer patients (benign-12.4% vs. cancer-16.6%; p <0.001) were more likely to be discharged to a rehab facility. Conclusion The data demonstrates that the payment methodology for colectomy under the CMS MS-DRG system does not accurately reflect the episode cost of care for benign versus malignant disease, especially with respect to post-discharge costs for cancer patients. A transition to value-based payments will require a better understanding of unique costs experienced by colon cancer patients before adoption.

QS30

The Magnitude of Postoperative Mortality After Colorectal Cancer Surgery in Elderly Patients Revised N.P. Brouwer,[1]* F. van Erning,[2] E. Bastiaannet,[3] J. Dekker,[4] H. Rutten,[5] H. de Wilt.[1] *1. Surgery, Radboud University Medical Center, Nijmegen, Netherlands; 2. Netherlands Comprehensive Cancer Organization, Utrecht, Netherlands; 3. Leiden University Medical Center, Leiden, Netherlands; 4. Reinier de Graaf Gasthuis, Delft, Netherlands; 5. Maastricht University Medical Center, Maastricht, Netherlands.*

Background: Previous studies have shown that elderly benefit less from surgical treatment for colorectal cancer (CRC) as reflected in higher postoperative mortality rates after surgical resection. The aim of the present study is to investigate trends over time for postoperative mortality and to assess whether the high postoperative mortality among elderly is still present. Methods: Patients with primary stage I-III CRC, who received surgery and were diagnosed between 2005 and 2014 were selected from the Netherlands Cancer Registry (N=99,012). Trends in 30-, 60-, and 90-day postoperative mortality were calculated by age group (<75 versus ≥75 years) and tumor location (colon versus rectum). Multivariable logistic regressions were used to correct for gender, tumor stage and histology. Relative postoperative mortality rates will be added to adjust for the background mortality in the elderly. Results: For both colon and rectal cancer, the 30-, 60- and 90-day postoperative mortality decreased between 2005-2006 and 2013-2014 for patients aged <75 years, as well as for patients aged ≥75 years. For colon cancer patients aged <75 years, logistic regression analysis yielded odds ratios (OR) for 30-, 60- and 90-day postoperative mortality in 2013-2014 versus 2005-2006 of 0.43, 0.44, and 0.48, respectively, and for colon cancer patients aged ≥ 75 years ORs of 0.52, 0.49, and 0.49, respectively. For rectal cancer patients aged <75 years, ORs for 30-, 60- and 90-day postoperative mortality in 2005-2006 and 2013-2014 were 0.50, 0.58, and 0.61, respectively, and for rectal cancer patients aged ≥ 75 years the ORs were 0.36, 0.43, and 0.57, respectively. Conclusion: The high postoperative mortality rates among elderly CRC patients have decreased, as both absolute postoperative mortality as well as differences in postoperative mortality between younger and elderly patients have diminished over time. More research is needed as to what has caused these improvements.

	Patients aged <75 years				Patients aged ≥75 years			
	2005-2006 (%)	2013-2014 (%)	OR	(95% CI)	2005-2006 (%)	2013-2014 (%)	OR	(95% CI)
Colon cancer								
30-day mortality	1.9	0.9	0.43	(0.31-0.58)	9.7	5.1	0.52	(0.44-0.61)
60-day mortality	2.9	1.3	0.44	(0.34-0.57)	12.3	6.2	0.49	(0.42-0.56)
90-day mortality	3.2	1.6	0.48	(0.30-0.60)	13.4	6.9	0.49	(0.42-0.56)
Rectal cancer								
30-day mortality	1.3	0.7	0.50	(0.31-0.80)	7.9	3.0	0.36	(0.26-0.51)
60-day mortality	1.8	1.1	0.58	(0.40-0.86)	10.2	4.6	0.43	(0.32-0.57)
90-day mortality	2.2	1.4	0.61	(0.46-0.91)	11.1	5.3	0.57	(0.35-0.60)

Figure 1 Logistic regression analysis for 30-, 60- and 90-day postoperative mortality in 2013-2014 versus 2005-2006 for both colon and rectal cancer patients, stratified to age; patients aged <75 years versus patients aged ≥75 years.

QS31

Management of Sentinel Node Metastasis in Merkel Cell Carcinoma: Completion Lymphadenectomy, Radiation or Both? M. Perez,* D.E. Oliver, E. Weitman, D. Boulware, J.L. Messina, J. Torres-Roca, C. Cruse, R. Gonzalez, A.A. Sarnaik, V.K. Sondak, L.B. Harrison, J.S. Zager. *Moffitt Cancer Center, Tampa, FL.*

Background An estimated 25-30% of patients with Merkel cell carcinoma (MCC) will have regional lymph node involvement on sentinel lymph node biopsy (SLNB). Optimal management of microscopic regional disease has not been clearly defined. We compared outcomes of patients treated with completion lymphadenectomy (CLND) alone, radiation (XRT) monotherapy or CLND + adjuvant XRT after positive SLNB. Methods All patients treated at a single institution for SLN-positive MCC (1998-2015) were retrospectively evaluated. Patient demographics, clinicopathologic characteristics, outcomes and regional toxicity were reviewed. Results 71 patients were found to have SLN-positive disease. Median age was 76 years, 76.1% were male. 11 (15.5%) patients underwent CLND, 40 (56.3%) patients underwent XRT monotherapy and 20 (28.2%) patients underwent both CLND and adjuvant XRT. Clinicopathologic features for each treatment group are shown in Table 1. Median follow up was 16.8 months. Only 2 patients, both treated with XRT monotherapy, recurred in their regional nodal basin. Lymphovascular invasion was the only clinicopathologic feature significantly more common in those who received XRT (p=0.04) and there was a trend toward a higher burden of nodal disease seen in the CLND+XRT group with 2%, 10% and 30% median burden of disease in the SLNs seen in the CLND, XRT and CLND+XRT groups, respectively (p=0.06). There was no observed difference in development of distant metastases (p= 0.82) or overall survival (p= 0.69) between the three treatment groups. 7 patients experienced wound infections (4 CLND + XRT, 2 CLND, 1 XRT). 3 patients developed symptomatic lymphedema (1 CLND, 2 CLND+XRT). Conclusions Regional nodal basin failure was low (≤ 10%) in all treatment groups, and morbidity appears low with all modalities. Given that multiple management strategies can be successful in regional control of micrometastatic MCC, future efforts should be directed at prospectively allocating patients to a specific modality, or possibly no further nodal treatment, based upon predefined selection criteria, all in an effort to maximize regional control at the lowest cost and morbidity.

Table 1: Clinicopathologic characteristics for each treatment group

	CLND alone (n=11)	XRT Monotherapy (n=40)	CLND + XRT (n=20)	p-value
Age – Median (range)	79.0 (46.0-83.0)	75.0 (54.0-90.0)	75.5 (57.0-84.0)	0.89
Gender Female (%) Male (%)	3 (27.3) 8 (72.7)	10 (25.0) 30 (75.0)	4 (20.0) 16 (80.0)	0.86
Immunosuppression Status + (%) - (%)	1 (9.1) 10 (90.9)	7 (17.5) 33 (82.5)	2 (10.0) 18 (90.0)	0.72
Primary Tumor Site Head & Neck (%) Trunk (%) Upper Extremity (%) Lower Extremity (%)	3 (27.3) 0 5 (45.4) 3 (27.3)	12 (30.0) 3 (7.5) 13 (32.5) 12 (30.0)	10 (50.0) 2 (10.0) 5 (25.0) 3 (15.0)	0.61
Primary Tumor Depth (cm) – Median (range)	0.6 (0.1- 1.7)	0.5 (0.05-1.8)	0.4 (0.1-2.0)	0.80
Lymphovascular Invasion Y (%) N (%)	1 (9.1) 10 (90.9)	18 (45.0) 22 (55.0)	5 (25.0) 15 (75.0)	0.04
Number + SLN – Median (range)	1.0 (1.0-6.0)	1.0 (1.0-4.0)	1.0 (1.0-9.0)	0.44
% Nodal Involvement (SLN) – Median (range)	2.0 (1.0- 20.0)	10.0 (1.0-70.0)	30.0 (1.0-75.0)	0.06
Extracapsular Extension Y (%) N (%)	2 (20.0) 8 (80.0)	5 (13.2) 33 (86.8)	5 (31.2) 11 (68.8)	0.32
CLND status + (%) - (%)	1 (9.1) 10 (90.9)	NA NA	6 (31.6) 13 (68.4)	0.21
Follow-up Time (Median)	1.54 years	1.40 years	1.42 years	0.79

QS32

Patient and Treatment Factors Associated with Survival in Patients with Malignant Cutaneous Adnexal Carcinoma: A National Cancer Database Analysis D. Schuitevoerder,[2]* E. Latour,[2] J. Youn Lim,[2] J.T. Vetto,[2] K. Massimino.[1] *1. Providence Medical Center, Portland, OR; 2. Oregon Health & Science University, Portland, OR.*

Background Malignant cutaneous adnexal tumors (MCATs) are rare non-epithelial skin cancers. The aim of this study was to utilize a large multicenter-database to determine factors associated with overall survival (OS) in patients with MCATs. A secondary aim was to determine whether provid-

ers in the United States are using sentinel lymph node biopsy (SLNBx) for staging in this rare skin tumor. Methods Patients with MCATs of the skin treated in years 2003-2013 were identified from the American College of Surgeons National Cancer Database. Data regarding the use of SLNBx were available for patients treated in years 2012-2013. Demographic and clinical characteristics of the study sample were summarized. Survival analysis was performed to evaluate the association between patient and treatment factors and OS using Kaplan-Meier curves, log-rank test, and the Cox-proportional hazard regression. Results 6083 patients met our inclusion criteria. Most patients were ≥ 70 years of age (45.7%) and had a sebaceous carcinoma (36.7%) of the head, neck or face (58.4%). Median survival of 66 months was reached for patients ≥ 70 years of age. Median survival was not reached for patients < 70 years of age. Data regarding SLNBx were available for 1425 patients. Of these 183 (12.8%) underwent SLNBx, 127 (8.9%) underwent non-SLNBx and 1115 (78.2%) did not undergo SLNBx. 21.9% of patients who underwent sampling had positive lymph nodes. Patient age, tumor histology, grade and surgical treatment were significantly associated with OS ($p<0.05$) in the multivariate model. Compared to patients with no surgical treatment, patients with ablation/ local excision and patients with wide excision/major amputation experienced longer OS (HR 0.20, 95% CI 0.09 to 0.45; and HR 0.23, 95% CI 0.10 to 0.55; respectively). Conclusion Overall survival among patients with MCATs of the skin is associated with patient and tumor factors. Treatment of the primary tumor is associated with OS suggesting that these tumors should be treated if feasible. Few patients in the United States undergo SLNBx for MCAT. The role for SLNBx in this rare malignancy remains unclear.

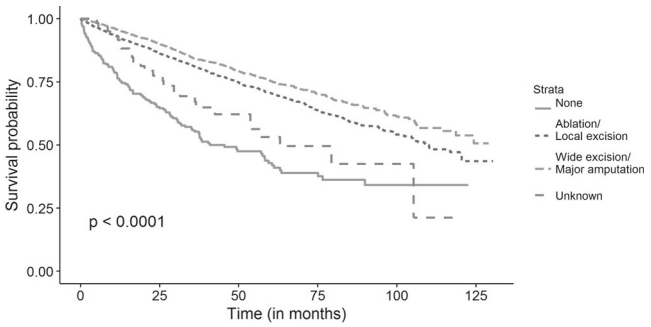


Figure 1. Survival of patients with adnexal carcinoma of the skin is associated with treatment of the primary site.

QS33

Negative Sentinel Lymph Node Biopsy in Patients with Melanoma: The Patient's Perspective S. Banting,* D. Milne, T. Thorpe, A. Herschtal, J. Spillane, D. Speakman, M.A. Henderson, D. Gyorki. *Division of Cancer Surgery, Peter MacCallum Cancer Centre, Melbourne, VIC, Australia.*

Introduction Over 80% of patients undergoing sentinel lymph node biopsy (SLNB) for melanoma will have no disease detected within their excised lymph nodes (negative SLNB). For these patients, the procedure results in risk stratification to a lower disease stage. This study sought to identify the physical and psychological impact of a negative SLNB. Method A prospective, cross-sectional study was performed in the melanoma outpatient clinic. Patients who had undergone a negative SLNB, completed a validated quality of life questionnaire (FACT-M) and underwent limb measurements at a single time point. Results 102 patients were recruited during 5 post-operative time intervals; <3 months (18.6%), 3-6 months (12.7%), 6-12 months (20.6%), 12-24 months (23.5%), >24 months (24.5%). Males predominated (55%), with a median age of 60 (range 29-81). Melanomas were located on the upper limb (30%), lower limb (35%), trunk (22%), head and neck region (13%). Most patients underwent primary wound closure (75%). One nodal basin was sampled in 87% of patients. SLN were identified in the axilla (46%), groin (39%), neck (18%) and other (2%). 25% of patients had acute, self-limiting wound complications. A single patient had a major cardiac event. Quality of life scores were lowest in the first 3 months following surgery and then improved across all domains (table 1). 3% of patients would be reluctant to undergo the procedure again. The mean discrepancy in limb circumference was 0.71cm in the upper limb (range 0-2.3) and 0.91cm in the lower limb (range 0-9.5). 2 patients had lymphedema (>3cm difference). Conclusion Patients with a negative SLNB are generally satisfied with the procedure. 97% of patients would have the procedure again. There was a trend to improved symptoms and quality of life from 3 months after surgery.

Table 1

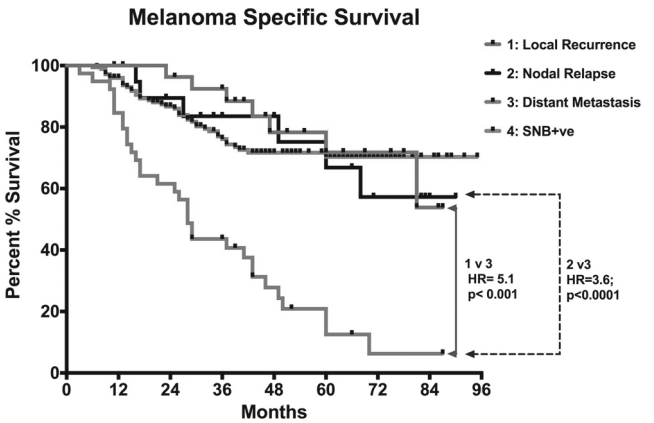
	Time (months)				
	0-3	3-6	6-12	12-24	>24
FACT-M total	137	154	148	154	159
Physical Well-Being	24	28	26	27	28
Functional Well-Being	20	25	24	25.5	26

Quality of life scores. FACT-M total includes physical, social, emotional, functional well-being and melanoma specific questions related to quality of life.

QS34

Melanoma Recurrence and Outcomes Following Negative Sentinel Node Biopsy F.M. O'Leary,* M.J. Heaton, M.D. Moncrieff. *Plastic Surgery, Norfolk And Norwich Hospital, Norwich, United Kingdom.*

Introduction There is a subset of patients who develop recurrences despite a negative sentinel node biopsy (SNB-ve). These patients putatively develop distant disease via hematogenous spread, bypassing the regional lymph node basin, and have poorer outcomes overall. We reviewed the outcomes of all patients who underwent wide local excision and sentinel node biopsy in a University Hospital cancer center, specifically examining patterns and sites of first recurrence. Methods A retrospective review of prospectively collected data on 1014 patients undergoing SNB was undertaken at a tertiary referral cancer center. Specific parameters examined included demographics, primary tumor characteristics, melanoma-specific survival (MSS) and overall survival (OS). Results We identified 87/837 (10.4%) histologically-proven SNB-ve patients who developed recurrence. The median time to disease progression from SNB was 20 months. Age and Breslow thickness were significant independent predictors of relapse. Patients were divided into three groups according to initial site of recurrence: local recurrence only (1: n=27), nodal relapse (2: n=21) and distant metastatic disease (3: n=39). Patients presenting initially with distant disease had a significantly worse MSS (1 v 3: HR=5.1; $p<0.0001$ and 2 v 3: HR=3.6; $p=0.0001$) than patients presenting with local or regional recurrences. Multivariate analysis demonstrated the site of initial recurrence and Breslow thickness were independent prognostic indicator for MSS. Patients who developed distant disease had a similar MSS and PFS survival curves regardless of initial SNB status with no significant lead time bias. Conclusion Our data suggests the development of distant disease is a process independent of sentinel node metastasis. Accordingly, a significant proportion of patients do not benefit from the prognostic information provided by the procedure, despite the Breslow thickness indicating it. The development of primary-derived biomarkers is needed to help to identify these patients at risk of hematogenous disease and avoid an unhelpful SNB.



Melanoma specific survival (MSS) in SLNB -ve patients with 1.local recurrence, 2. nodal recurrence, 3. distant recurrence compared to SLNB +ve patients

QS35

Outcomes Following Observation of Melanoma Patients with a Positive Sentinel Lymph Node Biopsy: A Large, Single Institution Experience K.E. Isaacs,* S. Pasquali, J.F. Thompson. *Melanoma Institute of Australia, The University of Sydney, NSW, Australia.*

Introduction: Results from second the Multicenter Selective Lymphadenectomy Trial and the DeCOG study are changing the treatment landscape for patients with stage III melanoma. We sought to establish outcomes of melanoma patients who did not proceed to a completion lymph node dissection (CLND) after a positive sentinel lymph node biopsy (SLNB). Methods: Data were obtained from a prospectively maintained database. We included melanoma patients with a positive SLNB treated from January 1993 to December 2014, who did not proceed to a CLND. We assessed disease-free survival (DFS) and overall survival (OS). We also investigated the subgroup of patients who recurred in the regional lymph nodes, to investigate the effect of therapeutic lymph node dissection (TLND) on patient outcomes. Results: 276 patients underwent observation with a median follow up of 84 months. The five-year DFS was 41% (95%CI 0.35-0.47). Older age (HR=1.03, P<0.001), a greater number of positive sentinel lymph nodes (SLNs) (HR=1.38, P=0.044) and larger SLN metastasis diameter (HR=1.17, P<0.001) were independently associated with worse DFS. The five-year OS was 63% (95%CI 0.56-0.68). Older age (HR=1.02, P=0.005), greater primary tumor thickness (HR=1.11, P=0.044), and larger SLN metastasis diameter (HR=1.14, P=0.005) were independently associated with worse OS. 92 patients developed a recurrence in the regional lymph nodes, with older age (HR=1.02, P=0.01) and larger SLN metastasis diameter (HR=1.15, P=0.008) being independent predictors of regional lymph node recurrence. 87 of these patients underwent a TLND, of whom 23 had no further recurrence. Conclusions: In patients who are observed after a positive SLNB, approximately one third will not recur, one third will recur in their regional lymph nodes, and one third will die of melanoma. More than half of those who recur in their regional nodes will die of melanoma. The size of the SLN metastasis, patient age and primary tumor thickness are factors predicting survival outcome.

Table 1: Outcomes for patients with a positive sentinel lymph node biopsy who did not proceed to completion lymph node dissection

	All patients	Recurred in node field
	n (%)	n (%)
Alive, no recurrent melanoma[1]	94 (34%)	-
Alive, recurrent melanoma resected[2]	36 (13%)	23 (25%)
Alive, active melanoma treatment[3]	21 (8%)	12 (13%)
Dead, melanoma	89 (32%)	51 (55%)
Dead, not melanoma	27 (10%)	6 (7%)
Status unknown	9 (3%)	-
Totals	276 (100%)	92 (100%)

[1]Patients with no recurrent melanoma after wide excision of primary site and sentinel lymph node biopsy [2]Patients with no active melanoma but with resected recurrence(s) including loco-regional & distant metastasis [3]Patients on medical therapy or with in-transit metastasis

QS36

Outcomes of Immunosuppressed Patients Who Develop Melanoma: A Matched Cohort Study J. Austin,[1]* F. Wright,[2] S.Y. Cheng,[4] R. Sutradhar,[4] N. Baxter,[3] N. Look Hong.[2] *1. Surgical Oncology, University Of Toronto, Toronto, ON, Canada; 2. Sunnybrook Health Science Centre, Toronto, ON, Canada; 3. St. Michaels Hospital, Toronto, ON, Canada; 4. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada.*

Immunosuppressed patients are up to 8x more likely than the regular population to develop melanoma. Little is known about melanoma outcomes in immunosuppressed patients relative to patients who are non-immunosuppressed. The purpose of this study is to compare survival in immunosuppressed patients who develop melanoma to non-immunosuppressed patients with melanoma. Patients with invasive cutaneous melanoma were identified retrospectively from the Ontario Cancer Registry (2003–2012) and linked with administrative databases to identify demographics, treatment pathways, and outcomes. Immunosuppression was defined as a diagnosis of Solid Organ Transplant, Lymphoma, Leukemia, or HIV prior to the development of melanoma. Immunosuppressed patients were matched (5:1) with non-immunosuppressed patients based on age at diagnosis, sex, birth year, and propensity score, which was made up of year of diagnosis, anatomic site, and resource utilization band (a measure of co-morbidities). Primary outcome was overall survival (OS). Patients were censored at the earliest of death or end of follow-up. Cox proportional hazard models were used to identify factors associated with OS. Baseline characteristics were balanced in 318 immunosuppressed patients matched to 1590 controls. 630 (33%) patients were female and median age was 69 (IQR 60 – 78). With a median follow up of 4 years, 181 (56.9%) immunosuppressed patients died compared to 500 (31.4%) non-immunosuppressed patients (p <0.001). Melanoma was leading cause of death in both groups, comprising 20.1% and 12.7% of patients in the immunosuppressed and non-immunosuppressed groups. In multivariable analysis, immunosuppression was an independent predictor of death (HR 2.65, 95% CI 2.23-3.16). Visits to a dermatologist before (HR 0.59, 95% CI 0.49-0.71) or after melanoma diagnosis (HR 0.72, 95% CI 0.56-0.93) were associated with improved OS. Patients who are immunosuppressed and develop melanoma have worse outcomes. Current recommendations for transplant patients include a yearly skin check. No such recommendations exist for lymphoma, leukemia, or HIV patients. This research suggests that these recommendations be extended to other immunosuppressed groups.

QS37

Intraoperative Imaging with a Portable Gamma Camera Reduces the False-negative Rate for Melanoma Sentinel Lymph Node Surgery S.P. Leong,[1]* W. Max,[1] Y. Lu,[2] D.M. Torre,[1] A. von Bakonyi,[1] A. Wight,[1] J. Newson,[1] W. Luckett,[1] M. Kashani-Sabet.[1] *1. California Pacific Medical Center, San Francisco, CA; 2. Stanford University, Stanford, CA.*

Introduction: Preoperative imaging combined with intraoperative gamma probe (GP) localization is standard for identifying sentinel lymph nodes (SLNs) in melanoma patients. The primary aim of this prospective IRB-approved study is to investigate whether an intraoperative portable gamma camera (PGC) improves SLN detection in addition to the GP. Methods: Lymphoscintigraphy and SPECT/CT were performed after injection of 600 μCi (1-day protocol) or 2000 μCi (2-day protocol) of 99mTc-tilmanocept in melanoma patients (≥18 years, Breslow thickness ≥ 1.0 mm). A strict surgical protocol was followed for each draining SLN basin. A GP (Neoprobe 2000, Neoprobe Corp.) was used to localize the SLNs. The resection bed was then explored by the GP at 8 positions of the clock and center to ensure that the entire operative field was less than 10% counts of the hottest SLN. The PGC (Sentinella S102, Oncovision) was then used with a 60-second image acquisition time after a negative GP screening. Any visualized hotspots were considered as additional SLNs found by the PGC. Using the 10% rule, these SLNs were removed by the GP. Results: In this study, 100 patients (60 males, 40 females) were included. Preoperative imaging localized 138 SLN basins. Conventional surgery using the GP and palpation found 306 SLNs. The PGC found 89 additional SLNs in 54 patients after a negative GP screening. The use of the PGC increased the SLN identification rate by 29.1% (89/306, p<0.05). Four of these additional 89 SLNs showed micrometastasis in 4 patients. Two of the 4 patients had micrometastasis in 2 SLNs, one tumor-positive SLN found by the GP and the other by the PGC. In 2 other patients, the only tumor-positive SLN was found by the PGC, thus, preventing 2 false-negative cases. The overall SLN positive rate was 9.9% (39/395). The overall patient positive rate was increased by the PGC from 25% (25/100) to 27% (27/100). Conclusion: This study demonstrates that intraoperative PGC imaging yielded additional SLNs in a significant number of patients as compared to GP alone. Further, intraoperative imaging reduces the false-negative rate for melanoma SLN surgery.

QS38

Dynamic Control of Tumor Vasculature Augments Antitumor Responses in a Regional Model of Melanoma E. Gabriel,[1]* M. Kim,[2] D. Fisher,[2] C. Powers,[2] K. Attwood,[2] J. Skitzki.[2] *1. Surgery, Mayo Clinic Florida, Jacksonville, FL; 2. Roswell Park Cancer Institute, Buffalo, NY.*

Introduction Despite recent advances in therapy for in-transit (IT) melanoma, heterogeneous responses with limited durability represent a major gap in treatment outcomes. The purpose of this study was to augment drug delivery and improve tumor responses in a regional model of melanoma by developing a preclinical method of tumor vessel control. Methods Dynamic control of tumor vessels in B6 mice bearing B16 melanoma was performed using a protocol of volume expansion (500 μl saline bolus) followed by i.v. phenylephrine (10 μg/mouse x 2). Intravital microscopy (IVM) enhanced with dextran-con-

jugated fluorescein was used to observe changes directly in real time. This protocol was combined with melphalan using a model of limb perfusion to determine its effects on outcomes. Results Our approach to dynamic control (1) restored blood flow in non-functional tumor vessels and (2) transiently decreased blood flow in functional tumor vessels. The velocity within tumor vessels increased following the saline bolus, and then decreased or even reversed following phenylephrine. Taken together, we hypothesized that these temporal effects would increase the exposure time of tumor to melphalan. Indeed, dynamic control of tumor vessels resulted in increased melphalan activity, as measured by the formation of DNA adducts (via IHC staining with the MP5 antibody) and apoptosis (TUNEL staining) within tumor. This combination approach (phenylephrine plus melphalan) also resulted in superior survival compared to melphalan alone (median overall survival 40.0 vs 25.0 days, respectively, p=0.041). Moreover, 25% (3/12) of the mice treated with the combination approach showed complete tumor response and long-term cure. Importantly, the combined treatment with phenylephrine and melphalan did not result in increased adverse events or elevated serum creatinine kinase levels. Conclusion We showed for the first time that dynamic control of tumor vessels was feasible, and that this approach augmented tumor responses in a regional model of melanoma. Future studies will focus on using this protocol of dynamic control to optimize responses to lymphocyte trafficking to tumor in combination with immunotherapy.

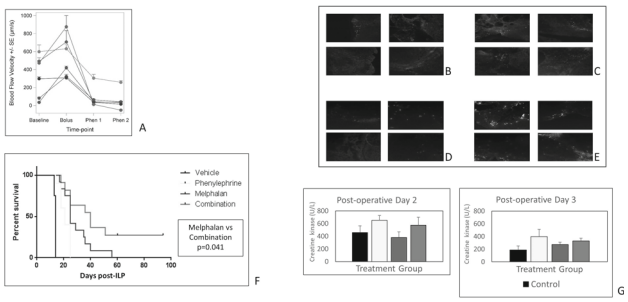


Figure: (A) Tumor blood flow velocity increased following the saline bolus and markedly decreased or even reversed following phenylephrine treatment, ANOVA p < 0.001. (B-E) Fluorescent staining of DNA adducts and apoptosis. Top panels show sections treated with melphalan alone (B) or melphalan plus phenylephrine (C) stained for DNA adducts with MP5. There was a significant increase in the number of observed DNA adducts with the combination treatment (the average number of observed DNA adducts per 20x field being 120.5 versus 30.3, respectively, Student's t test p = 0.029). The bottom panels show staining for apoptosis (TUNEL assay) of B16 tumors treated with melphalan alone (D) or melphalan plus phenylephrine (E). A similar increased pattern of fluorescence was observed for the combination treatment group. (F) Kaplan-Meier survival curve showing statistically superior survival for the combination group, even when compared to the melphalan alone group. There were 3 complete responses (25%) in the combination group, and no complete responses in any other group. (G) Creatine kinase (CK) levels following isolated limb perfusion on post-operative days 2 and 3. No significant differences were observed among the different treatment groups.

QS39

Exploring the Role of Gene Expression Profiling in the Prediction of Non-Sentinel Node Status in Cutaneous Melanoma J. Keller,* T. Schwartz, J. Lizalek, E. Hsueh. *Surgery, Saint Louis University School of Medicine, Saint Louis, MO.*

Introduction Nodal status in melanoma, as determined by sentinel lymph node (SLN) biopsy, is an important prognostic indicator. Although national guidelines recommend completion lymph node dissection (CLND) for SLN positivity, as 10-20% of SLN positive patients will have positive non-SLN (NSN) on CLND, the recent results of MSLT-2 have shown that nodal surveillance was equivalent to CLND. Gene Expression Profile (GEP) testing is used as a prognostic guide and determinant of metastatic risk in cutaneous melanoma. We evaluated the use of GEP testing in stratifying the risk of NSN metastases. Methods From 1/2013 to 6/2017, patients with primary cutaneous melanoma, ages 18-88, were evaluated at Saint Louis University. Patients with melanoma >1mm depth, along with select patients with melanoma <1mm, were included. GEP testing was done at time of wide excision and SLN biopsy. GEP results were reported as low risk (1), high risk (2) or insufficient sample (INS). Histological and qualitative characteristics of the primary sample and patients were collected. These characteristics were then used to calculate previously reported scoring systems--Size-Ulceration (SU) score, Non-sentinel node risk score (N-SNORE), Rotterdam criteria (RC) and Dewar classification (DC)--for determining NSN metastases. These variables were compared using Chi-square analysis. Results The cohort included 287 patients. Thirty-nine (13.6%) patients were found to have positive SLNs. Of these, 8 (20.5%) also had positive NSN on CLND. Seven (87.5%) of the 8 patients with positive NSN were found to be GEP class 2, while 1 was GEP class 1. This result was compared to the SU score, N-SNORE, RC and DC. The SU score (p=0.004) and GEP classification (p=0.047) were noted to be significant predictors of NSN metastases. Conclusion These results suggest that GEP classification has important implications in determining risk of NSN metastases. Further research into its role in guiding need for post-operative surveillance or adjuvant therapy is warranted.

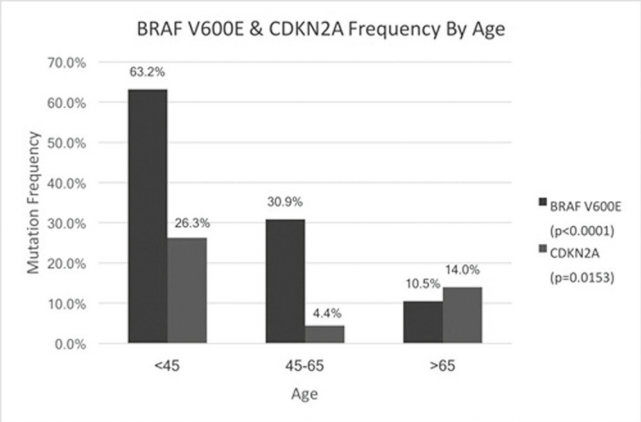
Table 1

	SN+NSN+	SN+NSN-	Chi-Square	p
Ulceration			11.657	0.003
No	1	23		
Yes	7	7		
GEP			3.931	0.047
Class I	1	15		
Class II	7	14		
NSNORE			5.77	0.217
0	0	0		
1-3	2	20		
4-5	6	9		
6-7	0	2		
>8	0	0		
SU			13.428	0.004
0	1	18		
1	0	7		
2	5	4		
Unknown	2	2		
Dewar			2.096	0.836
Subcapsular	4	13		
Parenchymal	0	4		
Combined	2	4		
Multifocal	0	0		
Extensive	1	3		
Unknown	1	7		
Rotterdam			5.477	0.142
<0.1	1	5		
0.1 to 1mm	0	12		
>1mm	5	11		
Unknown	2	3		

QS40

Comparing Age and Gender to Molecular Profile in Melanoma Patients I.A. Soliman,* N. Goel, K. Loo, M. Renzetti, T. Li, H. Wu, B. Luo, A. Olszanski, S. Movva, M. Lango, S. Reddy, J. Farma. *Fox Chase Cancer Center, Philadelphia, PA.*

INTRODUCTION: Next Generation Sequencing (NGS) is becoming a critical tool in the evaluation of primary cancers. Our cancer center uses NGS to detect mutations in 50 targetable cancer-related genes within various tumors. The objective of this study is to analyze molecular profiles of patients with malignant melanoma (MM) and determine how specific gene mutations and mutation burden correlate with age at diagnosis and gender. METHODS: This was a retrospective review of a prospective database analyzing the molecular profiles of patients with MM using NGS. Patients with MM of all stages were included in the study. Clinical and pathologic data were evaluated using Fisher's exact and Wilcoxon tests. RESULTS: The analytic cohort consisted of 173 patients with MM with sufficient molecular profiling data. Median age at diagnosis was 65 (range 21-94) and 64% were male (n=111). At diagnosis, 11% of the patients were <45 years old (Group A), 39% were 45-65 years old (Group B), and 50% were >65 years old (Group C). A total of 277 mutations were identified, affecting 34 unique genes. The most prevalent mutation in both males and females was NRAS, found in 33% of males and 32% of females. Males had an overall mutation burden of 1.71 while females had an overall mutation burden of 1.40 (p=0.105). The most common mutation was BRAF V600E in Group A (63%), NRAS in Group B (35%), and NRAS in Group C (35%). The BRAF V600E mutation was identified in 63% of patients in Group A, 31% of patients in Group B, and 11% of patients in Group C (p<0.0001). The CDKN2A mutation was detected in 26% of patients in Group A, 4% of patients in Group B, and 14% of patients in Group C (p=0.015). The overall mutation burden was 1.7 in Group A patients, 1.5 in Group B patients, and 1.7 in Group C patients (p=0.713). CONCLUSION: Using our NGS platform, we identified the most prevalent mutations and overall mutation burden in our cohort of patients based on age and gender. The analysis showed a statistically significant trend between BRAF V600E and age, as well as a statistically significant association between CDKN2A and age. These findings motivate investigation with a larger sample size and may provide prognostic value.



QS41

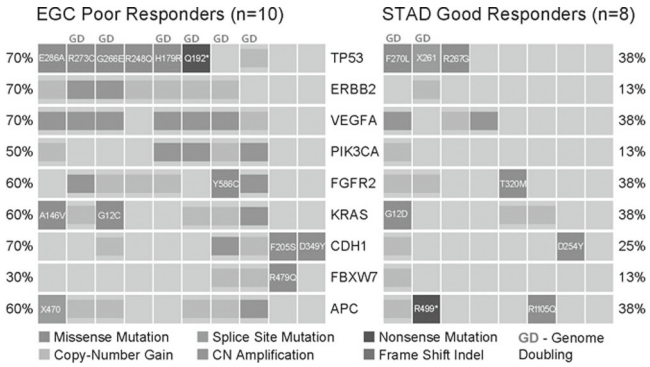
Long Term Follow Up of Patients with Pathological Complete Response Following Neoadjuvant Chemoradiation for Esophageal Cancer Y. Feferman,[1]* S. Morgenstern,[3] N. Menasherov,[1] O. Zlotnik,[1] S. Bard,[1] I. Ben-Aharon,[2] H. Kashtan.[1] *1. Department of General Surgery, Rabin Medical Center, Affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; 2. Oncology Division, The Davidoff Center, Rabin Medical Center, Affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; 3. Department of Pathology, Rabin Medical Center, Affiliated with Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.*

Background: Neoadjuvant chemoradiotherapy (nCRT) followed by surgery is standard of care for locally advanced esophageal cancer (EC). After nCRT up to one third of patients have pathological complete response (pathCR) in the resection specimen, raising the possibility of active surveillance over the standard surgery in all operable patients after nCRT. Methods: Patients treated with nCRT for EC between the years 2006-2017 were retrospectively reviewed from our institutional prospective database. A pathCR was defined as a surgical specimen with no residual carcinoma (primary or nodes). We describe long term outcomes. Results: Medical records of 436 patients with histologically proven EC were reviewed retrospectively. Two-hundred forty five (56%) patients received neoadjuvant therapy, of which 178 (73%) with Adenocarcinoma (AC) and 67 (27%) patients with Squamous Cell Carcinoma (SCC). A total of 46 (19%) patients achieved pathCR. Pre-operative lymph node status of these patients was N0 in 12 (26%) patients; N1 in 26 (57%) patients; Nx in 8 (17%) patients. The pathCR rate was 11% for AC and 39% for SCC ($p<0.001$). Five patients who achieved pathCR died within 90 days of surgery and thus were excluded. Of the remaining 41 patients, 9 (24%) had documented recurrence, with a median follow up time from surgery of 26 months. Six (15%) patients died with documented recurrence, 1 patient died of pneumonia with no evidence of disease recurrence and 2 are currently alive with confirmed recurrence. Median overall survival for patients with pathCR was 35 months and all but two patients with no recurrence are still in active follow-up. Conclusion: Our results indicate that long term survival is achieved for patients with pathCR although a quarter of patients will recur. This emphasizes the importance of developing molecular predictors for complete response.

QS42

Copy Number Gains in HER2 and VEGFα May Predict Poor Outcome in Early Gastric Cancer A.E. Russo,[1]* E.M. Da Silva,[1] C. Kandoth,[1] J.M. Hernandez,[2] E. Van Beek,[1] B.S. Taylor,[1] Y.Y. Janjigian,[1] L.H. Tang,[1] D. Solit,[1] V.E. Strong.[1] *1. Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; 2. National Cancer Institute, Bethesda, MD.*

Introduction: While most early gastric cancer (EGC) patients are cured with surgery, about 3% will relapse. We performed whole exome sequencing (WES) on curative intent resections to identify somatic mutations that may predict poor outcomes in EGC. Methods: Ten EGC cases were identified from a prospectively maintained institutional database. Paired tumor and normal DNA from FFPE tissue was isolated and hybridized for WES and compared to call somatic substitutions, indels, and copy-number variants including chromosomal instability (CIS) and genomic doubling (GD). Eight Stomach Adenocarcinoma (STAD) patients from The Cancer Genome Atlas served as controls. Early stage and good response were inferred from the absence of perioperative therapies and tumor-free status at follow up. Results: Study patients had a median time to recurrence of 11.7 months and median disease specific survival of 2.3 years. A median of 89.5 (21-212) somatic substitutions and indels were reported across the exomes in the study group compared to 90.5 (52-992) in the controls. TP53 mutations were more common in the study group (60 vs 38%). Oncogenic missense mutations in KRAS (20 vs 13%) and APC truncating mutations (10 vs 13%) were not significantly enriched in either group. Significant differences were revealed in copy-number variants (figure). Eight EGC samples reported CIS, 6 of which had GD events, and 2 STAD samples reported CIS, both of which had GD events. Gains in ERBB2 (HER2) with ≥3 copies of the gene were seen in 7 EGC and 1 STAD sample. Two of these 7 EGC samples reported >10 copies of ERBB2, while none of the STAD samples reported >3 copies. VEGFα gains were seen in 7 EGC versus 3 STAD samples. The gains in HER2 and VEGFα were more often co-occurrent in EGC (60%) versus STAD (0%) samples. Conclusions: The presence of CIS causing events, namely GD and TP53 mutations, as well as co-occurrent copy number gains in HER2 and VEGFα in ECG poor responders may be useful biomarkers in identifying those with an increased risk of recurrence following surgery. Utilization of these biomarkers may present an opportunity to offer more frequent surveillance and targeted adjuvant therapies to high risk patients.



QS43

Surgical Management of T1b Gallbladder Cancer: Are We Doing the Right Thing? E. Vo,* S.A. Curley, N.N. Massarweh, H.S. Tran Cao. *Surgery, Baylor College of Medicine, Sugar Land, TX.*

Background Current guidelines recommend radical cholecystectomy with regional lymphadenectomy (RC-RL) for patients with T1b gallbladder cancer (GBC). However, the extent to which these guidelines are followed is unclear. We sought to evaluate current surgical practices for T1b GBC, and their implications on overall management strategies and associated outcomes. Methods We conducted a retrospective cohort study of GBC patients with a pathology-proven T1b primary lesion who did not have metastatic disease in the National Cancer Database (2004-2012). Patients were categorized based on the type of surgical treatment received as having undergone simple cholecystectomy without lymphadenectomy (SC) or RC-RL. Among patients who had lymph nodes pathologically examined, nodal status was classified as pN0 or pN+. Utilization of any adjuvant therapy (chemotherapy and/or radiation) was ascertained. Overall survival (OS) was compared based on the type of surgical treatment and nodal status using the Kaplan-Meier method and log-rank test. Results The cohort comprised 464 patients (SC: n=247; RC-RL: n=217). RC-RL was more likely to be performed at academic/research hospitals (44.7% RC-RL vs. 28.3% SC, p=0.005). There was no difference in positive margin status (6.1% SC vs. 2.3% RC-RL, p=0.128). Among RC-RL patients, the pN+ rate was 14.8%. Adjuvant therapies were used more frequently in pN+ patients (54.8% compared to 9.7% of RC-RL patients with pN0). By comparison, 10.9% of SC patients received adjuvant therapy. OS for pN0 RC-RL patients (5-year OS 64.4%) was significantly better than pN+ RC-RL patients (5-year OS 15.7%) or SC patients (5-year OS 48.3%) ($p<0.001$; Figure). Conclusion Less than 50% of patients with a T1b GBC primary undergo the recommended surgical treatment. Given that nearly 15% of these patients have nodal metastasis, and in light of the previously described benefits of adjuvant therapy for

node positive GBC, failure to perform RC-RL risks incompletely staging, and thus undertreating, patients with T1b GBC.

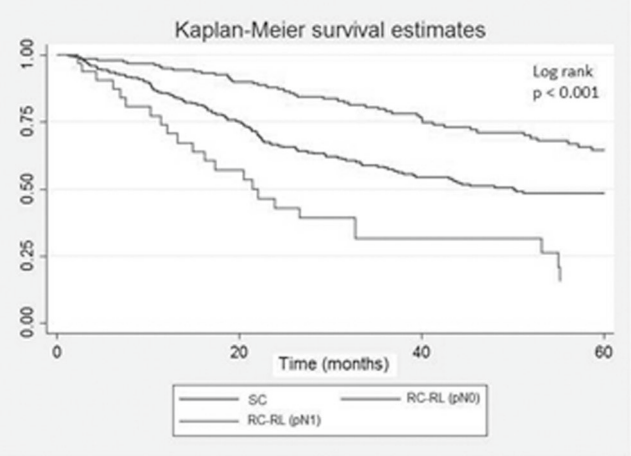


Figure. Survival analysis among T1b gallbladder cancer. SC = simple cholecystectomy; RC-RL (pN0) = radical cholecystectomy with regional lymphadenectomy with pN0; RC-RL (pN1) = radical cholecystectomy with regional lymphadenectomy with pN1.

QS44

Exome Sequencing Demonstrates Patterns of APC Mutation in Gastric Adenocarcinoma: A Novel Paradigm of Analysis
J.C. Rubinstein,* C. Cha. *Surgery, Yale School of Medicine, New Haven, CT.*

Introduction: Mutation of the tumor suppressor gene Adenomatous Polyposis Coli (APC) has long been associated with Familial Adenomatous Polyposis and is a recurrent somatic event across numerous tumors, including gastric adenocarcinoma. Severity of disease in FAP has been correlated with specific APC mutation, but the impact of a given mutation on phenotype in gastric cancer is not well studied. Using exome sequencing data from the Genomic Data Commons (GDC), a data sharing platform hosted by the NCI, we evaluate patterns of APC mutation in gastric cancer, demonstrating a distribution of variants that differs significantly from that seen in colon cancer. Methods: Exome sequencing data from APC-mutant colon and gastric adenocarcinomas was downloaded from the GDC and filtered for Simple Nucleotide Variants generated with MuTect2 Variant Aggregation and Masking in the Somatic Aggregation Workflow. Results: APC mutations were found in 56/347 gastric (12.8%) and 295/399 colon adenocarcinomas (73.9%). There was a significant difference in the proportion of stop gain, frameshift, and missense mutations between tumor types ($p<0.0001$). Colon tumors were predominated by frameshift and stopgains, comprising 35.8% and 47.9%, respectively. In contrast, 47.1% of gastric mutations were missense. Gastric tumors harboring missense mutations showed decreased median survival relative to stop gain and frameshift mutations (8.0 vs. 13.3 vs. 18.2 months, respectively, $p=0.03$). In the gastric samples, 17.6% of frameshift and stopgain mutations are in the 3' portion of the gene, compared to only 1.8% of colon samples. Conclusions: APC mutations demonstrate a markedly different distribution in gastric and colon adenocarcinoma, with a shift toward missense variants in gastric tumors and worse survival in those gastric tumors with missense mutations. Different mutations confer variable degrees of protein dysfunction, resulting in variable clinical manifestations. Expanding this type of high-resolution investigation of specific mutational patterns will prove integral to risk stratification of patients with gastric cancer in the future and will help direct therapeutic intervention.

QS45

Measuring the Quality of Gastric Cancer Care in the United States
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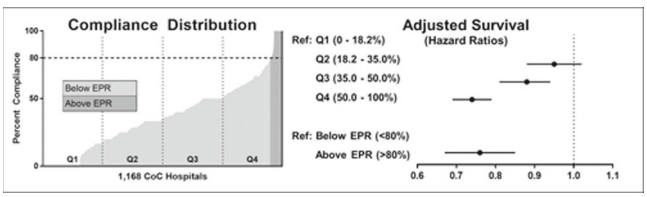
INTRODUCTION: The Commission on Cancer (CoC) has established quality measures required for accreditation. For gastric cancer, hospitals are evaluated on lymph node retrieval at gastrectomy (≥15 nodes), with an Expected Performance Rate (EPR) of 80%. We sought to evaluate whether this discriminates hospital performance based on actual patient outcomes. METHODS: Eligible cases were identified by CoC criteria from the 2006-2012 National Cancer Data Base. Hospital-level compliance was calculated and hospital quartiles were defined; hospitals were also stratified by EPR. Cox models were developed to estimate the relationship between performance and outcomes. The primary endpoint was overall survival (OS). Secondary endpoints included lymph node retrieval, margin status, short-term mortality, and length of stay (LOS). RESULTS: In total, 17,795 patients were included at 1,168 CoC hospitals. Median hospital compliance was 35% (IQR 18-50%), with 179 hospitals (15%) reporting a 0% compliance rate and only 60 hospitals (5%) meeting the EPR. Relative to the lowest performing hospitals (Q1), treatment at the highest performing hospitals (Q4) was associated with a 33% reduced risk of unadjusted mortality (HR 0.67, $p<0.001$). Similarly, treatment at hospitals above the EPR was associated with a 32% reduced risk of unadjusted mortality (HR 0.68, $p<0.001$). Following multivariable adjustment, treatment at Q4 hospitals and hospitals above the EPR remained associated with improved OS (HR 0.74 and 0.76, respectively, both $p<0.001$). Treatment at these hospitals was also associated with improvements across all secondary outcomes, including greater lymph node yield, fewer positive margins, lower 30- and 90-day mortality, and shorter LOS (all $p<0.001$). These patients were also more likely to receive multimodal treatment, including chemotherapy and radiation. CONCLUSIONS: The CoC's gastric cancer measure is highly discriminative for identifying hospitals with the best (and worst) patient outcomes. Beyond its intended purpose for CoC-accreditation, this measure may be a useful surrogate for quality gastric cancer care. These data highlight the large disparities that still exist in treatment quality for this complex disease.



QS46

Linking Circadian Rhythm Biology with Metastatic Tumor Cell Dormancy in a Novel Murine Model of Resectable Pancreatic Cancer Using Single Cell Transcriptomics
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Introduction Metastatic recurrence following surgery with curative intent is one of most significant clinical problems in oncology. These recurrences are due to tumor cells that have disseminated to distant sites that are occult at the time of surgery. Tumor relapse can occur at extended periods of time after surgery, indicating that these cells are dormant. The mechanisms of metastatic tumor cell dormancy (MTCD) are poorly understood. Currently there are no models of MTCD that involve dissemination of tumor cells after surgical resection in an immunocompetent animal. Methods/Results We established a model of MTCD using an orthotopic-syngeneic murine model of pancreatic cancer (PC) in which the tumor cells ($Kras^{G12D}$/$INK4a^{-/-}$) have been labeled with a vector expressing luciferase and mCherry. Mice develop primary tumors by injecting the cells in the tail of the pancreas and subsequently undergo resection. The majority of these mice (65%) go on to succumb to recurrent PC (early recurrences) with a median survival (MS) of 21 days while 35% go on to survive with a MS of 568 days (latent recurrences). Using fluorescence activated cell sorting, we isolated dormant metastatic pancreatic cancer cells from the livers of latent recurring mice, with a frequency of 0.001-0.004%. MRI performed prior to sacrifice confirmed no detectable metastatic disease. We confirmed the identity of these cells using PCR for $KRAS^{G12D}$, and luciferase. We performed single cell RNAseq on these cells to study their transcriptome

and identified Dec2 as the most highly expressed gene. We confirmed Dec2 overexpression in these cells by flow cytometry in comparison to the parental cell line. Dec2 is a basic helix-loop-helix transcriptional repressor that is involved in numerous biological processes including regulation of circadian rhythm and MTCD. Conclusions We have not only created the first mouse model of pancreatic cancer MTCD but also provide the first use of single cell next generation sequencing techniques to investigate MTCD. Further mechanistic studies focusing on the role of Dec2 in dormancy in this model are forthcoming.

QS47

Validation of AJCC 8 Staging System and Prognostic Value of Lymph Node Ratio for Resectable Pancreatic Adenocarcinoma after Neoadjuvant Therapy A. Lee,* Y. Chiang, M. Kim, C. Conrad, T. Aloia, J. Vauthey, M. Katz, J.E. Lee, C. Tzeng. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

INTRODUCTION The American Joint Committee on Cancer 8th edition (AJCC 8) staging system for pancreatic adenocarcinoma (PDAC), which adopted new size-based tumor and number-based nodal classifications, was generated with data from patients treated with upfront surgery. Thus, its validity after neoadjuvant therapy (NT) is unknown, as preoperative therapy often downstages the final pathologic tumor and lymph node (LN) status. In this context, we aimed to validate the AJCC 8 and compare the impact of lymph node ratio (LNR) vs. LN counts on overall survival (OS) in PDAC patients treated with NT. METHODS Utilizing the National Cancer Data Base (NCDB), we identified all clinical stage I and II pancreatic adenocarcinoma patients who received NT and subsequently underwent pancreaticoduodenectomy in 2006-2013. Kaplan-Meier survival analysis was performed according to AJCC 8 staging and compared to AJCC 7. Nodal status, nodal counts, and LNR's were used to stratify patients' OS. RESULTS A total of 2,121 patients met the inclusion criteria. AJCC 8 had a c-index of 0.91 and provided similar OS discrimination compared to AJCC 7 (c-index 0.92). Nationally, 53.8% had post-NT pathologic (yp) node-negative (N0) disease, 33.8% had ypN1 (1-3 LN positive) disease, and 12.4% had ypN2 (≥4 LN positive) disease, which correlated with 5-year OS rates of 30.2%, 13.3% and 12.0%, respectively (p<0.001 overall trend). However, there was no OS difference between ypN1 and ypN2 patients (p=0.14). Instead, when patients with nodal disease were stratified by LNR quartile cutoffs (LNR >0-0.08, >0.08-0.13, >0.13-0.25, >0.025), there was good discrimination of OS across quartiles (p<0.001). CONCLUSIONS This is the first large-scale study validating the use of AJCC 8 for resectable PDAC treated with NT. However, compared to count-based nodal staging in AJCC 8, the calculated LNR provides improved prognostic discrimination for patients with nodal disease following NT. The improved classification of patients using LNR could further inform decisions on adjuvant therapy and surveillance intensity.

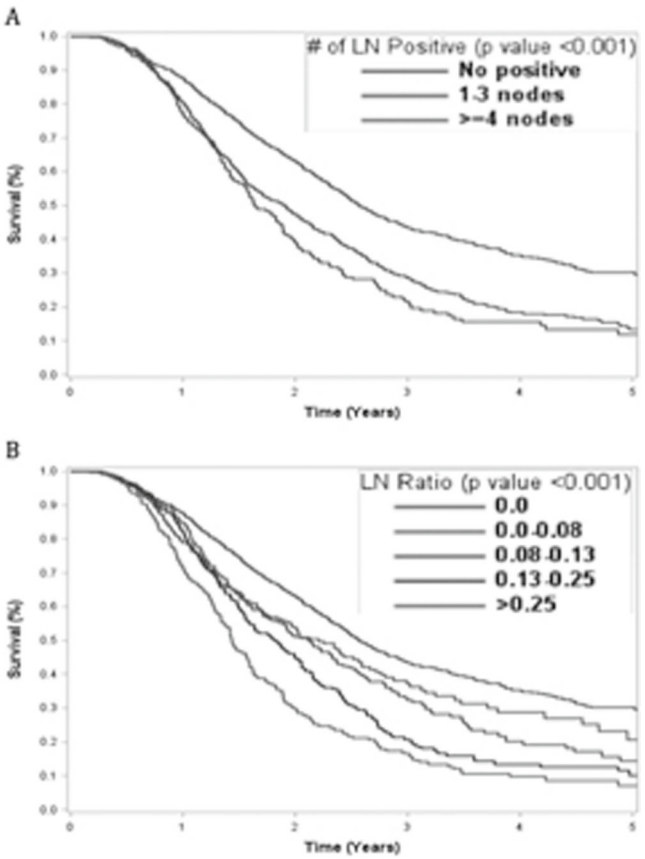


FIGURE: Patient survival after neoadjuvant therapy stratified by A) number of positive lymph nodes, and B) lymph node ratio quartiles

QS48

Differential MicroRNA Expression in Pancreatic Cancer of Eastern European and African American Populations C. Velazquez,[1]* T. Xiao,[1] w. grizzle,[2] M. Howard-McNatt,[1] A. Chiba,[1] L. McNally.[1] *1. Wake Forest Baptist Health, Winston Salem, NC; 2. university of alabama, Tuscaloosa, AL.*

Background: Pancreatic cancer has the lowest 5-year survival rate of all cancers and remains the 4th leading cause of cancer-related deaths in the United States. Incidence and mortality rates for pancreatic cancer are highest for African Americans (AA). MicroRNA expression varies greatly among malignant tissues, which may play a role in diagnosis, prognosis, classification, and screening for pancreatic cancer. We evaluated differences in microRNA expression among tumors from AA and European American (EA) patients, in attempts to elucidate the effects of race on microRNA expression in pancreatic adenocarcinoma. Methods: Specimens of pancreatic adenocarcinoma from 12 patients (6 AA, 6 EA) were used. Paired frozen and formalin paraffin embedded (FFPF) tissues were obtained from each patient, a total of 24 specimens. Samples were analyzed to determine differences in microRNA expression between frozen and FFPE samples. Laser capture microdissection (LCM) was used to isolate malignant cells from stromal cells, allowing only the malignant component to be analyzed for microRNA. Results: A panel of 119 microRNAs was examined, and 14 were found to be expressed differentially between EA and AA patients. MicroRNA expression profiles showed statistically significant up-regulation of microRNA-10b, -29a, -30c, -142-3p, -191, -203, -206, -361, -378, and -1291 in pancreatic adenocarcinomas in EAs and -205, -224, -520, and -576 in pancreatic adenocarcinomas from AAs. MicroRNA obtained from FFPE yielded higher quantity of microRNA compared to frozen samples among both races. Conclusion: We found that microRNA expression varies in pancreatic tumor samples among EA and AA, and may assist in diagnosis, prognosis, and patient-targeted therapeutic agents. FFPE samples are more readily available when compared to frozen samples since it can be stored in

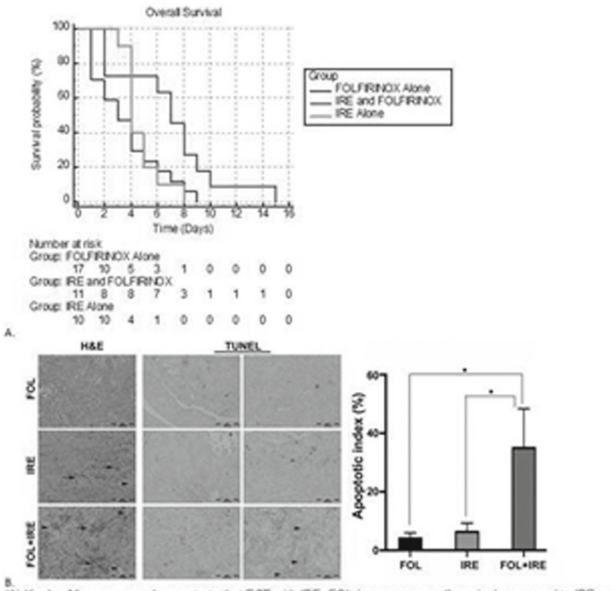
room temperature, and more microRNA were recovered in FFPE samples. This study is the first, to our knowledge, to use LCM to effectively recover and compare microRNAs in a purified sample of malignant pancreas cells. We anticipate the use of LCM will improve upon current models of tumor microRNA expression analysis.

QS49

Electrochemotherapy with Irreversible Electroporation and Folfirinox Improves Survival in Murine Pancreatic Adenocarcinoma by Increasing Apoptosis and Decreasing Tumor Cell Proliferation N. Bhutiani,* H. Pandit, Q. Zheng, S. Li, Y. Li, R.C.G. Martin. *Surgery, University of Louisville, Louisville, KY.*

Introduction: Combining gemcitabine (gem) with irreversible electroporation (IRE) has been shown to result in increased tumor cell apoptosis in a murine model of pancreatic adenocarcinoma (PDAC). However, it remains unclear whether this effect can be augmented locally and systemically by utilizing more active chemotherapies. The objective of this study was to evaluate the efficacy of IRE+FOLFIRINOX (FOL: 5-FU, leucovorin, irinotecan, and oxaliplatin). Methods: Athymic nude mice underwent intrapancreatic injection with S2-013 PDAC cells. After 7-10 days, tumors were confirmed with ultrasound and mice were treated with chemotherapy (gem or FOL), IRE, or chemotherapy+IRE. Four hours after last chemotherapy, pancreas was evaluated histologically. Levels of irinotecan and its active metabolite (SN-38) were evaluated in organs of mice treated with FOL and IRE+FOL. Experiments were repeated and survival analyses performed to evaluate long-term efficacy. Pancreas was harvested for histology and evaluation of apoptotic machinery, cell cycle proteins, and tumor cell proliferation. Results: IRE+FOL (ECT) resulted in increased tumor cells apoptosis compared to gem, gem+IRE, or FOL (apoptotic index (AI) 34.6% vs. 3.8%, 7.3%, 5.8%, respectively, $p<0.001$). HPLC demonstrated a 1.5-2-fold increase in irinotecan and SN-38 in the pancreas and a 4-fold increase of both compounds in the liver in mice treated with ECT vs. FOL. ECT significantly improved overall survival when compared to mice treated with IRE or FOL (Figure 1A). Histology demonstrated increased tumor cell apoptosis at time of death (Figure 1B). Western blot demonstrated an increase in active caspase 3 (0.14 ECT vs. 0.00 IRE vs. 0.03 FOL fold change/GAPDH, $p=0.02$). ECT resulted in lower cell proliferation compared to IRE or FOL (0.2% vs. 0.3% vs. 0.9, $p<0.001$). Conclusions: ECT with IRE and FOL causes significant tumor cell apoptosis, decreases tumor cell proliferation, enhances systemic FOL exposure, and improves overall survival. Human Phase 1 trials have been initiated to evaluate safety and efficacy of this therapeutic modality.

Figure 1 – Electrochemotherapy with IRE and FOLFIRINOX results in improved overall survival and prolonged cytotoxicity in murine pancreatic adenocarcinoma



(A) Kaplan-Meyer curves demonstrate that ECT with IRE+FOL improves overall survival compared to IRE or FOL alone (median = 7 days IRE+FOL vs. 4 days IRE vs. 3 days FOL, $p=0.03$). In all mice, death or euthanasia was a result of tumor growth and not of treatment itself.

(B) H&E and TUNEL analysis of pancreatic tumor tissue at the time of death from mice treated as part of the survival study. Arrows demonstrate areas of hemorrhage. Arrowheads indicate areas of necrosis. Brown foci on TUNEL analysis indicate areas of apoptotic cell death. ECT with IRE+FOL resulted in increased apoptosis compared to either treatment modality alone (AI = 34.2% ECT vs. 13.2% IRE vs. 4.4% FOL, $p=0.026$).

QS50

Is Adjuvant Therapy Needed for Surgically Resected Ampullary Tumors? V.K. Dhar,* K. Wima, L.K. Winer, T.C. Lee, B.G. Childers, M.C. Morris, S.A. Shah, S.H. Patel, S.A. Ahmad. *Surgery, University of Cincinnati, Cincinnati, OH.*

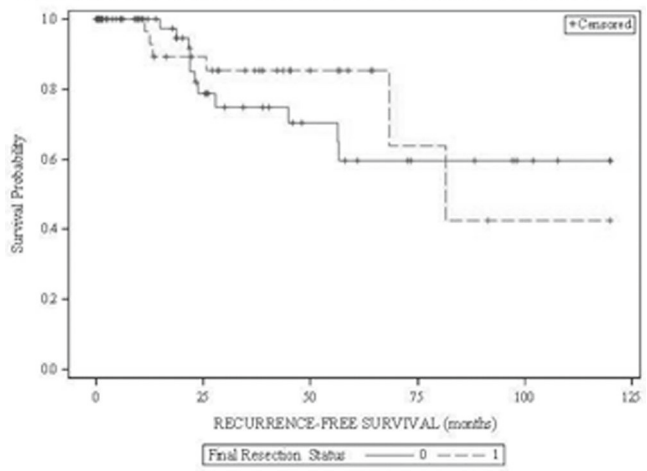
Objective: Due to a lack of randomized clinical trials, the role of adjuvant therapy in the treatment of patients with resected ampullary tumors is poorly defined. Methods: The American College of Surgeons National Cancer Database was used to identify patients with resected ampullary tumors (pathologic stage I – III) from 1998 – 2006 (n=5298). Patients receiving surgery alone (SA, n=3785), surgery with adjuvant chemotherapy (AC, n=316), and surgery with adjuvant chemotherapy and radiation therapy (ACR, n=1197) were compared. Univariate and Cox regression analyses were used to determine covariates associated with overall survival (OS). Results: Over the study period, 29% (n=1513) of patients undergoing surgical resection for ampullary tumors received adjuvant therapy. Adjuvant therapy was more often utilized in patients with stage 3 disease (SA, 22.5% vs. AC, 42.1% vs. ACR, 47.1%), positive lymph nodes (SA, 33.1% vs. AC, 70.7% vs. ACR, 70.9%), and positive surgical margins (SA 1.9% vs. AC 2.8% vs. ACR 4.3%) (all $p < 0.01$). On multivariate analysis, no significant differences in stage-specific OS were noted between patients receiving SA, AC, or ACR for pathologic stage I, II, or III disease (all $p > 0.05$). Similarly, no survival benefit was found for patients with positive resection margins or node positive disease receiving adjuvant therapy (both $p > 0.05$). Conclusion: This national analysis demonstrates that adjuvant therapy for surgically resected ampullary tumors, even when utilized in patients with aggressive disease, ultimately does not confer any survival benefit. Further studies evaluating histologic subtypes and modern systemic therapies need to be performed.

QS51

Resection Status Does Not Impact Recurrence in Well-Differentiated Liposarcoma of the Extremity L.P. Suarez-Kelly,[1]* R.D. Shelby,[1] P.Y. Yu,[1] T. Hughes,[1] M. Palettas,[1] C.G. Ethun,[2] T.B. Tran,[3] G. Poultsides,[3] J. Tseng,[4] K.K. Roggin,[4] K. Chouliaras,[5] K. Votanopoulos,[5] B.A. Krasnick,[6] R. Fields,[6] D. King,[7] M. Bedi,[7] R. Pollock,[1] V.P. Grignol,[1] K. Cardona,[2] J. Howard.[1] *1. The Ohio State University, Columbus, OH; 2. Emory University, Atlanta, GA; 3. Stanford University, Palo Alto, CA; 4. University of Chicago Medicine, Chicago, IL; 5. Wake Forest University, Winston-Salem, NC; 6. Washington University School of Medicine, St. Louis, MO; 7. Medical College of Wisconsin, Milwaukee, WI.*

Background: Well-differentiated liposarcoma (WDLPS) of the extremity is a low-grade malignant soft tissue tumor treated with surgical resection but has a tendency for local recurrence. The necessity of obtaining microscopically free surgical margins (R0) to minimize local recurrence is not clear. In this study we evaluate recurrence free survival (RFS) of extremity WDLPS in relation to resection status. Methods: A retrospective review of adult patients with surgically resected extremity WDLPS at 7 U.S institutions from 2000-2016 was performed. Patients with incomplete resection (R2) were excluded from analysis. Categorical variables were compared using chi-square tests. Continuous variables were compared using two-sample t-tests. Cox proportional hazard regression models were used to assess the impact of resection status on RFS and overall survival (OS). Results: 101 patients with surgically resected extremity WDLPS were identified: 62 (61.4%) had R0, 35 (34.7%) had complete gross resection with microscopically positive margins (R1) and 2 (3.9%) had R2 resections. Mean tumor size was 18.2±8.9cm. Patients with R0 resection had significantly smaller tumors vs those with R1 (16.6 vs 20.7cm, p=0.029). One patient underwent neoadjuvant radiation and 9 underwent adjuvant radiation with no difference in receipt of radiation between R0 vs R1 groups. There was an overall 9.9% complication rate with no difference in number or type of complication between R0 vs R1. Fourteen patients (13.9%) developed a local recurrence with no difference in recurrence rate or RFS between R0 vs R1 resection (Figure 1). Five and ten year RFS was 59.5% and 59.5% for R0 vs 85.2% and 42.6% for R1. A total of 7 deaths (6.9%) occurred with only one related to disease. There was no difference in OS between R0 vs R1 resection. Conclusion: In this large multi-institutional study of surgical resection of extremity WDLPS, microscopically positive margins were not associated with an increased risk of recurrence. R1 resection for extremity WDLPS can yield similar rates of local control while avoiding a radical approach to obtain microscopically negative margins.

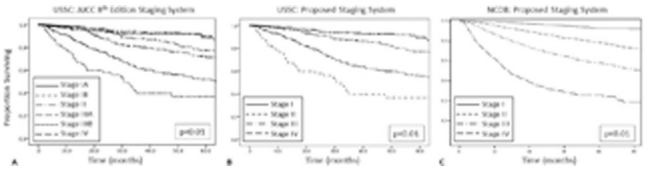
Figure 1. Extremity WDLPS recurrence free survival based on resection status



QS52

A Novel, Simplified, Externally-Validated Staging System for Truncal/Extremity Soft Tissue Sarcomas: An Analysis of the U.S. Sarcoma Collaborative Database A.C. Johnson,[1]* C.G. Ethun,[1] Y. Liu,[1] A.G. Lopez-Aguiar,[1] T.B. Tran,[2] G. Poultsides,[2] V.P. Grignol,[3] J.H. Howard,[3] M. Bedi,[4] J. Charlson,[4] J. Tseng,[5] K.K. Roggin,[5] K. Chouliaras,[6] K. Votanopoulos,[6] D.R. Cullinan,[7] R.C. Fields,[7] D.K. Monson,[1] S.V. Oskouei,[1] N.B. Reimer,[1] S.K. Maithel,[1] K. Cardona.[1] *1. Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 2. Department of Surgery, Stanford University Medical Center, Stanford, CA; 3. Division of Surgical Oncology, The Ohio State University Comprehensive Cancer Center, Columbus, OH; 4. Division of Surgical Oncology, Department of Surgery, Medical College of Wisconsin, Milwaukee, WI; 5. Department of Surgery, University of Chicago Medicine, Chicago, IL; 6. Wake Forest University, Winston-Salem, NC; 7. Department of Surgery, Washington University School of Medicine, St. Louis, MO.*

Background: The updated 8th ed. AJCC staging for soft tissue sarcoma (STS) maintains the same classification as the 7th ed. for low-grade (LG) tumors, but stratifies high-grade (HG) tumors into a complex 3-tier system (<5cm, 5-10cm, & >10cm). This revision may not provide optimal discrimination between stages. Our aim was to create a novel, simplified staging system. Methods: All pts with truncal/extremity STS who underwent resection from 2000-2016 at 7 institutions of the US Sarcoma Collaborative were analyzed. External validation of our proposed staging system was performed with the NCDB. Results: Of 1318pts identified, mean age was 59yrs and 54% were male. Median tumor size was 11cm and 72% were high-grade. When applying the 8th ed. staging, there was no difference between LG tumors (stages IA/B, p=0.92); there was risk stratification of HG tumors (Fig.1A). Although the 8th ed. stratified HG tumors, the separation into 3 size categories may be un-necessarily complicated as the difference in 5-yr OS was not that clinically significant (II: 77% and IIIA: 71%). ROC analysis identified 7.5cm as the ideal tumor size threshold for discriminating 5-yr OS for HG tumors. 5-yr OS was similar for HG <5cm and <7.5cm tumors (each 77%), and for HG >7.5cm and >10cm tumors (56% and 52%). Based on this, a simplified staging system that defined all LG tumors as stage I regardless of size, HG tumors <7.5cm as stage II, HG >7.5cm as stage III, and metastatic disease as stage IV improved stratification between all stages (Fig.1B:all p <0.05). The C-statistic was non-inferior to the 8th ed. (0.69 v. 0.70, p=0.08). External validation using a similar cohort of 9229pts from the NCDB confirmed the optimal stratification of pts between each stage (Fig.1C:all p<0.01). Conclusion: Our novel proposed staging system maintains prognostic significance between all stages within a simplified system. For high-grade tumors, a cutoff of 7.5cm, as opposed to 5cm, maintains discrimination for survival and could be a more clinically applicable cutoff for allocation of patients for multimodality therapies or future clinical trials.



Overall survival by stage for the AJCC 8th edition system in the USSC patient population (A), for the proposed staging system in the USSC patient population (B), and for the proposed staging system in the NCDB patient population (C).

QS53

Perioperative Outcomes After Extremity Sarcoma Resection - Results of a Contemporary Multi-Institutional Experience

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Introduction: Soft tissue extremity sarcoma (STES) is rare with few multi-institutional experiences contributing to our understanding of perioperative outcomes after resection. Our aim was to identify pre- and intraoperative predictors of perioperative morbidity and mortality after STES resection. Methods: Patients who underwent resection of STES from 2000-2016 were identified from a retrospective multi-institutional sarcoma database (United States Sarcoma Collaboration). 90-day morbidity and mortality were assessed, based on pre- and intraoperative risk factors, using Chi Squared and Fischer's Exact test. Statistically significant variables ($p \leq 0.05$) were used in multinomial regression analysis to determine independent predictors of morbidity and mortality. Results: 1334 patients underwent primary STES resection with a median age of 57.0 years. The most common histologic subtypes were undifferentiated pleomorphic sarcoma (28.9%), liposarcoma (16.1%), and leiomyosarcoma (8.1%). Overall 90-day morbidity was 22.5% and 90-day mortality was 1.3%. On multivariate analysis, independent predictors of increased 90-day morbidity were age > 65 years (OR=1.57, p=0.003), white v. other race (OR=1.74, p=0.01), obesity (OR=1.74, p=<0.001), lower versus upper extremity (OR=2.22, p<0.001), tumor size > 10 cm (OR=1.80, p<0.001), TNM/FNCLCC grade (OR=1.45, p=0.02), positive nodal status (OR=3.03, p=0.02), R1 v. R0 resection (OR 1.49, p=0.03), and vascular reconstruction (OR=4.52, p<0.001). Independent predictors of increased 90-day mortality on multivariate analysis were age > 65 years (OR=4.59, p=0.01), smoking (OR=5.65, p=0.003), emergency surgery (OR=27.03, p=0.04), tumor size > 10 cm (OR=4.10, p=0.03), and amputation (OR 6.45, p=0.001). Conclusion: Based on the unique strengths of a multi-institutional collaborative with large numbers of STES patients, we identified factors associated with 90-day morbidity and mortality after resection. These data should guide patient counseling regarding perioperative outcomes in order to better align patient expectation and inform treatment sequencing.

	90-day Morbidity		90-day Mortality	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Age > 65	1.57 (1.17-2.11)	0.003	4.59 (1.44-14.71)	0.010
Race				
White v. Black	0.81 (0.54-1.20)	0.296	-	-
White v. Other	1.74 (1.15-2.64)	0.009	-	-
Obese	1.74 (1.29-2.36)	<0.001	-	-
Smoking	-	-	5.65 (1.81-17.54)	0.003
Emergency Surgery	-	-	27.03 (1.22-500.00)	0.037
Lower v. Upper	2.22 (1.51-3.25)	<0.001	-	-
Size > 10 cm	1.80 (1.36-2.38)	<0.001	4.10 (1.18-14.29)	0.027
Deep v. Superficial	1.30 (0.80-2.10)	0.287	-	-
Grade	1.45 (1.07-1.97)	0.016	-	-
Histology	-	-	3.13 (0.81- 12.04)	0.098
Positive Nodal status	3.03 (1.16-7.88)	0.023	3.31 (0.56-19.61)	0.188
Neoadjuvant Therapy	1.45 (0.98-2.16)	0.066	-	-
Margin				
R1 v. R0	1.49 (1.05-2.11)	0.026	0.97 (0.22-4.30)	0.966
R2 v. R0	1.45 (0.65-3.21)	0.367	<0.00	0.998
Vascular Reconstruction	4.52 (2.35-9.52)	<0.001	-	-
Amputation	-	-	6.45 (2.05-20.28)	0.001

Table 1. Multinomial regression analysis of factors influencing 90-day morbidity and mortality. Factors not significant on univariate analysis denoted with (-). For histology, no subtype was statistically significant in the model. The lowest p-value is shown with its associated odds ratio.

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Accuracy and Safety of Percutaneous Biopsy in Retroperitoneal Soft Tissue Sarcomas (RPS)

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Background. Surgery is the mainstay of treatment for RPS, but neoadjuvant treatments have to be considered in advanced/high risk cases. Since chemotherapy is chosen based on histotype and grade, a correct diagnosis is critical. The aim of this study was to analyze accuracy and safety of percutaneous biopsy (PB) in RPS. Methods. Primary RPS patients who underwent PB between 2005 and 2016 at our institution were analyzed. PB approach and morbidity were recorded. Accuracy was calculated comparing PB diagnosis with final pathology on surgical specimen (SS). Histotypes were grouped as well-differentiated liposarcoma (WDLPS), dedifferentiated LPS (DDLPS), leiomyosarcoma (LMS), other/indeterminate RPS. Sensitivity (Se), specificity (Sp), and positive predictive value (PPV) of PB for histotypes were investigated, as well as PPV for malignancy grade. Results. Out of the 163 patients biopsied in the study period, in 143 (87.7%) PB result was either RPS or non diagnostic. Histotypes, PB approach and type of core needle are detailed in Table 1. In 9 cases (6.3%) a diagnosis could not be made on the PB material. Se and Sp of PB were 92.9% and 72.2% for WDLPS, 38.3% and 100% for DDLPS, 80.1% and 98.4% for LMS, and 83.3% and 92% for other/indeterminate RPS. PB had a PPV of 44.8% for WDLPS, 100% for DDLPS, 89.5% for LMS, and 73.5% for other RPS. PPV for malignancy grades 1, 2 and 3 were 50.8%, 61.3% and 90.9%. Grade 1 false positive PB were upgraded to grade 2 in 31.3% and to grade 3 in 17.9% on SS. Grade 2 false positive PB were upgraded to G3 in 100% on SS. Grade 3 false positive PB were downgraded to grade 2 in 100% on SS. Out of 58 WDLPS on PB, 29 (50%) had a DDLPS on SS. CTCAE G1/2 complications occurred in 4% of cases; no G3 complications occurred. No biopsy track seeding was found at a median follow up of 26 months. Conclusions. PB in suspected RPS is safe and informative in 93.7% of cases. Core needle 14-16 Gauge is recommended. Biopsy results of grade 3 DDLPS and LMS are highly reliable. While, WDLPS on biopsy may underestimate DDLPS in half of cases, and grade 2 on biopsy may underestimate grade 3 in one third of cases.

Percutaneous Biopsy	CT-guided		US-guided		Overall	
	Total (%)	Sensitivity	Total (%)	Sensitivity	Total (%)	Sensitivity
Biopsy Diagnosis						
Non diagnostic	5 (3.5%)	-	4 (2.8%)	-	9 (6.3%)	-
WDLPS	23 (16.1%)	90.9%	35 (24.5%)	94.1%	58 (40.6%)	92.9%
DDLPS	11 (7.7%)	42.3%	12 (8.4%)	35.3%	23 (16.1%)	38.3%
LMS	12 (8.4%)	92.3%	7 (4.9%)	62.5%	19 (13.3%)	80.9%
Other/Indet. RPS	12 (8.4%)	81.8%	22 (15.4%)	84.2%	34 (23.8%)	83.3%
Total	63 (44%)	63.6%	80 (56%)	59.8%	143 (100%)	61.5%
Core Needle type	Total	Non diagnostic	Total	Non diagnostic	Total	Non diagnostic
14-16 Gauge	45	2 (4.4%)	64	2 (3.1%)	109 (76.2%)	4 (3.7%)
18-22 Gauge	15	3 (20%)	8	1 (12.5%)	23 (16.1%)	4 (17.4%)
Not available	3	0	8	1 (12.5%)	11 (7.7%)	1 (9.1%)
Total	63 (44%)	5 (7.9%)	80 (56%)	4 (5%)	143 (100%)	9 (6.3%)

Table 1: Percutaneus biopsy results according to radiologic approach and core needle type.

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Eighth Edition of the AJCC Staging System for Retroperitoneal Sarcoma: Validation Using the U.S. Sarcoma Collaborative and Recommendations for Refinement

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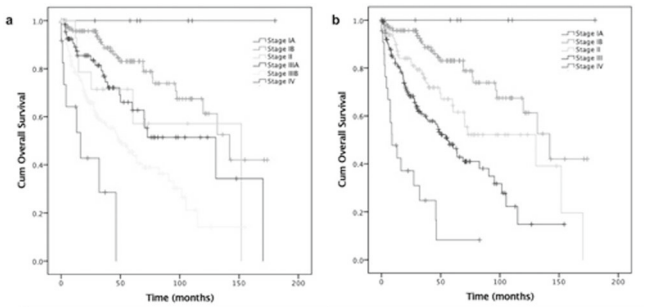
Introduction: The latest edition of the AJCC manual has introduced a specific staging system for retroperitoneal sarcomas (RPS), based on TNM status and tumor grade. We sought to utilize a US multi-institutional database in order to validate this 8th edition of the AJCC RPS staging system and potentially identify areas for improvement. Methods: Data from all patients with RPS who underwent curative-intent resection from 2000-2016 at the eight academic

institutions participating in the US Sarcoma Collaborative were analyzed. Only patients with the specific histology codes included in the RPS AJCC staging system were included. Overall survival curves for each stage grouping were compared using the Kaplan-Meier method. Results: Of 400 patients identified, 50% were males with a median age of 60 years. Median tumor size was 15.0 cm, 62% were grade G2/G3, 3% were N1, and 3% were M1. The 8th edition AJCC staging system did not provide significant separation between stages IB and II (P=0.106), or II and IIIA (P=0.943) (Fig. 1a & 1c). In addition, T(any)N1M0, G(any) and T(any)N(any)M1, G(any) patients were noted to have superimposed survical curves. After moving T2N0M0, G2/3 patients into Stage II (from IIIA), N1 patients into stage IV (from IIIB), and merging stage IIIA and IIIb into a single stage III, more effective discrimination was achieved (Fig. 1b & 1c). Conclusion: Adopting site-specific staging systems for sarcoma is a step in the right direction; however, when applied to this multi-institutional US cohort, the 8th edition of the AJCC staging system for retroperitoneal sarcoma was found to provide limited discrimination between stages IB and II, as well as stages II and IIIA. The proposed refinements in subgrouping allocation can offer improved stratification between stages and more accurate prognostic information.



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Current AJCC Staging System for Retroperitoneal Sarcoma			Proposed Staging System for Retroperitoneal Sarcoma		
Stage	Groupings	P value*	Stage	Groupings	P value*
IA (n=8)	T1N0M0, G1 or GX (n=8)	0.0137	IA (n=8)	T1N0M0, G1 or GX (n=8)	0.0137
IB (n=128)	T2N0M0, G1 or GX (n=27)	0.106	IB (n=128)	T2N0M0, G1 or GX (n=27)	0.005
	T3N0M0, G1 or GX (n=25)			T3N0M0, G1 or GX (n=25)	
	T4N0M0, G1 or GX (n=76)			T4N0M0, G1 or GX (n=76)	
II (n=18)	T1N0M0, G2 or G3 (n=18)	0.943	II (n=88)	T1N0M0, G2 or G3 (n=18)	0.01
IIIA (n=70)	T2N0M0, G2 or G3 (n=70)	0.006		T2N0M0, G2 or G3 (n=70)	
IIIB (n =164)	T3N0M0, G2 or G3 (n=45)	0.007	III (n=154)	T3N0M0, G2 or G3 (n=45)	<0.001
	T4N0M0, G2 or G3 (n=109)			T4N0M0, G2 or G3 (n=109)	
	T(any)N1M0, G(any) (n=10)		IV (n=22)	T(any)N1M0, G(any) (n=10)	
IV (n=12)	T(any)N(any)M1, G(any) (n=12)			T(any)N(any)M1, G(any) (n=12)	

*compared with row below

Figure 1: a. Overall survival (OS) curves following resection of retroperitoneal sarcoma (RPS) stratified by the eighth edition AJCC staging system. b. OS curves following resection of RPS stratified by the proposed staging system. c. Distribution of subgroups and comparison of OS by stage for the eighth edition AJCC and the proposed staging systems.

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An Evaluation of the 8th Edition of the American Joint Committee on Cancer (AJCC) Staging System for Retroperitoneal Sarcomas Using the National Cancer Data Base (NCDB): Does Size Matter?

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Introduction: Retroperitoneal (RP) sarcomas are often large at diagnosis calling into question the 7th edition AJCC size classification of these tumors as <5cm (T1) or ≥5cm (T2). The 8th edition expands T stage into 4 categories (T1:<5cm, T2:5<x≤10cm, T3:10<x≤15cm, T4:>15cm). We evaluated the prognostic ability of the 8th edition using the NCDB. Methods: Patients with RP sarcoma between 1998–2011 were identified from the NCDB and staged according to the AJCC 7th & 8th editions. Kaplan-Meier curves and Cox proportional hazard models were used to compare overall survival (OS). Results: Of the 6,427 patients identified, 9% had tumors <5cm(n=580), 19.4% had tumors 5<x≤10cm(n=1,246), 20.2% had tumors 10<x≤15cm(n=1,298) and 47.4% had tumors >15cm(n=3,045). The 8th edition redistributed patients who were previously staged as IIB(n=636) or III(n=2,129) into new stages IIIA(n=608) and IIIB(n=2,157). In the 7th edition, stage IIB patients (intermediate grade [G2] >10cm) had better OS than stage IIA patients (intermediate/high grade [G2/3] ≤5cm). With the 8th edition, stage II patients (G2/3 ≤5cm) have a similar OS to stage IIIA patients (G2/3 5cm<x≤10cm), and patients with larger tumors (stage IIIB, G2/3 >10cm) show a decrease in OS (Table). Stage IIIB also includes patients with nodal disease (n=106). There was no difference in OS within stage IIIB when stratified by nodal status (p=0.931). Five-year OS based on T stage alone was 57.5%, 55.1%, 51.8%, and 51.5% for T1, T2, T3, and T4 patients, respectively, p=0.007. After excluding patients with metastatic disease and accounting for margin status, grade, chemotherapy, and radiation, higher T-stage was associated with decreased OS (T2 HR 1.02, T3 1.11, and T4 1.25, p=0.004); high grade was the strongest prognostic factor (HR 2.64, p<0.001). The c-index for both editions were similar (80.13 8th vs 80.08 7th). Conclusion: The 8th edition of the AJCC staging system for retroperitoneal sarcoma incorporates larger tumor size parameters that better characterize the majority of patients, but tumor size alone is only a modest predictor of outcome.

Overall survival stratified by the American Joint Committee on Cancer 7th and 8th edition staging systems for retroperitoneal sarcoma

	Stage	HR for Death	5-Year OS	95% CI
AJCC 7th Edition	IA (T1N0M0G1)	Ref	65.9	Ref
	IB (T2N0M0G1)	1.19	63.0	0.9 - 1.5
	IIA (T1N0M0G2/3)	1.89	47.3	1.4 - 2.5
	IIB (T2N0M0G2)	1.40	60.9	1.1 - 1.8
	III (T2N0M0G3 or N1)	2.68	37.0	2.1 - 3.4
	IV (M1)	7.52	12.7	5.9 - 9.5
AJCC 8th Edition	IA (T1N0M0G1)	Ref	65.9	Ref
	IB (T2/3/4N0M0G1)	1.19	63.0	0.9 - 1.5
	II (T1N0M0G2/3)	1.88	47.3	1.4 - 2.5
	IIIA (T2N0M0G2/3)	1.84	49.5	1.4 - 2.4
	IIIB (T3/4N0M0G2/3 or N1)	2.47	40.0	2.0 - 3.1
	IV (M1)	7.49	12.7	5.9 - 9.5

HR: hazard ratio. OS: overall survival. CI: confidence interval. AJCC: American Joint Committee on Cancer. Ref: reference

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Tumor Size and Survival After Resection of Adipocytic and Smooth Muscle Retroperitoneal Sarcoma

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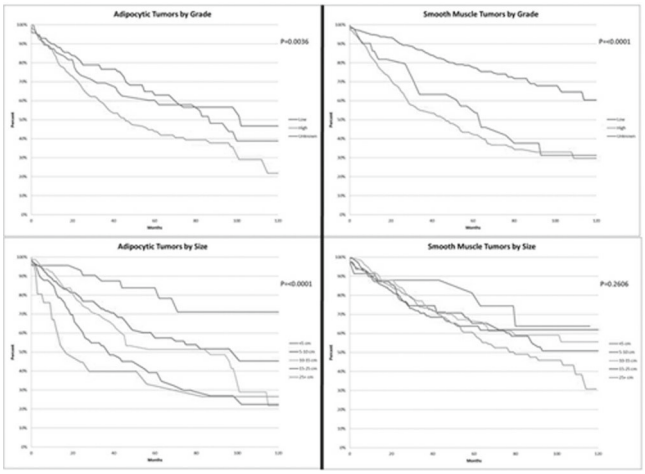
Introduction: American Joint Committee on Cancer (AJCC) staging has limited utility in Retroperitoneal Sarcoma (PRS) given the various histologic and behavioral subtypes. Important changes to the 8th Edition of the AJCC staging system include RPS-specific staging and new parameters such as T-stage for tumors >15 cm (T4). However, prognostic significance of "massive" RPS (>25cm) is unknown. We aimed to identify factors associated with survival of the most common subtypes. Methods: Patients who underwent resection of non-metastatic, primary RPS from 2004-2014 were identified from the Surveillance, Epidemiology, and End Results (SEER) database. Only liposarcoma (LPS) and leiomyosarcoma (LMS) were included, accounting for 81.5% of RPS. Primary outcome was overall survival (OS). Kaplan-Meier survival analysis was performed. Cox proportional hazards regression controlled for age, sex, histology, grade, adjacent tissue invasion, radiation, and size. Results: Of the 1193 patients undergoing resection of primary RPS, 797 (66.8%) had LPS histology and 393 (33.2%) were LMS. Median age was 60 (IQR 52,70) with 56.7% female sex. Patients with LPS were more likely to be older (61 vs 59, p=0.049) and female (52.3% vs 25.3% vs LMS, both p<0.001). LMS tended to be higher grade (49.0% vs 34.9%, p<0.001) and smaller in size (32.1% vs 67.8% >15 cm, p<0.001) as compared to LPS but had similar rates of adjacent tissue invasion (46.5% vs 48.7%, p=0.39). Median OS was 96 months with 3-yr, 5-yr, and 10-yr OS of 70.9%, 60.1%, and 42.2% respectively. While higher grade conferred worse OS in both subtypes, tumor grade was more prognostic in LMS, while size was more prognostic in LPS (Figure). On multivariable analysis, the highest mortality hazard was observed for massive tumors (size 15-25 cm, HR 2.51, p=0.004; and size >25 cm, HR 2.82, p=0.03). Conclusion: Tumor size beyond the current T-stage classifications impacted survival for patients undergoing RPS resection, particularly for LPS, while tumor grade appeared more important than tumor size for patients with LMS. Further refinement of AJCC staging for RPS provides additional information with regards to differences in outcomes in LPS and LMS.



Overall 10-year survival by size in patient with resected retroperitoneal sarcoma by grade and histologic subtype.

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Natural History of Undifferentiated Pleomorphic Sarcoma: Experience from the US Sarcoma Collaborative E.A. Makris,[1]* T.B. Tran,[1] J.A. Norton,[1] C.G. Ethun,[2] V.P. Grignol,[3] J.H. Howard,[3] M. Bedi,[4] T.C. Gamblin,[4] J. Tseng,[5] K.K. Roggin,[5] K. Chouliaras,[6] K. Votanopoulos,[6] D.R. Cullinan,[7] R.C. Fields,[7] E.R. Winslow,[8] S. Weber,[8] K. Cardona,[2] G.A. Poultsides.[1] *1. Stanford University, Redwood City, CA; 2. Winship Cancer Institute, Emory University, Atlanta, GA; 3. Ohio State University, Columbus, OH; 4. Medical College of Wisconsin, Milwaukee, WI; 5. University of Chicago Medicine, Chicago, IL; 6. Wake Forest University, Winston-Salem, NC; 7. Washington University, St. Louis, MO; 8. University of Wisconsin, Madison, WI.*

Introduction: Undifferentiated pleomorphic sarcoma (UPS) is a relatively common and aggressive sarcoma. Previously known as malignant fibrous histiocytoma, UPS is often studied together with other sarcoma histologic subtypes. We sought to utilize a modern, multi-institutional US cohort of sarcoma patients to examine predictors of survival and recurrence patterns after resection specifically for UPS. Methods: From 2000 to 2016, patients with UPS undergoing curative-intent surgical resection at 8 academic institutions were identified. Epidemiologic and clinicopathologic factors, overall survival (OS), time-to-local recurrence (TTLR), time-to-distal recurrence (TTDR), and patterns of recurrence were analyzed by site of origin (extremity, retroperitoneum and trunk). Results: Of the 580 UPS patients identified, 54% were male, with a median age of 56. There was no difference in demographics among extremity (n=478), retroperitoneum (n=39), and trunk (n=59) patients. Administration of neoadjuvant/adjuvant chemotherapy (19%/18%) and radiation (33%/23%) for the entire cohort) was similar among the 3 different sites. However, compared with extremity and trunk, retroperitoneal tumors were larger (median 9 cm, 7.25 cm, and 13.7 cm, P=0.033), more commonly multifocal (1%, 2%, and 10%, P=0.006) and less commonly amenable to R0 resection (86%, 74%, and 52%, P<0.001). Overall survival after resection of retroperitoneal tumors (5-yr 39%) was lower than for tumors arising in the extremity (66%) or trunk (60%, P=0.001, Fig 1a). This difference was explained by a shorter TTLR for retroperitoneal tumors (Fig 1b), whereas TTDR appeared similar between the 3 groups (Fig 1c). On multivariate analysis, multifocality (P<0.001), size > 5 cm (P=0.027), and R1 resection (P=0.023), but not location (P=0.949), were independent predictors of OS. Conclusion: This is the largest reported cohort examining the natural history of patients with resected undifferentiated pleomorphic sarcoma. Retroperitoneal tumors are larger and more commonly multifocal at diagnosis compared with extremity and trunk tumors, leading to a higher incidence of R1 resection and local recurrence.

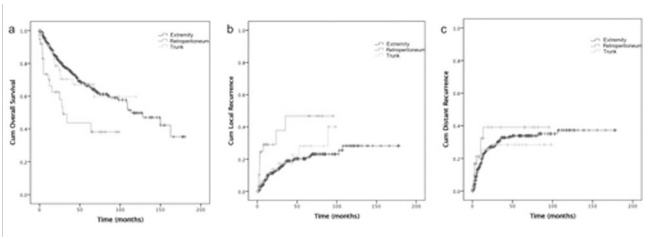

Figure 1: a. Overall survival curves following resection of undifffferentiated pleomorphic sarcoma stratified by the location of the tumor. b. Time-to-local recurrence curves following resection of undifffferentiated pleomorphic sarcoma stratified by the location of the tumor. c. Time-to-distant recurrence curves following resection of undifffferentiated pleomorphic sarcoma stratified by the location of the tumor.

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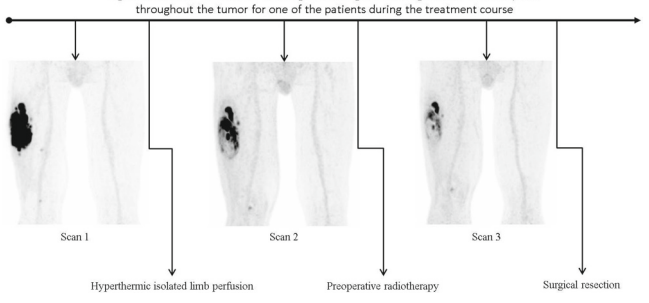
Various Volume of Interest Delineation Techniques to Study Changes in Metabolic Tumor Activity using 18F-FDG PET-CT Scans during Neoadjuvant Extremity Soft Tissue Sarcoma Treatment M.G. Stevenson,[1]* L.B. Been,[1] H. Hoekstra,[1] A.J. Suurmeijer,[2] R. Boellaard,[3] A.H. Brouwers.[3] *1. University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands; 2. University of Groningen, University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, Netherlands; 3. University of Groningen, University Medical Center Groningen, Department of Nuclear Medicine and Molecular Imaging, Groningen, Netherlands.*

Introduction: This study aims to investigate various volume of interest (VOI) delineation techniques for fluorine-18-fluorodeoxyglucose positron emission tomography with computed tomography (^{18}F-FDG PET-CT) scans to study changes in metabolic tumor activity during the neoadjuvant treatment of locally advanced extremity soft tissue sarcoma (ESTS). Furthermore, the relationship between metabolic tumor activity and histopathologic tumor responses was explored. Methods: During neoadjuvant treatment, consisting of hyperthermic isolated limb perfusion (HILP) and preoperative external beam radiotherapy (EBRT), 11 patients underwent three ^{18}F-FDG PET-CT scans. The first scan was made prior to the HILP, the second after the HILP but prior to the start of the EBRT and the third prior to the surgical resection. An automatically drawn VOI_{auto}, a manually drawn VOI_{man}, and two ^{18}F-FDG gradient-based semi-automatically drawn VOIs (VOI_{grad} and VOI_{grad+}) were obtained for each tumor. Maximum standardized uptake value (SUVmax), SUVmean, SUVpeak, metabolically active tumor-volume (MATV) and total lesion glycolysis (TLG) were calculated from each VOI. The correlation and level of agreement between VOI delineation techniques was explored. Lastly, the changes in metabolic tumor activity were related to the histopathologic response. Results: A decline in SUVmax, SUVpeak, SUVmean, TLG and MATV (all $p<0.05$) was found between the three scans. The strongest correlation and an acceptable level of agreement was found between the VOI_{man} and the VOI_{grad+} delineation techniques. A >75% decline in TLG between scan 1 and scan 3 seems to identify histopathologic response. Conclusions: A significant decline in metabolic tumor activity during the multimodality treatment of locally advanced ESTS was found. The VOI_{grad+} delineation technique was identified as most reliable considering reproducibility when compared with the other VOI delineation techniques. TLG seems promising as predictor for histopathologic response after multimodality ESTS treatment.

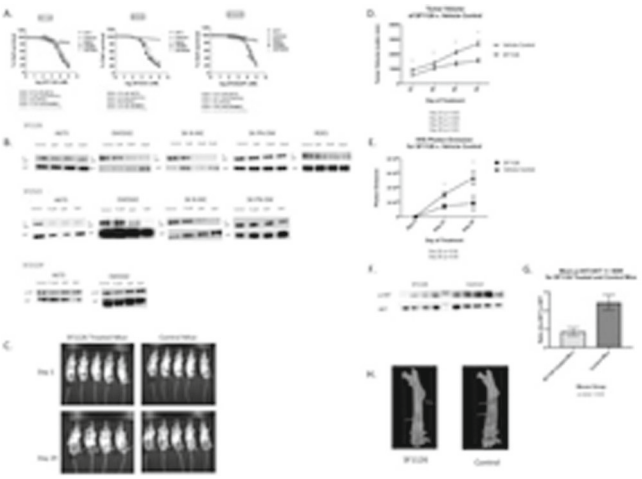
Figure 1: Coronal ^{18}F-FDG PET-CT images showing the heterogeneous ^{18}F-FDG uptake throughout the tumor for one of the patients during the treatment course



QS60

Anti-Tumor Activity for Novel Dual PI3K/BET Inhibitors, SF2523 and SF1126, in Ewing Sarcoma A.N. Goldin,* A.R. Singh, M. Muldong, S. Joshi, C. Jamieson, D.L. Durden. *Orthopaedic Surgery, University of California San Diego, San Diego, CA.*

Background: Ewing sarcoma (ES) shows increased activity of the phosphoinositide 3-kinase (PI3K) pathway and bromodomain and extraterminal domain (BET) proteins; however, there are no drugs that target these pathways. The goal of this study involves showing the efficacy of dual PI3K/BET inhibitors, SF1126 and SF2523, in ES. Methods: ES cell lines A673, EWS502, SK-N-MC, SK-PN-DW, and RDES were treated with SF1126 or SF2523, and IC_{50} values were determined after 48 hours. In western blot (WB) analysis, cells were treated with increasing concentrations of SF1126 or SF2523. Proteins were probed for p-AKT, and AKT. A673 cells were transfected with luciferase and injected into RAG-2 IL2Rgammac deficient mice intrafemorally. 50mg/kg of SF1126 versus control was injected subcutaneously daily for 30 days. Tumors were monitored via IVIS® in vivo imaging and caliper measurements. Tissue was homogenized to undergo WB evaluation and compared with densitometry. Femurs underwent CT scan analysis. Results: Logarithmic dose-response curves showed an IC_{50} of 6.73μM (A673), 13.88μM (EWS502), 11.39μM (SK-N-MC), and 13.39μM (SK-PN-DW) for SF1126; 3.5μM (A673), 5.9μM (EWS502) 3.8μM (SK-N-MC), and 6.2μM (SK-PN-DW) for SF2523. The drugs decreased phospho-protein expression in vitro. SF1126 slows tumor progression in vivo. Caliper measurements showed a significant difference in tumor volume, with p-values of 0.02, 0.03, 0.004, and 0.002 at day 23, 26, 29, and 30 of treatment, respectively. Difference in IVIS luciferase photon signal between the groups provided p-values of 0.8, 0.008, and 0.03 at day 8, 23, and 29 of treatment, respectively. WB tissue analysis showed significantly decreased levels of phospho-proteins (p=0.02). CT scans show greater bone damage to control than SF1126 femurs (Figure 1). Conclusion: Dual PI3K/BET inhibitors have tumor-suppressing effects in ES cells. Phospho-protein levels were decreased in 5 cell lines of ES and in a mouse model. SF1126 has completed phase I clinical trials in adults and entered phase I clinical trials in children with neuroblastoma; thus the present study acts as an indication that clinical trials are reasonable to consider with SF1126 and ES.



A. IC50 curves for 5 ES cell lines with dual PI3K/BET inhibitors SF1126 and SF2523 and single BET inhibitor SF2523P with dose dependent responses. B. WB data with decreasing quantities of p-AKT with drugs SF1126 and SF2523. No decrease in p-AKT with SF2523P, as it is not a PI3K inhibitor. C. in vivo drug trial. At Day 1 there is an equal appearance of tumors. At Day 29 there is more red in the control group, indicating higher tumor activity. D. The difference in volume between control and experimental groups was significant from Day 23 onward. E. The diffrernence in photon emission was significantly lower in the experimental group compared to the control group from Day 23 onward. F. WB data from tumor tissue, with higher levels of p-AKT in the control group. This is quantified in G. and shown to be significant. H. CT results of mouse femurs. There is a greater periosteal reaction in the control group, indicating greater tumor activity in the bone of the control compared to the treatment group.

ABSTRACTS

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VIDEO PRESENTATIONS

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V1

Restoration of Functional Lymphatic Flow Following Axillary Node Dissection with Lymphatico-Venous Bypass S.R. Grobmyer,[1]* S.A. Valente,[1] M. Djohan,[2] C. Cakmakoglu,[3] G. Schwarz,[3] R. Djohan.[3] *1. Cleveland Clinic, Division of Surgical Oncology, Department of Surgery, Cleveland, OH; 2. University of Toledo, Toledo, OH; 3. Cleveland Clinic, Department of Plastic Surgery, Cleveland, OH.*

Upper extremity lymphedema is a feared sequela of axillary lymph node dissection. In traditional axillary node dissection, no effort is made to preserve or restore arm lymphatic flow. We hypothesize that reverse axillary mapping with lymphatico-venous bypass is reproducible technique for preserving functional lymphatic flow following axillary node dissection. We present a case of a 65 year female with axillary recurrence following breast cancer treatment highlighting the technical approach to lymphatico-venous bypass following complete axillary node dissection. 4 cc of isosulfan blue dye is injected at the beginning of the case in the upper inner arm. Axillary node dissection is performed sharply with care to preserve blue arm lymphatic vessels along with small crossing veins in the axillary region representing a new approach to axillary node dissection. Following completion of the dissection, lymphatico-venous bypass is performed using high power operative microscropy. Functional lymphatic flow through the lymphatico-venous anastomosis is demonstrated from the arm using fluorescence microscopy following injection of ICG into the upper inner arm. This technique is reproducible as we have successfully completed this procedure in 13 of 13 consecutive cases. Restoration of lymphatic flow following axillary node dissection represents a new approach to decreasing the burden of post-surgical upper extremity lymphedema.

V2

Level III Axillary Lymph Node Dissection by Infraclavicular Approach Using an Iodine-125 Radioactive Seed K. Boulva,* A. Godin, M. El Khoury, A. Christopoulos, E. Patocskai. *University of Montreal, Montreal, QC, Canada.*

Level III axillary lymph node dissection (ALND) is recommended in patients with proven or suspected metastasis to these lymph nodes. A variety of approaches have been described to access the superior region the axilla, medial to pectoralis minor. The most commonly used approaches are the transpectoral approach described by Patey and the retropectoral approach described by Madden-Auchincloss. Both use an axillary incision, rendering access to the apex of the axilla a challenge in certain patients and putting them at risk of injury to pectoral nerves. We describe an innovative technique for level III ALND which uses an infraclavicular approach, guided by an iodine-125 radioactive seed. Using a radioactive seed to locate a previously biopsied and clipped metastatic lymph node both facilitates its identification during ALND and ensures its removal. We believe that this approach facilitates level III ALND, rendering it accessible to a select group of patients who require excision of lymph nodes which are difficult to access and may otherwise be considered non resectable. Furthermore, this technique demonstrates collaboration with our radiology department which has developed an expertise in positioning radioactive seeds. The following case is that of a patient with a history of breast cancer treated by partial mastectomy, level I and II ALND several years prior. She presents with locoregional recurrence in level II and level III axillary nodes, proven by imaging and lymph node biopsy. Using radioactive seed guidance, we perform level III ALND by infraclavicular approach using an incision 2 cm below the clavicle, centered on the mid-clavicular line.

V3

Minimally Invasive Revision of Choledochojejunostomy Stricture After Pancreaticoduodenectomy: Using All the Tools in the Toolbox E.M. Aleassa,* R. Walsh, S. Chalikonda, K.M. El-Hayek. *Digestive Disease and Surgery Institute, Cleveland Clinic Foundation, Cleveland, OH.*

Introduction: Revisional hepato-pancreato-biliary (HPB) surgery is technically demanding and requires multiple resources. Applications of technological advances in surgery help orient surgeons through distorted anatomy. This video presentation of a robotic-assisted laparoscopic revision of a choledochojejunostomy stricture after a prior pancreaticoduodenectomy illustrates multiple modalities to assist in the identification and management of complex anatomy. We also describe the novel use of indocyanine green (ICG) fluorescence to delineate the choledochoenteric anatomy. Patient and Methods: The patient is a 77 year-old male who underwent a prior robotic-assisted pancreaticoduodenectomy for a malignant duodenal gastrointestinal stromal tumor (GIST) 6 months prior. This index operation was complicated by a grade C pancreatic fistula managed with operative drainage. Following a prolonged recovery, the patient presented six months later with obstructive jaundice secondary to a stricture at the choledochojejunal anastomosis. Multiple percutaneous transhepatic attempts at crossing the stricture were unsuccessful. The decision was made to proceed with a robotic-assisted laparoscopic revision of the anastomosis. Intraoperative ICG was used to delineate the precise location of the stricture. This was further confirmed by fine needle aspiration, laparoscopic ultrasonography, and intraoperative cholangiogram. Results: Successful identification of the stricture allowed for robotic reconstruction using an end-to-side technique. The length of the procedure was 330 minutes with minimal blood loss. The patient recovered well and was discharged on post-operative day 4. No procedure complications were noted during the outpatient follow-up period of 18 months. Conclusion: Complex revisional HPB surgery requires multiple modalities to develop an optimal treatment plan. To our knowledge, this is the first description of ICG fluoroscopy as a valuable adjunct in minimally invasive revisional HPB surgery.

V4

Lateral Laparoscopic Spleen-Sparing Distal Pancreatectomy for Neuroendocrine Tumor J.L. Hallet,[1]* U. Hameed,[2] C. Law.[1] *1. Sunnybrook Health Sciences Centre, Toronto, ON, Canada; 2. North York General Hospital, Toronto, ON, Canada.*

Introduction: Laparoscopic distal pancreatectomy is now commonly performed for benign and malignant disease. Spleen preservation is favoured when possible but technically challenging. A lateral approach to pancreatic dissection may enhance surgical efficiency and results. Methods: This video highlights the lateral approach to laparoscopic spleen-sparing distal pancreatectomy. Results: We herein present the case of a 69 year-old gentleman presenting with a neuroendocrine tumor in the pancreatic tail. A lateral laparoscopic approach was chosen. The patient is positioned in the right lateral decubitus. The procedure begins with mobilization of the splenic flexure. The inferior border of the pancreas is then dissected, followed by the superior pancreatic edge. The lesser sac is entered and short gastric vessels are divided. The pancreatic gland is encircled proximal to the tumor. The tumor localization is confirmed with intra-operative ultrasound. Elevation of the pancreatic gland from the retroperitoneum is then carried out in a lateral to medial fashion anterior to the splenic vessels. Branches from the splenic vein are controlled sequentially. Once the pancreas is fully mobilized from the splenic vessels, it is divided with a buttresed stapler device. The specimen is protected in an endobag and extracted through the optical port. Post-operative course was uneventful and the patient was discharged on post-operative day three. Pathology revealed a 1.5 cm G1 pancreatic neuroendocrine tumor. Conclusion: Lateral laparoscopic distal pancreatectomy represents a safe and feasible approach and an alternative to the traditional laparoscopic distal pancreatectomy. It presents potential advantages over the medial approach, including easier dissection for spleen preservation. With easier and quicker dissection, this technique can increase the uptake laparoscopic spleen-sparing distal pancreatectomy.

V5

Peritonectomy Procedures for Cytoreductive Surgery: Upper Abdomen M. Alkhuziem,* J. Baumgartner, K.J. Kelly, A. Lowy, J. Veerapong. *Surgical Oncology, University of California San Diego, La Jolla, CA.*

Introduction: Cytoreductive surgery (CRS) is utilized to treat a variety of peritoneal surface malignancies, often with the combined use of hyperthermic intraperitoneal chemoperfusion (HIPEC). Oncologic outcomes are integrally tied to a complete cytoreduction, or complete resection of all gross visible disease. Knowledge of potential peritoneal metastatic sites is crucial in being able to obtain a complete cytoreduction. We present a video of cytoreductive surgery with a focus on clearing upper abdominal disease. Methods: A 70 year-old man with Stage IV mucinous colon adenocarcinoma with disease metastatic to the peritoneum is taken to the operating room for CRS/HIPEC. A total parietal peritonectomy is performed, including left diaphragmatic peritonectomy with Gerota's fascia, right diaphragmatic peritonectomy with Morison's Pouch, and pelvic peritonectomy en bloc with the rectosigmoid. A greater omentectomy, lesser omentectomy, and resection of disease in the caudate

recess are also performed. This video highlights cytoreduction techniques of the upper abdomen. Results: The patient was estimated to have a Peritoneal Cancer Index (PCI) Score of 11 out of 39 on exploration. The completeness of cytoreduction score was CC-0 at the end of the case. Conclusion: Aggressive cytoreductive techniques are required to ensure maximal clearance of gross disease in CRS for peritoneal surface malignancies. Long-term survival is dependent on a complete cytoreduction. Our video demonstrates standard techniques for cytoreduction of the upper abdomen.

V6

Robotic Assisted Radical Resection of Recurrent Rectal Cancer A. Saunders,* J. Kuechle, R. Lohman, S. Nurkin. *Roswell Park Cancer Institute, Buffalo, NY.*

Introduction Robotic assisted surgery has become a fairly well-established modality in the treatment of rectal cancers. However, the role of robotic technology in technically complex cases such as locally recurrent rectal cancer is less clearly understood. Methods We report the case of a 47 year old male with recurrent rectal cancer who was referred for treatment. He was evaluated with magnetic resonance imaging and endoscopy, and repeat staging found no evidence of metastatic disease. He was treated with short-course radiation followed by robotic assisted completion abdominoperineal resection en bloc with a partial sacrectomy followed by bilateral gluteus fasciocutaneous flaps. We submit a video recording of the key portions of the patient's surgical treatment. Results The operation began with a transabdominal robotic assisted dissection to mobilize the residual sigmoid colon and rectum en bloc with the presacral tissues and Denonvillier's fascia. The transabdominal dissection was carried down to and through the levator complex bilaterally. The end colostomy was then matured, and the perineal dissection was initiated. The patient was then rotated to a prone position and the resection was completed with a partial sacrectomy. The defect was closed with bilateral gluteus fasciocutaneous flaps. Operating room time was 7.5 hours and estimated blood loss was 500mL. Final pathology showed a 3.4cm tumor, with margin-negative resection and 12 lymph nodes negative for carcinoma. Conclusion We report a successful robotic assisted radical resection for recurrent rectal cancer. Further experience is necessary to further elucidate the role of robotic surgical technology in similar patients.

V7

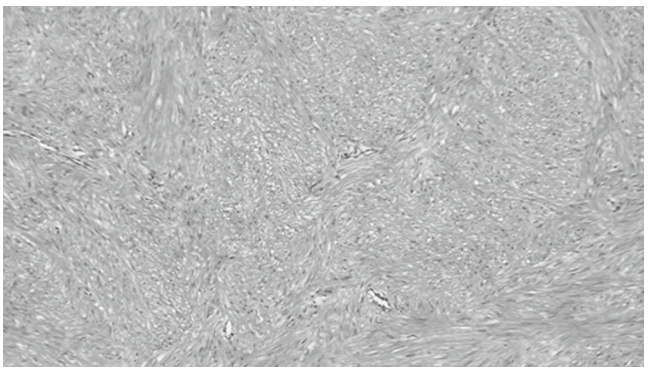
Peritonectomy Procedures for Cytoreductive Surgery: Lower Abdomen and Pelvis E. Chang,[2]* J. Baumgartner,[1] K.J. Kelly,[1] A. Lowy,[1] J. Veerapong.[1] *1. Surgical Oncology, University of California San Diego, La Jolla, CA; 2. Saint Louis University, St. Louis, MO.*

Introduction: Cytoreductive surgery (CRS) is utilized to treat a variety of peritoneal surface malignancies, often with the combined use of hyperthermic intraperitoneal chemoperfusion (HIPEC). Oncologic outcomes are integrally tied to a complete cytoreduction, or complete resection of all gross visible disease. Knowledge of potential peritoneal metastatic sites is crucial in being able to obtain a complete cytoreduction. We present a video of cytoreductive surgery with a focus on clearing lower abdominal and pelvic disease. Methods: A 70 year-old man with Stage IV mucinous colon adenocarcinoma with disease metastatic to the peritoneum is taken to the operating room for CRS/HIPEC. A total parietal peritonectomy is performed, including left diaphragmatic peritonectomy with Gerota's fascia, right diaphragmatic peritonectomy with Morison's Pouch, and pelvic peritonectomy en bloc with the rectosigmoid. A greater omentectomy, lesser omentectomy, and resection of disease in the caudate recess are also performed. This video highlights cytoreduction techniques of the lower abdomen and pelvis. Results: The patient was estimated to have a Peritoneal Cancer Index (PCI) Score of 11 out of 39 on exploration. The completeness of cytoreduction score was CC-0 at the end of the case. Conclusion: Aggressive cytoreductive techniques are required to ensure maximal clearance of gross disease in CRS for peritoneal surface malignancies. Long-term survival is dependent on a complete cytoreduction. Our video demonstrates techniques for cytoreduction of the lower abdomen and pelvis.

V8

Robotic Transgastric Resection of Gastroesophageal Junction Tumor in a Jehovah's Witness Y. Vigneswaran,* M. Hussain, K.K. Roggin. *University of Chicago Medicine, Chicago, IL.*

Here we describe a robotic assisted transgastric resection technique for a gastroesophageal junction tumor. A 66 year old female presented with epigastric discomfort and work up included CT and upper endoscopy which demonstrated submucosal mass at the gastroesophageal junction on the stomach side. Endoscopic ultrasound measured a 4.0 x 2.4cm mass that appeared to arise from the intramuscular wall. Given the location and size this was not amenable to endoscopic resection. Endoscopic ultrasound guided biopsy was consistent with leiomyoma. The patient was a Jehovah's Witness and given her symptoms and anemia, the decision was made to resect her mass. This was done with the use of robotic assistance through a transgastric approach. Port placement was done under direct guidance using laparoscopy. Adhesions from her previous operations were removed to safely place our ports. A Nathanson liver retractor was used to provide exposure to the hiatus. At this time an endoscopy was performed to localize the tumor. The robot was docked and we proceeded with an anterior longitudinal gastrotomy. Two stay sutures were placed to evert the edges of the gastrotomy and the tumor was everted through the gastotomy. The mass was then removed with three fires of the laparoscopic stapler across the pedicle of the mass. The gastrotomy was closed using the Connell suture pattern. At this time an endoscopy was repeated to inspect the staple line and gastrotomy, which confirmed a negative leak test. The port sites were closed. The patient was admitted postoperatively with no complications. Final pathology revealed a 6.7cm smooth muscle tumor with negative margins. The immunostains were strongly reactive for desmin and weakly reactive for c-kit, consistent with a leiomyoma. Additional molecular analysis for c-kit and PDGFRA mutation completely excluded the posibility of GIST.



Sections showed a well-circumscribed submucosal lesion consisting of spindle cells arranged in fascicles

EHV1

Repair of Soft Tissue Defects of the Chest and Breast with Rhomboid Flap C. Ridgeway.* *Breast Center, Lovelace Women's Hospital, Albuquerque, NM.*

The rhomboid flap is used often for closure of skin defects after removal of small cutaneous malignancies. It's utility for closure of more substantial defects after resection of soft tissue is frequently not recognized. This video will demonstrate two cases where it is useful.

EHV2

Resection of a Perirectal Leiomyosarcoma via Trans-Coccygeal Posterior Approach E.A. Asare,* V.J. Tim, B. Feig. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: Surgical management of perirectal tumors often require a significant resection of rectal wall itself and, sometimes a complete proctectomy is required. One way to access posterior perirectal masses while avoiding dissection of the intraperitoneal rectum is to use a posterior, transcoccygeal approach (also known as a Kraske procedure). Patient: The patient is a 63yo M who initially presented to his primary care physician with perirectal pain in May of 2016. He was treated with stool softeners and local therapies for about 4 months, when he was subsequently noted to have a mass on digital

rectal exam. This was initially thought to be related to an anal fissure, which was treated with fissurectomy and lateral internal sphincterotomy in November of 2016. He had an MRI in December of 2016, followed by multiple biopsies, which finally led to a diagnosis of leiomyosarcoma and a referral to our institution. EUS done in January of 2017 showed a 5.2 x 3.8 cm mass and a metastatic lesion in the left ilium. The patient was treated with preoperative Adriamycin/ Dacarbazine (ADIC) for a total of 6 cycles with a significant clinical and radiographic response. This was followed by radiation in August (50 Gy/25Fractions) to the rectal mass, and SBRT to the left Ilium for the metastatic tumor deposit. The patient was taken to the operating room for a Kraske procedure with radical resection of the perirectal mass. An R0 resection was performed with primary repair of the rectal wall using interrupted silk sutures. The incision was closed in multiple layers over a drain. We also performed a laparoscopic diverting loop ileostomy to protect the rectal repair. The patient did well post-operatively. His drain was removed on POD#3. Conclusion: Posterior transcoccygeal approach to a posterior perirectal mass allows for adequate resection, while avoiding the morbidity of trans-abdominal approach and allowing patient to maintain a continent rectum.

EHV3

Surgeon Assessment of Gastric Cancer Lymph Node Specimens

N. Ikoma,* J. Estrella, W. Hofstetter, J. Ajani, K. Fournier, P. Mansfield, J. Skibber, B. Badgwell. *Surgical Oncology, UT MDACC, Houston, TX.*

Background: In the majority of US institutions, gastrectomy specimens are sent for pathologic examination without surgeon assessment or standardized technique of lymph nodes (LNs) assessment for gastric cancer. We conducted a quality improvement project at a US cancer center utilizing surgeon assessment of gastric LNs, and created a video with the intention to help standardization of gastric LN assessment in the United States. Methods: Convenience sampling was employed among patients with gastric adenocarcinomas who underwent curative-intent D2 gastrectomy between July 2016-June 2017. For each patient, a surgeon assessed gastric LNs by harvesting individual LNs, followed by conventional evaluation by a pathologist. Patients who underwent curative-intent D2 gastrectomy during the preceding 2-year period served as the historical cohort. Results: The number of examined LNs was higher in the study cohort (n=17) than in the historical cohort (n=67) (median number of LNs, 43 vs. 36; p=0.031). The proportions of patients who had ≥30 LNs examined were 88% in the study cohort and 70% in the historical cohort. By linear regression analyses, surgeon assessment of LNs was the only factor that was associated with a higher number of LNs examined by the pathologist (beta coefficient 9.2, 95% confidence interval 2.2-17.3; p=0.012). Conclusion: Surgeon assessment of gastric LN specimens increased the number of LNs examined after gastrectomy in gastric adenocarcinoma patients. Standardization of the technical methods for gastric LN evaluation is needed to improve the accuracy and quality of gastric cancer staging in the US. The presented video can help inform standardization of gastric LNs assessment.

EHV4

Laparoscopic D3+CME Procedure for Right Hemicolectomy

J. Gong,* Y. Tong. *Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.*

D3 lymphadenectomy and complete mesocolic excision (CME) are two main surgical procedures for right colon cancer. Both have been demonstrated to have good oncological benefits. However, they were considered to be complex and hard to implement, because they have greater intraoperative and postoperative complication rates. This is especially true when they were performed in laparoscopic surgery. Here we present D3+CME approach during laparoscopic right hemicolectomy. There are three main components to D3+CME approach. 1) Meticulous dissection between the mesocolon and its contiguous dorsal mesenteric structure in situ (mesentery bed), and maintain its intact on both sides. 2) Expose the feeding vessles along SMA and SMV, and ligate them at their bifurcation points. 3) En bloc removal of all the lymphatic drainage area along the left side of SMA. We performed laparoscopic colectomy using D3+CME approach for 79 patients with right-sided colon cancer. The mean operative time and blood loss were 115±19.5 min and 7.2 ± 3.6ml, respectively. The mean number of harvested LNs was 24.5±9.7. The postoperative complication rate was 11.1%. The median hospital stay was 11.8±4.9days. No patients underwent conversion during laparoscopic surgery. There were no recurrent cases at a median follow-up period of 12 months. We consider this approach to be safe and feasible for radical excision for right-sided colon cancers.

EHV5

Robotic-Assisted Low Anterior Resection for Locally Invasive Rectal Cancer in a Lynch Syndrome Patient After Neoadjuvant Chemoradiation

A.A. Castelli,* V. Martinez Zavala, J. Estrada, J. Kaminski. *Advocate Illinois Masonic Medical Center, University of Illinois - Chicago Metropolitan Group Hospitals, Chicago, IL.*

Locally invasive rectal cancer remains one of the most challenging diseases to treat and manage. Neoadjuvant therapy and total mesorectal excision decrease the risk of local recurrence as well as increase the probability of an R0 resection especially in locally invasive rectal cancer. However, radiation-induced fibrosis may increase the technical difficulties of the procedure while increasing the risk of complications and locoregional recurrence. In this video, we present a 45 year-old male with Lynch syndrome and a locally invasive rectosigmoid adenocarcinoma extending into the bladder who underwent a robotic-assisted low anterior resection after neoadjuvant chemoradiation. An elegant robotic-assisted dissection demonstrates an adequate resection in the background of radiation-induced fibrosis as well as a locally invasive rectal cancer. A complete pathological response to neoadjuvant therapy was seen on final pathological evaluation. These findings demonstrate a potential inconsistency that can result from neoadjuvant therapy when comparing imaging studies and final pathological results.

ABSTRACTS

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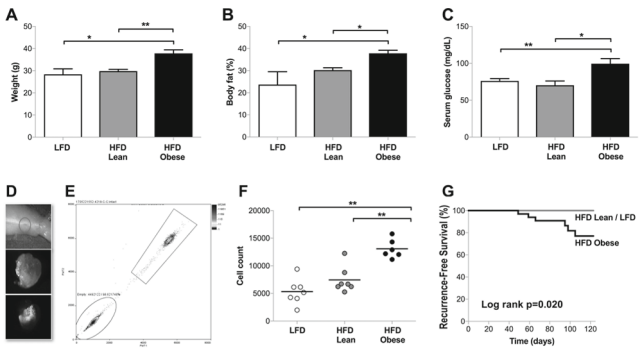
PT1

Impact of Obesity on Breast Cancer Recurrence and Minimal Residual Disease B. Ecker,[1]* A. Solomon,[2] J.Y. Lee,[2] C. Sterner,[2] G. Belka,[2] E. Cho,[2] J. Peraza,[2] F. Shen,[2] D. Pant,[2] T. Pant,[2] L. Chodosh.[2] *1. Surgery, University of Pennsylvania, Philadelphia, PA; 2. University of Pennsylvania, Philadelphia, PA.*

Background: Obesity is associated with an increased risk of breast cancer recurrence and cancer death. Cancer recurrences arise from the pool of minimal residual disease (MRD) that survives primary treatment. Mechanistic understanding of the impact of obesity on MRD and subsequent clinical recurrence is not known. Methods: Doxycycline-inducible primary tumors were formed in intact MMTV-rtTA;TetO-HER2/neu (MTB/TAN) and orthotopic TAN mice fed a high-fat diet (HFD; 60% kcal from fat) or control low-fat diet (LFD; 10% kcal from fat). Following oncogene downregulation and clinical regression, mice were followed for clinical recurrence. Body weight was measured twice weekly and used to segregate HFD mice into obese (i.e. responders) and lean (i.e. non-responders) study arms, and obesity was correlated with body fat percentage, glucose tolerance (measured by intraperitoneal glucose tolerance testing), serum biomarkers (measured by ELISA), and tissue transcriptomics (assessed by RNA sequencing). Minimal residual disease was quantified by droplet digital PCR. Results: HFD-Obese mice weighed significantly more than HFD-Lean and LFD controls ($p<0.001$) and had increased body fat percentage ($p<0.001$). Obese mice exhibited fasting hyperglycemia, hyperinsulinemia and impaired glucose tolerance, as well as decreased serum levels of adiponectin and increased levels of leptin, resistin and IGF-1. HFD-Obese mice developed recurrent tumors earlier than HFD-Lean and LFD mice (median RFS: 53.0 days vs. 87.0 days vs. 80.0 days, log rank $p<0.001$). HFD-Obese mice harbored a significantly larger number of residual tumor cells compared to HFD-Lean and LFD mice (12,550±991 vs. 7,339±2,182 vs. 4,6793±1,618 cells, $p<0.001$). Conclusions: Diet-induced obesity in a transgenic mouse model for human breast cancer progression is causally associated with an increased rate of spontaneous mammary tumor recurrence, as well as physiological changes characteristic of obese patients. The acceleration of tumor recurrence was associated with an obesity-induced increase in the number of dormant residual tumor cells that persist following therapy.



A. HFD-Obese, HFD-Lean and LFD *TAN* mice (n=5/arm) were sacrificed following primary tumor regression to assess residual disease. HFD-Obese mice weighed significantly more than HFD-Lean and LFD mice (37.9±5.3 g vs. 29.8±1.6 g vs. 28.4±4.9 g, respectively; p=0.004); B. HFD-Obese *TAN* mice had elevated body fat percentage relative to HFD-Lean and LFD mice (37.9±4.5% vs. 30.1±2.0% vs. 23.7±11.5%, respectively, p=0.004); C. HFD-Obese *TAN* mice had elevated fasting serum glucose levels relative to HFD-Lean and LFD mice (99.6±15.3 mg/dL vs. 70.3±10.0 mg/dL vs. 76.2±6.8 mg/dL, respectively, p=0.009); D. Representative bright field and fluorescence imaging of residual disease within the mammary glands of mice following tumor regression; E. Representative quantification of *rtTA*-positive droplets by ddPCR; F. HFD-Obese mice harbored a significantly greater number of *rtTA*-positive tumor cells in residual lesions relative to HFD-Lean and LFD mice (12,550±991 vs. 7,339±2,182 vs. 4,6793±1,618 cells, p<0.001); G. Recurrence-free survival of *TAN* mice (n=15/arm) following primary tumor induction of orthotopic injection of *MTB/TAN* tumor cells and subsequent doxycycline withdrawal. Recurrence-free survival was significantly worse for HFD-Obese mice, with no recurrences observed in the LFD or HFD-Lean mice (log rank p=0.020). Error bars represent the standard error of the mean (SEM); p-values <0.05 (*), <0.01 (**), and <0.001 (***).

PT2

Utility of Radiofrequency Spectroscopy for Intraoperative Lumpectomy Margin Assessment E. LeeVan,[1]* S. Seto,[1] F. Tan,[1] J. Shen.[2] *1. General Surgery, Huntington Hospital, Pasadena, CA; 2. University of California Los Angeles Department of Surgical Oncology, Los Angeles, CA.*

Introduction: Women undergoing lumpectomy for breast cancer treatment have a decreased risk of local recurrence with negative surgical margins. However, there is no standard technique for intraoperative margin assessment, and 20% of lumpectomies result in positive margins. MarginProbe is a novel tool that utilizes radiofrequency spectroscopy to provide real-time evaluation of lumpectomy margins. The current study aims to determine the impact of MarginProbe on re-excision rates, and evaluate its accuracy compared to other margin assessment tools. Methods: After IRB approval, a phase II study was conducted in 60 women diagnosed with breast cancer, scheduled for lumpectomy. During surgery, the six margins of the lumpectomy specimen were assessed using gross pathologic evaluation, specimen Xray, and MarginProbe, resulting in 360 margin data points. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were evaluated and compared by T-test. Results: The median age was 63.5 years. The median tumor size was 1.1cm. The majority (86.7%) of tumors were not palpable. 14 patients (23.3%) had DCIS. 4 patients (6.7%) had multifocal disease. 15 patients (25%) had dense breasts. The re-excision rate in the overall cohort was 6.6%, compared to a historical re-excision rate of 8.6% ($p < 0.01$). MarginProbe demonstrated a sensitivity of 67%, specificity of 60%, PPV of 16%, and NPV of 94%, which paralleled the accuracy of combined gross pathologic examination and specimen Xray. The sensitivity of MarginProbe was higher in patients with dense breasts (89% vs. 59%, $p < 0.01$), but the specificity was lower (47% vs. 64%, $p < 0.01$). Both the sensitivity and specificity of MarginProbe were lower in patients with DCIS compared to those with invasive ductal cancer (36% vs. 100%, 46% vs. 76%, $p < 0.01$). 2 patients avoided a positive margin as a result of MarginProbe utilization. Conclusion: The clinical impact of MarginProbe was small in a single surgeon cohort with historically low re-excision rates. MarginProbe has a low PPV, but high NPV across all tumor subtypes and breast densities. Thus, MarginProbe may be better utilized to determine completeness of resection.

Accuracy of Margin Assessment Techniques

	MarginProbe	Xray	Gross Pathology	Xray & Gross Pathology	Xray & Gross Pathology & MarginProbe
Sensitivity	67%	31%	53%	67%	89%
Specificity	60%	83%	71%	61%	43%
Positive Predictive Value	16%	17%	17%	16%	15%
Negative Predictive Value	94%	92%	93%	94%	97%

PT3

Conditional Survival in Women with Breast Cancer: An Analysis of 12,154 Patients from a Single Institution M. Reintgen,[1]* L. Kerivan,[2] E. Reintgen,[1] S. Shivers,[1] C. Cox,[1] D.S. Reintgen.[1] *1. Surgery, University of South Florida, Morsani School of Medicine, Tampa, FL; 2. Georgetown Medical Center, Washington, DC.*

Introduction: Conditional survival (CS) estimates are more meaningful for patients as they progress in their follow-up from a cancer diagnosis. Methods: A retrospective query of a prospective database was used to abstract patients diagnosed with breast cancer during the years 1988-2017. Patients were stratified by Stage of Disease at diagnosis. Data was generated based on 5 year disease-free survival (DFS) and overall survival (OS) from the date of diagnosis, as well as 5 year DFS and OS if patients survive 1,2,3, 4 and 5 years without recurrence or death (Conditional Survival). The best prognosis groups were compared to life tables of survival for the normal US population. There were a total of 12,154 breast cancer patients in the study who received their care from the University of South Florida. Results: For all stages of disease as patients with breast cancer were followed without recurrence or death, the prognosis improved. 5-year OS at any period of time during the recurrence free follow-up period for Stage I patients was (85.8%, 87.8%, 90.2%, 93.1%, and 96.3%) as patients survive their disease without recurrence. The 5-year OS for patients with Stage II disease rose from 70.9%, 74.1%, 80.1%. 86.4%, and 93.3% as patients survive 1-4 years without recurrence. Stage IV patients improved their 5 year OS from 14.9% to 54.4% if they had no progression for 4 years of follow-up, but numbers were small. The best prognostic groups, those patients with Stage 0 and I breast cancer who survive without recurrence for the first 4 years of follow-up, continued to have an increased death rate compared to the normal population. Conclusion: Prognosis improves for breast cancer patients if they survive during the follow-up period without recurrence. For all women with breast cancer who survive without recurrence during their follow-up period, DFS and OS approach a common point for Stage 0-III disease. This data provides more meaningful recurrence and survival information for patients and their families, for clinicians, for lawyers in the medical/legal system and for the insurance industry.

PT4

Enhanced Axillary Evaluation Using Reflector-Guided Sentinel Lymph Node Biopsy: A Prospective Feasibility Study and Comparison to Conventional Lymphatic Mapping Techniques
P. Jadeja,* R. Ha, B. Taback. *Columbia University Medical Center, New York, NY.*

Background: Recently there are efforts to utilize sentinel lymph node biopsy (SLNB) techniques after neoadjuvant chemotherapy (NAC) to minimize axillary surgery. However, studies have demonstrated higher false-negative rates in this scenario, which may result in inaccurate assessment of treatment response and patient prognosis as well as leaving residual disease behind. In this study, we describe the use of reflector-guided excision of the percutaneously biopsied node (PBN) as an aide to conventional SLNB and its predictor of the axillary status following NAC. Methods: This is a single-institution analysis of patients undergoing axillary fiducial-reflector placement and subsequent SLNB. Results: Thirteen patients in the reflector-group were retrospectively matched with 19 patients who underwent conventional SLNB(conventional-group). The PBN was identified in the SLNB in 13 patients (100%) in the reflector-group and in 9 patients (47.3%) in the conventional-group (p=0.002). In the remaining 10 patients in the conventional-group, the PBN was identified in the axillary lymph node dissection (ALND) specimen in 4 patients (21%) and not identified in 6 patients (31.7%). Among 32 patients, traditional mapping failed to identify the PBN in 11 patients (34.4%). The PBN was negative in 11 patients (57.9%) and positive in 8 patients (42.1%), correctly reflecting the status of the axilla in 100% of cases, resulting in a false negative rate (FNR) of 0% in the reflector-group and 33% in the conventional-group. (p=0.2). Conclusion: Reflector-guided excision of the PBN is not only facile and feasible, but more accurately reflects the status of the axilla following NAC.

PT5

Performance Comparison of Sentinel Lymph Node Biopsy After Neoadjuvant Treatment Between Patients with cN2 and cN1 Breast Cancer Disease
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Purpose Accumulating evidence supports usage of sentinel lymph node biopsy (SLNB) for cN1 breast cancer (BC) patients, who become ycN0 after neoadjuvant chemotherapy (NAC). Performing SLNB in patients with an initial cN2 disease remains to be controversial. The aim of this study is to compare the performance of SLNB after NAC both in cN1 and cN2 patients. Method Patients, who presented to our clinic between January 2014 and December 2016 with cN1 and cN2 disease, became ycN0 after NAC and underwent SLNB were included in the study. Treatment outcome measurements (overall survival, local recurrence and distant recurrence) were compared between cN1 and cN2 patients. Results 74 patients were included in the study. Median follow up time was 16.68±12.31 [1-36] months. 30% of patients were cN2. 54% of the cN1 patients had a negative SLNB, while this rate was 45% in cN2 patients. False negative rates for USG and MRI imaging in assessing the axilla after NAC were 43% and 57%, respectively. No axillary recurrence occurred after a negative SLNB in both cN1 and cN2 patients. Two cN2 patients had a local recurrence in breast. One cN1 patient developed a distant recurrence and died after 20 months following surgery. No distant metastasis or death were seen in the cN2 group. Conclusion SLNB is a reliable staging method after NAC both in cN1 and cN2 disease. Longer follow up results will also be analyzed.

Treatment outcomes of patients with a negative SLNB after neoadjuvant treatment

N stage during presentation	Overall Recurrence		Local-Regional Recurrence		Distant Recurrence		Overall Survival	
	No	Yes	No	Yes	No	Yes	Alive	Exitus
cN1	26 (96)	1 (4)	27 (100)	0	26 (96)	1 (4)	26 (96)	1 (4)
cN2	7 (78)	2 (22)	7 (78)	2 (22)	9 (100)	0	9 (100)	0

Data are presented as n(%)

PT6

Effect of Decision-making Resources on Satisfaction with Decision to Undergo Contralateral Prophylactic Mastectomy
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Introduction: Rates of contralateral prophylactic mastectomy (CPM) are increasing, yet few studies have evaluated factors associated with patient satisfaction with their decision to pursue for CPM. Methods: Patients who had undergone CPM at a large academic institution were surveyed regarding factors associated with their decision to pursue CPM, and their satisfaction with this was evaluated using the Satisfaction with Decision (SWD) scale. Results: Of the 58 CPM patients approached to participate, 55 (94.8%) completed the survey. Median age at surgery was 46 (range 29-62), and mean SWD score was 4.85 (range 3.00-5.00). Patients who had reconstruction were more likely to have a SWD score > 4.85 (81.3% vs. 28.6%, p=0.018). Also, those who used the experiences of other cancer patients in their surgical decision-making more often had a SWD > 4.85 (95.2% vs. 61.8%, p=0.009). There was also a correlation between higher SWD and increased patient income (p=0.024). SWD scores did not differ according to disease stage (p=0.384), receipt of neoadjuvant chemotherapy (p=0.755), age at surgery (p=0.555), race (p=0.712), education (p=0.698), insurance type (p=0.243), family history of disease (p=0.975), reported out of pocket (OOP) costs (p=0.150), financial burden (p=1.000), and doctor's communication style (p=0.651). Additionally, SWD scores were similar whether or not patients sought a second physician's opinion (p=0.193), or requested photographs of anticipated cosmetic results (p=1.000). Similarly, the opinion of patients' spouse (p=1.000), other family members (p=0.762), friends (p=0.255), online forums (p=0.664), support groups (p=1.000), and informational websites (p=0.205) did not affect SWD. On multivariate analysis, controlling for patient income and the pursuit of reconstruction, only use of other cancer patients' experiences predicted an above average SWD score (OR 9.397, 95% CI 1.008-87.579, p=0.049). Conclusion: Patients who use other cancer patients' experiences to aid in their surgical decision-making regarding CPM enjoy a higher satisfaction with their decision.

PT7

Long-term Outcome of Patients Undergoing Contralateral Mastectomy with and without Sentinel Lymph Node Biopsy: Impact on Axillary Status
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Introduction Along with the increase use of MRI in breast cancer diagnosis, there has been a dramatic rise in patients electing for bilateral mastectomies (BM) for contralateral prophylaxis. The role of sentinel lymph node biopsy (SLNB) is controversial for the side of contralateral prophylactic mastectomy (CPM) with high-risk lesions. The purpose of this study is to evaluate the utility of SLNB in this patient population and their long-term outcomes. Methods This single institution IRB approved retrospective-review identified patients who underwent BM from January 2010 to February 2017. Known carcinoma and occult findings were observed along with whether a SLNB was performed in CPM. Patient age, primary tumor size, and axillary recurrence were evaluated. Patients who received neoadjuvant chemotherapy or who had bilateral invasive cancer were excluded. Results Among 1127 mastectomies performed 174 (15%) were bilateral; 87 patients. Median age was 55 years old (range: 30 - 84 years old). Primary tumor size was 1.5 cm (range: 0.25 cm - 4.5 cm). Among the BM, 28 (32%) patients had SLNB in the CPM, of these, 12 (43%) had known DCIS and/or LCIS in the CPM preoperatively and 16 (57%) had occult findings postoperatively. In the 28 SLNBs in the CPM performed none were positive. Of the remaining patients that did not undergo SLNB on the CPM, final pathology revealed LCIS in 40 (69%) patients, DCIS in 18 (31%) patients, and occult invasive lobular carcinoma in one patient. At a median follow-up of 60.6 months there were no axillary recurrences regardless of whether SLNB was performed. Conclusion Among patients undergoing BM for known unilateral invasive cancer and a CPM with a high risk lesion, contralateral SLNB did not identify any evidence of metastatic disease. Furthermore, there was no axillary recurrence in any patient regardless of whether contralateral SLNB was performed. In this contemporary cohort of BM for unilateral cancer, SLNB has limited utility in prophylaxis or for the contralateral breast with non-invasive high risk lesions.

PT8

Doppler Ultrasound-Visible Microshells are More Rapidly Identified than Standard B-mode Ultrasound-Visible Markers in a Simulated Intraoperative Setting R.K. Voss,* E.P. Ward, S.L. Blair, H. Ojeda-Fournier. *Dept of Surgery, University of California San Diego, San Diego, CA.*

Background: The majority of nonpalpable breast tumors are localized with wires, clips, or radioactive implanted seeds. HydroMARK clips were developed to minimize the need for an external wire, as gelatin around the clip expands to allow for easier visualization with B-mode ultrasound. Signalmark is a novel, gas-filled microparticle localization system developed as an alternative marker with a unique signal on Doppler ultrasound. We aimed to evaluate the intraoperative identification of ultrasound-visible microshells (Signalmark) as compared to the commercially-available HydroMARK. Methods: Signalmark microshells consisted of 2mg/ml concentration of 2μm View Point Spheres in gelatin. Three 5 mm pellets, one of which was wrapped with a radiographic coil, were inserted in a standard 14-gauge injector. Breasts of lactating pigs were injected with either Signalmark or a HydroMARK clip by a breast radiologist and identified by 3 blinded surgeons using ultrasound. The time to identification of each marker was recorded, with a maximum allotted time of 300 seconds (s). The mean time ± SE to identification of each marker was calculated. The 2-sample t-test and Fisher's exact test were used to analyze the data. Results: A total of 8 Signalmark microshells and 4 HydroMARK clips were searched for by each blinded surgeon using ultrasound (Figure 1). Time to localization of each marker was recorded. Overall, the surgeons correctly identified Signalmark 95.8% of the time (n=23/24) and HydroMARK 41.7% of the time (n=5/12) within 300s (P<0.001). Assuming a maximum allotted time of 300s, the mean time to identification was significantly faster for Signalmark (80.8±20.1s) than for HydroMARK (209.4±35.2s) (P<0.002). Conclusion: Surgeons located ultrasound-visible Signalmark microshells in significantly less time than HydroMARK clips in a simulated intraoperative setting. These results suggest that Signalmark is a feasible option for rapid intraoperative localization of nonpalpable breast tumors using ultrasound guidance. It has the potential to be more convenient for surgeons and patients and potentially requires less operative time.

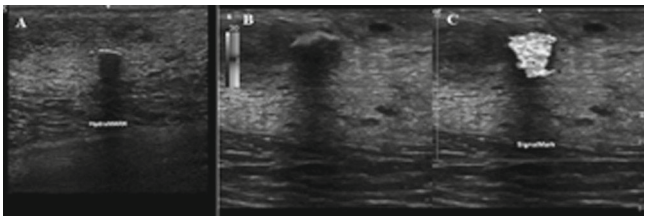

Figure 1: Ultrasound images of A) HydroMARK and B) Signalmark in standard B-mode ultrasound, as well as C) Signalmark viewed with Doppler ultrasound.

PT11

Are Current Practice Patterns Leading to Axillary Overtreatment in Early Stage Breast Cancer? D. Percy,[1]* A. Roberts,[3] J. Pao,[2] E. McKevitt,[2] U. Kuusk,[2] C. Dingee,[2] R. Cheifetz,[1] R. Warburton.[2] *1. General Surgery, University of British Columbia, Vancouver, BC, Canada; 2. Mount Saint Joseph Hospital, Vancouver, BC, Canada; 3. University of Ottawa, Ottawa, ON, Canada.*

Introduction: The objective was to examine the proportion of patients with early invasive breast cancer and preoperatively positive axilla by ultrasound/fine needle aspirate (US/FNA) or clinical exam, who could potentially be spared ALND based on pathologic nodal burden. Methods: A retrospective review of patients with cT1-T2N1 primary invasive breast cancer treated with up-front ALND was completed. Patients were identified from a prospectively maintained institutional database. Node positive disease was identified by either clinical exam or US/FNA. Patients who received neoadjuvant treatment were excluded. Patients were identified as either low nodal burden (<3 positive LNs) or high burden (≥3 positive LNs) on final pathology. Results: 283 patients underwent ALND for primary T1-T2 invasive breast cancer from 2012-2016. 178 were excluded for neoadjuvant therapy, and 14 were excluded due to ALND for failed sentinel node biopsy (SLNB). Of the remaining 91, 52 (57%) patients had clinically palpable axillary lymphadenopathy, and 39 (43%) had a positive US/FNA in the absence of palpable lymphadenopathy. There were no significant differences in clinicopathologic characteristics between the groups (see Table 1). For the US/FNA group and the palpable adenopathy group there was no significant difference in number of nodes removed (mean ± standard deviation; 16±5, 14±7, p=0.60) or number of positive nodes (4±6, 4±5, p=0.84). 17/39 (44%) of the US/FNA group and 26/52 (50%) of the palpable group had low nodal burden on final pathology (NS, p=0.54). The positive-predictive value for high nodal burden was 0.56 for US/FNA, and 0.50 for clinical exam alone. Conclusion: Current practice patterns which include ALND for all patients with positive lymph nodes by either clinical exam or US/FNA resulted in over treatment of 47% of our patients. Further study is required to identify patients who would benefit from strategies to reduce the rate of ALND in low nodal burden breast cancer including omission of preoperative axillary imaging when SLNB will be performed, use of neoadjuvant chemotherapy in appropriate patients or novel targeted axillary dissection techniques in conjunction with SLNB.

Table 1: Clinicopathologic characteristics of patients receiving up-front ALND

	Palpable (n = 52)	US/FNA (n = 39)	p
Age (years) (mean ± SD)	61 ± 15	60 ± 13	0.85
BCS	25 (48%)	25 (64%)	0.12
Histology			
IDC	47 (90%)	33 (85%)	0.40
ILC	2 (4%)	3 (8%)	0.42
Other	3 (6%)	3 (8%)	0.71
Size (mm) (mean ± SD)	27.8 ± 15.2	20.1 ± 13.1	0.66
Grade I	5 (10%)	3 (8%)	0.74
Grade II	19 (37%)	16 (41%)	0.66
Grade III	28 (54%)	17 (44%)	0.81
LVI	28 (54%)	17 (44%)	0.33
ER+	37 (71%)	25 (64%)	0.48
HER2+	11 (21%)	7 (18%)	0.70

BCS breast conserving surgery; IDC invasive ductal carcinoma; ILC invasive lobular carcinoma; LVI lymphovascular invasion; ER estrogen receptor; HER2 human epidermal growth factor 2

PT12

Response to Treatment and Outcomes in a Contemporary Cohort of Metaplastic Breast Cancer A. Salamat,* P. McAuliffe, J. Steiman, C. Nikas, D. Keenan, A. Soran, M. Bonaventura, R.R. Johnson, E. Diego. *Breast Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA.*

Introduction: Metaplastic breast cancer (MBC) represents <1% of all breast cancers (BC). Limited historical data suggests that MBC presents with a larger tumor size (≥T2), higher histologic grade, and higher likelihood of triple negative (TN) phenotype. Patients (pts) are more likely to have a total mastectomy (TM) and receive chemotherapy, but despite more aggressive therapy, have lower disease free survival (DFS) and overall survival (OS) compared to other BC subtypes. There is minimal information about response to neoadjuvant chemotherapy (NAC) in this group. We sought to evaluate a contemporary cohort of pts with MBC to determine whether outcomes are improved in an era of modern multimodality treatment, specifically examining rates of pathologic complete response (pCR), TM, OS, and DFS. Methods: An institutional data collection system and tumor registry was retrospectively queried for the term "metaplastic" in BC pathology reports from 2011-2016. Two groups of pts were identified: MBC and invasive ductal carcinoma with metaplastic features (IDC-M). Demographics, clinicopathologic features and outcomes were compared using standard statistical analysis. Results: Of 122 pts, 112 had treatment and follow-up data available; 57 and 55 pts had MBC and IDC-M, respectively. The groups were similar in terms of age, clinical T and N stage (Table 1). In both groups, most pts had TN phenotype. Systemic chemotherapy was administered to 60% of MBC and 62% of IDC-M pts. In 22% of MBCs, and 38% of IDC-Ms, it was given as NAC. The pCR rate was 0 in the MBC group and 19% in the IDC-M group. The proportion of patients receiving TM and breast conservation were also similar between the two groups. With a median follow-up of 2 years, OS was 69% and 75% in the MBC and IDC-M groups, respectively. DFS was 67% for both groups. 61% of deaths in the MBC group and 60% in the IDC-M group were breast cancer related deaths. Conclusions: MBC and IDC-Ms continue to carry a poor prognosis with low rates of pCR, OS, and DFS. There were no pCRs in the MBC group. Whether

biologic differences compared to other types of BC may explain the poor response rates is a topic for future investigation.

Table 1. Clinicopathologic features and outcomes

	Metaplastic Breast Cancer	IDC with Metaplastic Features	p Value
No of patients	57	55	
Median Age, years (Range)	61 (36-104)	65 (36-94)	0.08
Tumor Size			0.92
T1	12 (21%)	14 (25%)	
T2	26 (46%)	25 (45%)	
T3	15 (26%)	12 (22%)	
T4	4 (7%)	4 (7%)	
cLN Status			0.79
N0	50 (88%)	43 (78%)	
N1	7 (12%)	8 (15%)	
N2	0 (0%)	2 (4%)	
N3	0 (0%)	2 (4%)	
Phenotype			0.87
ER+/HER2-	5 (9%)	3 (5%)	
ER-/Her2+	2 (2%)	1 (2%)	
ER+/Her2+	0 (0%)	1 (2%)	
Triple negative	50 (88%)	50 (91%)	
Chemotherapy (total)	35 (60%)	34 (62%)	0.87
Neoadjuvant (NAC)	13 (22%)	21 (38%)	
pCR	0/13 (0%)	4/21 (19%)	0.14
Breast Surgery			0.84
Breast Conservation (BCS)	24 (41%)	21 (38%)	
Total Mastectomy (TM)	30 (53%)	32 (58%)	
Not known	3 (5%)	2 (4%)	
Axillary Surgery			0.58
Sentinel Lymph node bx	40 (69%)	36 (65%)	
ALND	15 (26%)	17 (31%)	
Radiation therapy			0.85
Whole Breast Radiation Therapy (WBRT) after BCS	17 (71%)	18 (85%)	
Post Mastectomy Radiation Therapy (PMRT)	14 (45%)	17 (31%)	
Median Follow-up	2yrs (1-6yrs)	2yrs (1-6yrs)	
Overall survival (OS)	39 (69%)	41 (75%)	
Disease Free Survival (DFS)	38 (67%)	37 (67%)	
# of Deaths	18 (31%)	15 (27%)	
BC specific deaths	11 (61%)	9 (60%)	

PT13

Tomosynthesis Finds More Radial Scars, But Do We Care?
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Introduction: Radial scars (RS) are benign lesions of uncertain etiology which usually present mammographically as architectural distortion. Prior studies have shown that these lesions can be associated with occult noninvasive and invasive breast cancer. Advancements in mammographic technology, such as digital breast tomosynthesis (DBT), have resulted in higher rates of detection of architectural distortion especially in dense breast tissue. We hypothesized that the rate of identifying treatment relevant lesions has decreased since the introduction of DBT. Methods: We performed a retrospective review identifying core biopsies (CB) from 2007-2016 with a histologic diagnosis of RS with or without atypia. We evaluated the upgrade rate to atypical proliferative lesions and invasive/noninvasive breast cancer over time since the utilization of DBT. Results: We identified 339 CB showing RS. 161 of these were excluded: 77 for additional findings including atypical hyperplasia (AH), papilloma, flat epithelial atypia, and lobular carcinoma in situ (LCIS), and 84 were excluded for having surgery at an outside facility. We included 178 CB in our analysis. The upstage rate on surgical specimen to noninvasive/invasive cancer was 2.8% (N=5). The rate of finding AH/LCIS was 16.3% (N=29). The number of CB with findings of RS has progressively increased from 2014 with the introduction of DBT at our institution. 67 RS were identified over a 7-year time frame prior to DBT with 112 identified over 3 years after widespread adoption. The rate of upstage to AH and LCIS increased after DBT implementation:12.9% to 18.8% (p= 0.297). The rate of upstage to cancer decreased: 6% to <1% (p= 0.064). Conclusion: Although the rate of diagnostic upgrade to breast cancer has decreased since the adoption of DBT in mammographic evaluation of breast lesions, the finding of lesions such as ADH, ALH, and LCIS has increased. We believe that the lack of statistical significance is due to low patient numbers, and future analysis allowing for more time will show significance. However, given these trends with the addition of DBT, we recommend performing an excisional biopsy in the presence of RS on CB until larger-scale studies are performed.

Year	Core biopsy with radial scar	Surgical specimen with cancer N (%)	Surgical specimen with ADH, ALH, LCIS N (%)
2007	3	1 (33%)	1 (33%)
2008	12	1 (8.3%)	1 (8.3%)
2009	16	1 (6.3%)	1 (6.3%)
2010	10	0	1 (10%)
2011	10	1 (10%)	2 (20%)
2012	9	0	1 (11.1%)
2013	6	0	1(16.7%)
2014**	22	0	3 (13.6%)
2015	35	1 (2.9%)	10 (25.7%)
2016	55	0	8 (14.5%)
Total	178	5	29

*Digital breast tomosynthesis was adopted at our facility in 2014

PT14

Distribution of 21-Gene Recurrence Scores in Male Breast Cancer in the United States A.M. Altman,* S. Kizy, J. Yuan, J.W. Denbo, E.H. Jensen, J. Hui, T.M. Tuttle, S. Marmor. *University of Minnesota, Minneapolis, MN.*

Introduction: The 21-gene recurrence score (RS) (Oncotype DX, Genomic Health, Redwood City, Ca) is a RT-PCR assay estimating the risk of distant recurrence in patients with estrogen receptor positive (ER+), human epidermal growth factor receptor 2 negative (HER2-) breast cancer (BC). Studies validating RS use are limited to women with BC. The objective of this study was to assess RS distribution and determine factors associated with high-risk RS in male BC. Methods: Using an augmented version of the Surveillance, Epidemiology, and End Results Program, we identified men and women diagnosed with ER+/HER2- BC from 2010-2014. RS was categorized by risk groups using the traditional and the Trial Assigning Individualized Options for Treatment (TAILORx) cutoffs. Multivariable logistic regression was used to determine factors associated with utilization of testing and a high-risk TAILORx RS. Results: We identified 1,388 men and 154,196 women with ER+/HER2- BC, among which 25% of men and 30% of women had RS testing. The mean age of tested men was 63; most were non-Hispanic white (81%), had grade I or II tumors (67%), and stage I or II (95%) BC. The mean age of tested women was 58; most were white (83%), had grade I or II tumors (82%), and stage I or II BC (97%). Factors associated with a lower likelihood of RS testing in men were older age, lymph node (LN) positivity and stage III BC ($p \leq 0.05$). In women, these factors were older age, diagnosis before 2012, non-white race, larger tumors, LN positivity, progesterone receptor (PR) negativity, grade III tumors, and stage III BC. Among tested men, 21% had high-risk RS compared to 14% of tested women (Table 1). Men with positive PR status and grade III tumors were more likely to have a high-risk RS ($p \leq 0.05$). In women, high-risk RS was associated with younger age, black race, diagnosis before 2012, LN negativity, PR negativity, and grade III tumors ($p \leq 0.05$). Conclusions: Using a large population-based dataset, we characterized RS distribution of ER+/HER2- male BC patients. Men are more likely to have a high-risk RS and factors associated with high-risk RS differ between men and women. Future work on the utility and validity of RS in men is needed.

Table 1: 21-gene recurrence score (RS) distributions among estrogen receptor (ER) positive, human epidermal growth factor receptor 2 (HER2) negative male (n=343) and female (n=46,064) breast cancer patients by traditional and TAILORx cutoffs from 2010-2014.

	Men		Women		
	n	%	n	%	p-value
Traditional RS Cutoffs					<.0001
High (>30)	44	13	3,087	7	
Intermediate (18-30)	112	33	15,993	35	
Low (<18)	187	54	26,984	58	
TAILORx RS Cutoffs					<.0001
High (>25)	74	21	6,320	14	
Intermediate (11-25)	139	41	27,468	59	
Low (<11)	130	38	12,276	27	

TAILORx = Trial Assigning Individualized Options for Treatment

PT15

Women Who have Undergone Bariatric Surgery have a Lower Incidence of Breast Cancer Compared to Their Counterparts: A Retrospective Case-Control Analysis A.D. Williams,* C. Hill, M. Goldbach, A. Malinovitch, J. Tchou. *University of Pennsylvania, Philadelphia, PA.*

Introduction: Bariatric surgery, in addition to offering women a durable weight loss solution, is associated with regression of medical comorbidities such as diabetes and hypertension. Other benefits of bariatric surgery include a reduction in the incidence of common cancers, such as breast cancer (BC). However, studies of the impact of bariatric surgery on BC incidence have had mixed results. We hypothesized that women who undergo bariatric surgery would have a decreased incidence of BC compared to their obese counterparts. Methods: We identified 191 women 40 years of age or older who underwent sleeve gastrectomy or gastric bypass between 2010 and 2014 who also had at least two postoperative mammograms in our health system. Using our multi-hospital medical records database, we then matched each bariatric patient with three control patients (n=573) based on age, and race. The BMI of our cases (bariatric patient) was matched with the BMI of our control (non-bariatric patients) recorded within 1 month of bariatric surgery. The incidence of ductal carcinoma in situ (DCIS) and invasive breast cancer (IBC), mammography data and follow-up were collected and compared between the groups. Results: Our case and control cohorts were similar in demographics and length of follow-up (Table 1). BMI did not differ between the groups at the time of matching (p=0.42). As expected, the BMI at the last follow-up date and the change in BMI differed between the groups (p=0.04 and p=0.003), demonstrating that the bariatric patients lost weight after their surgery. Within a mean of 58.1 months of follow-up for the bariatric group and 56.8 months of follow-up for the control group, patients underwent a mean of 2.9 and 2.6 screening mammograms, respectively (p=0.53). Finally, 3.1% of bariatric patients and 5.0% of control patients were diagnosed with DCIS or IBC (p=0.28). Conclusion: Our preliminary results suggest that women after bariatric surgery may have a lower incidence of BC and warrant a larger analysis, such as multi-institutional study, to examine the potential benefit of bariatric surgery in women at risk for breast cancer.

Table 1

		Bariatric	*Non-bariatric*	*p*
n		191	575	
Age		50.8 ± 8.3	50.0 ± 8.1	0.82
Race	White	73 (38.2)	217 (37.7)	0.81
	Black	115 (60.2)	356 (61.9)	
	Other	3 (1.6)	2 (0.3)	
BMI	Initial	45.2 ± 7.1	45.4 ± 7.3	0.42
	Last follow-up	35.7 ± 7.4	44.8 ± 8.2	0.04
	Change in BMI	-8.9 ± 6.1	-1.5 ± 5.5	0.004
Follow-up (months)		58.1 ± 18.0	56.8 ± 23.2	0.74
Number of mamograms		2.9 ± 1.6	2.6 ± 1.5	0.53
Breast cancer diagnoses		6 (3.1)	29 (5.0)	0.28
	DCIS	2 (1.0)	6 (1.0)	0.13
	Invasive cancer	4 (2.1)	23 (4.0)	

Values are n (%) or mean ± S.D.

PT16

Factors Associated with Local-Regional Recurrence Following Sentinel Lymph Node Dissection (SLND) in Clinically Node Negative Breast Cancer Patients Treated with Neoadjuvant Chemotherapy S. Nurudeen,* M. Yi, I. Bedrosian, A. Caudle, S. DeSnyder, H.M. Kuerer, E.A. Mittendorf, K. Hunt. *Breast Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: The role of SLND for axillary staging following neoadjuvant chemotherapy (NAC) has been questioned. Studies have demonstrated efficacy, however limited data exists on rates of local-regional recurrence (LRR) in patients undergoing SLND alone after NAC. We sought to determine the rate of LRR in a large clinically node negative breast cancer cohort undergoing SLND following NAC and to examine factors associated with increased risk of LRR. Methods: The study population included clinically node negative patients undergoing SLND from 1993 to 2012. Patients with pathologically node positive disease were included. Patients were monitored for LRR and Cox proportional hazard ratios were utilized to identify factors associated with LRR. Clinicopathologic factors assessed for local regional failure risk included patient age, race, tumor stage, sentinel node positivity, tumor grade, receptor status, tumor size and presence of lymphovascular invasion. Results: A total of 7,294 clinically node negative patients were identified. Median age was 56 years and median follow-up was 7.2 years. There were 6315 (86.6%) patients undergoing surgery first and 979 (13.4%) who had NAC. The rate of LRR was 3.3% in the entire cohort. The LRR rate for the group receiving NAC was 4.4% overall, with a rate of 3.7% for local and 1.7% for regional recurrence. For patients receiving NAC, 447 (45.7%) underwent total mastectomy, 501 (51.2%) underwent breast conserving therapy (BCT), and 31 (3.2%) underwent breast conserving surgery (BCS) without adjuvant radiation. In the NAC group, multivariate analysis revealed PR negativity and tumor size as risk factors for LRR. There was no significant difference in LRR between patients undergoing BCT and BCS. Patients undergoing TM were found to be at decreased risk for LRR in comparison to breast-conserving procedures. Conclusions: The incidence of LRR in clinically node negative breast cancer patients undergoing SLND following NAC is low. Factors most associated with LRR are related to tumor size, hormone receptor status, and surgery type.

Multivariate Analysis of Factors Associated with Local and Regional Recurrence in Breast Cancer Patients Undergoing Sentinel Lymph Node Dissection Alone Following Neoadjuvant Chemotherapy

	Neoadjuvant Chemotherapy		
	N=979		
Factor	Hazard Ratio (95% CI)	Standard Error	p-value
PR Negative	2.6 (1.2-5.8)	1.1	0.02
Tumor Size	1.2 (1.1-1.4)	0.1	0.001
Surgery Type			
BCT	Reference		
BCS	0.9 (0.1-7.0)	1.0	0.9
TM	0.4 (0.2-0.96)	0.2	0.04

Progesterone Receptor (PR), Breast Conserving Therapy (BCT), Breast Conserving Surgery (BCS), Total Mastectomy (TM)

PT17

Contralateral Prophylactic Mastectomy in Young Breast Cancer Patients: Is there a Difference Between Public and Private Hospitals? E. Warnack,* S. Ma, F. Schnabel, K. Joseph, D. Axelrod, S. Dhage. *NYU School of Medicine, Department of Surgery, New York, NY.*

Introduction: The rate of CPM (contralateral prophylactic mastectomy) has increased. We examined the rate and characteristics of young cancer patients who elect for CPM at a public safety-net hospital (SNH) and a private hospital (PH) that vary in race, educational background, and English proficiency (EP); that are staffed by specialty- trained providers from the same institution. Methods: Data from 257 breast cancer patients with invasive breast cancer < 45 years old treated from 2011-2015, were obtained and reviewed from institution databases. There were 206 patients from PH and 51 patients from SNH. Chi square test was used to compare qualitative variables. Logistic regression was used to determine factors associated with CPM. Results: Patients at SNH were predominantly Hispanic and Asian, 70% had low EP, 98 % underinsured (public/uninsured), and 18% had college degrees. PH patients were predominantly Caucasian, 100% EP, 100% insured, and 82% had college degrees.

There was no significant difference in number of patients who elected for CPM at SNH vs. PH (23.5% versus 25.2%, p = .8). The ratio of CPM over total mastectomies performed over time did not increase at both hospitals (p= .608,) nor the private hospital alone (p= .074,) nor the public hospital alone (p= .557,) when controlling for patient race, English proficiency, and education. Overall, CPM was associated with the likelihood of having reconstruction (p < .01). Patients at PH who received CPM were approximately 8 times more likely to elect for reconstruction (OR 7.7, p <.01,) but there was no significant association between reconstruction and CPM at SNH (p = .996,) even when controlling for education, stage and race. Most patients at both hospitals were BRCA negative. Patients with positive BRCA status were 4.1 times more likely (OR 4.1, p = .01) to undergo CPM. Conclusions: The rate of CPM regardless of hospital type, patient's race, English proficiency, and education was the same and did not change over time. This suggests that the decision for CPM may be more patient- driven, rather than clinician based.

PT18

Outcome of African American (AA) Compared to White American (WA) Patients with Early-Stage Breast Cancer, Stratified by Phenotype A. Lehrberg,[1]* D. Nathanson,[2] F. Baidoun,[1] L. Petersen,[2] L. Susick,[2] M. Davis,[2] T. Ivanics,[2] I. Rakitin,[2] J. Bensenhaver,[2] E. Proctor,[2] L. Newman.[2] *1. General Surgery, Henry Ford Wyandotte Hospital, Wyandotte, MI; 2. Henry Ford Hospital, Detroit, MI.*

Introduction: Population-based breast cancer mortality rates are approximately 40% higher for AA compared to WA women. The extent to which these outcome disparities are related to the two-fold higher incidence of triple negative breast cancer (TNBC) in AAs is unclear. Methods: We evaluated survival among AA and WA pts presenting with clinically early-stage/node negative breast cancer, stratified by having TNBC versus non-TNBC phenotype from a prospectively-maintained, IRB-approved database in an employee health plan-based hospital system serving a diverse community; Median follow-up was 60 months. Results: A total of 2,847 cases were analyzed; 1,061 (37%) AA and 1,786 (63%) WA. Frequency of TNBC was higher among the AA patients compared to WA patients (15% versus 10%; p<0.05) and frequency of non-TNBC/HER2-negative disease was lower among AA compared to WA patients (53% versus 62%; p<0.05). Median survival of AA compared to WA pts was shorter (median survival 1175 versus 1691 days; Wilcoxon p-value 0.002), but median survival of AA and WA TNBC pts was not statistically different (1094 versus 1636 days; p-value 0.397). Outcome disparities re-emerged for AA compared to WA pts with HER2-positive/non-TNBC (median survival 1210 versus 1717 days; p-value 0.015), and for HER2-negative/non-TNBC (median survival 1722 versus 2088 days; p-value 0.10) although the difference was not statistically significant for the latter. Conclusions: Variation in TNBC prevalence likely contributes to race-associated breast cancer disparities overall, but outcome differences associated with HER2-positive and hormone receptor-positive disease suggest that variations in delivery of targeted therapy or response to targeted therapy may also be playing a role.

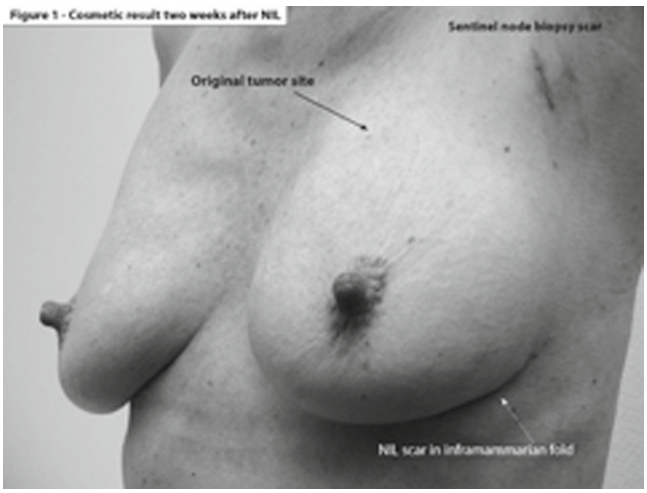
Table 1. Survival comparison between African American (AA) and White American (WA) women with early-stage breast cancer. Triple-Negative Breast Cancer (TNBC)

Group		Median Survival (Days)	Wilcoxon p-value
All Cases	AA	1175	0.002
	WA	1691	
TNBC	AA	1094	0.397
	WA	1636	
Non-TNBC, HER2-positive	AA	1210	0.015
	WA	1717	
Non-TNBC, HER2-negative	AA	1722	0.10
	WA	2088	

PT19

Safety of Nearly Invisible Lumpectomy (NIL) Procedure in Non-Palpable Early Breast Cancer A.A.G. Nijhuis,* M.M.F. Aubuchon, P.H.A. Nijhuis. *VieCuri MC, Venlo, Netherlands.*

The Nearly Invisible Lumpectomy (NIL) technique proved to be feasible and safe in patients with palpable breast tumors. The purpose of this study was to analyze the NIL-technique and its safety in patients with non-palpable tumors. Method: The first 48 early breast cancer patients with non-palpable tumors were treated with NIL between February 2012 and August 2017. Initially, wire localization was used to localize tumors. In patients treated after November 2015, radio-guided localization with ^{125}Iodine seeds was used. Follow-up was according to Dutch national guidelines. Informed consent was obtained in all patients. Technique: 1) Incision inframmarian fold; 2) separation of the breast from pectoral fascia; 3) identification of the tumor; 4) tumor removal; 5) breast reconstruction. Results: All patients were female and the average age was 53 years. Mean tumor size was 1.3 cm; 25 tumors were localized with wire localization and 23 using radioactive seeds. Staging was as follows: six patients with ypT0, one ypT1mic, two ypT1b, one ypT1c, eight pT1b, twenty-seven pT1c and three pT2. Nine cases were staged yN0, two yN1, twenty-six N0, five N1mic, five N1 and one unknown. Pathohistological margins were involved in two cases. In one of these, ablative surgery showed multifocal disease. The other patient had focally involved margins; she rejected adjuvant radiotherapy and underwent re-excision. Ten patients had neoadjuvant chemotherapy, all had clear margins. Three postoperative complications occurred. Two women had a bleeding necessitating re-operation and one developed thrombosis in the external jugular vein. No patient has recurred after a median follow-up of 31 months. Cosmetic results are excellent, there is no dimpling of breast tissue and no visible scar (figure 1). Conclusion: The current study demonstrates the safety of the NIL-procedure in non-palpable tumors, both using wire localization and radio-active seed guidance. This new procedure should be offered to early breast cancer patients, even with non-palpable tumors; especially if tumors are located deep in the breast or in the upper quadrants and cosmetic results with conventional surgery will be less satisfactory.



PT20

Decreasing Rates of Axillary Lymph Node Dissections Over Time: Implications for Surgical Trainee Exposure and Operative Skills Development L.H. Rosenberger,[1]* S.M. Thomas,[2] L.M. Youngwirth,[1] J.K. Plichta,[1] O.M. Fayanju,[1] R.A. Greenup,[1] E.S. Hwang.[1] *1. Department of Surgery, Duke University Medical Center, Durham, NC; 2. Biostatistics and Bioinformatics, Duke University, Durham, NC.*

BACKGROUND Sentinel lymph node biopsy (SLNB) is now a widely accepted means of axillary staging in women with clinically node-negative breast cancer and has become incorporated into the care of select women with node-positive disease. We hypothesized that national rates of axillary lymph node dissection (ALND) are decreasing over time. METHODS We identified all adult patients with clinical Stage I-III breast cancer in the National Cancer Data Base (NCDB 2004-2014). ALND was defined as removal of 10 or more lymph nodes, and a comparison group of patients with 0-9 LN removed was also defined. Hospital volume was defined as low (<148 breast cases/year), moderate (148-298 breast cases/year), and high (>298 breast cases/year) based on previously published thresholds defined by restricted cubic spline analysis. Adjusted logistic models were used to estimate the effect of volume and facility type on receipt and non-receipt of ALND. Adjusted interaction models were used to determine if the changes over time in odds of ALND differed based on facility volume or type. RESULTS 1,131,363 patients were identified; 255,306 received ALND and 876,057 underwent removal of 0-9 lymph nodes. Median age was 61 years, and tumor size was 1.6 cm. Among those who received ALND, 29.9% received neoadjuvant chemotherapy, and the number of positive and total nodes retrieved were 2 and 15, respectively. Rates of ALND

declined from 2004 (32%) to 2014 (16%), with the largest decline occurring between 2010 and 2011 (24% to 20%) across all facility types and hospital volume groups (Figure 1). After adjustment, this effect was maintained, with ALND decreasing with each additional year (OR=0.90, 95% CI 0.89-0.90). The change over time did not differ by facility type or hospital volume (interaction p's>0.05). CONCLUSIONS Over the past decade, there has been a significant decline in the rates of ALND. This trend may have an adverse impact on surgical education and intraoperative skill development. This may have subsequent impact on patient and oncologic outcomes, as ALNDs are being performed in ever more challenging oncologic scenarios.

Figure 1. Axillary Lymph Node Dissection Rates Over Time by Hospital Volume.

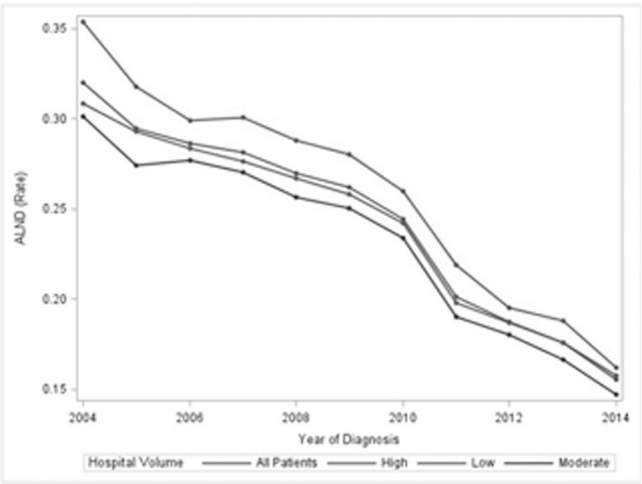
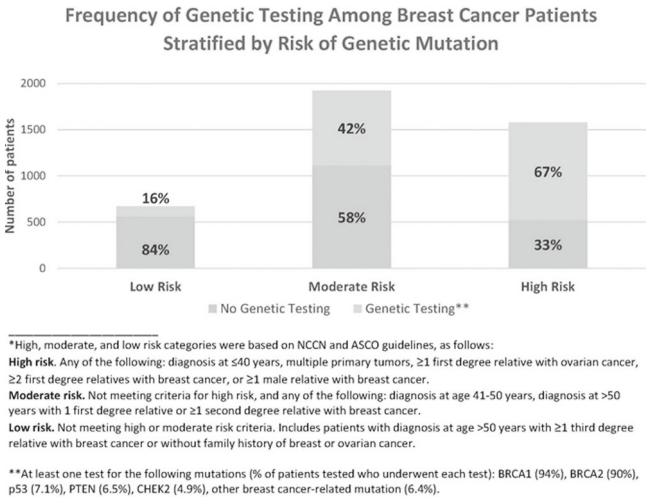


Figure 1. Axillary Lymph Node Dissection Rates Over Time by Hospital Volume.

PT21

Genetic Testing for Hereditary Breast Cancer: Stratified but Underutilized Among High Risk Patients F.C. Verdial,[1]* M. Bartek,[1] S.H. Javid.[2] *1. Surgical Outcomes Research Center, Department of Surgery, University of Washington, Seattle, WA; 2. Department of Surgery, University of Washington, Seattle, WA.*

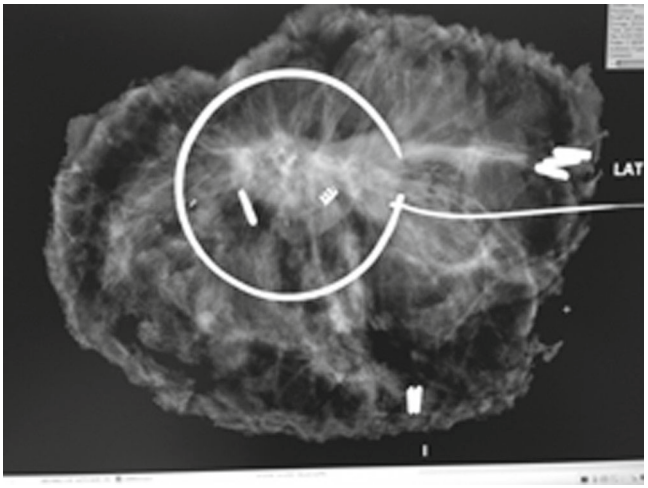
Assessing risk of hereditary breast cancer has significant implications for breast cancer treatment and surveillance. Rates of genetic testing and stratification of testing based on risk of hereditary breast cancer in practice remain poorly understood. The current study aims to examine genetic testing rates and factors associated with testing among breast cancer patients at high risk of a genetic mutation. We identified patients diagnosed with breast cancer at age ≥21 from 2000-2015 from The Health of Women (HOW) Study™, a cohort study led by the Dr. Susan Love Research Foundation. We categorized patients as high, moderate, or low risk of harboring a genetic mutation based on criteria outlined in NCCN and ASCO practice guidelines and compared patient characteristics and testing rates across groups using Fisher's exact and Chi-square tests. Multivariate logistic regression was used to estimate the odds of testing by various patient characteristics. Among 4,170 patients, 38% met criteria for high risk of a genetic mutation and 67% of high risk patients had a genetic test (Figure 1). Risk of carrying a mutation was strongly associated with receipt of genetic testing (p<0.001). High risk patients comprised 54% of those tested and were more likely to have had genetic counseling, result disclosure by a genetic counselor, and a positive test than individuals at moderate and low risk of a mutation (all p<0.001). Among patients at high risk of a mutation, the odds of testing were increased with higher level of education (OR 1.21, 95% CI 1.07–1.37), white race (OR 1.86, 95% CI 1.10–3.14), history of marriage (OR 1.83 95% CI 1.27–2.62), and younger age at diagnosis (OR 0.93 each year beyond age 21, 95% CI 0.90–0.98). Overall, genetic testing rates were appropriately higher among individuals at high risk of harboring a genetic mutation as defined by national guidelines. However, testing rates among high risk breast cancer patients remain relatively low. Focused efforts to increase genetic testing rates among high risk patients, particularly among non-white, less educated, and never married individuals, present opportunities for improvement in the care of these patients.



PT22

Feasibility of a New Method for Localization of Non-Palpable Breast Lesions M. Cross,[1]* C. Kaufman,[4] J. Lopez,[2] K. Pierce,[3] L. Snyder,[2] G. Lebovic.[5] *1. Breast Treatment Center of Northwest Arkansas, Fayetteville, AR; 2. Hoag Memorial Hospital, Newport Beach, CA; 3. The Breast Center - Medical Assoc. of Northwest Arkansas, Fayetteville, AR; 4. University of Washington, Seattle, WA; 5. Surgery, Focal Therapeutics, Inc, Frisco, TX.*

Introduction: Wire localization has been the standard of care to assist surgeons with excision of non-palpable lesions of the breast. However, difficulties associated with the procedure include: scheduling, accuracy in targeting the lesion, potential for dislodgement of the wire, delays in surgery start time, and overall inconvenience for patients and clinicians. These issues warrant examination of alternative methods of preoperative localization. Methods: We describe a novel approach to localization using a nitinol ring deployed into the breast. A needle cannula that houses the ring is advanced into the breast and the ring is manually deployed into the breast tissue forming a circle, leaving a highly flexible tail portion emerging from the skin. The device is designed for single handed use with delivery of the ring under ultrasound or mammographic guidance. The deployed nitinol ring encircles the lesion as opposed to penetrating the center or localizing a single point near the edge of the lesion. We evaluated 21 deployments in 19 patients prospectively and performance data of the device were collected for both the placement and surgical removal of the device. Results: Surrounding the lesion in this manner provided visual and tactile cues for the surgeon while its shape and flexible tail portion provided protection against migration or discomfort when placed prior to surgery. 11 of 21 placements were performed by the radiologist while 10 of 21 were placed by the surgeon. All placements were performed using ultrasound guidance with an average placement time of 6.5 minutes. All deployments were accurately situated at the intended target with no evidence of migration. Complete excision with negative margins on final histologic examination occurred in 21 of 21 lesions. No re-excisions were necessary. The average time from skin incision to completion of surgery was 22 minutes. Conclusions: This pilot study describes a novel and efficient method of localization for non-palpable breast lesions. The ring can be placed up to 30 days prior to surgical removal allowing for flexibility in scheduling for both surgeons and radiologists. Further evaluation of this unique device is warranted.



Specimen x-ray showing nitinol ring (courtesy of Dr. Cary Kaufman)

PT23

Axillary Management Following Mastectomy in Patients with One to Two Positive Sentinel Nodes: Evolution in Practice Patterns

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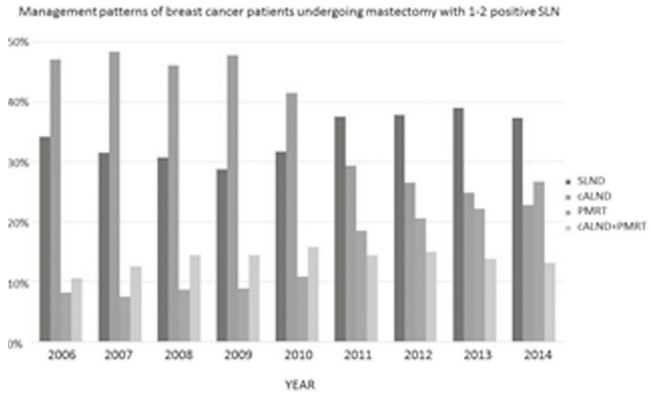
Background: The optimal management of breast cancer patients with a positive sentinel lymph node (SLN) who undergo mastectomy remains controversial. This study was undertaken to describe the treatment patterns of patients with +SLNs who undergo mastectomy using the National Cancer Database (NCDB). Methods: The NCDB was queried for cT1-2N0 breast cancer patients treated with mastectomy between 2006-2014 who had 1-2 +SLNs. Patients receiving neoadjuvant chemotherapy were excluded. Axillary management included SLN dissection (SLND) alone, completion axillary lymph node dissection (cALND), post-mastectomy radiation (PMRT) alone, and cALND+PMRT. Trends over time and patient characteristics were examined. The risk of additional +LNs was calculated for SLND and PMRT patients using a published nomogram. Results: Among 12,190 +SLN patients, use of cALND decreased after 2010 with a corresponding increase in other approaches. In 2006 34% of patients had SLND alone, 47% cALND, 8% PMRT and 11% cALND+PMRT. By 2014, treatment patterns shifted to SLND alone in 37%, 23% cALND, 27% PMRT and 13% cALND+PMRT (Figure 1). By univariate analysis, patients who underwent SLND alone tended to be older (mean 60.6 years, P<.001) with more medical comorbidities (Charlson-Deyo score >2, P<.001). They more frequently had a smaller primary tumor (mean 2.1 cm, P<.001) that was well differentiated (P<.001), hormone receptor positive (P<.001), HER2 negative (P=.003), with only 1 +SLN (P<.001) with micrometastatic disease (P<.001) and no lymphovascular invasion (P<.001). Patients who underwent SLND alone had a 17-29% predicted risk of additional metastatic lymph nodes, and this risk did not change over time (17-29% in 2011 versus 18-30% 2014, P=.14). SLND alone was more likely to be performed at community centers than academic centers (P<.001). Conclusions: The management of breast cancer patients with +SLNs undergoing mastectomy has evolved over time with decreased use of cALND and increased use of radiation. Further clinical trials are needed to evaluate the oncologic safety of these various treatment strategies.

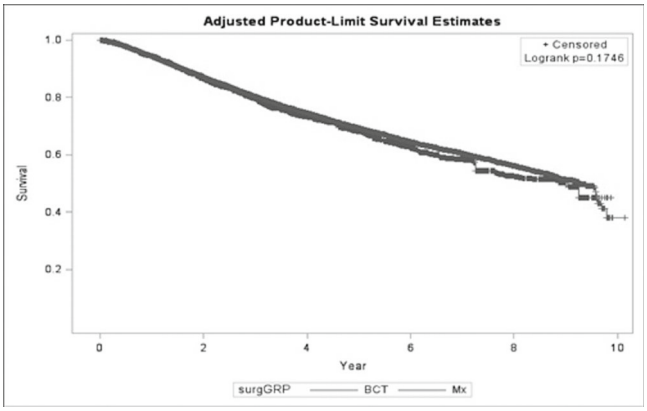


PT24

Breast Conservation Versus Mastectomy in Patients with T3 Breast Cancers (>5 cm): An Analysis of 37,268 Patients from the National Cancer Database

A.M. Mazor,* A. Mateo, L. Demora, E.R. Sigurdson, E. Handorf, J.M. Daly, A. Aggon, P.R. Anderson, S.E. Weiss, R.J. Bleicher. *Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Breast conservation therapy (BCT) is standard for T1-T2 tumors, but prospective randomized trials excluded breast cancers >5 cm. It is unlikely that similar clinical trials will be performed for T3 tumors, and so this study was performed to assess patterns and outcomes of BCT vs mastectomy (Mtx) for breast cancers >5 cm. Methods: We reviewed the National Cancer Database (NCDB) for noninflammatory breast cancers >5 cm, diagnosed 2004-2011 who underwent BCT or Mtx. Male patients, and those receiving preoperative endocrine or radiation therapy were excluded. The Wilcoxon rank sum test was used to compare groups. Multivariable logistic regression was used to identify BCT predictors based on patient demographics and tumor characteristics in patients with clinical T3 stage. The Cochran-Armitage test and Spearman's correlation assessed trends over time. Overall survival (OS) was analyzed using multivariable Cox proportional hazards models, and adjusted survival curves were estimated using inverse probability weighting. Results: 37,268 patients remained after exclusions. Median age and tumor size for BCT vs Mtx was 54 vs 56 years (p<0.001), and 6.0 vs 6.5 cm (p<0.001), respectively. Predictors of BCT in cT3 tumors included age, race, insurance, location, facility type, year of diagnosis, tumor size, grade, histology, nodes examined and positive, and administration of chemotherapy and radiotherapy. OS for all patients having pT3 breast cancers (irrespective of cT stage) was similar between Mtx and BCT (p=0.36). This held true for the subset that was cT3 and pT3 (p=0.55), and when the 6,424 neoadjuvant chemotherapy patients were excluded (p=0.39). The percentages having BCT declined over time (p<0.001) while tumor sizes remained the same (p=0.77). Median follow up was 51.4 months. Conclusions: In this largest series to date, OS for patients with T3 breast cancers is similar whether patients received Mtx or BCT, confirming that in properly selected patients, tumor size should not be a BCT exclusion. Declining use of BCT for tumors >5 cm in younger patients may be accounted for by recent trends towards mastectomy.



Overall Survival: Breast Conservation vs Mastectomy

PT25

Change in Systemic Therapy for HER2+ Breast Cancer Based on Choice for Upfront Surgery H. Schmidt,* K. Pisapati, C. Ezratty, D. Orringer, C. Weltz, E. Port. *Mount Sinai Medical Center, New York, NY.*

Background: While use of neoadjuvant chemotherapy is standard with larger tumors and/or node-positive disease, for smaller, node negative tumors, optimal sequencing of treatment for Her2-positive breast cancers remains a challenge. Specifically, decision-making regarding the need for chemotherapy and/or which agents to give (adriamycin vs non-adriamycin based regimens, the addition or omission of pertuzumab) can be influenced by results obtained from surgery related to tumor size and/or lymph node status. Conversely, patients with positive nodes may benefit from neoadjuvant therapy to downstage the axilla thereby obviating the need for axillary dissection (AD) We investigated the outcome of upfront surgery and how often results potentially changed subsequent medical management for Her2-positive patients. Methods: Between 2010-2017, 82 patients with Her2-positive tumors underwent primary surgery. Patients who were not known to be Her2-positive on biopsy and those upgraded from DCIS or benign findings on biopsy were excluded. Results: Mean patient age was 53.2 (range 30-86). Mean tumor size on final pathology was 14.1mm (range 0-48mm). 22/82 (27%) were found to be node positive at surgery. 62/82 (76%) were treated with adjuvant chemotherapy, 15 of whom received Adriamycin. 14/82 (17%) were found on final pathology to have tumor ≤5mm, and were node negative. 10 of these 14 had preoperative imaging indicating tumor larger than 5mm, 4 of which had size differential greater than 1cm. 75 (91%) patients in the total population had preoperative imaging suggesting tumor >5mm. 7/75 (9%) subsequently received no systemic therapy due to smaller tumor size than on preoperative imaging, thereby potentially changing medical management. Conclusions: A proportion of patients with Her2-positive, clinically node negative breast cancer may benefit from upfront surgery regarding management change related to clarifying node status and tumor size prior to decisions regarding chemotherapy. Consideration should be given to upfront surgery in this group of patients.

PT26

Can MRI Predict Pathologic Complete Response After Neoadjuvant Chemotherapy for Locally Advanced Breast Cancer? C. Lee,* V. Le-Tran, Y. Olimpiadi, N. Zaremba, M. Nelson, J.E. Lang, S.F. Sener. *Surgery, USC LAC + Keck, Los Angeles, CA.*

Introduction: Neo-adjuvant chemotherapy (NAC) for locally advanced breast cancer is associated with pathologic complete response (pCR) to varying degrees prior to surgical intervention. This study was designed to assess whether MRI could accurately predict pCR after NAC, as a prelude to considering development of clinical trials omitting surgical excision of the primary tumor site. Methods: A single-institution retrospective analysis was performed including clinical, radiographic, and pathologic parameters for all breast cancer patients treated with NAC from 2015-'17, all of whom had pre-and post-NAC MRI. Post-NAC imaging data were abstracted from preoperative reports, so radiologists were blinded as to pathologic findings after operation. Radiologic complete response (rCR) after NAC was defined as the absence of suspicious MRI findings in the ipsilateral breast or nodes. pCR was defined as absence of invasive cancer or DCIS in breast or nodes after operation (ypT0N0M0). True-positive was defined as tumor on both MRI and path, true-negative was defined as rCR and pCR, false-positive was defined as tumor on MRI but had pCR, and false-negative was rCr with tumor on path. Results: Data for 64 patients demonstrated that 25 (39.1%) had rCR and 25 (39.1%) had pCR. pCR occurred in 20 (51.3%) of 39 ER- patients and in 15 (48.4%) of 31 HER2+ patients. Overall, for MRI the sensitivity (tumor on MRI and path) and specificity (rCR and pCR) were 87.1% and 80%. For 19 ER-patients who had rCR, 17 (89.5%) had pCR, and for 16 HER2+ patients who had rCR, 13 (81.3%) had pCR. Conclusion: Patients who achieve rCR after NAC, especially with ER- or HER2+ cancers, are likely to have pCR. rCR might be a reasonable criterion for including ER- and perhaps HER2+ patients into clinical trials employing a non-surgical arm after NAC.

PT27

The Impact of Choosing Wisely on Utilization of Ineffective or Unproven Breast Cancer Care T. Yen,* J. Neuner, M. Nattinger, E. McGinley, A. Nattinger, P. Laud, L. Pezzin. *Medical College of Wisconsin, Milwaukee, WI.*

BACKGROUND: Since 2012, about 80 specialty societies have released Choosing Wisely (CW) recommendations aimed at reducing the use of low value, unproven or ineffective tests/procedures. The extent to which these recommendations have influenced the behavior of physicians and patients remains largely unknown. METHODS: Using data from the 2010-2015 MarketScan Commercial Claims and Medicare Supplemental and Coordination of Benefits databases, we identified annual cohorts of women with incident breast cancer to estimate the prevalence of low-value breast cancer services (initial diagnosis, treatment and surveillance; Table) and to examine temporal trends in their utilization, with a special focus on the impact of CW. RESULTS: Among 133,580 women, mean age was 58 years (SD 12); 68% had no comorbidities; 58% underwent breast-conserving surgery (BCS) and 26% underwent axillary node dissection (ALND). In 2010, 13% underwent diagnostic excisional biopsy and 23% had ALND without an initial sentinel node biopsy (SLNB). Over time (before and after release of 2013 CW recommendations), these percents dropped to 7% and 16%, respectively in 2015. However, the percent of IMRT remained stable at 8% and increased to 12% in 2015. In 2010, 12% underwent contralateral prophylactic mastectomy (CPM); this decreased to 10% in 2015, prior to the 2016 CW recommendation. In 2011, 25% had surveillance tumor markers, 17% underwent CT scan, 5% PET/PET CT, and 5% bone scan. After the 2012 CW recommendation, these percents decreased to 20%, 16%, 4%, and 4%, respectively in 2014. Among patients who received BCS and radiation, 41% underwent more than one mammogram annually in 2011; by 2014, this decreased to 27%, largely prior to the 9/2014 CW recommendation. CONCLUSIONS: Compliance with all but one CW recommendation improved over time. CW recommendations led to declines in surveillance metrics but the use of several low-value services (excisional biopsy, ALND, CPM, mammography) were already declining before the CW recommendation release dates. These trends likely reflect changes in clinical practice patterns attributable to NCCN, ASCO, ASBrS, and SSO guidelines that existed prior to 2010.

Metric	Choosing Wisely release date	2010	2011	2012	2013	2014	2015
INITIAL DIAGNOSIS AND TREATMENT							
Diagnostic excisional biopsy without attempted needle biopsy-1	9/4/13	13%	11%*	10%*	9%*	8%*	7%*
ALND without attempted SLNB (excludes neoadjuvant cases)-1	9/4/13	23%	20%*	19%*	19%*	17%*	16%*
Contralateral prophylactic mastectomy in mastectomy cases (excludes patients with family history/genetic predisposition/ counseling/testing)-2	6/27/16	12%	12%	12%	11%	12%	10%*
Intensity modulated radiation therapy (IMRT) after BCS-2	9/23/13	8%	8%	8%	8%	8%	12%*
SURVEILLANCE-3							
CA 15-3, CA 27.29, CEA	4/4/12	-	25%	25%	22%*	20%*	X
PET or PET-CT scan	4/4/12	-	5%	5%*	4%*	4%*	X
CT scan	4/4/12	-	17%	17%	16%*	16%*	X
Bone scan	4/4/12	-	5%	5%	4%*	4%*	X
Mammography performed more frequently than annually after BCS and radiation	9/15/14	-	41%	39%*	37%*	27%*	X
Abbreviations: ALND, axillary lymph node dissection; BCS, breast-conserving surgery; SLNB, sentinel lymph node biopsy							
1 - Years refer to diagnosis year, 2010 as reference							
2 - Years refer to surgery year, 2010 as reference							
3 - Years refer to surveillance year, 2011 as reference							
* Significant difference from reference year ($p<0.05$)							
X - Omitted							

PT28

Prognostic Significance of Micrometastatic Disease After Neoadjuvant Chemotherapy N. Almana,* H. Gagnon, A. Shen, J. Choi, J. Hu, W. Barry, S.D. DeSantis, J. Bellon, M. Golshan, L. Dominici, T.A. King. *Dana Farber Cancer Institute, Boston, MA.*

Background: Increasing use of neoadjuvant chemotherapy (NACT) in both biopsy proven node positive (cN1) and node negative (cN0) patients undergoing mastectomy has led to questions regarding the management and prognostic significance of residual micrometastatic nodal disease. Methods: All patients receiving NACT and mastectomy (2001-2014) were identified from institutional databases. Patients with T4d and Stage IV disease, those who had nodal surgery prior to NACT or no nodal surgery were excluded. Clinical, pathologic and treatment data were obtained from the medical record. Bilateral cancers were captured once per the highest clinical stage. Local regional recurrence free survival (LRRFS), distant recurrence free survival (DRFS) and disease free survival (DFS) were examined by pathologic nodal status (negative (ypN0), micromets (ypNmi), macromets (ypN1)). Results: 1026 patients received NACT for primary breast cancer during the study period; 608 met eligibility criteria. Median patient age 46.5yrs(range 21-86), mean tumor size 3.3cm, 341(56%) patients were cN1. Tumor subtypes included 256(42%) HR+/HER2-, 189(31%) HER2+, and 163(27%) TNBC. Among cN1 patients, 23 (7%) had SLN only and 318 (93%) had ALND; 105(31%) were ypN0, 39(11%) were ypNmi and 197(58%) were ypN1. Among cN0 patients, 138 (52%) had SLN only and 129 (48%) had ALND; 171(64%) were ypN0, 16(6%) were ypNmi and 79(30%) were ypN1. Overall, 182(30%) patients received adjuvant chemotherapy, 498 (82%) received PMRT and 90% ER+ pts received endocrine therapy (ET). In both cN0 and cN1 patients, 5yr DRFS and DFS decreased with increasing residual nodal burden; whereas there was no difference in 5yr LRRFS between ypN0 and ypNmi groups(table). These patterns did not change when adjusting for adjuvant ET or PMRT. Conclusion: In this cohort of patients treated with NACT, 11% of cN1 patients and 6% of cN0 patients had residual micrometastatic nodal disease. The presence of ypNmi disease was associated with inferior DRFS and DFS but was not associated with inferior LRRFS. As most post-NACT node positive patients received ALND during this time period, the impact of ypNmi disease on LRR in patients not receiving ALND remains unknown.

	5yr LRRFS (95%C)	5yr DRFS (95%CI)	5yr DFS (95%CI)
cN1 (n=341)			
ypN0	0.87 (0.80-0.95)	0.89 (0.83-0.96)	0.86 (0.79--0.94)
ypNmi	0.93 (0.84-1.00)	0.79 (0.66-0.95)	0.79 (0.66-0.95)
ypN1	0.72 (0.66-0.80)	0.67 (0.60-0.74)	0.64(0.57-0.72)
	P<0.001	P<0.001	P<0.001
cN0 (n=267)			
ypN0	0.90 (0.85-0.95)	0.90 (0.85-0.95)	0.87 (0.82-0.93)
ypNmi	1.00 (1.00-1.00)	0.83 (0.63-1.00)	0.83 (0.63-1.00)
ypN1	0.63 (0.51-0.77)	0.66 (0.54-0.80)	0.64 (0.52-0.79)
	P<0.001	P<0.001	P<0.001

PT29

Contralateral Prophylactic Mastectomy Rates Among Surgeons at a Single Institution L. Stelle,* S. Cologer, C. Mylander, J. Wellington, K. Waite, L. Martino, M. Rosman, C. Harris, L. Tafra, W. Liang, R. Buras, R. Jackson. *Anne Arundel Medical Center, Annapolis, MD.*

Background: Nationally, rates of contralateral prophylactic mastectomy (CPM) have been increasing over time. In 2016, an American Society of Breast Surgeons consensus guideline advised against routine CPM in average-risk patients with unilateral breast cancer (BC), as there is no oncologic benefit. Previous research shows that patients strongly consider surgeon recommendations in deciding about CPM. We investigated whether CPM rates varied between our institution's four surgeons. Methods: This was a review of all mastectomies for BC at a single breast center offering comprehensive reconstruction options, from 9/2015-4/2017. Cases were identified from our institution's BC database and EHR. We excluded males, bilateral BC, BRCA+, patients with a history of BC and patients initially evaluated at our satellite location. We assessed the univariate association of multiple factors with CPM and significant factors were selected for multivariate logistic regression. Results: Of 172 patients undergoing mastectomy for unilateral BC, 89 (51.7%) underwent CPM and 126 (73.3%) had immediate reconstruction (IR). Surgeon-specific CPM rate ranged from 26% to 67% (p=0.03). Other factors associated with increased CPM rate on univariate analysis were younger age, IR, N0 status, and married status (Table). History of atypia, MRI, T-size, family history of BC, and multicentricity were not associated with CPM. On multivariate analysis, IR was significantly associated with CPM and N0 status approached significance (Table). Although the effect of surgeon considered globally did not reach statistical significance in the multivariate model, the surgeon with lowest CPM rate had a lower adjusted relative odds of CPM (OR 0.21) compared to the reference surgeon (p=0.02). Conclusion: Breast reconstruction was the strongest predictor of CPM, and previous literature has shown that CPM rates are higher at institutions offering comprehensive reconstruction options. We found a substantial difference in CPM rates between surgeons, but this difference diminished on adjusted analysis. Breast centers that choose to look at surgeon variability as an internal quality review should control for known predictors of CPM.

Univariate and multivariate analysis for unilateral versus bilateral mastectomy. For univariate analysis, the table shows only factors with p</=0.05.

Univariate analysis			
	Bilateral %	Unilateral %	p-value
Age: <41 41-55 >55	59.1% 64.5% 36.5%	40.9% 35.5% 63.5%	0.002
Surgeon: 1 2 3 4	53.6% 48.3% 66.7% 26.3%	46.4% 51.7% 33.3% 73.7%	0.03
Immediate reconstruction completed:	63.5%	36.5%	<0.0001
Married:	57.3%	42.7%	0.05
N0 status	57.4%	42.6%	0.04
Multivariate analysis			
	Odds Ratio	Odds Ratio p-value	Effect Likelihood Ratio p-value
Age: 41-55 (vs 55 (vs	1.62 1.12	0.37 0.84	0.53
Surgeon: 2 (vs 1) 3 (vs 1) 4 (vs 1)	0.84 1.17 0.25	0.69 0.75 0.02	0.10
Immediate reconstruction completed:	5.89	0.0001	0.0001
Married:	1.42	0.37	0.37
N0 status:	2.03	0.06	0.06

PT30

Magnetic Seed Localization as an Alternative to Wire Localization for Non-Palpable Breast Lesions T.L. Spivey,[1]* L.R. Lamb,[1] O. Viramontes Sandoval,[2] C.D. Lehman,[1] K.S. Hughes,[1] M.A. Gadd,[1] B.L. Smith,[1] M.C. Specht.[1] *1. Surgical Oncology, Massachusetts General Hospital, Boston, MA; 2. Harvard Medical School, Boston, MA.*

Introduction: Increasingly, seed localization is replacing wire localization to guide excision of non-palpable breast lesions. Seed localization benefits both the patient and surgeon by decoupling the localization procedure from the operative day. To our knowledge, there have been no previously published studies on magnetic seed localization systems. We sought to evaluate differences between magnetic seed and wire localization. Methods: With IRB approval, retrospective single institution data was collected for 174 patients undergoing magnetic seed localization (3/2017 – 8/2017) and 191 patients undergoing wire localization (4/2016 – 12/2016). Pre-op localization procedure times (mins), total operative times (mins), and specimen volumes (cm^3) were recorded. For invasive cancers, volume in excess of tumor size was calculated by subtracting invasive tumor volume (cm^3) from total specimen volume (cm^3). Pain was recorded as the number of narcotic doses administered in the recovery room. Re-excision rates were determined by the need to return to the operating room for additional tissue excision. Results: All localized lesions were successfully excised in both the wire and magnetic seed groups. Mean localization times were not significantly different (41 vs. 41 mins, p=0.7607). Length of surgery for excisional biopsies was significantly shorter for the wire group (30 vs. 39 mins, p=0.0001), whereas, the operative time for lumpectomy with or without axillary surgery did not differ (see table). In patients undergoing lumpectomy with sentinel lymph node biopsy, pain was significantly higher in the wire group versus magnetic seed group (1.3 vs 0.71 doses, p=0.0006). Re-excision rate for positive margins was significantly lower in the wire versus magnetic seed group (14.8% vs 26.4%, p=0.0322). Conclusions: Magnetic seed localization is a novel technique for localizing non-palpable breast lesions. While post-operative pain was decreased with utilization of magnetic seeds, the overall volume of tissue removed to achieve negative margins and the increased

need for a second procedure demonstrate that refinement is necessary to meet the standards achieved with wire localization.

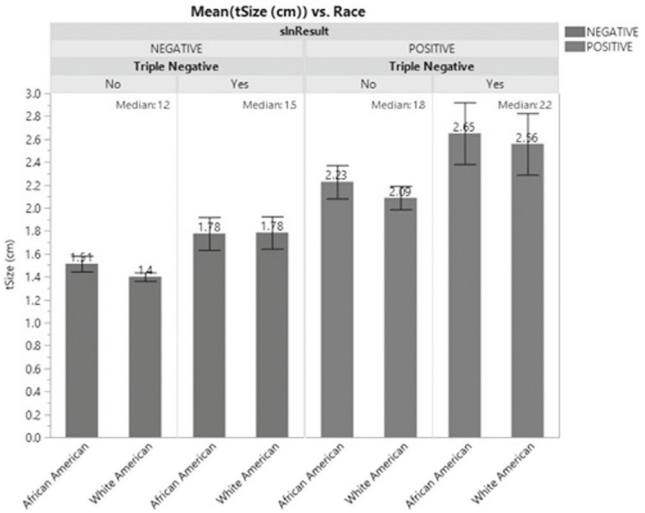
Comparative Outcomes Between Wire Localization and Magnetic Seed Localization Techniques for Non-Palpable Breast Lesions

	WIRE (n=191)	MAGNETIC SEED (n=174)	p-value
LOCALIZATION TIME (mean)			
Pre-operative procedure 1 localization marker	41 minutes (n=171)	41 minutes (n=155)	p=0.7607
Pre-operative procedure >1 localization marker	61 minutes (n=20)	75 minutes (n=19)	p=0.1140
OPERATIVE TIME (mean)			
Excisional biopsy	30 minutes (n=69)	39 minutes (n=68)	p=0.0001
Lumpectomy (without axillary surgery)	43 minutes (n=47)	45 minutes (n=40)	p=0.7282
Lumpectomy + SLNB	57 minutes (n=73)	62 minutes (n=64)	p=0.0911
Lumpectomy + ALND	110 minutes (n=2)	89 minutes (n=2)	p=0.0817
SPECIMEN VOLUME (mean)			
Volume in excess of size of tumor in invasive cancers	54.9 cm3 (n=93)	66 cm3 (n=75)	p=0.3461
Total volume of tissue for excisional biopsies	34 cm3 (n=69)	27 cm3 (n=68)	p=0.2577
PAIN (number of narcotic doses administered in the recovery room)			
Excisional biopsy	0.13 (n=69)	0.14 (n=68)	p=0.8114
Lumpectomy (without axillary surgery)	0.26 (n=47)	0.35 (n=40)	p=0.5425
Lumpectomy + SLNB	1.3 (n=73)	0.71 (n=64)	p=0.0006
Lumpectomy + ALND	1.5 (n=2)	0 (n=2)	p=0.0955
RE-EXCISION RATE			
Re-excision rate	14.8% (n=122)	26.4% (n=106)	p=0.0322

PT31

Frequency of Sentinel Lymph Node (SLN) Metastases in Triple Negative Breast Cancer (TNBC) Versus Non-TNBC T. Ivanics,* L. Petersen, D. Nathanson, M. Davis, L. Susick, A. Lehrberg, I. Rakitin, J. Bensenhaver, E. Proctor, L. Newman. *Surgery, Henry Ford Hospital, Detroit, MI.*

Introduction: Primary tumor size has historically had a direct correlation with risk of nodal metastatic disease, and adjuvant chemotherapy is recommended for the majority of node-positive breast cancers. The published literature to date however, has revealed inconsistent data regarding associations between nodal status and size of TNBC tumors. Studies revealing high rates of nodal metastases among cases of small TNBC therefore raise questions regarding the value of breast cancer screening to detect subclinical TNBC among populations at increased risk for this phenotype, such as African Americans (AAs). Our goal was to evaluate nodal status correlated with primary tumor size in a diverse population treated in metropolitan multi-hospital health care system. Methods: We utilized an IRB-approved, prospectively-maintained database of patients (pts) undergoing SLN biopsy for clinically node-negative breast cancer. Results: A total of 2,438 SLN pts 1998 to 2017 were evaluated (median age 61, range 24-94 years); 897 AA (36.8%; median age 60 years) and 1,541 WA (63.2%; median age 63 years). Frequency of TNBC was 17.3% (155/897) among the AAs compared to 11.4% (175/1541) among White Americans (WAs) ($P<0.01$). Overall frequency of metastatic SLNs was similar for TNBC compared to non-TNBC pts (19.9% versus 21.0%) and for AAs compared to WAs (19.7% versus 21.5%). Mean tumor size (cm) was larger for the SLN-positive compared to SLN-negative cases (2.28 versus 1.58; $p<0.01$). Mean primary tumor size was also larger for the TNBC compared to non-TNBC cases (2.1 versus 1.8; $p<0.05$). Correlations between larger primary tumor size and increased frequency of SLN mets persisted after stratifying for race and for TNBC versus non-TNBC phenotype (see figure). Conclusion: In contrast to studies demonstrating that risk of nodal metastases is similar regardless of tumor size in TNBC, we found a direct correlation between tumor size and nodal status which was similar for AA and WA women. Early detection of TNBC can therefore reduce the likelihood of pts needing adjuvant chemotherapy and may reduce breast cancer outcome disparities between AA and WA pts.



Correlation between primary tumor size and SLN metastases after stratifying for race and for TNBC vs. non-TNBC phenotype

PT32

Effect of the Affordable Care Act on Breast Cancer Care in a Safety Net Hospital V. Satyananda,* G. Eckel, C. Dauphine, J. Ozao-Choy, K.T. Chen. *Harbor UCLA Medical Center, Torrance, CA.*

Background: The Affordable Care Act (ACA) mandated expansion of Medicaid and allowed for creation of healthcare exchanges in order to increase access to basic health care services, such as cancer screening, for uninsured, underserved populations. We hypothesized that the effect on overall breast cancer care would be increased utilization of cancer services and earlier detection rates. We sought to evaluate the actual effect of the ACA on breast cancer care at a tertiary care, safety net hospital in Los Angeles County Methods:We performed a retrospective review of our tumor registry patients who were diagnosed with breast cancer between 2011 through 2016. We divided the patients into two cohorts; those diagnosed in the years 2011-2012 (pre-ACA implementation, group 1) and 2015-2016 (post-ACA implementation, group 2). Patient and clinical data, including payer source, method of diagnosis, and stage at presentation, were collected, and the two cohorts were analyzed and compared Results:After the implementation of the ACA, there was a decrease in number of breast cancer cases treated, from 309 patients in group 1 to 203 patients in group 2 ($p<0.008$), although there were no differences in number of screening mammograms performed (average per year, 2384 vs. 2864, p NS). There were no differences between groups in age at diagnosis (median 54 vs. 55 years), mammography detected cancers (40% vs. 37%), or clinical stage at diagnosis (Table 1). The number of patients who reported as self-pay at the time of diagnosis was 28% in group 1 and 5% in group 2 ($p<0.0001$). Conclusion:There was a significant decrease in the number of breast cancer cases treated at a safety net hospital immediately following implementation of the ACA, although there were no differences in number of screening mammograms performed. This may have been due to expanded insurance options for patients. There was also a significant decrease in the number of patients who reported as self-pay. Although there was a slight trend towards earlier stage at diagnosis, this was not significant. Long-term follow up across different health care systems will be necessary to fully evaluate the global impact of the ACA on breast cancer care.

Table 1. Clinical stage at diagnosis, Group 1 vs. Group 2

Clinical Stage	Group 1(n=309)*	Group 2 (n=203)	p value
Stage 0	38(12%)	23(11%)	NS
Stage 1	82(27%)	56(28%)	NS
Stage 2	89(29%)	67(33%)	NS
Stage 3	47(15%)	23(11%)	NS
Stage 4	36(12%)	17(8%)	NS

*insufficient data for 34 patients overall

PT33

Expression of miR34a Predicts Breast Cancer Survival J.C. Sporn,* E. Katsuta, L. Yan, K. Takabe. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

INTRODUCTION: miRNAs are a diverse family of RNA molecules. They are about 18 to 24 nucleotides in length and regulate translation and stability of partially complementary target mRNAs. It has been shown that miRNA expression is severely dysregulated in cancer cells. miR-34a was found to be a direct target of p53 exhibiting tumor suppressor activity in certain models. Downregulation of miR-34a was shown to be associated with worse prognosis in select breast cancer cohorts. Interestingly, miR-34a expression was also linked to downregulation of SIRT1, an NAD+-dependent enzyme involved in a variety of cellular pathways including stress-response and chromatin-silencing. SIRT1 itself was found to be downregulated in BRCA1-associated breast cancer compared with normal controls which led to an increased expression of survivin. Inhibition of BRCA1-mutant tumor growth was on the other hand associated with upregulation of SIRT1 activity. This suggests a more complex role of miR34a in breast cancer than what it is explained solely by its tumor suppressor function. METHODS: We utilized the TCGA dataset and analyzed the expression of miR-34a-5p in human breast cancer patients. To link the expression levels with the provided survival data, we used the OncoLnc platform. 988 patients were divided into two equal groups (low versus high expression). Cox regression was performed and a Kaplan plot was calculated. We further analyzed the expression levels of SIRT1 to SIRT7 in the groups with low and high expression of miR-34a. RESULTS: miR-34a expression ranged from 13.9 to 134.6 in the 'low' and from 134.7 to 639.1 in the 'high' expression group. Survival analysis showed that high expression of miR-34a was associated with worse prognosis (p-value=0.0123). Interestingly, high expression correlated with older age and diminished SIRT1 levels (both $p<0.001$). CONCLUSION: Contrary to prior findings, our analysis shows that high expression of miR34a was associated with worse outcome in a large breast cancer cohort. High levels of miR-34a were associated with downregulation of SIRT1 which is in line with prior findings. Our data supports the important link between miR-34a and SIRT1 and argues for a complex role of miR34a in breast cancer.

PT34

Immediate Breast Reconstruction and Post-mastectomy Radiation Therapy: Two Safe and Complementary Entities K. Boulva,* N. Shahvary, L. Meloche-Dumas, D. Mathieu, N. Cote, M. Al Khaldi, I. Fortin, R. Younan, E. Patocskai. *University of Montreal, Montreal, QC, Canada.*

Adjuvant radiotherapy post-mastectomy has been proven to increase disease-free survival (DFS) and overall survival (OS) rates in women with locally advanced breast cancer. Also, immediate breast reconstruction (IBR) post-mastectomy offers important psychosocial benefits and decreased morbidity as compared to delayed reconstructive surgery. There is currently controversy in the literature regarding the safety of post-mastectomy radiotherapy (PMRT) after IBR with regards to compromised treatment plans and the possibility of increased radiation toxicity. An increasing number of centers promote PMRT after IBR, but some remain reluctant. This study aims to demonstrate that, with advances in radiotherapy technologies, adequate and safe PMRT can be offered to patients after IBR. This retrospective study includes patients with breast cancer who underwent IBR post-mastectomy with adjuvant radiotherapy. Whole breast irradiation at 50 Gy in 25 fractions was used, with lymph node coverage when indicated. Treatments were delivered by tangential irradiation, tomotherapy or deep inspiration breath-hold (DIBH). Toxicities were graded according to the Common Terminology Criteria for Adverse Effects v4.0. Disease control and survival rates were calculated by Kaplan Meier curves. Seventy-one patients treated with PMRT after IBR between August 2006 and April 2015 were included. Median follow-up was 39 months. An adequate radiotherapy dose was administered without treatment delay to 66 (93%) patients. Fifty-seven patients received lymph node coverage. Tangential irradiation was used in 59 patients, whereas 10 patients were treated with tomotherapy and 2 in DIBH to reduce cardiac doses induced by treatment of left breast lesions or coverage of internal mammary chains. Grade ≤ 2 skin toxicities were observed in 49 patients. At 3 years, local control, DFS and OS were respectively 98%, 87% and 94%. With newly developed radiotherapy technologies, the vast majority of IBR post-mastectomy patients can obtain adequate radiotherapy without treatment delay. In our experience, only low-grade skin toxicities were reported with excellent tumor control.

PT35

Comparing Breast Surgery Choices After Neoadjuvant Therapy and a Surgery First Approach A. Elias,* T. Lasseter, T. Gibson, Z. Li, E. Gabriel, S. Bagaria, S.A. McLaughlin. *Surgery, Mayo Clinic, Jacksonville, FL.*

Background Clinicians cite the opportunity to downstage breast cancers (BrCa) and improve breast conservation (BCS) rates as the reason for recommending neoadjuvant chemotherapy (NAC). However, prospective NAC BrCa studies have not demonstrated higher rates of BCS than a surgery first (SF) approach and are unable to quantify post-NAC eligible BCS patients who chose mastectomy (Mx). Herein, we sought to compare patient surgical choices and outcomes after NAC or SF. Method We retrospectively identified 1473 women with operable BrCa undergoing surgery at our institution from 7/07-6/16. Two surgeons prospectively recorded patient BCS eligibility, use of NAC, and final surgery performed. We analyzed surgical outcomes, pathological variables, and local recurrences. Results Overall, 160/1473 (11%) women had NAC while the remaining 1313 had SF. Those having NAC were more likely ER-/HER2- or HER2+, younger, larger tumor sizes (median 2.6 vs 1.2cm), and node positive (59% vs 4%), all $p<0.0001$. Pathologic complete response occurred in 44% HER2+, 21% ER-/HER2-, and 10% ER+/HER2- NAC patients. At presentation 28/160(19%) NAC and 1002/1313(79%) SF pts were eligible for BCS ($p<0.0001$). NAC downstaged 63/132 (48%) patients making BCS ultimately possible in 90/160(58%) and chosen by 66/91(73%) NAC women. Downstaged tumors were equally distributed among ER/HER2 subtypes ($p=0.72$). Table 1 categorizes final surgical outcomes by eligibility and choice. Overall, fewer women chose BCS after NAC than SF (73% vs 80%, $p = 0.001$). Need for re-excision, 30d complications, and 5yr LRR rates were not statistically different among all BCS cohorts (all $p>0.10$) but those having BCS after NAC had larger specimen volumes (40 vs 30cm^3, $p=0.018$). Conclusion NAC increases eligibility for BCS, however statistically fewer women chose BCS after NAC than SF despite similar outcomes. Understanding patient preferences is critical to appropriately educating patients on surgical decisions after NAC.

	NAC Initially BCS eligible N=28/160 (18%)	NAC Downstaged made BCS eligible N=63/132 (48%)	Surgery first Eligible for BCS N=1002/1313 (79%)	P
Progressed	1(4%)			
Chose Mx	2(7%)	22(35%)	201(20%)	0.008
Chose BCS	25(89%)	41(65%)	801(80%)	

PT36

Advanced Breast Cancer at Diagnosis: Over 1/3 of Patients Adherent to Screening Recommendations O. Friedman-Eldar,[1]* S. Gur,[2] H. Giy-Chen,[2] E. Sharon,[1] N. Ben Baruch,[3] T.M. Allweis.[4] *1. Dept of Surgery, Rabin Medical Center, Petah Tikva, Israel; 2. Dept of Plastic Surgery, Kaplan Medical Center, Rehovot, Israel; 3. Dept of Oncology, Kaplan Medical Center, Rehovot, Israel; 4. Sarah Markowitz Breast Health Center, Kaplan Medical Center, Rehovot, Israel.*

Background: Advanced breast cancer (BC) at the time of diagnosis carries a worse prognosis. Delay in diagnosis (over 3 months between onset of symptoms and diagnosis) may be patient or physician dependent, but advanced BC at diagnosis is not necessarily the result of a delay. Better understanding of the factors related to advanced BC at diagnosis could help in decreasing the proportion of such cases. Patients & Methods: This is a retrospective single institution study of patients diagnosed with BC between 2012 - 2015. Data were collected from medical records and phone interviews, and included demographics, clinical and tumor related data, and knowledge of and adherence to screening guidelines. Results:Five hundred fifty five consecutive newly diagnosed BC patients were identified, 390 patients (70.2%) with early BC, and 165 (29.7%) with advanced or metastatic BC (stage IIb-IV). The average age was similar in both groups (61.8 vs. 60.6 years, $p=0.36$). However, 74 (19%) of patients diagnosed early were under the age of 50, compared with 48 (29.2%) of those diagnosed late ($p=0.006$). Late diagnosis was also associated with higher grade and proliferation rate, Her2/neu over expression, luminal B like and triple negative phenotype. Among patients with advanced BC at diagnosis, 38.7% had had a mammogram within the 30 months prior to diagnosis, compared with 67.5% of patients diagnosed early ($p=0.003$). Only 10.3% of patients with advanced BC at diagnosis were diagnosed by screening, while 84.8% were diagnosed following clinical symptoms. Of the 140 patients who were diagnosed following clinical symptoms, a delay in diagnosis occurred in 36 (25.7%), and the majority of delays were patient related. Conclusions: Early

diagnosis of BC is associated with higher adherence to screening mammography, bur over 30% of patients with advanced BC at diagnosis had undergone a screening mammogram every 2 years as recommended. Further research is needed to fully elucidate the factors related with advanced BC at diagnosis, current screening guidelines need to be reviewed, and more effective screening modalities need to be developed.

PT37

The Role of Tattooing Biopsied Axillary Lymph Nodes in Patients Undergoing Neoadjuvant Therapy R. Patel,* N. Choy, J. Tsai, S. Pal, J. Lipson, I. Wapnir. *Surgery, Stanford University, Menlo Park, CA.*

Background. Preoperative evaluation of axillary lymph node (ALN) status is crucial to accurate clinical staging in breast cancer and plays a pivotal role in guiding treatment. Many patients presenting with clinically positive nodal disease that undergo neoadjuvant therapy (NAT) have a favorable response that can make excision of previously involved axillary lymph nodes difficult at the time of surgery. Methods. Women who planned to undergo NAT that presented with palpable or suspicious ALNs on preoperative imaging were tattooed with black ink (GI Spot ink) at the time of fine needle aspiration or core biopsy. A total of 0.1 to 0.5 ml of ink was injected into the cortex of the biopsied ALN and perinodal soft tissue after sampling was completed. The anterior surface of the node was targeted. Lymphatic mapping was carried out using injection of both peritumoral Isosulfan blue dye and periareolar Technetium sulfur colloid injections. The concordance between sentinel and tattooed nodes were evaluated. Results. Fifty-nine patients have been tattooed preoperatively and 40 patients underwent post-NAT (38 chemotherapy, 2 endocrine/targeted therapy) surgery to date. Of these, 34 (82.5%) were node positive before and 15 (37.5%) remained node positive after NAT. The average number of days from tattoo to surgery was 142 days (71 to 223 days). The tattooed node(s) were identified in all cases. The tattooed node identified a lymph node with carcinoma or treatment effect in 7 nodes that did not take up the Isosulfan blue or radiotracer. All sentinel nodes in node positive cases contained black ink tattoo within the node or perinodal fat. Of the 17 patients whose nodes were initially positive and were subsequently downstaged as node negative following NAT, 5 (29.4%) demonstrated histologic treatment effect. Conclusion. Tattooed ALNs that have been biopsied in patients undergoing NAT are easily identified at the time of definitive surgery and complement lymphatic mapping procedures while decreasing the patient discomfort and added hospital costs associated with additional localization procedures utilized to ensure excision of biopsy proven lymph node metastasis.

PT38

Clinical and Pathologic Stage Discordance is Associated with Breast Cancer Prognosis J.K. Plichta,* S.M. Thomas, R.A. Greenup, O.M. Fayanju, L.H. Rosenberger, N. Tamirisa, T. Hyslop, E.S. Hwang. *Surgery, Duke University Medical Center, Durham, NC.*

Background: Clinical staging is often used to estimate prognosis when breast cancer is diagnosed, although staging may change following surgery. The concordance of clinical and pathologic staging is unknown. We aim to compare overall survival (OS) between the clinical stage at diagnosis and pathologic stage following surgery. Methods: Adults with clinical stage I-III breast cancer were identified from the National Cancer Data Base (2004-2014), excluding those who received neoadjuvant therapy. Stages were defined by the AJCC 8th ed. Concordance was defined as equivalent clinical and pathologic stages; discordance was defined as any difference in stages. Multivariate logistic regression was used to identify factors associated with stage discordance. The Kaplan-Meier method was used to estimate 5y and 10y OS. A Cox proportional hazards model was used to estimate the effect of stage discordance on the adjusted OS. Results: 398,796 patients were identified; median age 62y; median followup 38 months. The majority were women with early-stage, ER+, PR+, HER2-, invasive ductal carcinoma. Stage concordance was observed for 81.1%, while 14.9% were upstaged (varying by stage 12.9-22.6%) and 4% were downstaged (0.1-11.6%). Discordance was associated with race/ethnicity, HER2- status, and higher clinical stage. Concordance was associated with older age, ER- status, PR- status, and lumpectomy receipt. Unadjusted OS was worse for upstaged patients (5y OS rate: 0.83 upstage-discordance vs 0.88 downstage-discordance vs 0.9 concordance). After adjusting for covariates, downstaging was protective (HR 0.75, 95% CI 0.69-0.81), while upstaging portended a worse prognosis (HR 1.75, 95% CI 1.69-1.82; p<0.001). When comparing the same clinical and pathologic stages, differences in 5y OS were smaller (median 2.2%, range 0.1-5%) than those at 10y (median 5%, range 2-12.6%; Table). Conclusions: Surgical staging remains an important aspect of breast cancer treatment, as it often changes the disease stage. Among patients having surgery first, discordance in pathologic and clinical staging is associated with a worse overall survival, which may be important in counseling and multidisciplinary treatment planning.

Stage changes and overall survival rates by clinical and pathologic stage

	Downstage N (%)	Upstage N (%)	Any Stage Change N (%)	5- Year Survival Rate (95% CI)		10-Year Survival Rate (95% CI)	
				Clinical	Pathologic	Clinical	Pathologic
Stage IA	299 (0.1%)	27885 (12.9%)	28184 (13%)	0.925 (0.922-0.927)	0.926 (0.924-0.929)	0.764 (0.714-0.805)	0.792 (0.755-0.824)
Stage IB	9006 (10.6%)	13836 (16.2%)	22842 (26.8%)	0.894 (0.890-0.898)	0.905 (0.902-0.909)	0.733 (0.677-0.781)	0.713 (0.640-0.774)
Stage IIA	1931 (3.9%)	9278 (18.5%)	11209 (22.4%)	0.855 (0.849-0.860)	0.877 (0.871-0.882)	0.651 (0.572-0.720)	0.701 (0.616-0.770)
Stage IIB	844 (7.2%)	2683 (22.6%)	3527 (30%)	0.826 (0.814-0.837)	0.848 (0.837-0.858)	0.594 (0.462-0.703)	0.699 (0.623-0.763)
Stage IIIA	2565 (11.1%)	5019 (21.6%)	7584 (32.9%)	0.770 (0.761-0.779)	0.797 (0.788-0.806)	0.612 (0.544-0.672)	0.558 (0.466-0.641)
Stage IIIB	476 (10.4%)	669 (13.8%)	1145 (25.1%)	0.691 (0.668-0.713)	0.741 (0.726-0.756)	0.514 (0.403-0.615)	0.481 (0.343-0.605)
Stage IIIC	922 (11.6%)	101 (0.1%)	1023 (12.8%)	0.588 (0.572-0.604)	0.598 (0.585-0.611)	0.361 (0.202-0.522)	0.487 (0.443-0.529)

PT40

Radiation Therapy After Breast Conserving Therapy in Women 70 and Older: How Wisely Do We Choose? S. Downs-Canner,* E. Zabor, T. Wind, A. Cobovic, M. Morrow, A. Heerdt. *Memorial Sloan Kettering Cancer Institute, New York, NY.*

Introduction: Despite 10 year data from randomized trials supporting omission of radiation therapy (RT) for women >=70 with T1, estrogen receptor positive (ER+) tumors undergoing breast conserving therapy (BCT), RT usage nationally remains high. We reviewed our single institution experience to determine if factors associated with risk of local recurrence (LR) or decreased patient mortality risk informed RT use. Methods: Women 70 and older with T1, ER+, Her2 negative tumors undergoing BCT in 2010-2012 were identified from a prospectively maintained database. 10 year estimated mortality was calculated using the Suemoto index. The associations of clinicopathological features and mortality risk on receipt of RT were examined. Results: 329 patients with 333 tumors were identified. Median patient age was 75.9 (range 70-100), median tumor size was 1cm, and all patients were clinically node negative. 87.7% of patients had axillary evaluation (97.9% sentinel lymph node biopsy) and of those, 96.2% were pathologically node negative. 181 of 333 (54.4%) cancers were treated with RT. RT usage did not differ significantly by year of treatment. Use of RT decreased with age (74.6% in 70-74 year olds, 50.0% in 75-79 year olds, 32.7% in 80-84 year olds, and 10.7% in those over 85, p<0.001). Also, on univariable analysis, lower estimate of 10 year mortality (37% vs 51%, p<0.001), larger tumor size (1.1cm vs 0.9cm, p=0.024), and need for re-excision (71.1% versus 28.8%, p=0.009) were associated with use of RT. Factors associated with risk of LR (lymphovascular invasion and higher grade) were not associated with RT use. On multivariable logistic regression analysis, younger age (p<0.001), larger tumor size (p=0.002), and more re-excisions (p=0.045) were significantly associated with RT use. Conclusions: Over 50% of women received RT during the study period. No consistent features such as increased LR risk or lower mortality risk correlated with RT use. Future work should attempt to combine tumor features with competing mortality risk and patient preference to define which women in this age group will best benefit from RT.

Table: Clinicopathologic features associated with receipt of RT

	Overall (n=333)	No radiation (n=152)	Radiation (n=181)
Median age at surgery**	75	78	74
Receipt of RT by age**			
70-74	142 (42.6%)	36 (25.4%)	106 (74.6%)
75-79	108 (32.4%)	54 (50%)	54 (50%)
80-84	55 (16.5%)	37 (67.3%)	18 (32.7%)
85 and older	28 (8.4%)	25 (89.3%)	3 (10.7%)
Estimated 10-year mortality risk*	43%	51%	37%
70-74		32%	29%
75-79		48.5%	43%
80-84		71%	63%
85 and older		79%	85%
Tumor size**	1 cm	0.9 cm	1.1 cm
Lymphovascular invasion			
Not Present	283 (85%)	133 (47%)	150 (53%)
Present	50 (15%)	19 (38%)	31 (62%)
Grade			
Well differentiated	40 (12%)	21 (52.5%)	19 (47.5%)
Moderately differentiated	93 (27.9%)	44 (47.3%)	49 (52.7%)
Poorly differentiated	160 (48%)	68 (42.5%)	92 (57.5%)
Unknown	39 (11.7%)	19 (48.7%)	20 (51.3%)
Re-excision**			
No	281 (84.4%)	137 (48.8%)	144 (51.2%)
Yes	52 (15.6%)	15 (28.8%)	37 (71.2%)

**Significant on univariable and multivariable analysis

*Significant on univariable analysis only

PT41

The Impact of Insurance Status on Time to Surgery Among Breast Cancer Patients in Indiana S. Obeng Gyasi,[1]* L. Timsina,[1] K.P. Lipking,[1] K.K. Ludwig,[1] C.S. Fisher,[1] D.A. Haggstrom.[2] *1. Indiana University School Of Medicine, Indianapolis, IN; 2. VA HSR&D Center for Health Information and Communication, Indianapolis, IN.*

Introduction: Timeliness of care among breast cancer patients has been shown to affect overall and disease-specific mortality. However, there is a paucity of research on the interaction between insurance status at diagnosis and time to treatment. The objective of this study is to understand the implications of insurance status at diagnosis on time to surgery (TTS) among breast cancer patients in Indiana. Methods: Data was obtained using the Indiana cancer registry and the Indiana Network for Patient Care. Women, ages 18-90, diagnosed with stage 0-III breast cancer from 01/01/2008-12/31/2014 were included in the study. Patients who received neoadjuvant chemotherapy were excluded. The timeframe from biopsy proven diagnosis of breast cancer to first definitive surgery was assessed. Surgical delay was defined as TTS ≥ 60 days. The data was divided into four insurance groups: uninsured, private, Medicaid, and Medicare. Bivariate intergroup analysis and a multivariable logistic regression model were used to evaluate factors associated with surgical delay. Results: The total study sample included 11,877 breast cancer patients. 11% of subjects in the study experienced surgical delay and the median TTS was 29 days (IQR 20-43). Patients with Medicaid and private insurance were more likely to have their diagnostic biopsy and definitive surgery at different institutions (p=0.0001). There was significant variation in TTS among insurance groups (p=0.0001). The median time to surgery was 25 days uninsured (IQR 16-40), 28 days Medicare (IQR 20-42), 29 days private (IQR 20-44), and 34 days for Medicaid (IQR 21-52). In multivariable analysis, Medicaid insurance (OR 0.55; 95% CI: 0.42, 0.74), black race (OR 0.45; 95% CI: 0.36, 0.56), mastectomy (OR 0.66; 95% CI: 0.54, 0.81), plastic surgery consult (OR 0.40; 95% CI: 0.30, 0.52) and multiple comorbidities (OR 0.35; 95% CI: 0.22, 0.57) reduced the probability of surgery within 60 days of biopsy. Conclusion: Breast cancer patients in Indiana with Medicaid are the most likely insurance group to experience surgical delay. This suggests Indiana Medicaid patients may experience disproportionate barriers in access to definitive surgical treatment.

PT42

3-D Tomosynthesis for Intra-Operative Margin Assessment During Breast Conserving Surgery D. Black,* G. Rauch, J. Leung, C. Park, A. Sahin, H.M. Kuerer. *Breast Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Background: Intra-operative margin assessment for breast cancer patients undergoing segmental mastectomy (SM) enables excision of additional tissue during the first surgery to obtain clear margins. Returning to the operating room for re-excision ranges from 15-40%, resulting in increased complications and healthcare costs. This study's aim is to determine the ability of 3-D tomosynthesis (tomo) to detect positive margins compared to 2-D imaging. Methods: With IRB approval, SM specimens underwent intra-operative processing with 2-D imaging of the intact and sliced tissue with review by a breast radiologist. Gross assessment of the margins was performed by a breast pathologist. These findings guided the surgeon to excise additional tissue. 3-D tomo images of intact specimens were prospectively obtained and retrospectively reviewed by a breast radiologist. Results: From November 2016 to September 2017, 98 patients underwent 99 SMs. Fourteen (14%) initial specimens had tumor at ink; all were identified intra-operatively (100%) with standard extensive processing (SEP). With additional tissue excised based on SEP guidance, 6 cases (6%) had final margins with tumor at ink. 3-D tomo identified 13 of the 14 initial specimens with tumor at ink (93%). Ten patients (10%) had a second surgery for positive/close margins. With SEP, 75 (76%) cases had additional tissue excised with 16 (21%) having malignancy. With 3-D tomo, 32 cases were read as having tumor at ink (32%), correctly identifying 11 of the 16 cases (69%) with malignancy in the additional excised tissue. For the five specimens in which 3-D tomo did not identify tumor at ink, four had DCIS in the additional excised tissue and 1 had invasive disease. Conclusions: 3-D tomo is an accurate method for detecting positive SM margins intra-operatively, performing similar to more labor intensive processing. It resulted in potentially 38% fewer cases being recommended for unnecessary additional tissue excision. 3-D tomo primarily missed residual DCIS. Prospective studies are needed to evaluate the surgeon's ability to analyze 3-D tomo specimen images for obtaining negative margins during the first surgery.

PT43

National Trends in Radiation Treatment for DCIS R.L. Arlow,[1]* A.D. Williams,[1] S. Reyes,[1] K. Yoon-Flannery,[2] R. Mustafa,[3] L.M. De La Cruz,[1] D.N. Anderson,[1] S. Ugras,[1] A.D. Brooks,[1] D. Sataloff,[1] G.M. Freedman,[1] J. Tchou.[1] *1. University of Pennsylvania, Philadelphia, PA; 2. Kennedy Comprehensive Breast Center, Sewell, NJ; 3. Saint Peter's University Hospital, New Brunswick, NJ.*

Introduction: Treatment of ductal carcinoma in situ (DCIS) is one of the most controversial topics in the field of breast surgery. Adjuvant radiation therapy for the treatment of DCIS varies, with current recommendation deeming it safe for older patients with low grade, small tumors and at least 3 mm negative margins to forego radiation. The purpose of this study was to examine recent national trends in adjuvant radiation therapy for DCIS. Methods: Using the National Cancer Database (NCDB) we conducted a retrospective review of all patients with DCIS who underwent lumpectomy from 2004 to 2014. Patients were stratified into groups based on whether or not they had undergone radiation. We compared the demographic and clinical characteristics of these groups using chi-square and independent t-tests. Results: Of the 164,930 patients who underwent lumpectomy for DCIS, 70% (115,621 patients) underwent adjuvant radiation therapy and 28% (46,494 patients) did not. We found statistically significant differences between the two groups in age, ethnicity, facility location and type, patient insurance, educational attainment for the region, income, distance between the patient's residence and hospital, and Charlson co-morbidity score. Expected trends such as older patients, those that lived further from the treatment center, and those with a higher co-morbidity score, for example, were more likely to have radiation omitted ($P < 0.001$). Interestingly, a larger percentage of patients who had radiation omitted had positive margins (4.8%, versus 3.2% with radiation, $P < 0.001$). In addition, 22 percent of patients who did not receive radiation had poorly differentiated or undifferentiated tumors ($P < 0.001$). Conclusion: Patients who underwent adjuvant radiation therapy for DCIS have statistically different baseline characteristics than those who did not receive radiation. This study demonstrates that the omission of adjuvant radiation therapy extends beyond our current national treatment guidelines, including those with high-grade tumors and positive margins. Further investigation is warranted to determine the lack of adherence to treatment guidelines for DCIS, particularly in the setting of adjuvant radiation therapy.

	Radiation (N = 115621)	No Radiation (N = 46494)	P-Value
Age (Years)	59.6 ± 11	64.1 ± 13	<0.001
Race/Ethnicity (Number (Percent))	95917		
White	(83.0)	38243 (82.3)	
Black	13542	5567 (12.0)	<0.001
Other	(11.7)	2059 (4.4)	
Unknown	4990 (4.3)	625 (1.3)	
	1172 (1.0)		
Facility Location (Number (Percent))	8437 (7.3)		
New England	17109		
Middle Atlantic	(14.8)	3487 (7.5)	
South Atlantic	26554	7920 (17.0)	
East North Central	(23.0)	11447 (24.6)	
East South Central	23490	7055 (15.2)	<0.001
West North Central	(20.3)	2468 (5.3)	
West South Central	6244 (5.4)	1937 (4.2)	
Mountain	8462 (7.3)	3501 (7.5)	
Pacific	6777 (5.9)	2123 (4.6)	
	4739 (4.1)	5803 (12.5)	
	11854		
	(10.3)		
Facility Type (Number (Percent))	12557		
Community Cancer Program	(10.9)		
Comprehensive Community Cancer Program	57609	5283 (11.3)	
Academic/Research Program	(49.8)	22361 (48.1)	<0.001
(includes NCI-designated comprehensive cancer centers)	30719	12899 (27.7)	
Integrated Network Cancer Program	(26.6)	5198 (11.1)	
	12781		
	(11.1)		
Primary Insurance (Number (Percent))	1661 (1.4)		
Not Insured	70211	659 (1.4)	
Private Insurance / Managed Care	(60.7)	22311 (48.0)	
Medicaid	4709 (4.1)	1680 (3.6)	<0.001
Medicare	36169	20586 (44.3)	
Other Government	(31.3)	360 (0.8)	
Insurance Status Unknown	1106 (1.0)	898 (1.9)	
	1765 (1.5)		
Educational Attainment for Patient's Area of Residence (Number (Percent))	14582		
21% or more	(12.6)		
13% - 20.9%	26612	6523 (14.0)	
7%-12.9%	(23.0)	10631 (22.9)	<0.001
Less than 7%	39273	15204 (32.7)	
	(34.0)	13598 (29.2)	
	34270		
	(29.6)		
Income (Number (Percent))	15806		
Less than $38,000	(13.7)		
$38,000 - $47,999	23722	6679 (14.4)	
$48,000 - $62,999	(20.5)	9029 (19.4)	
$63,000 +	31015	11905 (25.6)	<0.001
	(26.8)	18327 (39.4)	
	44153		
	(38.2)		

Demographic and clinical characteristics of all patients in NCDB who underwent lumpectomy for DCIS between 2004 to 2014, with and without radiation.

PT44

Breast MRI After Neoadjuvant Chemotherapy Does Not Change Clinical or Surgical Management and May Be Eliminated in Patients Desiring Mastectomy A.Y. Merrill,[1]* S. Renfroe,[1] E. Hill,[1] R. Henry-Tillman,[1] D. Ochoa,[1] V.S. Klimberg,[2] M. Preston,[1] I. Makhoul,[1] A. Pennisi,[1] L. Peacock,[1] S.G. Routon,[1] G. Bryant-Smith.[1]
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Background: Neoadjuvant chemotherapy (NAC) downstages breast and axillary disease to improve operability and eligibility for breast-conserving surgery (BCS) in both locally advanced and early-stage breast cancer. Despite the ability of MRI to identify candidates for BCS and predict a pathologic complete response (pCR), women whose cancers are downstaged with NAC continue to choose mastectomy. The objective of this study was to determine if MRIs obtained after NAC result in a change in clinical or surgical management. Methods: We identified 164 women with stage I-IV invasive breast cancer who underwent breast MRI before and/or after NAC and surgical resection at our institution between May 1, 2014 and June 30, 2017. We evaluated eligibility for BCS, pre-treatment surgical preference, the use of breast MRI, the frequency that MRI changed clinical or surgical management, and pathologic response. Results: Of the 164 cohort, 114 subjects (69.5%) presented with locally advanced, node-positive, or metastatic breast cancer. Prior to NAC, 97 patients (59.1%) had a preference for mastectomy, 18 (11.0%) for BCS, and 49 (29.9%) were unstated. 150 of the 164 (91.5%) had an MRI after completion of NAC. None resulted in a clinical change, and only 4 (2.7%) resulted in a surgical change (3 from mastectomy to lumpectomy and 1 from lumpectomy to mastectomy). 39 of 94 patients (41.5%) who were not eligible for BCS upon presentation became eligible after NAC. Of the 109 patients eligible for BCS after NAC, 72 (66.1%) underwent bilateral and 5 (4.9%) unilateral mastectomy, and 32 (29.4%) underwent lumpectomy. Similarly, in the 42 patients with a pCR, 32 (76.2%) underwent bilateral and 1 (2.4%) unilateral mastectomy, and 9 (21.4%) underwent lumpectomy. Conclusions: Breast MRI obtained after NAC does not change management in patients with a pre-treatment preference for mastectomy. We recommend a highly selective rather than routine use of MRI after NAC to identify patients who are appropriate candidates for and willing to undergo BCS. Eliminating MRIs that do not impact clinical or surgical management will save on overall healthcare costs.

PT45

Genetic Testing in Breast Cancer Patients: Do Mutations Other than BRCA Make a Difference in Surgical Decision Making? A.C. Beck,* P. Imperiale-Hagerman, K. shipley, L. Erdahl, S.L. Sugg, R.J. Weigel, I.M. Lizarraga. *University of Iowa, Iowa City, IA.*

Introduction The use of multi-gene panel testing in management of breast cancer is increasing. Some moderate penetrance gene mutations are associated with increased breast cancer risk but evidence is lacking regarding the rate of contralateral prophylactic mastectomy (CPM). We examined results of panel testing and the rate of CPM in patients with breast cancer. Methods All subjects with genetic testing between January 2008 and December 2015 at a single institution were reviewed; 368 were identified, 191 of whom had unilateral breast cancer prior to testing and had surgery. Patients received genetic counseling based on NCCN guidelines after review in clinic or at tumor board. Testing modality, specifically multigene panel vs. BRCA only, was decided after discussion with the patient. A retrospective chart review examined demographics, tumor characteristics and genetic testing results. Associations were analyzed using Pearson's chi-squared test and multinomial logistic regression. Results Seventy of the 191 breast cancer patients (36.6%) had panel testing. Panel testing was done in 2/86 (2.3%) patients from 2008-2013 and 68/105 (64.7%) from 2014-2015. Testing identified 3 (4.2%) deleterious BRCA mutations, 8 (11.4%) deleterious mutations in a non-BRCA gene, 0 BRCA variants of unknown significance (VUS), and 15 (21.4%) non-BRCA VUS. The other deleterious mutations detected were in PMS2, PALB2, APC, PTEN, MUTYH, ATM, CHEK2 and BARD1. Of the 121 patients who underwent BRCA testing alone, 9 (7.4%) were found to have a deleterious mutation. Rate of CPM by mutation type is shown in Table 1. Only patients with a deleterious BRCA mutation had a significantly higher rate of CPM (p=0.012). This persisted on multivariate analysis with tumor stage and grade (p=0.018). Three patients with an abnormal finding in a non-BRCA gene elected CPM; only 1 had a mutation known to increase breast cancer risk. Conclusion Panel testing has become more common in breast cancer management and mutations in moderate risk genes have a higher prevalence rate than mutations in BRCA genes. Deleterious mutations in genes other than BRCA did not appear to inform the decision for CPM.

Table 1. Surgical Management after Genetic Testing

	Breast Conservation	Unilateral Mastectomy	Bilateral Mastectomy	p value
Total population (n=191)	90 (47.1%)	58 (30.4%)	43 (22.5%)	
BRCA deleterious mutation (n=12)*	4 (33.3%)	1 (8.3%)	7 (58.3%)	0.012
BRCA VUS (n=7)*	5 (71.4%)	1 (14.3%)	1 (14.3%)	0.316
Multi-gene panel testing (n=70)	34 (48.6%)	24 (34.3%)	12 (17.1%)	
Other deleterious mutation (n=8)	3 (37.5%)	3 (37.5%)	2 (25.0%)	0.680
Other gene VUS (n=15)	10 (66.7%)	4 (26.7%)	1 (6.7%)	0.082
No abnormality with testing (n=149)*	68 (45.6%)	49 (32.9%)	32 (21.5%)	

*Includes results from multi-gene panel testing and BRCA only testing.

PT46

Papillary Neoplasms Identified on Core Needle Biopsy Should be Excised Unless Atypia is Excluded R. Sidhu, K. Liu, R. Warburton, J. Pao, U. Kuusk, C. Dingee, E. McKevitt.* *Providence Health Care, Vancouver, BC, Canada.*

BACKGROUND: The management of papillary neoplasms (PN) of the breast identified on core needle biopsy (CNB) has evolved and routine excision of all PN is being questioned. Upstage rates to malignancy following excision of PN on CNB are reported between 5-38%. The purpose of this study was to evaluate the presence of malignancy following excision of CNB diagnosed PN at our center and to evaluate factors predictive of malignancy. METHODS: Patients having excision of high risk breast lesions at our regional breast center were identified from OR lists and chart review was performed to identify patients with PN identified on CNB between 2014 and 2017. The primary endpoint was rate of upstage to malignancy. The association of age,

center where CNB was performed, palpability, discharge, clinical exam size, imaging size, family history of breast cancer, and presence of atypia with upstage to cancer was evaluated. RESULTS: 959 patients having surgery for high risk lesions were identified with 195 having CNB diagnosis of PN. 171 patients had CNB diagnosis of papillary neoplasm, 7 patients CNB diagnosis of PN associated with atypical ductal hyperplasia/atypical lobular hyperplasia/ flat epithelial atypia, and 27 patients having a CNB diagnosis of atypical PN (APN). Twenty-three patients were upstaged to malignancy (11.8%) with 6 having invasive cancer, 1 encapsulated papillary carcinoma, and 16 with DCIS. Patients with a CNB diagnosis of APN had an upstage to malignancy rate of 58% (5 invasive cancer, 1 encapsulated papillary carcinoma, 13 DCIS). APN on CNB was associated with malignancy ($p<0.0001$) and other factors were not. When all APNs and other atypias were excluded from the analysis the upstage to malignancy rate was 1.2%. Atypia was not mentioned on the CNB report for these 2 patients. CONCLUSION: CNB diagnosis of APN has a 58% rate of upstage to malignancy at our regional center and we recommend excision for these patients. Papillary lesions without atypia have a low upstage to malignancy rate but the presence or absence of atypia is not always reported on CNB pathology reports. Clarification of the absence of atypia is needed prior to considering conservative management.

PT47

Utility of HER2 Retesting of Histologic Grade 3 Invasive Breast Carcinomas R. Gologorsky,[1]* K. Axelsson,[2] E. Hosfield,[2] V. Shim.[2]
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Current American Society of Clinical Oncology and College of American Pathologists guidelines recommend repeat evaluation of human epidermal growth factor receptor 2 (HER2) status on surgical specimens from patients diagnosed by core needle biopsy with grade 3 invasive breast tumors. Proper diagnosis of HER2 status is critical to treatment planning. Though these guidelines were designed to improve the accuracy of HER2 identification, doubt exists as to whether reflexive testing of grade 3 tumors achieves this goal. As a quality improvement project, we evaluated 98 patients from a single institution who were diagnosed between 2015-2017 with grade 3 invasive carcinomas of the breast to compare HER2 status on core biopsy versus excisional biopsy. HER2 testing was performed in accordance with ASCO/CAP guidelines via immunohistochemistry or fluorescent in-situ hybridization. Two of 98 patient specimens (2%) demonstrated positive - negative status discordance between core and excisional biopsy, both of whom were treated with trastuzumab. One of these patients, who had a history of contralateral invasive ductal carcinoma, had two concomitant invasive breast tumors with different hormone receptor profiles. The other patient was a BRCA1 mutation carrier. Four out of 98 specimens were HER2 equivocal by core biopsy and negative by surgical excision. One patient was HER2 negative by core biopsy and HER2 equivocal by surgical excision, and one patient was HER2 positive by core biopsy and HER2 equivocal by surgical excision; both patients were treated with trastuzumab. The treatment of one patient out of 98 was affected by HER2 retesting. Our findings suggest limited utility of standard HER2 retesting for all patients with grade 3 carcinomas of the breast due to low rates of clinically significant discordance. Patients whose core biopsy specimens are HER2 positive will likely receive HER2-targeted therapy regardless of the result of surgical specimen retesting, and therefore do not benefit from retesting. Further evaluation of patients who are HER2 negative by core biopsy and HER2 positive by surgical specimen may elucidate a population that benefits from reflexive retesting.

	CORE BIOPSY			SURGICAL BIOPSY			
CASE #	IHC	FISH	Interpretation	IHC	FISH	Interpretation	Trastuzumab
1	3+	N/A	P	0-1+	N/A	N	YES
2	1-2+	2.0	P	1-2+	1.8	E	YES
3	1+	N/A	N	1-2+	0.9	E	NO
4	2+	1.4	E	1+	N/A	N	NO
5	1+	N/A	N	2+	2.1	P	YES
6	2+	1.6	E	1+	N/A	N	NO
7	2+	1.9	E	1+	N/A	N	NO
8	2+	N/A	E	1+	N/A	N	NO

PT48

A Randomized Controlled Trial Evaluating the Impact of Pre-Consult Information on Patient Participation in Decision-making T. Stankowski-Drengler,[1]* J. Tucholka,[1] J. Bruce,[4] N.M. Steffens,[3] J.R. Schumacher,[1] C. Greenberg,[1] L. Wilke,[1] J. Steiman,[2] H. Neuman.[1]
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Introduction: We hypothesized that providing high quality treatment information to breast cancer patients prior to surgical consult would facilitate active participation in decision-making. The objective was to examine the impact of pre-consult information on patients' role in decision-making and the relationship between role and satisfaction with the decision process. Methods: Stage 0-3 breast cancer patients were randomized to be emailed prior to the surgical consult a link to standard websites (e.g. National Cancer Institute) versus a decision aid (n=227). 68% completed surveys after surgical consult and treatment completion (n=154) that assessed patients' perceptions on being asked preference for surgery type, role in decision-making, and satisfaction with the decision process. Chi square tests compared role in decision-making by randomization arm. Multivariable logistic regression assessed the relationship between satisfaction with the decision process and patient factors (demographics, surgery, role in decision-making), randomization arm, and surgeon. Results: Median age was 59 (27-80) years, 99% were white, and 88% had at least some college education. The majority perceived a shared role in decision-making (83%), though fewer reported being asked their surgical preference (63%). 62% were satisfied with the decision process (Table). Randomization arm was not associated with these outcomes ($p>0.05$). Whether patients reported being asked their surgical preference varied by surgeon ($p=0.001$) and education ($p=0.05$), with more educated patients less likely to report being asked. Patients not asked their preference reported less active roles in decision-making ($p<0.005$). There was no association between patient factors, randomization arm, or surgeon with satisfaction with the decision process. Conclusion: Although the majority of women reported a shared role in decision-making, only 62% were satisfied with the decision process. Further research must identify factors contributing to the low satisfaction with the decision process observed in order to identify opportunities to intervene.

Table. Satisfaction with Decision Process

	Agree %(n)	Disagree %(n)
I wish I had given more consideration to other surgical treatment options	39% (n=60)	61% (n=94)
I would like to have had more information when the decision about surgery was made	45% (n=70)	55% (n=84)
I would like to have been more active in making the decision about what kind of surgery to have	38% (n=59)	62% (n=95)
I did not have as much to say about what kind of surgery to have as I wanted	29% (n=44)	71% (n=110)
Overall satisfaction with decision process*	Low: 38% (n=58)	High: 62% (n=96)

*Satisfaction with Decision Process scale is scored on a Likert scale from 1-5 with the overall satisfaction score representing an average of the 4 individual questions; low satisfaction is defined as a score of <3

PT49

Is Sentinel Node Biopsy Necessary When Ductal Carcinoma In Situ with Microinvasion is Found on Core Biopsy? A. Phantana-Angkool,[1]* Y.E. Warren,[1] A.E. Voci,[1] C.A. Livasy,[2] L. Hadzikadic-Gusic,[1] T. Sarantou,[1] M.R. Forster,[1] D. Sarma,[1] I.N. Perry,[1] R.L. White.[1] *1. Levine Cancer Institute at Carolinas Medical Center, Charlotte, NC; 2. Carolinas Pathology, Charlotte, NC.*

Introduction: The aim of the study was to assess the upgrade rate to invasion and axillary lymph node metastasis in patients with ductal carcinoma in situ with microinvasion (DCISM) diagnosed by core-needle biopsy. We hypothesize the rate of metastasis to lymph node in patients diagnosed with DCISM on core biopsy is low and axillary surgery is not necessary. Methods: From 2006-2017, we retrospectively identified 137 patients with DCISM diagnosed on core biopsy, 70 of which were included in the study. 67 patients were excluded due to additional findings of macro invasive disease or prior history of breast cancer. Outcome data were analyzed. Fisher's exact tests for categorical factors and median two sample tests for continuous factors were utilized to identify characteristics associated with upstaging and positive nodes on final pathology. Time to event distributions were summarized with Kaplan Meier methods and factors associated with recurrence free survival were identified

with log rank tests. Results: All patients underwent breast conserving surgery or mastectomy: lumpectomy alone (N=2, 3%), lumpectomy with sentinel node biopsy (N=51, 73%), mastectomy with sentinel lymph node (SLN) biopsy (N =17, 24%). One patient had mastectomy with axillary dissection. 93% (N=65) had one focus of microinvasion. 7%(N=5) had multiple foci (>1) of microinvasion. 30%(N=21) were upgraded to invasive cancer at surgical excision (T1a =8,T1b=4,T1c=3,T2=2.). Of those with invasive cancer, 81% (N=17) had negative SLN biopsy; 19% (N=4) had SLN metastasis. 1 patient who was not upstaged to cancer had SLN metastasis. A total of 5 patients (7%) had SLN metastasis. Conclusion: With improvements in technology, DCISM on core biopsy is becoming more common. We reviewed our experience to find that while our upstage rate to invasive cancer is 30%, the likelihood of a positive SLN in the overall population of DCIS with microinvasion on core biopsy remains low (7%). In the ongoing discussion of utilization of healthcare dollars admixed to continued controversy over the management of DCIS, this warrants further discussion and evaluation with larger scale studies.

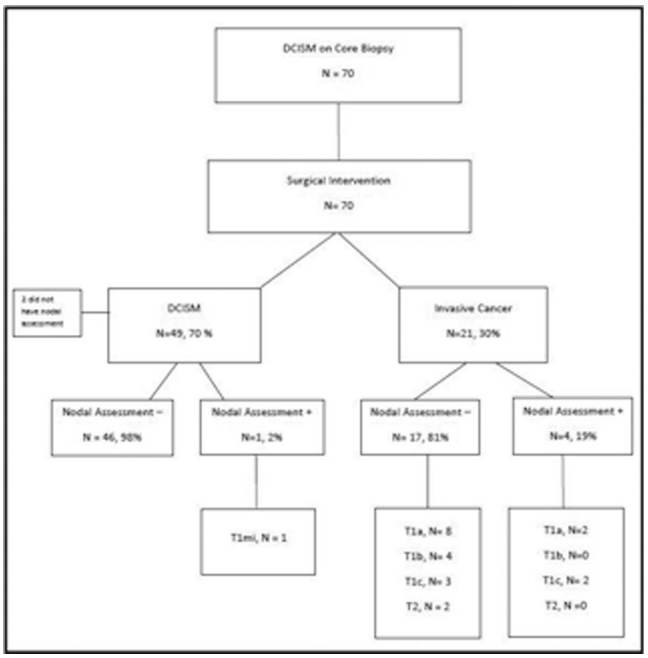


Diagram illustrating final pathology and nodal assessment results with associated tumor sizes of patients with DCISM found on core biopsy.

PT50

Comparison of Survival Outcomes in Node-Negative T1a and T1b High-risk Breast Cancer Treated with and without Adjuvant Chemotherapy K.A. Carlson,[1]* C.K. Thompson,[1] E.L. Siegel,[1] S. Kim,[1] J.J. Bao,[2] F. Amersi,[1] A. Giuliano,[1] A. Chung.[1] *1. Surgery, Cedars Sinai Medical Center, Los Angeles, CA; 2. University of Chicago, Chicago, IL.*

Introduction: There is controversy whether patients with early stage high-risk breast cancer (BC) benefit from adjuvant chemotherapy. This study aims to compare outcomes in patients with node-negative triple negative (TN) or HER2 positive (HER2+) T1a or T1b BC treated with and without adjuvant chemotherapy. Methods: Review of a prospectively maintained database identified 110 female patients with node negative T1a or T1b HER2+ or TN BC between 2000-2011. Data regarding patient and tumor characteristics and treatment received were collected. Overall survival (OS) and disease free survival (DFS) were compared between those who received adjuvant chemotherapy (Group 1) and those who did not (Group 2). Univariate and multivariable analyses were performed to identify factors that were associated with OS and DFS. Results: Among the 110 patients with high-risk tumors, 67 (60.9%) had HER2+ disease and 43 (39.1%) had TN breast cancer. Group 1: 31 (46.3%) patients with HER2+ BC, 17 (39.5%) patients with TN BC; Group 2: 36 (53.7%) patients with HER2+ BC, 26 (60.5%) patients with TN BC. Patients in Group 1 were younger (mean age: 53.7yrs vs. 60.6yrs, p=0.008) and had larger tumors (median: 7mm vs. 4mm, p=0.003). Of the patients with HER2+ BC, those in Group 1 were more likely to have also received hormone therapy (37.5% vs. 17.7%, p=0.20) and Herceptin (55.6% vs 0%, p <0.001) compared to Group 2. With a median follow up time of 6.98 years (95%CI:5.98-8.27) five-year DFS and OS rates were 89.66% and 93.18%, respectively. There was no difference in DFS (p = 0.268) or OS (p = 0.454) between Group 1 and Group 2. Tumor subtype (HER2+ or TN) was not associated with improved DFS (p = 0.213) or OS (p = 0.674). The use of adjuvant radiation therapy was associated with improved OS (HR: 0.19; 95% CI: 0.04-0.97;p=0.046) while there was a trend towards an improved OS in younger patients (p = 0.088). Conclusion: OS and DFS remain excellent for patients with Her2+ and TN node-negative T1a and T1b breast cancer regardless of the use of adjuvant chemotherapy. The addition of adjuvant chemotherapy may not confer a survival benefit in this patient population.

PT51

Racial Disparities and Survival Outcomes in Triple Negative Breast Cancer M. Nunez,[1]* G. Ortega,[1] A.R. McDowell,[2] L. Wilson.[2] *1. Howard University College Of Medicine, Clive O. Callender Howard-Harvard Health Sciences Outcomes Research Center, Washington, DC; 2. Howard University Hospital & College of Medicine, Washington, DC.*

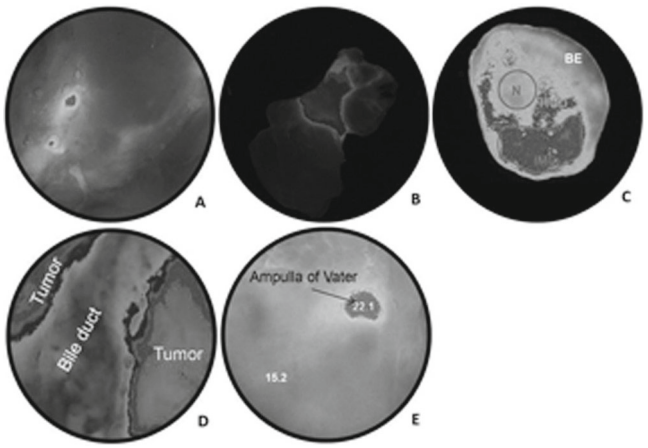
INTRODUCTION: Triple-negative breast cancer (TNBC) is responsible for a relatively large proportion of breast cancer deaths, despite its relatively small proportion among all breast cancer. The aim of this study is to analyze a large national database to evaluate the role of race/ethnicity on prognostic factors and survival outcomes in patients with TNBC. METHODS: We conducted a retrospective analysis using the U.S. National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) database. Inclusion criteria included female patients with a diagnosis of TNBC from 2010-2014. Patients were divided according to race in White or Black. Unadjusted and adjusted analysis were performed to determine the association of patient demographics, tumor characteristics and staging classifications with cancer specific mortality. RESULTS: A total of 32,933 patients were included, mean age at diagnosis was 59 years. Of these, 71.9% were White and 20.2% were Black. The most common histology and grade were ductal and lobular (91.7%) and Grade III: Poorly differentiated (74.4%), respectively. Stage Ia was the most common 33.9%, followed by Stage IIa 27.7%. Overall crude mortality rate was 16% and the cancer specific mortality rate was 10.6%. Mean age was 59 years and 57 years among Whites and Blacks respectively (p<0.001). Stage Ia was the most common for both groups (35.7% vs 28.3%). Regarding advanced stages, there was a higher prevalence in Black patients: Stage IIa 27.4%, vs. 27.5, Stage IIb 12.1% vs. 14.7%, Stage IIIa 6.5% vs. 8.6%, Stage IIIb 3.4% vs. 4.3%, Stage IIIc 3.5% vs. 3.9%, Stage IV 5.9% vs. 7.8%. Mean survival for White and Black patients was 26.4 and 25.3 months, respectively (p<0.001). Specific breast cancer related death was 61.63% and 65.91% among Whites and Black patients respectively. CONCLUSION: TNBC is not restricted to a specific age or ethnic group. However, advanced stages and increased in death rate are observed on women of African ancestry. These results might lead to the development of models that specifically capture the risk of Black women for TNBC, to increased access to effective early detection and to the implementation of health policies to eliminate disparities.

PT52

Use of a Cathepsin-Activatable Fluorescent Agent to Rapidly Distinguish Tumor Versus Normal Tissue in Multiple Tumor Types C. Lanahan,[1]* M.C. Specht,[1] M.A. Gadd,[1] B. Brigman,[2] D. Kirsch,[2] A.T. Chan,[1] D.A. Drew,[1] R. Tang,[1] D. Strasfeld,[3] E. Brachtel,[1] B.L. Smith.[1] *1. Massachusetts General Hospital, Boston, MA; 2. Duke University Medical Center, Durham, NC; 3. Lumicell, Inc., Wellesley, MA.*

Background: Improved options for real time detection of residual tumor at surgical margins and during endoscopy are needed. We assessed the LUM Imaging System for detection of malignancies in sarcoma, breast, esophagus, colorectal and pancreas specimens. This system detects far-red fluorescence produced at tumor sites by LUM015, a cathepsin-activatable imaging agent, allowing instantaneous tumor detection. Methods: Patients received intravenous LUM015 4±2 hours before surgical resection at 0.5, 1.0 or 1.5 mg/kg. Using the LUM Imaging System (Lumicell Inc., Wellesley MA), breast lumpectomy cavities were imaged in vivo and excised breast, sarcoma and GI malignancies were imaged ex vivo. The hand-held probe and LUM software

can acquire a 2.6 cm diameter image that detects and analyzes fluorescent signal in approximately 1 second. Tumor-to-normal, or signal-to-background, ratios were calculated and compared with standard histopathology. Results: 12 excised sarcoma specimens were imaged a mean 17.9 hours (range 4.8-30.9) after injection. Sarcomas imaged included malignant peripheral nerve sheath tumor, metastatic clear cell sarcoma, spindle cell carcinoma, myxofibrosarcoma, myxoinflammatory fibroblastic sarcoma, synovial sarcoma, undifferentiated pleomorphic sarcoma and well differentiated liposarcoma. Tumor-to-normal tissue signal ratios for sarcomas were 4.3±2.4 (n=12). 34 breast lesions (25 invasive ductal with or without ductal carcinoma in situ (DCIS), 4 invasive lobular and 5 pure DCIS) were imaged on average 4.6 hours (range 2.9-7.7) after injection. Tumor-to-normal tissue signal ratios were 4.3±3.2, similar to that seen for sarcomas. Preliminary evaluation of excised GI malignancies (3 esophagus, 4 pancreas, and 5 colorectal) also shows promising tumor-to-normal signal ratios. Conclusions: Imaging with a novel cathepsin-activatable agent LUM015 can rapidly distinguish tumor from surrounding normal tissue in multiple tumor types. Additional studies are underway to assess this platform for real-time detection of residual tumor during surgical and endoscopic procedures.



A. In vivo LUM image of several invasive lobular carcinoma foci in the cavity margin B. Ex vivo LUM image of transected lumpectomy specimen with invasive ductal carcinoma and DCIS C. Ex vivo LUM image of esophageal nodule. BE: Barrett's Esophagus. HGD: High Grade Dysplasia. IMC: Intramucosal Carcinoma. N: Nodule D. Ex vivo LUM image of an uninvolved bile duct surrounded by pancreatic adenocarcinoma E. Ex vivo LUM image of pancreatic carcinoma protruding through Ampulla of Vater in a background of normal small intestinal mucosa

PT53

Interim Report of a Clinical Registry: 669 Patients Implanted with a 3-D Bioabsorbable Marker C. Kaufman,[2]* J. Barone,[10] M. Cross,[1] N. Dekhne,[7] K. Devisetty,[6] J. Dilworth,[7] D. Edmonson,[8] F. Eladoumikdachi,[5] J. Gass,[8] R. Hong,[9] R. Kuske,[3] B. Patton,[10] R. Phillips,[11] L. Tafra,[12] A. Smith,[13] L.A. Smith.[4] *1. Breast Treatment Associates, Fayetteville, AR; 2. University of Washington, Seattle, WA; 3. Arizona Breast Cancer Specialists, Scottsdale, AZ; 4. Linda Ann Smith, Albuquerque, NM; 5. Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; 6. Karmanos Cancer Institute, Flint, MI; 7. William Beaumont Hospital, Royal Oak, MI; 8. Women and Infants Hospital of Rhode Island, Providence, RI; 9. Virginia Hospital Center, Arlington, VA; 10. Saint Joseph Hospital, Denver, CO; 11. Metro Surgical Associates, Atlanta, GA; 12. Anne Arundel Health System, Baltimore, MD; 13. Highlands Oncology Group, Fayetteville, AR.*

Introduction: Studies show Oncoplastic (OPS) reconstruction improves patient outcomes following breast conserving surgery (BCS). Previous reports indicate that a 3-D bioabsorbable implant placed during lumpectomy facilitates OPS by providing a dependable tumor bed target for radiation, a scaffold for OPS closure with consistent reports of good/excellent cosmesis. This interim report summarizes data collected in an IRB-approved Registry started in 2012. Methods: A bioabsorbable 3-D implant was implanted at the tumor excision site during lumpectomy and was used for planning and targeting breast irradiation. Data includes patient demographics, breast size, tumor characteristics, surgical and radiotherapy techniques, cosmesis and follow-up. Results: Following informed consent, 669 patients from 13 centers were enrolled in the implant registry. Median follow-up is 10 months with 148 subjects approaching 2 years. Tumor characteristics were T-1 (57%), T-2 (19%), DCIS (21%), node positivity (14%) and tumor location (upper outer 49%). Radiation oncologists verified the implant as "easily seen" on CT in 96% of cases and 96% found "improved accuracy" in boost targeting. 87% of radiation oncologists rated the device as fairly or very useful for boost planning. Oncoplastic closure was used in 98% of patients with 63% using the device as a scaffold for tissue support. Cosmesis was highly rated as "good" or "excellent" at 6, 12, and 24 months by surgeons (95%, 94%, 90%) and by patients (96%, 93%, 88%). The device contributed to the cosmetic benefit for each time period (89%, 93%, and 91%). Table 1 summarizes the data as well as surgical complication and re-excision rates. Conclusion: This interim report notes benefits of a 3-D bioabsorbable implant placed during lumpectomy. The device provides a dependable target for radiation, a scaffold for oncoplastic tissue rearrangement with reported good/excellent cosmesis in >90% of patients. This report of 669 patients describes evidence that this device may help to achieve multiple goals. Further collection of data over time will validate these interim findings.

Category	Patients
Enrollment	669
Surgery	665
Surgical Follow Up	514
Positive Nodes	14%
Oncoplastic Closure	98%
Good/Excellent Cosmesis (physician rated @ 6,12,24 mos.)	95%, 94%, 90%
Re-excision Rate	8.3%
Complication Rate (Infection, etc)	2.0%
Radiation Toxicity > Grade 2	None reported
Exit/Lost to Follow Up	23

PT54

Pathology Results of Architectural Distortion Detected with Digital Breast Tomosynthesis without Definite Sonographic Correlate S. Walcott-Sapp,[2]* J.R. Garreau,[1] N. Johnson,[1] K. Thomas.[1] *1. Surgical Oncology, Legacy Cancer Institue, Portland, OR; 2. Oregon Health & Science University, Portland, OR.*

Introduction Digital breast tomosynthesis (DBT) is an advanced mammographic technique which has been shown to have a high positive predictive value for malignancy, especially in patients with dense tissue. Architectural distortion, in particular, is readily detected by DBT, but can be occult with traditional 2D mammography and ultrasound. We hypothesized that the use of DBT would improve the sensitivity for cancer detection compared to traditional 2D mammography. Methods In a retrospective imaging database review, 110 patients who underwent 116 DBT-guided needle biopsies for architectural distortion were identified between June 2014 and August 2017. Medical records including imaging findings, biopsy results, and final surgical pathology were reviewed. Results Ninety-four lesions (81%) were

not visible on ultrasonography and 8 were not imaged with ultrasound within the preceding 6 months. Three biopsies were performed after discordance of imaging and ultrasound-guided biopsy pathology results. Of these biopsies, 60 (52%) were positive in 55 patients, including 22 invasive malignancies, 2 ductal carcinoma in situ (DCIS), 5 atypical ductal hyperplasia, 5 atypical lobular hyperplasia, and 2 other lesions. Forty-seven lesions in 44 patients were excised, while 9 patients with single radial scars chose ongoing surveillance. Two patients transferred care after the biopsy and excluded from analysis. Final surgical pathology revealed malignancy in 21 lesions, including 19 invasive carcinomas and 2 DCIS. The mean malignant lesion size was 0.79 ± 0.39cm. Imaging findings were concordant with DBT-guided biopsy pathology in all lesions, and surgical pathology in 45 (95%) lesions. One complication, a large hematoma, was noted in relation to the DBT-guided biopsy. Conclusion DBT-guided biopsy for architectural distortion was well tolerated with a low rate of complications, and detected a malignancy in 18% of lesions. These findings demonstrate the importance of pursing pathologic diagnosis in patients with architectural distortion detected on DBT, even in the absence of abnormality on sonographic imaging.

PT55

A Tissue microRNAs Profile That Predict Breast Cancer Bone Recurrence and Poor Prognosis T. Kawaguchi, L. Yan, Q. Qi, X. Peng, J. Young, S. Liu, K. Takabe.* *Roswell Park Cancer Institute, Buffalo, NY.*

Purpose: MicroRNAs (miRNAs) are known to play roles in almost all aspects of cancer biology, including metastasis. The aim of this study is to identify miRNAs signature that can predict patient survival utilizing integrated transcriptomics analyses. Experimental Design: Integrated and unbiased transcriptomics approach was conducted on genomic/epi-genomic and clinicopathological information of 2580 breast cancer patients derived from The Cancer Genome Atlas (TCGA), Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) and Gene Expression Omnibus (GEO) dataset. Results: A novel risk scoring model of three miRNAs signature (miR-19a, miR-93, and miR-106a) was identified to predict extremely poor prognosis using TCGA cohort (p=0.0005), and it was validated using another three independent cohorts (GSE19536, p=0.0009; GSE22220, p=0.0003; and METABRIC, p=0.0023, respectively). The three miRNAs score was served as an independent prognostic factor by multivariable Cox regression in TCGA and METABRIC cohort. Competing risk analysis for tumor recurrences demonstrated that the score could be significantly associated with bone metastasis/recurrence (p=0.0052). The predictive potential for bone recurrence using the score was validated by miRNA-Seq on primary breast tumor from patients who developed bone recurrence and age/stage-matched patients without any recurrence (sensitivity, 0.90; specificity, 0.65; accuracy 0.75). Gene Set Enrichment Analysis (GSEA) identified high level of the score significantly associated with several critical gene sets related to metastasis; angiogenesis, epithelial mesenchymal transition, focal adhesion, ECM receptor interaction, TGF beta signaling pathway, MTOR signaling pathway. Conclusions: These data provide a promising miRNAs signature as a novel biomarker to predict worse survival and bone-recurrence potentiality in breast cancer.

PT56

Does Inflammatory Breast Cancer have a Worse Prognosis than Other T4 Cancers? A. Romanoff,* O. Petruolo, M. El-Tamer, E. Zabor, M. Morrow, A.V. Barrio. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction Both inflammatory (IFL) and non-inflammatory T4 (non-IFL) breast cancers have a heavy disease burden in the breast, but it is uncertain whether the unique biology of IFL conveys a higher risk of locoregional (LRR) recurrence and worse outcome than in other T4 lesions. Here we compare outcomes in patients with IFL and non-IFL breast cancer treated with modern multimodality therapy. Methods Patients with non-metastatic T4 breast cancer treated with neoadjuvant chemotherapy (NAC), mastectomy, and radiation therapy between 2006 and 2016 were identified. Recurrences and survival were compared between IFL and non-IFL patients overall, and stratified by receptor subtype. Results Of 199 T4 patients, median age was 52 and median clinical tumor size was 7 cm. 117 (59%) had IFL. Characteristics of IFL and non-IFL are compared in the Table. At a median follow-up of 35 months, 4 patients had an isolated locoregional recurrence (LRR), all of which occurred in IFL patients. The 5-year LRR rate in IFL patients was 4.8%. Overall, 14 patients had both LRR and distant recurrence, and 47 had distant (DR) recurrence only. The 5-year distant recurrence free survival (DRFS) was similar between IFL and non-IFL patients (63% vs 71%, p = 0.14). When stratified by receptor subtype, 5-year LRR did not differ. The 5-year DRFS was lowest (43%) among triple negative (TN) patients, and was significantly lower for TN IFL than non-IFL patients (28% vs 62%, p = 0.02); DRFS did not vary between IFL and non-IFL for other subtypes. Overall survival (71% vs 74%, p = 0.4) and cause-specific survival (74% vs 79%, p = 0.23) did not differ between IFL and non-IFL. Conclusion Although IFL breast cancer is often considered a unique biologic subtype, IFL and non-IFL patients had similar outcomes with modern multimodality therapy, and isolated LRR was uncommon. TN subtype in IFL patients is associated with poor outcome, indicating the need for new treatment approaches in this group.

Characteristics of IFL and non-IFL patients

	Overall (n = 199)	non-IFL (n = 82)	IFL (n = 117)	p-value
Tumor size, cm (median, range)	7 (1.5, 15)	7 (1.5, 15)	7 (2, 15)	0.84
Histology (n, %)				0.72
Ductal	175 (88%)	71 (87%)	104 (89%)	
Lobular	13 (7%)	7 (8%)	6 (5%)	
Mixed	9 (4%)	3 (4%)	6 (5%)	
Other	2 (1%)	1 (1%)	1 (1%)	
Tumor subtype (n, %)				0.02
HR+/HER2-	85 (43%)	44 (54%)	41 (35%)	
HR+/HER2+	36 (18%)	11 (13%)	25 (21%)	
HR-/HER2+	46 (23%)	12 (15%)	34 (29%)	
HR-/HER2-	32 (16%)	15 (18%)	17 (15%)	
Clinical nodal status (n, %)				0.67
cN0	9 (4%)	4 (5%)	5 (4%)	
cN1	137 (69%)	54 (66%)	83 (71%)	
cN2	25 (13%)	13 (16%)	12 (10%)	
cN3	28 (14%)	11 (13%)	17 (15%)	
Path nodal status (n, %)				0.19
pN0	79 (40%)	28 (34%)	51 (44%)	
pN+	120 (60%)	54 (66%)	66 (56%)	
Systemic chemotherapy (n, %)				0.92
AC-T	167 (84%)	71 (87%)	96 (82%)	
TC	18 (9%)	6 (7%)	12 (10%)	
Taxane	9 (5%)	3 (4%)	6 (5%)	
Other	5 (2%)	2 (2%)	3 (3%)	
Anti-her2 therapy* (n, %)				1.0
Trastuzumab	55 (28%)	16 (20%)	39 (33%)	
Trastuzumab / pertuzumab	21 (11%)	6 (7%)	15 (13%)	
Other	6 (3%)	1 (1%)	5 (4%)	
NA	117 (59%)	59 (72%)	58 (50%)	

*Calculated for the HER2 positive patients overall (n = 82), non-IFL (n = 23) and IFL (n = 59). IFL, inflammatory breast cancer; non-IFL, non-inflammatory T4 breast cancer; HR, hormone receptor; HER human epidermal growth factor

PT57

Optimal Implantation Sites and Source Tumor for Breast Cancer Patient-Derived Xenografts M. Okano,* T. Kawaguchi, E. Katsuta, I. Okano, K. Takabe. *Roswell Park Cancer Institute, Buffalo, NY.*

Backgrounds: Many compounds proved to be effective in animal models often fails in humans. This is partly because murine models do not mimic human patients. Patient-Derived Xenograft (PDX) has emerged to address these issues, however, the optimal site of implantation remains controversial. We hypothesized that breast PDX tumor survives and grows better when implanted orthotopically in mammary fat pad (MFP) compared to dorsal subcutaneous space (SQ). Methods: We xenografted 10 patient breast cancer tumors into NSG mice. Two tumors were derived from brain metastasis (B-met), whereas the others were from Primary. 3 tumors were ER(+)HER2(-) and 7 tumors were triple negative (TN). Using 2-3 mice per each patient sample, $1mm^3$ tumor fragments were implanted surgically into four sites in SQ and four sites in MFP. Tumors resected at the day when the biggest tumor grew up to 1.5cm. Results: PDX tumors were established in 6 out of 10 tumors, which were all pathological grade 3. The average take time for Primary tumor was significantly longer in 1^{st} generation compared to 2^{nd} or 3^{rd} generation (117.3 vs 60.1 days, p<0.0001). The overall take rate of Primary tumor was 53.6% (170/317 site), which was significantly better in MFP compared to SQ (63.3% (107/169) vs 42.3% (63/148), p<0.001). Tumor weight were significantly heavier in MFP compared to SQ (0.60g vs 0.10g, p<0.0001). Take rate from Primary TN and ER positive tumors were 59.0% (170/288 site) and 0%

(0/39 site) respectively, but that of ER positive B-met was 89.6% (86/96 site). In B-met, take rate was significantly better in MFP than SQ (96.4%, 54/56 vs 73.2%, 41/56, p=0.001), and tumor weight were significantly heavier in MFP compared to SQ (0.20g vs 0.57g, p<0.0001). Take rate from B-met was significantly higher in both MFP and SQ (p<0.0001, respectively). SQ tumor weight from B-met was heavier (p<0.0001) than from Primary tumor but there was no difference in MFP tumors. Conclusions: Triple negative breast cancers were more successful than ER positive tumors in establishing PDX. Brain metastasis tumor had the best take rate. Implantation of metastatic tumor to MPF is better than SQ to develop breast PDX model.

PT58

Axillary Staging: Tissue Diagnosis Versus Lymph Node Morphology, is Ultrasound Enough? E. Hill,[1]* D. Ochoa,[1] A. Merrill,[1] J. Watson,[1] M. Preston,[1] I. Makhoul,[1] A. Pennisi,[1] L. Peacock,[1] S. Korourian,[1] G. Bryant-Smith,[1] K. Glover-Collins,[2] V.S. Klimberg,[3] R. Henry-Tillman.[1] *1. University of Arkansas for Medical Sciences, North Little Rock, AR; 2. Washington University Physicians, St. Louis, MO; 3. University of Texas Medical Branch at Galveston, Galveston, TX.*

Background: The most important prognostic indicator after a diagnosis of invasive breast cancer is metastasis to the axillary lymph nodes (ALN). Currently, staging of the axilla is performed by image guided core needle biopsy (CNB) or sentinel lymph node biopsy (SLNB). Recent studies have shown that ultrasound (US) guided (G) CNB is a less morbid and more cost-efficient alternative to SLNB, contributing to the increasing interest in the accuracy of staging with less invasive means. Our objective is to evaluate the accuracy of identifying metastasis to the axilla by sonographic characterization of lymph nodes to eliminate the need for pre-treatment pathologic confirmation. Methods: This IRB-approved retrospective review included a total of 248 patients with invasive breast cancer undergoing preoperative staging of the axilla using US at our institution from 2007 to 2016. A surgeon performed USG CNB was obtained in patients with suspicious ALN. Lymph nodes were deemed suspicious if they demonstrated a round, irregular shape with cortical thickening and/or a loss of fatty hilum. Comparisons were made between morphology on US and pathology on CNB and SLNB. Results: The cohort of 248 patients was divided into 2 groups: 95 (38%) clinically positive (CP) and 153 (62%) negative (CN) axilla. In the CP group, 75 (80%) had suspicious ALN on US, and of those, 68 (89%) had a positive biopsy. In the CN group, 120 (78%) had suspicious ALN on US, and of those, 85 (71%) had a positive biopsy. The number of patients with lymph node positivity in this cohort is 161 (65%). The positive and negative predictive values for identifying metastasis by ALN morphology is 87% and 84%, with a sensitivity and specificity of 95% and 61%. Less benefit was seen when axillary staging is not completed at the time of breast biopsy for the initial diagnosis of cancer, allowing the lymph nodes to react and appear falsely suspicious. Conclusion: Preoperative US examination of ALN was successful in identifying metastasis in 95% of cases. Axillary staging by sonographic morphology is a non-invasive, sensitive tool that can successfully be used to facilitate the management of breast cancer.

PT60

G2M Checkpoint and MYC Targets Gene Sets are Found to be Enriched in Young (<40 yo) Breast Cancer Patients J. Young,* T. Kawaguchi, L. Yan, X. Peng, Q. Qi, K. Takabe. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

INTRODUCTION: Though the incidence of breast cancer in young women is relatively rare, it tends to be diagnosed in advanced stages, have more aggressive subtypes, and have higher mortality rates. This study investigates the biologic differences between younger and older patients with breast cancer, and aims to find genomic subtypes that may cause increased aggressiveness. MATERIALS AND METHODS: The Cancer Genome Atlas (TCGA; n=1092) was used for analysis. Gene Set Enrichment Analysis (GSEA) was performed on breast cancer patients in TCGA. RESULTS: We separated the breast cancer patients in TCGA into Young (<40 yo) and non-Young (>40 yo). There were 98 (8.9%) Young and 994 (91%) non-Young patients in TCGA. We found that the Young patients were less likely to be ER-positive (69.5% vs 77.9%) and PR-positive (60.8% vs 68.4%). They were more likely to be Her2-positive (22.2% vs 22.6%). There were less Young patients with Luminal A (41.6% vs 49.7%) and Luminal B (17.8% vs 22.9%) subtypes. There was an increased number of basal-like subtype in Young patients (17.8% vs 16.1%). There were less Stage I (13.5% vs 17.3%) and II (54.2% vs 58.3%) patients and more Stage III (31.2% vs 22.4%) patients in the Young patients as compared to the non-Young. Young patients were also found to have a lower disease-free median survival than their non-Young counterparts (NA vs 214.7 mo, p=0.027). GSEA was then used to analyze 50 Hallmark gene sets in the Young patients. 97 patients were analyzed. Of the 50 gene sets, two gene sets were found to be enriched. The G2M Checkpoint gene set was found to be enriched in this population (p=0.004), as well as the MYC Targets gene set (p=0.033). CONCLUSION: We used a large dataset to compare Young (<40 yo) vs non-Young (>40 yo) patients with breast cancer, which confirmed that Young patients were more likely to have unfavorable subtypes, advanced stage, and lower disease free survival as compared to their older counterparts. Using this valid database, we were then able to find two gene sets that are enriched in the Young population, which may be the mechanism for their more aggressive subtypes and worse survival.

PT61

Equivalent Outcomes in Autologous Free Flap Post-Mastectomy Breast Reconstruction Despite Differences in Pre-Operative Risk Factors Among Racial Minorities L.M. Winton,* R. Warren, C.A. Hester, R. Wooldridge, N. Haddock, S. Teotia, H. Zhu, M. Leitch. *Surgical Oncology, Univ of Texas Southwestern, Dallas, TX.*

Background: Recent studies demonstrate racial and socioeconomic disparities in breast cancer treatment and reconstruction despite attempts to narrow this gap. African American women are 30% less likely to receive breast reconstruction after mastectomy, whereas Hispanic women have similar reconstruction rates as white women. There is limited data regarding clinical decision making for breast reconstruction. Available studies show African American women perceive greater barriers to reconstruction, including that surgeons persuaded them against breast reconstruction. The aim of this study is to validate that African American and Hispanic women, despite having more comorbidities than white women, have equivalent outcomes following autologous free flap breast reconstruction. Methods: Women (376) who underwent autologous free flap reconstruction following mastectomy at a single institution from 2008 to 2016 were identified from a prospectively maintained database. Patient demographics, comorbidities, TNM stage, receipt of preoperative chemotherapy or radiation, major and minor surgical complications, and medical complications were compared after women were stratified by race. Results: The three racially ethnic groups were comparable with respect to cancer data including TNM stage, tumor Ki67, and receipt of preoperative chemotherapy or radiation. Black and Hispanic women had higher rates of multiple comorbidities compared to white women (41.51% and 23.68% vs 18%, p=0.003). Analysis showed no difference in major immediate surgical complications, minor surgical complications, flap loss, prolonged breast wound healing, or medical complications including DVT, pulmonary embolism, and need for post-operative transfusion. Conclusion: Despite an overall higher rate of comorbid conditions in minority women, measurable outcomes following autologous free flap reconstruction are equivalent. Based on this data, minority women should be offered equivalent post-mastectomy reconstructive options.

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BRCA1 Low Expression Breast Cancer Increased Tumor Clonality and Immune Gene Signatures in the Tumors T. Kawaguchi, X. Peng, Q. Qi, S. Narayanan, K. McDonald, J. Young, S. Liu, L. Yan, K. Takabe.* *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Background: BRCA1 gene is known to play a critical role in repairing DNA double strand breaks. In agreement, triple-negative breast cancer with decreased BRCA1 expression was reported to be cisplatin sensitive due to increased genetic mutations in the tumor. However, the association of BRCA1 gene expression, tumor clonality and immune gene signature has not yet been elucidated in breast cancer patients. We hypothesized that less BRCA1 expression with less DNA repair is associated with tumor clonality and increased immune gene signatures. Patients and Methods: A transcriptomics approach was conducted on genomic and clinicopathological information of 3614 breast cancer patients. We utilized The Cancer Genome Atlas (TCGA) and the Molecular Taxonomy of Breast Cancer International Consortium (METABRIC) to evaluate the association between BRCA1 expression and molecular signature of the tumor immune microenvironment in breast tumors. Tumor clonality of cancer cells were evaluated utilizing Mutant Allele Tumor Heterogeneity

(MATH) index. Results: Tumors with low expression of BRCA1 contained higher mutation burden in ER negative patients (p=0.0357), but did not in the ER positive population. Intra-tumoral clonality was associated with low expression of BRCA1 (p=0.00033) and high composition of CD8+ T-cells (p=0.013). This suggests that low BRCA1 expression leads to robust tumor-associated antigen (TAA) which impacts the tumor immune microenvironment. We then evaluated the association between BRCA1 expression and immune gene signature, HLA-A, GZMA, GZMB, PRF1, in the breast tumor. Low expression of BRCA1 significantly associated with high expression of HLA-A, GZMA, GZMB, and PRF1 (TCGA, p<0.0001, p<0.0001, p<0.0001, and p=0.0001, respectively; METABRIC, p=0.0003, p<0.0001, p<0.0001, p<0.0001, respectively). Conclusions: We conclude that low BRCA1 expression increases intra-tumoral genomic instability that leads to increased clonal mutation that result in alteration of the tumor immune microenvironment.

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Management of Positive Margins for Invasive Lobular Carcinoma of the Breast: A Single Institution Cohort Study of 481 Women
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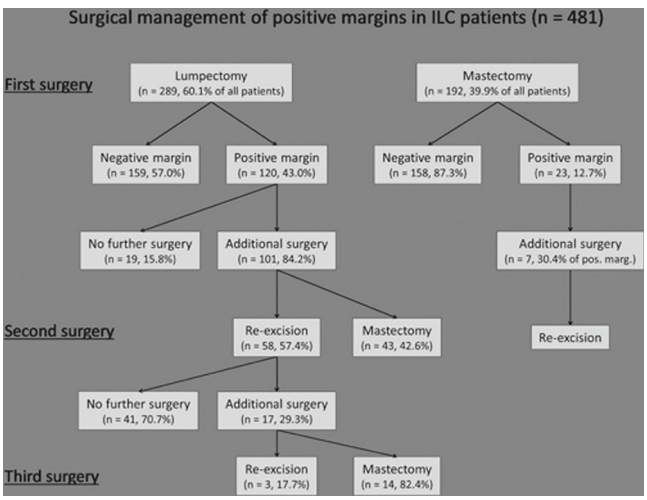
Background: Women with invasive lobular carcinoma (ILC) of the breast have high rates of positive margins after surgery, likely due to ILC's diffuse nature. When faced with a positive margin, the optimal next step is unclear. We sought to determine the success rate of re-excision for ILC, and impact of surgical management. Methods: We queried pathology databases at UCSF and identified 531 women treated for ILC from 1996-2016. We excluded those with < 6 months follow up, stage 4 disease, or missing data, leaving 481 cases. Data were analyzed in Stata 14.2. Results: Average age was 59.2 years and most tumors were ER+PR+Her2- (74.2%) and stage 1-2 (84.7%). Of the 289 women who had breast conservation therapy (BCT) as their first operation, 43% had a positive margin. Of those, just over half had attempt at re-excision, and the remainder had mastectomy (Figure 1). Ultimately, BCT was successful in 80% of women who attempted it, with 25% undergoing 1 re-excision and 1.2% undergoing 2 re-excisions. Of the 181 patients who had mastectomy as the initial operation, positive margins were seen in 12.7%. Among BCT patients, margin status was not associated with chemotherapy or radiation. Among mastectomy patients, positive margins were associated with post-mastectomy radiation (64% vs 29%, p=0.006). Positive margins were associated with stage (p<0.001), but not with tumor subtype or grade. There was no difference in time to recurrence between those with negative margins, and the 57 patients who had un-resected positive margins. Conclusions: In a large cohort of women with ILC, we found high rates of positive margins. However, the majority of women who sought BCT were able to achieve it with a single re-excision. This is important information for surgeons and patients who face difficult decisions in treating these diffuse tumors. Our observation that a group of women with un-resected positive margins had no difference in recurrence is intriguing, and raises the possibility that adjuvant therapy may adequately treat this low cellularity disease type in the absence of further surgical resection—a hypothesis that requires further evaluation.



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Satisfaction with Breast-Conserving Therapy After Re-excision: A Study Using the Breast-Q, A Patient Reported Outcomes Measure in Breast Surgery
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Background Many factors affect breast satisfaction in women who undergo breast-conservation therapy (BCT) for invasive breast cancer. Although SSO/ASTRO consensus guidelines defining "no ink on tumor" as a negative margin have led to a decreased rate of re-excision, some women need additional surgery. Re-excision surgery may have negative impacts, including adjuvant treatment delays, psychosocial stress, increased costs, and effects on cosmetic outcomes. The purpose of this study was to examine the effect of re-excision on breast satisfaction using the BREAST-Q 'Satisfaction with Breast' scale that evaluates breast satisfaction of patients who undergo BCT. Methods We identified 2538 women with invasive breast cancer who had BCT between March 2013 and December 2016 and completed the BREAST-Q at least once after BCT. Clinical, pathologic and treatment factors were collected, and BREAST-Q scores were used to assess factors that were associated with lower breast satisfaction. The BREAST-Q scores were summarized over time using line plots for each individual patient with a locally weighted scatterplot smooth to show the average trend, and linear mixed models were used for comparisons over time. Results The median age of women in our study was 57(range 26-97). Median tumor size was 1.2(.02-9.9); 58% of women had stage I disease with 88% of women receiving radiation therapy (RT). Number of re-excisions was significantly associated with lower BREAST-Q scores (Table, p<.001). Increased age (p=.003), increased tumor size (p=.003), any axillary surgery (p=.001), adjuvant radiation (p=.009) and increased time from surgery (p<.001) were all significantly associated with reduced breast satisfaction. Age, RT and number of re-excisions remained significant on multivariate analysis. Conclusions Re-excision was significantly associated with a decrease in breast satisfaction among women receiving BCT. This finding will help in counseling women who require re-excision surgery regarding breast satisfaction. We found an overall decrease in breast satisfaction over time; further research is necessary to identify factors associated with this effect.

Number of re-excisions	N (%)	BREAST-Q score	P value
None	2421(78.9%)	ref	<001
1	574 (18.7%)	-3.81	
≥2	73 (2.4)	-4.47	

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What Would This Patient's Prognosis have Been If Her Breast Cancer Had Been Diagnosed When It Was Smaller?
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Introduction: Delay in diagnosis of breast cancer is the most common cause of medical malpractice suits in the United States. In almost all these cases, an "expert" uses cancer staging data to testify about what the patient's prognosis would have been if diagnosed earlier. However recently we have shown that many small breast cancers are small, not because they were diagnosed early, but because they have favorable biology. The purpose of the present study is to estimate what effect this might have on retrospective estimates of prognosis. Methods: SEER data on invasive breast cancers diagnosed from 2001 – 2014 were used to evaluate how the biological factors ER, PR, and grade interact with tumor size to influence 10-year breast cancer specific survival. Results: As seen in the table, T1 tumors had a higher percentage of ER+, PR+, and low-grade tumors whereas T2 tumors had a higher percentage of ER-, PR-, and high-grade tumors. The survival for T1 tumors was 16 percent higher than T2 tumors. We used the observed survival for each of 12 subsets within T1 tumors to calculate what their survival would have been if they had had the same distribution of biological types as the T2 tumors. The survival for T1 tumors would have been 0.5% worse using just one biological variable in the model, and this increased to 1.5% worse using all three variables. Although these 3 simple variables accounted for only about 10% of the difference in survival between T1 and T2 tumors, it is likely that more sophisticated molecular tests such as Oncotype or MammaPrint, as well as undiscovered prognostic factors, would account for a higher, but unknown, fraction of the difference. Even without known risk factors, a tumor that has grown from T1 to T2 must have had a worse than average prognosis when it was T1 since a significant percentage of T1 tumors will not progress to T2. Conclusions: Cancer staging

data is useful to estimate the prognosis for a group of patients going forward. It is not valid, however, to use it to estimate retrospectively what an individual patient's prognosis would have been. Attempts to do this will usually overestimate the value of early detection.

Prognostic variables by tumor size

	T1 (0.1 - 2.0 cm)		T2 (2.1 - 5.0 cm)		P value for incidence
	Number (%)	Survival*	Number (%)	Survival*	
All patients	406,396 (100%)	94%	203,100 (100%)	78%	
ER+	345,648 (85.1%)	95%	150,301 (74.0%)	80%	p < 0.001
ER-	60,748 (14.9%)	88%	52,799 (26.0%)	73%	
PR+	301,846 (74.3%)	95%	127,065 (62.6%)	81%	p < 0.001
PR-	104,550 (25.7%)	90%	76,035 (37.4%)	74%	
Grade 1	119,790 (29.5%)	97%	21,842 (10.8%)	89%	p < 0.001
Grade 2	184,278 (45.3%)	94%	81,335 (40.0%)	81%	
Grade 3	102,328 (25.2%)	89%	99,923 (49.2%)	74%	

*10-year breast cancer specific survival

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Does Lymph Node Status Prior to Neoadjuvant Chemotherapy Influence the Number of Sentinel Nodes Removed? J.L. Baker,* S. Muhsen, E. Zabor, M. Stempel, M.L. Gemignani. *Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction Recent randomized trials support the use of sentinel lymph node biopsy (SLNB) post neoadjuvant chemotherapy (NAC) in patients (pts) with invasive breast cancer with clinically positive (CN+) axillary nodes prior to chemotherapy with a lower false negative rate if at least 2 SLNs are obtained. Here we sought to investigate whether the pre-NAC axillary lymph node status influences the number of sentinel nodes removed. Methods Retrospective review of our prospective NAC database identified 350 pts who received NAC and were eligible for SLNB at our institution from May 2014 to April 2016. Clinically node-negative (CN-) and CN+ pts who converted to CN- after receipt of NAC and had an SLNB were included in our analysis. Dual mapping with blue dye and isotope was used in all cases. Clinicopathologic factors were collected and compared with number of SLNs removed. Generalized linear mixed models analyzed factors associated with number of SLNs removed, incorporating a random surgeon effect to account for inter-surgeon variability in node removal. Results Of the 350 pts 343 had at least one SLN identified for an identification rate of 98.0%; 7 pts had a failed mapping procedure and were excluded from analysis. 343 patients had 348 SLN procedures (5 were bilateral). Clinicopathologic characteristics were compared between 145 (42%) CN- and 203 (58%) CN+ pts (Table). Overall, only 24% of pts underwent ALND after SLNB, with 34% in the CN+ group vs 10% in the CN- group($p<.001$). The median number of SLNs removed was 4 (range 1-14) in both CN+ and CN- pts ($p=0.18$). The number of SLNs removed was similar across year of surgery in this study. On univariable analysis, only younger age ($p=0.02$) and lower BMI ($p=0.04$) were significantly associated with removal of >4 vs ≤4 nodes. Conclusions Our study confirms that SLNB was successfully performed in 98% of our pts with breast cancer after NAC with very few failed mapping procedures. In the post NAC setting, the median number of SLNs removed was 4, and the status of the axilla prior to NAC did not affect the number of SLNs removed.

	Overall (n = 348)	CN- (n = 145)	CN+ (n = 203)	p-value
Age	50 (27, 82)	51 (28, 72)	50 (27, 82)	0.309
BMI	25.9 (15.1, 55)	25 (17, 55)	26 (15.1, 48.3)	0.429
Clinical tumor size (cm)	4 (0.7, 15)	3.6 (1.1, 11)	4 (0.7, 15)	0.263
Tumor subtype				0.018
HR-/HER2-	109 (31.3)	51 (35.2)	58 (28.6)	
HR-/HER2+	43 (12.4)	11 (7.6)	32 (15.8)	
HR+/HER2-	101 (29)	36 (24.8)	65 (32)	
HR+/HER2+	94 (27)	47 (32.4)	47 (23.2)	
NA	1 (0.3)	0 (0)	1 (0.5)	
Breast Surgery				0.081
BCT	158 (45.4)	74 (51)	84 (41.4)	
Mastectomy	190 (54.6)	71 (49)	119 (58.6)	
Axillary surgery				<001
SLNB	265 (76.1)	130 (89.7)	135 (66.5)	
SLNB, ALND	83 (23.9)	15 (10.3)	68 (33.5)	

CN-, clinically negative; CN+, clinically positive; BMI, body mass index,; HR, hormone receptor; NA, not available; BCT, breast-conserving therapy; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection

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Incidence of Bilateral Breast Cancer Based on Pathologic Subtypes M.S. Rashid,[1] J. Li,[1] D. Kekulawala,[2] A. Giles,[1] S. Salsabila,[1] G. Gohla,[1] B. Heller.[1]* *1. Surgical Oncology, McMaster University, Hamilton, ON, Canada; 2. Western University, London, ON, Canada.*

Introduction Breast cancer is the most common cancer diagnosed in women. The incidence of the three predominant subtypes is 72-80% invasive ductal carcinoma (IDC), 5-15% invasive lobular carcinoma (ILC) and 3-6% invasive ductal carcinoma with lobular features (IDC-L). Studies have shown IDC is associated with bilateral breast cancer in 11% of patients, ILC in 10-29%, and none reported for IDC-L thus far. These quoted rates are high, and bilaterality of breast cancer has significant implications for investigation and treatment. The incidence of breast tumour subtype and bilaterality is defined by historical literature. This retrospective cohort study was initiated to challenge the historic incidence of bilateral breast cancer by pathological subtype. Methods All consecutive breast pathology reports submitted between May 2015 and May 2016 at St. Joseph's Hospital, Canada were reviewed. Patient demographics, peri- and post-diagnostic imaging and pathology was collected on patients identified with an invasive breast malignancy. The incidence of histological subtype and pathologic bilaterality was determined with univariate analysis. Results 963 total patients had breast pathology submitted during the study period. Of these, 271 had invasive breast cancers: 163 (75%) IDC, 28 (13%) ILC, and 26 (11.98%) IDC-L. Baseline characteristics were similar. No differences were observed for surgical or nodal management (Table). Estrogen receptor positivity was higher among ILC and IDC-L (100% and 89%, respectively, versus 78% IDC; $p=0.004$). Receptor status for other markers was equivocal. Lymphovascular invasion was similar (17% IDC, 7% ILC, 20% IDC-L; $p=0.376$). Higher proportion of Grade III tumours were noted in the IDC group (29% vs 11% ILC and 12%IDC-L, $p=0.033$). Pathologic confirmed bilaterality was 5% for IDC, 7% for ILC, and 8% for IDC-L ($p=0.677$). Multifocality was similar between groups ($p=0.434$) and overcalled on imaging (26% vs 17% on pathology, $p=0.012$). Conclusion Review of the experience of a single Canadian centre revealed lower rates of bilateral breast cancer than those historically quoted. This carries implications for patient counselling, investigations and management of the contralateral breast.

Patients and tumour biological characteristics by pathologic subtype

	IDC	ILC	IDC-L	p
Patients, N (%)	163 (75.11)	28 (12.90)	26 (11.98)	-
Demographics	-	-	-	-
Age, mean (SD)	63.82 (11.72)	66.07 (13.12)	60.35 (11.06)	0.208*
Sex, N (%)	-	-	-	-
Male	2 (1.36)	0 (0)	0 (0)	1.000†
Female	145 (98.64)	25 (100)	23 (100)	
Tumour Identification, N (%)	-	-	-	
Asymptomatic Screening	105 (64.42)	21 (75.00)	17 (65.38)	0.550**
Symptomatic Work-up	58 (35.58)	7 (25.00)	9 (34.62)	
Surgical Treatment Modality, N (%)	-	-	-	-
Non-surgical management	0 (0)	0 (0)	1 (3.85)	0.120†
BCS	123 (75.93)	23 (82.14)	15 (57.69)	0.086**
Mastectomy	39 (24.07)	5 (17.86)	10 (38.46)	0.187**
Nodal Management, N (%)	-	-	-	-
None	12 (7.41)	2 (7.14)	4 (15.38)	0.372†
SLNB	115 (70.99)	23 (82.14)	19 (73.08)	0.473**
ALND	35 (21.60)	3 (10.71)	3 (11.54)	0.306†
Receptor Status, N (%)	-	-	-	-
ER +	126 (77.78)	28 (100)	23 (88.46)	0.004†
PR +	114 (70.37)	21 (75.00)	22 (84.62)	0.337†
HER2/neu +	20 (12.35)	2 (7.14)	1 (3.85)	0.496†
Lymphovascular Invasion	27 (16.56)	2 (7.14)	5 (20.00)	0.376†
Grade, N (%)	-	-	-	-
0	2 (1.25)	1 (3.57)	1 (4.00)	0.259†
1	38 (23.75)	8 (28.57)	7 (28.00)	0.801**
2	73 (45.63)	16 (57.14)	14 (56.00)	0.381**
3	47 (29.38)	3 (10.71)	3 (12.00)	0.033†
Pathology Evidence of Bilaterality, N (%)	8 (4.91)	2 (7.14)	2 (7.69)	0.677†
Multifocality **	-	-	-	-
Imaging	43 (26.38)	5 (17.86)	10 (38.46)	0.227†
Pathology	30 (18.52)	2 (7.41)	4 (15.38)	0.434†

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; IDC-L, invasive ductal carcinoma with lobular features; BCS, breast conserving surgery; SLNB, sentinel lymph node biopsy; ALND, axillary lymph node dissection. * ANOVA (two-tailed, independent samples); † Fisher's Exact Test; ** Chi-squared test comparing multifocality on imaging to pathology p = 0.012

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The Role of Mastectomy in Stage IV Inflammatory Breast Cancer

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INTRO De novo stage IV inflammatory breast cancer (IBC) is viewed as incurable and the role of mastectomy often questioned. We evaluated the impact of modified radical mastectomy (MRM) on outcome in this population. METHODS 97 women with stage IV IBC (T4d N0-3 M1) were identified in a prospective database from 2007-2016. To address for selection bias in receipt of MRM, response to chemotherapy (partial/complete vs. stable/progressive) and number of metastatic sites were accounted for. Outcomes were analyzed by Cox regression. RESULTS Women who underwent MRM (n=52) had significantly improved overall survival (OS) compared to no MRM (n=45) (58 vs.19 months HR 0.301, p<0.0001), and more local-regional (LR) failures (21.2% vs. 8.9%) but this difference was not statistically significant (p=NS). Median follow up was 70 months in the MRM group vs 47.5 months with no MRM. The MRM group had fewer metastatic sites (median 1 vs. 2, p=0.010), more hormone receptor (HR) positivity (63.5% vs. 35.6%, p=0.006), and favorable clinical response to neoadjuvant chemotherapy (NAC) (p<0.001). On univariate analysis, MRM (HR [95% CI], 0.3 [0.176-0.51] p<0.001) and clinical response to NAC both LR (HR 0.462 [0.245-0.869] p=0.0166) and distant (HR 0.467 [0.253-0.859] p=0.0144), were associated with decreased risk of death. Increased number of metastases (HR 1.134 [1.011-1.27] p=0.03) and triple-negative (TN) subtype (HR 11.1 [2.61-47.3] p=0.01) were associated with increased risk of death. On multivariate analysis, MRM (HR 0.519 [0.291-0.926] p=0.0265) remained significant for OS when adjusting for N3 disease (HR 2.162 [1.072-4.372] p=0.0313), tumor subtype (TN vs. HR+/Her2+ HR 7.175 [1.657-31.070] p=0.0084; HR+/Her2- vs. HR+/Her2+ HR 4.977 [1.154-21.466] p=0.0314), and distant response to NAC (HR 0.433 [0.243-0.771] p=0.0045). CONCLUSIONS MRM in de novo stage IV IBC is associated with significantly improved OS in patients with response to NAC and limited metastatic disease. The higher rate of LR recurrence after MRM may be explained by these patients living longer. Our findings strongly support the need for a prospective randomized trial evaluating the utility of MRM in de novo stage IV IBC after favorable response to NAC.

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Increase in Utilization of Nipple Sparing Mastectomy for Breast Cancer: Indications, Complications, and Oncologic Outcomes

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Background Nipple-sparing mastectomy (NSM) is increasingly performed for invasive breast cancer. A growing body of evidence supporting the oncologic safety of NSM has lead to widespread use and broadened indications. We reviewed our institutional experience with NSM and examined rates of postoperative complications and recurrence. Methods From 2003-2016, women undergoing NSM for invasive cancer or DCIS were identified from a prospectively maintained database. Rates of postoperative complications and recurrence were examined using the Kruskal-Wallis test and Fisher's exact test. Kaplan–Meier (KM) estimates and log-rank tests were used to evaluate overall survival. Results Of the 467 therapeutic NSM, 337 (72%) were invasive cancer, 126 (27%) were DCIS and 4 (1%) were phyllodes tumors. Median age was 45 (range, 24-75). Median follow-up time among survivors was 39.4 months. The nipple areolar complex (NAC) was entirely preserved in 446 mastectomies (96%). There was a total of 21 (4.5%) nipple excisions, of which 14 (3%) were performed due to cancer at the nipple margin. 38 (8.1%) had skin necrosis requiring debridement. 44 (9.4%) had a complication that required a re-operation, of which 16 breasts (3.4%) necessitated implant removal. 28 patients (6%) were treated for infection. 344 (76.6%) cases were performed after 2011. When comparing between NSM performed before and after 2011 (Table), there was a significant increase in the therapeutic NSM performed for invasive tumor histology in recent years (58% vs 77%, p <.001). There was no difference in regards to family history, genetic mutations, smoking status, neoadjuvant chemotherapy, prior radiation, nodal involvement, or invasive tumor subtype. 15 patients had a local regional recurrence (LRR) or distant metastasis. Of these, 3 were LRR only, 11 were distant metastasis only, and 1 was an LRR and distant metastasis. Conclusion The use of NSM for invasive carcinoma has doubled at our institution since 2011 while postoperative complications and recurrence rates remain low. Our experience supports the selective use of NSM in the malignant setting with careful patient selection.

Patient and Tumor Characteristics by Surgery Year

	Overall (n=449)	NSM before 2011 (n=105)	NSM after 2011 (n=344)	p-value
Age	45 (range, 24-75)	44 (range, 25-64)	45 (range, 24-75)	0.51
Family History, Breast Cancer (1st Degree)	118 (26.2%)	27 (25.7%)	90 (26.2%)	0.90
Family History, Ovarian Cancer (1st Degree)	11 (2.4%)	6 (5.7%)	5 (1.5%)	0.03
Genetic Testing, No	179 (39.9%)	50 (47.6%)	129 (37.5%)	0.07
Genetic Testing, Yes	270 (60.1%)	55 (52.4%)	215 (62.5%)	
Mutations Detected, BRCA1	28 (6.2%)	6 (5.7%)	22 (6.4%)	0.81
Mutations Detected, BRCA2	18 (4.0%)	5 (4.8%)	13 (3.8%)	0.38
Smoking Status, Current Smoker	25 (5.6%)	6 (5.7%)	19 (5.5%)	0.83
Smoking Status, Never Smoked	326 (72.6%)	74 (70.5%)	252 (73.3%)	
Smoking Status, Quit	98 (21.8%)	25 (23.8%)	73 (21.2%)	
Neoadjuvant Chemotherapy, Yes	33 (7.3%)	4 (3.8%)	29 (8.4%)	0.14
Neoadjuvant Chemotherapy, No	416 (92.7%)	101 (96.2%)	315 (91.6%)	
Prior Radiation, Yes	32 (7.1%)	12 (11.4%)	20 (5.8%)	0.08
Prior Radiation, No	417 (92.8%)	93 (88.6%)	324 (94.2%)	
Tumor Histology, Invasive Cancer	337 (72.2%)	64 (58.2%)	273 (76.5%)	<001
Tumor Histology, DCIS	126 (27%)	44 (40%)	82 (23%)	
Tumor Histology, Phyllodes	4 (0.9%)	2 (1.8%)	2 (0.6%)	
Nodal Status, N0	390 (83.5%)	92 (83.6%)	273 (76.5%)	1.0
Nodal Status, N+	77 (16.5%)	18 (16.4%)	82 (23%)	
Invasive Tumor Subtype, HR+/HER2-	237 (64.1%)	43 (57.3%)	194 (65.8%)	0.8
Invasive Tumor Subtype, HR+/HER2+	38 (10.3%)	4 (5.3%)	34 (11.5%)	
Invasive Tumor Subtype, HR-/HER2-	35 (9.5%)	12 (16%)	23 (7.8%)	
Invasive Tumor Subtype, HR-/HER2+	17 (4.6%)	3 (4%)	14 (4.7%)	
Invasive Tumor Subtype, Unknown	43 (11.6%)	13 (17.3%)	30 (10.2%)	
Contralateral Prophylactic NSM, Yes	310 (69%)	75 (71.4%)	235 (68.3%)	0.63
Contralateral Prophylactic NSM, No	139 (31%)	30 (28.6%)	109 (31.7%)	

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Adolescents and Young Adults with Breast Cancer have More Aggressive Disease and Treatment than Adult Patients

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Background: Less than 2% of breast cancer diagnoses are made in adolescents and young adults (AYA) (<30 years old). Due to its rarity, little is known about tumor characteristics and care provided to AYA patients. We sought to compare demographic, tumor, and treatment between AYA and adult patients age 30-49. Methods: We identified patients aged 18-49 with breast cancer 2010-2014 from the National Cancer Database (NCDB). Patient and tumor factors were compared between patients aged 18-29 and 30-49 using chi-square tests. Multivariable logistic regression was used to model the effect of age group on treatment while adjusting for confounding variables. Results: 4,582 AYA and 185,106 patients aged 30-49 years were identified. AYA were significantly more likely to present with stage IV disease (8.6% vs 3.8%, p<0.001). Among patients with stage 0-III disease (Table), DCIS was less common in AYA (6.8% vs 19.2%, p<0.001). AYA were more likely to be cN+ (34.7% vs 19.6%) and had higher overall clinical stage (64.4% vs 40.4% stage II/III). Triple negative (23.5% vs 15.2%) or HER2+ (28.6% vs 19.7%) disease was more common, as was high grade disease (63.7% vs 42.4%). Mastectomy was more likely in AYA (76.4% vs 54.9%) and among those with mastectomy, contralateral prophylactic mastectomy rate was higher (62.5% vs 54.1%), while reconstruction rates were similar (63.7% vs 63.6%). Both neoadjuvant (25.5% vs 12.6%) and adjuvant (55.7% vs. 41.1%) chemotherapy were more common in AYA, while smaller differences were observed for hormone therapy (81.2% vs 79.3%, p=0.02) and radiation (83.6% vs. 88.5%, p<0.001) where indicated. After adjustment for confounding factors including stage and biologic subtype, AYA remained more likely to undergo mastectomy (OR 2.20, 95% CI: 2.04-2.38) and more likely to receive chemotherapy (OR 2.23, 95% CI: 1.96-2.53), but less likely to receive radiation therapy (OR 0.63, 95% CI: 0.53-0.74). Conclusion: AYA with breast cancer presented with more advanced disease and had more aggressive tumor biology. AYA had higher rates of mastectomy and use of chemotherapy.

	Age 18-29 (N=39960)	Age 30-49 (N=171157)	p value
Race			<0.0001[1]
Missing	45	1828	
White	2790 (71.3%)	133056 (78.6%)	
Black	797 (20.4%)	23685 (14.0%)	
Other	328 (8.4%)	12588 (7.4%)	
Primary Payer			<0.0001[1]
Missing	71	3121	
Not insured	218 (5.6%)	5850 (3.5%)	
Private Insurance	2715 (69.8%)	136387 (81.2%)	
Medicaid	815 (21.0%)	18824 (11.2%)	
Medicare	64 (1.6%)	4706 (2.8%)	
Other Government	77 (2.0%)	2269 (1.4%)	
Clinical Stage			<0.0001[1]
Missing	276	13493	
0	336 (9.1%)	33993 (21.6%)	
1	976 (26.5%)	59913 (38.0%)	
2	1744 (47.3%)	50355 (31.9%)	
3	628 (17.0%)	13403 (8.5%)	
Pathologic Stage			<0.0001[1]
Missing	529	17754	
0	378 (11.0%)	29895 (19.5%)	
1	1121 (32.7%)	59783 (39.0%)	
2	1402 (40.9%)	47690 (31.1%)	
3	530 (15.4%)	16035 (10.5%)	
Biologic Subtype			<0.0001[1]
Missing	449	37723	
HER2+	1004 (28.6%)	26272 (19.7%)	
Triple Negative	826 (23.5%)	20285 (15.2%)	
HR+/HER2-	1681 (47.9%)	86877 (65.1%)	
Histology			<0.0001[1]
DCIS	270 (6.8%)	32896 (19.2%)	
IDC	3218 (81.3%)	111729 (65.3%)	
ILC	30 (0.8%)	8715 (5.1%)	
IMC	74 (1.9%)	6161 (3.6%)	
Mucinous/Tubular/Papillary	58 (1.5%)	2434 (1.4%)	
Other	310 (7.8%)	9232 (5.4%)	
Grade			<0.0001[1]
Missing	335	15569	
Well differentiated	208 (5.7%)	25014 (16.1%)	
Moderately differentiated	1108 (30.6%)	64561 (41.5%)	
Poorly differentiated/Undifferentiated	2309 (63.7%)	66013 (42.4%)	
Surgery Type			<0.0001[1]
Missing	7	196	
BCS	934 (23.6%)	77038 (45.1%)	
Mastectomy	3019 (76.4%)	93923 (54.9%)	
Axillary Surgery			<0.0001[1]
Missing	24	1257	
No nodes removed	257 (6.5%)	20679 (12.2%)	
1-5 nodes	1844 (46.8%)	94224 (55.5%)	
>5 nodes	1835 (46.6%)	54997 (32.4%)	
Reconstruction (among mastectomy only)			0.91[1]
Missing	155	6334	
Mastectomy: No reconstruction	1041 (36.3%)	31926 (36.4%)	
Mastectomy: Reconstruction	1823 (63.7%)	55663 (63.6%)	
Removal of uninvolved contralateral (among mastectomy patients)			<0.0001[1]
Missing	303	10498	
No removal of uninvolved contralateral	1018 (37.5%)	38275 (45.9%)	
Removal of uninvolved contralateral	1698 (62.5%)	45150 (54.1%)	
Chemotherapy Treatment			<0.0001[1]
Missing	73	3819	
None	646 (16.6%)	74798 (44.7%)	
Neoadjuvant chemotherapy	993 (25.5%)	21050 (12.6%)	
Adjuvant chemotherapy	2164 (55.7%)	68850 (41.1%)	
Chemotherapy given, unknown timing	84 (2.2%)	2640 (1.6%)	
Hormone Therapy Treatment (among HR+ patients)			0.02[1]
Missing	103	5091	
No	495 (18.9%)	26695 (20.7%)	
Yes	2143 (81.2%)	102495 (79.3%)	
Radiation Therapy (among patients with BCS or 4+ nodes positive)			<0.0001[1]
Missing	6	462	
No	224 (16.4%)	10185 (11.5%)	
Yes	1138 (83.6%)	78090 (88.5%)	

[1]Chi-Square

Table. Comparison of demographic, tumor, and treatment characteristics between patients age 18-29 versus age 30-49 for stage 0-III breast cancer patients undergoing surgery.

PT71

Diabetes Mellitus and Metformin Are Not Associated with Complete Pathologic Response Following Neoadjuvant Chemotherapy for Breast Cancer T. Hassinger,[1]* A. Berger,[2] A. Christopher,[2] A. Knisely,[1] J. Mehaffey,[1] H. Witmer,[2] M. Lazar,[2] T. Tsangaris,[2] D. Brenin,[1] A. Schreon,[1] S.L. Showalter.[1] *1. Surgery, University of Virginia, Charlottesville, VA; 2. Thomas Jefferson University, Philadelphia, PA.*

Introduction Recent data have linked metformin use to increased rates of pCR in cancer patients treated with neoadjuvant chemotherapy. A large single-institution study showed benefit of metformin specifically in breast cancer patients. We aimed to investigate the association of both diabetes mellitus (DM) and metformin use to pCR in breast cancer patients in a 2-institution series. Methods All breast cancer patients who received neoadjuvant chemotherapy between June 2013 and October 2016 at 2 academic medical centers were identified. A retrospective cohort study was conducted to evaluate patients who did and did not achieve pCR. Univariate analyses compared patients with and without pCR. Multivariable analysis (MVA) was performed to identify independent predictors of pCR. Results Three hundred fifty-two breast cancer patients received neoadjuvant chemotherapy during the study period, with 108 (30.7%) achieving pCR. The rate of DM did not differ between those with and without pCR [10 (9.3%) vs. 25 (10.3%); p=0.78], nor did rate of metformin use [5 (4.6%) vs. 15 (6.2%); p=0.57]. HER2+ tumors were more common among patients with pCR. Patients with pCR were less likely to have infiltrating ductal carcinoma (p=0.044) as well as estrogen receptor (ER) (p<0.0001) and progesterone receptor positive (p<0.0001) tumors. Locoregional, and distant recurrence rates were lower in the pCR group (1.9 vs 9.4% p=0.011; 0.9 vs 10.3% p=0.002; 6.5 vs 27.5% p<0.0001). Mortality was decreased in patients with pCR [61 (6 (5.6% vs. 61 (25.0%)); p=<0.0001]. MVA identified HER2+ tumors and small tumor size (p=0.012) as predictors of pCR. ER+ and multifocal disease were associated with an absence of pCR. Neither diabetes mellitus nor metformin use were predictive of pCR. Conclusion This 2-institution study supports previous data of factors known to be associated with pCR (invasive ductal carcinoma, estrogen negative, HER2 positive, unifocal disease). The current study did not find DM or metformin to be independently associated with pCR. Thus additional studies are warranted to support this association prior to validating metformin as an antitumor agent.

Table. Predictors of Complete Pathologic Response Following Neoadjuvant Chemotherapy for Breast Cancer

	OR (95% CI)	p value
Age at diagnosis (years)	1.00 (0.97 - 1.02)	0.86
Pre-chemotherapy BMI (kg/m2)	0.99 (0.95 - 1.03)	0.53
Type II diabetes mellitus	1.13 (0.33 - 3.85)	0.85
Metformin	0.86 (0.17 - 4.47)	0.86
ER+	0.28 (0.16 - 0.48)	<0.0001
HER2+	2.11 (1.18 - 3.78)	0.01
IDC	1.88 (0.75 - 4.77)	0.18
Preoperative tumor size (cm)	0.83 (0.71 - 0.95)	0.01
Multifocal disease	0.41 (0.22 - 0.77)	0.006
Completed neoadjuvant chemotherapy	1.40 (0.76 - 2.59)	0.28

BMI = body mass index; ER+ = estrogen receptor positive; HER2+ = human epidermal growth factor receptor 2 positive

PT72

Annexin A1 Expression Associate with EMT and Poor Prognosis in Patients of Triple Negative Breast Cancer M. Okano,[1]* E. Katsuta,[1] T. Ohtake,[2] K. Takabe.[1] *1. Roswell Park Cancer Institute, Buffalo, NY; 2. Fukushima Medical University, Fukushima, Japan.*

Introduction: Annexin A1 (ANXA1) is a phospholipid-linked protein, involved in anti-inflammatory effects and tumorigenesis. Recently, we reported that ANXA1 is associated with triple-negative breast cancer (TNBC) and its poor prognosis in 211 Japanese breast cancer cases. ANXA1 was reported to relate with epithelial mesenchymal transition (EMT) in cells and animal studies but has never been shown in patients. We hypothesized that ANXA1 expression associate with EMT that reads to poor prognosis of TNBC patients. Methods: Clinical and RNA-seq data were all obtained from the Cancer Genome Atlas (TCGA). Patients were classified as either high or low expression of ANXA1 determined by automated scanning and selecting the threshold yielding the lowest p-value. Overall survival (OS) and Gene set enrichment analysis (GSEA) were conducted comparing high and low expression group. ANXA1 protein expression was assessed by Immunohistochemistry (IHC) in 48 TNBC patients. Results: TNBC patients had significantly higher levels of ANXA1 expression compare to non-TNBC patients in TCGA cohort (p<0.001). ANXA1 high and low expression group were 140 and 20 patients in TNBC, and 540 and 245 in non-TNBC in TCGA cohort, respectively. High expression of ANXA1 group showed significantly worse OS (5-year OS rate: 68.6% vs 100%, p=0.035) in TNBC patients, whereas it demonstrated better OS in non-TNBC patients (5-year OS rate: 88.4% vs 78.7%, p=0.004). Among 48 cases of TNBC patients 17 cases (35.4%) had high expression of ANXA1 protein. OS was significantly shorter in patients with ANXA1 protein high tumors compared with ANXA1 protein low tumors (p=0.008), which was in agreement with transcriptome analysis. To explore the mechanism of worse survival of TNBC patients with ANXA1 high expression, GSEA was conducted between ANXA1 high and low expression group. GSEA demonstrated that high expression of ANXA1 group enriched EMT related genes (NES=1.916, p=0.004). Conclusions: For the first time we demonstrate high expression of ANXA1 transcriptome and protein enriched EMT signaling related gene expression in TNBC patients that associated with worse OS.

PT73

Elevated Expression of High Mobility Group Protein B1 (HMGB1) Attracts Tumor Infiltrating Lymphocytes (TILs) and Predicts Improved Response to Neoadjuvant Chemotherapy (NAC) in Breast Cancer K. McDonald,* E. Katsuta, L. Yan, Q. Qi, X. Peng, K. Takabe. *Surgery, Roswell Park Cancer Insititute, Buffalo, NY.*

Introduction: HMGB1 is an evolutionarily conserved protein present in the nucleus of eukaryotic cells. HMGB1 is released from damaged cells and detected by the TLR4 receptor. We previously showed that high expression of HMGB1 is significantly associated with improved survival in ER-positive, luminal A, and luminal B cancers, but not TLR4. We sought a mechanistic explanation of this survival benefit. Previous studies have shown that HMGB1 attracts lymphocytes by release after cell destruction and tumors with high TILs have an improved response to NAC. Thus, we hypothesize that HMGB1-high expression attracts TILs independent of TLR4 and that tumors with a good response to NAC produce high HMGB1 that attracts TILs. Methods: TCGA dataset used to evaluate the expression of HMGB1 in ER+ cancers. HMGB1 high vs. low cutoffs were used to analyze CIBERSORT to obtain TIL composition. Gene set enrichment analysis (GSEA) was used to obtain gene enrichment data. GSE cohorts used to analyze the relationship between HMGB1 and response to NAC. Results: HMGB1-high expression associated with a statistically significant increase in CD4 activated memory T cells (p=<1e-04), gamma delta T cells (p=<1e-04), macrophage M1 cells (p=.00748), and decreased macrophage M2 cells (p=.002726). HMGB1-high expression attracted T cells that inhibit tumor growth. HMGB1-high expression also associated with statistically significant enrichment of MYC (p=.014257) and E2F (p=.024145) genes which may be reflective of immune behavior. In the NAC cohort that received taxane and anthracycline, HMGB1 was significantly elevated in tumors with a pathological complete response. However, doxorubicin cohorts had no statistical difference in HMGB1 expression. Conclusions: By utilizing a big dataset with sufficient statistical power, HMGB1 high expression facilitated the trafficking of tumor suppressive TILs and improved response to NAC. Our study supports the novel role of HMGB1 as a tumor suppressor in breast cancer.

PT74

Extreme Oncoplasty: Expanding Indications for Breast Conservation A. Crown,* J. Grumley. *General, Thoracic and Vascular Surgery, Virginia Mason Medical Center, Seattle, WA.*

INTRODUCTION: Breast cancer patients with multiple lesions and tumor span greater than 5 cm are often advised to undergo mastectomy. Patient desire for breast conservation has increased the interest in extreme oncoplastic breast conserving surgery (EOBCS) as a way to avoid mastectomy. METHODS: This is a single institution retrospective review of breast cancer patients with multiple lesions and disease span ≥5 cm who underwent EOBCS. Patient demographics, tumor preoperative imaging and final pathology size, margin width, mastectomy and re-excision rates, and cosmesis were evaluated. Patients were treated with adjuvant therapies as appropriate. RESULTS: 111 patients underwent EOBCS between November 1, 2012 and September 15, 2017. Average patient age was 58.5 ± 11.7 years. 94 patients had invasive cancers and 17 had DCIS. 82 patients presented with multifocal or multicentric disease with an average imaging span of 60 mm (range 35-117 mm) and with an average of 3.2 lesions per breast (range 2-13 lesions). 18 patients presented with unifocal tumors measuring an average of 67.6 mm (range 50-160 mm) on imaging. 11 patients with an imaging size of <5 cm had a disease span ≥ 5 cm on final pathology. Surgical approaches included 49 reduction mammoplasties, 30 racquet mammoplasties, 22 mastopexies and 10 other incisions. Clear margins with no tumor on ink were achieved in 87 (78.3%) patients. 57 (51.4%) patients had additional surgery for margins <2 mm. 15 (12.6%) patients elected to have mastectomy while 42 (37.8%) patients opted for re-excision. 33 (29.7%) patients required a single re-excision while 9 (8.1%) patients required multiple re-excisions. Good to excellent cosmesis was accomplished in 95% of patients who ultimately achieved breast conservation. 16 (14.4%) patients had surgical site complications; 2 patients had operative interventions. There were 2 recurrences during the follow-up interval which averaged 24 months. CONCLUSION: EOBCS can allow for breast conservation in patients who are traditionally counseled to undergo mastectomy. Although the rate of inadequate margins is significant, re-excision can be successfully performed and the vast majority of patients can avoid mastectomy.

Lesion Characteristics

	Number of patients (n=111)	Percent of patients (%)
Invasive Lobular Carcinoma	17	15.3%
Invasive Ductal Carcinoma	68	61.3%
Invasive Carcinoma with Ductal and Lobular Features	9	8.1%
Ductal carcinoma-in-situ	17	15.3%
Node Positive	38	34.2%
ER Positive	94	84.7%
PR Positive	72	64.9%
Her2 Positive	16	14.4%

PT75

Disparities in Survival From Stage IV Breast Cancer Are Influenced More by Patient Factors Than Treating Facility B. McDevitt,* P. Subhedar, S. Gabram-Mendola, J. Kramer, C. Arciero. *Breast Surgical Oncology, Emory, Atlanta, GA.*

Background: Prognosis for women with Stage IV breast cancer may differ based on many factors including the resources of a given hospital system. In a previously studied, unadjusted survival analysis comparing three urban teaching hospitals, we found worse outcomes associated with patients treated at the under-resourced safety net hospital in our system. In this population-based study, we aimed to assess the effects of hospital type (academic, safety-net, or mixed academic/safety-net) stratified by age, race, size of tumor and treatment on overall survival. Methods: An institutional database was used to collect data on all stage IV breast cancers diagnosed from 2004-2016. A Cox proportional hazard model was used with time to death as the outcome, hospital location, race, age, receipt of radiation, and receipt of breast surgery as fixed covariates, and receipt of systemic therapy as a time dependent covariate. Differences in frequencies of covariates by hospital were assessed by chi(2) tests of independence. Results: 834 women with Stage IV disease were seen at one of three hospital types; academic (n=313), mixed academic/safety net (n=265) and safety net (n=256). At the safety net hospital, the patients were more likely to be older (p=0.029), of African American in race (P<0.001), less likely to undergo surgery (P<0.001), and less likely to receive systemic therapy (P=0.05). On multivariate analysis; African American race (p=0.02), presence of T4 disease (P=0.0025), older age (P<0.0001), and lack of systemic therapy use (P=0.0001) was associated with an increased hazard of death. Association with hospital type did not reach statistical significance. Conclusion: Poorer overall survival appears to be associated with African American race, lack of systemic therapy use, presence of T4 disease and older age at diagnosis compared to the treating hospital type. Attention should therefore be focused on improving modifiable risk factors such as breast cancer awareness, treatment compliance and screening programs especially in known at risk African American populations.

Multivariate Analysis

Covariate	Hazard Ratio of Death	P-value
Hospital		
reference (academic hospital)		
mixed safety net/academic hospital	0.98 (0.79-1.26)	0.89
safety net hospital	1.27 (0.99-1.63)	0.06
African American Race	1.32 (1.04-1.68)	0.02
Systemic Therapy	0.67 (0.52-0.85)	0.0001
T4 disease	1.37 (1.12-1.69)	0.0025
Age	1.02 (1.01-1.02)	<0.0001
Breast Surgery	0.78 (0.58-1.05)	0.0993
Radiation	0.95 (0.77-1.18)	0.65

PT76

In Breast Recurrence in DCIS Patients Treated with APBI Using Balloon Brachytherapy K. Williams,[1]* W.B. Carter,[1] A.V. Barrio,[2] R. Carella,[1] L. Li.[1] *1. Bryn Mawr Hospital, Bryn Mawr, PA; 2. Memorial Sloan Kettering, New York, NY.*

INTRODUCTION: Patients undergoing breast conservation have traditionally been treated with whole breast radiation. A newer alternative is accelerated partial breast irradiation, which delivers radiation directly to the target tissue over a shorter time period. Recently, ASTRO issued updated clinical practice guidelines including patients with low risk DCIS (low/intermediate grade, less than 2.5cm, margin width of 2mm) as "suitable" candidates for APBI. Data is emerging suggesting that the application of APBI is much broader than first

anticipated. METHODS: This is a retrospective longitudinal single institution study that evaluates patient factors, disease characteristics, and treatment outcomes in DCIS patients treated with APBI using brachytherapy. RESULTS: Between 2004 and 2014, 529 patients were treated with balloon brachytherapy to 34Gy (10 fractions twice daily). Of these, 68 patients had pure DCIS. 6/68 patients had in-breast recurrence (8.8%). Recurrence rate for high grade DCIS was 13% and 6.7% for low/intermediate. Average time to recurrence was 4.5 years. Only one patient had a 0.3mm margin; all others had negative margins. DCIS was less than 2cm in size in all patients. 2/6 patients took anti-estrogen therapy as recommended. 3/6 either refused therapy or stopped early from side effects. 1/6 had hormone receptor negative disease. All recurrences were invasive ductal. 3/6 had positive lymph nodes and 3/6 had HER2 positive tumors. All of the high grade DCIS patients had either positive nodes or HER2 disease. 5/6 patients required adjuvant cytotoxic chemotherapy. CONCLUSION: Local recurrence with APBI was similar to whole breast radiation. In our study, size and margin of DCIS were not significant risks for in-breast recurrence. However, high grade DCIS treated with APBI was twice as likely to have a recurrence as low/intermediate grade DCIS. Those with high grade DCIS also had recurrent disease with more aggressive features (lymph node positivity and HER2+ disease). All high grade DCIS patients who had in-breast recurrence required cytotoxic chemotherapy. APBI is a promising alternative to whole breast radiation in carefully selected patients with DCIS.

PT77

Elevated Expression of High Mobility Group Protein B1 (HMGB1) Attracts Tumor Infiltrating Lymphocytes (TIL) in Breast Cancer

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Introduction: HMGB1 is an evolutionarily conserved protein present in the nucleus of eukaryotic cells. HMGB1 is released by either active or passive secretion from damaged cells. Extracellular HMGB1 is detected by the TLR4 receptor. Not yet fully elucidated whether the HMGB1/TLR4 interaction promotes or inhibits breast cancer tumorigenesis. We previously showed that high expression of HMGB1 is significantly associated with improved survival in ER-positive cancers, but not TLR4. Previous studies showed that TILs represent the most important immunological response in tumor growth and suppression. We hypothesize that high expression of HMGB1 attracts TILs, independent of TLR4, partly accounting for the improved survival. Methods: All data obtained from the Cancer Genome Atlas (TCGA) dataset. Expression of HMGB1 retrieved from the Genomic Data Commons (GDC). HMGB1 thresholds were derived and used to group ER positive/negative breast cancers into high- or low-expression groups. CIBERSORT estimated TIL composition based on gene expression profiles. The relationship between CIBERSORT cell composition and gene expression calculated using the Pearson correlation and the Two-Samples Wilcoxon Test. Results: High HMGB1 expression was associated with a statistically significant improvement in overall survival (high = 462, low = 628; p=.036). HMGB1-high expression associated with a statistically significant increase in CD4 activated memory T cells (p=<1e-04), gamma delta T cells (p=<1e-04), macrophage M1 cells (p=.00748), and decreased macrophage M2 cells (p=.002726). HMGB1-high expression attracted T cells that inhibit tumor growth. Cancers with low HMGB1expression had more CD4 resting T cells (p=.024) and more Tregs (p=<1e-04). Low levels of HMGB1 attracted T cells whose function is to promote tumor growth. Conclusions: By utilizing a big dataset with sufficient statistical power, we found that high expression of HMGB1 facilitates trafficking of tumor suppressive TILs. Our study supports the novel role of HMGB1 as a tumor suppressor in breast cancer.

PT78

Improving Access to Care for Breast Cancer Patients Through Telemedicine Occupational Therapy

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Objective: To determine feasibility of telemedicine in breast cancer rehabilitation Background: In geographically remote areas, access to rehabilitation after breast surgery remains limited. To address this need, we initiated a feasibility study to provide telemedicine services in "Hub and Spoke" model linking patients with the occupational therapist (OT). Methods: The sites, located 75 miles apart, were equipped with videoconferencing equipment, to connect the therapist, located at the Hub site, with the patient at the Spoke site. An OT assistant helped with the videoconferencing, patient evaluation, and data acquisition. Feasibility of telemedicine sessions was assessed though patient participation and completion rates, time to return to baseline function, and overall patient satisfaction. Results: During a 9-month period, 26 female patients consented to participate, 22 initiated therapy, and 18 completed post-operative sessions. Average distance from patients' home to the site was 16 (range 3 – 85) miles. 50% (11/22) and 32% (7/22) of the treated patients underwent mastectomies and axillary dissections, respectively. Measurements, functional assessments, exercises and education were completed at pre- and post-operative sessions. Patients regained baseline functional status within a mean of 42 days after surgery and after a mean of 3 telemedicine sessions. The patient survey was completed by 54% (12/22) patients who attended all prescribed sessions. All of the patients rated their satisfaction level with the program at the highest level. Conclusions: Telemedicine breast surgery rehabilitation using videoconferencing is feasible and acceptable to patients. Our study adds to emerging data about the acceptability and utility of telemedicine in cancer care.

PT79

Relationship Between Ductal Carcinoma In Situ Associated Calcifications, and Margin Status in Breast Conserving Surgery

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Background: Up to a third of women undergoing lumpectomy for Ductal Carcinoma In Situ (DCIS) will undergo re-excision. DCIS associated microcalcifications (DCIS-AMC) at the lumpectomy margin could be detected during intraoperative specimen radiograph as a surrogate of margin involvement. We evaluated the frequency and predictive histologic factors of DCIS-AMC at lumpectomy margins. Methods: Women from a prospective database diagnosed with DCIS with microcalcifications, treated with breast conserving surgery between 2009 and 2017 were identified. Patients with DCIS without calcifications, upgraded to invasive cancer or incomplete slides were excluded. Patients demographic and pathologic characteristics, including age, grade, size, estrogen receptor (ER), progesterone receptor (PR), and margin status, were collected. Histologic slides were reviewed by a breast pathologist to evaluate distance of DCIS from each margin (6 per specimen) and the co-existence of DCIS-AMC. Results: After exclusions, a total of 30 patients with 180 margins were evaluated. Median age was 60 years, median DCIS size was 2 cm (0.3-7.5 cm), 93% were ER+ and 83% were PR+. Grade was low in 4 (13.3%), intermediate in 17 (56.7%), and high on 9 (30%). 14 (46.75%) speciment had DCIS <2 mm from at least 1 margin; 3 patients (10%) had 4 (2.2%) positive margins, with one positive margin with DCIS-AMC. 15 patients (50%) underwent additional margin excisions, with 25 new margins all negative for DCIS. Overall, 13/30 patients (43%) had DCIS-AMC present in at least one margin, and 41/180 margins (23%) had DCIS-AMC. When comparing margins with and without calcifications, DCIS-AMC were closer to the surgical margin than those with DCIS not associated with calcifications (median 5.0 mm vs. >10 mm, p<0.001). Groups did not differ in any other parameter. Most DCIS-AMC were at the anterior (13, 32%), superior (9, 22%), and posterior (8, 20%) margins. Conclusions: In patients undergoing BCS for DCIS, the presence of DCIS-AMC at margins does not accurately predict margin positivity or the need for re-excision at that margin; no histologic factors predict their presence at the surgical margins.

Tumor Characteristics of Specimens with and without Calcifications Associated with DCIS at Margins

	Margins with DCIS-AMC (n=41)	Margins without DCIS-AMC (n=139)	p-value
ER+	39 (95%)	129 (93%)	1.00
PR+	36 (88%)	114 (82%)	0.48
Median Tumor Size (mm)	1.6 (0.3-7.5)	2.0 (0.3-7.5)	0.51
Tumor Grade			
Low	7 (17%)	17 (12%)	0.56
Intermediate	24 (59%)	78 (56%)	
High	10 (24%)	44 (32%)	
Comedo Architecture	5 (12%)	19 (14%)	1.00
Distance from Closest DCIS Focus to Margin (mm)	5 (0.1-14.0)	>10 (0->10)	<0.001

*Continuous variable expressed as median (range). Categorical variables expressed as n (%).

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Effect on Re-Excision Rates After Adoption of SSO: ASTRO-ASCO Ductal Carcinoma in Situ (DCIS) Margin Consensus Guidelines
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Introduction Approximately one-third of women who have breast-conserving surgery (BCS) for ductal carcinoma in situ (DCIS) undergo re-excision for close or positive margins. In 2016, the SSO, ASTRO, and ASCO published a consensus guideline recommending a 2mm margin in patients with DCIS undergoing BCS and whole-breast irradiation. The aim of this study was to determine re-excision rates before and after guideline adoption at a single institution. Methods Patients undergoing BCS for DCIS prior to adoption of the consensus guideline (January 1, 2016-June 30, 2016) and after adoption of the guideline (January 1, 2017-June 30, 2017) were identified. Margins were defined as positive (tumor on ink), close (≤1mm), 1-1.9mm or negative (≥2mm). Clinical and pathologic characteristics, and rates of re-excision were compared using generalized mixed models incorporating a random surgeon effect. Results 212 patients met inclusion criteria for the study: 105 before and 107 after guideline adoption. Median age was 58 years (range 30-85). DCIS was estrogen receptor positive (ER+) in 85%. 53% of patients received radiation therapy (RT). There was no significant difference in age, breast density, method of diagnosis, nuclear grade, necrosis, ER+, RT or endocrine therapy between the two groups. 45 (21%) patients underwent re-excision: 26 before, and 19 after guideline adoption (p=0.23). The table shows additional surgery per group. The most common reason for re-excision in both groups was close margins (≤1mm), followed by tumor on ink. The only factor significantly associated with re-excision was high nuclear grade (OR=2.42). Of patients who underwent initial re-excision for close or positive margins, 23/45 (51%) had no residual DCIS in their re-excision specimens. Conclusion There was no significant change in re-excision rates following guideline implementation, and higher nuclear grade was the only independent variable associated with re-excision. We found low re-excision rates in both groups, reflecting that the DCIS margin consensus guideline appropriately allows for flexibility and clinical judgment in determining the need for re-excision of <2mm margins.

Table 1. Patterns of re-excision.

	Overall n=212	Pre-guideline n=105	Post-guideline n=107	p-value
Re-excision (n, %)				0.23
Yes	45 (21%)	26 (25%)	19 (18%)	
1 re-excision	40	23	17	
2 or more re-excisions	5	3	2	
Final mastectomy	10	3	7	
No	167 (79%)	79 (75%)	88 (82%)	
Residual close/positive margins after final re-excision	21	13	8	0.19

PT81

Bone Morphogenetic Protein Expression is Altered in Relation to ER Status and Affects Overall Prognosis A.A. Maawy,* E. Katsuta, L. Yan, K. Takabe. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction Bone morphogenetic proteins are members of the TGFβ family of signaling pathways. Differential expression noted in some forms of breast cancer and is known to affect tumor biology in multiple in-vitro studies. This study investigates the association of BMP6 & 7 gene expression with breast cancer survival in a large patient cohort Methods 1096 patients with breast cancer had treatment naïve samples of the tumors undergo genetic sequencing and the results of their sequencing stored in The Cancer Genome Atlas (TCGA) dataset. These patients were followed for a period of 10 years to allow for assessment of Overall survival (OS) in this time frame. OS was compared to expression of BMP6 & 7 and ER status based upon RNA-sequencing data in the Cancer Genome Atlas (TCGA). Results BMP6 & 7 (both $p<0.001$) significantly affected OS in the entire cohort. High BMP6 expression is associated with decreased OS and BMP7 with improved OS. In ER+ tumors BMP6 expression with improved OS (p=0.004) while in ER- tumors a decrease in OS (p=0.006). BMP7 expression was associated with improved OS in ER+ and ER- tumors. Gene Set Enrichment Analysis (GSEA) with $p<0.05$ was performed. In the entire cohort, BMP6 high tumors showed enrichment of myc, G2-M checkpoint and E2F targets. The BMP6 low group showed enrichment of estrogen response pathways. In ER+ tumors, multiple myriad pathways were enriched. In ER- tumors, BMP6 enriched myc targets and the BMP6 low group with multiple myriad pathways. GSEA of the entire cohort in the BMP7 showed enrichment of multiple myriad pathways, the BMP7 low group with none. In ER+ tumors, BMP7 high showed enrichment of multiple myriad pathways, the BMP7 low group none. In ER- tumors the BMP7 enriched for wnt-β-catenin and notch signaling pathways; the BMP7 low group with multiple pathways Conclusion BMP6 & 7 expression affect tumor biology and OS. Both molecules are significantly altered and affected by ER receptor status. ER positivity has an overall favorable prognosis with BMP expression and in triple negative tumors BMP6 expression associated with different effectors and pathways that negatively impact OS and may serve as a prognostic marker.

PT83

Evidence Does Not Support Enhanced Breast Cancer Surveillance in Patients with Multiple Endocrine Neoplasia Type 1 M.A. Romero Arenas,[1]* A.M. Silva Figueroa,[2] S.M. Hyde,[1] P.H. Graham,[1] E.G. Grubbs,[1] H.M. Kuerer,[1] J.E. Lee,[1] N.D. Perrier.[1] *1. Surgical Oncology, UT MD Anderson Cancer Center, Houston, TX; 2. Hospital Barros Luco-Trudeau, Santiago de Chile, Chile.*

Intro: Multiple endocrine neoplasia type 1 (MEN1) is an autosomal dominant syndrome that has been linked to over 20 mostly benign neoplasms. Recent reports suggest both an increased incidence of female breast cancer and an earlier age of onset in patients with MEN1. We aimed to determine if an increased prevalence of breast disease or breast cancer was observed in female patients with MEN1 from our institution. Methods: Adult female patients (age >18 years) with MEN1 confirmed by genetic testing were identified from institutional databases between 1993-2016. Clinical data were abstracted from the medical record including MEN1-related diagnoses, age at diagnosis, clinical details regarding documented breast disease, and associated treatment. Secondary neoplasms to the breast were excluded. Descriptive statistics were performed. Results: Eighty-eight adult women with MEN1 met the eligibility criteria. Breast disease was documented in 10/88 (11.4%) and 5 of these 10 women had a primary breast carcinoma. The median age at diagnosis for breast cancer was 58 (range 41-64) years and for benign breast lesions was 41 (range 26-67) years. In the cohort of MEN1 patients without breast lesions, 31/78 (40%) were age <40 years and the median age at last follow-up was 32 (range 18-39) years; the median age at last follow up for those >40 years of age was 53 (range 40-70) years. Conclusion: Our patients with MEN1 had a lower prevalence of breast cancer compared to the average US population (12.4%). Breast cancer in our patients with MEN1 did not appear to present at an earlier age than the average US population, although our cohort included a significant portion of younger women who would be ineligible for screening mammography by age alone. Nonetheless, half of patients with MEN1 and a documented breast lesion had breast cancer. Our data do not currently support altering standard screening for breast cancer in patients with MEN1, however, a high index of suspicion should be maintained for any breast lesion in these patients. Further research on the prevalence of breast disease in patients with MEN1 compared to the general population is warranted.

PT84

Stage and Disease-Free Interval are Useful in Selecting Patients for Surgical Management of Locally Recurrent and Metastatic Adrenocortical Carcinoma W. Lo,[1]* C. Kariya,[1] M.L. Good,[1] S.M. Steinberg,[2] J.L. Davis,[1] R.T. Ripley,[1] J.M. Hernandez.[1] *1. National Cancer Institute, Bethesda, MD; 2. National Cancer Institute, Bethesda, MD.*

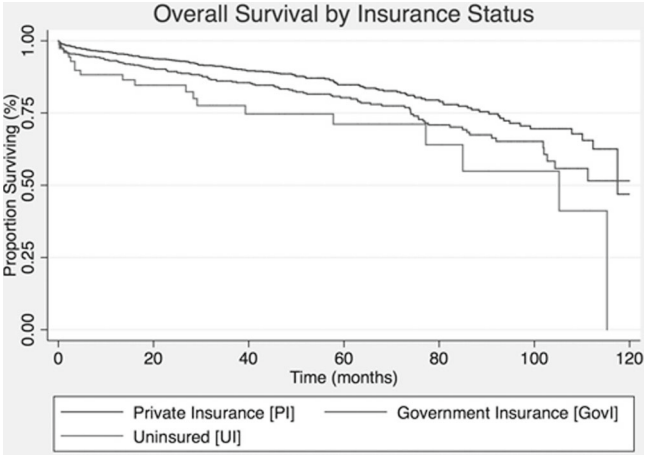
Introduction Systemic therapy options for patients with recurrent and metastatic adrenocortical carcinoma (ACC) are limited, often leading to consideration for re-resection/metastasectomy. We undertook this analysis of patients with surgically managed locally recurrent or metastatic ACC to determine characteristics associated with a two-fold increase in overall survival (OS) compared to what has been reported with chemotherapy alone. Methods All patients undergoing resection for recurrent ACC from 1988 to 2016 were identified from an institutional database. Patients were stratified by survival time from the date of first re-resection/metastasectomy: ≤12mo (~OS with chemotherapy alone) vs. > 24mo. Tumor stage, size, functional status, intent at operation, resection margin, initial disease-free interval (DFI), adjuvant radiation, and chemotherapy regimens were assessed for associations with survival Logistic regression was used to create a predictive model. Results Of the 84 patients with recurrent or metastatic ACC managed surgically at our institution, 58 patients were included in the analysis. Forty-three patients

survived >24 months and 15 patients died within 12 months from the time of re-operation. Early stage tumors at diagnosis (p = 0.01) and DFI from index adrenalectomy (p<0.0001) were associated with OS beyond 24 months. Tumor stage, size, functional status, intent at operation, margin status, treatment with neoadjuvant chemotherapy, adjuvant radiation/radioablative therapy, and adjuvant mitotane (all p >0.05) were not associated with OS. Initial DFI and stage at diagnosis jointly predicted survival beyond 24 months with approximately 70% accuracy. Patients who survived more than 24 months after reoperation underwent more subsequent procedures for recurrence than patients who died within 12 months (median 3 vs 0, p < 0.0001). Conclusion Stage at diagnosis and DFI can be employed to select patients who may derive a survival advantage from re-resection/metastasectomy. Patients treated surgically should be informed of the likelihood of requiring subsequent interventions.

PT85

Impact of Insurance Status on Survival in Gastrointestinal Neuroendocrine Tumors: A Multi-Institutional Study from the U.S. Neuroendocrine Study Group P. Marincola Smith,[1]* C.E. Bailey,[1] C. Solorzano,[1] A.G. Lopez-Aguiar,[3] M. Dillhoff,[2] E.W. Beal,[2] G. Poultsides,[4] E.A. Makris,[4] F.G. Rocha,[5] A. Crown,[5] C.S. Cho,[6] M. Beems,[6] E.R. Winslow,[7] V.R. Rendell,[7] B.A. Krasnick,[8] R. Fields,[8] S.K. Maithel,[3] K. Idrees.[1] *1. Department of Surgery, Vanderbilt University Medical Center, Nashville, TN; 2. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 3. Department of Surgery, Winship Cancer Institute, Emory University, Atlanta, GA; 4. Stanford University Medical Center, Stanford, CA; 5. Virginia Mason Medical Center, Seattle, WA; 6. Division of Hepatopancreatobiliary and Advanced Gastrointestinal Surgery, Department of Surgery, University of Michigan, Ann Arbor, MI; 7. University of Wisconsin School of Medicine and Public Health, Madison, WI; 8. Washington University School of Medicine, St Louis, MO.*

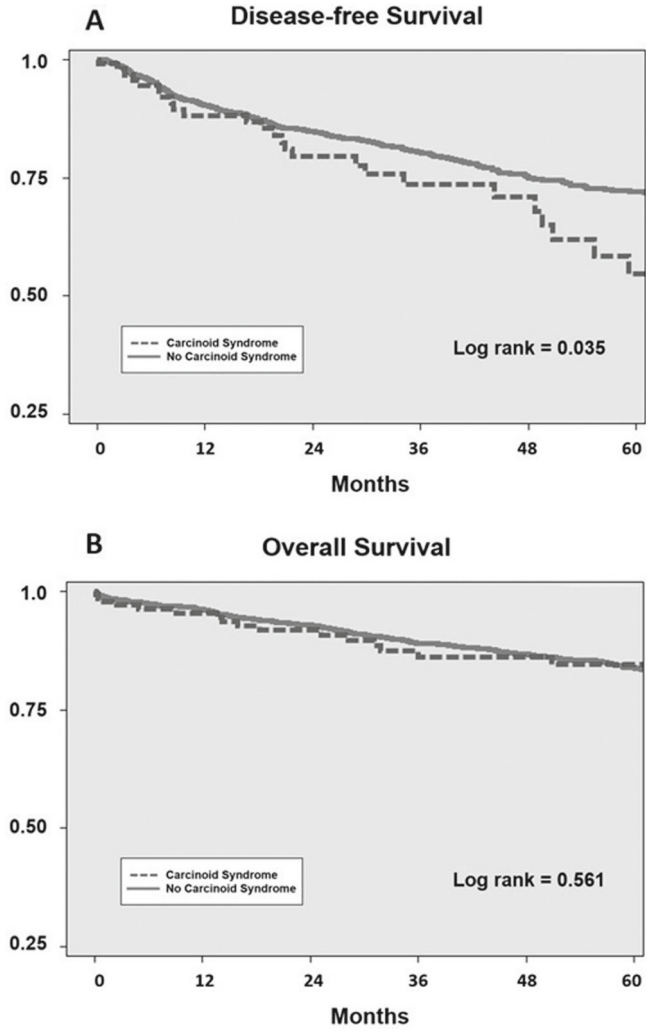
BACKGROUND: Insurance status predicts access to medical care in the U.S. Previous studies have shown uninsured and government insured patients with certain gastrointestinal malignancies have worse outcomes than patients with private insurance. However, the impact of insurance status on survival in patients with Gastrointestinal Neuroendocrine Tumors (GI-NETs) is unclear. We aim to evaluate the association between insurance status and survival in patients with GI-NETs. METHODS: A retrospective cohort study of adult patients with resected GI-NETs was performed using the U.S. Neuroendocrine Study Group database (2000-2016). Demographic and clinical factors were compared according to insurance status (private insurance [PI], government insurance [GovI], uninsured [UI]). Kaplan-Meier and log-rank analysis were used for survival analysis. Logistic regression analysis was used to assess factors associated with survival. RESULTS: The cohort included 2,022 patients with resected GI-NETs. The median age for GovI, PI and UI was 66, 54 and 56 years respectively (p<0.01). UI patients were more likely African American (21.5%) or Latino (5%) compared to PI and GovI patients (p<0.01). UI patients were more likely to undergo no post-operative surveillance imaging (39%) compared to PI and GovI patients (both 26%), but this was not statistically significant (p=0.15). There was no difference in ECOG performance status, tumor size at presentation, or operative intent (curative vs. palliative) between groups. Five-year overall survival was 86% for PI, 82% for GovI, and 73% for UI patients (p<0.01) (Figure 1). On multivariate regression analysis, being UI was independently associated with reduced survival (Hazard ratio 1.39, 95% confidence interval 1.08 – 1.80, p=0.012). CONCLUSION: In this study, insurance status appeared to be a predictor of survival in GI-NET patients. UI and GovI patients have worse OS compared to PI patients. Our study highlights the importance of access to medical care and disparities related to insurance status. Further studies are needed to investigate how to mitigate these disparities.



PT86

Influence of Carcinoid Syndrome on the Clinical Characteristics and Outcomes of Patients with Gastroenteropancreatic Neuroendocrine Tumors Undergoing Surgical Resection C. Kimbrough,[1]* E.W. Beal,[1] M. Dillhoff,[1] A.G. Lopez-Aguiar,[2] G. Poultsides,[3] E.A. Makris,[3] F.G. Rocha,[4] A. Crown,[4] D. Abbott,[5] A. Fisher,[5] R. Fields,[6] B.A. Krasnick,[6] K. Idrees,[7] P. Marincola Smith,[7] C.S. Cho,[8] M. Beems,[8] S.K. Maithel,[2] C.R. Schmidt,[1] T.M. Pawlik,[1] J. Cloyd.[1] *1. Ohio State University Wexner Medical Center, Columbus, OH; 2. Winship Cancer Institute, Emory University, Atlanta, GA; 3. Stanford University Medical Center, Stanford, CA; 4. Virginia Mason Medical Center, Seattle, WA; 5. University of Wisconsin School of Medicine and Public Health, Madison, WI; 6. Washington University School of Medicine, St. Louis, MO; 7. Vanderbilt University Medical Center, Nashville, TN; 8. University of Michigan, Ann Arbor, MI.*

Introduction: The incidence, clinical characteristics, and long term outcomes of patients with gastroenteropancreatic neuroendrocrine tumors (GEP-NETs) with carcinoid syndrome undergoing surgical resection have not been well characterized. Methods: Patients undergoing resection of primary and/or metastatic GEP-NETs between 2000-2016 were identified from an 8 institute collaborative database. Carcinoid syndrome was defined clinically as the presence of preoperative flushing, diarrhea, or other pathognomonic symptoms attributable to their neuroendocrine tumor. Clinicopathologic and postoperative characteristics, as well as overall survival (OS) and disease-free survival (DFS), were compared between patients with and without carcinoid syndrome. Results: Among 2,182 patients who underwent resection, 139 (6.4%) had preoperative carcinoid syndrome. Patients with carcinoid syndrome were more likely to be white (86.8% vs. 77.9%, p=0.02), have midgut primary tumors (41.0% vs. 19.0%, p<0.001), lymph node metastasis (63.4% vs. 44.3%, p<0.001), and radiographic evidence of metastatic disease (62.8% vs. 26.7%, p <0.001). There was no difference in tumor differentiation, grade, or Ki67 status. Patients with carcinoid syndrome had higher preoperative serum serotonin levels (1107 ng/mL vs. 357 ng/mL, p<0.05) and were more likely to be on preoperative somatostatin analogues (24.0% vs. 3.1%, p<0.001). Perioperative carcinoid crisis was rare (1.6% vs 0%, p<0.01), and the presence of preoperative carcinoid syndrome was not associated with postoperative morbidity (38.8% vs. 45.5%, p=0.129). Despite an association with worse DFS on univariate analysis (Fig 1A), carcinoid syndrome was not independently associated with DFS on multivariate Cox regression analysis (OR 1.07, 95% CI 0.64-1.80). Carcinoid syndrome was also not associated with OS (Fig 1B). Conclusion: Among patients undergoing surgical resection of GEP-NETs, the incidence of carcinoid syndrome was low. After controlling for measures of tumor burden, carcinoid syndrome was not independently associated with worse DFS or OS.



PT88

Underutilization of Surgery for Primary Hyperparathyroidism

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INTRODUCTION: Primary hyperparathyroidism is a common condition with associated morbidity. Clear guidelines exist for selecting patients who would benefit from parathyroidectomy, but many patients are not referred to surgery. The aim of this study was to evaluate differences between patients with biochemical evidence of hyperparathyroidism (HPT) who did and did not have parathyroidectomy. METHODS: Patients treated in a university-affiliated hospital system between 2006 and 2015 with serum calcium ≥10.3 mg/dL and parathyroid hormone level ≥66 pg/mL were identified. End-stage renal disease patients were excluded. Patients who underwent surgery were compared to those who did not. Multivariate logistic regression was performed to determine factors independently associated with not undergoing surgery. RESULTS: A total of 2906 patients with HPT were identified; 2191 (75.4%) did not undergo surgery. Among patients not having surgery, 1277 (58.3%) had at least one accepted criteria for parathyroidectomy: age<50 years, history of nephrolithiasis, renal insufficiency, osteoporosis, and serum calcium ≥11.3mg/dL. Patients who did not undergo surgery were older (70 v. 61 years, p<0.01), had lower serum calcium levels (10.7 vs. 11.0, P<0.01), and were less likely to have nephrolithiasis (12.9% vs. 17.3%, p<0.01) or osteopenia (38.3% vs. 43.4%, p=0.02). On univariate analysis, several comorbidities were negatively associated with having surgery: diabetes, hypertension, stroke, coronary artery disease, and renal disease. On multivariate analysis, factors associated with not having surgery included: older age, lower calcium, history of renal disease, absence of nephrolithiasis, and absence of osteopenia. CONCLUSIONS: Most patients meeting consensus guidelines for hyperparathyroidism did not undergo surgery. Education of health care providers is needed to improve patient care.

PT89

Quantitative CT Analysis for the Preoperative Prediction of Pathologic Grade in Pancreatic Neuroendocrine Tumors

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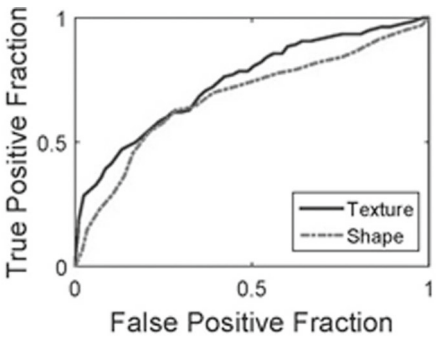
INTRODUCTION The prognosis for patients with pancreatic neuroendocrine tumors (PanNETs) is dependent on both tumor stage and grade (G1, G2, G3). Preoperative staging techniques have been established; however, determination of tumor grade can be difficult. Quantitative Analysis (QA) of CT imaging is an emerging field based on the concept that medical images may reflect pathophysiological characteristics of tissue that can be revealed by analyzing the intensity and distribution of the pixels and geometric features within tumors. The aim of this study was to evaluate whether QA can determine preoperative grade in PanNETs. METHODS Consecutive patients who underwent resection for G1/G2 (2015-2017) and G3 PanNET (2000-2017) who had available preoperative arterial phase CT imaging were reviewed. The tumor was manually segmented from the CT scan and the texture and shape-based features were extracted. Features were selected using fuzzy maximum relevance and minimum redundancy, and a classifier was created for the categorization of G1/G2 and G3 PanNETs. The classification performance was evaluated with area under the curve (AUC) and the model was validated with 10-fold cross-validation RESULTS There were 55 patients with PanNET and a preoperative CT scan identified. The study cohort included patients with G1 (n=24), G2 (n=18), and G3 (n=13) tumors. Overall, seven patients had a functional PanNET, in four cases the tumors were multifocal and arose in the context of a hereditary syndrome. Radiologically, the tumor appearance was solid in 35 cases, solid/cystic in 14 and cystic in six. The median size was 2.8 cm (IQR 1.8-4.5). At QA, four texture-features (G_7, L_{64}, L_{83} and L_{85}) and one shape-feature (S_2) was selected. The model based on shape features obtained an AUC of 0.69 while the model based on the texture features demonstrated the best performance obtaining an AUC of 0.74 (Figure 1). The inclusion of the tumor size in the two models did not improve performance. CONCLUSION CT quantitative analysis may be helpful in predicting pathologic grade in PanNETs. Further validation is needed to elucidate the role of QA as an imaging biomarker in patients with PanNETs.



	AUC	Accuracy	Sens.	Spec.	PPV	NPV
Texture	0.74	72	58	76	45	84
Shape	0.69	74	41	86	49	81

PT90

Validation of a Survival Nomogram for Adrenocortical Carcinoma

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Background:A published nomogram predicts 5-year overall survival (OS) in adrenocortical carcinoma (ACC) using tumor size, margins, and nodal status. It performed well in its developmental dataset (DD) (n=148 at 13 institutions), but was not externally validated. We sought to independently vali-

date this nomogram in a large cohort using the National Cancer Database (NCDB). Methods:NCDB records from 2004-13 were reviewed. Exclusion criteria matched those of DD. Survival and 95% confidence intervals (CI) were determined by Kaplan-Meier method and compared to nomogram-supplied OS predictions. Harrell's c-index tested discrimination. Calibration was assessed graphically and by percent deviance in predicted to observed OS. Results:Median age in 1145 included patients was 54 years and 61% were female, similar to DD (53 years, 66%). Median follow-up was longer in NCDB (58.7 vs. 23.0 months in DD). Margins were negative in 88.1% and median tumor size was 10.2cm, with 60.3% <12cm. Nodes were not reported (Nx) in 76.9%, with N0 and N1 in 17.6 and 5.6% (65, 26, and 9% in DD, P<0.01 by Chi-squared). Median OS was lower in NCDB compared to DD (64.1 vs. 86.3 months), as was 5-year OS (51.9 vs. 54.5%). The nomogram assigned 45% of NCDB patients the same OS prediction (70.5% 5-year OS in <12cm, Nx, R0 tumors). Nomogram discrimination was lower in NCDB than DD (c-index 0.58 vs. 0.70). Calibration plots showed predictions within CI for observed results in 5 of 7 groups.(Figure) The nomogram accurately identified high-risk patients, but struggled to distinguish patients at lower risk. For these patients, the nomogram overestimated survival. Deviance of nomogram predictions was +14.8% (mean 59.6 predicted vs. 51.9% observed). Conclusions:The ACC survival nomogram performed worse on independent validation with NCDB data than in DD due to its assignment of the same OS prediction to nearly half of NCDB patients. Smaller sample sizes or better outcomes in patients treated at DD centers compared to all of NCDB could explain overestimates of OS in lower-risk patients and warrants study. Complete nodal staging data and adding variables that better separate lower-risk patients could improve performance and clinical utility.

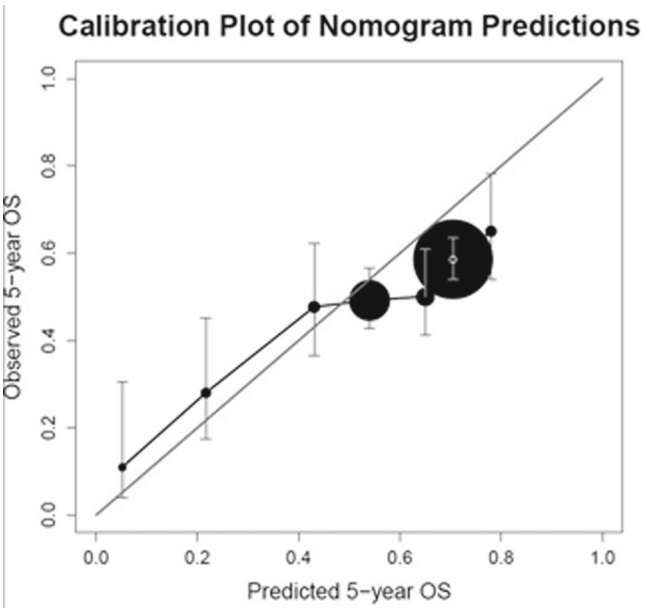

Figure:Calibration plot of nomogram predictions. Predicted 5-year overall survival in NCDB Adrenocortical Carcinoma patients (OS) is plotted on the x-axis with observed Kaplan-Meier 5-year OS on the y-axis. Perfect calibration, as indicated by the 45-degree red line, occurs when predicted survival is equal to observed. Point size is scaled relative to the number of patients in each group. Bars indicate the 95% confidence intervals for observed 5-year OS. For two points (representing 55% of patients), survival predictions fall outside the confidence interval of the observed survival. The largest patient group fell outside of the CI for true KM-observed survival (70.5% predicted vs. 58.6% observed, CI 54.0-63.6%).

PT91

Survival for Small, Well-Differentiated PNETs Does Not Differ by Treatment B.T. Julian,[1]* P. ituarte,[2] Z. Jutric,[2] G. Singh,[2] I.B. Paz,[2] A. Lewis.[2] *1. General Surgery, Huntington Memorial Hospital, Pasadena, CA; 2. City of Hope, Duarte, CA.*

Background Management of small well-differentiated pancreatic neuroendocrine tumors (PNETs) is controversial, and the malignant potential remains uncertain. Treatment options include observation (OB), enucleation (EN), and formal resection (Distal pancreatectomy – DP, Whipple/ Total pancreatectomy – PD). Our objective was to analyze the association between treatment types of small PNETs and overall survival (OS). Methods The California Cancer Registry linked with the Office of Statewide Health Planning and Development inpatient database was queried from 2000-2012 for patients with <3 cm, nonfunctional, stage I–II PNETs. Exclusion: poorly-differentiated PNETs or metastases within 6 months. Non-parametric statistics (Kruskal-Wallis) or Fisher's exact test were used to determine if any patient characteristics were associated with type of treatment (surgery or observation). Ten-year OS was estimated by the Kaplan-Meier method. A multivariate model was performed using Cox proportional hazards. Results Of 1,862 patients with PNETs, 204 were small, well-differentiated. Treatments include: OB n=41, EN n=20, DP n=106, or PD n=67. Few patients developed distant recurrences past 6 months (OB, n=0; EN, n=0; DP, n=2; PD, n=1). On bivariate analysis, comorbidities (2 or more, p=0.024), insurance type (p=0.018), and mean number of lymph nodes retrieved (EN=1.8 +/- 4.1; DP=6.3 +/- 7.63; PD=11.0 +/-8.5) were associated with treatment. Patient gender, race, socio-economic status, hospital type, tumor size, grade (well vs. moderate), and lymph node status at diagnosis were not associated with treatment type. On multivariate analysis, treatment type was not associated with worse OS (p=0.098). Ten-year OS is similar between treatment groups (Figure 1, p = 0.18). Conclusion In this unique study accounting for time of metastasis in patients who present with early stage, well-differentiated PNETs, observation, enucleation, and resection are equally associated with long-term survival. In the appropriately selected patient group, enucleation or observation may be alternatives to more aggressive surgery.

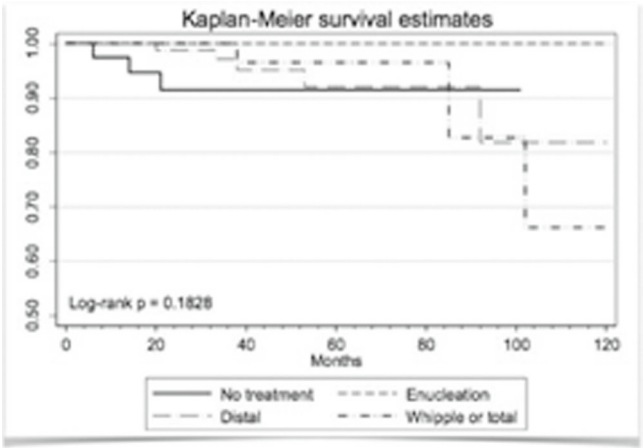

Figure 1. Overall survival of PNETs at 10 years by treatment type

PT92

Well-Differentiated Thyroid Cancer and Robotic-Assisted Surgery: a Retrospective Review of Safety and Feasibility at Two Western Institutions M.E. Garstka,[1]* P. Aidan,[2] K. Ibraheem,[1] M. Bechara,[2] K. Mohsin,[1] D. Bu Ali,[1] H. Shalaby,[1] M.A. Farag,[1] S. Kang,[1] E. Kandil.[1] *1. Department of Surgery, Tulane University School of Medicine, New Orleans, LA; 2. American Hospital of Paris, Paris, France.*

Introduction: Many recent studies report the safety and feasibility of robotic-assisted approaches for thyroid cancer surgeries, but most of these studies were performed in Asia. The aim of our study is to report the safety and feasibility of robotic-assisted thyroid surgery for well-differentiated thyroid cancer patients at two Western institutions. Methods: We performed a retrospective cohort study using prospectively collected clinical databases from two academic medical centers, one in North America and one in Europe. We included all well-differentiated thyroid cancer patients who underwent

surgery from January 2015 to June 2017. Patient demographics and perioperative data were collected and analyzed. Results: A total of 255 surgeries for thyroid cancer were performed; 143 (56.0%) were robotic. Central neck dissections were performed in 41 (28.7%) robotic and 32 (28.6%) cervical surgeries. Combined central and lateral dissections were performed in 8 (5.6%) robotic and 12 (10.7%) cervical cases. Patients undergoing robotic surgery were significantly younger (45.7±12.1 years vs 52.7±14.5 years, p <0.001) and had a significantly lower BMI (24.6±4.3 kg/m^2 vs 32.2±8.1 kg/m^2, p<0.001). Thyroid volume was significantly less for robotic procedures at 26.2±17.7 cm^3 compared to 33.4±23.1 cm^3 for cervical approach (p=0.02), but there was no significant difference in size of the primary tumor. There were no significant differences in estimated blood loss or operative time (153.1±52.8 minutes for robotic vs 145.1±87.7 minutes for cervical, p=0.4). Overall mean length of stay for the North American institution was significantly shorter for robotic procedures (0.6±0.9 days vs 1.1±1.2 days, p=0.009). Mean follow-up duration was 10.7±7.3 months, and there were three episodes of recurrence after cervical procedures. Conclusions: Robot-assisted thyroid surgery is a safe and feasible approach for a select group of well-differentiated thyroid cancer patients in Western populations. Future multi-institutional studies and long-term oncologic follow-up studies are needed.

PT93

Characteristics and Outcomes Associated with Tumor Size in Small Bowel Neuroendocrine Neoplasms N. Manguso,[1]* A. Gangi,[1] E.L. Siegel,[1] A. Harit,[1] A. Hendifar,[2] F. Amersi.[1] *1. Cedars-Sinai Medical Center, Department of Surgery, Los Angeles, CA; 2. Cedars-Sinai Medical Center, Division of Hematology and Oncology, Department of Medicine, Los Angeles, CA.*

Introduction: Patients with small bowel neuroendocrine tumors (SBNET) are often diagnosed with advanced disease due to the slow growing nature of these neoplasms. The association of tumor size on pathologic characteristics and long-term outcomes is not well described. Methods: Database review identified 261 patients with a primary SBNET from 1990 to 2015. Patients with Stage IV disease at diagnosis were excluded. Patients with primary tumors less than or equal to 1 cm (≤1cm) and those with tumors larger than 1 cm (>1cm) were compared. Clinical, pathologic and long-term outcomes were evaluated. Survival estimates were performed using the Kaplan-Meier method. Results: 132 patients were identified with a median age of 59 years (range 21-91). Most primary tumors were in the ileum (76.5%). Median tumor size was 1.5 cm (range 0.1-5.5). 35 (26.5%) patients had primary tumors ≤1 cm and 97 (73.5%) had tumors >1 cm. No significant differences in age, race, operation performed or tumor location were identified. Additionally, there was no difference in tumor grade (p=0.56), positive margins (p=0.7) or presence of multifocal disease (p=0.13). Patients with tumors ≤1 cm were significantly less likely to have lymphovascular invasion (LVI) (21.2% vs 71.4%, p<0.001), perineural invasion (PNI) (9.4% vs 50.6%, p<0.001), and mesenteric disease (40.0%, vs 84.5%, p<0.001). 118 (89.4%) patients had lymph nodes resected with 96 (81.3%) having nodal disease. Tumors ≤1 cm were less likely to be associated with positive lymph nodes (48% vs 92%, p <0.001). With a median follow-up of 4.6 years, there were 40 (30.3%) recurrences, all in the >1cm group. Eleven (8.3%) deaths occurred, 10 (10.8%) of which were in the >1cm group. 10-year disease-free survival (DFS) was significantly better in the ≤1cm group (100% vs 37.5%, p=0.001); however, there was no difference in overall survival at 10 years (96% ≤1cm vs 83.4% >1cm, p=0.44). Conclusions: Primary tumors >1 cm are more likely to be associated with nodal disease, LVI and PNI, and patients in this group have a lower 10-year DFS. Despite these findings, patients with tumors >1cm have comparable 10-year OS to those with tumors ≤1 cm.

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Integrating Patient Reported Outcomes in Neuroendocrine Tumors Care: An Assessment of Cognitive and Psychological Screening Tools During Follow-up J.L. Hallet,* E. Isenberg-Grzeda, J. Kazdan, K. Beyfuss, S. Myrehaug, S. Singh, D. Chan, C. Law. *Sunnybrook Health Sciences Centre, Toronto, ON, Canada.*

Background: An association between neuroendocrine tumors (NETs) and neuropsychological symptoms is suggested, but objective data is limited. We aimed to assess the burden of neuropsychological symptoms in NETs using validated patient reported outcomes (PRO). Methods: We conducted a prospective cohort study of adult patients with WHO grade 1 and 2 NETs. The validated Beck Depression Inventory (BDI-II), Functional Assessment of Cancer Treatment Cognitive domain (FACT-Cog), and EORTC-GEPNET 21 were administered to patients by phone. An exploratory preliminary analysis was conducted after 2 months. Patients were also asked about their preference for psycho-social support. Results: Of 80 patients, 27.5% had BP and 65.2% GEP primary NETs. Metastases were present in 65% and 30% were hormonally active (elevated 24-hour urinary 5-HIAA). No patients had an established cognitive or psychiatric diagnosis. Median time from NETs diagnosis to PROs measure was 82 (IQRL: 64.5-125) months. Using the BDI-II, 16.3% of patients presented mood disturbances, 17.5% signs at or above the level of clinical borderline depression, and 8.8% moderate to severe depression. FACT-Cog assessment revealed moderate perceived cognitive impairment (median 61, IQR: 50-68, possible range 0 to 72) and considerable reduction in perceived cognitive ability (median 5, IQR: 2-10, possible score 0 to 28). On the EORTC-GEPNET21, social functioning was the most impacted domain (median 16.7, IQRL 8.3-33.3). Gastro-intestinal, endocrine and treatment related symptoms were mildly impacted. Patients preference (very likely/likely to use) for psycho-social support was: social work 23.8%, psychology services 32.6%, psychiatry services 36.2%, and patient support group 36.3%. Conclusion: Using validated PROs, one out of 5 patients presented signs of clinical depression and perceived cognitive ability was impaired, during the maintenance phase of care. While symptoms appeared controlled, social functioning was impacted. These results provide insight into the need to routinely screen NETs during follow-up in order to offer support and improve patient-centred longitudinal care

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Clinical Outcome of Thyroid Atypia of Undetermined Significance and Role of Molecular Genotyping: Single Institution Experience Y.K. Hong,* W. Kim, M.R. Nowacki, M. Kelecy, R.C. Martin II, A.R. Quillo. *Surgery, University of Louisville, Louisville, KY.*

Background: Thyroid atypia of undetermined significance(AUS) or follicular lesion of undetermined significance (FLUS) presents a clinical management dilemma of whether to repeat an FNA biopsy versus resection for this indeterminate category. Molecular genotyping has been proposed to predict malignancy from FNA results in these situations. We aim to describe the incidence of AUS and their risk for malignancy on final pathology with correlation with their molecular genotype. Method: We reviewed our prospective Endocrine database for fine needle aspiration (FNA) of thyroid nodules from 2010 to 2017 for AUS/FLUS. Patients were evaluated for surgical management, molecular genotyping, and predictive incidence of malignancy on final pathology. Result: There was a total of 1732 thyroid nodules evaluated by FNA with 253 (14.6%) AUS. Of the 100 patients who underwent thyroidectomy, the overall malignancy rate was 28% (28/100) on final pathology with 96.4% (27/28) papillary carcinoma. There was no correlation of malignancy on final pathology with gender (female 26.1% vs male 45.4%; p = 0.284), size of nodule (malignant 1.75cm vs benign 2.09; p = 0.183), or age (malignant 56.7 yrs vs. benign 56.8 yrs; p=0.972). The frequency of gene mutation was BRAF V600E (2.2%), NRAS (18.5%), KRAS (2.2%), and HRAS (2.2%). Of those with genetic mutation who underwent thyroidectomy, the malignancy rate on final pathology was 100% (1/1 BRAF), 36.4% (4/11 NRAS), 0% HRAS (0/1), and 0% KRAS (0/1). The malignancy rate on surgical pathology without a genetic mutation was 18.5% (5/27). Conclusion: Thyroid atypia of undetermined significance does not have an insignificant incidence of malignancy potential with a higher probability when a molecular genetic mutation is present. Clinical management with molecular profiling results should facilitate the decision of surgical resection versus observation given the increased potential of malignancy in AUS/FLUS.

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Survival After Surgery for Metastatic Small Bowel Compared to Pancreatic Neuroendocrine Tumors S.J. Concors,* B. Ecker, A.J. Sinnamon, D.L. Fraker, G. Karakousis, C.M. Vollmer, R. Roses. *Hospital of the University of Pennsylvania, Philadelphia, PA.*

Background Surgical management of small bowel (mSBNET) and pancreatic (mPNET) neuroendocrine tumors with hepatic metastases remains controversial. Previous studies, often drawn from single institution experiences, combine outcomes mSBNET and mPNET cohorts, despite ample evidence indicating discreet biology and natural history. This study aimed to define and contrast survival outcomes after surgery in patients with mSBNET and

mPNET using a large national dataset. Methods Patients with hepatic metastases from SBNET and PNET who underwent surgical (n= 1063; n= 556, respectively) or non-surgical management (n= 456; n= 2593, respectively) were identified in the National Cancer Database (1998-2014). Surgical and non-surgical cohorts were matched (1:1) by propensity scores based on the likelihood of receiving surgery and survival hazard. Kaplan-Meier estimates of overall survival (OS) were compared. Results After adjustment for potential cofounders (age, Charleston comorbidity index, tumor differentiation and administration of chemotherapy or radiotherapy), nonsurgical management was associated with worse survival in SBNET (HR 2 95%CI 1.5-2.7) and in PNET (HR 3.6, 98%CI 2.8-4.5). In the propensity matched cohort, there was a significant survival advantage for patients who received surgery for both SBNET and PNET (p<0.001, Figure 1). In SBNET, mean survival in the non-surgical cohort was 33.9 months (SD 1.3, 95%CI 31.5-36.4), and 39.3 months in the surgical cohort (SD 0.8, 95%CI 36.1-39.1). In PNET, mean survival in the non-surgical cohort was 32.7 months (SD 1.6, 95%CI 29.5-35.8), and 55.1 months in the surgical cohort (SD 1.4, 95%CI 52.4-57.7). Conclusions Surgical selection or management are associated with a survival advantage in both mPNET and mSBNET; this advantage is greater in mPNET. The relative contributions of patient selection and therapeutic benefit require further elucidation.

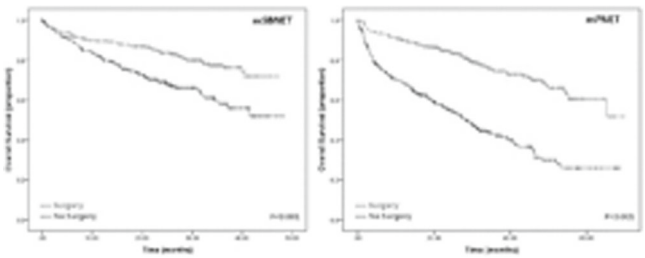

Figure 1. Impact of surgery on overall survival in mSBNET (257 [nonsurgical] v. 343 [surgical]) and mPNET (363 [non-surgical] v. 383 [surgical]) in the propensity matched cohort.

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Disparity in the Use of Adjuvant Radioactive Iodine Ablation Among High-Risk Thyroid Cancer Patients A.S. Moten,[1]* H. Zhao,[2] A.I. Willis.[3] *1. Temple University Hospital, Philadelphia, PA; 2. Lewis Katz School of Medicine at Temple University, Philadelphia, PA; 3. Thomas Jefferson University, Philadelphia, PA.*

Background: The American Thyroid Association (ATA) Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer in 2015 have implications on the use of adjuvant radioactive iodine ablation (RAI). Our aim was to identify treatment disparities existing prior to publication of these guidelines in order to identify patient groups at risk for receiving inadequate treatment. Methods: Patients diagnosed with papillary thyroid cancer from 2011-2013 were identified using the Surveillance, Epidemiology and End Results database. High-risk disease was defined as T4, NI, or M1. Chi-square tests compared both the characteristics of patients with and without high-risk disease and the characteristics of high-risk patients who did and did not receive RAI. Logistic and Cox regressions were used to determine odds of having high-risk disease, odds of receiving RAI for high-risk disease, and risk of death associated with receipt of RAI. Results: Sample included 32,229 individuals; 7,894 (24.5%) had high-risk disease. Mean (SD) age was 50.0 (14.8) years, 24,815 (77.0%) were female, and 21,318 (66.2%) were white. Odds of high-risk disease were greater among males (OR:2.04; 95% CI:1.92–2.16), Hispanics (OR:1.67; 95% CI:1.56–1.79) and Asians (OR:1.49; 95% CI:1.37–1.62), and uninsured (OR:1.24; 95% CI:1.07–1.43). Odds of high-risk disease were lower among patients ages 45-64 (OR:0.57; 95% CI:0.53-0.60), and ≥65 years (OR:0.54; 95% CI:0.50-0.59), and Blacks (OR:0.46; 95% CI:0.40-0.53). Most (69.3%) high-risk patients received RAI. Odds of receiving RAI among high-risk patients were lower among patients age ≥65 years (OR:0.67; 95% CI:0.58–0.77), the uninsured (OR:0.52; 95% CI:0.41–0.67), or Medicaid (OR:0.58; 95% CI:0.50–0.69). Use of RAI among high-risk patients reduced the risk of mortality in all age groups (HR:0.29; 95% CI:0.18–0.47). Conclusion: High-risk thyroid cancer patients were less likely to receive RAI if they were older, uninsured, or had Medicaid. Knowledge of these treatment disparities will allow recognition of groups at risk for high-risk disease and receiving inadequate treatment.

Characteristics of high-risk patients by radioactive iodine (RAI) category

	All, n (%)	No RAI, n (%)	RAI, n (%)	Chi Square p-value	Adjusted** Odds of Receiving RAI, Odds Ratio (95% CI)
High Risk Population	7,894 (100)	2,422 (30.7)	5,472 (69.3)		
Mean (SD) Age (years)	46.8 (15.7)	48.3 (16.7)	46.2 (15.3)	< 0.001*	0.992 (0.989 – 0.995)*
Age Group (years)				< 0.001*	
< 45	3,707 (47.0)	1,082 (44.7)	2,625 (48.0)		Reference
45 – 64	3,017 (38.2)	887 (36.6)	2,130 (38.9)		0.990 (0.889 – 1.103)
≥ 65	1,170 (14.8)	453 (18.7)	717 (13.1)		0.670 (0.580 – 0.773)*
Sex				0.22	
Female	5,392 (68.3)	1,631 (67.3)	3,761 (68.7)		Reference
Male	2,502 (31.7)	791 (32.7)	1,711 (31.3)		0.940 (0.846 – 1.045)
Race				0.03*	
White	4,825 (61.1)	1,449 (59.8)	3,376 (61.7)		Reference
Black	230 (2.9)	83 (3.4)	147 (2.7)		0.846 (0.638 – 1.121)
Hispanic	1,673 (21.2)	543 (22.4)	1,130 (20.7)		0.958 (0.845 – 1.087)
Asian	1,029 (13.0)	296 (12.2)	733 (13.4)		1.047 (0.901 – 1.218)
Other/Unknown	137 (1.7)	51 (2.1)	86 (1.6)		0.809 (0.563 – 1.161)
Insurance Type				< 0.001*	
Insured	6,754 (85.6)	1,930 (79.7)	4,824 (88.2)		Reference
Uninsured	294 (3.7)	125 (5.2)	169 (3.1)		0.525 (0.412 – 0.669)*
Medicaid	731 (9.3)	298 (12.3)	433 (7.9)		0.585 (0.498 – 0.688)*
Unknown	115 (1.5)	69 (2.9)	46 (0.8)		0.279 (0.191 – 0.408)*

*p-value significant at the < 0.05 level.
**Adjusted for age, sex, race, insurance type, surgery type and number of nodes removed.

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The Pancreas as a Site of Metastasis or Second Primary in Patients with Small Bowel Neuroendocrine Tumors A.T. Scott,[3]* D. Pelletier,[4] J.E. Maxwell,[3] S.K. Sherman,[2] K.J. Keck,[3] G. Li,[3] J.S. Dillon,[1] T.M. O'Dorisio,[1] A.M. Bellizzi,[4] J.R. Howe.[3] *1. University of Iowa Carver College of Medicine, Department of Internal Medicine, Iowa City, IA; 2. University of Chicago, Department of Surgery, Chicago, IL; 3. University of Iowa Carver College of Medicine, Department of Surgery, Iowa City, IA; 4. University of Iowa Carver College of Medicine, Department of Pathology, Iowa City, IA.*

Introduction: The small bowel and pancreas are the most common primary sites of neuroendocrine tumors (NETs) giving rise to metastatic disease. We have observed that some patients with small bowel NETs (SBNETs) present with synchronous or metachronous pancreatic NETs (PNETs), and it is unclear whether these are separate primaries or metastases from one site to the other. We examined this question using gene expression and immunohistochemistry (IHC) in patients with both SBNETs and PNETs. Methods: A surgical NET database including patients undergoing operations for SBNETs or PNETs was reviewed. Patients with synchronous or metachronous SBNETs and PNETs at exploration or on follow-up imaging were identified, and available tissues from primary tumors and metastases were examined using a previously validated 6-gene qPCR and immunohistochemistry (IHC) panel developed for evaluating tumors of unknown primary. Results: Of 338 patients undergoing exploration, 11 had both SBNETs and PNETs. Synchronous lesions were found in 8, while 3 presented with SBNETs followed by PNETs. Tissues from 11 SBNETs, 9 PNETs and 10 metastases were analyzed. qPCR and IHC data revealed that 3 patients had separate SBNET and PNET primaries, and 5 patients had SBNETs which metastasized to the pancreas (Table). In the other 3 patients, pancreatic tissue was unavailable in 2, and qPCR and IHC gave discrepant results in 1. Separate primary PNETs all presented synchronously and tended to be larger, but this difference was not significant (p=0.2). Conclusions: Both SBNETs and PNETs were found in 3% of our patients, none of whom had MEN1 or VHL. In nearly two thirds of evaluable patients the pancreatic tumor was a metastasis from the SBNET primary, while in the other third of patients it represented a separate primary. In patients where pancreatic tumors are suspected to be metastatic from SBNETs, such as those with smaller tumors, metachronous presentation, or CDX2 positivity by IHC, a less aggressive surgical approach to the PNET should be considered, especially in the setting of widely metastatic disease. Preoperative core biopsy with IHC may aid in this decision making.

Primary Tumor Site as Predicted by qPCR/IHC

Pt. ID	Presentation	SBNET	PNET	PNET Size (cm)	Classification
517-1	Synchronous	na/SB	na/Pa	10	Separate
133-1	Synchronous	SB/SB	Pa/Pa	3.2	Separate
256-1	Metachronous (83 mos)	SB/SB	SB/SB	1.2	SB Metastasis
137-1	Metachronous (96 mos)	SB/SB	na/na	3.1	Unknown
339-1	Synchronous	SB/SB	SB/SB	3	SB Metastasis
494-1	Synchronous	SB/SB	Pa/SB	2.5	Discrepant
220-1	Metachronous (27 mos)	SB/SB	na/SB	1.8	SB Metastasis
506-1	Synchronous	SB/SB	SB/SB	2.7	SB Metastasis
518-1	Synchronous	SB/SB	SB/SB	3.8	SB Metastasis
547-1	Synchronous	SB/SB	Pa/Pa	5.1	Separate
408-1	Synchronous	SB/na	na/na	1.6	Unknown

na=not available; SB=small bowel; Pa=Pancreas; mos=months to PNET appearance after SBNET diagnosis

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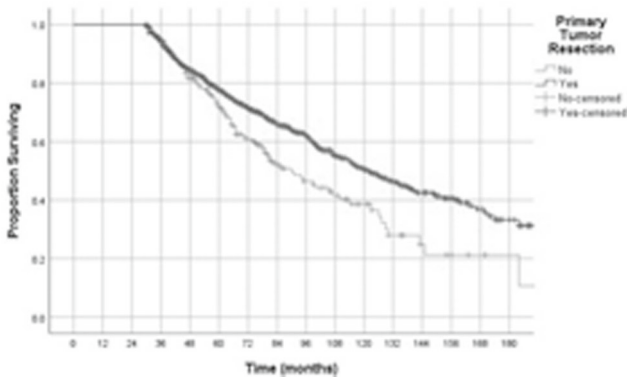
Outcome of Primary Tumor Resection in Patients with Metastatic Midgut Neuroendocrine Tumors C. Schlegel,* K. Idrees, C.E. Bailey. *Vanderbilt University, Nashville, TN.*

Introduction: Approximately 30% of patients with gastrointestinal neuroendocrine tumors (NET) present with metastatic disease, most commonly to the liver. Successful resection of these metastatic foci can lead to improved long-term survival, but a significant number of patients present with unresectable metastatic disease. Much debate remains regarding the role of primary tumor resection (PTR) in these patients. The primary aim of this study was to evaluate the prevalence and impact of PTR in patients with metastatic midgut NET. Methods: A retrospective cohort study of patients diagnosed with metastatic midgut NET was performed using the Surveillance, Epidemiology, and End Results database (1998-2014). Demographic and clinical factors were compared for patients who underwent PTR and those who had not. Kaplan-Meier and log-rank analysis was used for survival analysis. Logistic regression analysis was used to assess factors associated with PTR. Results: The cohort included 1,023 patients with midgut NET and synchronous, non-resected distant metastasis. A total of 810 (79.2%) patients underwent PTR. There was no difference in age, gender, race, and marital status between the two groups. Patients who underwent PTR were more likely to have well/moderately differentiated tumors compared to patients who did not undergo PTR (39.6% vs. 20.2%, p<0.001). Median overall survival (OS) was significantly improved for patients who underwent PTR compared to those who did not (122 vs 90 months, p=0.001)[Figure]. In multivariate analysis, tumor location to the proximal colon (OR 1.75, 95% CI 1.12 to 2.74, p=0.015) was associated with increased PTR and increasing year of diagnosis (OR 0.86, 95% CI 0.83 to 0.91, p<0.001) was associated with decreased PTR. Conclusion: Resection of the primary neoplasm is associated with improved OS in patients with midgut NET and non-resected metastatic disease. Despite this survival improvement, 1 in 5 patients do not undergo PTR. Further work is needed to better understand and improve this disparity in care.

Figure. Overall survival stratified by primary tumor resection.



PT100

Hepatic Resection Versus TACE in Hepatitis B Virus Related UICC Stage T3 Hepatocellular Carcinoma Patients: A Propensity Score Matching Study C. Zhong,[1]* Y. Zhang,[2] R. Guo.[3] *1. Hepato-pancreato-biliary, The First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China; 2. Fudan University Shanghai Cancer Center, Shanghai, China; 3. Cancer Center of Sun Yat-sen University, Guangzhou, China.*

ABSTRACT Objectives: The optimal therapeutic strategy in hepatitis B virus related UICC stage (7th) T3 hepatocellular carcinoma that maximizes both safety and long-term outcome has not yet been determined. The aim of this study was to compare the clinical outcomes following hepatic resection (HR) versus transcatheter arterial chemoembolization (TACE) for those stage HCC. Methods: From 2005 to 2013, 1179 patients with hepatitis B virus related UICC stage T3 HCC who underwent HR or TACE were divided into two groups, HR (n=280) or TACE (n=899). The clinical outcomes were compared before and after propensity score matching. Results: The propensity model matched 244 patients with HR and TACE, respectively, for further analyses. After matching, medium overall survival (OS), 1, 3, and 5-year OS rates in TACE group were 11.8 months (95%CI, 9.9, 13.7), 49.6%, 16.5%, and 8.4%, respectively, which HR group were 17.8 months (95% CI, 14.8-20.8), 63.1%, 33.3%, and 26.4%, respectively; (log rank=19.908, P<0.01). Patients in HR group were more likely to developed pleural effusion, compared with those of TACE group (0.4% vs. 5.3%, P=0.01). However, no significant difference between the two groups was found for other AEs. Similar results were also demonstrated prior to the matched analysis. Multivariate analysis indicated that PT (HR=1.425; 95%CI, 1.128-1.800; P=0.003), tumor size (HR=1.406; 95%CI, 1.125-1.757; P=0.003), tumor number (HR=1.435; 95%CI, 1.014-2.030; P=0.042), TNM staging (HR=1.831; 95%CI, 1.311-2.559; P=0.000), and initial treatment of HR (HR=0.646; 95%CI, 0.522-0.798; P=0.000) were independent prognostic factors. Conclusions: Hepatic resection was safe and yielded a survival benefic compared with TACE in hepatitis B virus related UICC stage T3 HCC patients. Keywords: carcinoma, hepatocellular; hepatic resection; TACE; propensity score matching study

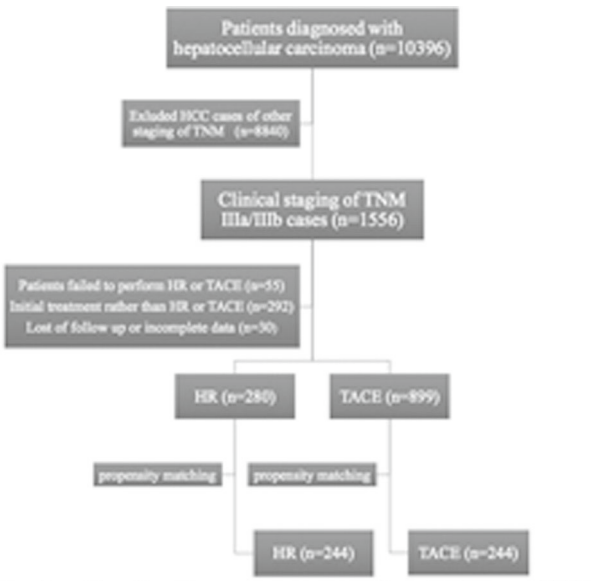


Fig 1. Flow chart of the study and the treatment strategies of patients with UICC stage T3 HCC.

Figure 1. Flow chart of the study and the treatment strategies of patients with UICC stage T3 HCC.

PT101

A Comparative Analysis of Discrepancies in Research Funding Among Cancers with High Mortality B. Hall,[1]* A. Cannon,[1] P. Atri,[1] A.K. Ganti,[2] C. Wichman,[1] L. Smith,[1] H. Wang,[1] A. Sasson,[3] C. Are,[1] S. Kumar,[1] S.K. Batra.[1] *1. University of Nebraska Medical Center, Omaha, NE; 2. VA Nebraska-Western Iowa Health Care System, Omaha, NE; 3. Stony Brook School of Medicine, Stony Brook, NY.*

Introduction: Discrepancies in research funding contribute to stagnant survival rates in pancreatic ductal adenocarcinoma (PDAC). Comparative analyses of survival and funding in cancers with high mortality were performed to quantify discrepancies and identify areas for intervention. Methods: The Surveillance, Epidemiology, and End Results database was queried for survival statistics. Funding data were obtained from the National Cancer Institute (NCI). Clinical trial data were obtained from www.clinicaltrials.gov. Inflation rates were obtained from the Federal Bureau of Labor Statistics. Cancers with high mortality were included for analyses. Results: We found that since 1997, 5-year overall survival (5Y-OS) rates have exceeded 90% for breast, melanoma, and prostate cancer; however, it remains less than 9% in PDAC. We estimate that PDAC will surpass breast and colorectal cancer in terms of years of life lost by 2024 at that point, over 800,000 years of life lost will be attributable to PDAC alone. Since 1997, fewer clinical trials have been completed in PDAC (n=680) compared to breast (n=2,077) and lung (n=2,046) cancer. Research funding emphasizing 'early detection and diagnosis' in PDAC has decreased by 50% since 2007 and presently accounts for only 6.9% of total PDAC funding. This trend was not observed in other cancers. Incremental cost effectiveness analysis demonstrated that research dollars invested in PDAC translated to a significantly greater increase in 5Y-OS when compared to dollars invested for melanoma, uterine, prostate, ovarian and female breast cancer (Table). Increases in annual NCI research funding have not matched inflation rates in over ten years, resulting in a cumulative deficit of $3.74 billion in all-cancer NCI research funding. Conclusions: The results of our study demonstrate that funding for pancreatic cancer lags behind other cancers. We also noted that research dollars invested in pancreatic cancer resulted in a greater return on investment as noted by the higher differential rate of improvement in 5Y-OS. The findings of this study provide the much needed objective data to support the multiple calls for increased funding for PDAC.

Incremental Cost Effectiveness Ratio (ICER) Analysis of NCI Funding in Cancer Research, 1997-2009

	Total NCI funding (Millions)	5Y-OS rate increase (%)	5Y-OS difference (%)	Funding difference (Millions)	ICER (Millions)
Pancreas	$603	3.92			
Uterine	$247	-0.70			
Melanoma	$1,084	2.74	-1.17	$482	
Prostate	$3,136	1.29	-2.62	$2,533	
Ovarian	$1,074	2.23	-1.69	$471	
Female breast	$6,509	2.18	-1.73	$5,906	
Liver	$739	10.33	6.42	$136	$21
Non-Hodgkin	$1,194	14.23	10.31	$591	$57
Lung	$2,822	4.95	1.03	$2,220	$2,158
Colorectal	$2,823	4.09	0.18	$2,220	$12,498

ICER demonstrates that millions (liver, non-Hodgkin's lymphoma) and billions (lung, colorectal) of dollars were needed for each additional percent increase in 5Y-OS relative to pancreatic cancer. Dollars spent in pancreatic cancer research more efficiently increased the 5Y-OS compared to melanoma, prostate, ovarian, and female breast cancer.

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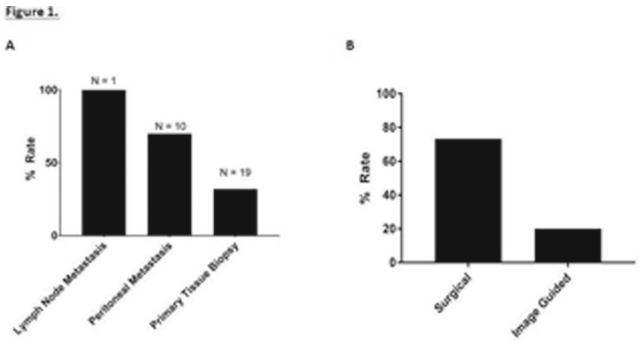
Biopsy Patient-Derived Xenografts for Hepatopancreatobiliary Cancers M. Hernandez, L. Yang, J. Leiting,* J. Bergquist, M. Truty. *Department of Hepatobiliary and Pancreas Surgery, Mayo Clinic, Rochester, MN.*

Introduction: Patient-derived xenografts are a robust translational platform that amplifies patient tumor tissue and provides a clinically relevant model to guide individualized medicine. Prior PDX series rely on surgical resected tissue and are limited to resectable cancers. We hypothesized that biopsy specimens (surgical/image-guided (IG)) could provide sufficient tissue for PDX generation in order to expand the phenotypic repertoire. Methods: We maintain a prospective GI cancer PDX program. With informed consent and IRB approval, surgical and IG biopsies were obtained from patients with either unresectable or metastatic tumors: pancreatic adenocarcinoma (PDAC), colorectal cancer, gastric cancer, cholangiocarcinoma (CCA), and gallbladder carcinoma. Biopsies were implanted into subcutaneous flanks of immunocompromised mice. Tumor growth was monitored, viable tumor was passed into subsequent generations, and histopathology was confirmed. Outcomes reported include 1) ischemic time (IT - retrieval to implantation), 2) time to tumor formation (TTF – days until first palpable PDX), 3) time to tumor harvest (TTH – days from implantation to harvest), and 4) engraftment ratio (ER - % of successful engraftment). Results: 30 patients underwent biopsy PDX engraftment. Overall ER was 0-100%. Gallbladder carcinoma and gastric cancers were most likely to engraft (100% ER) whereas PDAC and CCA demonstrated more engraftment rate variability (33% ER). For PDAC median TTF/TTH was (54, 105 days) respectively, in cases of gall bladder carcinoma (32,119 days) and in gastric carcinoma (136, 186 days). Increased engraftment was displayed in models derived from metastatic compared to primary tissue (71% versus 15.4%, p=0.001). The type of tissue biopsied (primary tissue, lymph node, or peritoneal metastases) demonstrated variability in ER, Fig 1A. ER was increased in surgical compared to IG specimens (p=0.003) Fig 1B. Conclusions: PDX of metastatic or unresectable tumors can be successfully created from clinical biopsies. Biopsy PDX technology may be increasingly offered in the preoperative setting, for unresectable disease, or for recurrent disease where conventional methods are impossible due to clinical constraints.



A. Variability of engraftment based on type of biopsied tissue B. Surgical biopsies are associated with increased engraftment compared to image-guided

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Macrophages Promote Aggressive Pancreatic Carcinoma L.F. Reed,* C.J. Freeburg, M.S. Husain, P. Dickson, J.L. Deneve, D. Shibata, E.S. Glazer. *College of Medicine, University of Tennessee Health Science Center, Memphis, TN.*

Introduction: Pancreatic Ductal Adenocarcinoma (PDAC) is expected to be the second leading cause of cancer related deaths by 2030. TGF-β is a well-studied PDAC mediator with a context dependent role as initially a tumor suppressor with potential to convert to a tumor promoter in later stages. Tumor associated macrophages and interleukins, such as the pro-inflammatory interleukin, IL23, are not well studied regarding PDAC. We hypothesized PDAC treated with TGF-β and macrophages would induce a more aggressive phenotype. Methods: We investigated aggressive behavior with a primary PDAC cell line in vivo and a metastatic PDAC cell line in vitro. A primary pancreatic cell line, Panc-1 cells, were pre-treated with PBS, IL23, macrophages (10:1 ratio of Panc-1 cells to macrophages), IL23 + macrophages, TGF-ß, TGF-ß + macrophages, or TGF-ß + macrophages + IL23. After treatment, cells were orthotopically implanted into the pancreas of NOD SCID gamma mice with 5 mice per group. Mice weights were recorded twice weekly for 4-weeks. Primary lesions and metastasis were investigated with ANOVA. AsPC-1 cells, a metastatic pancreatic cell line, were pre-treated with the same seven treatments. We investigated pSTAT3 expression and the streak closure in vitro. Results: Panc-1 cells treated with macrophages had the largest pancreatic tumor weight and diameter compared to PBS control, IL23 alone, and TGF-β alone ($P<0.001$). When macrophages treatment included TGF-β, pancreatic tumor weights and diameters decreased as compared to macrophages alone and macrophages + IL23 ($P<0.001$). Macrophage treatment induced higher liver weights and higher number of surface liver metastatic lesions suggesting higher metastatic disease burden ($P<0.03$). AsPC-1 cells treated with combinations of macrophages and TGF-β increased pSTAT3 expression compared to PBS control (see Figure). AsPC-1 cells treated with macrophages closed the gap in the scratch assay faster than PBS control 24 hours after treatment ($P<0.001$).

Conclusions. We demonstrated macrophages have a key role in converting primary pancreatic cancer into a more aggressive phenotype in vivo whereas they have less effect on metastatic pancreatic cancer in vitro.

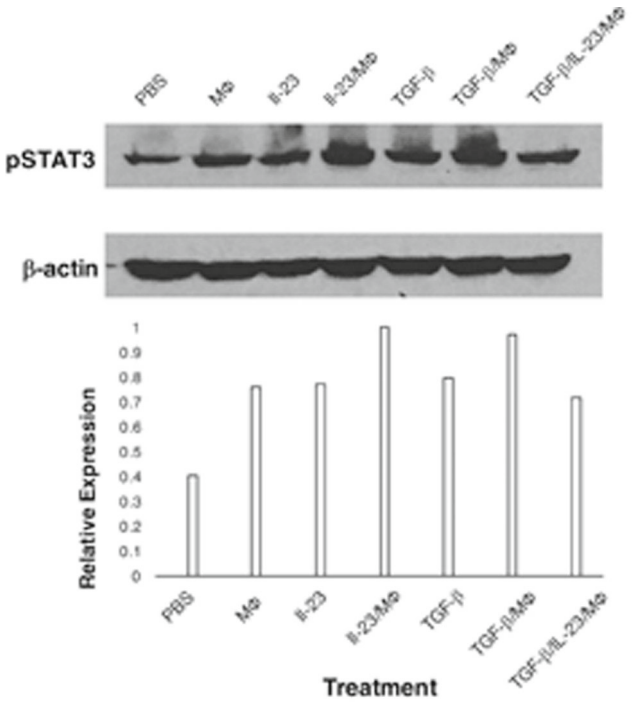


Figure 1: Expression of pSTAT3 in treated AsPC-1 cells normalized to β-actin controls.

PT104

Association of Adjuvant Chemotherapy with Overall Survival in Resected Pancreatic Adenocarcinoma Previously Treated with Neoadjuvant Therapy D.S. Swords,[1]* I. Garrido-Laguna,[1] S.J. Mulvihill,[1] G.J. Stoddard,[2] M.A. Firpo,[2] C.L. Scaife.[1] *1. Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; 2. University of Utah, Salt Lake City, UT.*

Background: Guidelines for adjuvant chemotherapy in patients with resected pancreatic adenocarcinoma (PDAC) who received neoadjuvant chemotherapy are equivocal. A lymph node ratio (LNR) ≥ 0.15 may predict lack of benefit, but conflicting results are reported. Methods: The National Cancer Database was searched to identify patients who were resected after neoadjuvant chemotherapy between 2006-2013. Exclusions were metastases at surgery, 90-day postoperative mortality, adjuvant radiation, and outlier interval from diagnosis to surgery (< 2.5 or > 10 months). The association between adjuvant chemotherapy and overall survival (OS) from diagnosis was examined using multivariable Cox regression and inverse propensity of treatment weighted (IPTW) Cox regression. An IPTW-based estimator of the average treatment effect (ATE) was used to quantify the population average survival benefit of treatment. Outcomes were examined in all patients and in patients with LNR < 0.15 and ≥ 0.15. Results: Of 2,488 patients, 681 (27.4%) received adjuvant chemotherapy. Adjuvant chemotherapy was administered to 357/1,518 (23.5%) node negative patients, 198/560 (35.4%) with LNR > 0 and < 0.15, and 126/410 (30.7%) with LNR ≥ 0.15. In multivariable Cox regression, adjuvant chemotherapy was associated with improved survival in the overall cohort and in patients with LNR < 0.15. A trend towards improved OS was also observed for those with LNR ≥ 0.15. After accounting for indication bias using IPTW, a significant survival benefit for was observed only for patients with LNR < 0.15. The ATE among LNR < 0.15 patients was 3.3 months (95% confidence interval 1.0, 5.7), indicating that the average survival of the population would be 3.3 months longer if all received treatment. Conclusions: Adjuvant chemotherapy in resected PDAC patients who received neoadjuvant therapy appears to be beneficial in patients with negative lymph nodes or minimal nodal burden. High LNR after neoadjuvant therapy may be an indicator of adverse tumor biology that is less likely to derive a therapeutic benefit.

Summary of the Association of Adjuvant Chemotherapy with Survival

	Hazard Ratio (95% Confidence Interval)	P Value
Multivariable Cox regression *		
Overall cohort (N=2,488)	0.84 (0.75, 0.94)	0.002
LNR < 0.15 (N=2,078)	0.84 (0.73, 0.96)	0.009
LNR ≥ 0.15 (N=410)	0.75 (0.56, 1.00)	0.05
Inverse Propensity of Treatment Weighted Cox regression**		
Overall cohort	0.88 (0.78, 1.00)	0.05
LNR < 0.15	0.86 (0.75, 0.99)	0.03
LNR ≥ 0.15	1.04 (0.82,1.33)	0.74

*Adjusted for sex, age, race/ethnicity, insurance status, Charlson/Deyo score, area income, area education, census region, year, clinical T and N stages, neoadjuvant radiation, surgical procedure, tumor location, pathologic T stage, LNR, size, grade, margin status, 30-day readmissions, and treatment at multiple CoC facilities.
**The above variables were used to predict propensity for adjuvant chemotherapy in the IPTW models.

PT105

Predictors of Adjuvant Treatment and Survival in Patients with Intrahepatic Cholangiocarcinoma Who Undergo Resection G.C. Lee,[1]* P.A. Vagefi,[1] C.R. Ferrone,[1] K.K. Tanabe,[1] K.D. Lillemoe,[1] D.C. Chang,[1] L.S. Blaszkowsky,[2] A.X. Zhu,[1] T.S. Hong,[2] M. Qadan.[1] *1. Surgery, Massachusetts General Hospital, Boston, MA; 2. Newton-Wellesley Hospital, Newton, MA.*

Background: Recent data from the BILCAP study recommends use of adjuvant capecitabine following resection of intrahepatic cholangiocarcinoma (ICC). However, administration of adjuvant therapy (AT) in patients with ICC remains controversial, with no clear practice guidelines. This study investigates predictors of receipt of AT in patients with resected ICC, and implications on survival. Methods: Patients with ICC who underwent resection, defined as any type of hepatectomy, were identified using the NCDB (2004-2014). Logistic regression and Cox proportional hazard analysis were used to determine predictors of AT, defined as receipt of chemotherapy and/or radiation after surgery, and overall survival. Results: A total of 3,292 patients with ICC who underwent resection were identified, of whom 1,335 (40.6%) received AT. Patients with positive margins, positive lymph nodes, age <65 years, fewer comorbidities, and higher clinical stage were more likely to receive AT (p<0.001). Black patients and patients with Medicare or Medicaid insurance were less likely to receive AT (p=0.008, p=0.024, and p=0.006, respectively). AT was associated with lower overall mortality in resected ICC patients (HR 0.67 for chemotherapy alone, HR 0.66 for chemoradiation, both p<0.001). On subgroup analyses of patients with negative margins, positive margins, and positive nodes, AT was significantly correlated with a survival benefit (all p<0.05). Interestingly, AT was associated with improved 1-year survival (81.3% with AT, 72.2% without AT, p<0.05) but worse 5-year survival (25.6% with AT, 33.3% without AT, p<0.05). Kaplan Meier curves suggest that the initial survival benefit offered by AT loses effect at approximately 20 months after diagnosis. Other factors associated with improved survival were negative margins, negative nodes, age <65 years, female gender, fewer comorbidities, tumor size <5 cm, and treatment at an academic center. Conclusions: Adjuvant therapy after resection of intrahepatic cholangiocarcinoma is associated with significant survival improvement, regardless of margin status. Interestingly, this survival benefit does not persist beyond 20 months after diagnosis.

Table 1. Cox proportional multivariable analysis of predictors of mortality in patients with resected intrahepatic cholangiocarcinoma (n = 1,965)

Characteristic	Hazard Ratio	P-value	95% Confidence Interval	
Type of adjuvant therapy				
None	Reference			
Chemotherapy alone	0.67	<0.001	0.57	0.78
Chemoradiation	0.66	<0.001	0.56	0.78
Positive resection margin	1.74	<0.001	1.52	1.99
Lymph node status				
Negative	Reference			
Positive	2.03	<0.001	1.71	2.42
Not examined	1.09	0.243	0.95	1.25
Age >65	1.30	0.002	1.10	1.54
Male	1.30	<0.001	1.16	1.46
Race				
White	Reference			
Black	0.86	0.262	0.66	1.12
Hispanic	0.98	0.870	0.75	1.27
Asian	0.91	0.484	0.69	1.19
Charlson/Deyo score (CDCC)				
CDCC 0	Reference			
CDCC 1	1.21	0.010	1.05	1.41
CDCC >=2	1.41	<0.001	1.17	1.69
Clinical stage				
1	Reference			
2	1.67	<0.001	1.43	1.96
3	1.87	<0.001	1.57	2.23
4	2.13	<0.001	1.72	2.62
Tumor size >5 cm	1.38	<0.001	1.23	1.55
Insurance type				
Private	Reference			
Medicare	0.93	0.393	0.79	1.10
Medicaid	1.16	0.338	0.86	1.56
Other government	0.71	0.207	0.42	1.21
None	1.20	0.414	0.78	1.85
Median income quartiles (by zip code)				
$63,000+	Reference			
$48,000-$62,999	1.16	0.096	0.97	1.37
$38,000-$47,999	1.14	0.178	0.94	1.39
<$38,000	1.37	0.013	1.07	1.76
Education level (% of region without high school degree)				
Higher education level (<7%)	Reference			
7-12.9%	1.12	0.199	0.94	1.32
13-20.9%	1.13	0.235	0.93	1.39
Lower education level (>=21%)	0.89	0.368	0.69	1.15
Facility type				
Community cancer program	Reference			
Comprehensive community cancer program	0.56	0.002	0.38	0.81
Academic/research program	0.48	<0.001	0.33	0.69
Integrated network cancer program	0.67	0.048	0.45	1.00
Distance between patient zipcode and hospital (miles)				
<10 miles	Reference			
10-40 miles	1.02	0.829	0.87	1.18
>40 miles	1.02	0.844	0.87	1.19
Year of diagnosis				
2004-2009	Reference			
2010-2014	0.86	0.028	0.75	0.98

PT106

Subcategorizing T1 Pancreatic Cancer Predicts Survival: An Analysis of the National Cancer Database M.M. Shah,[1]* R. NeMoyer,[2] S.H. Greco,[1] C. Chen,[1] D.F. Moore,[3] M.S. Grandhi,[1] T.J. Kennedy,[1] P. Javidian,[2] S.K. Jabbour,[1] D.A. August,[1] D.R. Carpizo.[1] *1. Surgical Oncology, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; 2. Robertwood Johnson Medical School, New Brunswick, NJ; 3. Rutgers School of Public Health, Piscataway, NJ.*

Introduction According to the AJCC 7th edition, T1 staging of pancreatic adenocarcinoma (PC) is defined as tumor limited to the pancreas, 2cm or less in greatest dimension. AJCC 8th edition subcategorizes T1 staging into T1a (< 5mm), T1b (< 1cm), T1c (< 2cm) for PC. We sought to determine if the subcategorization of T1 staging has prognostic significance. In addition, we sought to evaluate the impact of adjuvant therapy on overall survival (OS). Methods A retrospective review of patients undergoing definitive surgery for PC was performed using the National Cancer Database (NCDB) from 2004-2014. Of the 58 histology codes provided by NCDB, we used 22 codes associated with PC after consultation with our gastrointestinal pathologist. Kaplan-Meier survival was calculated. Survival was stratified by T1 subcategory for lymph node negative and positive patients, individually and collectively. Multivariate analysis was performed in stepwise regression for clinical variables that associated with OS. Results We captured 41,552 stage I and II patients that underwent definitive surgery for PC. The median OS was 20.1 months. 1,924 of these patients were pT1N0 PC. The 5-year OS for patients with T1a (n = 319), T1b (n = 296), and T1c (n = 1309) PC was statistically significantly different (68.8%, 57%, and 46.6%, respectively) [Fig. 1]. These differences in OS lost significance in node positive patients alone. There was no statistically significant association between patients receiving chemotherapy and OS. In the T1a subcategory, radiation therapy (RT) was statistically significantly associated with worse OS compared to no RT. Age (18-50, 51-65 vs. >65), geographic location (Midwest/South/West vs. North East), grade (2-4 vs. 1) and surgical margins were statistically significantly associated with OS. Conclusion Subcategorization of the T1 stage into T1a, T1b and T1c significantly stratifies patients by OS in node negative patients undergoing surgery for PC. This significance is lost in node positive patients. Adjuvant chemotherapy has no additional impact on the predictive power of T1 subcategorization. RT is negatively associated with OS in the T1a subcategory of patients.

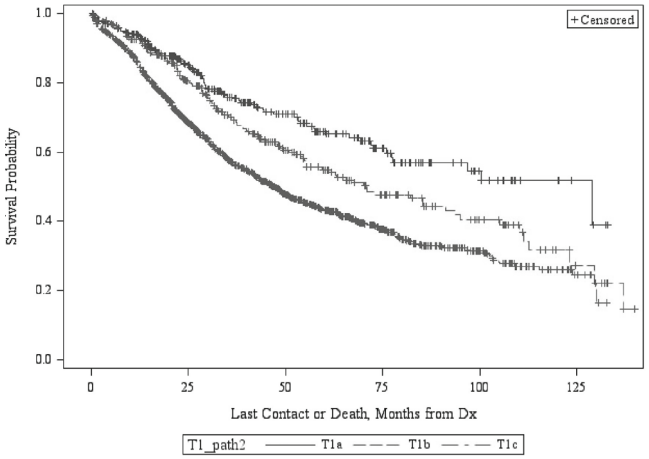


Figure 1. Kaplan-Meier Survival Curve for T1a, T1b and T1c Pancreatic Adenocarcinoma.

PT107

Inhibition of the Autotaxin/Lysophosphatidic Acid (ATX/LPA) Pathway Reduces Pancreatic Cancer Tumor Size and Desmoplastic Response in Mice D.J. Erstad,* M. Sojoodi, S. Li, M. Lanuti, K.K. Tanabe, B.C. Fuchs. *Surgery, Massachusetts General Hospital, Cambridge, MA.*

Introduction Pancreatic ductal adenocarcinoma (PDAC) desmoplasia is driven by stellate cell activation, and is characterized by dense fibrosis and elevated interstitial fluid pressure, hindering drug delivery to tumor cells. Lysophosphatidic acid (LPA), a lipid-signaling molecule synthesized by the enzyme autotaxin (ATX), is a known driver of fibrosis with high expression in the pancreas. We hypothesize that the ATX/LPA pathway plays a critical role in the desmoplastic response in pancreatic cancer. Methods C57B/6 mice (n = 10 per group) were orthotopically implanted with 10^4 syngeneic Hy15549 PDAC cells (Ptf1-Cre; LSL-KRAS-G12D; p53 Lox/+). Tumors grew for 14 days (approx. 5 mm). Mice were randomized to receive an ATX inhibitor (AM063), or vehicle by daily oral gavage (2.5 mg/kg) starting on postoperative day 1 and continuing to the study endpoint. Results In vitro, the proliferative and pro-fibrotic effects of LPA were confirmed in primary murine and immortalized human pancreatic stellate cells (PSCs). LPA dose-dependently increased cellular proliferation (1-10 μM, $p < 0.01$), mRNA expression of the proliferation marker, Ki67 ($P < 0.01$), and markers of activation including αSMA ($p < 0.01$) and COL1A1 ($p < 0.01$), and reduced lipid droplets on microscopy. Phosphokinase analysis revealed that LPA signals primarily through AKT, ERK and Rho pathways via the LPA1 receptor in PSCs. In vivo, AM063-treated tumors were smaller by size ($404 \pm 145 m^3$ vs. $234 \pm 58 m^3$, $p < 0.01$) and weight (0.25 ± 0.12g vs. 0.15 ± 0.03g, $p < 0.05$), and contained less collagen Sirius Red staining ($24.8 \pm 9.8\%$ vs. $16.5 \pm 5.3\%$, $p < 0.05$) and decreased αSMA by immunofluorescence ($9.6 \pm 1.9\%$ vs. $7.9 \pm 1.8\%$, $p < 0.05$), commensurate with reduced fibroblastic activation. There were no differences in staining for apoptosis or angiogenesis. Conclusion These findings strongly support the role of the ATX/LPA pathway in the desmoplastic response in pancreatic cancer. Inhibition of this pathway with well-tolerated agents like AM063 reduces

tumor size and stromal activation in a syngeneic orthotopic murine PDAC model, providing strong support for evaluation in clinical trial.

PT108

Near Infrared Intraoperative Imaging with Second Window Indocyanine Green Can Improve Visualization of Pancreatic Neoplasms During Distal Pancreatectomy A.D. Newton,[1]* J.D. Predina,[1] C.T. Connolly,[1] M.T. Shin,[1] L. Frenzel-Sulyok,[1] J. Drebin,[2] S. Singhal,[1] M.K. Lee IV.[1] *1. University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA; 2. Memorial Sloan Kettering Cancer Center, New York, NY.*

Introduction: Surgical resection of pancreatic neoplasms is hindered by high rates of margin positivity and distant recurrence from unrecognized metastases. Improved ability to visualize the primary tumor and small metastases could improve outcomes. We used near infrared (NIR) intraoperative imaging with an FDA approved optical contrast agent (indocyanine green [ICG]) to visualize pancreatic neoplasms during pancreatic resections. Methods: Ten patients with radiographic pancreatic lesions were enrolled in a phase I clinical trial from July 2016 to August 2017. Subjects received ICG (5mg/kg) 24 hours prior to resection. A laparoscopy was generally performed to triage the abdomen. After mobilization, tumors were imaged in situ and ex vivo. Tumor fluorescence was quantified using signal-to-background ratio (SBR). Postoperatively, surgeons completed a questionnaire to determine utility of NIR imaging. Results: Imaging with ICG was safe, with no drug-related toxicity observed. Procedures included 5 pancreaticoduodenectomies and 5 distal pancreatectomies. Final pathologies were pancreatic adenocarcinoma (N=6), intrapancreatic cholangiocarcinoma (N=1), pancreatic neuroendocrine tumor (N=1), intraductal papillary mucinous neoplasm (N=1), and microcystic serous cystadenoma (N=1). Nine of ten pancreatic lesions displayed strong fluorescence compared to normal pancreas (mean SBR 4.72 ± 1.97). In patients receiving neoadjuvant therapy, two of three had mostly viable tumor and strong tumor fluorescence (mean SBR 4.17); a third patient had only 10% remaining viable tumor and no significant tumor fluorescence (SBR 1.53). Imaging did not significantly prolong the procedures. Surgeons found that NIR imaging improved localization and margin assessment in 4/5 distal pancreatectomies, but background fluorescence from the bowel and bile ducts limited use during pancreaticoduodenectomy. Conclusions: ICG reliably accumulates in a variety of pancreatic neoplasms and provides real-time fluorescence feedback that can improve visualization during distal pancreatectomy. NIR imaging can also help to assess the response to neoadjuvant therapy.

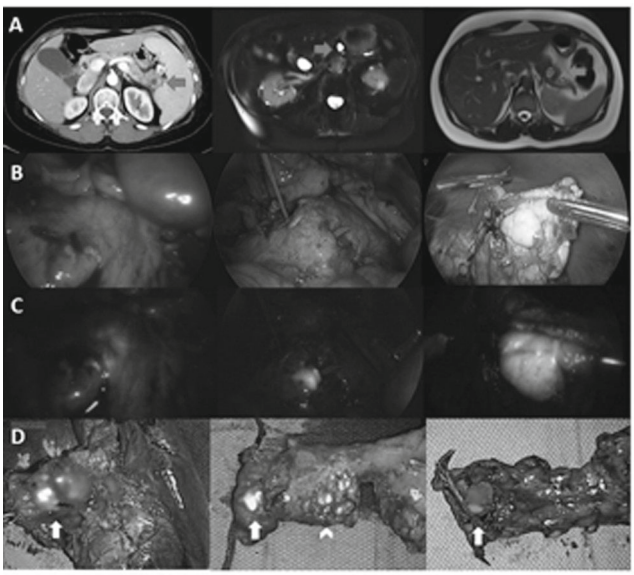
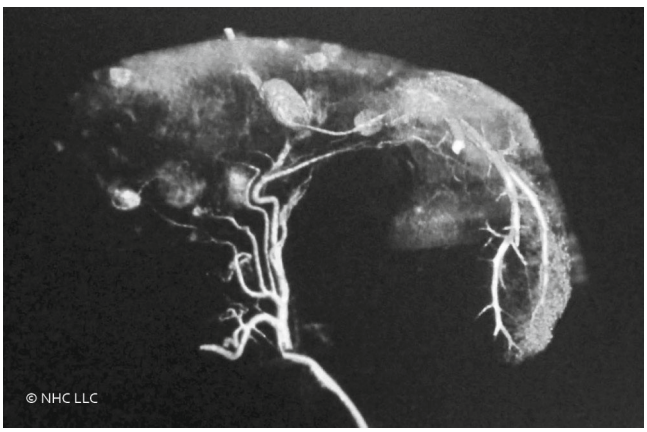


Figure 1: A) Preoperative CT or MRI from 3 patients with pancreatic lesions (noted by arrows). B) Intraoperative white light images during pancreatic resection. C) Intraoperative NIR fluorescence images for localization of pancreatic lesions. D) Back table fluorescence imaging for 3 distal pancreatectomy specimens (arrows denote primary pancreatic lesion, arrowhead denotes additional pancreatic cysts).

PT109

Venous-to-Venous Loco-Regional Delivery of Contrast Agents to Simulate Chemotherapy Delivery in a Carcinogen-Induced Hepatocellular Carcinoma Pig Model S. Corr,[1] B. Toombs,[2] J. Ho,[1] M. Ware,[1] A. Anderson,[1] S.A. Curley.[1]* *1. Baylor College of Medicine, Houston, TX; 2. Baylor St. Luke's Medical Center, Houston, TX.*

Introduction: Novel methods are needed to disrupt the physiologically challenging hemodynamics of hepatic tumor vasculature and microcirculation to optimize drug penetration, and reduced systemic toxicity. We demonstrate venous-to-venous loco-regional delivery of computed tomography (CT) contrast agents in an accelerated hepatocellular carcinoma (HCC) Yucatan minipig model, using a novel catheter-based delivery system (Otricath). Methods: Yucatan miniature swine were treated concurrently with diethynitrosamine once weekly for 3 months and phenobarbital 5 times weekly for 4 months. At 18 months post-treatment, animals with HCC tumor lesions > 2 cm were evaluation with the Otricath system. An arteriogram was performed prior to catheterization to visualize the tumors and their vasculature. The catheter was fluoroscopically positioned in the left hepatic vein, and the retrograde closed loop delivery circuit was confirmed. A 3D digital subtraction angiography was then performed concurrently with this injection. Results/Conclusion: Otricath uses a venous-to-venous approach for closed-loop delivery. The triple-lumen catheter features a distal balloon catheter for infusion, a central sheath for monitoring pressures, and a proximal balloon catheter for aspiration (see image). The catheter delivered Omnipaque 300 CT contrast agent via a major hepatic vein to a target liver site, monitored key pressure and flow variables over time, and retrieved the unabsorbed CT agent to minimize systemic toxicity. A syringe infusion pump, withdrawal pump, and pressure transducer controlled flow rates and pressures. Critical study criteria were to assess functional and performance characteristics while confirming the venous-venous closed loop circuit, the results of which can be seen in the image, which shows a compelling 3-D rendering of the dual circuits, confirming the viability of the design in controlling pressure and flow dynamics in the hepatic circulation. These results suggest Otricath can be utilized as a novel device for localized HCC drug delivery to enhance therapeutic index while reducing systemic toxicity.



PT110

Modern Trends in Neoadjuvant Therapy Utilization for Pancreatic Cancer K.S. Cools,* U. Maduekwe, P. Strassle, R.C. Chen, K. Stitzenberg. *University of North Carolina, Chapel Hill, NC.*

Introduction: While complete surgical resection remains the only potentially curative treatment for pancreatic adenocarcinoma; there has been an increasing use of neoadjuvant therapy (pre-operative chemotherapy and/or radiation) with early stage tumors. Modern trends in neoadjuvant therapy use have not been well described. The aim of this study is to examine trends in neoadjuvant therapy use over time among patients with early stage pancreatic cancer. Methods: Retrospective analysis of adults diagnosed between 2010 and 2013 with clinical stage I and IIA pancreatic adenocarcinoma and who underwent pancreatic surgery in the National Cancer Database. Primary outcome was receipt of neoadjuvant chemotherapy and/or radiation therapy. Trends in neoadjuvant therapy and tumor characteristics were assessed using multivariable logistic regression, adjusting for patient, hospital, and cancer characteristics. Results: Overall, 5,269 patients were included in the analy-

sis and 20% (n=1044) received neoadjuvant therapy (69.9% chemoradiation, 29.7% chemotherapy alone, 0.4% radiation alone). Neoadjuvant therapy use increased from 18.7% in 2010 to 28.4% in 2013 (p=0.01). Those in the neoadjuvant group were younger (64.3 vs 67.3, p<0.001), and had more advanced preoperative stage (IIA, 55.4% vs 35.9%, p<0.001). They were also more likely to be treated in an academic center (57.9% vs 50.3%, p<0.001), have private insurance (42.3% vs 33.9%, p<0.001), and live in the Northeast (23.4% vs 16.1%, p=0.02). The neoadjuvant group was more likely to have negative margins (79.6% vs 76.3%, p<0.001) and had lower 30-day readmissions (5.7% vs 7.6%, p=0.04). On multivariable analysis, neoadjuvant was more likely to be used in 2013 compared to 2010 (OR 1.45, 95% CI 1.11-1.90) and less likely to be used among patients with low income (OR 0.68, 95% CI 0.49-0.93), and those treated at a community cancer center (OR 0.69, 95% CI 0.56-0.84) (Table 1). Conclusions: Neoadjuvant therapy use has been increasing over time and is associated with more negative margin resections. Patients with low income and seeking treatment at a community cancer center are less likely to receive neoadjuvant therapy for pancreatic cancer.

Table 1: Multivariate Analysis of Neoadjuvant Therapy Utilization in Stage I and IIA Pancreatic Adenocarcinoma from 2010-2013.

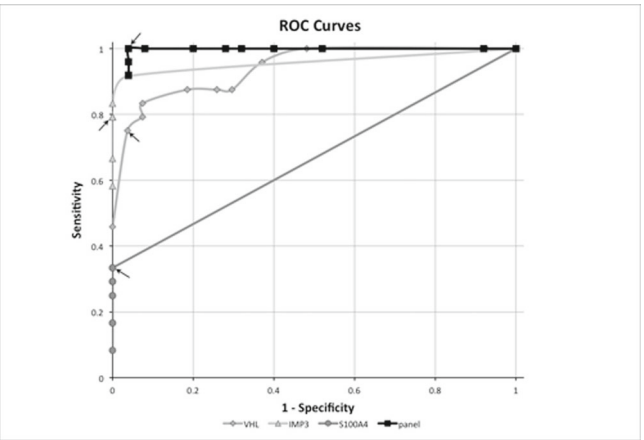
	Crude		Adjusted*	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Race:				
non-Hispanic White	ref	--	ref	--
Other	0.85 (0.71, 1.03)	0.09	0.91 (0.71, 1.20)	0.53
Insurance:				
Private	ref	--	ref	--
Medicare	0.68 (0.59, 0.79)	<0.0001	0.89 (0.69, 1.14)	0.36
Medicaid	0.83 (0.60, 1.17)	0.29	0.83 (0.54, 1.28)	0.4
Year of Diagnosis:				
2010	ref	--	ref	--
2011	1.29 (1.05, 1.58)	0.02	1.30 (0.99, 1.72)	0.06
2012	1.36 (1.12, 1.66)	0.003	1.61 (1.24, 2.09)	**0.0004**
2013	1.48 (1.22, 1.81)	0.0001	1.45 (1.11, 1.90)	**0.006**
Facility Type/Program:				
Community/Comprehensive Community	0.75 (0.65, 0.86)	<0.0001	0.69 (0.56, 0.84)	**0.0003**
Academic/Integrated Network	ref	--	ref	--
Region:				
Northeast	1.19 (0.98, 1.45)	0.08	1.22 (0.95, 1.58)	0.13
Southeast	0.93 (0.77, 1.13)	0.48	0.94 (0.73, 1.21)	0.62
Central East	ref	--	ref	--
Central West	0.96 (0.77, 1.19)	0.71	0.68 (0.50, 0.93)	**0.01**
West	1.05 (0.84, 1.32)	0.67	0.94 (0.69, 1.27)	0.69
Median Income Quartile:				
<$38,000	0.79 (0.64, 0.98)	0.03	0.68 (0.49, 0.93)	**0.02**
$38,000 - $47,999	0.98 (0.81, 1.17)	0.81	0.76 (0.58, 0.98)	**0.04**
$48,000 - $62,999	0.99 (0.83, 1.17)	0.86	0.97 (0.69, 1.09)	0.23
$63,000 +	ref	--	ref	--

*Controlling for all variables listed above and age, sex, Charlson-Deyo Score, clinical Stage (IA, IB, or IIB), and CA 19-9; age and CA 19-9 were modeled as restricted cubic splines

PT112

A Highly Sensitive Biomarker Panel is able to Distinguish Pancreaticobiliary Malignancies from Benign Disease A. Burnett,[1]* D. Ajibade,[2] S. Peters,[2] S. Ahlawat,[2] O. Mahmoud,[2] R. Chokshi.[2]
1. Oncology, McGill University Health Centre, Montreal, QC, Canada; 2. Rutgers New Jersey Medical School, Newark, NJ.

Background: Biliary strictures present a diagnostic challenge to differentiate benign disease from hepatopancreaticobiliary (HPB) malignancies. Cytology from Endoscopic retrograde cholangiopancreatography (ERCP) or Endoscopic ultrasound with fine needle aspiration (EUS-FNA) have both been plagued by poor sensitivity and high false negative rates. In a review of over 80 adjunct molecular biology tests that have been attempted on ERCP and EUS-FNA samples, four immunohistochemistry biomarkers with sensitivities ranging 74-80% were identified; von Hippel Lindau loss of expression (VHL), over-expression of insulin-like growth factor 2 mRNA-binding Protein 3 (IMP3), and EF-hand Calcium 2+ binding S100 subfamily members A4 (S100A4) and P (S100P). We sought to determine if these results could be validated in a tumor explant model and furthermore if combining these tests into a biomarker panel could boost overall diagnostic sensitivity to 100%. Methods: Tumor tissue and normal surrounding pancreas from 27 pancreaticoduodenectomy specimens were selected by an experienced pathologist, subjected to immunohistochemistry staining with VHL, IMP3, S100A4, S100P, and the intensity and percent of cells staining was graded. Using ROC curve analysis, threshold criteria were chosen for each biomarker to differentiate between tumor and normal pancreas. Biomarkers were then evaluated as a panel for their ability to discriminate malignant from benign specimens. Results: Individual sensitivity of VHL, IMP3, S100A4, and S100P were found to be 75.0%, 79.2%, 45.8%, and 0%. When VHL, IMP3, and S100A4 were grouped into a panel, they were able to distinguish cancer from normal tissue with a sensitivity of 100% and a specificity of 96%. S100P was dispensable in our assay and only VHL, IMP3, and S100A4 staining were required to achieve 100% sensitivity. Conclusions: A panel of three biomarkers, VHL, IMP3, and S100A4, were able to distinguish pancreatic cancer from surrounding normal tissue with 100% sensitivity in our tumor explant model. Prospective studies on patient biopsy specimens are required to further validate the clinical use of this biomarker panel.



PT114

A Population-Based Cohort Study of Overall Survival Following Curative-Intent Resection and Adjuvant Therapy for Pancreas Adenocarcinoma N. Vela,[1]* D. Kagedan,[1] L.D. Bubis,[1] L. Davis,[2] Y. Liu,[3] A. Mahar,[2] N. Coburn.[2] *1. University of Toronto, Toronto, ON, Canada; 2. Sunnybrook Research Institute, Toronto, ON, Canada; 3. Institute for Clinical Evaluative Sciences, Toronto, ON, Canada.*

Introduction: The effectiveness of adjuvant chemotherapy and chemoradiation following resection of pancreas adenocarcinoma (PC) is debated. We describe survival by adjuvant therapy following curative-intent resection for PC. Methods: All patients with resected PC in Ontario, Canada diagnosed between 2004 and 2014 were identified and linked to administrative healthcare databases containing treatment and vital status information. Patients receiving neoadjuvant therapy were excluded. Patients were categorized as receiving chemotherapy (CT), chemoradiation therapy (CRT), or no adjuvant treatment (NAT) following resection. Stratified Kaplan—Meier survival curves and log-rank test compared survival across treatment categories in a subset of patients surviving ≥6 months after PC resection. Results: 13,916 PC patients were identified; of these, 1648 (11.8%) underwent curative-intent resection. After applying all exclusion criteria, the final cohort consisted of 1272 patients. 37% received NAT, 49% CT, and 14% CRT. Patients receiving CT and CRT were younger than patients receiving NAT (p<0.001), and patients receiving CRT were less likely to have high comorbidity burden (ACG ≥10) than CT and NAT patients (p<0.01). Median survival for the 1084 patients who survived ≥6 months after resection was 22.1, 22.7, and 22.4 months for the NAT, CT, and CRT groups respectively (p value n.s.) (Figure 1). Conclusion: Patients who survived ≥6 months after resection for PC had similar median survival whether they received adjuvant CT, CRT, or NAT. Differences in disease biology may identify subgroups who benefit from more aggressive adjuvant therapy. Alternatively, there may be cause for less treatment in particular subsets of lower-risk patients.

Figure 1 - Survival analysis in patients who survived ≥6 months after curative-intent resection for pancreas adenocarcinoma, stratified by adjuvant therapy. There was no significant difference in median survival based on adjuvant therapy. CRT: Chemoradiation therapy; CT: Chemotherapy; NAT: No adjuvant therapy.

PT115

Src Family Kinase Lck Phosphorylation of Yes Associated Protein (YAP) Leads to Early Recurrence in Intrahepatic Cholangiocarcinoma L. Yohanathan,* T. Sugihara, N.W. Werneburg, C. Sosa, V. George, M. Truty, G.J. Gores, R.L. Smoot. *Hepatobiliary Surgery, Mayo Clinic, Rochester, MN.*

Background: YAP is a transcriptional co-activator and the effector protein of the hippo pathway. Hippo pathway is important for organ size control. Dysregulation has been associated with tissue overgrowth and cancer and has been seen in human intrahepatic cholangiocarcinoma (ICC). We have demonstrated a unique association between receptor tyrosine kinase signaling and regulation of YAP subcellular localization/activity by tyrosine phosphorylation via Src family kinases (SFK) which functions in signal transduction and have mixed expression. The precise mediator of YAP tyrosine phosphorylation in ICC has been unknown. Methods: SFK expression was profiled in normal human cholangiocytes (NHC), the CCA cell line HuCCT-1, and multiple ICC patient derived xenografts (PDX) by RT-PCR. Downregulation of expressed SFK was undertaken by siRNA in HuCCT-1 cells and knockdown confirmed by RT-PCR. Evaluation of YAP tyrosine phosphorylation was done by immunoblot using phospho-specific antisera. RNA sequencing was undertaken in 13 resected ICC PDX. Clinicopathologic features, recurrence free and overall survival were abstracted for them. Differentially expressed genes were identified between early recurrence (<10months) and late recurrence with a $\log^2$ threshold of 1.5 with a p-value of <0.01. Results: Five SFK were expressed in NHC and HuCCT-1 cell lines (Src, Yes, Lyn, Fyn, and Lck). Multiple PDX showed the same five SFK. Downregulation by target specific siRNA for each of the five SFK showed significant reduction in each targeted SFK. si-Lck-HuCCT-1cells showed a significant reduction in YAP tyrosine phosphorylation compared to non-targeting siRNA and the other four targeted cell lines. RNA sequencing of 13 resected ICC PDX demonstrated significant upregulation of Lck in patients with early recurrence (<10months); $\log^2$ fold change 7.77, p=0.00005. Conclusions: Src family kinase Lck is associated with YAP tyrosine phosphorylation in ICC, a previously unrecognized function for Lck. The clinical importance of this association through RNAsequencing has identified upregulation of Lck in patients with early recurrence after resection of ICC.

PT116

Understaging of Clinical Stage I Pancreatic Cancer and the Impact on Multimodal Treatment K.A. Baugh,* H.S. Tran Cao, G. Van Buren, E. Silberfein, C. Hsu, C. Chai, O. Barakat, W. Fisher, N. Massarweh. *Michael E. DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX.*

Background: Clinical staging of early stage pancreatic cancer is suboptimal, yet it directs clinical decision-making at the point of care. We hypothesized that most clinical stage I patients actually have more advanced stage disease and benefit from multimodal therapy (MMT). Methods: Retrospective cohort study of surgically resected patients aged 18-79 years with clinical stage I (i.e.: T1N0 or T2N0) pancreatic adenocarcinoma in the National Cancer Database (2004-2012). The rate of primary and nodal understaging was ascertained by comparing pretreatment clinical stage to pathologic stage among those treated with upfront surgery. Among these upfront resection patients, the association between the use of MMT and overall risk of death was evaluated using multivariable Cox regression in patients who were pathologically truly stage I or were upstaged. Results: Among 3,983 clinical stage I patients, 58.0% were treated with surgery and some form of MMT (25.9% chemotherapy alone; 32.1% MMT included radiotherapy), 34.0% were treated with surgery alone, and 8.0% received neoadjuvant treatment. Among 3,665 patients treated with upfront resection, only 30.6% were also pathologic stage I (58.5% had primary upstaged; 51.0% had nodal disease). For those who were stage I on final pathology, 47.2% received MMT, but MMT was not associated with a survival benefit (Hazard Ratio [HR] 1.10; 95% Confidence Interval [0.91-1.32]). For upstaged patients, 69.6% received MMT, and in these patients MMT was associated with a significantly lower risk of death (Hazard Ratio [HR] 0.77 [0.67-0.89]). Conclusion: The majority of patients with clinical stage I pancreas cancer actually have higher stage disease and benefit from MMT. However, one third of those upstaged on final pathology do not receive MMT. In light of the high rate of clinical understaging, alternative management strategies that optimize receipt of MMT may be beneficial and merit further investigation.

PT117

Upregulation of CPT Family Genes Mediates the Mitochondrial Uptake of Linoleic Acid in Hepatic $CD4^+$ T Lymphocytes and Promotes HCC in the Context of NAFLD/NASH Z. Brown,* Q. Fu, B. Heinrich, C. Ma, S. Yu, Q. Zhang, T. Greten. *Thoracic and GI Oncology Branch, National Institutes of Health, Bethesda, MD.*

Introduction: Non-alcoholic fatty liver disease (NAFLD) is an increasing health problem worldwide as metabolic syndrome becomes more prevalent. As such, NAFLD has become a major risk factor for the development of HCC in the United States. A recent study showed linoleic acid (LA), a fatty acid accumulated in NAFLD, causes a selective loss of hepatic $CD4^+$ T lymphocytes initiated by excessive mitochondrial intake of LA followed by increased levels of mitochondrial reactive oxygen species (ROS) and cellular apoptosis. The carnitine palmitoyltransferase (CPT) system of enzymes consisting of CPT1a, CPT1b, and CPT2 is responsible for transporting long-chain fatty acids from the cytoplasm into the mitochondria to undergo beta-oxidation. The details of how CPT enzymes get upregulated and mediate the mitochondrial uptake of LA in the context of NAFLD are still largely unknown. Methods: Induction of CPT RNA was measured utilizing qPCR for in vitro and in vivo studies. Inducible liver-specific MYC oncogene transgenic mice were utilized for spontaneous tumor development. Results: We demonstrated LA upregulates CPT genes both in vitro and in mice fed with a high LA diet or a diet that causes NAFLD. This upregulation is mediated through the peroxisome proliferator-activated receptor alpha (PPAR-α), a lipid receptor and master regulator of lipid metabolism, as using GW6471, a PPAR-α antagonist, blocks this increase in CPT expression. In addition, bezafibrate, PPAR-α specific agonist, induces CPT production in both $CD4^+$ T lymphocytes and Jurkat cells where upon upregulation we demonstrate increase ROS and cell death. Furthermore, LA induced cell death could be rescued by knocking down CPT1a using lentiviral shRNA in Jurkat cells. In addition, genetically engineered mice to spontaneously develop liver tumors showed decreased tumor formation while on NAFLD producing diet when treated with perhexiline, a CPT1 antagonist. Conclusion: These results will provide useful information for targeting the CPT gene family or PPAR-α for NAFLD-promoted HCC therapy.

Linoleic acid upregulates CPT genes mediated through PPAR-α leading to increased ROS and $CD4^+$ T cell dead promoting HCC development. LA: linoleic acid, PPAR-α: peroxisome proliferator-activated receptor alpha, CPT: carnitine palmitoyltransferase, ROS: reactive oxygen species, HCC: hepatocellular carcinoma

PT118

Surgical Resection May Not Offer Survival Benefit Following Neoadjuvant Chemotherapy in Patients with Stage I-II Pancreatic Adenocarcinoma R.J. Hendrix,* E. Rouanet, K. Schultz, T. Ali, B. Switzer, V. Bathini, G. Whalen, J. LaFemina. *Surgery, University of Massachusetts Medical School, Worcester, MA.*

Background: Pancreatic adenocarcinoma (PDAC) is a lethal malignancy, representing the 4th leading cause of US cancer deaths. Our 2011 institutional protocol guides that patients with Stage I/II PDAC receive neoadjuvant chemotherapy (FOLFIRINOX or gemcitabine-nab-paclitaxel); a similar protocol is followed in locally unresectable, Stage III disease. The aim of the study is to determine if potentially curative surgery provides added survival benefit, compared to neoadjuvant chemotherapy alone. Methods: Patients who received neoadjuvant chemotherapy and who were diagnosed with Stage I-III PDAC from 2011-2017 at a tertiary medical center were included in this prospectively-collected, retrospective analysis. The primary endpoint was overall survival (OS). Kaplan-Meier curves were built and compared using Log-rank test. Cox proportional hazards were then used to adjust for potential confounders. Results: 105 patients met inclusion criteria: 38 (36%) had Stage I disease (n=18 had neoadjuvant chemotherapy and surgery [N+S], n=20 had neoadjuvant chemotherapy [N] alone), 44 (42%) had Stage II (N+S n= 20, N n=24), 23 (22%) had Stage III (N+S n=4, N n=19). There was no difference in 5-year overall survival (OS) regardless of treatment regimen in patients with Stage I (median OS N+S 22.5 mo vs N 27.9 mo; p=0.99, HR 1.00, 95%CI 0.74-1.35) or Stage II disease (median OS N+S 28.7 mo vs N 27.6 mo; p=0.69; HR 1.06, 95%CI 0.79-1.41; Fig. 1). A trend towards improved survival after N+S was noted in those with Stage III disease (median OS N+S 46.0 mo vs N 14.5 mo, p=0.08), but the number who underwent resection is low (17%). Conclusion: In patients with stage I-II PDAC, potentially curative surgery may not provide additional survival benefit beyond that afforded by modern day neoadjuvant chemotherapy. The analysis of stage III outcomes is limited by small numbers, and the impact of surgery is less clear. It might be possible that the uncommon locally unresectable tumor that is rendered resectable with neoadjuvant chemotherapy may be associated with a particularly favorable tumor biology, such that surgery offers added survival benefit.

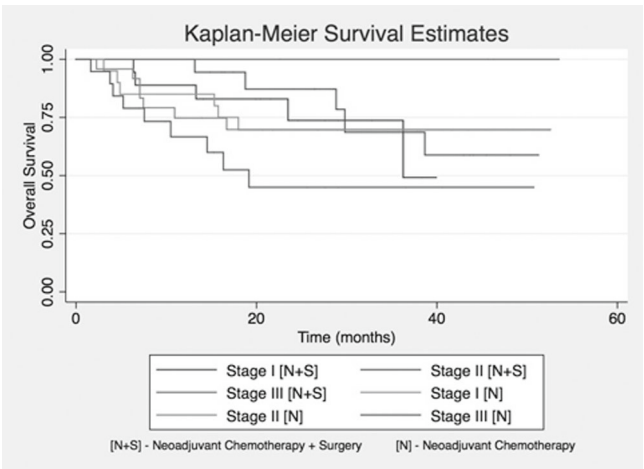


Figure 1: Kaplan-Meier Survival Curves representing OS (months) by stage of pancreatic disease at time of diagnosis.

PT119

Preoperative Opioid Use Associated with Increased Length of Stay After Pancreaticoduodenectomy C.A. Thiels,* E.B. Habermann, A.E. Glasgow, T.E. Grotz, S.P. Cleary, R.L. Smoot, M.L. Kendrick, D.M. Nagorney, M. Truty. *Surgery, Mayo Clinic, Rochester, MN.*

Introduction: Preoperative opioid use in patients undergoing low complexity operations is associated with increased complications, but its relationship to procedures of greater complexity is unclear. We aimed to assess this impact on outcomes following pancreaticoduodenectomy (PD). Methods: A single institution, retrospective cohort of adults undergoing elective PD for cancer (1/2009-9/2015). Preoperative users were defined as patients taking opioids 90 days preoperatively. Discharge prescriptions were converted into Oral Morphine Equivalents (OME) and ten-point pain scores were abstracted. Univariate and multivariable analyses compared outcomes of naïve and preoperative users overall and for laparoscopic vs open surgery. Results: Of 661 PD patients, 131 (19.8%) were preoperative users (Table). These patients had greater mean pain scores over the first three days after surgery (3.4±1.6, vs 2.8±1.4, p<0.001), max pain (7.9±1.9 vs 7.2±2.0, p<0.001), and discharge pain (2.3±1.9 vs 1.8±1.6, p=0.01) than naïve patients. The median OME prescribed was 300 (IQR 150,450) with preoperative users receiving more opioids at discharge (mean 496±764 vs 320±489 OME, p=0.03). Thirty-day refill rates were 12.6% (19.1% preoperative vs 10.9% naïve, p=0.02). Open and laparoscopic (n=261) PD had similar mean pain scores over the first three days (p=0.51), max pain score (p=0.11) and OME prescribed (p=0.50), but laparoscopic cases had slightly lower pain scores at discharge (1.7±1.6) vs open (1.9±1.7, p<0.01). After controlling for tumor type, texture, and duct size, naïve patients had similar odds of ISGPS grade B/C leak (OR 1.13, p=0.68) and delayed gastric emptying (OR 1.05, p=0.87). After controlling for age and complications, preoperative opioid use was associated with increased odds of LOS ≥9 days (OR 1.59, p=0.04). Conclusion: Following PD, preoperative users had worse pain scores, received more opioids at discharge, refilled prescriptions more frequently, and were more likely to have prolonged LOS. As most opioid utilization research has been focused on low complexity surgery, additional work aimed at optimizing opioid use in complex oncologic operations is warranted.

Table. Univariate comparison of opioid naïve patients to preoperative opioids users.

	All PD Patients n=661	Opioid Naïve Patients n=530	Preoperative Opioid Users n=131	P-value
Female	285 (43.1%)	224 (42.3%)	61 (46.6%)	0.38
Age, in years				**0.03**
<56	131 (19.8%)	98 (18.5%)	33 (25.2%)	
56-64	180 (27.2%)	136 (25.7%)	44 (33.6%)	
65-72	168 (25.4%)	140 (26.4%)	28 (21.4%)	
73-91	182 (27.5%)	156 (29.4%)	26 (19.8%)	
Estimated Blood Loss, in mL				0.67
≤400	299 (45.2%)	245 (46.2%)	54 (41.2%)	
401-700	152 (23.0%)	117 (22.1%)	35 (26.7%)	
701-1,000	104 (15.7%)	83 (15.7%)	21 (16.0%)	
>1,000	106 (16.0%)	85 (16.0%)	21 (16.0%)	
Diagnosis Group				**<0.001**
PDAC	352 (53.3%)	259 (48.9%)	93 (71.0%)	
Other Neoplasm	309 (46.7%)	271 (51.1%)	38 (29.0%)	
Pancreatic Duct Diameter (mm)				0.38
≥5	188 (28.4%)	156 (29.4%)	32 (24.4%)	
4.0-4.9	136 (20.6%)	104 (19.6%)	32 (24.4%)	
3.0-3.9	164 (24.8%)	127 (24.0%)	37 (28.2%)	
2.0-2.9	128 (19.4%)	104 (19.6%)	24 (18.3%)	
≤1	45 (6.8%)	39 (7.4%)	6 (4.6%)	
Gland Texture				**0.02**
Firm	386 (58.4%)	298 (56.2%)	88 (67.2%)	
Soft	275 (41.6%)	232 (43.8%)	43 (32.8%)	
POPF (grade B/C)	130 (19.7%)	108 (20.4%)	22 (16.8%)	0.39
Clinically Significant DGE	114 (17.2%)	92 (17.4%)	22 (16.8%)	1.00
Post-op Hemorrhage	44 (6.7%)	39 (7.4%)	5 (3.8%)	0.17
LOS, median (IQR) in days	8 (6,13)	8 (6, 13)	9 (6, 13)	0.84
LOS ≥ 9 days	308 (46.6%)	241 (45.5%)	67 (51.2%)	0.28
OME Prescribed at Discharge, median (IQR)	300 (150,450)	300 (150, 390)	300 (200, 470)	**0.03**
Refill Rate	83 (12.6%)	58 (10.9%)	25 (19.1%)	**0.02**

DGE, Delayed Gastric Emptying; IQR, Inter-Quartile Range; LOS, Length of Stay; PD, Pancreaticoduodenectomy; PDAC, Pancreatic Ductal Adenocarcinoma; POPF, Post-operative Pancreatic Fistula.

PT120

Portal Vein Circulating Tumor Cells (CTC) Conform Multi-Cellular Type Clusters in Patients with Peri-Ampullary Carcinomas

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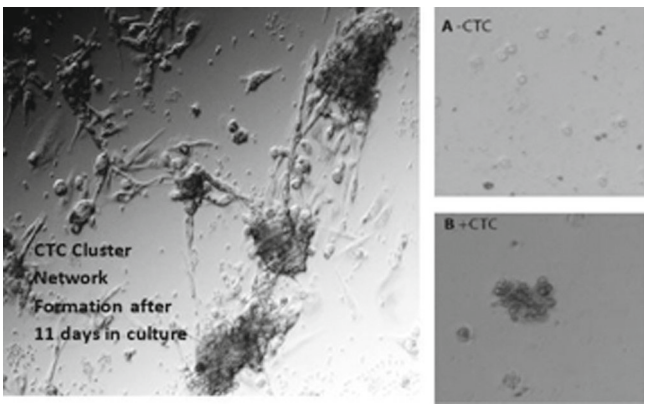
Pancreatic ductal adenocarcinoma (PDAC), distal cholangiocarcinoma (CC), and ampullary adenocarcinoma (AA) are often characterized as biologically aggressive tumors. We have shown that KRAS-mutated CTC thrive in the portal venous blood of PDAC patients and may represent a source of metastatic progression. We postulate CTC survival and metastatic potential are promoted by unique interactions with immune and stromal cells within the portal circulation. We analyzed portal venous blood collected during pancreatico-duodenectomy in 36 patients with various peri-ampullary pathologies (PDAC=9; AA=12; CC=6; IPMN=7; pancreatitis=2). Different portal circulation cell types were isolated by fluorescence-activated cell sorting (FACS), including neoplastic CTC (CD147+,CD44+, EPCAM+, CD45-); immune cells: dendritic cells (DC, CD11c+, MHCIIDR+), myeloid-derived suppressor cells (MDSC, CD33+, CD14+, CD11b+, MHCIIDR-) and T-cells (CD45+, CD3+); stromal cells: fibroblasts (FB, CD105+,CD14-) and myeloid-derived fibroblasts (MFB, CD105+,CD14+), collected aseptically and grown ex vivo in mixed cell reaction (MCR) cultures. During the first 48hr, PDAC, AA, and CC CTC were highly proliferative (mean 2.6 hr/ cell cycle, 65% growth, ±17%) and resistant to apoptosis (mean 37%, ±24%). PDAC CTC proliferation and resistance to T cell cytotoxicity were significantly augmented by MDSC and decreased by pre-operative chemotherapy (p=0.006, p=0.04, respectively), and by ex vivo treatment with indomethacin (p=0.01). After 5-7 days, cultured CTC spontaneously recruited multiple cell types, including MFB, to organize into spheroid-like clusters. Cluster formation promoted CTC survival, growth, and MFB differentiation, particularly in PDAC and CC patients. FACS-depletion of CTC or MFB from portal blood cell isolates eliminated cluster network formation, and MCR with re-introduction of these cell populations restored clustering ability. Our findings suggest that PDAC and CC CTC survival within the portal venous system is supported by their interactions with circulating immune and stromal cells conforming multi-cellular clusters that may constitute vectors of metastatic progression.



PT121

Racial and Ethnic Disparities of Pancreatic Adenocarcinoma in Florida

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Background: Pancreatic cancer is a fatal malignancy predominantly seen in men of advanced age with an aggressive course. Factors including race and cultural background can influence the survival of patients with pancreatic cancer, as Blacks have decreased overall survival with respect to Whites throughout the literature. Our study analyzes the Florida pancreatic cancer population, previously unrepresented in the literature and inclusive of the Hispanic population. We sought to analyze whether race and ethnicity are independent determinants of survival in patients with pancreatic cancer. Methods: A non-concurrent prospective observational study was performed utilizing all patients diagnosed with pancreatic adenocarcinoma between 1983-2013 in the Florida Cancer Data System (FCDS). Statistical analysis to assess the independent risk of dying was performed using Cox proportional hazard regression models. Kaplan-Meier survival analysis is also presented. SPSS software was used for analysis. Results: Of 36,756 patients identified with pancreatic adenocarcinoma in the FCDS, 90% of patients were White, 9% were Black, and 1% were other races. Compared to Whites, there was significantly decreased survival among Black patients (unadjusted HR 1.06, 95% CI 1.02 – 1.10, p = 0.002, adjusted HR 1.07, 95% CI 1.03 - 1.13, p = 0.003). Ethnicity was also associated with increased survival among Hispanics compared to non-Hispanics (unadjusted HR 0.83, 95% CI 0.80 – 0.86, adjusted HR 0.86, 95% CI 0.82 - 0.90, both p <0.001) with average survival of six versus five months respectively. Conclusion: Evidence supports ethnic and racial disparities in the survival of patients with pancreatic adenocarcinoma. Black race is associated with decreased survival when compared to White and Others. Additionally, Hispanic ethnicity is associated with increased survival when compared to Non-Hispanics. Future research into these disparities is warranted and clinically relevant.

Table 3 Cox proportional hazard model for overall survival

Characteristics	Unadjusted HR (95% CI)	p-value	Adjusted HR (95% CI)	p-value
Race				
White	Ref		Ref	
Black	1.06 (1.02-1.10)	0.002	1.07 (1.03-1.13)	0.003
Other	0.83 (0.73-0.94)	0.004	0.96 (0.81-1.12)	0.58
Age				
<=55	Ref			
56-65	1.09 (1.04-1.13)	<0.001	1.09 (1.04-1.14)	<0.001
66-75	1.22 (1.18-1.27)	<0.001	1.19 (1.14-1.25)	<0.001
>75	1.61 (1.55-1.67)	<0.001	1.47 (1.41-1.55)	<0.001
Sex				
Male	Ref			
Female	0.98 (0.96-1.00)	0.052	0.92 (0.89-0.94)	<0.001
Ethnicity				
Non-Hispanic	Ref			
Hispanic	0.83 (0.80-0.86)	<0.001	0.86 (0.82-0.90)	<.001
Marital Status				
Unmarried	1.16 (1.13-1.19)	<0.001	1.12 (1.08-1.15)	<0.001
Married	Ref			
Stage				
In-situ/localized	Ref			
Regional	1.10 (1.05-1.15)	<0.001	1.25 (1.18-1.31)	<0.001
Distant	2.03 (1.95-2.12)	<0.001	2.09 (1.99-2.21)	<0.001
Cigarette Smoking				
Never	Ref			
Former	0.95 (0.92-0.97)	<0.001	0.98 (0.95-1.01)	0.237
Current	1.03 (1.00-1.06)	0.085	1.08 (1.04-1.12)	<0.001
Decade of diagnosis				
1980-1989	Ref			
1990-1999	0.91 (0.88-0.94)	<0.001	0.94 (0.90-0.97))	0.001
2000-2009	0.87 (0.84-0.90)	<0.001	0.87 (0.83-0.90)	<0.001
2010-2013	0.55 (0.53-0.58)	<0.001	0.48 (0.45-0.50)	<0.001
Insurance*				
Private	Ref			
Medicaid	1.05 (0.98-1.13)	0.161	NA	
Medicare	1.21 (1.17-1.25)	<0.001	NA	
Government	0.98 (0.87-1.10)	0.713	NA	
None	1.10 (1.02-1.19)	0.02	NA	
Other	1.05 (0.99-1.11)	0.134	NA	
Treatment				
Surgery	1.70 (1.56-1.82)	<0.001	1.56 (1.44-1.69)	<0.001
Chemotherapy	2.33 (2.19-2.48)	<0.001	1.69 (1.57-1.83)	<0.001
Radiation	2.68 (2.46-2.91)	<0.001	2.12 (1.92-2.35)	<0.001
Surgery & chemotherapy	1.11 (1.01-1.23)	0.039	1.05 (0.93-1.18)	0.428
Surgery & radiation	1.44 (1.26-1.64)	<0.001	1.24 (1.06-1.46)	<0.001
Chemotherapy & radiation	1.83 (1.71-1.96)	<0.001	1.55 (1.43-1.67)	<0.001
All	Ref			
None	3.79 (3.57-4.03)	<0.001	2.90 (2.70-3.12)	<0.001

CI confidence interval, *Ref* referent value, *HR* hazard ratio
*excluded adjusted analysis due to missing values

PT122

Improved, Shorter Latency Carcinogen-Induced Hepatocellular Carcinoma Model in Pigs

J. Ho,* M. Ware, S. Corr, S.A. Curley, J. Law. *Surgery, Baylor College of Medicine, Houston, TX.*

Introduction: Large animal models serve important roles in translational research, particularly in liver tumors whereby catheter- and radiofrequency-based techniques are clinically utilized. Current large animal models for hepatocellular carcinoma (HCC) have a tumor latency period of 10-26 months,

imposing a restrictive time and cost barrier to effective research. We hypothesized that administration of phenobarbital (PB) with diethylnitrosamine (DENA) would more rapidly induce HCC in pigs. Methods: At 5-7 months, 9 Yucatan mini-swine were treated with DENA 15 mg/kg intraperitoneal once weekly for 3 months and concurrent PB 3-5 mg/kg oral 5 times weekly for 4 months. Tumor development was monitored with serial contrast-enhanced MRI every 2-4 months after treatment with T1 VIBE and T2 TSE sequences. Animals were euthanized at 10-18 post-treatment for gross and histopathological analysis. Data: See attached table Results/Conclusion: On final pathology, 8 out of 9 pigs were positive for HCC with tumors ranging 5 to 25 mm in size. Lesions were first identified on MRI by 5 to 11 months post-induction. The tumors were small, encapsulated, and multifocal in nature, arising from numerous foci throughout the liver parenchyma. Adenomas and focal nodular hyperplasias were also identified on pathology. At the time of euthanization of the pigs, no systemic toxicity or liver dysfunction were clinically observed or detected in serum analysis. The addition of PB, a P450 enzyme inducer, resulted in a significant accelerated improvement in HCC tumor latency in pigs compared to similar previous studies by Li et al (10 months) and Mitchell et al (15-26 months). Further reduction in tumor latency time might be achievable with dose optimization of PB and DENA. This model is now being used by our group in numerous preclinical therapeutic trials. Li, X. et al. N-nitrosodiethylamine-induced pig liver hepatocellular carcinoma model: radiological and histopathological studies. Cardiovasc. Intervent. Radiol. 29, 420–428 (2006). Mitchell, J. et al. Validation of a Preclinical Model of Diethylnitrosamine-Induced Hepatic Neoplasia in Yucatan Miniature Pigs. Oncology 91, 90–100 (2016).

DENA- and PB-induced HCC in pigs

Pig #	1	2	3	4	5	6	7	8	9
Months to MRI lesions	5	5	11	N/A	7	7	N/A	7	11
Months at Euthanization	10	10	18	10	12	12	15	12	17
HCC present on pathology	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes

N/A: not applicable; lesions not seen on imaging, but was identified on final pathology for pig #7

PT123

Histone Modulation by Triptolide Contributes to Cell Death in Pancreatic Ductal Adenocarcinoma S. Kurtom,* B. Giri, A. Ferrantella, V. Sethi, B. Garg, S. Banerjee, A. Saluja, V. Dudeja. *University of Miami, Miami, FL.*

Introduction: Triptolide and its water-soluble prodrug, Minnelide, have shown promising activity against pancreatic ductal adenocarcinoma (PDAC) in both in vitro and in vivo experiments. While results from the Phase I clinical trial for Minnelide have shown efficacy at clinically tolerable doses, understanding of its exact mechanism of action is still evolving. With recent focus on epigenetic changes in cancer, post-translational modification of histones including acetylation and methylation have been shown to regulate cancer growth. With this study, we aim to determine if triptolide interferes with epigenetic regulation via histone acetylation and methylation to affect cell growth and proliferation. Methods: Pancreatic cancer cell lines (Mia PaCA-2 and S2VP10) were treated independently with triptolide as well as C646, a selective histone acetyltransferase (HAT) inhibitor in vitro. Cell viability was measured using a tetrazolium dye. Apoptosis (via cleaved caspase-3) and cell cycle analysis was performed using flow cytometry. Histone acetylation and methylation were analyzed by western blotting and RT-qPCR. Results: Treatment with triptolide resulted in a dose-dependent increase in tri-methyl histones (H3K27me3, H3K9me3 and H3K4me3) and concurrent decrease in acetylated histones (Acetyl histones H3K9 and H3K18) in pancreatic cancer cell lines. This decrease in acetylation and increase in methylation was accompanied by increasing cytotoxicity in MiaPaca-2 and S2VP10 cells as well as an increase in apoptosis. This pattern corresponds to the effects seen in inhibition of histone acetylation. To confirm these phenomena, cancer cells were treated with C646. The results showed a similar decrease in cell viability and increase in apoptosis. Conclusion: Triptolide leads to cell death in pancreatic ductal adenocarcinoma through epigenetic mechanisms, one of which may be due to an effect on modulation of histone acetylation and methylation.

PT124

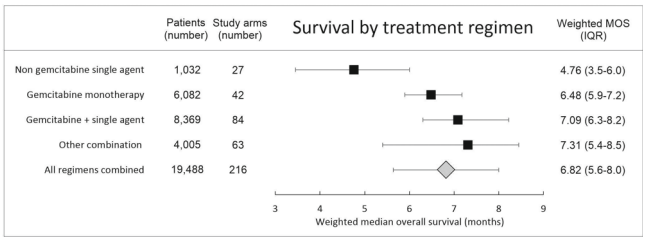
Implications of Peritoneal Lavage Cytology in Resectable Left-Sided Pancreatic Cancer Y. Iwagami,* H. Eguchi, D. Yamada, T. Asaoka, T. Noda, K. Kawamoto, K. Gotoh, S. Kobayashi, M. Mori, Y. Doki. *Gastroenterological Surgery, Graduate School of Medicine, Osaka University, Suita, Japan.*

Background: Peritoneal lavage cytology (CY) positive status is not currently included in stage evaluations in the Classification of Pancreatic Cancer in Japan. The aim of this study is to determine the utility of the CY findings for predicting the clinical outcomes of resectable left-sided pancreatic cancer. Methods: CY samples were collected from 92 consecutive patients who underwent surgery for left-sided pancreatic cancer between January 2000 and December 2015. We analyzed the correlations between disease-free survival (DFS), overall survival (OS) and clinicopathological factors including CY, under the criteria of General Rules for the Study of Pancreatic Cancer (the 6th edition, Japan Pancreas Society). Results: Eight patients had malignant cells in CY samples (CY(+)) and all cases were Stage IVa, while CY negative Stage IVa (CY(-)) included 53 cases, and CY (+) and CY(-) were compared below. Significant differences were found in portal vein, arterial infiltration and venous invasion in CY (+) (p=0.050, 0.027, 0.001). As recurrence types, peritoneal dissemination was more frequently occurred in CY (+) (p=0.008), however, there was no significance in distant metastases (except for peritoneal dissemination), and no local recurrence was occurred in CY (+). DFS was significantly shorter in CY (+) (CY (+): 0.6 ± 0.1 years, CY(-): 3.1 ± 0.6 years, p <0.0001), while there was no significance in OS (CY (+): 1.8 ± 0.4 years, CY(-): 4.9 ± 0.9 years, p=0.159). As a result of multivariate analysis, CY positive and positive venous invasion became independent prognostic factors in DFS (p=0.035, RR 2.871, 95% CI 1.083-7.247, p=0.022, RR 2.657, 95% CI 1.156-6.200, respectively), meanwhile, there was no factor that became an independent prognostic factor in OS. Conclusions: In this analysis, the peritoneal dissemination was significantly increased, and DFS was significantly shorter in CY (+), but no significance was observed in OS. It is suggested that therapeutic intervention for peritoneal dissemination of CY positive cases may contribute to improvement of prognosis.

PT126

Advanced Pancreatic Cancer: a Meta-Analysis of Clinical Trials Over Thirty Years B. Hall,[1]* A. Cannon,[1] P. Atri,[1] C. Wichman,[1] L. Smith,[1] A.K. Ganti,[1] C. Are,[1] A. Sasson,[2] S. Kumar,[1] S.K. Batra.[1] *1. University of Nebraska Medical Center, Omaha, NE; 2. Stony Brook School of Medicine, Stony Brook, NY.*

Introduction: In contrast to other cancers, survival rates for pancreatic ductal adenocarcinoma (PDAC) have improved but minimally over the past thirty years. The aim of this study was to perform a meta-analysis of clinical trials published since 1986 to determine trends in median overall survival in primarily metastatic PDAC. Methods: All Phase 2-4 clinical trials published during or after 1986 investigating first-line systemic chemotherapy in metastatic PDAC were included in the meta-analysis. Publications obtained through PubMed and www.ClinicalTrials.gov were cross-referenced to identify additional trials. Trials enrolling fewer than 50% of study participants with metastatic disease were excluded. Results: Of 19,488 patients enrolled in 151 clinical trials, 84% had metastatic disease and 16% had locally advanced pancreatic cancer. Fifty-six percent of patients were male and median age for all patients was 62.5 years. Forty percent (n=60) of all published trials originated from the United States. In clinical trials published from 1986 to 2016, the weighted median overall survival (wMOS) increased by 3.0 months. The median wMOS was higher in combination therapy (7.31 months, IQR 5.4 to 8.5) compared to non-gemcitabine, single-agent therapy (4.76 months, IQR 3.5 to 6.0), gemcitabine monotherapy (6.48 months, IQR 5.9 to 7.2), and gemcitabine plus single-agent therapy (7.09 months, IQR 6.3 to 8.2) (Figure). For all drugs or regimens used in two or more study arms, FOLFIRINOX was the most efficacious combination regimen (wMOS 10.9 months), S-1 was the most efficacious single agent regimen (wMOS 8.0 months), and nab-paclitaxel was the most efficacious agent when administered in addition to gemcitabine (wMOS 9.0 months). No significant difference was found between the number of study arms reporting biased-high MOS (n=6) versus biased-low MOS (n=10) (p=0.31). Conclusions: Regardless of treatment regimen, survival rates in metastatic PDAC have minimally improved over time. Of drugs used in two or more study arms, only FOLFIRINOX has a wMOS greater than ten months. Emphasis should, therefore, be placed on identification of novel targets that promote early diagnosis and intervention.



PT127

A Scoring System to Estimate Perioperative Mortality Following Liver Resection for Hepatocellular Carcinoma C.T. Ong,[1]* G. Li,[2] B. Clary,[3] A. Barbas.[1] *1. Surgery, Duke University, Durham, NC; 2. Harvard Medical School, Boston, MA; 3. University of California, San Diego, San Diego, CA.*

Introduction: Clinical decision-making regarding the optimal treatment modality for hepatocellular carcinoma (HCC) is complex, and considerations include the overall health of the patient, underlying liver function, and extent of disease. Although liver resection remains the primary approach for treating HCC with curative intent, resection can be associated with significant morbidity and mortality. The purpose of this study is to examine the association of variables available on preoperative assessment with mortality following liver resection for HCC, and to determine whether a simple scoring system based on MELD score and extent of resection can be generated to help guide risk assessment. Methods: The 2005-2010 National Surgical Quality Improvement Program database was queried for all patients undergoing liver resection for HCC. Univariate and multivariate analyses were performed to determine the association of several preoperative variables with perioperative mortality. MELD score and extent of resection (major or minor hepatectomy) were used to create a HCC Resection Risk Score (HRRS), and mortality was calculated as a function of HRRS. Results: 1,099 patients with complete preoperative data were included in the study. On multivariate analysis, preoperative variables significantly associated with mortality following liver resection included: age (OR 1.03 [1.01 – 1.06], p = 0.01), ASA score ≥ 3 (OR 3.01 [1.05 – 8.64], p = 0.04), steroid treatment (OR 4.69 [1.39 – 15.9], p = 0.01), albumin (OR 0.47 [0.29 – 0.77], p = 0.002), major hepatectomy (OR 2.55 [1.42 – 4.58], p = 0.002), and MELD > 10 (OR 2.79 [1.10 – 7.09], p = 0.03). The HCC Resection Risk Score (HRRS) was generated by assigning a value of 1-3 for MELD score (MELD 6, MELD 7-10, MELD > 10, respectively) and 0-1 for extent of resection (minor hepatectomy = 0, major hepatectomy = 1). Increasing HRRS was significantly associated with mortality (p < 0.001, Figure 1). Conclusions: MELD score and extent of hepatic resection are significant predictors of outcome following liver resection for HCC. A simple scoring system incorporating these two variables can be used to estimate perioperative mortality.

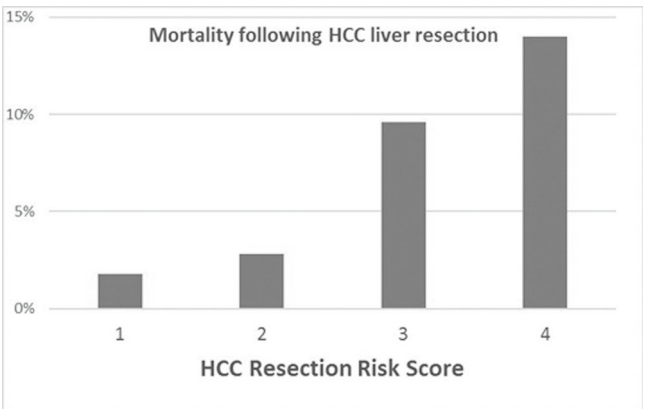
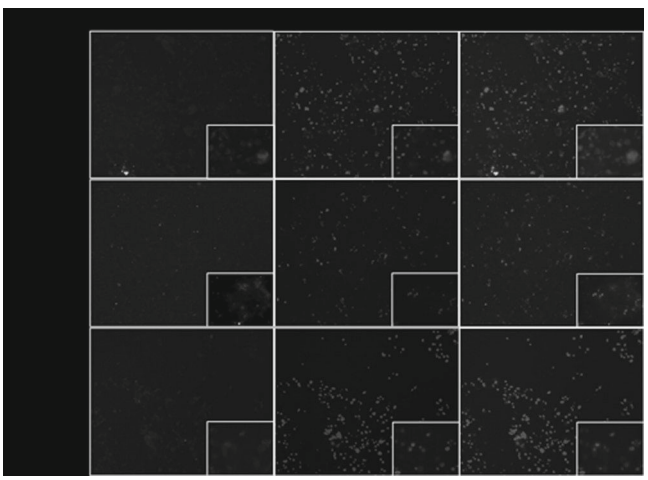


Figure 1. Mortality following liver resection by HCC resection risk score

PT128

The Peritoneal Pre-Metastatic Niche in Pancreatic Cancer: Exosomes Traffic to Mesothelial Cells In Vitro and In Vivo E. Khachatryan,* X. Jung, H. Chang, A. Moro, O. Hines, G. Eibl, J. King. *Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA.*

Introduction: Peritoneal metastases from pancreatic cancer (PC) are a common and morbid occurrence with few treatment options. There is evidence that PC exosomes are responsible for establishing a pre-metastatic niche in lung and liver but a peritoneal correlate is not described. We sought to determine the effects of PC exosomes on the peritoneum to improve understanding of peritoneal metastases in PC. Methods: Exosomes were isolated from PC cell supernatants (AsPC-1 and HPAF-II) by ultracentrifugation and labeled with the fluorescent membrane dye PKH67. Mesothelial cells (MeT-5A) were treated in vitro with exosomes and the dynamin inhibitor Dynasore to inhibit macropinocytosis. We assayed exosome uptake by immunofluorescence, proliferation by MTT incorporation and migration by scratch assay. Exosomes were injected intraperitoneally (IP) in nude mice and detected in peritoneal tissues by flow cytometry. Results: In vitro, MeT-5A cells internalized exosomes and this was reversed by treatment with Dynasore (Figure). Exosome-treated MeT-5A proliferation was inhibited by treatment with Dynasore (72.7±2.6%; p=0.004 vs vehicle control [DMSO]). Scratch assay wound closure was greatest with exosome-treated cells (61.5±0.1%; p=0.03 vs referent [DMSO]) and migration was inhibited by Dynasore cotreatment (-19.3±0.4%; p=0.5 vs DMSO). In vivo, exosomes accumulated in mesothelial cells as detected by flow cytometry (5.0±2.6% vs 1.1±0.8% [macrophages] vs 0.3±0.3% [fibroblasts]; p=0.04). Conclusions: PC exosomes traffic to mesothelial cells in vivo and induce changes that are reversed by inhibition of macropinocytosis in vitro. These findings correlate with features of mesothelial-mesenchymal transition and may represent formation of a pre-metastatic niche in the peritoneum. Further translational and clinical studies are planned to elucidate components of the peritoneal pre-metastatic niche in order to develop clinically useful therapeutics targeting the metastatic process in PC.



Pancreatic cancer exosomes are internalized by mesothelial cells in vitro. Exo = Exosome.

PT129

Systematic Review and Meta-Analysis of the Effect of Pre-Operative PET/PET-CT in the Management of Patients With Potentially Resectable Colorectal Cancer Liver Metastasis J.F. Daza,[1]* N.M. Solis,[1] S. Parpia,[1] S. Gallinger,[2] C. Moulton,[2] P. Serrano.[1] *1. McMaster University, Hamilton, ON, Canada; 2. University Health Network, Toronto, ON, Canada.*

Background: It has been proposed that PET with 18F-fluorodeoxyglucose alone or combined with CT improves detection of extrahepatic disease in the setting of colorectal cancer liver metastasis (CRCLM). However, there remains conflicting evidence on the added benefit of PET/PET-CT prior to liver resection, and its effect on long-term survival. Methods: From 2000 to April 2017, MEDLINE, EMBASE, and CENTRAL were searched for studies (prospective and retrospective) investigating the preoperative use of PET/PET-CT in the

management of patients with CRCLM. We excluded studies in which neoadjuvant chemotherapy was given 2 weeks prior to PET/PET-CT. Screening, data abstraction, and quality assessment were performed in duplicate. Primary outcome was overall survival (OS). Secondary outcomes included disease-free survival (DFS), pre-operative change in surgical management, and open-close surgery. Random effect models were used to pool treatment effects. A protocol was published in PROSPERO a priori. Results: Of 4034 articles reviewed, 37 met the inclusion criteria and were analyzed, and 8 compared PET/PET-CT to conventional imaging. All studies included PET (n=18), PET-CT (n=17), or both (n=2). OS was similar for all patients who were staged with or without PET/PET-CT prior to liver resection (HR 0.94, 95% CI 0.69 – 1.26). A similar effect was seen in the subgroup of patients who underwent surgery after staging with or without PET/PET-CT with respect to OS (HR 0.92, 95% CI 0.72 – 1.17) and also DFS (HR 0.93, 95% CI 0.81 – 1.08). PET/PET-CT changed the surgical management of 23.4% patients (95% CI 19.33 – 27.47), however, heterogeneity between studies was high (I^2 = 100%, P < 0.01) mostly due to different study designs. Compared to conventional imaging, PET/PET-CT reduced the odds of undergoing an open-close surgery (OR 0.52, 95% CI 0.35 – 0.76). Conclusions: Pre-operative PET/PET-CT may have a meaningful impact on surgical decision-making and prevent unnecessary surgeries in CRCLM. However, the addition of PET/PET-CT to routine pre-operative imaging does not improve OS or DFS.

PT130

Risk Factors for Major Post-Surgical Infection and Wound Dehiscence Following Pancreaticoduodenectomy A. Dosch,* D.K. Imagawa, A. Grigorian, E.J. Won, V. Gabriel, P.T. Delaplain. *Surgery, University of California Irvine Medical Center, Orange, CA.*

Introduction: Intra-abdominal infection (IAI) and surgical site infection (SSI) are common occurrences following pancreaticoduodenectomy (PD). The purpose of this study is to identify independent risk factors for both minor (superficial SSI) and major (deep SSI or IAI) infections in patients undergoing PD and examine the influence of these complications on fascial dehiscence. Methods: Patients who underwent PD from 2010 to 2015 were identified in the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. Logistic regression analysis was used to identify independent risk factors for developing infectious complications. Results: 21,339 patients underwent PD during this time period. Concurrent colon or hepatic resection was performed in 343 (1.6%) and 263 (1.2%) of patients. Minor and major infections occurred in 1992 (9.3%) and 3375 (15.8%) patients, respectively. The rate of post-operative fascial dehiscence was 1.7% (N=354). 254 (71.8%) patients with dehiscence had a coexisting minor or major infection. Of the 1304 patients requiring re-operation, 193 (14.8%) were due to a dehiscence. Multivariate analysis showed malignant diagnosis (OR 1.24, p<0.01), wound classification ≥3 (OR 1.23, p<0.01), and operative time ≥ 6 hours (OR 1.23, p<0.01) as independent risk factors for minor post-operative infection whereas male gender (OR 1.35, p<0.01), body mass index ≥ 35 (OR 1.72, p<0.01), and concurrent colectomy (OR 1.98, p<0.01) or hepatectomy (OR 1.59, p<0.05) were associated with major post-operative infection. Minor and major infections were strongly associated with post-operative dehiscence (OR 3.12 and OR 7.14, p<0.01). Concurrent colectomy (OR 1.78, p<0.01) and hepatectomy (OR 2.28, p<0.01) were independently associated with increased rate of dehiscence, regardless of infection status. Conclusion: Post-operative major and minor infections are both associated with serious morbidity and need for re-operation in patients undergoing PD. Concurrent colon or liver resection is independently associated with an increase in major infectious complications and these patients should be closely monitored for wound dehiscence.

Risk Factors for Minor and Major Infectious Complication following Pancreaticoduodenectomy

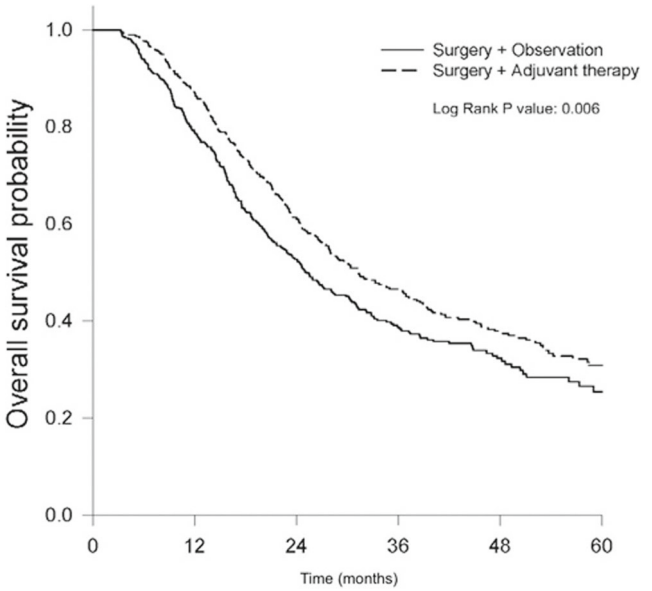
Minor Infectious Complication				Major Infectious Complication			
Risk Factor	OR	95% CI	P-val	Risk Factor	OR	95% CI	P-val
Bleeding Disorder	1.30	0.96-1.76	0.093	Male Gender	1.35	1.21-1.51	0.000
Pre-operative Transfusion	0.41	0.20-0.85	0.160	Black Race	0.87	0.71-1.05	0.149
Malignant Histology	1.24	1.08-1.43	0.003	Asian Race	1.18	0.89-1.57	0.243
Wound Class ≥ 3	1.42	1.23-1.64	0.000	Hispanic Ethnicity	1.24	0.95-1.62	0.113
Operative time ≥ 360 min	1.23	1.10-1.38	0.000	Hypertension	1.10	0.98-1.23	0.116
Concurrent Colectomy	1.15	0.76-1.74	0.519	IDDM	0.71	0.60-0.84	0.000
Concurrent Hepatectomy	1.46	0.93-2.28	0.098	Smoking	1.02	0.89-1.17	0.747
NPWT Placement	1.38	0.54-3.55	0.507	Disseminated cancer	1.24	0.97-1.59	0.084
				Bleeding Disorder	1.22	0.90-1.66	0.196
				≥10% Weight Loss in 6 months	0.92	0.78-1.07	0.275
				Pre-operative SIRS/Sepsis	1.21	0.80-1.85	0.369
				Malignant Histology	0.77	0.68-0.87	0.000
				ASA Score ≥ 3	1.12	0.98-1.27	0.108
				Pre-operative Bili ≥ 2.0	0.87	0.76-1.00	0.057
				Pre-operative Hct < 39	0.83	0.74-0.93	0.002
				Wound Class ≥ 3	1.09	0.93-1.26	0.280
				Operative time ≥ 360 min	1.09	0.98-1.22	0.128
				BMI ≥ 35	1.72	1.45-2.04	0.000
				Concurrent Colectomy	1.98	1.40-2.80	0.000
				Concurrent Hepatectomy	1.59	1.04-2.44	0.034

Table 1: Results of multivariate analysis performed for risk factors of minor/major infectious complications found to be significant on univariate analysis. OR odds ratio, CI 95% confidence interval, NPWT negative pressure wound therapy, IDDM insulin dependent diabetes mellitus, SIRS systemic inflammatory response syndrome, ASA American Society of Anesthesiologists, Bili total bilirubin, Hct hematocrit, BMI body mass index.

PT131

Improved Survival in a National Cohort of Resected Distal Cholangiocarcinoma Treated with Adjuvant Therapy I. Nassour,* C.A. Hester, R. Minter, P. Polanco, S. Wang, M. Porembka, M. Augustine, M.A. Choti, A. Yopp. *Surgery, University of Texas Southwestern, Dallas, TX.*

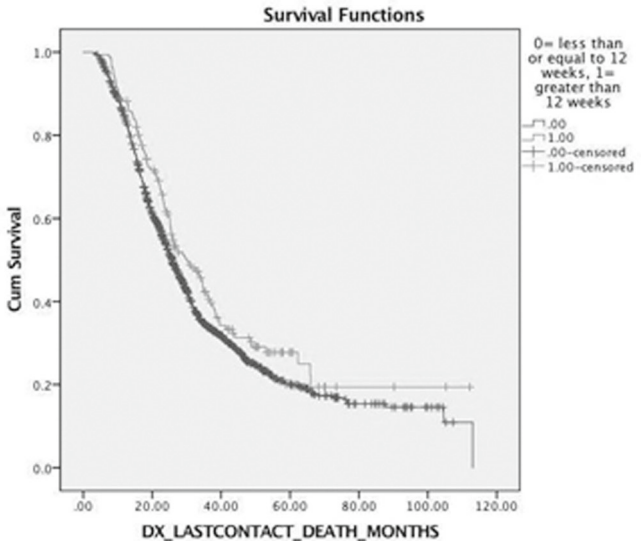
Introduction: The data on the efficacy of adjuvant therapy in distal cholangiocarcinoma is limited in the absence of randomized clinical trials. The aim of this study was to determine in what subgroups following surgically resected distal cholangiocarcinoma would adjuvant therapy be efficacious. Methods: We conducted a retrospective analysis of NCBD of patients diagnosed with surgically resected distal cholangiocarcinoma between 2006 and 2013. All patients who received adjuvant therapy (AT) or observation (OB) were included for analysis. 90-day mortality was excluded to minimize immortal time bias. Patients who received adjuvant therapy (AT) were matched to observation (OB) by propensity score to minimize selection bias. Results: Of the 1,782 patients identified with surgically resected distal cholangiocarcinoma, 840 patients (47%) were in the OB group and 942 (53%) in the AT group. The AT group was younger (p<0.001), had less comorbidities by Charlson-Deyo score (p<0.001), and was more likely to have private insurance (p<0.001). The AT group also was more likely to have T3/T4 disease (72% vs. 57%, p<0.001), N1/N2 disease (58% vs. 37%, p<0.001) and positive surgical margins (26% vs. 16%, p<0.001). After 1:1 propensity score matching, 500 OB patients were compared to 500 AT patients. The receipt of AT was associated with better overall survival compared to the OB group (HR=0.79; 95% CI:0.67-0.93). The median overall survival was 31.2 months for the AT group and 25.2 months for the observation group (P value = 0.006). The 1-, 3-, and 5-year survival were 87%, 46%, and 31% for the AT group; 79%, 39% and 24% for OB group. Subgroup analysis showed that the survival advantage for AT was evident in T3/T4 disease (HR=0.72; 95% CI:0.59-0.89), node positive disease (HR=0.70; 95% CI:0.56-0.87) and positive resection margin (HR=0.58; 95% CI:0.42-0.81). Conclusions: Adjuvant therapy is associated with improved overall survival in resected distal cholangiocarcinoma, especially in T3/T4 disease, node positive disease and positive resection margin. This study supports the use of adjuvant therapy in high-risk patients.



PT132

Implications of Prolonged Time to Pancreaticoduodenectomy After Neoadjuvant Chemoradiation: Analysis of the National Cancer Database A. Teng,[1]* T. Nguyen,[1] A. Bilchik,[1] V.V. O'Connor,[3] D.Y. Lee.[2] *1. John Wayne Cancer Institute, Santa Monica, CA; 2. TriHealth Cancer Institute, Cincinnati, OH; 3. Kaiser Los Angeles Medical Center, Los Angeles, CA.*

Background For patients with pancreatic adenocarcinoma (PA), the optimal time interval between neoadjuvant chemoradiation (CR) to surgical resection has not been well established. The National Cancer Database (NCDB) was used to evaluate the impact of radiation-surgery (RS) interval on outcomes. Methods The NCDB from 2006-2014 was queried for patients ≥18 years old diagnosed with PA who received CR prior to surgery. Survival and short-term outcomes were compared between patients who had a Whipple procedure performed ≤12 weeks and >12 weeks after completion of CR therapy. Results 1610 patients met selection criteria. Average RS interval was 58.2 ± 39.5 days. 1419 patients had RS interval ≤12 weeks (mean 47.4 days) and 191 had RS interval >12 weeks (mean 138.8 days). Age, race, gender, income, type of treatment facility, CA 19-9 levels, types of chemotherapy and radiation dosage administered were similar between the two groups. Mean tumor size was 32.2 mm in the ≤12 week group and 34.9 mm in the >12 week group (p=0.021). There was a higher proportion of patients with clinical stage III cancers in the >12 weeks group than in the ≤12 weeks group (33.5% vs 14%, respectively). Short-term morbidity and mortality was not significantly different between the two groups in terms of length of stay, readmission within 30 days, 30-day and 90-day mortality. However, a long-term survival benefit was observed in the >12 week group (median 25.8 months in ≤12 weeks vs 30.2 months in >12 weeks, p = 0.049) that appears to persist (Figure 1). An interval >12 weeks was associated with significantly prolonged survival on multivariate analysis (HR 0.80 (0.65-0.99 95% CI, p=0.042)). Higher clinical stage and positive surgical margins were independently associated with worse survival. Conclusion Surgical resection beyond 12 weeks after CR for PA did not worsen surgical outcomes. Waiting may contribute to better patient selection, especially those with larger tumors and higher clinical stage. In the absence of progressive disease, patients need to be continuously evaluated for surgical resection after CR.



PT133

Stromal SDF-1/CXCL12 Maintains an Immuno-Suppressive Microenvironment in Pancreatic Ductal Adenocarcinoma A. Ferrantella,* B. Garg, B. Giri, S. Modi, V. Sethi, S. Kurtom, S. Ramakrishnan, S. Banerjee, E. Gilboa, A. Saluja, V. Dudeja. *Surgery, University of Miami, Miami, FL.*

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is believed to be an immunologically 'cold' tumor. This, in part, is mediated by the dense stroma that helps create an immune-privileged sanctuary. CXCL12/SDF-1 has been shown to play an immunosuppressive role in several cancers. Here, we aim to delineate the role of stromal CXCL12/SDF-1 in mediating an immunosuppressive phenotype within the tumor. Methods: Pancreatic cancer cells derived from KPC, a genetically engineered mouse model for PDAC, were injected alone or co-injected with pancreatic stellate cells (PSCs) extracted from WT (C57/BL6) mice to induce tumors. IHC was used to evaluate SDF-1 expression in the tumor. AMD3100 (2mg/kg), an SDF-1 inhibitor or vehicle was administered i.p for 21 days in mice bearing tumors and at end point, tumor growth and immune infiltration were assessed by flow cytometry. In vitro, PSCs were pre-treated with SDF-1 neutralizing antibody, educated with KPC cancer cells and co-cultured with splenic CD3+ T cells in transwell system to evaluate T cell migration. Results: Mice co-injected with KPC cancer cells and PSCs had larger tumors with increased secretion of SDF-1 as compared to tumors from mice where cancer cells alone were injected. Interestingly, inhibiting the SDF-1/CXCR4 axis with AMD3100 led to reduced tumor growth and greater infiltration of activated CD8+ cytotoxic T cells compared to the saline-treated control mice. Secretion of SDF-1 by PSCs was confirmed in vitro, and neutralization of SDF-1 led to increased T cell migration when co-cultured with cancer cells and PSCs. Conclusion: Our findings indicate that stromal cells contribute to tumor progression by preventing the infiltration of cytotoxic immune effectors via SDF-1. Targeting SDF-1 or other stroma-derived immune repellents may render the 'cold' pancreatic tumors responsive to immunotherapy.

PT134

Lymph Node Harvest as a Measure of Quality and Effect on Overall Survival in Pancreas Cancer: a National Cancer Database Assessment S.H. Slipak,* M. Dudash, M. Fluck, M. Hunsinger, T. Arora, J. Wild, M. Shabahang, J. Blansfield. *General Surgery, Geisinger Health System, Danville, PA.*

Introduction: Surgical therapy for pancreas cancer is the cornerstone of treatment and the highest quality operation should lead to the highest cure rate. Evaluated lymph node (ELN) count is one quality measure that has been championed. The objective of this study was to explore ELN, examine predictors of a 12-ELN threshold in pancreatectomy and determine whether higher ELN improves overall survival (OS). Methods: ELN was examined in patients with resected pancreas cancer using the National Cancer Database from 2004 to

2013. Results: On multivariate (MV) analysis and adjusting for confounding variables, in node negative (N0) as well as node positive patients, a 12-ELN threshold is associated with significantly improved OS (HR 0.86, 95% CI [0.82, 0.89], HR 0.90, 95% CI [0.87, 0.93], respectively). ELN has improved over time with 40% of patients having 12 or more nodes examined in 2004 versus 68% of patients in 2013. Women were slightly more likely to meet the 12-ELN threshold (59.4% v 58% of men, p<0.008) and head resections were more likely to reach the 12-ELN threshold compared to tail resections (63% v 41%, p<0.0001). Neoadjuvant treatment affected ELN with neoadjuvant chemotherapy increasing ELN on MV analysis (HR 1.92, 95% CI [1.72,2.14]) and neoadjuvant radiation treatment decreasing ELN (HR 0.637, 95% CI [0.556,0.73]). Facility type also predicted ELN. On MV analysis, academic centers were more likely to meet the threshold compared to other facility types. High volume centers were also more likely to reach the threshold on MV (HR 1.43, 95% CI [1.35,1.51]). Quality predictors were improved when 12-ELNs were counted. Thirty day unplanned readmissions decreased (8.2% versus 7.6%, p<0.02) as did 30-day mortality (3.5% versus 2.6%, p<0.0001). Conclusions: Adjusted OS is improved in N0 patients when the 12-ELN threshold is reached, suggesting nodal yield is a good quality measure for pancreatectomy. High volume centers and academic facilities have the highest rates of nodal harvest but overall nodal harvest has improved over time.

Effect of Lymph Node Harvest on Overall Survival: Multivariate Analysis

Cox models for overall survival	All Patients			
	HR	95% CI		p value
		LL	UL	
Total Node Harvest*				**<0.0001**
Lymph Node Harvest < 12	Ref	Ref	Ref	
Lymph Node Harvest ≥ 12	0.884	0.862	0.906	
Positive Lymph Nodes*				**<0.0001**
0	0.701	0.677	0.726	
1	Ref	Ref	Ref	
≥ 2	1.278	1.238	0.32	
	All N0			
Total Node Harvest				**<0.0001**
Lymph Node Harvest < 12	Ref	Ref	Ref	
Lymph Node Harvest ≥ 12	0.856	0.821	0.894	
	All N1			
Total Node Harvest				**<0.0001**
Lymph Node Harvest < 12	Ref	Ref	Ref	
Lymph Node Harvest ≥ 12	0.898	0.871	0.926	
Positive Lymph Nodes				**<0.0001**
1	Ref	Ref	Ref	
≥ 2	1.29	1.249	1.332	

Hazard Ratio > 1 indicates increased risk of death

*Model adjusted for same variables as factors associated with 12 Node Harvest, with the addition of adjuvant chemo and radiation, and removal of TNM PATH N

PT135

Residual Tumor Index: A Significant Prognostic Parameter for Resected Neoadjuvant Treated Pancreatic Ductal Adenocarcinomas

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Background: Pancreatic ductal adenocarcinoma (PDAC) is an infiltrative tumor with a prominent desmoplastic stroma. Often the adjacent fibrotic stroma is exaggerated by neoadjuvant therapy (NAT). In this setting, accurate measurement of tumor size, and consequently staging based on AJCC 8th edition, is frequently very difficult. The aim of this study is to identify a prognostically meaningful pathologic parameter which can be an adjunct to tumor staging in the neoadjuvant setting. Methods: A cohort of patients with PDAC located in the head of pancreas, who underwent NAT followed by pancreaticoduodenectomy, was identified from a prospectively maintained database. Archival H&E slides were reviewed to assess the percentage of residual tumor, along with other usual pathologic parameters, and a record of tumor size and tumor bed size was noted by a pathologist. Residual tumor index (RTI) was arbitrarily defined as the product of residual tumor percentage and tumor bed. Univariate and multivariate analyses were performed to determine the association of RTI with overall survival (OS) and recurrence free survival (RFS). Results 105 cases were analyzed using clinical and pathologic (tumor grade, margin status, perineural invasion and lymphatic invasion) characteristics. On univariate analysis, total number of lymph nodes involved and RTI were significantly associated with RFS (p-value=0.0132 & 0.0027). On multivariate analysis, only RTI was identified as an independent predictor of RFS (HR=1.650 (1.189, 2.289), p=0.003). Lymphatic invasion, number of lymph nodes involved and RTI were also associated with OS on univariate analysis (p-value of <0.05, <0.002 and <0.0005) however, RTI was the only independent predictor of OS on multivariate model (HR=1.539 (1.115-2.126), p<0.01). Conclusion Our data suggest that RTI is a useful parameter for pathologic classification of PDAC post resection in patients undergoing NAT. Categorization of RTI and verification of these results in a large cohort will be useful to develop an adjunct to pathological staging for patients undergoing NAT.

PT136

Predicting Pancreatic Fistula in Patients Undergoing Pancreaticoduodenectomy for Pancreatic Ductal Adenocarcinoma

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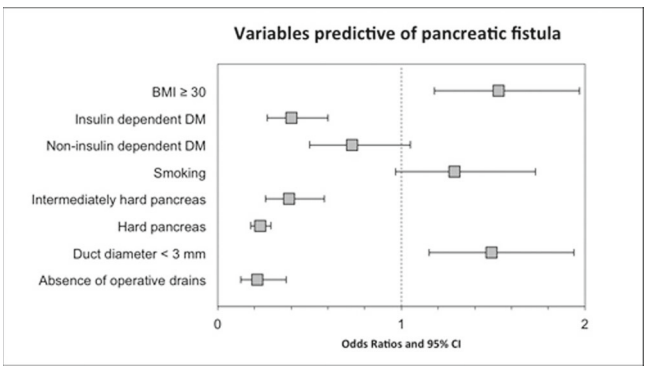
Introduction: Mortality following pancreatic resection is low; however, morbidity remains high. This study aims to identify patient and procedure-related factors predictive of pancreatic fistula (PF) following pancreaticoduodenectomy (PD). Methods: The 2014-2015 NSQIP pancreatic procedure targeted database was analyzed. Logistic regression models were created to identify risk factors predictive of PF for patients undergoing either classic or pylorus preserving PD for pancreatic ductal adenocarcinoma (PDAC). Results: A total of 3,037 patients were included, of whom 22.2% developed PF. Nearly 57% of patients were jaundiced prior to surgery. For all patients, median age was 66 years, median BMI was 26.8, and perioperative mortality rate was 1.2%. Twenty-five percent of all patients received neoadjuvant chemotherapy and 12.1% received neoadjuvant radiation therapy. On multivariate analysis, BMI (p=0.001), diabetes (p<0.001), pancreatic texture (p<0.001), pancreatic duct diameter (p=0.003), smoking (p=0.08), and placement of operative drains (p<0.001) were significantly associated with the development of PF and were carried forward for model creation. Our model predicts PF with good accuracy (C-statistic 0.75) and includes: BMI greater than or equal to 30 (OR 1.53, 95% CI 1.18-1.97), preoperative diagnosis of insulin-dependent diabetes (OR 0.40, 95% CI 0.27-0.60), preoperative diagnosis of non-insulin-dependent diabetes (OR 0.73, 95% CI 0.50-1.05), smoking (OR 1.29, 95% CI 0.97-1.73), intermediately hard pancreatic texture (OR 0.39, 95% CI 0.26-0.58), hard pancreatic texture (OR 0.23, 95% CI 0.18-0.29), pancreatic duct diameter less than three millimeters (OR 1.49, 95% CI 1.15-1.94), and placement of operative drains (OR 4.63, 95% CI 2.67-8.00) (Figure). Conclusions: This study has identified factors, some of which were previously unrecognized, that may predict the development of PF in patients undergoing PD for PDAC. Identification of high-risk patients will allow for early intervention to reduce the severity of, or prevent, the development of pancreatic fistula.



PT139

Identification of Risk Factors for Venous Thromboembolism in Pancreatic Ductal Adenocarcinoma Patients Undergoing Pre–Operative Chemotherapy B.A. Boone,* C. Rieser, A. Hamad, M.S. Zenati, A. Zureikat, M. Hogg, M.D. Neal, H. Zeh. *Surgery, University of Pittsburgh, Pittsburgh, PA.*

Introduction: Pancreatic ductal adenocarcinoma (PDA) is associated with a hypercoagulable state resulting in high risk of venous thromboembolism (VTE). VTE risk is well established for patients receiving chemotherapy for advanced disease and during the perioperative period for patients undergoing surgical resection. However, data is lacking for patients undergoing neoadjuvant treatment, who may have unique risk of VTE because of exposure to both the risks associated with chemotherapy and surgery. Methods: Patients with PDA treated with neoadjuvant therapy followed by surgery were identified from pancreatic surgical databases from 2007 to June 2016. VTE including any venous thrombosis were evaluated from the start of treatment through the 90-day postoperative period. Risk factors including clinical factors, treatment variables and laboratory values evaluated prior to treatment and prior to surgery were assessed. Results: 357 patients receiving pre-operative therapy prior to surgical resection were studied. Surgical resection included pancreaticoduodenectomy (76%), distal pancreatectomy (14%), distal pancreatectomy with celiac axis resection (DP-CAR, 9%), total pancreatectomy (<1%), and central pancreatectomy (<1%). 21% of patients had a VTE within 90 days postoperatively (n=75). VTEs (n=84) included PE (29%), DVT (31%), superficial vein thrombosis (5%), and thrombosis of the portal vein/SMV (35%), splenic vein (4%), and ovarian vein (1%). 73% of VTEs occurred during the postoperative period. Patients with VTE had significantly higher pretreatment neutrophil count, lower preoperative lymphocyte count, higher frequency of preoperative platelet/ lymphocyte ratio >260, longer operative times and were more likely to receive radiation and undergo total pancreatectomy or DP-CAR. Age >65, pretreatment hemoglobin <10 g/dL and resection with DP-CAR or total pancreatectomy were independent predictors of VTE on multivariate analysis. Conclusions: VTE during neoadjuvant treatment followed by surgery is common. Further study into novel thromboprophylaxis measures during neoadjuvant treatment and the perioperative period is warranted.

PT140

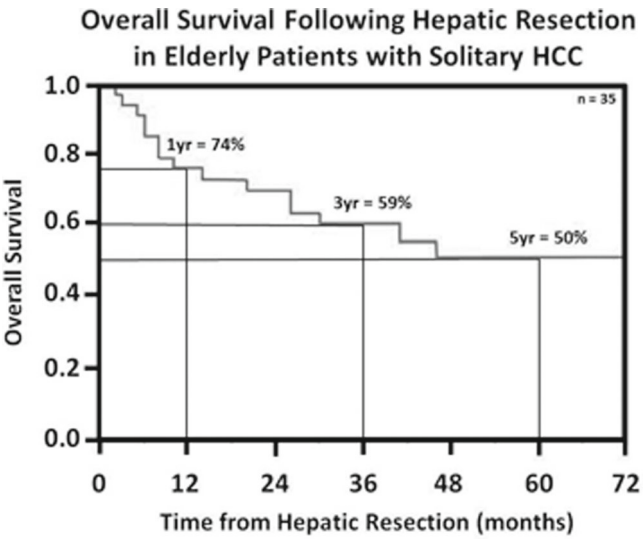
Clinicopathological Significance of Promoter DNA Hypermethylation of the Cysteine Dioxygenase 1 (CDO1) Gene in Primary Gallbladder Cancer and Gallbladder Disease K. Igarashi,* K. Yamashita, H. Katoh, K. Kojima, Y. Ooizumi, N. Nishizawa, Y. Kumamoto, M. Watanabe. *Surgery, Kitasato University Hospital, Sagamihara, Japan.*

Background CDO1 is a highly relevant methylation gene in human cancer, and postulated to be a novel tumor suppressor gene. We assessed for the first time the clinicopathological significance of CDO1 promoter DNA methylation in GBC and gallbladder disease. Materials and Methods We examined the transcriptional level of CDO1 by RT-PCR and performed 5-Aza-dC and TSA treatment in gallbladder cancer cell lines (G-415, TCGK2TKB). CDO1 DNA methylation was quantified using quantitative TaqMan methylation specific PCR in 99 primary GBC patients and 26 benign gallbladder disease patients who underwent surgical resection between 1986 and 2014. Tissue samples: GBC tumor tissue (T) (n=99), the corresponding non-cancerous mucosa (CN) (n=78), benign gallbladder disease tissue (NN) (n=26) including chronic cholecystitis, adenomyomatosis, xanthogranulomatous cholecystitis (XGc), of the formalin-fixed, paraffin embedded (FFPE) tissues. Results Silenced CDO1 was reactivated by pharmacological demethylation. The CDO1 methylation value of T (median 16.4) was significantly higher than those of CN (median 2.3) and those of NN (median 0), respectively (p<.0001). The AUROC that discriminates T from NN was 0.89. CDO1 methylation value of CN was significantly higher than those of NN (p=0.0084), in NN, CDO1 methylation value of XGc was significantly higher than those of others (p=0.014). The CDO1 methylation status of T showed significant differences between stage I and other stages (p=0.018). Using a cut-off value of 17.7, CDO1 hypermethylation showed significantly poorer prognosis than CDO1 hypomethylation (p=0.0023). Multivariate Cox proportional hazards analysis identified that CDO1 hypermethylation was an independent prognostic factor (HR 2.1). Notably, CDO1 hypermethylation showed prognostic relevance, especially in stage II GBC. Conclusions CDO1 was epigenetically inactivated in GBC celllines. Promoter DNA methylation of CDO1 was demonstrated to be a cancer-associated methylation in primary GBC. CDO1 methylation has the potential to be a prognostic biomarker of GBC for high-risk patients with stage II GBC.

PT141

Hepatic Resection of Solitary HCC in the Elderly: Disease Control and Survival in a Growing Population L. Zarour,[1]* K.G. Billingsley,[1] W. Naugler,[2] C.K. Enestvedt,[3] S.L. Orloff,[3] E. Maynard,[3] E. Dewey,[4] A. Fung,[5] G.M. Vaccaro,[6] S.C. Mayo.[1] *1. Division of Surgical Oncology, Hepatopancreatobiliary Surgery, Knight Cancer Institute at Oregon Health & Science University, Portland, OR; 2. Division of Hepatology at Oregon Health & Science University, Portland, OR; 3. Division of Abdominal Organ Transplantation at Oregon Health & Science University, Portland, OR; 4. Department of Surgery, Biostatistics at Oregon Health & Science University, Portland, OR; 5. Department of Radiology at Oregon Health & Science University, Portland, OR; 6. Division of Medical Oncology at Oregon Health & Science University, Portland, OR.*

INTRODUCTION: The management of elderly patients with a solitary hepatocellular carcinoma (SHCC) is challenging with perceived clinicopathologic differences driving treatment recommendations compared to younger patients and evidence suggesting underutilization of hepatic resection. We sought to assess peri-operative outcomes and determine factors predictive of disease control and survival in elderly patients after resection of SHCC METHODS: We identified n=45 elderly patients (^65-yo) with SHCC who underwent hepatic resection alone from our prospectively managed institutional database from 2003-16. Clinicopathologic data were analyzed and survival was assessed using Kaplan-Meier and Cox regression models. Significance was evaluated at P<0.05 RESULTS: The median age was 71-yo with the majority of patients (n=32; 71%) being men. Viral hepatitis was present in 47% (n=21) with the majority having no evidence of hepatic steatosis (n=34; 76%). At the time of resection, the median Child-Pugh score was A6 with a mean tumor size of 5.5cm (s.d. = 3.1cm) and a mean AFP of 1,050 ng/mL. Major hepatectomy was performed in 23 patients (51%) with R0 resection achieved in 96% and vascular invasion present in 39% (n=17) on final pathology. Two patients (4%) had a ^Grade III complication with no mortality at 30 days and one death (2.2%) at 90 days. After R0 resection 42% (n=19) of patients had an intrahepatic recurrence at a mean of 28 months with 20% (n=9) developing extrahepatic recurrence at a mean of 61 months. Following resection, the median survival was 72 months (95% CI: 30-108 mo). For patients with at least three years of follow-up (n=35), the 1-, 3-, and 5-year overall survival was 74%, 59%, and 50%, respectively (Figure). Intrahepatic recurrence was associated with a higher AFP and neutrophil to lymphocyte ratio and a lower prognostic nutritional index. Both increasing T-stage and tumor size were associated with higher extrahepatic recurrence CONCLUSIONS: Select elderly patients with a SHCC managed with hepatic resection alone can achieve excellent overall and recurrence-free survival with low morbidity and mortality that is comparable to younger patient cohorts



PT142

WNT-11 Negatively Regulates Cancer Cell Migration and Invasion in Pancreatic Ductal Adenocarcinoma T. Hughes,* C.R. Siangco, K. Das, Y. Kang, M. Kim. *Surgical Oncology, MD Anderson, Houston, TX.*

Introduction: WNT-11 is a secreted ligand that has been shown to affect cell migration and invasion in multiple types of cancer, but its role in non-canonical WNT-signaling and pancreatic ductal adenocarcinoma (PDAC) is not well understood. The goal of this study was to determine the effect of WNT-11 on PDAC cell invasion and migration. Methods: Relevant expression of WNT-11 in human PDAC was confirmed using gene expression data from the cancer genome atlas. WNT-11 expression was confirmed in 12 different human PDAC cell lines and in 4 PDAC cell lines generated from genetically engineered mouse models (GEMMs) of pancreatic cancer (KPC cell lines). Plasmids containing an empty backbone and Wnt11 cDNA were infected into KPC cell lines, and overexpression was confirmed by western blot analysis. MTT and transwell migration/invasion assays were performed in KPC cell lines to measure cell proliferation, migration and invasion relative to control vectors. The effect of exogenous WNT-11 ligand (500ng/mL for 24 hours) on KPC cell migration and invasion was measured using transwell migration/invasion assays. Unpaired student's t-tests were used to assess for statistically significant differences between control and treatment groups. Results: WNT-11 is expressed in human pancreatic cancer, PDAC GEMMs and all derived PDAC cell lines. Relative to control cell lines, WNT-11 overexpression did not affect cell proliferation in KPC cell lines as measured by MTT assay. WNT-11 overexpression resulted in a 73.1% and 45.73% reduction in migration and invasion relative to controls ($p=0.0094$ and $p=0.0316$ respectively) in tested KPC cell lines. Treatment of KPC cell lines with exogenous WNT-11 ligand resulted in reduced cell migration and invasion (48.16%, $p=0.008$; 50.23%, $p=0.0096$) relative to untreated controls. Conclusion: WNT-11 is expressed in human and mouse PDAC. Exogenous WNT-11 treatment and stable overexpression of WNT-11 in KPC cell lines results in reduced cancer cell migration and invasion without effects on cell proliferation. PDAC cell invasion and metastasis may be modulated by WNT-11 expression and requires additional in vivo testing in human and mouse model systems.

PT143

Identifying Different Patterns of Desmoplasia in Pancreatic Cancer Using Collagen 11A and Vitamin D Receptor Expression Levels M.N. Brakha,* E. Nizri, S. Bar-David, G. Lahat, A. Aizic, J.M. Klausner. *Tel-Aviv Sourasky Medical Center, Holon, Israel.*

Introduction: Desmoplasia is a prominent feature of pancreatic ductal adenocarcinoma (PDAC). While it is considered to be a contributor for tumor lethality and resistance to therapy, there is also evidence for its role against tumor progression. We hypothesized that desmoplasia is a heterogeneous process. We used the following markers to distinguish between different desmoplasia patterns: Collagen 11A (COL11A), a stromal protein expressed in various cancers; and Vitamin D receptor (VDR), a marker for activated pancreatic stellate cells. Methods: We retrospectively evaluated tumor specimen from 76 patients with PDAC and desmoplasia. Stromal peritumoral area was defined and analyzed for stromal cellularity (inflammatory cells and fibroblasts). COL11A+ and VDR+ cells were quantified using immunohistochemistry and digital imaging. Patients were divided into groups of COL11A high/low and VDR high/low according to the mean number of positive cells in the total cohort. Data was correlated with overall survival (OS) expressed in months. Results: Mean follow up time was 25.15±19 months. Perineural invasion (PNI) (n=51, 67%) was not associated with OS (OS=23.81±4.7 for PNI- vs. OS=28.4±3.9 for PNI+, $p=0.21$) whereas N1 stage (n=40, 52%) was almost significant (OS=34.9±5.3 for N0 vs. 21.7±2.6 for N1, $p=0.06$). Neither inflammatory nor fibroblastic cellularity was associated with clinical outcome. Both parameters of stromal activation demonstrated remarkable association with OS: for COL11A, OS=47.3±5.1 for COL11A-low vs. OS=14.3±2.1 for COL11A-high, $p<0.0001$; for VDR, OS=49.7±5.3 for VDR-low vs. OS=14.7±2 for VDR-high, $p<0.0001$. Multivariate analysis showed only VDR+ to be associated with OS significantly, with HR=1.2, $p<0.001$. Conclusions: PDAC-associated desmoplasia is a heterogeneous process, sub-classified here by COL11A and VDR expression. High COL11A and VDR expression appear to be negative prognostic factors. These results call for better understanding the heterogeneity of desmoplasia, and could guide future anti-stromal targeted therapies.

PT144

The Impact of Tumor Genomic Profile on the Effectiveness of Adjuvant Chemotherapy in Resectable Intrahepatic Cholangiocarcinoma (ICC) R.K. Marcus,* H.A. Lillemoe, R. Abdel-Wahab, R. Shroff, M. Javle, T. Aloia. *Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: The incidence and mortality of ICC is rising in the U.S. While surgical resection currently offers the only potential for cure, the role of adjuvant chemotherapy is not well defined. Tumor genomic profiling is increasingly used to make adjuvant therapy decisions for malignancies. We sought to evaluate the correlation between tumor genomic profile and the ability of adjuvant chemotherapy to prevent ICC recurrence after resection. Methods: A retrospective review of 49 patients with ICC undergoing surgical resection and comprehensive tumor genomic profiling was performed. The median age at diagnosis was 56 years (range: 21-72 yrs), 67% were female, and 67% were Caucasian. At resection, 20% had stage I disease, 43% stage II, 29% stage III, and 8% stage IV. Over 90% had moderately or poorly differentiated adenocarcinoma. Clinically relevant genetic mutations (those targeted by anticancer drugs currently on the market or required for entry into a mechanism-driven clinical trial) were evaluated using Foundation Medicine testing. Results: Median recurrence free survival (RFS) for the entire cohort was 9 months (range: 1-55 mo). 59% of patients received adjuvant chemotherapy – 66% gemcitabine- and 31% capecitabine-based. The most prevalent mutations were FGFR2 (28%), CDKN2A/B (24%), IDH1 (17%), and ARID1A (17%). Median RFS for the adjuvantly treated group was 12 months (range: 3-55 mo), and the presence of any clinically relevant mutation was associated with worse RFS (x vs y, $p=0.03$). IDH1 (30%), BAP1 (25%), and PBRM1 (20%) were most frequently mutated amongst patients who did not receive adjuvant therapy, and their median RFS was 5 months (range: 1-54 mo). Lack of an IDH1 mutation correlated with worse RFS ($p=0.02$), while lower stage correlated with improved RFS ($p=0.01$). Conclusions: For patients with ICC undergoing resection and adjuvant chemotherapy, the presence of clinically relevant genetic mutations is associated with reduced RFS. To gain further insight into the influence of tumor genomic profile on the effectiveness of adjuvant chemotherapy for this patient population, a multicenter collaborative effort is needed.

PT145

Prognostic Factors of Patients with Intrahepatic Cholangiocarcinoma After Hepatic Resection: 433 Cases for 10-Years S. Hwang,* J. Lee. *Asan Medical Center, Seoul, Korea (the Republic of).*

Purpose : The curative treatment option for patients who have intrahepatic cholangiocarcinoma is surgical resection. Unfortunately, even after curative resection, the clinical outcomes are disappointing with a 5-year survival rate of 20% to 35%. This study aims to assess clinicopathological factors associated with recurrence and survival of IHCC patients after hepatectomy. Methods : 433 patients with ICC who were treated surgically between January 2003 and December 2012 at our institution were retrospectively evaluated. The possible prognostic factors were analyzed by the univariate analysis and evaluated using the Kaplan-Meier method. The multivariate analysis was performed using the Cox proportional hazards model to identify the independent prognostic factors for survival and recurrence. Results: : The median age was 60 years (range 31 - 83) and male was dominant (69.6%). Solitary and mass-forming type of tumor were 89.5% and 69.2%, respectively. Median tumor size was 5.42cm and lymphnode metastasis was identified in 20.3%. R0 resection were obtrained in 79.0% accompanied by extrahepatic bile duct resection in 17.1%. 57.3% and 42.7% of patients were treated with postoperative chemotherapy and radiotherapy, respectively. The overall 1-, 3-, 5- and 10-years survival rate of patients were 76.5, 44.1, 33.3 and 25.1%, respectively, and disease free 1-, 3-, 5- and 10-years survival rate were 51.1, 31.0, 28.3 and 25.3%. Multivariate analysis showed that intraductal growing type($P=0.002$, $OR=0.495$), lymph node metastasis($P=0.020$, $OR=1.454$), perineural invasion($P=0.000$, $OR=1.618$), and lymphovascular invasion($P=0.004$, $OR=1.472$) were independent factors associated with overall survival. Intraductal growing type($P=0.006$, OR=0500), perineural invasion($P=0.000$, $OR=1.698$), and lymphovascular invasion($P=0.002$, $OR=1.641$) were independent factors associated with recurrence. Conclusions: The prognosis of IHCC was determined primarily by tumor factors. Intraductal growing type is associated with good prognosis. Perineural invasion, lymphovascular invasion and lymph node metastasis are associated with poor prognosis.

PT146

Frailty and Sarcopenia Are Separate and Distinct Biologic Parameters Affecting Outcomes in Patients Undergoing Surgery for Pancreatic Diseases J. Chakedis,* S.H. Sun, M.H. Squires, E.W. Beal, A. Chafitz, J. Galo, P. Rajasekera, E. Talbert, D. Guttridge, T.M. Pawlik, M. Dillhoff, C.R. Schmidt. *Surgery, The Ohio State University, Powell, OH.*

Frailty is a surrogate marker for decreased functional reserve after surgery which contributes to poor outcomes. Similarly, sarcopenia is associated with increased complication rates and survival after pancreatic resection. Serum cytokines MCP-1 and IL-8 are known predictors of poor survival after resection and therefore we measured frailty, sarcopenia and perioperative cytokine levels to determine relationships to short and long-term outcomes. In 118 patients undergoing pancreatic resection for malignant or benign peri-pancreatic disease, 25 serum cytokines were measured using a multiplex ELISA assay. Sarcopenia is defined by the lowest quintile psoas muscle are measured at L3 on preoperative CT imaging. Frailty is defined by ≥ 3 out of 11 fields positive using the modified frailty index (mFI). There were 99 patients who underwent pancreatic resection for periampullary malignancy and 19 had benign disease (cystic lesions and pancreatitis). The proportion of frail patients was not different at 20.2% in the cancer group and 36.8% in the benign group. Sarcopenia was only found in patients with cancer (21.7% versus 0%). Levels of IL-6 and Interferon-gamma were associated with frailty and levels of IL-4 and soluble RANK ligand were associated with sarcopenia (Table 1). Frail patients had increased visceral (p=0.023) and total fat (p=0.037) compared to non-frail patients, but frailty was not associated with sarcopenia or differing weight. Frailty was associated with increased short-term (30-day) mortality (14.8% vs 3.3%, p=0.026), unplanned intubation (18.5% vs. 4.4%, p=0.015) and prolonged mechanical ventilation (14.8% vs. 4.4%, p=0.059). Conversely, sarcopenia was not associated with complications or mortality but was associated with worse overall survival (median 10.6 vs 20.1 months, p 0.012). Patients with pancreatic diseases have high rates of complications and the contrasting contributions from frailty and sarcopenia emphasize the importance of measuring both given the uncertain prognosis. The differing associated cytokines also imply separate biologic mechanisms and causal factors deserving further investigation.

Frailty Predictor	OR (95% CI)	p value
Age	1.14 (1.04-1.26)	0.006
IL-6	4.0 (1.38-11.63)	0.011
IFN- gamma	0.08 (0.01-0.67)	0.021
Model c-statistic	0.840	<0.001

Sarcopenia Predictor	OR (95% CI)	p value
IL-4 detectable	5.7 (1.2-26.3)	0.025
sRANK Ligand detectable	3.8 (1.1-13.0)	0.034
Model c-statistic	0.659	0.055

Perioperative cytokines associated with frailty and sarcopenia are disparate and can be utilized in a predictive model.

PT147

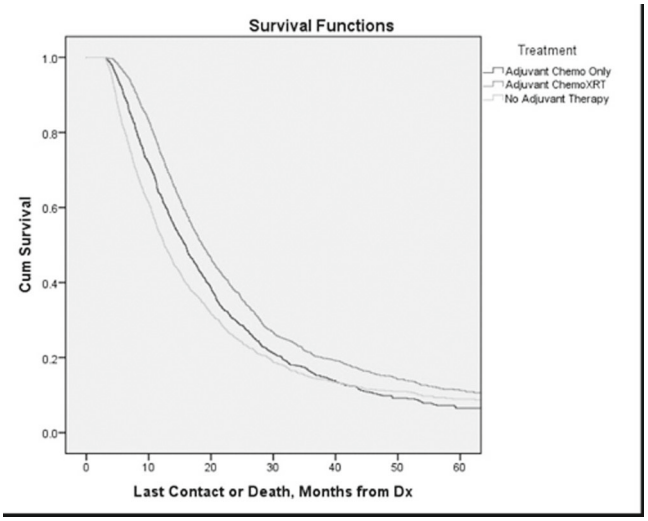
Racial and Ethnic Disparities in Hepatocellular Carcinoma Associated with Presentation and Prognosis C.A. Hester,* L. Winton, M. Augustine, M.A. Choti, J. Mansour, R. Minter, P. Polanco, M. Porembka, S. Wang, A. Yopp. *Surgical Oncology, University of Texas Southwestern, Dallas, TX.*

Background Prior studies demonstrate a disparity in HCC incidence among racial/ethnic groups but due to reliance on administrative datasets, which lack granular data on tumor characteristics and underlying liver dysfunction, a paucity of data exists comparing survival outcomes among non-Hispanic white (NHW), non-Hispanic black (NHB), and Hispanic white (HW) patients. The aim of this study is to characterize the racial/ethnic disparities in presentation and prognosis in HCC patients. Methods We conducted a retrospective review of a prospectively maintained HCC database at a safety-net and tertiary referral health system. Demographics, tumor characteristics, treatment regimens, and survival were compared between NHW, NHB, and HW patients diagnosed with HCC between January 2008 and July 2017 using ANOVA, Chi-squared, and Cox proportional hazard models. Survival curves were generated using Kaplan-Meier with log rank test. Results 1143 HCC patients were identified: 413 (36%) NHW, 397 (35%) NHB, and 333 (29%) HW. Compared to NHW and HW, NHB were more likely to have viral hepatitis (70% and 52% vs. 85%, p<0.001). HW patients were more likely to present with NASH compared to NHW and NHB (15% vs. 8% and 2%, p<0.001) and female gender (28% vs. 24% and 18%, p<0.003). At HCC presentation, HW patients were less likely to present with CTP A liver function than NHW and NHB (37% vs. 49% and 55%, p=0.002). There was no difference in early stage tumor presentation (BCLC 0/A or TNM stage I/II). After adjustment for BCLC stage, HW were less likely to receive curative treatment than NHW (OR 0.63, 95%CI 0.4-0.9). There was no difference in the receipt of curative treatment between NHW and NHB or NHB and HW patients. There was no difference in overall survival (OS) between NHB (11 months), NHW (17 months), and HW (12 months) when adjusted for tumor stage, degree of liver dysfunction, and receipt of treatment (HR 1.053, 95%CI 0.96-1.12). Conclusion NHB patients have similar tumor stage at presentation, receipt of curative therapy, and OS as NHW patients. HW patients have similar OS as NHW and NHB patients despite presenting with advanced liver dysfunction and receiving less curative therapy.

PT148

Adjuvant Therapy for Margin Positive Pancreatic Cancer C. Takahashi,[2]* J. Huston,[1] R. Shridhar,[3] A. Patel,[4] K. Meredith.[1] *1. Gastrointestinal Oncology, Florida State University/Sarasota Memorial Hospital, Sarasota, FL; 2. Midwestern University, Phoenix, AZ; 3. University of Central Florida, Orlando, FL; 4. Florida Cancer Specialists, Sarasota, FL.*

Purpose: Pancreatic cancer continues to have a dismal prognosis despite improvements in surgical care. Approximately 26% of patients are deemed resectable, and at the time of operation, 28% will have R1 resections. Adjuvant chemotherapy(AC) or chemoradiation(CRT) is recommended, however the magnitude of benefit is unclear. We sought to examine the impact these therapies on R1 resected pancreatic cancer. Methods: Utilizing the National Cancer Database we identified patients who underwent pancreatic resection for adenocarcinoma. Patients were stratified by resection status and adjuvant therapy. Baseline comparisons were made using Mann-Whitney U, Kruskal Wallis and Pearson's Chi-square test as appropriate. Survival analyses were performed using the Kaplan-Meier method. Multivariable cox proportional models(MVA) were developed to identify predictors of survival. All statistical tests were two-sided and α <0.05 was considered significant. Results: We identified 28,440 patients: 22,005(77.4%) underwent R0 resections and 6,435(22.4%) underwent R1 resections with a median age of 67.5 years(18-90) and median tumor size of 3.1 cm(2.4-4.2). Patients with tumor size >2cm were more likely to undergo R1 resections, p<0.001. Within the R1 resection group, AC was administered in 1,802(19.4%), CRT 2,153(28.5%), and no adjuvant therapy(NA) 2,480 (21.4%). Adjuvant therapy improved survival in all patients with median and 5-year survival of: AC(21.7 months, 17.45%), CRT(23.3 months, 20.9%) vs NA(19.5 months, 19.1%), p<0.001. In the R1 resection cohort survival was also improved with adjuvant therapy with CRT demonstrating the most significant improvement: AC(15.9 months, 6.5%), CRT(18.7 months. 11.2%) vs NA(12.5 months, 8.7%), p<0.001. Additionally CRT but not AC improved survival in the R1 node negative, p<0.004, and node positive, p<0.001. AC benefited survival in R1 node positive patients, p<0.001. MVA revealed age, tumor grade, tumor size >2cm, T-stage, N-stage, AC, and CRT were predictive of survival. Conclusions: Patients with pancreatic cancer who undergo R1 resection have significant improvement in survival when treated with adjuvant CRT and AC. However, benefits were greater in those receiving adjuvant CRT.



PT149

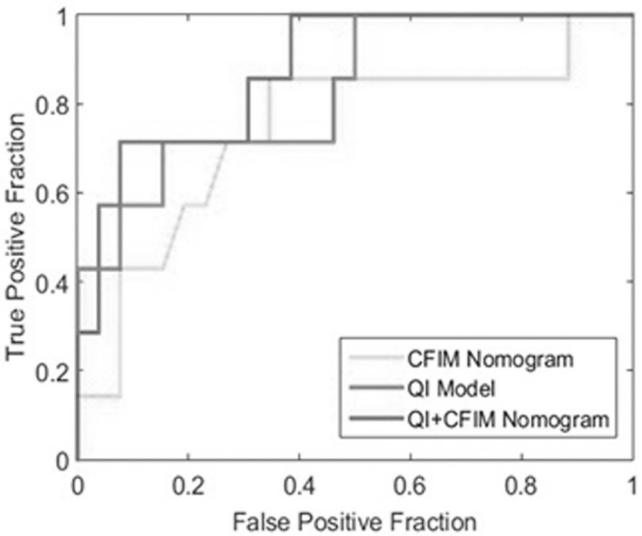
Neutrophil-to-Lymphocyte Ratio as a Predictor of Invasive Carcinoma in Patients with Intraductal Papillary Mucinous Neoplasms of the Pancreas C.A. McIntyre,* S.A. Lawrence, A. Pulvirenti, K. Seier, M. Gonen, M. D'Angelica, P. Kingham, V. Balachandran, J. Drebin, W. Jarnagin, P. Allen. *Memorial Sloan-Kettering Cancer Center, New York, NY.*

Introduction: Intraductal papillary mucinous neoplasms (IPMN) are cystic precursor lesions of pancreatic adenocarcinoma. Preoperative determination of the grade of dysplasia in patients with IPMN is difficult. Serum Neutrophil-to-Lymphocyte Ratio (NLR) has been shown to have prognostic significance in patients with pancreatic cancer, and early data have suggested an ability to predict invasive disease in patients with IPMN. Methods: A prospectively maintained database was queried for consecutive patients who underwent resection of a pathologically confirmed IPMN between 2000 and 2017. Exclusion criteria included diagnosis or treatment of cancer within six months of operation, documented infection or jaundice within one month of operation, immunosuppression or use of immunomodulatory mediations. All patients had a complete blood count (CBC) within one month of operation. Neutrophil-to-lymphocyte ratio was calculated by dividing absolute neutrophil count by absolute lymphocyte count. The Kruskal Wallis test was used to compare medians between groups. Results: Within the study period, 446 patients underwent resection for IPMN and 348 patients (78%) met the inclusion criteria. The median age was 68 years (interquartile range 60-75 years) and 166 patients (48%) had main-duct IPMN while 182 (52%) had branch-duct IPMN. Low-grade dysplasia was present in 60 patients (17%), 137 (39%) had moderate-grade dysplasia, 76 (22%) had high-grade dysplasia and 75 (22%) had invasive carcinoma. A higher median NLR was associated with invasive carcinoma as compared to dysplasia (3.00 vs 2.68, p=0.039). Comparison between those with high-grade dysplasia and those with less than high-grade dysplasia showed no difference (2.80 vs 2.43, p=0.10). Conclusion: In the current study, the median NLR was significantly higher in patients with IPMN-associated invasive carcinoma as compared to patients with non-invasive disease. We did not find NLR helpful in identification of the grade of dysplasia between those patients with non-invasive disease.

PT150

Use of Quantitative Image Analysis and Cyst Fluid Inflammatory Markers to Predict Risk in Intraductal Papillary Mucinous Neoplasms S.A. Lawrence,[1]* J. Chakraborty,[1] M. Al Efishat,[2] M. Attiyeh,[1] G. Askan,[1] Y. Chou,[1] A. Pulvirenti,[1] C.A. McIntyre,[1] M. Gonen,[1] O. Basturk,[1] V. Balachandran,[1] P. Kingham,[1] M. D'Angelica,[1] W. Jarnagin,[1] J. Drebin,[1] R.K. Do,[1] A.L. Simpson,[1] P. Allen.[1] *1. Surgery, Memorial Sloan Kettering Cancer Center, New York, NY; 2. Johns Hopkins Hospital, Baltimore, MD.*

Introduction: Intraductal papillary mucinous neoplasms (IPMNs) represent cystic precursor lesions of pancreatic cancer with varying levels of risk for progressing to malignancy based on degree of dysplasia. We sought to combine existing tools for identifying lesions with the highest risk of progression into one prediction model that can identify high-risk IPMNs. Methods: An institutional database was queried for patients with resected branch duct or mixed type IPMN, cyst fluid available for analysis, and high quality preoperative abdominal CT scans. A previously described predictive nomogram combining clinical features with cyst fluid inflammatory marker (CFIM) analysis was applied to patient data. CT scans were analyzed to extract quantitative imaging (QI) features describing variations in CT enhancement patterns known to be predictive of grade of dysplasia in IPMN and previously validated in a larger cohort. The nomogram predictive score and QI model risk score were than combined to build a predictive model. Results: Thirty-three patients were included in the final analysis, with 21% (n=7) classified as high-risk based on degree of dysplasia, and the remaining 79% (n=26) classified as low-risk. The cohort was 55% male (n=18), and median age at operation was 72 years (IQR 63-76). Worrisome radiographic features were present in 52% of patients (n=17). Combination of the clinical nomogram with CFIMs was predictive of high-risk lesions, with an area under the receiver operating characteristic curve (AUC) of 0.74. The addition of QI features further improved the predictive value of the preoperative model, yielding an AUC of 0.88. Conclusion: Quantitative imaging combined with clinical features and CFIMs may be developed to reliably predict which IPMNs are high-risk. Although further validation with a larger cohort is needed, this model may represent a highly accurate tool for preoperative patient assessment.



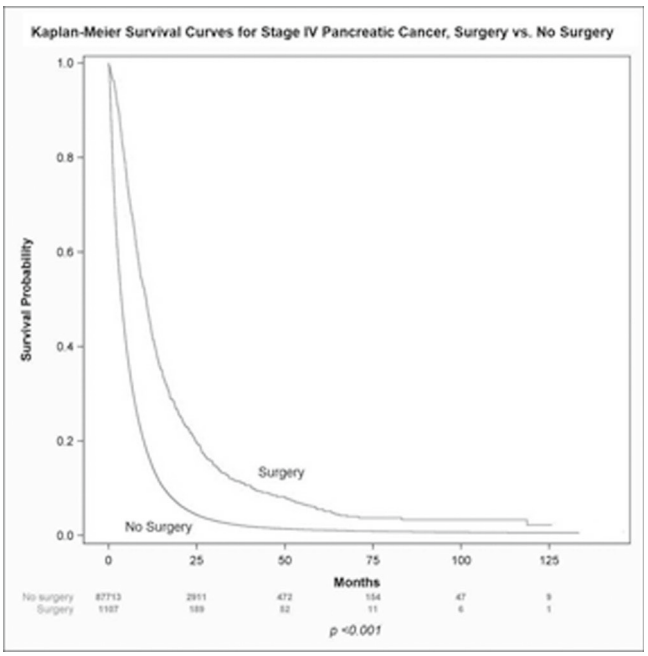
Model/Predictors	AUC
CFIM Nomogram	0.74
QI model	0.83
QI +CFIM Nomogram	0.88

Figure 1 - Top: Receiver operating characteristic (ROC) curves for various predictors of risk. Bottom: Area under ROC curve (AUC) for each predictor.

PT151

Surgical Resection in Stage IV Pancreatic Cancer: Analysis of the 2004-2014 National Cancer Data Base K.M. Turner,[2]* C.J. Joyce,[2] A.R. Dhanarajan,[2] J.L. Gnerlich.[1] *1. LSU Health Sciences Center, New Orleans, LA; 2. Loyola University Medical Center, Maywood, IL.*

Introduction: Pancreatic resection is not considered an option for management of Stage IV pancreatic cancer. Our aim is to determine if there is a survival advantage with surgical resection of the primary tumor in a large subset of patients with metastatic disease. Methods: We conducted a retrospective study of Stage IV pancreatic adenocarcinoma patients using the 2004-2014 National Cancer Data Base (NCDB) to compare patients who underwent surgical resection with patients who did not. The odds of surgery by patient characteristics were assessed for statistical significance in univariable generalized linear mixed effects models. Median survival time was calculated using the Kaplan-Meier method. Univariable and multivariable frailty survival models were used to determine hazard ratios for mortality. Results: Of the 100,877 NCDB patients with Stage IV pancreatic adenocarcinoma, 1,235 (1.2%) underwent pancreatic surgery and 99,642 (98.8%) did not receive surgery. Overall, 36.2% of patients received chemotherapy as first course therapy, 39.5% surgery group vs. 36.2% no surgery group (p=0.015). Patients who were younger, married, had private insurance or managed care, were treated at academic or research program facilities, had smaller tumors (<4cm), pancreatic head tumors, received single/multiagent chemotherapy as first course therapy, and those who received radiation were significantly more likely to undergo surgery (p<0.05 for each). On univariable modeling, single agent chemotherapy (HR: 0.75, 95% CI: 0.74-0.76), multiagent chemotherapy (HR: 0.53, 95% CI: 0.52-0.54), and surgery (HR: 0.48, 95% CI: 0.45-0.51) conferred a survival advantage. Median survival was longer for those who underwent surgery compared with those who did not undergo surgery (10.6 vs. 3.6 months, p<0.001). After adjustment for confounding variables, surgery was associated with improved survival (aHR: 0.48, 95% CI: 0.44-0.51). Conclusions: Analysis of the 2004-2014 NCDB data suggests that a subset of patients with Stage IV pancreatic cancer are undergoing surgery with improved survival. Future studies are needed to determine which patients with metastatic disease will benefit from resection.

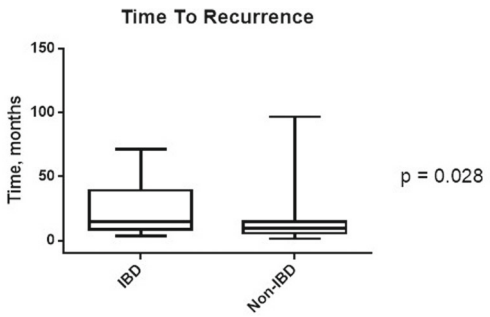


Kaplan-Meier curves showing overall survival in Stage IV pancreatic cancer for patients who underwent surgery compared with those who did not undergo surgery.

PT152

Prognosis of Inflammatory Bowel Disease–Related Colorectal Cancer Liver Metastases: A Propensity Score Matching Analysis G. Margonis,[1]* S. Buettner,[1] N. Andreatos,[1] S. Kazunari,[2] D. Wagner,[3] A. Ejaz,[1] J. Wang,[1] A. Deshwar,[1] G. Karagkounis,[2] A. Beer,[4] C. Damaskos,[5] M. Samaha,[1] J. He,[1] E. Antoniou,[5] T.M. Pawlik,[6] K. Kaczirek,[4] K. Hoffmann,[7] H. Mischinger,[3] J.L. Cameron,[1] F. Aucejo,[2] C.L. Wolfgang,[1] M. Weiss.[1] *1. Department of Surgery, Johns Hopkins University, School of Medicine, Baltimore, MD; 2. Department of General Surgery, Digestive Disease Institute, Cleveland Clinic, Cleveland, OH; 3. Department of General Surgery, Medical University of Graz, Graz, Austria; 4. Department of General Surgery, Medical University of Vienna, Vienna, Austria; 5. Second Department of Propaedeutic Surgery, Athens University Medical School, Athens, Greece; 6. Department of Surgery, The Ohio State University Wexner Medical Center, Columbus, OH; 7. Department of General, Visceral and Transplantation Surgery, University of Heidelberg, Heidelberg, Germany.*

Introduction: Inflammatory bowel disease (IBD)-related colorectal cancer (CRC) is characterized by distinct pathophysiology and clinical features compared to sporadic CRC. However, IBD-related colorectal cancer liver metastases (CRLM) have not been studied to date. We aimed to compare the baseline characteristics and outcomes of patients undergoing surgery for sporadic and IBD-related CRLM. Methods: Patients that underwent resection for IBD-related and sporadic CRLM (from 01/01/2000 to 12/31/2015) were identified from an international registry and matched for pertinent prognostic variables. The following outcomes were subsequently assessed: overall survival (OS), recurrence rate and time to recurrence (TTR). TTR was defined as the time from liver surgery to recurrence. Results: 25 patients had IBD-related CRLM (Crohn's disease: 14, Ulcerative Colitis: 11); they had a larger percentage of concurrent extrahepatic disease than patients with sporadic CRLM (32.0% vs. 8.0%; P < 0.001). The 25 patients with IBD–related CRLM were matched to 100 patients with sporadic CRLM according to age, gender, T stage, primary lymph node metastasis, primary tumor site, pre-hepatectomy chemotherapy, carcinoembryonic antigen level, tumor size, tumor number, KRAS mutational status, presence of extrahepatic disease, synchronous CRLM presentation and rate of R0 resection. After matching, no significant difference between the two groups existed for these variables. No significant difference in median OS and recurrence rate between the two groups was noted (51.6 months vs. 52.7 months; P = 0.609 and 68.0% vs 53.5%; P = 0.192). Interestingly, TTR was significantly longer among patients with IBD-related CRLM (14.6 IQR:8.4-39.1 vs 9.0 IQR:4.7-14.2; P = 0.028)(Figure). Conclusion: Patients with IBD-related CRLM had a longer time to recurrence, but similar survival compared to patients with sporadic CRLM. This suggests that IBD-related tumors might indeed have distinct biology and merit further study.



Median, months	14.6	9.0
IQR	8.4-39.1	4.7-14.2

PT153

Impact of Extra-Pancreatic Cysts on Risk of Pancreatic Cancer
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Introduction: Advancements in abdominal imaging have increased the detection of pancreatic cysts among adults. The impact of concurrent liver, kidney, or ovarian cysts on the risk of pancreatic cancer (PC) in these patients is unclear. We sought to define the risk of PC in patients with pancreatic cysts, with and without additional extra-pancreatic abdominal cysts. Methods: Abdominal CT/MRI records from 1996-2012 containing the keyword "cyst" in adult patients were compiled. Natural language processing stratified patients with cysts in the pancreas, liver, kidney, ovary, or in any combination. Cancer outcomes were identified by linkage with the California Cancer Registry (CCR). Age and sex adjusted multivariable logistic regression models were used to compute odds ratios (OR) as estimates of relative risk of PC. A multinomial logit model (OR_m; 95%CI) with outcome defined as no cancer (per CCR), non-pancreatic cancer, or PC was used when analyzing the cohort. Results: Of 15,000 patients identified, 3,315 patients had >=1 pancreatic cyst, 8,430 had extra-pancreatic cysts and 1,750 patients had a pancreatic cyst plus an extra-pancreatic cyst. Among those who developed cancer (n=4,535), patients with pancreatic cysts alone (OR=2.40, p=<0.0001) and those with an additional cyst (OR=1.52, p=0.0008), were more likely to develop PC compared to patients who only had an extra-pancreatic cyst. In the total cohort, cysts in the pancreas and kidney were independently associated with risk of PC. Specifically, risk of PC was more likely in those with pancreatic cysts (OR_m=1.72; 1.44-2.06) and less likely in those with renal cysts (OR_m=0.74; 0.62-0.87) compared with other cancers. In women, the association of ovarian cysts to PC was similar (OR_m=0.57; 0.32-1.03). Interestingly, compared to patients with pancreatic cysts alone, patients with pancreatic and abdominal cysts were ~40% less likely to be diagnosed with PC compared with other cancers (OR_m=0.63, p=0.0025). Conclusion: Patients with pancreatic cysts and additional abdominal cysts were less likely to have pancreatic cancer than other cancers. Prospective acquisition of data is needed to stratify the complexity of risks in patients with pancreatic cysts.

PT154

Neoadjuvant Treatment in Resectable Pancreatic Cancer: A Double-edged Sword?
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Background: Resectability criteria guide treatment decisions in pancreatic cancer (PC). While neoadjuvant treatment (NAT) is gaining acceptance as a treatment approach for early stage PC, its role in resectable patients remains unclear. Methods: Patients at our institution with non-metastatic PC from 2013 to 2016 were analyzed from a retrospective database. Tumor imaging was classified as resectable (R), borderline resectable (BR) or unresectable (UR) per AHPBA criteria. Patients receiving NAT were reassessed after treatment completion. Progression and response were defined as changes in resectability status. Results: 156 patients met inclusion criteria. 55% (n=85) underwent upfront surgery, while 45% (n=71) received NAT. In the NAT cohort, 25% (n=18), 44% (n=31) and 31% (n=22) were classified as R, BR and UR, respectively. In the R group, 78% (n=14) had stable disease at NAT completion; of these, only 1 patient experienced morbidity from NAT and was unable to undergo resection. Among BR patients, 23% (n=7) responded and 45% (n=14) demonstrated stable disease; resection was performed in 71% (n=15) of cases from these two subgroups. Progression after NAT occurred in 4 patients in R group and 10 in BR (20% combined); progression was local in 36% (n=5) and distant metastases were found in 64% (n=9). Interestingly, 14% (n=3) UR patients were able to undergo resection, of which 2 achieved an R0 resection. Overall, patients receiving NAT when compared to upfront surgery had more advanced pTNM stages (p=0.027) and underwent more vascular reconstructions (p=0.008); despite this, R0 resections were higher (p=0.039) in this group. Lymphovascular invasion (p=0.032) was also less frequent in NAT patients. Conclusions: Better surgical outcomes were observed in patients receiving NAT. Among the minority of R patients who received NAT and progressed, most developed distant metastasis in a short time interval and would likely not have benefitted from upfront surgery. Only a small percentage of patients progressed locally and were no longer deemed resectable. Our data suggests that NAT may provide clinical benefit in resectable PC patients.

Tumor response based on resectability criteria for non-metastatic PC patients.

n (%)	Total - 71	Resectable - 18 (25)	Borderline - 31 (44)	Unresectable -22 (31)
CTx Response*				
Progress	14 (19.7)	4 (22.2)	10 (32.2)	N/A
Stable	46 (64.8)	14 (78.0)	14 (45.2)	18 (81.8)
Respond	11 (15.5)	N/A	7 (22.6)	4 (18.2)
Surgery				
Total	31 (43.7)	13 (72.2)	15 (48.3)	3 (13.6)
R0 Resection	26 (83.9)	10 (76.9)	14 (93.3)	2 (66.6)

*Progression or response are defined as changes in resectability status

PT155

Pattern of Pathologic Response to Total Neoadjuvant Therapy in Distal Pancreatic Cancer
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Introduction: Several markers have been evaluated for pathologic response to neoadjuvant therapy of different types of cancers, such as necrosis and inflammatory reaction. In this case, we are interested in the different patterns of fibrosis response to neoadjuvant therapies versus surgery upfront. We hypothesize that total neoadjuvant therapy (TNT) could show superior regression compared to other therapies. In this pilot study, we report our experience with total neoadjuvant therapy in cancers of the body and the tail of the pancreas. We define total TNT as induction chemotherapy (Gemcitabine, FOLFOX or FOLFIRINOX), followed by chemoradiation. Methods: We conducted a retrospective chart review of the 54 patients who underwent a distal pancreatectomy in our tertiary care institution between 2000 and 2016. One patient was excluded due to loss to follow-up. Clinical and pathological information was reviewed, and fibrosis patterns and time to recurrence were examined and compared using chi-square and Anova tests. Results: 28 of the 53 patients (53.7%) underwent surgery first, and 25 (46.2%) had neoadjuvant treatment (NAT). Of the patients who received neoadjuvant treatment, 14 received TNT, 6 had neoadjuvant chemoradiation (CRT) and 5 had neoadjuvant chemotherapy (NAC) only. 100% of the TNT patients had a R0 resection, 89.3% with surgery first, 83.3% with CRT and 80% with NAC (p=.469). Fibrosis was seen in 0% of the surgery first and 68% with NAT (p<0.001). 78.8% of the TNT patients had fibrosis seen on pathology, 66.7% with CRT and 40% with chemotherapy alone (p=0.283). Fibrosis to tumor ratio was documented in 12 patients. The mean percentage of fibrosis was 86.0% with TNT, 79.8% with CRT and 61.5% with chemotherapy (p=0.260). The only 2 pathologic complete responses (pCR) were in the TNT group. Both showed fibrosis and the patients have not experienced recurrence. Conclusion: Fibrosis could be an important marker of response to neoadjuvant treatment in tumors of the body and tail of the pancreas. These preliminary results will guide future investigations to determine which patients would most benefit from TNT.

PT156

Pre- and Post-Operative Ki-67 and Tumor Grade in Patients with Primary Neuroendocrine Tumor: An Analysis of the U.S. Neuroendocrine Tumor Study Group
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Background: Gastroenteropancreatic neuroendocrine tumors (GEP-NET) comprise a heterogeneous group of tumors with variable prognosis. Ki-67 labeling index (Ki67) and tumor grade help stratify patient prognosis. We sought to compare preoperative Ki67 and tumor grade versus final pathological values and examine their ability to predict disease-free survival (DFS).

Methods: Using a multi-institutional database, data on pre- and post-operative values of Ki67 and/or tumor grade were compared for patients with primary non-metastatic GEP-NET. Concordance between preoperative and final pathological Ki67/tumor grade were compared using Kendall's tau coefficient; the ability of pre- versus postoperative Ki67 and tumor grade to predict DFS was assessed using the Harrel c-index. Results: 172 patients had pre- and post-operative Ki67 and tumor grade available. 5- and 10-year DFS were 80% and 67%, respectively. Preoperatively, 148 (87%) underwent fine needle aspiration (FNA), 15 (9%) core needle biopsy (CNB), and 8 (4%) both FNA and CNB. The distributions of preoperative and postoperative Ki67 and tumor grade are demonstrated in Table 1. When preoperative Ki67 was <3%, no patients had a Ki67 >20% on final pathology. There was moderate agreement between pre- and postoperative Ki67 values (Kendall tau, 0.41) and pre- and postoperative tumor grade (Kendall tau, 0.37). Sensitivity analyses including only patients with FNA and again including only CNB confirmed the moderate association between pre- and post-operative values of Ki67 and tumor grade. In examining disease-free survival, c-indexes for the preoperative Ki67 value and tumor grade were 0.571 and 0.533, compared with 0.771 and 0.759 for postoperative Ki67 and tumor grade. Conclusion: There was only moderate agreement between pre- and postoperative Ki67 and tumor grade. While preoperative Ki67 and tumor grade demonstrated a poor ability to predict patients' prognosis, postoperative Ki67 and tumor grade demonstrated a moderate to strong ability to predict patients' prognosis.

Table 1 - Pre- and Post-operative Ki-67 and Tumor Grade

Ki-67				Grade			
Preoperative Ki-67		Postoperative Ki-67		Preoperative Grade		Postoperative Grade	
<3%	110 (73%)	<3%	85 (77%)	G1	132 (77%)	G1	96 (73%)
		3-20%	25 (23%)			G2	35 (26%)
		>20%	0 (0%)			G3	1 (1%)
3-20%	39 (26%)	<3%	13 (33%)	G2	36 (21%)	G1	11 (31%)
		3-20%	24 (62%)			G2	22 (61%)
		>20%	2 (5%)			G3	4 (8%)
>20%	2 (1%)	<3%	1 (50%)	G3	4 (2%)	G1	2 (50%)
		3-20%	0 (0%)			G2	0 (0%)
		>20%	1 (50%)			G3	2 (50%)

PT157

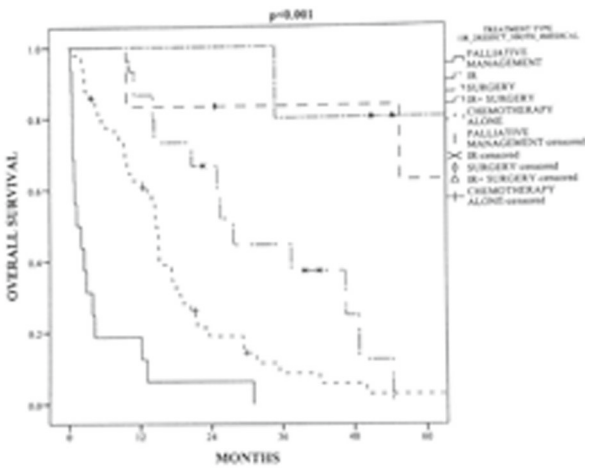
Adjuvant Radiation Improves Survival for Extra-Hepatic Cholangiocarcinoma C. Takahashi,[2]* R. Shridhar,[3] J. Huston,[1] K. Meredith.[1] *1. Gastrointestinal Oncology, Florida State University/ Sarasota Memorial Hospital, Sarasota, FL; 2. Midwestern University, Phoenix, AZ; 3. University of Central Florida, Orlando, FL.*

Purpose: Extra-hepatic cholangiocarcinomas(EHC) are low-incidence cancers that are difficult to diagnose and associated with a dismal prognosis. Surgery remains the only option for durable survival however R1 resections are high. We sought to examine the impact of adjuvant therapies on survival in patients with EHC. Methods: Utilizing the National Cancer Database we identified patients who underwent resection for EHC. We then stratified by adjuvant therapy chemo(AC) or chemoradiation(CRT). Baseline comparisons were made using Mann-Whitney U, Kruskal Wallis and Pearson's Chi-square test as appropriate. Survival analyses were performed using the Kaplan-Meier method. Multivariable cox proportional hazard models (MVA) were developed to identify predictors of survival. All statistical tests were two-sided and α <0.05 was considered significant. Results: We identified 4334 patients who underwent EHC resection: AC=775, CRT=1254, no adjuvant (NA) therapy=2305 and a median age of 67 (18-90) years. R0 resections was performed in 71.6% of patients and the median LN harvest was 9 (3-18). R0 resections and lymph node negative patients demonstrate improved survival p<0.001 and p<0.001. Adjuvant therapy did not improve survival in R0 resections, p=0.2. However survival was benefited in R1 patients, with those receiving CRT demonstrating the most significant improvement: median and overall 5-year survival AC=16.7 months 8%, CRT=23.1 months, 20.4%, and NA=16.1 months and 11.6% p<0.001. In LN- patients CRT (47.3 months, 47%) but not AC (45 months, 44.5%) demonstrated benefit in survival compared to NA (37.8 months, 40.1) p=0.04 and p=0.7. Additionally, patients with LN+ and R1 resection had survival benefit when treated with (CRT 24.9 months and 24.3%), compared to NA (20.2 and 21.1%), p=0.02. AC (24 months and 24%) did not demonstrate survival in these patients, p=0.21. MVA demonstrated that age, T-stage, LN+, R0 resection and CRT were predictors of survival. Conclusions: Adjuvant CRT improves survival for patients with EHC who underwent R1 resections, and in LN- and LN+ patients. However, AC only benefited LN+ patients with R0 resections. Patients with resected EHC should be referred for adjuvant CRT.

PT158

Optimal Management of Soft Tissue Sarcoma Liver Metastasis (STS LM) D.K. DePeralta,* R. Gonzalez, B. Kis, A. Naghavi, G. El-Haddad, A. Brohl, M. Druta. *Surgical Oncology, Moffitt Cancer Center, Boston, MA.*

Introduction: The estimated rate of STS LM is 25-40%. Optimal management of this heterogeneous population is unclear, and a comprehensive evaluation of outcomes has not been reported. We examined our institutional experience with a focus on long-term outcomes and evolving locoregional and surgical strategies for disease control. Methods: An IRB approved, single-institution retrospective review of patients with STS LM from 1/1999 to 8/2016 was conducted. Patients with gastrointestinal stromal tumor were excluded. Clinical-pathological factors, treatment approach, and follow-up data were collected. Outcomes including time to hepatic progression, progression free survival (PFS), and overall survival (OS) were estimated via Kaplan-Meier and compared via log-rank. Results: 92 patients were identified with STS LM. 11 underwent metastasectomy and 20 underwent locoregional therapy (10 transarterial chemoembolization, 5 radiofrequency ablation, 3 radioembolization, 1 bland embolization, 1 percutaneous hepatic perfusion.) 5 patients underwent combination locoregional therapy and resection. The majority of patients were treated with systemic therapy (n=72, 78.3%). Among the 26 patients that underwent surgery and/or locoregional therapy 88.5% also received chemoherapy (n=23). 25% of patients (n=23) in the series had no evidence of extrahepatic metastasis. In the medically managed group 15.2% (n=10) had solitary, liver metastasis and 84.6% (n=55) had multifocal liver metastases. In the interventionally managed group 53.8% (n=14) had unifocal metastasis and 46.2% (n=12) had multifocal disease. After median-follow-up of 14 mos (range 0-182), 2-year OS for all patients with STS liver metastases was 33.9% and PFS was 21.3%. (Median OS=14.8 months, PFS=6.7 months). By treatment approach, 2-yr OS and PFS were as follows: palliative management/ no chemotherapy OS 6.3%, PFS 0%; chemotherapy alone OS 18.9%, PFS 8.9%; non-surgical locoregional OS 66.7%, PFS 54.9%; Surgical resection OS 83.3%, PFS 66.7%; locoregional therapy+surgical resection OS 100%, PFS 80%. Conclusion: Long-term survival and control of hepatic tumor burden is possible in select patients with STS LM. A multimodal approach to care is recommended.



Kaplan-Meier curves of overall survival. From left to right: palliative management/ hospice, chemotherapy alone, locoregional therapy alone, surgical resection alone, surgical resection combined with locoregional therapy.

PT159

Impact of Postoperative Complications on Return to Intended Oncologic Treatment and Survival in Patients Undergoing Resection for Rectal Cancer with Synchronous Liver Metastases

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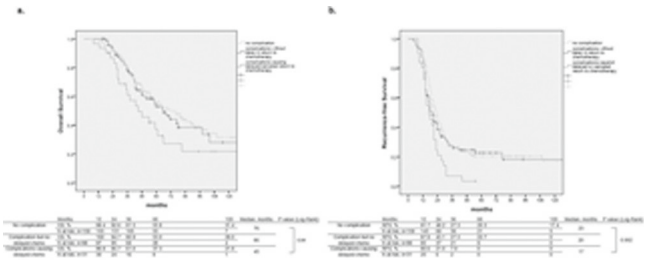
Background Patients undergoing multimodality treatment for rectal cancer with synchronous liver metastases (RCSLM) may experience delay in or cancelation of return-to-intended-oncologic-treatment (RIOT) due to complications of rectal or liver surgery. The causes and impact on survival of delayed or cancelled RIOT (dcRIOT) in this cohort have not been analyzed. Methods Institutional database was searched for patients who underwent oncologic resection for RCSLM with planned RIOT between 2000-2014. Reasons for dcRIOT, effect of dcRIOT on survival and the impact of postoperative complications on dcRIOT-risk were investigated using Log-Rank test and logistic-regression models. Results Of 287 patients, 64 (22%) had delayed (n=52) or canceled (n=12) RIOT after rectal or liver surgery. DcRIOT due to postoperative complications occurred in 31 patients (48%) and was associated with worse survival (median OS, 45 vs 65 months, p=0.04; median RFS, 17 vs 21 months, p=0.009). DcRIOT due to complications was an independent predictor of worse OS (OR=1.75, p=0.026) and RFS (OR=1.8, p=0.004). Patients with postoperative complications but RIOT<90days had similar survival to patients with no complications (median OS, 66 and 76 months, p=0.7; median RFS, 20 and 23 months, p=0.4). Among the 31 patients with complication-related dcRIOT were rectal-surgery-related complications in 19 (61%) and liver-surgery-related complications in 10 (32%) (p=0.001). Conclusion In patients undergoing oncologic resection for RCSLM, delay >90 days or cancellation of RIOT due to postoperative complications significantly impairs survival. The higher complication rate of rectal vs. liver surgery leading to delay or cancellation of RIOT necessitates thoughtful treatment sequencing to achieve optimal outcome.



Overall (a) and recurrence-free survival (b) according to postoperative complications and their impact on return to intended oncologic treatment (RIOT) in 287 patients undergoing surgical resection for rectal primary and synchronous LM.

PT160

Ratio of Cytotoxic to Regulatory T Lymphocytes Predicts Survival in Pancreas Cancer

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Introduction: It is well established that patients with pancreas cancer have higher levels of circulating and tumor infiltrating T-regulatory cells though impact on oncologic outcomes has not been determined. We sought to quantify immune cell subsets and interactions utilizing an 8 color in-situ immunophenotyping assay. Methods: Formalin fixed paraffin embedded tissue was prepared from 36 patients with resected pancreas cancer. Immunophenotyping was performed using the OPAL staining platform (Perkin Elmer) and images analyzed using InForm software. Serial staining was performed using antibodies to CD3, CD4, CD8, FoxP3, CD163, Pancytokeratin and PDL1. Associations between immune cell subsets, tumor pathology and survival were determined. Results: Of the 36 patients analyzed, 8 were alive with a median follow-up of 24 months. A majority of patients were stage 3 (60%) and 66% had positive lymph nodes. The mean tumor size was 2.8cm. The mean T-cell infiltration was 6.4% with cytotoxic T-cells and T-regulatory cells comprising 4.5% and 1%, respectively. The mean cytotoxic/regulatory T-cell ratio was 0.27 (0.02-0.51). On univariate analysis, predictors of survival included node status, stage and cytotoxic/regulatory T-cell ratio. On multivariate regression, only cytotoxic/regulatory T-cell ratio remained significant (OR 1.19, p=0.05). Conclusion: In-situ multiplex immunophenotyping allows for a more detailed analysis of the tumor microenvironment with the opportunity to examining multiple cell types in a single section. We present an example of its power demonstrating impact of two immune cell types on oncologic outcome.

PT161

Preoperative Prognostic Nutritional Index Predicts Survival of Patients With Intrahepatic Cholangiocarcinoma After Curative Resection

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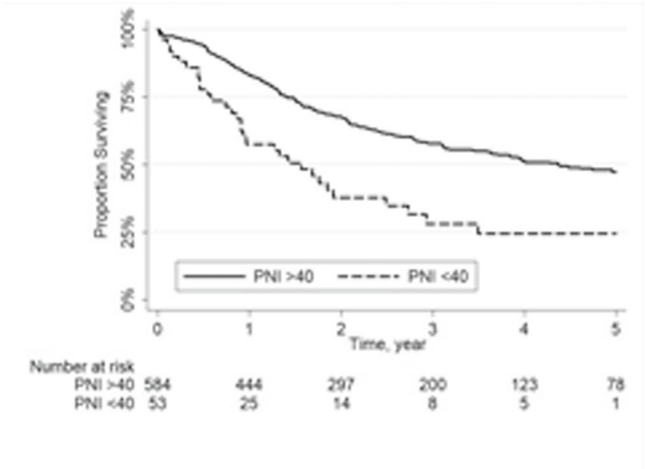
Background: Prognostic nutritional index (PNI) may be associated with long-term outcomes of cancer patients. The impact of PNI on the prognosis of patients with intrahepatic cholangiocarcinoma (ICC) has not been investigated. We sought to analyze the prognostic role of PNI among ICC patients undergoing curative intent liver resection. Methods: Patients who underwent hepatectomy for ICC between 1990-2015 who had available preoperative data on absolute lymphocyte count and serum albumin level were identified using an international database. PNI was calculated as 10×serum albumin (g/dL)+0.5%×total lymphocyte number (per mm^3). Patients were stratified by the previously established PNI threshold of 40 and outcomes were assessed using univariable and multivariable analyses. Results: Among 637 patients who underwent resection of ICC, the median preoperative albumin level was 4.1 g/dl and the median lymphocyte number was 1,614 per mm^3. In turn, 584 (92%) patients had PNI≥40 versus 53 (8%) who had PNI<40. Patients with PNI<40 were more likely to be older (median age, PNI<40: 64 yrs vs. PNI≥40: 57 yrs) and be ASA class 3-4 (PNI<40: 60% vs. PNI≥40: 27%)(both p<0.001). In addition, patients with PNI<40 patients also had more advanced disease (T2/T3/T4: PNI<40: 71% vs. PNI≥45: 13%)(p<0.001). Patients with PNI<40 also more often had multifocal disease (PNI<40: 30% vs. PNI≥40: 11%), moderate-undifferentiated tumor grade (PNI<40: 25% vs. PNI≥40: 13%), and perineural invasion (PNI<40: 32% vs. PNI≥40: 13%)(all p<0.001). Survival was associated with PNI status as 5-year survival among patients with PNI<40 was only 25% compared with 47% for patients with PNI≥40 (p<0.001)(Figure). On multivariable analysis, after controlling for T-category and nodal status, PNI<40 remained associated with an almost 2-fold higher hazard of death (HR 1.91, p=0.001). Conclusion: Among patients undergoing curative-intent resection of ICC, preoperative PNI was associated with adverse pathological features. In addition, preoperative PNI was an independent predictor of long-term prognosis of survival following resection.



PT162

Pathologic Complete Response after Total Neoadjuvant Therapy

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Introduction There is increasing interest in the role of total neoadjuvant therapy (TNT) for patients with pancreatic cancer. This entails systemic chemotherapy followed by chemoradiotherapy, and as long as their disease remains localized, then definitive surgery. The perceived benefits are that all patients receive multimodality therapy and the potential down staging for curative resection. The objective of this study is to evaluate overall survival (OS) in those with a pathologic complete response (pCR) after TNT. Methods This is a retrospective study of 66 TNT patients at our institution from 2000-2015 and then underwent definitive resection with a pancreatoduodenectomy or a total pancreatectomy for pancreatic adenocarcinoma. Clinical and pathological information was reviewed. Results The analytic cohort consisted of 10 patients (15%) who had a pCR. The analytic cohort was 60% female. Median age at surgery was 68 years (range 37-91). Five of these patients had locally advanced disease and two required an arterial or venous reconstruction at the time of surgery. Five were initially borderline resectable. The final pathology reports described three patients as having acellular mucin, one had no residual carcinoma, one had no viable tumor and necrotic debris, two had no residual carcinoma and several foci of pancreatic intraepithelial neoplasia, grade 2 (PanIN-2), two patient had residual multifocal IPMN with severe or high grade dysplasia but no invasive carcinoma, and one patient had acellular mucin with a fibrosis to cancer score of 100%. All patients completed TNT, however the treatment regimens varied from systemic therapy with gemcitabine alone, gemcitabine/nab-paclitaxel, or FOLFIRNINOX, along with capecitabene and/or bevacizumab with SBRT. The average initial CA19-9 pre-TNT was 221 and 25 post-TNT. Five-year OS is 89%. One patient died in the immediate postoperative period from sepsis and the other patient died from recurrence in the pancreatic body after a 6.5 year disease-free survival. Conclusion This is one of the largest studies to describe pCR after TNT in pancreatic adenocarcinoma. These results are promising and support the use of TNT and analyzing individual tumor response.

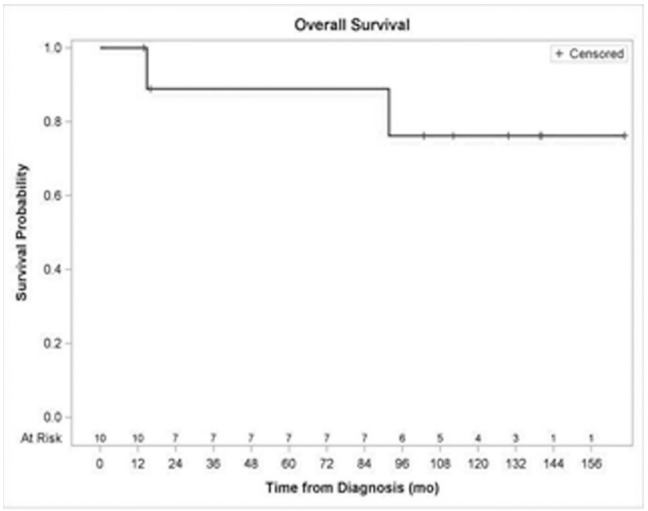

Figure 1: Kaplan-Meier Survival Curve in Patients with a Complete Pathologic Response after Total Neoadjuvant Therapy

PT163

Mice with Targeted Kras G12D and p53 Loss in the Liver: A Model for Studying Immunologic Interventions for Treating Cholangiocarcinoma

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Background Cholangiocarcinoma (CCA) is the most common liver malignancy within the biliary tree with few treatment options and a poor 5-year survival. CCA often develops following a liver insult and is characterized by a highly fibrotic stromal compartment inundated by inflammatory immune cells. In this age of cancer immunotherapeutics however, little is known about the immune system's response to CCA. Here we set out to characterize the immune dynamics and signaling pathways contributing to CCA development in order to identify potential targets for immune based therapies. Methods Histology and immunohistochemistry (IHC) were performed on tissue microarrays of 52 CCA specimens in order to identify the prognostic significance of cytokine and immune markers. Liver tumors, bone marrow, and blood were collected from genetically engineered mice that spontaneously develop CCA through Kras activation and p53 loss (Alb-Cre/LSL-KRAS^{G12D} /p53$^{-/-}$). These were used for histological, IHC, and flow cytometry analysis. Additionally, quantitative gene expression was performed through qRT-PCR. Results High levels of inflammatory leukocytes in human CCA were predominantly of monocytic and granulocytic origin including macrophages (TAM) and granulocytic-myeloid derived suppressor cells (G-MDSC), respectively. Malignant cells expressed high levels of CCL2 and TAMs stained positive for its cognate receptor CCR2. Kras-p53 mice developed CCA tumors histologically similar to human disease. There was a predominance of TAMs and G-MDSCs within tumor-burdened tissue when compared to normal littermate controls through flow cytometry (p=<0.001). Additionally, these tumors induced myelopoiesis leading to significantly more monocytes and granulocytes in the bone marrow, blood, and spleen in comparison to littermate controls (p=<0.01, 0.01, and 0.001). Tumors from Kras-p53 mice expressed higher levels of CCL2 and PD-L1 with more CCR2^{+} TAMs and PD-1^{+} T cells. Conclusion The inflammatory process seen in human CCA utilizes immune signaling pathways that are recapitulated in Kras-p53$^{-/-}$ mice providing an ideal model to study immune based therapies for CCA treatment.

PT164

Identification of Pancreatic Cancer Using a Urokinase Plasminogen Activator-Probe Detected via Multispectral Optoacoustic Tomography A. Chiba,[1]* P. Chuong,[2] T. Xiao,[1] c. Velazquez,[1] G. Mishra,[1] L. McNally.[1] *1. Surgical Oncology, Wake Forest Baptist Health, Winston-Salem, NC; 2. University of Louisville, Louisville, KY.*

Background: Current methods of pancreatic cancer screening, diagnosis and treatment have failed to improve outcome significantly. Possible causes stem from the hypovascularized nature of pancreatic cancer, making conventional chemotherapy and imaging suboptimal. A potential solution for improved imaging is through the use of a new imaging such as multispectral optoacoustic tomography (MSOT). We hypothesize that a using urokinase plasminogen activator (uPA) probe in MSOT imaging will improve identification of orthotopic pancreatic cancer in xenografts. Methods: Pancreatic tumor cell lines, Panc1, MiaPaca-2, S2VP10, and S2CP9, were evaluated for uPA receptor (uPAR) expression using western blot. A uPA targeted contrast was constructed using standard bioconjugation methods with the Hilite 750 near infrared (NIR) dye. Finally, SCID mice (5 mice/group) were orthotopically implanted with S2CP9 (1.5×10^5) or MiaPaCa2 (2.0×10^6) pancreatic tumor cells. After tumors reached 3mm, 200μL of 100 nM uPA-750 probe or 750 dye alone was injected into mice. Biodistribution and accumulation of the uPA-750 probe was visualized using MSOT imaged at 2-hour intervals for 8 hours and at 24 hours. UPA-750 probe accumulation in tumor, liver, and kidney was evaluated ex vivo using NIR fluorescent imaging. Results: Each pancreatic cancer cell line expressed uPAR with the highest relative abundance in S2CP9 cells (3.0x), S2VP10 (2.5x), Panc1 (1.77x) and MiaPaca-2 (1.3x). In vivo, uPA-750 probe was successfully detected by MSOT within the pancreas tumor in slices from 37mm-41mm with peak intensity at 4 hrs. By 8 hours, uPA-750 probe was undetectable within the tumor. Using ex vivo NIR fluorescence imaging, uPA-probe signal was detected within the pancreatic tumor, but not the liver or kidney. Conclusion: UPA-probe demonstrates potential as a contrast agent which may be used with MSOT imaging for pancreatic cancer screening, diagnosis and evaluating treatment response.

PT165

Geriatric Pancreatic Cancer Resection: The Impact of Frailty Syndrome and Age M. Khreiss,* M. Khan, M. Hamidi, B. Joseph. *Department of Surgery, University of Arizona, Tucson, AZ.*

Introduction: Frailty is highly prevalent in geriatric population and confers high risk for morbidity and mortality after operative intervention. Aim of study was to assess the impact of frailty on outcomes after pancreatic resection in geriatric pancreatic cancer patients. Methods: An 8-year (2005-12) analysis of NSQIP. Patients undergoing pancreatic resection for pancreatic cancer were analyzed. Patients older than 65 years were included. A modified frailty index (mFI) was defined by the 11 variables within the NSQIP previously used from the Canadian study of health and aging-frailty index. Frail status was defined as mFI≥0.27. Results: 4307 patients were included in the analysis. Mean age was 73.6±5.9 years, 72.9% had radical pancreaticoduodenectomy (PD) while 27.1% had distal pancreatectomy and 9.4% patients were frail. 4.8% patients received neoadjuvant treatment. 16.1% of patients had major complications, 5.2% died, and 24.8% were discharged to Rehab/SNF. Frail patients had higher major complication rate (22% vs. 11.5%, p<0.001), higher mortality rate (6.6% vs. 2.9%, p=0.002), and were more likely to be discharged to Rehab/SNF (41% vs 22%, p<0.001). Frail patients had a longer hospital length of stay (15 days vs. 8 days, p=0.02) and a higher 30-day readmission rate (5% vs. 2.9%, p=0.03) compared to the non-frail. On regression analysis after controlling for age, gender, albumin level, type of surgery, and ASA class, frail status was an independent predictor of major complications, adverse disposition, and 30-d mortality(Table 1). On sub-analysis of frail patients, the adjusted rates of complications were higher in those who underwent PD compared to distal pancreatectomy (OR: 2.9 [1.7-3.8]). Frail patients who received neoadjuvant treatment had higher complications (OR: 2.2 [1.2-4.9]) compared to those who did not. Conclusions: Frailty is associated with higher complications and mortality in geriatric patients undergoing pancreatic surgery for pancreatic cancer. We recommend the use of modified frailty index instead of age alone to guide risk stratification, perioperative optimization, and counseling and while considering treatment options for patients with pancreatic cancer.

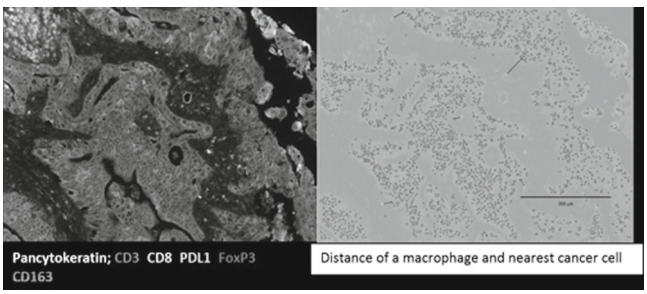
Table 1. Multivariate Regression analysis

Frailty	OR	95%Confidence Interval	*p-value*
Major complications	1.9	1.5-2.7	0.01
Discharge to Rehab/SNF	2.3	1.8-2.9	0.01
30-day mortality	2.2	1.7-2.9	0.01

PT166

Multiplex Fluorescent Immunohistochemistry Allows for Analysis of Spatial Distribution Patterns of Immune Cells in Pancreas Cancer J. Lazarus,* T. Maj, M. Perusina Lanfranca, L. Delrosario, J. Shi, W. Zou, T. Frankel. *Surgery, University of Michigan, Ann Arbor, MI.*

Introduction: Pancreas adenocarcinoma (PDAC) is known for its immunosuppressive environment and poor survival. However, the knowledge of the cell-to-cell interactions within the tumor microenvironment is limited. We used a novel multiplex immunohistochemistry staining system (Opal) with multiplex imaging and trainable cell phenotyping software (InForm) to evaluate the interactions among immune cells and cancer cells in PDAC. Methods: A formalin-fixed paraffin-embedded tissue microarray (TMA) consisting of pancreatic cancer specimens underwent 7 rounds of multiplex fluorescent staining. Each step consisted of primary antibody incubation (pancytokeratin, CD3, FoxP3, CD8, PDL1, CD163, and DAPI), secondary horseradish peroxidase-conjugated polymer, followed by Opal tyramide signal amplification (TSA) which covalently binds to the epitope. After each TSA step antibodies were removed in subsequent antigen retrieval steps eliminating antibody cross reactivity. Multispectral imaging was followed by phenotyping of immune and cancer cells using InForm software. Software was used to analyze the location and distances from all phenotyped cells. Results: Multispectral imaging and subsequent analysis by InForm software allowed for clear cell phenotyping of T-cells, macrophages, T-regulatory cells, and cancer cells. Cells could be further phenotyped for co-localization with PDL1 (immune checkpoint marker). All cell phenotypes were located using X and Y coordinates and its nearest neighboring identified and distance calculated. Conclusion: Multiplex immunohistochemistry used in combination with multispectral imaging and trainable cell phenotyping software has allowed for essential insight into the interactions between immune cells and cancer cells in the tumor microenvironment. This coupled with patient clinical data will give rise to a greater understanding of the immunosuppressive environment and its correlation with patient morbidity and survival.



PT167

Drain After Pancreatic Resection: Friend or Foe? Perioperative Hemorrhage and Infection from ACS NSQIP R. El Khoury,* C. Kabir, V.K. Maker, M. Banulescu, M. Wasserman, A.V. Maker. *Department of Surgery, Advocate Illinois Masonic Medical Center, Chicago, IL.*

INTRODUCTION Controversy remains on drain placement after pancreatic resection. While proponents of drains utilize them to manage the risks of pancreatic fistula, they could present a pathway for retrograde infection. In this study, we aimed to identify perioperative hemorrhage, infection and need for reintervention after pancreatic resection with versus without drain placement. METHODS Patient characteristics, perioperative and outcomes data were obtained from the ACS NSQIP database. Fisher's exact test was performed using a p<0.05 for statistical significance. RESULTS 5013 pancre-

atic resections were reviewed with 87% receiving drains. The majority of surgeries were proximal while 33% were distal pancreatectomies. Surgical site infection was more likely after distal pancreatectomy with a drain vs. without (4.2% vs. 1.2%, p=0.038) while an opposite trend was identified after pancreatoduodenectomy (8.7% vs. 11.5%, p=0.089). Deep, organ/space infections and reintervention for infectious complications (p=0.68) did not differ with vs. without drains. Sepsis (6.6% vs. 5.2%, p=0.20) and septic shock (2.8% vs. 3.4%, p=0.39) were uncommon. Wound disruption (1.2% vs. 1.6%) and incisional hernia (0.2% vs. 0.1%) were rare and carried equivalent need for reoperation (0.6% vs. 0.4%, p=0.79). While patients with a drain underwent more vascular resections (p=0.022), re-exploration for postoperative hemorrhage was not different (p=0.68). Mortality was significantly higher among patients without drains (1.2% vs. 2.8%, p<0.01). CONCLUSION While little difference in infectious and hemorrhagic complication rates was found between patients with and without a drain, perioperative mortality was higher in the no drain group. There is an ongoing need for refined criteria for drain placement.

PT168

Impact of Tumor Location and Extent of Hepatic Resection on Survival Rates in Patients with T2 Gallbladder Carcinoma
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BACKGROUND: National guidelines recommend en-bloc hepatectomy and lymphadenectomy for gallbladder cancer (GBC) greater than T1b. However, controversies remain regarding the relationship between the location of the tumor, peritoneal-sided (PS) and hepatic-sided (HS), on extent of resection and survival for T2 GBC. METHODS: National Cancer Database (NCDB) was queried for patients with T2 disease who underwent resection for GBC from 2004 to 2014. Kaplan-Meier log-rank analyses assessed the impact of hepatic resection on survival rates. Multivariable Cox regression analyses were performed to investigate the factors affecting survival based on location of the tumor. RESULTS: Of the 11,532 patients identified with GBC, 618 subjects with T2 tumors were included. Among them, 198 (32.1%) were PS and 420 (67.9%) were HS tumors. Factors negatively affecting survival in HS tumors were high grade (p <0.001, HR 5.519), N1 stage (p=0.007, HR 1.366), absence of liver resection (p=0.002, HR 1.686), comorbidity status (p=0.045, HR 1.578), and presence of lymphovascular invasion (p=0.018, HR1.340). In PS tumors, factors negatively affecting survival were advanced age (p=0.009, HR 1.027), comorbidity status (p=0.049, HR 1.882) and N1 stage (p=0.014, HR 1.962). There was a trend towards improved survival rates of PS tumors undergoing hepatectomy, however, it did not reach statistical difference (p=0.057, HR 1.840) CONCLUSION: Hepatectomy and lymphadenectomy result in improved outcomes in hepatic-sided GBC, however its benefits on survival in PS tumors are equivocal. In PS tumors, radical cholecystectomy with lymphadenectomy without liver resection may be an acceptable option, especially in elderly patients or those unfit for major liver resections.

PT169

Current Practice Patterns in the Surgical Management of Gallbladder Carcinoma
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BACKGROUND: National guidelines recommend en-bloc hepatectomy and lymphadenectomy for stage IB and higher gallbladder cancer (GBC). Compliance with these guidelines has been poor and the data is mostly outdated. We sought to reassess the current national trends and evaluate whether there has been an improvement in practice patterns in the treatment of T2 GBC. METHODS: National Cancer Database (NCDB) was queried for patients with T2 disease who underwent resection for GBC from 2004 to 2014. Kaplan-Meier log-rank analyses assessed the impact of hepatic resection on survival rates. RESULTS: Of the 11,532 patients identified with GBC, 618 subjects with T2 tumors were included. Overall median survival was 32.7 months. Patients undergoing hepatectomy had improved survival (51.7 vs. 25.3 months, p<0.001). However, only 230 patients (37.2%) underwent hepatectomy, 24.7% for peritoneal-sided (PS) tumors and 43.1% for hepatic-sided (HS) tumors. Portal lymphadenectomy was performed in only 50.1% (56.6% and 61.2% in PS and HS tumors, respectively). Among these, 49.1% had N1 disease (41.2% and 42% in PS and HS tumors, respectively). CONCLUSION: Major discrepancies remain regarding the actual management of GBC based on recommendations from national guidelines. Only one third of patients with T2 GBC undergo appropriate hepatectomy and half of them undergo portal lymphadenectomy. Efforts should be directed towards standardization of practice patterns in GBC.

PT170

Clinical Score Predicting Survival Following Resection of Sarcoma Liver Metastases
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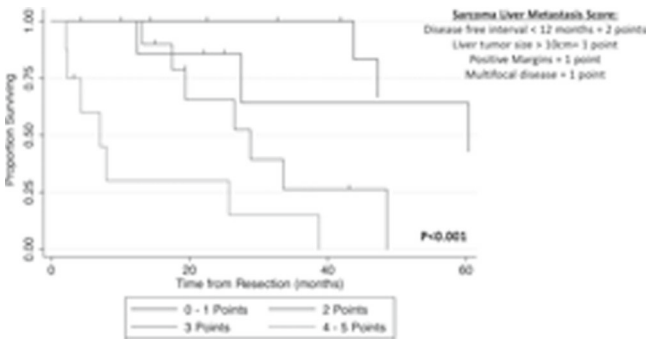
Introduction: The oncologic value of hepatectomy in patients with sarcoma liver metastases remains poorly understood. The aim of this study was to create a preoperative clinical risk score to facilitate selection of patients with metastatic sarcoma for liver resection. Methods: Patients who underwent liver resection for metastatic sarcoma in one of 8 academic institutions participating in the US Sarcoma Collaborative were identified. Morbidity, mortality, and survival outcomes were evaluated. Kaplan Meier survival analysis and multivariate Cox regression was used to identify predictors of survival and create the clinical risk score. Results: From 2000-2016, 58 patients underwent hepatectomy for liver sarcoma metastases, 45 (77.6%) of which were metachronous. Median age was 57 years. Most common histologies were: leiomyosarcoma (48%), liposarcoma (14%), and undifferentiated pleomorphic sarcoma (10%). Sites of primary tumor included retroperitoneal (76%), uterine (10%) extremity (10%), and trunk (4%). Median size of largest liver tumor was 6 cm (range 1-17cm). Multiple hepatic metastases were present in 63%. R0 margins were achieved in 70.5%. Major hepatectomy (>3 segments) was performed in 22% and concomitant liver ablation in 20% of cases. Overall morbidity, major morbidity, and mortality rates were 38%, 22%, and 1.8%, respectively. Multivariate cox regression analysis revealed that disease free interval < 12 months, positive margins, liver tumor > 10cm, and multifocal disease were independent predictors of poor survival. A clinical score created from the above 4 variables based on each variable's regression coefficient demonstrated good discrimination in predicting survival after hepatectomy (3-year: 100% for 0-1 points, 62% for 2 points, 40% for 3 points, and 15% for 4-5 points, P<0.001, AUC =0.72, Figure). Conclusion: Disease free survival > 12 months, solitary metastasis, negative margins, and tumor size < 10 cm are useful parameters in selecting patients with sarcoma liver metastases for hepatic resection.



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Outcomes After Upper Abdominal Debulking in Ovarian Malignancies
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Introduction Cytoreductive surgery with complete macroscopic resection in patients with ovarian cancer is associated with improved survival. The presence of upper gastrointestinal disease remains a major reason why optimal cytoreduction may not be achieved. We sought to investigate outcomes in

patients undergoing cytoreductive surgery with upper abdominal debulking at our institution. Methods Patients who underwent cytoreductive surgery for ovarian malignancies from 2009-2015 were retrospectively identified from an institutional database at a comprehensive cancer center. Upper abdominal debulking was defined anatomically as debulking of disease proximal to the ligament of Treitz. Perioperative outcomes were compared between patients who did and did not undergo cytoreductive surgery with upper abdominal debulking. Results A total of 258 operations were performed in 226 patients. Median age was 61 years (IQR 53-68), and the majority of patients had a diagnosis of serous ovarian carcinoma (70%). 53% of the operations were primary cytoreductions. In operations with upper abdominal debulking (96, 37%), compared to operations without, patients were more likely to have an ASA of 3 (56% vs. 49%, p=0.037), peritoneal implants (92% vs. 55%, p<0.001), liver/spleen metastases (42% vs. 6%, p<0.001), and ascites (60% vs. 47% p=0.017). Preoperative chemotherapy (25% vs. 28%, p=0.553) and optimal cytoreduction (80% vs. 72%, p=0.337) were similar between groups. Twenty-five patients (26%) in the upper abdominal debulking group underwent liver resection and/or ablation. As demonstrated in Table 1, median length of stay was greater in the upper abdominal debulking group (10 vs. 8 days, p<0.001), but complications, readmissions, and perioperative mortality were not significantly different between groups. Conclusions Upper abdominal debulking in patients with ovarian malignancies is safe, feasible, and should be performed if needed to achieve an optimal cytoreduction.

Table 1. Perioperative Outcomes Stratified by Extent of Debulking

CHARACTERISTIC	Lower (N=162)	Upper+Lower (N=96)	p-value
Length of stay (days), median (IQR)	8 (7-12)	10 (9-14)	<0.001
Any complication, n (%)	25 (15)	17 (17)	0.825
Complication type, n (%)			0.813
Cardiac	1 (1)	0 (0)	
Gastrointestinal	1 (1)	0 (0)	
Infectious	6 (4)	6 (6)	
Procedural	8 (5)	5 (5)	
Respiratory	4 (2)	3 (3)	
Vascular	0 (0)	2 (2)	
Other	5 (3)	1 (1)	
Clavien-Dindo Grade, n (%)			0.274
I	2 (1)	0 (0)	
II	8 (5)	3 (3)	
IIIA	11 (7)	10 (10)	
IIIB	1 (1)	2 (2)	
IVA	0 (0)	1 (1)	
V	3 (2)	1 (1)	
Readmission at 30 days, n (%)	29 (18)	11 (11)	0.167
Mortality at 30 days, n (%)	3 (2)	1 (1)	0.524

PT172

Role of Serum HE 4 as a Marker for Response and Recurrence in Carcinoma Ovary M. Lakshmanan,* V. Kumar, S. Gupta, N. Akhtar, S. Rajan, A. Chaturvedi, S. Misra, K. Jain, S. Garg. *Department of Surgical Oncology, King George's Medical University, Lucknow, India.*

INTRODUCTION: Epithelial ovarian cancer is the second most common gynecological cancer and accounts for 4% of cancers affecting women worldwide. Carbohydrate Antigen 125 (CA 125) is currently considered the standard biomarker for detecting ovarian cancer recurrence. However, the application of CA125 is compromised by its low accuracy. Human Epididymis Protein 4 (HE 4) is a novel biomarker which has been noted to rise in ovarian cancer. The present study aims to explore the role of HE4 in assessing response and predicting recurrence. MATERIALS and METHODS: A total of 149 patients with epithelial ovarian carcinoma treated in the Department of Surgical Oncology, King George's Medical University, Lucknow between January 2014 and March 2016 were enrolled in the study. Baseline HE 4 and CA 125 values were recorded and tests were repeated after surgery, during chemotherapy and every three months during follow up. HE4 levels were correlated with clinicopathological profile including stage, platinum sensitivity, optimal debulking & disease free survival. RESULTS: Median age at diagnosis was 45 years (24-80). Mean baseline CA 125 was 1201.91 + 189.46 and baseline HE 4 was 1132.75 + 271.26. Stage distribution was as follows, Stage I (3.35%, n=5), Stage II (14.76%, n=22), Stage III (64.42%, n=96) and Stage IV (17.44%, n=26). In patients receiving neoadjuvant chemotherapy there was a significant decline in HE 4 values (1132.75 + 271.26 vs 132.45 + 23.56, p=0.001) and it correlated well with response to chemotherapy and prediction of optimal cytoreduction. Recurrence was seen in 38.25%(n=57) patients. HE 4 was elevated in all patients with recurrence, versus elevation of CA 125 in only 73.68%(n=42) patients and had a lead time of 3 months over CA 125. CONCLUSION: Although both CA 125 and HE 4 can be used to predict recurrence, HE 4 has been found to be better in terms of accuracy and lead time. Changes in pre cytoreduction HE 4 accurately predicts response to neoadjuvant chemotherapy, optimal cytoreduction and disease free survival. Longer follow up is needed to explore the role of HE 4 in predicting overall survival.

PT173

Prognostic Pre-Operative Factors for Patients with Ovarian/Primary Peritoneal Cancers Considered for Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) W. Wang,* J.C. Seo, G. Tan, C. Chia Shulyn, J. Ong, K. Soo, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: CRS and HIPEC confer survival benefit in selected patients with ovarian/primary peritoneal cancers but are not universally accepted as standard of care in an exquisitely chemosensitive cancer. Selection of only patients who derive significant survival benefit may help to justify this treatment. This paper aims to identify the pre-operative factors that affect survival outcomes after CRS and HIPEC. Methods: All patients with ovarian/primary peritoneal cancers who have undergone CRS and HIPEC at our institution between January 2001 and December 2016 were included. Demographic and clinicopathological data were collected. Survival analyses were performed using Kaplan-Meier curves and cox regression proportional hazards model to identify the pre-operative factors associated with overall survival (OS). Results: 86 patients were included and followed up for a median of 34 months. During the follow-up period, 57 (66.3%) patients remained alive and 29 (33.7%) were disease-free. The following factors were associated with better OS on multivariate analysis: absence of ascites on radiological imaging (HR:0.200 95% CI: 0.076 - 0.528, p=0.001), NLR (neutrophil lymphocyte ratio) less than 5 (HR: 0.146, 95% CI: 0.018 – 1.000; p=0.05) and normal CA125 (HR 0.324, 95% CI 0.117 – 0.891, p=0.029). Age, performance status, disease-free interval, neoadjuvant treatment, histological subtype, pre-operative albumin and platelet-lympyhocyte ratio were not significantly associated with OS. DIscussion: Preoperative selection of patients with ovarian/primary peritoneal cancers may be improved by considering presence of ascites on imaging, NLR and CA125 levels.

PT174

Early Postoperative Intraperitoneal Chemotherapy (EPIC) for Peritoneal Mesothelioma P.K. Shah,* S. DESSUREAULT. *Complex General Surgical Oncology, H Lee Moffitt Cancer Center, Tampa, FL.*

Introduction: Peritoneal Mesothelioma (PM) is a rare neoplasm with few therapeutic options that include debulking and Heated Intraperitoneal Chemotherapy (HIPEC). The utility of Early Postoperative Intraperitoneal Chemotherapy (EPIC) for PM is not well characterized. We reviewed our experience with EPIC for PM to investigate the procedure's morbidity and its impact on overall survival. Methods: From a prospective database of 99 patients undergoing HIPEC (2004-2017), 42 patients had PM and were considered for EPIC following HIPEC. EPIC involved administering Paclitaxel and 5-Fluorouracil on post-operative day 7 via an intraperitoneal drain inserted at the time of debulking and HIPEC with Cisplatin. Clinical variables were analyzed for morbidity and mortality. Results: Median age of patients with PM undergoing debulking with HIPEC was 64 years; 54% were females. The Median Peritoneal Cancer Index (PCI) was 15 and the median Completeness of Cytoreduction (CC) score was 1. Median post-operative hospital stay was 10 days with no deaths reported within 30 days after the surgery. Eight patients (19%) did not receive EPIC following HIPEC most commonly (63%) from early postoperative renal insufficiency attributed to Cisplatin toxicity. In the 34 patients (81%) that received EPIC following HIPEC, the median PCI was 21 and the median CC score was 1. Fourteen of these patients (41%) had debulking prior to the referral for HIPEC. The most common 30-day complications in this group were fever and ileus. Of the 15 patients (44%) who received pre-operative chemotherapy in this group, 10 patients (67%) went on to receive post-operative chemotherapy. At a median follow up of 23 months, 21 patients (62%) were alive at the last follow up. Of the patients who underwent HIPEC with EPIC, 11 patients (32%) underwent a repeat HIPEC with EPIC at a later date. Two patients (6%) underwent a third HIPEC with EPIC. Median overall survival in the patients receiving EPIC with HIPEC was 28 months. Conclusion: Patients undergoing EPIC in addition to HIPEC for PM have an appre-

ciable overall survival without any major postoperative complication. EPIC should be considered for patients with PM undergoing HIPEC.

PT175

The Evolution of CRS and HIPEC for Ovarian Peritoneal Carcinomatosis in a Single Institution T. Skanthakumar,* G. Tan, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Background: CytoReductive Surgery (CRS) and Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC) have been utilised in the management of selected patients with peritoneal metastasis from ovarian cancer. This study describes the evolution of CRS-HIPEC for ovarian peritoneal carcinomatosis in our institution. Methods: The institution's prospectively-maintained CRS-HIPEC database was retrospectively reviewed. Metastatic ovarian cancer patients who underwent CRS-HIPEC were identified and stratified into two groups. Group 1 consisted of patients treated in our initial 100 cases of CRS-HIPEC surgeries while Group 2 consisted of the subsequent 178 cases. Pre-, intra- and post-operative prognostic factors as well as overall- (OS) and disease-free survival (DFS) outcomes were analysed. Results: Between March 2005 to July 2017, 74 CRS-HIPEC procedures were performed on 64 ovarian cancer patients. Five patients had undergone CRS-HIPEC twice while one patient underwent the procedure thrice. 34 (45.9%) and 40 (54.1%) CRS-HIPECs were performed for Groups 1 (median age 50, range 24-69) and 2 (median age 55, range 19-74) patients respectively. 17 patients presented with comorbidities at time of HIPEC in both Groups 1 (50%) and 2 (42.5%) respectively. Groups 1 and 2 had median follow-up duration of 67 and 22 months (mths) respectively. There was a significant difference in OS in group 1 compared to group 2 (37mths vs not reached, $p = 0.034$). However, DFS between the groups (15mths vs 12mths, $p = 0.456$) was not significantly different. Post-operatively, fewer patients in Group 2 developed high grade (Clavien-Dindo III-V) complications (44.1% vs 5.0%, $p < 0.001$), had shorter hospitalisation (18 days vs 12 days, $p < 0.001$) and SICU stay (2 days vs 1 day, $p=0.009$). Significantly fewer patients in Group 2 recurred following their surgery (76.5% vs 40.0%, $p=0.002$), especially locoregionally (50.0% vs 20.0%, $p = 0.007$) as compared to patients in Group 1. Conclusion: Improved peri- and post- operative survival outcomes were seen in the latter cohort that can likely be attributed to overcoming of the learning curve and better patient selection.

PT176

Hypothermia is Associated with Surgical Site Infection in Cytoreductive Surgery with Hyperthermic Intraperitoneal Chemotherapy O.S. Eng,* M.P. O'Leary, M. Raoof, M. Lew, M.T. Wakabayashi, I.B. Paz, L.G. Melstrom, B. Lee. *City of Hope National Medical Center, Duarte, CA.*

Introduction Maintenance of perioperative normothermia remains a global quality metric for hospitals. Hypothermia is associated with surgical site infections (SSI) in colorectal surgery. Patients undergoing cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) can experience multiple complications postoperatively. We sought to investigate the association of perioperative hypothermia with SSI in patients undergoing CRS/HIPEC. Methods Patients undergoing CRS/HIPEC from 2009-2017 were retrospectively identified from a prospectively collected institutional database. Demographics and perioperative variables were recorded, with hypothermia defined as <36.0°C in accordance with the Agency for Healthcare Research and Quality metric. Regression analyses were performed with SSI diagnosed within 30 days postoperatively as the primary outcome. Results A total of 170 patients were identified, 14 (8.2%) of whom developed an SSI. All patients received perioperative antibiotics within 60 minutes of incision per National Surgical Quality Improvement Program guidelines. Median perioperative nadir temperature was 35.0°C (IQR 35.0°C-35.7°C), with a median percentage of time <36.0°C of 42.3% (IQR 12.9%-57.9%). Patients with SSIs experienced lower median temperatures (35.7°C vs. 36.1°C, $p=0.020$), greater percentage of operative time at nadir (18.7% vs. 11.1%, $p=0.030$), and greater percentage of operative time in hypothermia (55.8% vs. 35.3%, $p=0.003$). On a multivariate analysis adjusting for other risk factors for SSI (age, diabetes mellitus, body mass index, total operative time), total operative time (OR 1.33, 95%CI 1.04-1.70, $p=0.024$) and percentage of operative time in hypothermia (OR 1.04, 95%CI 1.01-1.07, $p=0.011$) were significantly associated with SSI within 30 days postoperatively. Conclusions Hypothermia is associated with the development of SSI in patients undergoing CRS/HIPEC. Our findings suggest that minimizing perioperative temperatures <36.0°C may decrease perioperative morbidity in the context of SSI in this high-risk patient population.

PT177

Variability in Sentinel Lymph Node Biopsy (SLNB) Retrieval for Breast Cancer (BC) in a Large Midwest Hospital System A. Chevinsky,* J.A. Tjoe, W. Owens, J.M. Weese. *Surgical Oncology, Aurora Cancer Care, Mequon, WI.*

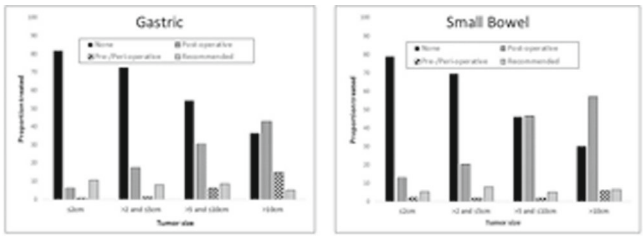
Background: SLNB for staging and treatment of BC is the standard of care. Interpretation of results to guide therapy is evolving including the need for completion axillary lymph node dissection (ALND) after removal of a positive SLN and, the need to perform SLNB in patients (PTS) over age 70 with small ER+ tumors. Methods: A retrospective chart review revealed that from 1/1-6/30/2016, 25 general surgeons (GS) and 4 dedicated breast surgeons (BS) performed 282 SLN operations (OPS) for Stages I-III BC (181 lumpectomies (LUMP) and 101 mastectomies (MAST)) Results: In the 282 BC OPS, 234 SLNBs were attempted (LUMP-157, MAST-77). In the LUMP group 9 PTS had neither SLNB nor ALND (6 declined, 3 had in situ disease) and were excluded from analysis. A mean of 2.53 and a median of 2 SLNs/PT were removed in the LUMP group. The number of SLNs retrieved was: 0-11 PTS, 1-45, 2-42, 3-36, 4-18, 5-9, 6+-7. 17 PTS were SLN+ (10.8%) and 13 PTS had ALND. In the MAST group 2 PTS had neither SLN nor ALND (both declined). A mean of 3.52 and a median of 2 SLNs/PT were removed. The number of SLNs retrieved was: 0-2 PTS, 1-19, 2-25, 3-10, 4-7, 5-5, 6+-9. 15 PTS were SLNB+ (19.5%) and 24 PTS had ALND. The BS did 129 of the OPS (46%) ranging 22-43 OPS/surgeon. The GS did 153 OPS (54%) ranging 1-18 OPS/surgeon. The SLNB variability between groups showed the BS had a mean of 2.4 SLN/PT for LUMP and 4.0 SLN/PT for MAST. The GS had a mean of 3.29 SLN/PT for LUMP and 3.05 SLN/PT for MAST. The variability amongst the GS was higher compared to the BS group. Conclusions: Based on these findings and a review of the literature the following recommendations were made: Dual tracer should be used; 1 SLN was felt to be insufficient for complete evaluation and >4 SLN did not improve staging; goal is to remove SLNs which are hot, blue or palpable with a goal of 2-4 SLNs per PT; a completion ALND can be omitted in Stage I-II PTS having LUMP with radiation with only 1-2 SLNs involved; PTS >70 with T1-2 ER+ tumors do not require SLNB; SLN after Neoadjuvant therapy can be done even with an initially positive LN, however, attempt to remove the initially positive LN should be done.

PT178

Trends in Utilization of Multimodal Therapy for Gastric and Small Bowel Gastrointestinal Stromal Tumors S. Bansal,[1]* J.I. Portuondo,[1] H.S. Tran Cao,[1] Y.H. Sada,[1] C. Roland,[2] C. Chai,[1] N.N. Massarweh.[1] *1. Michael E DeBakey Department of Surgery, Baylor College of Medicine, Houston, TX; 2. University of Texas MD Anderson Cancer Center, Houston, TX.*

Background: Imatinib is commonly used in multimodal management of patients with gastrointestinal stromal tumors (GISTs). However, the frequency of adjuvant therapy utilization and sequence of treatment for patients with gastric and small bowel GISTs are presently unknown. Methods: Retrospective cohort study of patients with non-metastatic gastric (n=3,182) or small bowel (n=1,465) GIST in the National Cancer Data Base (2006-2012). Patients were stratified by primary tumor site, size (≤2cm, >2 and ≤5cm, >5 and ≤10cm, and >10cm), and sequence of multimodal treatment (surgery only, post-operative, and pre- or perioperative). Factors associated with adjuvant therapy use (regardless of sequence) were evaluated using hierarchical regression. Results: Over the study period, adjuvant therapy use significantly increased among patients with gastric GISTs >10cm (51.6% in 2006 vs 68.2% 2012; trend test, $p=0.001$) and small bowel GISTs >5 and ≤10cm (31.9% vs 57.3%; trend test, $p=0.02$). Utilization significantly decreased among patients with small bowel GISTs >2 and ≤5cm (26.3% vs 19.4%; trend test, $p=0.04$). Among patients with gastric and small bowel GIST >10cm, 36.6% and 30.1%, respectively, did not receive adjuvant treatment (Figure). A minority of patients with >10cm tumors (gastric—15%; small bowel—6.1%) received pre- or perioperative therapy. Factors associated with adjuvant treatment included small bowel primary (Odds Ratio [OR] 1.28, 95% Confidence Interval [1.09-1.50]), tumor size (>2 and ≤5cm—OR 1.73 [1.27-2.35]; >5 and ≤10cm—OR 4.75 [3.48-6.49]; >10cm—OR 10.10 [1.56-2.35]), and a positive surgical margin (OR 2.12 [1.56-2.89]). Patients treated at a Community Cancer Center were less likely to receive adjuvant treatment (OR 0.65 [0.47-0.90]). Conclusions: While adju-

vant therapy utilization has increased for certain patients with gastric and small bowel GISTs, there remains underuse among patients with tumors >10cm—the vast minority of whom do not receive preoperative treatment. Further work is needed to delineate drivers of adjuvant therapy use and to better characterize any potential benefit associated with preoperative treatment of large or high risk GIST.



Sequence of multimodal therapy for gastric and small bowel GIST.

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Preventable Readmissions Following Common Cancer Operations in New York State Y. Feferman,[1]* M. Katz,[2] N. Egorova,[3] U. Sarpel,[1] N. Bickell.[3] *1. Icahn School of Medicine at Mount Sinai, New York, NY; 2. Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY; 3. Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, New York, NY.*

Potentially preventable readmissions of surgical oncology patients offer opportunities to improve quality of care. Identifying and subsequently addressing remediable causes of readmissions may improve patient-centered care. We sought to identify factors associated with potentially preventable readmissions after index cancer operation. Methods: The New York State hospital discharge database was used to identify patients undergoing common cancer operations via principal diagnosis and procedure codes between the years 2010 and 2014. The 30-day readmissions were identified and risk factors for potentially preventable readmissions were analyzed using competing risk analysis. Results : A total of 53,740 cancer operations performed for the following tumor types were analyzed: colorectal (CRC) (42%), kidney (22%), liver (2%), lung (25%), ovary (4%), pancreas (4%), and uterine (1%). The 30-day readmission rate was 11.97%, 47% of which were identified as potentially preventable. The most common cause of potentially preventable readmissions was sepsis (48%). Pancreatic cancer had the highest overall readmission rate (22%) and CRC had the highest percentage of potentially preventable readmissions (51%, Hazard Ration (HR)=1.42; 1.28-1.61). Risk factors associated with preventable readmissions included discharge disposition to a skilled nursing facility (HR=2.22; 1.99-2.48) and the need for home health care (HR=1.61; 1.48-1.75). Years prior to the Affordable Care Act's Hospital Readmissions Reduction Program were associated with higher readmission rates (HR=1.13; 1.03-1.23). Conclusion: Almost half of the 30-day readmissions were potentially preventable and attributed to high rates of sepsis, surgical site infections, dehydration and electrolyte disorders. These results may be generalized to other institutions in the United States and can be further validated for identifying broad targets for improvement.

PT180

Intraoperative Fluid Restriction for Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Surgery T. Almerey,* E. Gabriel, S. Bagaria. *General Surgery, Mayo Clinic, Jacksonville, FL.*

Introduction: Multiple studies highlight the importance of liberal fluid administration to replace the large volume lost during cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) and reduce end organ damage such as acute renal failure. Unfortunately, over-resuscitation can result in deleterious effects on gastrointestinal function recovery, wound healing, and length of hospital stay. In this study, we introduce a novel intraoperative protocol for CRS-HIPEC procedure that minimizes intravenous fluid administration. Methods: Retrospective analysis of 35 patients that underwent CRS-HIPEC for curative intent under fluid restrictive protocol from June 2015 to July 2017 was performed. The protocol consists of 1) continuous infusion of vasopressin 0.02 units/hour and 2) maintaining urine output at 0.5 ml/kg/hr through the judicious use of crystalloid and colloid. Endpoint measured was Clavien Dindo ≥ 3 adverse events within 30 days of the procedure. Results: Median age was 56 years and 71% were female. Malignancies treated included appendix (49%), colon (31%), and other (20%). The median peritoneal cancer index was 15 and complete cytoreduction was achieved in 91% of patients. There was a total of 28 bowel anastomoses. The median operative time was 520 minutes, and the median estimated blood loss was 400 cc. The median intraoperative administration of crystalloid, colloid, and packed red blood cells were 1900 cc, 1500 cc, and 700 cc, respectively. Clavien Dindo grade 3-4 adverse events occurred in 5 (14%) of patients: these include anastomotic leak (n=1) and acute kidney injury (n=1). The median time for return of bowel function (flatus) was 5 days, and the median length of hospital stay was 7 days. Three patients (9%) were readmitted and there were no deaths 30 days after surgery (Table 1). Conclusion: A fluid restriction protocol appears to be safe and feasible in the setting of CRS-HIPEC for curative intent. Larger series are needed to validate this intraoperative approach. Future studies comparing the outcomes of this protocol with liberal fluid administration are recommended.

Table 1. HIPEC patients treated with intra-operative fluid restriction.

Variable	Total=35, N (%)
Demographics	
• Age (years), median (range)	56 (21-74)
• Female	25 (71)
Primary tumor	
• Appendix	17 (49)
• Colon	11 (31)
• other	7 (20)
Intraoperative characteristics	
• Peritoneal cancer index (Median)	15
• Operative time (Median, mins)	520
• Estimated blood loss (Median, cc)	400
• Number of anastomosis	28
• Crystalloids used (Median, cc)	1900
• Colloids used (Median, cc)	1500
• PRBCs used (Median, cc)	700
Return of bowel function (Median, days)	5
Length of stay (days)	7 (6, 8.5)[a]
30 days complications	
• Mortality	0 (0)
• Grade III/IV Clavien Dindo	5 (14)
• Bowel anastomotic leakage	1 (2.8)
• Abdominal collection	3 (8.5)
• Renal injury	1 (2.8)
• Readmission	3 (8.5)
• Reoperation	3 (8.5)

[a] Median, (Interquartile range)

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The Impact of Hospital Volume on Outcomes in Patients with Retroperitoneal Sarcoma (RPS) E. Keung,* Y. Chiang, J. Cormier, K. Torres, K. Hunt, B. Feig, C. Roland. *Surgical Oncology, MD Anderson Cancer Center, Houston, TX.*

Introduction: RPS are rare tumors for which complete surgical resection remains the mainstay of treatment. Given their low incidence, it has been recommended that RPS be referred to high volume sarcoma centers for management. We sought to determine the impact of hospital case volume on outcomes among patients with primary RPS. Methods: We identified 8861 patients diagnosed with primary RPS from the National Cancer Data Base between 1998-2011. Treating hospitals were classified by annual case volume (low, mid, and high volume defined as 0-5, 6-10, and >10 cases/year, respectively). Overall survival was compared using Kaplan-Meier curves and Cox proportional hazard models were created to compare risks. Results: Of 1131 reporting hospitals, 1120 (99%) were low volume institutions while 7 (0.6%) and 4 (0.4%) were mid and high volume centers, respectively. The majority

of patients (n=7427; 83.8%) were treated at low volume compared to mid (n=562; 6.3%) and high volume hospitals (n=872; 9.8%). Patients treated at mid and high volume hospitals experienced longer median duration between diagnosis and definitive surgical procedure (32 and 36 vs 8 days). Among patients undergoing surgical resection (n=6950), those treated at higher volume hospitals were more likely to have higher grade and larger tumors, and less likely to have radiation therapy. Patients treated at high volume hospitals were also less likely to have an incomplete gross (R2) resection (1.6% vs 3.6% and 4.5%). Patients treated at low and mid volume hospitals were more likely to die within 90 days of surgery than those treated at high volume hospitals (5.7 % and 6.5% vs 3.2%). After controlling for margin status, tumor size, grade, chemotherapy and radiation administration, treatment at a high volume hospital was independently associated with a reduced risk of death (HR 0.67, 95% CI 0.59-0.76; Table). Conclusion: Primary RPS are rare tumors for which few surgeons and institutions have significant experience and expertise in their multidisciplinary management and surgical resection. Although further studies are needed, oncologic and patient outcomes may be impacted by treating facility case volume and experience.

Factors associated with overall survival among patients undergoing surgery for primary retroperitoneal sarcoma

Overall survival (n=6950)								
	Univariate model				Multivariate Model			
Description	HR	95% CI		p value	HR	95% CI		p value
Margin (ref. R0/R1)				<0.001				<0.001
R2	2.39	2.08	2.76		2.30	1.99	2.65	
RX	1.42	1.32	1.53		1.46	1.36	1.57	
Hospital Volume (ref.0-5/year)				<0.001				<0.001
6-10/year	0.83	0.72	0.96		0.76	0.66	0.88	
>10/year	0.82	0.73	0.93		0.67	0.59	0.76	
Tumor stage (ref. <= 5 cm)				<0.001				0.002
> 5 cm	1.20	1.06	1.37		1.12	0.99	1.27	
Unknown	1.50	1.28	1.76		1.32	1.12	1.54	
XRT (ref. No)				<0.001				<0.001
Yes	0.84	0.78	0.91		0.71	0.66	0.77	
Chemotherapy (ref. No)				<0.001				<0.001
Yes	1.60	1.46	1.74		1.25	1.14	1.37	
Unknown	0.71	0.58	0.88		0.94	0.75	1.17	
Grade (ref. Low)				<0.001				<0.001
Intermediate	1.16	1.03	1.31		1.24	1.11	1.40	
High	2.23	2.08	2.40		2.36	2.19	2.55	

R0/R1: complete gross resection; R2: incomplete gross resection; XRT: radiation therapy

PT182

Incidence and Predictors of Incisional Hernia After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Malignancies J. Huang,* S. Kizy, A.M. Altman, H. Nalluri, S. Marmor, W. Gaertner, E.H. Jensen, J. Hui, T.M. Tuttle. *Surgery, University of Minnesota, Minneapolis, MN.*

Background: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is increasingly used for primary and metastatic peritoneal malignancies. The combination of major abdominal surgery, malignancy, and immunosuppressive chemotherapy may predispose patients to incisional hernias (IH); however, this rate has not been well reported. We analyzed our institution's experience with IH after CRS/HIPEC and factors associated with its development. Methods: All patients who had CRS/HIPEC from March 2002 to June 2016 through a midline laparotomy incision for peritoneal cancer were reviewed. Incisional hernias were diagnosed by clinical exam and follow up computed tomography (CT) scans. Univariate analysis was performed to assess predictors of IH formation. Results: We identified 155 patients who had a midline incision and primary closure for CRS/HIPEC. The most common method of fascial closure was with a running 0-looped polydioxanone suture. The median age was 52 years. 58% of patients were female and the mean body mass index (BMI) was 28.5 kg/m^2. After a median follow-up of 6.3 years, we identified 23 (15%) incisional hernias with 7 (30%) of these ultimately requiring repair. The median time to IH formation was 230 days, and all hernias were identified within 1.5 years after CRS/HIPEC. Factors associated with IH included older age and BMI >35 (both p<0.05). In contrast, pre- and post-operative chemotherapy, smoking, diabetes, albumin level, and Peritoneal Cancer Index scores were not significantly associated with IH formation. Conclusions: The development of an incisional hernia affects quality of life and may lead to another surgery after CRS/HIPEC. The IH rate in our study was moderately high, but similar to the hernia rate after other major abdominal operations. Perhaps, alternative midline closure techniques ("small bites" or prophylactic mesh placement) will reduce the IH rates, especially in high-risk (older age, obese) patients.

PT183

Quality of Life After Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Mesothelioma Y. Ali,* J. Sweeney, K.C. Perry, K. Votanopoulos, P. Shen, E.A. Levine. *Wake Forest Baptist Medical Center, Chapel Hill, NC.*

Introduction: Peritoneal mesothelioma is a rare condition, for which cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) is an accepted treatment. There is little data on quality of life (QOL) in this setting. The purpose of this study was to evaluate QOL after HIPEC for peritoneal mesothelioma. Methods: This was a prospective study of patients who underwent HIPEC for peritoneal mesothelioma between 2002 and 2015. Patients completed QOL surveys, including the Short Form-36 (SF-36), Functional Assessment of Cancer Therapy (FACT-C), Brief Pain Inventory (BPI), and Center for Epidemiologic Studies Depression scale (CES-D), preoperatively and at 3, 6, 12, and 24 months postoperatively. Results: There were 46 patients who underwent HIPEC for peritoneal mesothelioma and completed QOL surveys prior to and following surgery. Mean age was 52.8±13.8 years. Percentage of males was 52.2%. Preoperative functional status (ECOG 0 or 1) was 69.6%. The median survival was 3.4 years; 1, 3 and 5-year survivals were 77.4%, 55.2% and 36.5%, respectively. CES-D score decreased at 3 months following HIPEC, but increased at 24 months (p=0.014). SF-36 physical functioning scale decreased at 3 months but returned to baseline at 12 months (p=0.0045); general health scale decreased at 3 months, returned to baseline by 6 months, but then decreased again at 24 months (p=0.0034). Emotional well-being (p=0.0051), role limitations due to emotional problems (p=0.0006), and social functioning (p=0.0022) improved following HIPEC. BPI (p=0.025), least pain (p=0.045), and worst pain (p<0.0001) improved following HIPEC and continued to improve at each time point. FACT-C physical well-being decreased at 3 months but returned to baseline at 6 months (p=0.020) and there was continued improvement of the total FACT-C score beginning at 6 months (p=0.05). Conclusion: Though HIPEC is associated with significant morbidity, QOL returns to baseline or improves from baseline between 3 months and 1 year following surgery. This suggests that despite the risks associated with this operation, patients tolerate the operation well and have good overall QOL following the procedure.

PT184

Outcomes After Elective Major Cancer Surgeries: Prediction through Parsimony N. Goel,* W.H. Ward, L. Demora, S. Manstein, M.C. Smaldone, J. Farma, C.S. Chu, A. Kutikov, D.Y.T. Chen, M. Lango, R. Viterbo, J.A. Ridge, E. Ross, R.G. Uzzo, N. Esnaola. *Fox Chase Cancer Center, Philadelphia, PA.*

Introduction Major cancer surgery is associated with significant risks of morbidity/mortality. Retrospective studies have demonstrated an association between Surgical Apgar Score (SAS, based on intraoperative blood loss, heart rate, and blood pressure) and postoperative risk of serious complications(SC). This study prospectively evaluated the predictive value of SAS to predict SC–as well as other adverse postoperative outcomes and length of stay(LOS)-both singly and in combination with parsimonious measures of "fitness for surgery" (American Society of Anesthesiology [ASA] classification) and surgical complexity (work relative value units [wRVU]). Methods Demographic, comorbidity, procedure, intraoperative, and outcome data was collected prospectively for 442 cancer patients undergoing elective major surgery between 2014-17. ASA and wRVU were assigned preoperatively; SAS was calculated immediately postoperatively. Logistic regression was used to analyze association of ASA vs wRVU vs SAS vs ASA/wRVU/SAS (combined) with SC, return to the operating room(ROR), not discharged home, and unplanned readmission; areas under receiver operator characteristic curves(AUC) were calculated to assess predictive accuracy. Accelerated failure time models were used to analyze associations with LOS and compared using Harrell's concordance index. Results The predictive accuracy of SAS for SC was modest(AUC 0.650) and not improved when controlling for ASA and wRVU(both had poor predictive accuracy for SC;see Table). Both wRVU(AUC 0.634) and SAS(AUC 0.663) had modest predictive accuracies for ROR, whereas the predictive accuracy of ASA(AUC 0.749) surpassed that of wRVU(AUC 0.630) for not discharged home. All 3 measures were

poor at predicting readmission. In contrast, the predictive accuracy of ASA, wRVU, and SAS for LOS was highest when combined(AUC 0.699). Conclusion Commonly used, simple measures of comorbidity, functional status, and surgical complexity can help predict risk of ROR and not discharged home (respectively), whereas only SAS has sufficient discriminatory ability to predict risk of SC. All 3 measures are too coarse to predict unplanned readmission, but when used in combination, can help predict LOS.

Univariate and Multivariate Predictors of Outcomes After Elective Major Cancer Surgery

Outcome	OR (univariate)	aOR (multivariate)	Lower CI 95%	Upper CI 95%	P-value	AUC
Serious Complication (SC)						
ASA	1.481		0.808	2.714	0.204	0.533
wRVU	1.036		1.005	1.068	0.022	0.564
SAS	0.704		0.584	0.848	0.0002	0.650
ASA		1.286	0.692	2.390	0.426	0.655
wRVU		1.014	0.980	1.048	0.434	
SAS		0.733	0.598	0.899	0.003	
Return to the Operating Room (ROR)						
ASA	1.786		0.671	4.752	0.245	0.564
wRVU	1.053		1.004	1.104	0.035	0.634
SAS	0.685		0.511	0.918	0.011	0.663
Not Discharged Home						
ASA	7.383		2.514	21.680	0.0003	0.749
wRVU	1.055		1.003	1.111	0.040	0.630
SAS	0.988		0.684	1.426	0.947	0.490
Unplanned Readmission						
ASA	1.308		0.667	2.564	0.4346	0.5178
wRVU	1.031		0.997	1.066	0.0721	0.5440
SAS	0.874		0.710	1.075	0.2022	0.5673
ASA		0.935	0.744	1.176	0.5667	0.5752
wRVU		1.209	0.613	2.383	0.5843	
SAS		1.025	0.988	1.064	0.1821	
Length of Stay (LOS)	TR (univariate)	TR (multivariate)	Lower CI 95%	Upper CI 95%	P-value	Harrell's C
ASA	1.463		1.233	1.736	<0.001	0.554
wRVU	1.053		1.045	1.061	<0.001	0.641
SAS	0.817		0.776	0.859	<0.001	0.630
ASA		1.260	1.091	1.456	0.002	0.699
wRVU		1.044	1.036	1.053	<0.001	
SAS		0.901	0.859	0.944	<0.001	

OR: Odds Ratio
aOR: Adjusted Odds Ratio
TR: Time Ratio
CI: Confidence Interval
AUC: Area Under the Receiver Operating Characteristic Curve
Harrell's C: Harrell's concordance index

PT185

Carcinoembryonic Antigen, Peritoneal Cancer Index and Pre-operative Disease-free Interval as Predictors of Post-operative Outcomes in Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy K. Chin,* G. Tan, C. Chia Shulyn, J. Ong, M. Teo. *Department of Surgical Oncology, Singapore General Hospital, Singapore, Singapore.*

Background: The combination of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) has significantly improved prognosis of patients with peritoneal carcinomatosis, a diagnosis once deemed to have few therapeutic options. Patient selection is key to improved survival outcomes. We aimed to identify pre- and peri-operative parameters with predictive value for post-CRS-HIPEC disease-free and overall survivals. Methods: A single-institution review of prospectively collected data from all patients who underwent CRS-HIPEC between Oct 2005-Oct 2017 was conducted. Pre- and peri-operative parameters (e.g. age, nodal status, neoadjuvant chemoradiotherapy, carcinoembryonic antigen (CEA), peritoneal cancer index (PCI), pre-operative disease free interval (DFI: time between primary tumour resection and peritoneal disease recurrence)) for patients who underwent CRS-HIPEC for recurrent cancers were assessed and analyzed for their predictive value of post-CRS-HIPEC disease-free survival (DFS) and overall survival (OS). Univariate and multivariate analyses were used to identify significant predictors and ROC curves to identify cutoffs most significantly associated with DFS and OS. Results: 278 patients underwent CRS-HIPEC, of which 178 for recurrent cancers. CEA (p=0.006) and PCI (p=0.025) were independent predictors of 2-year OS. CEA (p=0.011) was an independent predictor of 5-year OS. CEA, PCI and DFI were all independent predictors of DFS (CEA, p=0.079; PCI, p=0.048; DFI, p=0.002). CEA less than 2.7 (p=0.03, sensitivity and specificity of 65%) and PCI less than 10 (p<0.001; sensitivity and specificity of 82% and 64%) were significantly predictive of 2-year OS. PCI less than 11.5 (p=0.0015, sensitivity and specificity of 78% and 73%) and DFI greater than 17 months (p<0.029; sensitivity and specificity of 56% and 79%) were significantly predictive of 5-year OS. Conclusion: CEA, PCI and DFI have significant predictive value for post-CRS-HIPEC survival outcomes. Consideration of these parameters could allow for more prudent patient selection.

PT186

Rapid Rise of Robotic Surgery in Gastrointestinal (GI) Malignancies: Are We Maintaining Perioperative and Oncologic Safety? I. Konstantinidis,* Y. Woo, S. Warner, K. Melstrom, J. Kim, G. Singh, Y. Fong, L.G. Melstrom. *Surgery, City of Hope National Cancer Center, Duarte, CA.*

Introduction: Minimally invasive surgery (MIS) continues to gain traction as a feasible approach for the operative management of GI malignancies. The aim of this study is to quantify national trends and perioperative outcomes of MIS for the most common GI malignancies including the esophagus, stomach, pancreas, colon and rectum. We hypothesize that with more widespread use of MIS techniques, perioperative outcomes and resection quality are still maintained. Methods: The National Cancer Database (2010-2014) was utilized to assess perioperative outcomes and pathologic quality of MIS (robotic and laparoscopic) compared to open, in patients who underwent resection for cancers of the esophagus, stomach, pancreas, colon, and rectum. Results: Data from 11,023 esophageal, 3,0664 gastric, 30,689 pancreas, 260,669 colon and 52,239 rectal resections were analyzed. Although, laparoscopy is the most prevalent MIS approach, the number of robotic resections increased nearly four-fold from 2010 to 2014 in all organ sites (increase by factor: esophagus:3.8, stomach:4.4, pancreas:4.4, colon:3.8 and rectum: 4). The number of laparoscopic resections increased at a slower rate (factor:1.3-1.9), whereas the number of open resections decreased (factor:0.67-0.77). Patients who underwent robotic assisted resections were younger for stomach and colorectal surgeries and with lower Charlson Comorbidity Index across all sites. Patients who underwent robotic or laparoscopic resections had shorter hospitalizations, fewer re-admissions (with the exception of rectal surgeries) and lower postoperative mortality at 90 days. Robotic assisted resections had comparable negative margin resections and lymph node number to laparoscopic resections across all sites (Table). Conclusion: The utilization of robotic assisted resections of gastrointestinal cancers is rapidly increasing with more frequent use in younger and healthier patients. This study demonstrates that with rising utilization of robotic-assisted resections, perioperative outcomes and oncologic safety have not been compromised

Clinicopathologic and Perioperative Outcomes in Robotic (ROB), Laparoscopic (LAP) and Open Approach (OPEN)

Variable, N ROB/LAP/ OPEN	Esophagus 771/2601/ 7651	Stomach 1249/6409/ 23006	Pancreas 859/4265/ 25565	Colon 7180/96760/ 156729	Rectal 5495/13987/ 32757
Median Age (y)	64/64/64	65/66/67**	66/66/66	67/69/70**	60/61/62**
CCI 0(%)	74.1/69.9/70	67.3/66.4/66.2	65.2/65.2/64.7	70.2/68/67.4**	77.7/77/74.3**
Inpatient stay (days)	9/9/10**	7/6/8**	6/6/8**	4/4/6**	5/5/6**
Readmission within 30d (%)	5.2/6.2/7.3*	4.9/5.6/7**	8.6/7.4/9.4**	4.3/5.2/6.4**	8.1/6.9/7.5*
90d Mortality (%)	8.6/7.3/8.9	5.3/5.2/8.7**	3/4.3/7**	3.1/3.7/8.7**	1.7/2.2/3.4**
R0 surgical Margin	95.8/93.9/92.9*	95.4/94.7/90.6**	90.6/91.3/85.7**	97.7/97.6/94.5**	96.7/96.7/94.5**
Median Nodes	16/15/13**	13/10/13**	13/13/14**	17/18/17	15/14/14**

*p<0.05, ** P<0.01, CCI: Charlson Comorbidity Index

PT187

Beliefs and Practices of Surgical Oncologists in the Care of Obese Patients T. Hughes,* J.J. Idrees, E. Palmer, s. Abdel-Misih, Q. Capers, A. Harzman, E.W. Beal, D.M. Agnese, J. Cloyd, M. Dillhoff, V.P. Grignol, J.H. Howard, R. Pollock, L. Shirley, A.M. Terando, T.M. Pawlik. *Ohio State University Wexner Medical Center, Columbus, OH.*

Introduction: The impact of obesity on decision-making in the care of surgical oncology patients is not well understood. We sought to characterize surgeon beliefs and practices in the care of obese cancer patients. Methods: A survey tool was developed and distributed to a national sample of surgical

oncologists to evaluate attitudes and practices in the treatment of obese cancer patients. Data were tabulated and analyses were performed. Results: Among 172 providers who accessed the survey, 157 completed the survey (response rate: 91.3%). Among respondents, 58% were male and the median years in practice was 9.5. Providers treated a wide range of disease sites (hepatopancreaticobiliary, 27%; melanoma/sarcoma, 26%; breast, 21%; colorectal, 10%). Of note, 66% believed obese patients were more prone to present with more advanced disease. Providers were more likely to attribute later disease presentation to patient factors (e.g. "other family/social priorities" or "other medical priorities") versus provider factors (e.g. "received sub-optimal care from previous providers" or "mistrust of the medical community") (28% v 16%, p<0.001). While one-third of providers (34%) noted obesity may sometimes affect the timing of surgery relative to other therapies, most respondents did not believe obesity significantly impacted operative factors such as blood loss (77%), surgical margin status (84%), or ability to perform an adequate lymphadenectomy (77%). In contrast, 34% of respondents did consider obesity a risk factor for worse oncologic outcomes, with 30% and 42% believing obesity was a risk factor for recurrence and worse overall survival, respectively. In addition, 72% of respondents reported obesity was a major risk factor for perioperative complications, yet only 16% reported routinely advising patients to lose weight prior to an operation. Conclusions: Many providers of surgical oncology care believe that obesity has an important impact on disease presentation, risk of operative complications, as well as long-term oncological outcomes. Given the epidemic of obesity, more research is needed on provider attitudes and biases in the care of obese cancer patients.

PT188

Survey of Surgical Oncology Fellowship Graduates, 2005-2016: Insight into Initial Practice S. Ilyas,[1] S. Ruff,[1]* J.M. Hernandez,[1] S.M. Steinberg,[1] C. Cummings,[2] P. Stella,[2] C.R. Schmidt,[2] M. D'Angelica,[2] C. Raut,[2] K. Delman,[2] J.L. Davis.[1] *1. Surgical Oncology Section, TGIB, National Cancer Institute, Bethesda, MD; 2. Society of Surgical Oncology, Rosemont, IL.*

Introduction: Geographic and practice choices of Complex General Surgical Oncology (CGSO) graduates are unreported. We sought to characterize recent graduates' first practices and analyze factors associated with choice of practice. Methods: A NCI- and SSO-approved survey was distributed to graduates of CGSO programs in the U.S. and Canada from 2005-2016. Relevant statistical analyses were undertaken using SPSS. Results: Out of 509 survey recipients, 237 (47%) individual responses were collected. The response rate per graduating year ranged from 35-55%. Forty percent of respondents completed two years of dedicated research in residency and 61% published 1-10 papers. Research sabbaticals during residency increased over the study period. Sixty-two percent of respondents completed fellowship before board certification was available and 76% of all respondents felt it was a professional asset. Forty-six percent described their first job as faculty at a university-based hospital and 62% reported employment where they had no prior history of education or training. Respondents often chose to pursue their first job in a similar environment to their surgery residency. For example, 64% of respondents who trained at an academic center pursued a career in the same setting. Respondents ranked type of practice, personal factors and opportunity for professional advancement (80%, 70%, and 67%, respectively) as top factors influencing job choice (Figure 1). Number of publications prior to fellowship did not correlate with the pursuit of clinical research, however it did predict pursuit of basic science positions. Debt level, dedicated research time, and type of residency were not associated with how respondents ranked top reasons for choice of job. Conclusion: Type of practice, personal factors and opportunity for professional advancement are the most frequent factors cited by CGSO graduates for choosing a first job. More than half of responding graduates began their surgical oncology careers in an academic setting. Understanding factors that influence job choice along with geographic trends related to education, training, and first practice location may also prove informative.

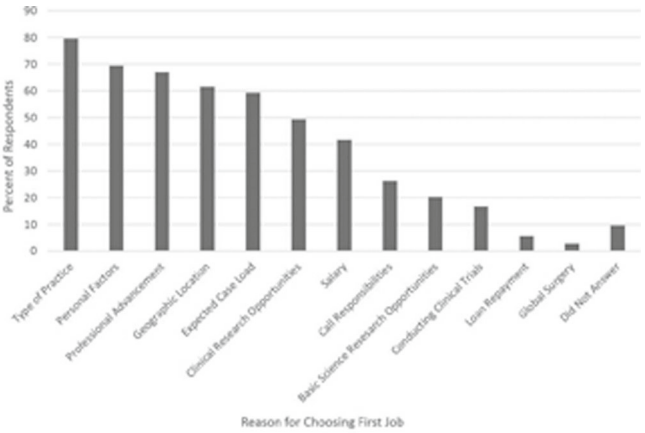

Figure 1: Factors that influenced respondents' choice of first job

PT189

Preoperative Anxiety in Patients Undergoing Surgery for Malignant Disease: Causes and Coping Mechanisms K. Cole,[1]* N. Kulkarni,[2] K. Lehmann.[1] *1. Mercy Hospital, Portland, ME; 2. Atlanticare, Atlantic City, NJ.*

Background: Psychosocial distress screening is an essential component of multidisciplinary cancer care and a requirement for accreditation of cancer programs by the CoC. The perioperative period has been identified as a key time for identifying emotional distress, as interventions may have an impact on outcomes. The purpose of this study is to investigate self-reported anxiety level, sources of anxiety and coping mechanisms in surgical oncology patients at our institution. Methods: All elective major cases performed by a single surgeon in a community hospital setting from January 2016 to May 2017 were included. Patients completed a single-page survey at their pre-op visit, rating their anxiety level (0-10) on a visual analog scale (VAS), and selecting from a list of 9 reasons for anxiety related to surgery. On the day of surgery, a similar survey with a choice of 10 coping strategies was completed. Results: Of 198 patients, 55 (28%) had malignant disease. Similar rates of anxiety history and anxiolytic medication use were reported in patients with benign and malignant disease. The pre-op anxiety score was significantly higher in malignant versus benign disease; 4.5 vs. 3.1 (p=0.0002, student's t-test). The frequency with which various causes for anxiety were reported in both groups is shown in table 1. Of 36 patients in the malignant group who scored ≥4 on the VAS, only 13 (36%) had indicated anxiety as a symptom or diagnosis on their patient intake form. Average DOS score was 3.7, and was not significantly different in malignant versus benign patients. In both groups, the most common coping mechanism reported was "talking with friends or family" (83% of patients in the malignant group; 76% in the benign group). Conclusion: Despite its small size, this study does provide insight into the heightened anxiety experienced by surgical oncology patients and the unique factors contributing to it, and suggests that a typical patient intake form does not adequately screen for anxiety in patients with malignant disease. Future studies should be directed at methods for reducing perioperative distress in this subgroup.

Patient-reported causes of preoperative anxiety

	Malignant disease (n=55)	Benign disease (n=143)	p*
"Worried about unexpected findings during surgery"	33 (60%)	39 (27%)	<0.001
"Worried about my diagnosis and my future health"	28 (51%)	25 (17%)	<0.001
"Worried about pain after surgery"	22 (40%)	42 (29%)	0.15
"Worried about complications of surgery or anesthesia"	18 (33%)	36 (25%)	0.29
"Worried about impact on family members"	18 (33%)	20 (14%)	0.003
"Worried about impact on personal finances"	15 (27%)	29 (20%)	0.29
"Worried about recovery period after surgery"	12 (22%)	44 (31%)	0.21
"Worried about the hospital stay"	8 (15%)	15 (10%)	0.43
"Worried about 'loss of control' while under anesthesia"	3 (5%)	9 (6%)	0.82

Table 1: Frequency with which different causes of pre-operative anxiety were reported by patients scheduled for surgery with malignant vs. benign disease.
*calculated using Chi square test

PT190

Impact of Restricted Fluid Administration During Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemoperfusion on Perioperative Outcomes for Patients with Extensive Carcinomatosis

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Introduction: Excessive fluid administration in the perioperative period has been associated with increased morbidity and mortality, however liberal fluid administration is common practice during CRS/HIPEC for peritoneal malignancies. Methods: Single institution retrospective review of patients undergoing CRS/HIPEC for appendiceal or colorectal carcinomatosis between 2006 and 2017. Patients included had a peritoneal cancer index >=18 and a minimum operative time of 5 hours. Patients receiving cisplatin chemoperfusion were excluded. Patients were grouped into tertiles (low, intermediate, high) based on IV fluids given intraoperatively. Primary outcomes during the index admission were analyzed using the Kruskal-Wallis test and linear regression analysis. Results: A total of 203 patients were analyzed. 69 patients in the low volume group with median fluids received of 12.1 (IQR 10.5 – 13.9) ml/kg/h, 67 patients in the intermediate volume group with a median of 19 (17.4 – 20.8) ml/kg/h and 67 in the high volume group with a median 29.7 (25.7 – 37.5) ml/kg/h. No differences were noted in the incidence of postoperative outcomes including: wound infections (p=0.515), prolonged ileus (p=0.719), delayed gastric emptying (p=0.607), sepsis (p=0.934), acute kidney injury (p=0.695), cardiac complications (p=0.739), or Clavien-Dindo grade 3 and 4 morbidity (p=0.652). A positive trend was noted towards increasing rates of re-intubation (4.3%, 4.5%, 8.9%, p=0.436), readmission to the ICU (10.1%, 16.4%, 20.9%, p=0.225), and unplanned return to the OR (10.1%, 14.9%, 23.9%, p=0.089) with liberal use of intraoperative fluids. A restrictive use of fluids correlated with higher rates of early (POD 0) extubation (81%, 64%, 36%, p=0.001), and shorter (<3 days) ICU stay (42%, 54%, 63%, p=0.048). Amount of volume administered was predictive of extubation (r=6.26, p<0.001) and ICU stay (r=2.36, p=0.014) by regression analysis. Conclusions: Restrictive goal-directed fluid administration during CRS/HIPEC leads to earlier extubation and decreased ICU length of stay for patients with extensive carcinomatosis.

PT191

Inability to Predict Recurrence among Patients with Completely Resected Node Negative Non-Small Cell Lung Cancer

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Introduction: One in five patients who undergo a complete resection of early-stage node-negative non-small cell lung cancer (NSCLC) will recur within two years. However, there is no systematic risk-stratified approach to the early-detection and/or treatment of recurrence for these patients. We sought to develop a prediction model for recurrence based on five previously described clinical variables (tumor size & grade, visceral pleural invasion, lymphovascular invasion, and sublobar resection) and to explore whether the addition of potential biomarkers could enhance prediction (vascular endothelial growth factor-C, miR-1, miR-486, miR-499, miR-30d). Methods: We performed a cohort study of patients from three academic centers with completely resected, node-negative NSCLC (May 2011-Aug. 2014, follow-up through Oct. 2016). Clinical data and RNA samples were collected from resected specimens in a Department of Defense-funded lung cancer biorepository. Cox-regression was used to estimate the two-year risk of recurrence. The optimism-corrected c-statistic was used as our primary measure of model performance. Results: For 173 patients, the distribution of five known risk factors for recurrence was as follows: mean tumor size 3.6 cm, 32% poorly differentiated, 26% visceral pleural invasion, 16% lymphovascular invasion, and 12% sublobar resection. With a median 30 months of follow-up, 49 people experienced a recurrence for a two-year recurrence rate of 23% (Figure, 95% confidence interval [CI] 17-31%). A prediction model using five known risk-factors for recurrence performed only slightly better than chance in predicting recurrence (optimism-corrected c-statistic 0.542, 95% CI: 0.511-0.683). The addition of biomarkers did not significantly change the model's ability to predict recurrence (corrected c-statistic 0.548, 95% CI: 0.519-0.707) (likelihood ratio test p=0.36). Conclusions: We were unable to predict lung cancer recurrence using five known risk factors and potential molecular markers for recurrence. Novel predictors of recurrence are needed in order to personalize the surveillance and treatment of patients with completely resected early-stage lung cancer.

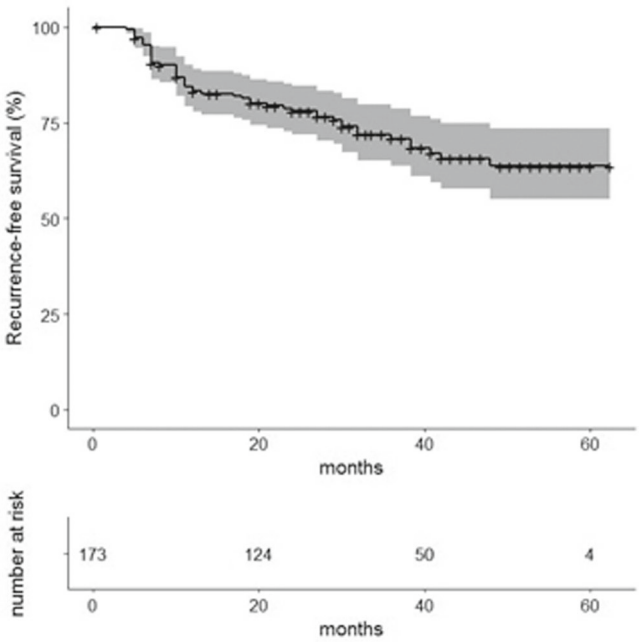

Figure: Kaplan-Meier curve for recurrence-free survival after complete resection of node-negative non-small cell lung cancer.

PT192

Redefining the Learning Curve for Robotic Ivor Lewis Esophagectomy

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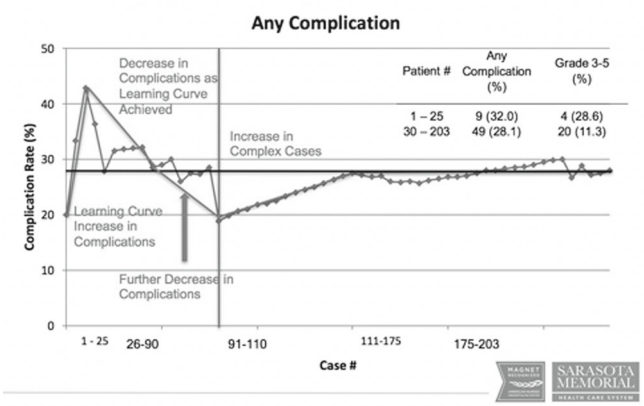
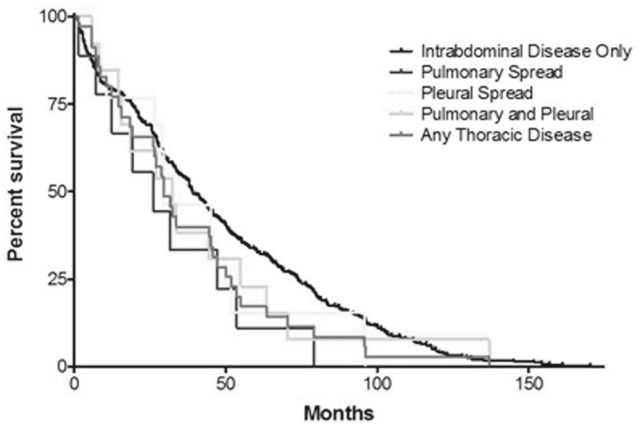
Background: Minimally invasive esophagectomy(MIE) has demonstrated superior outcomes compared to open approaches. The myriad of techniques has precluded the recommendation of a standard approach. The robotic approach has increased steadily. We have previously published our series defining the learning curve for this approach. The purpose of this study is to redefine the learning curve for robotic-assisted esophagogastrectomy with respect to operative time, conversion rates, and patient safety. METHODS: We have prospectively followed patients undergoing robotic-assisted esophagectomy and compared operations performed at our institutions by a single surgeon in successive cohorts. Our measures of proficiency included: operative times, conversion rates, and complications. Statistical analyses were undertaken utilizing Spearman regression analysis and Mann-Whitney U test. Significance was accepted with 95 % confidence. RESULTS: We identified 203 patients (166 (81.8%) male: 37 (18.2%)female) with a median age of 67<30–90⟩ years who underwent robotic-assisted esophagogastrectomy for malignant esophageal disease. One-hundred sixty six were adenocarcinoma, 26 were squamous cell carcinoma and 11 were other. R0 resections was performed in 202 (99.5%) of patients. The median lymph node harvest was 18 (6–63). Neoadjuvant chemoradiation was administered to 157 <77.4 %⟩ patients. A significant reduction in operative times (p <0.005) following completion of 20 procedures was identified <514±106 and 415±91⟩ minutes compared to subsequent 80 cases and further reduced with the subsequent 100 cases 397± 72 minutes p%0.001. Complications decreased after the initial learning curve of 29 cases, p=0.04. However there was an increase in complications after 90 cases in which there was an increase in the Charleson morbidity index, p<0.01 indicating higher risk patients which tapered after case 115. CONCLUSIONS: For surgeons proficient in performing minimally-invasive esophagogastrectomies, the learning curve for a robotic-assisted procedure appears to begin near proficiency after 20 cases however as more complex cases are undertake there appears to be an additional learning curve which is surpassed after 115 cases.



PT193

Thoracic Extension of Appendiceal Mucinous Tumor Following Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy J.D. Beane,[1]* G.C. Wilson,[1] J.M. Sutton,[1] L. Ramalingam,[1] H.L. Jones,[1] J. Pingpank,[1] M. holtzman,[1] A. Zureikat,[1] S. Ahrendt,[2] H. Zeh,[1] D. Bartlett,[1] H. Choudry.[1] *1. University of Pittsburgh Medical Center, Pittsburgh, PA; 2. University of Colorado, Denver, CO.*

Background: Intrathoracic extension of appendiceal mucinous tumor following cytoreductive surgery and heated intraperitoneal chemotherapy (CRS/HIPEC) is rare, difficult to predict, and results in significant morbidity and mortality. The aim of this analysis is to report factors associated with intrathoracic recurrence of appendiceal mucinous neoplasm and compare survival to patients with intraabdominal disease. Methods: A retrospective review of a prospective database was performed to identify patients with appendiceal pseudomyxoma peritonei who underwent CRS/HIPEC between November 2000 and April 2017. Patient demographics, operative details, and tumor specific variables were reviewed. Kaplan-Meier survival curves were generated to compare outcomes in patients with and without intrathoracic extension of their tumor. Results: Of 413 evaluable patients, 41 (9.9%) had intrathoracic tumor involvement. Median age at time of CRS/HIPEC was 56. All patients had appendiceal mucinous tumors and PMP. Most were AJCC Grade II (42.5%), 37.5% were Grade I, and 20% were Grade III. Median PCI score was 25 (7-39) and median CC score was 1 (1-3). Six (14.6%) patients presented with pleural involvement at the time of surgery. Of the 35 remaining patients, there were 13 (37.1%) with pulmonary metastases, 9 (25.7%) with pleural progression, and 13 (37.1%) with both pleural and pulmonary progression. Of the 22 patients with pleural progression, 7 (31.9%) had an ipsilateral diaphragm resection at the time of CRS. The median survival in patients with pulmonary metastases was 26.8 months, 29.6 months for those with pleural progression, 32.6 months for patients with both pleural and pulmonary disease, and 39.3 months for those without thoracic recurrences. Conclusion: While thoracic extension of appendiceal mucinous tumor is rare, it portends a poorer prognosis. Patients who undergo diaphragm resection at the time of cytoreductive surgery may benefit from routine surveillance for pleural progression of disease.



PF2

Minimally Invasive Surgery for T4 Colon Cancer is Associated with Better Outcomes in the National Cancer Database F. El-Sharkawy,[1]* L. Bijelic,[2] T.A. Plerhoples,[2] C. Liu,[2] C. Birisan,[2] E.L. Emery,[2] D.T. Collins,[2] V. Gushchin.[1] *1. Surgical Oncology, Mercy Medical Center, Baltimore, MD; 2. Inova Fairfax Hospital, Falls Church, VA.*

Introduction: Minimally invasive surgery for T4 colon cancer remains controversial due to a lack of clinical trials or large datasets assessing outcomes specifically in T4 tumors. We compared outcomes in pT4 colon cancer patients treated with minimally invasive surgery (MIS) or open surgery (OS) and examined factors associated with survival. Methods: The National Cancer Database (NCDB) was used to analyze outcomes by intention to treat analysis in patients undergoing MIS or OS for pT4 colon cancer between 2010 and 2014. Patients aged 18 years or older with Stage II or III adenocarcinoma of the colon were included. Cases with missing data regarding histology, stage, surgery or survival were excluded. A Cox proportional hazard model assessed the impact of various factors on patient survival and a logistic regression model evaluated 30-day outcomes. Results: A total of 21,998 patients with pT4 colon cancer were identified. Of these, 7,532 (34.2%) underwent MIS (includes MIS converted to open) and 14,466 (65.8%) underwent OS. Postoperative mortality at 30 days was 3.4% for MIS and 7.0% for OS (p<0.001). The rate of readmission within 30 days was not significantly different between MIS and OS (10% vs. 9.6%; p=0.56). When controlling for clinically relevant prognostic factors (AJCC stage, Charlson comorbidity score, resection margin status, and adjuvant chemotherapy), MIS was associated with significantly longer survival compared to OS (Table 1). Median overall survival was 57.8 months for MIS and 41.7 months for OS (p<0.001). The incidence of positive surgical margins was lower for MIS compared to OS (18.6% vs 22.3%; p<0.001). Conclusions: Our study is the largest dataset comparing MIS to OS for pT4 colon cancer. It shows that MIS is associated with a longer overall survival compared to OS. Acknowledging the limitations of database analyses, pT4 colon cancer should not be a contraindication for MIS, and this provides rationale for prospective studies.

Impact of clinical factors on patient survival and 30-day postoperative readmission

	Overall Survival			30-day Readmission		
Variables	Adjusted HR	95% CI	p-value	Adjusted OR	95% CI	p-value
Open surgery	1.33	1.27 - 1.4	<0.001	0.92	0.83 - 1.02	0.1
pStage III	2.08	1.99 - 2.19	<0.001	1.11	1 - 1.22	0.05
Systemic Therapy Before Surgery	0.5	0.38 - 0.65	<0.001	0.94	0.58 - 1.52	0.79
Systemic Therapy After Surgery	0.44	0.42 - 0.47	<0.001	0.92	0.82 - 1.03	0.14
Radiation Before Surgery	0.96	0.59 - 1.57	0.87	0.53	0.18 - 1.59	0.26
Radiation After Surgery	0.86	0.75 - 0.98	0.02	0.88	0.69 - 1.14	0.33
Comorbidity (Charlson) score = 1	1.1	1.04 - 1.15	<0.001	1.05	0.94 - 1.18	0.37
Comorbidity (Charlson) score ≥ 2	1.47	1.37 - 1.57	<0.001	1.35	1.15 - 1.59	<0.001
Colectomy + Contiguous Organ	1.06	1 - 1.13	0.04	1.15	1.01 - 1.3	0.03
Proctocolectomy	0.9	0.54 - 1.49	0.67	2.94	1.56 - 5.53	0.001
Proctocolectomy + Contiguous Organ	0.98	0.81 - 1.2	0.86	1.27	0.89 - 1.81	0.18
Microscopic residual tumor	1.49	1.4 - 1.58	<0.001	1.26	1.09 - 1.45	0.002
Macroscopic residual tumor	2.36	2.04 - 2.74	<0.001	1.52	1.07 - 2.15	0.02

PF3

Routine Splenic Flexure Mobilization Increases Compliance with Pathologic Quality Metrics in Patients Undergoing Low Anterior Resection T.J. Mouw,[1]* C.L. King,[2] J.H. Ashcraft,[1] J.D. Valentino,[1] P.J. DiPasco,[1] M. Al-Kasspooles.[1] *1. Department of General Surgery, University of Kansas Medical Center, Kansas City, KS; 2. The University of Kansas School of Medicine, Kansas City, Kansas City, MO.*

Background: The need for mandatory splenic flexure mobilization (SFM) has been a topic of debate among surgeons treating distal colon and rectal cancers. Proponents of mandatory SFM argue that additional mobilization facilitates creating a tension-free anastomosis, however this is weighed against the longer operative times and the morbidity of increased dissection. Very little is known about how the specifics of surgical technique impacts oncologic outcomes and quality metrics. Methods: This study is a retrospective chart review of patients selected via a query of the University of Kansas Medical Center electronic medical record (EMR). Patients who had undergone high anterior resection (HAR) and low anterior resection (LAR) for distal colon or rectal adenocarcinoma during billing years 2009-2016 were included. A manual chart review was conducted to extract basic patient demographic data

and pathology data including surgical margins and node yield. The operative reports were also read to determine whether SFM had been performed. Primary outcomes were node yield > 12 and length of lowest longitudinal margin. A secondary analysis was conducted to determine if patient factors were likely to influence the decision to perform SFM. Results: There were 146 patients who met inclusion criteria. SFM was associated with wider longitudinal margins (3.52cm vs 2.51cm in LAR, 5.37cm vs 3.77cm in HAR, p <0.001). Additionally, SFM was associated with a decreased rate of inadequate nodal staging in patients undergoing LAR (3.7% vs 19.3% p=0.008). Conclusions: The decision to perform SFM can impact surgical quality metrics in patients undergoing distal colon and rectal resections. These findings support the routine use of SFM when surgically treating distal colon and rectal cancers. Further study is warranted to determine if these quality and pathology differences translate into differences in oncologic outcomes.

PF4

Anti-Oncogenic Function of MAF in Colorectal Cancer T. Hata,* H. Yamamoto, H. Takahashi, K. Iso, N. Haraguchi, J. Nishimura, T. Hata, C. Matsuda, T. Mizushima, Y. Doki, M. Mori. *Osaka University Graduate School of Medicine, Suita, Japan.*

Introduction; c-Maf (MAF) is an AP-1 family DNA binding transcription factor, a member of large MAF, involved in gene expression and differentiation in the retina, lens, sensory neuron, and immune T cells. In terms of cancer, previous studies showed that MAF acted as an oncogene in breast cancer and multiple myeloma, however, its function in colorectal cancer (CRC) has not been established at present. The aim of study is to investigate the role of MAF in CRC and analyze the underlying mechanism of its regulation. Materials and methods; Immunohistochemistry was performed with a subset of resected specimens from patients who received colorectal surgery at our Osaka University. In vitro experiments, we performed proliferation assay using a normal intestinal cell line and CRC cell lines with wild-type p53 and with null p53. Cells were transfected with MAF siRNA, MAF expression vector, or mutated p53 (R175H, R248W) expression vector. Results; Immunohistochemistry for MAF protein revealed that nuclear MAF expression was significantly decreased in tumor tissues as compared to the normal counterparts (P=0.024), which was validated with the public database. In vitro, knockdown of MAF increased cell proliferation and colony formation in normal intestinal cells, IEC18. Overexpression of MAF in p53-wild HCT116 and LS174T CRC cells led to significantly decreased cell proliferation, while no effect was observed in p53-null HCT116 cells. In immunohistochemistry, we also found that MAF expression was inversely correlated to intense p53 staining, compatible to the existence of mutant p53 (P=0.023). In vitro experiment, introduction of mutated p53 (R175H, R248W) in p53-null HCT116 cells lead to a decrease of MAF expression. In addition, it also upregulated the expression of miR-155, which targets MAF by binding to the 3'-UTR of its mRNA. Conclusions; Our findings suggest that MAF protein appears to function as tumor suppressor rather than oncogene in CRC. MAF may suppress cell proliferation in cooperation with wild-type p53, and p53 mutation may suppress MAF expression through miR-155 upregulation, which may further enhance malignant potential.

PF5

Reprofiling of Antimalarial Drug is a Novel Therapeutic Target for Colon Cancer Stem Cell M. Takeda,[1]* N. Haraguchi,[1] H. Takahashi,[1] N. Miyoshi,[1] T. Hata,[1] C. Matsuda,[1] T. Mizushima,[2] H. Yamamoto,[3] Y. Doki,[1] M. Mori.[1] *1. Department of Surgery, Osaka University Graduate School of Medicine, Osaka, Japan; 2. Department of Therapeutics for Inflammatory Bowel Diseases, Graduate School of Medicine, Osaka University, Suita, Japan; 3. Department of Molecular Pathology, Division of Health Sciences, Graduate School of Medicine and Health Science, Osaka University, Suita, Japan.*

Introduction; Cancer stem cells (CSCs) are deeply involved in various biological properties such as cancer development, resistance to treatment and recurrence, and are the most important target cells in cancer treatment. The metabolic mechanism of reactive oxygen species (ROS) plays an important role in the chemo-radiation resistance and maintenance of cancer stem cells. In the previous study, we identified LAMP1, a lysosome marker, as a marker of lower ROS expressing colon cancer cells, hence we focused on autophagy and lysosomal activity of CSCs in this study. We also focused on colon CSC targeting by drug repositioning. Materials and Methods; Autophagy and lysosome were labeled by LC3B imaging vector and Lysotracker respectively. Flowcytometry, single cell sphere formation assay, limiting dilution assay, chemosensitivity assay were performed. Chemical screening and isobologram analysis were performed. Additionally, anti-tumor effect was assessed. Results; Both $LC3B^+$ and $Lysotracker^+$ cells were characteristically existed in $CD44V9^+$/$CD133^+$ CSC fraction as a small cell subpopulation. $Lysotracker^+$/$CD44v9^+$ cells showed higher sphere formation and tumorigenic activity than $LC3B^+$/$CD44v9^+$ cells. During the process of screening of antimalarial drugs, anti-lysosomal effect of mefloquine was identified. Mefloquine treatment significantly decreased $CD44v9^+$/ $CD133^+$ cell number than representative antimalarial drugs, chloroquine and hydrochloroquine. Mefloquine demonstrated the synergic effect on oxaliplatin and irinotecan, and induced caspase mediated apoptosis via upregulation of intracellular ROS level. In the HCT116 colon cancer cell line and two patient-derived colon cancer tissue xenografted (PDX) mice, combined treatment of mefloquine with oxaliplatin drastically abrogated the tumorigenic activity of cancer cells. Conclusions; Cells of higher lysosome activity possess higher stem cell like properties than autophagy activated cells in colon cancer. Lysosomal activity in CSCs is a promising therapeutic target, and repositioning of mefloquine to colon cancer together with conventional chemotherapeutic agent will be a promising strategy for cure of colon cancer.

PF7

Does Positive Radial Resection Margins in Locally Advanced Colorectal Cancer Correlate with Development of Peritoneal Carcinomatosis? A Propensity Score Matched Comparison S. Thorp,[1]* A. Witte,[2] m. chung,[1] M. Assifi.[1] *1. Division of Surgical Oncology, Department of Surgery, Spectrum Health Medical Center, Grand Rapids, MI; 2. Michigan State University College of Human Medicine, Lansing, MI.*

Background The peritoneum is a common site of disease spread in colorectal cancer (CRC). There is little data on the role of positive radial resection margins (+RM) as a risk factor for the development of peritoneal carcinomatosis (PC). This study examined the development of PC in those patients with +RM compared to negative radial resection margins (-RM) patients. Methods Seventy-seven consecutive patients with locally advanced, nonmetastatic CRC with +RM between 2010 and 2015 were case matched (age, sex, tumor site, stage) using propensity scoring to 77 patients with negative radial resection margins (-RM). Patients with unknown PC status or less than 6 months follow-up, as well as prior CRC, were excluded from analysis. Results Data for 71 +RM and 74 -RM patients were analyzed. Demographic and clinical variables were comparable between the groups (p>0.05). Median follow up was 37.7 (5.2 – 84.4) months. No significant differences were noted for histologic type, tumor grade, lymphovascular invasion, completeness of mesorectal excision, macroscopic perforation or microsatellite instability. There was no significant difference in the rate of development of PC (+RM 7/71 (9.9%) vs -RM 3/74 (4.1%); p=0.203) or time to development of PC (p=0.161) per Kaplan-Meier analysis. Overall median time to PC was 20 (5.2 – 43.6) months. Conclusion Patients with +RM developed PC more than twice as frequently as –RM. This trend did not meet significance likely due to low study power. Further collaborative study is needed to define the role of +RM as a risk factor for PC development in CRC patients.

PF8

Feasibility of Extended Dissection of Lateral Pelvic Lymph Nodes During Laparoscopic Total Mesorectal Excision in Patients with Locally Advanced Lower Rectal Cancer: a Single-Center Pilot Study After Neoadjuvant Chemotherapy Y. Aisu,* T. Hori, T. Kitano, Y. Takamatsu, Y. Kimura, D. Yasukawa, S. Kato, Y. Kadokawa, T. Hata, T. Ito, T. Machimoto, T. Yoshimura. *Tenriyorozusoudanjo Hospital, Tenri, Japan.*

Background The feasibility of additional dissection of the lateral pelvic lymph nodes (LPLNs) in patients undergoing total mesorectal excision (TME) combined with neoadjuvant chemotherapy (NAC) for locally advanced rectal cancer (LARC) is controversial. The use of laparoscopic surgery is also debated because of its technical difficulties. In the present study, we evaluated the utility of laparoscopic dissection of LPLNs during TME for patients with LARC and metastatic LPLNs after NAC. Methods Twenty-five patients with LARC with swollen LPLNs who underwent laparoscopic TME and LPLN dissection were enrolled in this study. The patients were divided into two groups: those patients with NAC (n = 19) and without NAC (n = 6). Our NAC regimen involved four to six courses of FOLFOX plus panitumumab, cetuximab, or

bevacizumab. Results The operative duration was significantly longer in the NAC group than in the non-NAC group (648 vs. 558 minutes, respectively; p = 0.022). The rate of major complications, defined as grade ≥3 according to the Clavien–Dindo classification, was similar between the two groups (15.8% vs. 33.3%, respectively; p = 0.4016). No conversion to conventional laparotomy occurred in either group. In the NAC group, a histopathological complete response was obtained in two patients (10.5%), and a nearly complete response (Tis N0 M0) was observed in one patient (5.3%). Although the operation time was prolonged in the NAC group, the other perioperative factors showed no differences between the two groups. Conclusion In patients with LARC who received NAC, laparoscopic dissection of LPLNs was not accompanied by disadvantageous perioperative factors except for a longer operative time. Laparoscopic LPLN dissection is feasible in patients with LARC and clinically swollen LPLNs, even at the state after NAC.

PF9

Synergistic Anti-Tumor Efficacy of Toll-like Receptor and CD40 Stimulation with an Immunogenic Neoantigen Vaccine T. Hoki, T. Yamauchi, C. Eppolito, A.J. Francois, K. Odunsi, F. Ito.* *Roswell Park Cancer Institute, Buffalo, NY.*

Cancer neoantigens are derived from nonsynonymous, tumor-specific mutations that create de novo epitopes for T cells, and bypass central thymic tolerance. Although they are highly immunogenic and induce immune responses in humans, the overall success of vaccination studies that target cancer neoantigens has so far been limited. To boost cell-mediated immunity against epithelial tumors, toll-like receptor (TLR) agonists have been implemented as adjuvants. Signaling through CD40 has also been used with promising results. Furthermore, combinatorial stimulation of TLRs and CD40 generates expansion of $CD8^+$ T cells targeting nonmutated self-antigens compared with either agonist alone. However, therapeutic efficacy of combined TLR/CD40 stimulation in the setting of neoantigen vaccine remains elusive. To this end, we used murine MC38 colon adenocarcinoma cells that harbor a single-epitope mutation within the Adpgk protein with the neo-epitope presented in MHC-I $H\text{-}2D^b$ molecules. C57BL/6 mice were inoculated subcutaneously with MC38 cells. MC38 tumor-bearing mice were treated with soluble Adpgk mutant epitope in combination with TLR agonist, anti-CD40 antibody or both. Therapeutic vaccination with the Adpgk mutant peptide combined with TLR agonist and an anti-CD40 antibody (TLR/CD40) significantly improved survival compared with TLR agonist or anti-CD40 antibody alone. This was associated with expansion and differentiation of $CD8^+$ T cells in the periphery as well as in the tumor microenvironment. Significantly increased terminally differentiated neoantigen-specific $CD8^+$ T cells in blood and spleen were identified using the tetramer staining assay. Interestingly, frequency of neoantigen-specific $CD8^+$ T cells in blood was inversely correlated with the tumor volume, suggesting epitope spreading and broadening T-cell clonality induced by TLR/CD40 stimulation. These studies provide the rational basis for the use of combined TLR and CD40 agonists together as essential adjuvants to optimize vaccines designed to elicit therapeutic immunity against cancer neoantigens.

PF10

Body Weight and Composition Changes, Primary Tumor Side and Resection As Survival Predictors in Metastatic Colorectal Cancer J. Franko,[1]* T. Graff,[1] C. McClairen.[2] *1. Surgical Oncology, Mercy Medical Center, Des Moines, IA; 2. Meharry Medical College, Nashville, TN.*

BACKGROUND: Common symptoms of metastatic colorectal cancer (mCRC) are sarcopenia and weight loss. We investigated whether weight loss, sarcopenia and primary tumor resection can predict overall survival among patients (pts) with mCRC. METHODS: Consecutive pts newly diagnosed with mCRC in a community hospital between 2012-2014 we reviewed. We gathered initial and 6-month follow up data on weight, standardized muscle mass measure (estimated psoas muscle area/m^2 height, sEPA) and subcutaneous fat (SQ). RESULTS: There were 109 pts (age 66.9±14.5, range 37-93 years). Chemotherapy recipients were younger (n=59, 61.2±13.3 years) and survived longer (22.3 versus 5.3 months, p<0.001) as compared to best supportive care patients (n=50, 73.6±13.0 years, p<0.001). There were no baseline and 6-month differences between pts with resected versus in situ primary tumor in age (p=0.074), baseline weight (p=0.728) or percent weight loss (p=0.404), albumin (p=0.322), hemoglobin (p=0.301), creatinine (p=0.791), initial standardized EPA (p=0.866), percent of sEPA loss (p=0.952), and percent subcutaneous thickness loss (p=0.477). Cohort was further dichotomized by median anthropometric changes at 6 months: -7.1% for weight loss, -6.2% sEPA, -3.3% SQ fat. Cox proportional hazard models demonstrated that anthropometric measures and receipt of systemic chemotherapy were the strongest predictors of survival with their predictive strength surpassing traditional predictors as age, tumor sidedness, primary tumor resection, initial BMI and serum albumin level. CONCLUSION: Weight loss and anthropometric changes are strongly associated with shorter survival. Prognostic characteristics of loss of weight, muscle and fat should be investigated further using more robust datasets.

Regression model for overall survival

	aHR	95% CI for aHR	p
Age (per year)	1.010	0.975-1.045	0.571
Gender	0.660	0.236-1.843	0.428
Left side vs right (base right)	0.864	0.350-2.133	0.752
Chemotherapy	0.262	0.865-0.794	0.018*
BMI	0.486	0.059-3.962	0.501
Initial serum albumin	1.228	0.508-2.966	0.647
≥6% psoas muscle loss	1.800	0.685-4.728	0.233
≥3% subcutaneous fat loss	4.113	1.577-10.724	0.004*
≥7% weight loss	2.859	1.043-7.835	0.041*

PF11

Expansion of Tumor-Infiltrating Lymphocytes and Their Potential for Application to Adoptive Cell Therapy in Patients with Colorectal Cancer S. Kim,[1] J. Baek.[2]* *1. Reserch and Development center, GNSBIO, Seongnam-si, Korea (the Republic of); 2. Gachon University Gil Medical Center, Incheon, Korea (the Republic of).*

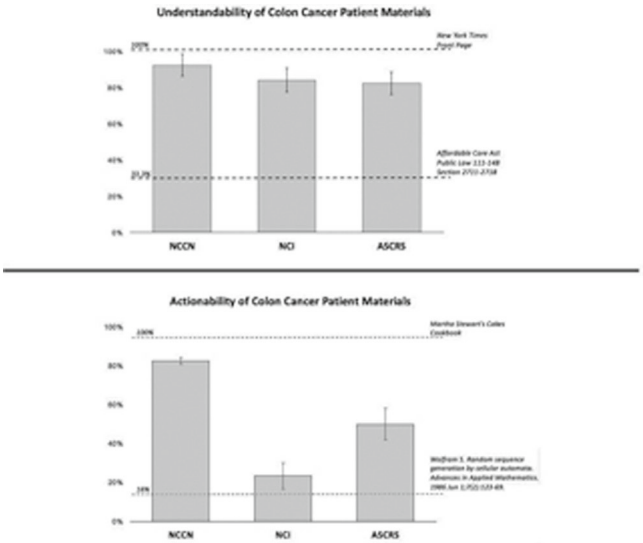
Purpose: Tumor-infiltrating lymphocytes (TILs) are immune cells that composed of several types of mononuclear cell including T cells, B cells, NK cells, macrophages and dendritic cells. They can be found in stroma and within the tumor tissue. Adoptive cell therapy (ACT) of ex vivo expanded TILs has been successful in treating a considerable proportion of patients with metastatic melanoma. In addition, some patients with several other solid tumors have been recently reported to have benefited clinically from such ACT. The purpose of this study is to obtain TILs from patients with colorectal cancer (CRC) and to evaluate their potential as an immunotherapeutic modalities. Methods: Samples of resected colorectal cancers were collected from 20 patients. Tumors were minced into fragments and cultured in media containing high dose interleukin-2 (IL-2) for up to 5 weeks. T cell phenotype, activation markers, and reactivity were measured. Results: TILs were successfully isolated from at least one plated fragment in all of the 20 patient tumors (100 %) in the presence of high dose IL-2 (6000 IU/mL) after 2 to 3 weeks of culture. TILs yield varied between patient samples with an average yield of 1.37×10^6 TILs from an average of just over 20 fragments per patient. 18 samples of the 20 (90 %) measured gave rise to at least 10 million TIL, the minimum number required for initiation of a clinical scale rapid expansion protocol (REP). Extrapolated to the 48 fragments typically set up during a clinical scale expansion, the average yield increased to over 65.8 million TILs. The majority of these expanded TIL were CD8+ T cells and CD4+ T cells. Especially, greater than 80 % of CD8+ T cells were producing IFN-g and CD107a Conclusion: In this study, we successfully expanded TILs from CRC tissue and showed that the ex vivo expanded TILs contained mostly effector memory T cells and they were found the functional potential to elicit an anti-tumor response. These results together indicate that TILs could be alternative medicine for patients with refractory CRC.

PF12

Colon Cancer Patient Education Materials: Assessing Understandability and Actionability Using a Validated Assessment Tool R. Kang,[1]* J.A. Columbo,[1] R. Turjoman,[2] A.M. Habib,[2] S.W. Trooboff,[1] P.P. Goodney,[1] S.L. Wong.[1] *1. Dartmouth-Hitchcock Medical Center, Lebanon, NH; 2. The Dartmouth Institute, Hanover, NH.*

Background: Colon cancer patients are better able to participate in their care if they understand their diagnosis and its implications. Printed patient education materials (PEM) are often used to complement the information provided by surgeons, but whether available materials inform patients in an actionable way is not known. Our objective was to assess the understandability and actionability of colon cancer PEM. Methods: We reviewed patient

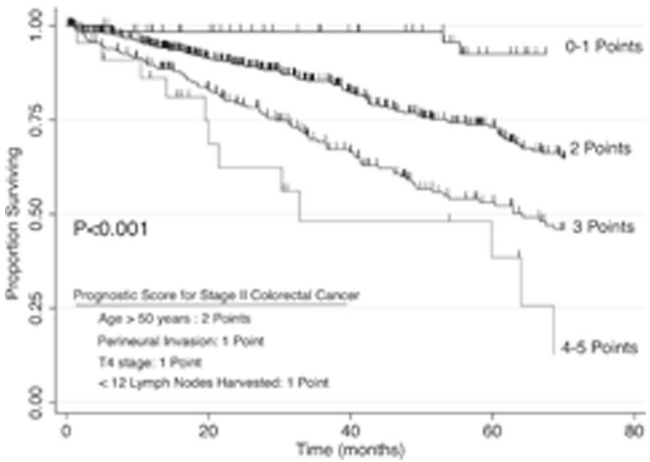
materials from the National Comprehensive Cancer Network (NCCN), the National Cancer Institute (NCI), and the American Society of Colon and Rectal Surgeons (ASCRS). We assessed the reading level using the Flesch–Kincaid readability formula, and used the Patient Education Material Assessment Tool (PEMAT), a validated tool from the AHRQ, to evaluate and score understandability and actionability (range 0% to 100%, higher scores preferred). Highly actionable materials identify what the patient can do based on the information given. Four independent reviewers evaluated all colon PEM. Interrater per-item agreement was evaluated using the kappa (k) statistic. To provide context, two reviewers evaluated nonmedical materials as comparators with PEMAT. Results: The reading grade levels for the NCCN, NCI, and ASCRS materials were 6.8, 8.9 and 10.6, respectively. The understandability score was highest for NCCN (mean ± SD: 92.2 ± 6.1%) and lowest for ASCRS materials, 82.2 ± 6.3%. For context, the New York Times scored 100% for understandability, while the Affordable Care Act-Sections 2711-2718 scored 33.3% (Figure 1). Actionability scores were higher for NCCN materials (82.5 ± 1.7%) than ASCRS and NCI, 50.0 ± 8.2%, and 23.3 ± 6.7%, respectively. Interrater agreement was moderate (k 0.21-0.52, p<0.005). Conclusion: Two of the three colon cancer PEM were written at a higher than 8th-grade reading level. While all materials scored well in the understandability domain, there was substantial variation in actionability. The NCCN materials scored highest, while the NCI materials were not as actionable. Surgeons should consider these qualities when using patient-education materials as adjunct to in-person counseling.



PF13

Prognostic Clinical Score for Stage II Colon Cancer: Who Should Receive Adjuvant Chemotherapy? T. Tran,* A. Ejaz, V.K. Maker, A.V. Maker. *University of Illinois in Chicago, Chicago, IL.*

Introduction: Adjuvant chemotherapy is not routinely recommended for patients with stage II colon cancer after resection, however, guidelines recommend consideration in the setting of certain high-risk pathological features. Quantification of "risk" is challenging and adjuvant chemotherapy use remains a clinical dilemma. The objective of this study is to design a prognostic score to identify high-risk patients for clinical decision making. Methods: Patients with stage II colon cancer with histologically proven adenocarcinoma who underwent curative intent resection were retrospectively identified and analyzed from a multi-institutional database. Kaplan Meier method was used to estimate survival. Univariate and multivariate Cox regression analyses were performed to identify predictors of poor survival to incorporate into a clinical prognostic score. The prognostic performance of the clinical score was internally validated using the area under the curve (AUC). Results: A total of 862 patients who underwent curative intent treatment for stage II colorectal cancer were identified. The median age was 74 years and 52% were female. The median number of lymph nodes examined was 17 nodes. Only 3.8% had R1 margins, 4% had perineural invasion, and 12% had high-grade tumors. Four risk factors were identified as independent predictors of poor survival on multivariate analysis: age greater than 50 years, insufficient lymphadenectomy (<12 nodes), perineural invasion, and T4 stage. Assigning points based on each variable's beta coefficient, a clinical risk score for stage II colon cancer was created. The 5-year survival rates were 92% for 0-1 points, 73% for 2 points, 53% for 3 points, and 38% for 4-5 points (P<0.001). The model was validated and demonstrated an AUC of 0.64, indicating good discriminatory and predictive ability for the prognostic score (P<0.001). Conclusion: A clinical risk score was developed for stage II colon cancer patients that can quantify risk of death based on clinicopathologic features. This clinical score adequately stratifies patients into 4 risk groups that may help clinicians to facilitate individualized treatment and improve selection for adjuvant therapy.



PF14

Circumferential Tumor Growth is a Negative Predictive and Prognostic Factor for Rectal Cancer Patients Treated with Neoadjuvant Chemoradiation G. Karagkounis,* D. Liska, M.F. Kalady. *Colorectal Surgery, Cleveland Clinic, Cleveland, OH.*

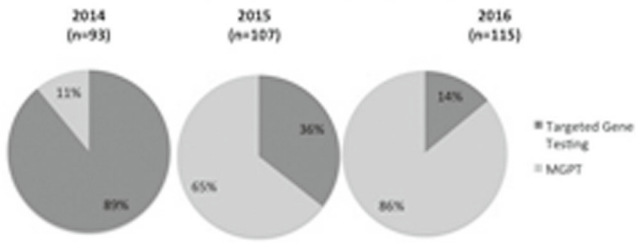
Objective Axial tumor location within the rectum (anterior, posterior, lateral, or circumferential) is known to be associated with specific operative challenges and distinct patterns of recurrence. However, its importance in patients who received neoadjuvant chemoradiation (nCRT) is less clear. The purpose of this study was to evaluate the correlation between axial tumor site and nCRT response and the impact of site on survival in patients with rectal cancer. Methods Patient demographics, tumor characteristics, and nCRT regression scores were assessed from rectal cancer patients treated by nCRT followed by surgery at a single institution. Tumor location was determined by the surgeon at the pretreatment visit based on clinical examination and imaging. Survival analyses were performed using Cox proportional hazards models. Results Three hundred ninety-five patients were included (median age 57 years, range 26-85, 28.9% female). Rectal cancer location was as follows: anterior in 109 (27.6%), posterior in 102 (25.8%), lateral in 106 (26.8%) and circumferential in 78 (19.8%) patients. Median follow-up was 5.2 years. There was no association between axial location and nCRT response, but pathologic complete response was significantly less common in patients with circumferential tumors (9.0% vs 23.3%, p=0.005). There was no survival difference between the different non-circumferential locations. However, circumferential tumors were associated with worse overall survival on univariable analysis (hazard ratio 2.0, 95% confidence interval 1.43-2.90) and on multivariable analysis (HR 1.68, 95% confidence interval 1.16-2.43), along with poor differentiation, worse nCRT response score, greater pathologic stage, positive margin, and abdominoperineal resection. Conclusion Circumferential rectal cancers are less likely to obtain a complete pathologic response to nCRT and are independently associated with worse long-term survival. This study provides important predictive and prognostic information, particularly for surgeons or patients wishing to pursue watch and wait approaches.

PF15

The Evolving Application of Panel-Based Tests for Defining Hereditary Colorectal Cancer Susceptibility C. Scally,* M. Rodriguez-Bigas, S.T. Nguyen, G. Chang, B.K. Bednarski, C.A. Messick, P.M. Lynch, E. Vilar Sanchez, Y. You. *University of Texas MD Anderson Cancer Center, Houston, TX.*

Introduction: Multigene panel testing (MGPT) evaluates multiple genes simultaneously and has become an efficient option for identifying germline cancer susceptibility. MGPT offers particular advantages in cases with ambiguous phenotype or multiple differential diagnoses, while traditional targeted gene testing (TGT) is optimal for cases with classic phenotypes. We aimed to investigate the evolving integration of MGPT with TGT for assessing hereditary susceptibility to colorectal cancer (CRC) over time. Methods: Distinct index probands with CRC who had been referred by their treating physicians for genetic risk assessment and underwent clinically indicated germline genetic testing between 2014-2016 (N=315) were identified from a prospectively maintained database. MGPTs of 6-67 genes were performed at four commercial laboratories. The evolving use of and findings from MGPT vs. TGT were examined using chi-squared test. Results: Overall, hereditary CRC susceptibility was evaluated through MGPT in 178 (56.5%) and through TGT in 137 (43.5%) patients. MGPT utilization increased over time, from 11% in 2014 to 86% in 2016 (Figure; p<0.001). There was no significant change over time in the median age of patients tested (47 years, interquartile range: 21-80) nor in the proportion of colon vs. rectal cancers (74 vs. 26%; p=0.52). A pathogenic mutation was detected in 91 (28.9%) patients, 53 (58.2%) through TGT and 38 (41.8%) through MGPT. Mutations were in traditional high-penetrance CRC susceptibility genes in all but 4 patients (BRCA2, 4.4%). At least one variant of unknown significance (VUS) was detected in 46 (14.6%) patients, the vast majority (38, 82.6%) through MGPT. Conclusions: MGPT has rapidly been integrated with TGT for clinical assessment of germline CRC susceptibility. Clinically indicated testing by mix of MGPTs and TGTs detected pathogenic mutation in 28.9% of high-risk CRC patients. The application of MGPT must be coupled with clinical cancer genetics expertise to ensure appropriate triage and selection of patients for MGPT vs. TGT in order to maintain a high diagnostic yield of clinically actionable pathogenic mutations, while minimizing the frequency of VUS.

Figure. Relative Use of Multigene panel testing vs targeted gene testing by year



PF16

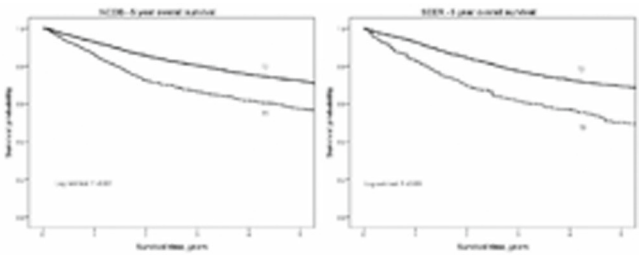
Does Increased Erythrocyte Phospholipid Membrane Arachidonic Acid Levels Correspond to Increased Risk for Colorectal Adenomas? C. Isom,* M. Shrubsole, Q. Cai, W. Zheng, H. Murff. *Vanderbilt University Medical Center, Nashville, TN.*

Background: Previous studies have shown a link between increased levels of arachidonic acid (ARA) and colorectal adenomas. Levels of ARA are affected by both diet, and thus susceptible to potential confounders, as well as genetics. To determine if a casual association exists between erythrocyte membrane ARA levels and colorectal adenoma we conducted a Mendelian Randomization (MR) analysis using a functional genetic variant in Fatty Acid Desaturase (FADS) (rs174547) as an instrumental variable. By using genetic markers as a proxy for an environmental exposure, the MR design helps to minimize potential confounding factors. Variants in FADS have been shown to explain almost 30% of the additive variance in tissue ARA levels. Methods: A case-control study was performed using the Tennessee Colorectal Polyps Study. Patients were matched on age, gender, race, site of colonoscopy and time frame. Cases were defined as any colorectal polyp on colonoscopy (n=909) and controls were polyp free (n=855). A logistic regression was conducted using rs174547 regressed on erythrocyte membrane ARA as an instrumental variable with the dependent variable being the presence of a colorectal adenoma on colonoscopy. Results: Cases were statistically older, (58.92yrs vs 56.6yrs, p<0.0001), more likely to be a current drinker (47.41% vs 19.77%, p=0.001) and to have a history of smoking (77.01% vs 66.9%, p<0.0001). The presence of the G allele showed a statistically significant dose increase in ARA levels (p<0.0001). The GG allele was more common in African-Americans compared to whites (p<0.0001). However between all three alleles there was no statistically significant difference in the following: age, sex, alcohol use, BMI, or NSAID use. A strong statistically significant correlation between the ARA levels and rs174547 alleles (p<0.0001) was found. We found no evidence of an association between our instrumental variable and colorectal adenomas (p=0.9268). Conclusion: In our Mendelian Randomization study increased arachidonic acid levels were not associated with of the risk of colorectal adenomas.

PF17

A Population-Based Validation of the New AJCC Subclassification of Anal Squamous Cell Cancer Stage II A and B P. Goffredo,[1]* M. Garancini,[2] T. Robinson,[3] J.M. Frakes,[3] H. Hoshi,[1] I. Hassan.[1] *1. University of Iowa Hospitals & Clinics, Iowa City, IA; 2. University of Milano-Bicocca, Monza, Italy; 3. Moffitt Cancer Center, Tampa, FL.*

Intro: The 8th edition of the American Joint Committee on Cancer (AJCC) has updated the staging system of anal squamous cell cancer (ASCC) by subdividing stage II into A (T2N0) and B (T3N0). This was based on the RTOG9811 trial in which T3 tumors (>5 cm) were found to have worse overall (OS) and disease free survival (DSS) than T2 cancers (between 2 and 5 cm). We aimed to validate this new subclassification within the general ASCC population utilizing two population-based databases. Materials: The National Cancer Database (NCDB) [2004-2014] and the Surveillance Epidemiology and End Results (SEER) database [1988-2013] were queried to identify patients with stage II ASCC. Overall survival was compared between patients with T2 vs T3 tumors via log-rank test and Cox proportional hazards regression. Results: A total of 6,651 and 2,579 stage II A and 1,777 and 641 stage IIB patients were identified in the NCDB and SEER databases, respectively. Compared with stage IIB patients, stage IIA pts within the NCDB were characterized by a higher proportion of females, fewer comorbidities, and were less likely to undergo APR (all p<0.001). No significant differences were observed between age, race, receipt of chemotherapy, and radiation therapy/dose. In the SEER database, the demographic, clinical, and pathologic characteristics were comparable to those of the NCDB. OS at 5y was 72 and 69% for stage IIA vs 57 and 50% for IIB for the NCDB and the SEER databases (Figure 1) (p<0.001). For the SEER database, in which DSS was available, the 5y DSS was 82 (IIA) vs 68% (IIB) (p<0.001). After adjustment for available confounders, stage IIB was significantly associated with worse OS in both cohorts (HR 1.58 and 2.01, both p<0.001). Conclusion: This study confirms the RTOG9811 secondary findings of T3 ASCCs having worse survival than T2 tumors at a national level. Therefore, the new AJCC subclassification of stage II anal cancer into A and B based on size less or greater than 5 cm remains prognostically accurate in the general ASCC population. AJCC stage IIB pts represent a higher risk category that should be the target of more aggressive treatment regimens and novel therapies.



PF18

Sidedness of Colorectal Cancer Impacts Risk of Second Primary Gastrointestinal Malignancy K.K. Broman,[1]* C.E. Bailey,[1] A. Parikh.[2] *1. Surgery, Vanderbilt University Medical Center, Nashville, TN; 2. Greenville Health System, Greenville, SC.*

Introduction: Recent studies have shown that cancers of the right colon, left colon, and rectum differ according to molecular changes, responses to treatment, and outcomes. The purpose of this study was to determine if colorectal cancer (CRC) location is associated with differential risk for subsequent gastrointestinal (GI) malignancy. Methods: A retrospective cohort study of adult patients diagnosed with CRC was performed using the Surveillance, Epidemiology, and End Results database (1973-2013). Standardized incidence ratios (SIR) for subsequent GI malignancies were compared based on location of the index CRC. Statistical significance was determined based on the upper and lower confidence limits for each SIR estimate. Results: The cohort included 343,750 patients with CRC (32.7% right colon, 33.8% left colon, 33.5% rectum). In a median follow-up of 4.17 years (interquartile range 1.3-10.6), 14,164 (4.1%) patients developed a second primary GI malignancy (2.7% recurrent/second primary CRC, 1.4% non-CRC). Relative to an age-adjusted standardized population, patients with CRC at any location had a higher than expected incidence of small intestinal, other colorectal, and anal cancers and a lower incidence of gallbladder cancer. The SIR for small intestinal cancer was higher after right colon than after left colon or rectal cancer. There was an increased incidence of gastric and bile duct cancer after right and left colon, but not rectal cancer. The incidence of esophageal cancer was higher than expected after left colon cancer diagnosis. The incidence of pancreas cancer was higher than expected for patients with right colon cancer, but lower with left colon and rectal cancer (Table). Conclusions: The location of CRC leads to differences in incidence and location of second primary GI malignancies and may be related to similarities in the associated carcinogenesis and molecular pathways. CRC location not only impacts treatment response and outcomes, but should also be considered during subsequent surveillance.

Table. Standardized incidence ratios for second primary malignancies based on location of colorectal cancer (ref=1.00)

Second Primary	Right	Left	Rectal
Esophagus	0.96 (0.88-1.04)	1.20 (1.12-1.28)	0.96 (0.89-1.04)
Stomach	1.18 (1.12-1.24)	1.17 (1.12-1.23)	1.01 (0.96-1.07)
Small intestine	4.40 (4.13-4.69)	2.69 (2.49-2.90)	2.39 (2.19-2.61)
Cecum	0.26 (0.23-0.29)	1.84 (1.78-1.91)	1.75 (1.68-1.82)
Ascending colon	0.43 (0.39-0.47)	2.23 (2.15-2.32)	1.70 (1.62-1.79)
Hepatic flexure	0.74 (0.65-0.84)	2.35 (2.20-2.51)	1.77 (1.62-1.93)
Splenic flexure	3.34 (3.09-3.61)	2.20 (2.02-2.40)	1.73 (1.55-1.93)
Descending colon	3.03 (2.85-3.23)	2.40 (2.25-2.56)	2.02 (1.87-2.18)
Sigmoid colon	1.73 (1.66-1.80)	0.80 (0.76-0.84)	0.74 (0.70-0.78)
Rectosigmoid	1.44 (1.34-1.54)	1.11 (1.03-1.19)	0.62 (0.56-0.69)
Rectum	1.30 (1.24-1.37)	1.57 (1.51-1.63)	1.67 (1.60-1.74)
Anus	1.43 (1.23-1.66)	1.18 (1.01-1.37)	2.34 (2.08-2.63)
Liver	0.80 (0.73-0.88)	0.82 (0.75-0.89)	0.65 (0.59-0.72)
Gallbladder	0.68 (0.57-0.81)	0.73 (0.62-0.86)	0.69 (0.57-0.83)
Intra- and Extrahepatic Bile Duct	1.48 (1.36-1.61)	1.33 (1.22-1.45)	1.10 (0.99-1.22)
Pancreas	1.16 (1.11-1.21)	0.92 (0.88-0.96)	0.84 (0.80-0.89)

Standardized Incidence Ratio (SIR) = Age-adjusted ratio of observed to expected incidence rates based on general population

PF19

Restrictive Fluid Therapy Decreases Morbidity and Length of Stay After HIPEC A. Damle,[2] C. Williams,[1] R.J. Hendrix,[1]* A. Harris,[1] S. Spanakis,[1] D. Lambert,[3] L. Lambert.[1] *1. Surgery, University of Massachusetts Medical School, Worcester, MA; 2. Washington University in St. Louis, St. Louis, MO; 3. Boston Medical Center, Boston, MA.*

Introduction Recent data has demonstrated multiple benefits of intra- and post-operative fluid restriction. However, data regarding the outcomes of fluid restriction and cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemoperfusion (HIPEC) are limited. This study evaluates clinical outcomes of restricted fluid therapy in CRS/HIPEC. Methods This is a single institution retrospective chart review of all CRS/HIPEC procedures performed at our institution between January 2009 and July 2017. Recorded variables included demographic information, intra-operative factors, post-operative complications as defined by NSQIP (recorded for 60 days post op), and length of stay (LOS). Outcomes based upon the use of permissive fluid resuscitation (PFR) versus restrictive fluid resuscitation (RFR) were compared. Results 169 CRS/HIPEC cases were reviewed. 84 cases were managed with PFR and 85 with RFR. No significant differences were identified in patient demographics or intra-operative factors except for a decrease in intra-operative administration of crystalloid (8.0L vs 4.4L, $p<0.01$), colloid (900mL vs 300mL, $p<0.01$), and blood transfusion (0.9u vs 0.3u, $p<0.01$) in the RFR. LOS was reduced from 11.5 days to 9.7 days ($p<0.01$) and the incidence of any 60-day complication decreased from 45% to 28% ($p=0.02$) in the RFR compared with the PFR. The 90-day mortality rate was 0.6%. When adjusting for age, sex, prior chemotherapy, length of surgery, intra-operative blood loss, and specific intraoperative chemotherapeutic agent, the odds ratio of having a Clavien-Dindo class 3, 4, or 5 complication was 0.31 (95% CI 0.1-0.95) with RFR. Conclusion RFR can be used safely in CRS/HIPEC and is associated with a decreased LOS, and decreased rate of post-operative complications.

PF20

Real-World Impact of Laparoscopic Surgery for Rectal Cancer on Short-term Outcomes: A Population-Based Analysis A. Drohan,* P. Johnson, M. Hoogerboord, G. Flowerdew, G. Porter. *Dalhousie University, Halifax, NS, Canada.*

BACKGROUND: Over the past decade, randomized controlled trials have demonstrated equivalent oncologic results but decreased morbidity in rectal cancer patients undergoing laparoscopic surgery (LS) compared to open surgery (OS). The objective of this study was to compare short-term outcomes following LS and OS for rectal cancer in a real-world, population-based setting. METHODS: A national discharge database was used to identify all patients undergoing rectal cancer resection (LS or OS) in Canada (excluding Quebec) from 2004 to 2014. In an attempt to identify a cohort eligible for both OS and LS, exclusion criteria included pregnancy, emergency surgery, complex resections, and transanal approaches. Short-term outcomes examined included same-admission death and length of stay (LOS) after surgery. RESULTS: Among the 27,521 patients, 23,501 (85.4%) underwent OS and 4,020 (14.6%) underwent LS; the use of LS increased from 1.4% in 2004 to 34% in 2014 ($p<0.0001$). Use of LS was associated with female gender, younger age, less comorbidity, and higher surgeon/hospital volume. Overall, same-admission mortality was lower among LS compared to OS patients (0.87% and 1.95%, respectively; $p<0.0001$). On multivariate analysis (Table 1) controlling for age, sex, comorbidity, surgeon/hospital volume, surgery type, province and year, the odds of in-hospital mortality with LS was approximately half of that with OS (OR 0.52; $p<0.0001$). Median LOS was shorter in patients who underwent LS compared to OS (5 days and 8 days, respectively; $p=0.0001$) This strong association of LS with shorter LOS was maintained on multivariable analysis ($p<0.0001$), where high surgeon volume ($p=0.002$), female gender ($p<0.0001$), sphincter-preserving surgery ($p<0.0001$), year ($p<0.0001$) and specific province ($p<0.0001$) were also associated with reduced LOS. CONCLUSION: This study suggests that the short-term outcome benefits of LS demonstrated in randomized controlled trials have been realized, or perhaps exceeded, in a real world setting. Although some differences in patient selection for LS exist, these do not completely explain the short-term outcome differences between LS and OS.

Multivariate logistic regression of factors associated with in-hospital mortality among patients undergoing rectal cancer surgery in Canada from 2004-2014

	OR	p value
Laparoscopic surgery		
OS (N=23,501)	ref	
LS (N=4,020)	0.52	<0.0001
Charlson Comorbidity Index		
0-1 (N=18,688)	ref	
2-5 (N=1,817)	3.39	<0.0001
≥6 (N=7,016)	1.71	<0.0001
Age		
19-50 (N=2,663)	ref	
51-65 (N=10,047)	1.82	0.11
66-80 (N=11,491)	6.01	<0.0001
>80 (N=3,320)	17.97	<0.0001
Surgeon Volume		
Low (N=13,916)	ref	
High (N=13,605)	0.99	0.89
Hospital Volume		
Low (N=3,107)	ref	
High (N=24,414)	1.09	0.57
Sex		
Male (N=18,639)	ref	
Female (N=8,882)	0.72	0.002
Surgery Type		
Non-sphincter sparing (N=6,959)	ref	
Sphincter-sparing (N=20,562)	1.08	0.48
Province		
NL (N=883)	ref	
PE (N=175)		
NS (N=1,323)		
NB (N=1,029)		
ON (N=12,346)		
MB (N=1,459)	0.69	0.57
SK (N=1,226)	0.85	0.60
AB (N=3,459)	1.00	0.99
BC (N=5,621)	0.70	0.15
	0.92	0.79
	1.10	0.78
	0.67	0.16
	0.76	0.30
Year	0.98	0.16

PF21

Prognostic Value of Neutrophil-to-Lymphocyte Ratio (NLR) in Intestinal Neuroendocrine Tumors: An Analysis of the U.S. Neuroendocrine Tumor Study Group B.A. Krasnick,[1]* J. Davidson,[1] R.Z. Panni,[1] M. McGilvray,[1] J. Rodriguez,[1] A.G. Lopez-Aguiar,[2] M. Dillhoff,[3] E.W. Beal,[3] G. Poultsides,[4] E.A. Makris,[4] F.G. Rocha,[5] A. Crown,[5] K. Idrees,[6] P.M. Smith,[6] C.S. Cho,[7] M. Beems,[7] S. Weber,[8] A. Fisher,[8] W. Hawkins,[1] S.M. Strasberg,[1] C. Hammill,[1] W. Chapman,[1] M.B. Doyle,[1] S.K. Maithel,[2] R. Fields.[1] *1. Washington University School of Medicine, St. Louis, MO; 2. Emory University, Atlanta, GA; 3. The Ohio State University, Columbus, OH; 4. Stanford University Medical Center, Stanford, CA; 5. Virginia Mason Medical Center, Seattle, WA; 6. Vanderbilt University Medical Center, Nashville, TN; 7. University of Michigan Medical Center, Ann Arbor, MI; 8. University of Wisconsin School of Medicine and Public Health, Madison, WI.*

Introduction: Intestinal neuroendocrine tumors (Int. NETs) can be indolent, with survival often exceeding 10 years. However, a subset can be more aggressive. A prognostic test based on preoperative lab results would be of benefit. An elevated NLR has been found to be predictive of diminished overall survival (OS) in several cancers, and we hypothesized that this would hold true for Int. NETs. Methods: Utilizing the 8 member institutions of the retrospective U.S. NET Study Group, patients undergoing resection of Int. NETs were included. After excluding patients undergoing emergent surgery, those with preoperative sepsis or distant metastases (mets), and those with missing NLR lab values, 281 patients were included for analysis. The cutoff values for NLR were determined using receiver operator curve (ROC) analysis. Univariate analysis was performed based on these groups. A Kaplan-Meier survival curve was created based off optimal NLR from ROC analysis. OS was calculated as date of surgery to date of death/ last follow-up. SPSS 23 was used for analysis. Results: Of the 281 patients identified, 9% were appendiceal, 9% colonic, 21% duodenal, 5% rectal, and 56% jejunal/ileal. Using a NLR of >2.47, the ROC area under the curve was 0.609 (p=0.002). Median survival for the 130 patients in the <2.47 group was 159.8 months, versus 115.6 months in the ≥2.47 group (p=0.009). When comparing the NLR <2.47 and ≥2.47 groups, mean age (57.5 vs. 59.0 years, respectively, p=0.642), ASA status (89% ASA 2 /3 in both groups, p=0.314), tumor Ki-67 status (Ki-67>3% in 30% vs. 26%, respectively, p=0.57), and post-op complications (36 vs. 42%, respectively, p=0.310) were similar between groups. A significantly greater number of patients in the NLR high group had positive lymph nodes (60 vs. 47%, p=0.002). Conclusion: For patients undergoing curative planned resection of Int. NETs with no distant mets, a preoperative NLR of ≥2.47 was significantly predictive of decreased OS, with those in the elevated NLR group having an OS 3.7 years less than those in the <2.47 group. Future prospective data is warranted to further validate these findings.

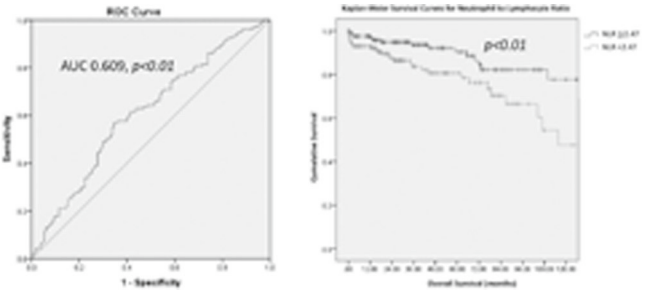


Figure. Left depicts the ROC curve for NLR and survival for intestinal neuroendocrine tumors, and Right depicts the Kaplan-Meier survival curves for overall survival based on a preoperative NLR ratio cutoff of 2.47. AUC, area under curve.

PF22

Enhanced Recovery Protocol Improves Outcomes for Colorectal Cancer Surgery Patients A.D. Jung,* V.K. Dhar, M.C. Daly, T.C. Rice, J.R. Snyder, I.M. Paquette, J.F. Rafferty. *Surgery, University of Cincinnati, Cincinnati, OH.*

BACKGROUND: Prolonged recovery due to complications following surgery may delay initiation of adjuvant chemotherapy for colorectal cancer (CRC) patients. While enhanced recovery pathways (ERPs) have been shown to hasten recovery following elective colorectal surgery, their specific benefit in CRC patients remains poorly defined. METHODS: In January 2016, an ERP was implemented for CRC patients undergoing surgical resection. Perioperative outcomes and costs for all consecutive CRC resections performed one year prior to adoption of ERP (n=75) and after universal adoption of ERP (n=75). Procedures were grouped as low anterior resection (LAR), abdominal perineal resection (APR), right hemicolectomy (RC), left hemicolectomy (LC), sigmoid colectomy (SC), and total abdominal proctocolectomy (TPC). Surgical complications were defined as surgical site infection, anastomotic leak, and ileus. RESULTS: Except for APR (18.7% vs 5.3%; p = 0.01), there were no differences in types of resection performed prior to and following ERP implementation (LAR 32.0% vs 36.0% ; RC 32.0% vs 29.3% ; LC 5.3% vs 9.3% ; SC 6.7% vs 13.3% ; TAC 5.3% vs 6.7% ; all p > 0.05). No differences were found regarding frequency of laparoscopic (66.7% vs 80.0%; p = 0.07), open (33.3% vs 20.0%; p = 0.07), or converted cases (16.0% vs 10.0%; p = 0.35). Both median length of stay (5.0 days vs 3.0; p < 0.001) and 30-day complications (26.7% vs. 12.0%; p = 0.02) were reduced after initiation of the ERP. 30-day readmission was unchanged (10.5% vs 10.7%; p = 0.98). ERP patients required less narcotics during their index hospitalization (84.8 morphine equivalence units [MEU] vs 686.2 MEU; p < 0.001) and tolerated a regular diet 2 days earlier (day 3 vs day 1; p < 0.001). Despite comparable pharmacy costs ($1,934 vs $1,632; p = 0.15), total direct cost of index hospitalization was less for ERP patients ($12,172 vs $10,430; p = 0.04). CONCLUSION: Implementation of ERP for CRC patients undergoing resection led to reduced lengths of stay, narcotic use, 30-day complications, and lowered total cost of admission. ERP following CRC resection has both clinical and financial benefits, and should be considered for widespread implementation.

	COLON CANCER		RECTAL CANCER	
	pre-ERP (n = 35) n (%) ; mean ± STD	post-ERP (n = 40) n (%) ; mean ± STD	pre-ERP (n = 40) n (%) ; mean ± STD	post-ERP (n = 35) n (%) ; mean ± STD
Type of Resection				
Low Anterior Resection	0 (0%)	1 (2.5%)	24 (60.0%)	26 (74.3%)
Abdominal Perineal Resection	1 (2.9%)	0 (0%)	13 (32.5%)	4 (11.4%)
Right Hemicolectomy	24 (68.7%)	22 (55.0%)	0 (0%)	0 (0%)
Left Hemicolectomy	4 (11.4%)	7 (17.5%)	0 (0%)	0 (0%)
Sigmoid Colectomy	5 (14.3%)	8 (20.0%)	0 (0%)	2 (5.7%)
Total Abdominal Proctocolectomy	1 (2.9%)	2 (5.0%)	3 (7.5%)	3 (8.6%)
Type of Surgery				
Laparoscopic	25 (71.4%)	32 (80.0%)	25 (62.5%)	28 (80.0%)
Converted	0 (0%)	2 (6.3%)	8 (32.0%)	4 (14.3%)
Open	10 (28.6%)	8 (20.0%)	15 (37.5%)	7 (20.0%)
LOS (d)	4	3	5	4
Day Diet Advanced	3	1	3	2
Narcotic Use (MEU)	284.6 ± 407.5	68.5 ± 118.4	1,149.7 ± 1,605.5	105.2 ± 104.6
30-day Complication	7 (20.0%)	4 (10.0%)	13 (32.5%)	5 (14.3%)
30-day Readmission	1 (2.9%)	2 (5.0%)	7 (17.5%)	6 (17.1%)
Total Direct Cost ($)	9,765 ± 4,832	9,213 ± 4,697	14,374 ± 6,055	11,821 ± 4,050
Labor ($)	5,005 ± 2,882	4,275 ± 2,502	7,133 ± 3,570	5,253 ± 2,301
Supply ($)	3,342 ± 1,683	3,009 ± 1,415	5,070 ± 2,474	4,433 ± 1,630
Drugs ($)	625 ± 809	1,097 ± 685	957 ± 1,014	1,159 ± 446
Other ($)	794 ± 350	833 ± 435	1,214 ± 561	977 ± 493
Detail Pharmacy Cost ($)	1,655 ± 1,448	1,598 ± 947	2,222 ± 1,633	1,671 ± 881

PF23

Facility Variation in Clinical Staging of Rectal Adenocarcinoma and its Contribution to Underutilization of Neoadjuvant Therapy

D.S. Swords,[4]* D.E. Skarda,[1] G.J. Stoddard,[2] H.T. Kim,[1] W.T. Sause,[3] C.L. Scaife.[4] *1. Intermountain Healthcare, Surgical Services, Salt Lake City, UT; 2. University of Utah, Division of Epidemiolgy, Salt Lake City, UT; 3. Intermountain Healthcare, Oncology Services, Salt Lake City, UT; 4. Huntsman Cancer Institute, University of Utah, Department of Surgery, Salt Lake City, UT.*

Background: Studies of the National Cancer Database (NCDB) found that neoadjuvant therapy (NAT) for clinical stage II-III rectal adenocarcinoma is underutilized, but they reclassified patients without clinical staging by pathologic stage. Methods: Retrospective study of patients < 80 with clinically non-metastatic rectal adenocarcinoma resected between 2010-2014 in the NCDB. Reliability-adjusted (RA) facility rates of clinical staging were calculated. Then, patients with clinical stage I, unknown clinical stage/pathologic stage 0-1, and contraindications to or refusal of NAT were excluded. Multivariable Poisson regression was used to examine predictors of NAT in patient- and hospital-level models. Multiple imputation by chained equations was used to account for missing data. RA facility rates of NAT were calculated. Variance partitioning analysis was used to examine causes of omission of NAT. Results: Of 26,220 patients with clinical stage II-III or unknown clinical stage/pathologic stage II-III, 3,634 (13.9%) were not clinically staged. RA facility clinical staging rates ranged from 17%-99% (mean 82%). NAT was delivered to 20,415/22,586 (90.4%) patients who were clinical stage II-III vs. 1,372/3,634 (37.8%) of those without clinical staging. Of 4,443 patients who did not receive NAT, 2,262 (50.9%) did not have clinical staging. Clinical staging was associated with 2.4-fold higher rates of NAT in the patient-level model. Treatment at facilities with higher clinical staging rates was associated with delivery of NAT (facility-level model). Treatment at higher volume facilities was associated with delivery of NAT, but facility type was not. RA facility NAT rates ranged from 33%-96% (mean 83%). Patient factors explained 15% of the variance in facility NAT rates, facility type/volume 16%, and adjusted facility clinical staging rates 23%. Conclusions: A single process (omission of clinical staging) is present in half of cases omitted NAT (Pareto principle). Facility NAT rates vary 2.9-fold, and adjusted facility clinical staging rates explain much of the variation in use of NAT. Efforts to increase utilization of clinical staging are warranted.

Selected Factors Associated with Delivery of Neoadjuvant Therapy

	Patient-level Model*	Hospital-level Model*
	Relative Risk (95% Confidence Interval)	Relative Risk (95% Confidence Interval)
Clinically staged (Ref no)		
Yes	2.35 (2.26, 2.45)	-----
Facility reliability adjusted rate of clinical staging (Ref 1st quintile [≤ 68.3%])		
2nd quintile (68.4%-79.2%)	-----	1.12 (1.09, 1.14)
3rd quintile (79.3%-85.7%)	-----	1.17 (1.14, 1.19)
4th quintile (85.8-90.8%)	-----	1.21 (1.18, 1.23)
5th quintile (≥ 90.9%)	-----	1.20 (1.17, 1.22)
Facility type (Ref Comprehensive Community)		
Community	0.98 (0.96, 1.01)	0.97 (0.94, 1.00)
Academic	1.00 (0.98, 1.01)	0.99 (0.98, 1.01)
Integrated Network	1.00 (0.99, 1.02)	1.02 (0.995, 1.04)
Facility volume (Ref 1st quartile [≤ 4.8 cases/year])		
2nd quintile (4.9-9.5 cases/year)	1.05 (1.03, 1.07)	1.06 (1.04, 1.09)
3rd quintile (9.6-14.7 cases/year)	1.07 (1.05, 1.09)	1.09 (1.07, 1.11)
4th quintile (14.8-23.3 cases/year)	1.09 (1.07, 1.11)	1.11 (1.09, 1.14)
5th quintile (23.4 ≥ cases/year)	1.07 (1.05, 1.10)	1.11 (1.09, 1.14)

*Both models also adjusted for age, sex, race/ethnicity, insurance status, median area income, median area education, census region, urban/rural status, travel distance, Charlson/Deyo score, histology, CEA, year, and treatment at > 1 CoC facility.

PF24

Cytoreductive Surgery and HIPEC in Poorly Differentiated Carcinomatosis: Favorable or Futile?

O.S. Eng,* M.P. O'Leary, A. Lewis, A.M. Blakely, I.B. Paz, B. Lee, M. Raoof. *City of Hope National Medical Center, Duarte, CA.*

Introduction Cytoreductive surgery with hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is utilized in locoregional management of colorectal and appendiceal cancer with peritoneal carcinomatosis. Poorly differentiated adenocarcinoma is a histology that is associated with a poor prognosis. We sought to investigate oncologic outcomes in these patients after CRS/HIPEC. Methods Patients undergoing CRS/HIPEC from July 2009 to January 2016 were retrospectively identified from a prospectively collected institutional database. Patient information and final histologic pathology were collected and analyzed. Overall survival was determined using the Kaplan-Meier method and compared between sub-groups using a Cox proportional hazards model. Results A total of 123 consecutive patients were identified, 28 (23%) of whom were found to have poorly differentiated adenocarcinoma of colorectal or appendiceal primary. Median age was 52 years (IQR 48 to 62). Mitomycin C and platinum-based chemotherapeutic perfusion were used in 68% and 32% of patients respectively. Median peritoneal cancer index (PCI) was 12 (IQR 7 to 20). CC-0 cytoreduction was achieved in 20 (71%) patients. Median length of hospital stay was 10 days (IQR 8 to 19). There were no mortalities at 30 days. Median recurrence-free survival was 7.5 months (IQR 5.3 to 18.9 months). Median overall survival was 25.3 months (IQR 14.3 to 45.8 months). Response to preoperative chemotherapy was not associated with overall survival (p=0.55). Four patients (14%) at a median follow-up of 58.6 months remain without evidence of disease. When stratified by the median PCI, median overall survival in patients with a PCI ≤12 was 32.5 months compared to 14.8 months in patients with a PCI>12 (HR 4.79, 95% CI 1.71-13.4; p=0.001). Conclusion CRS/HIPEC in carefully selected patients with poorly differentiated colorectal or appendiceal carcinoma and a PCI ≤12 can result in an overall survival of almost three years, with the potential for long-term control of disease. CRS/HIPEC should be considered in this sub-set of patients.

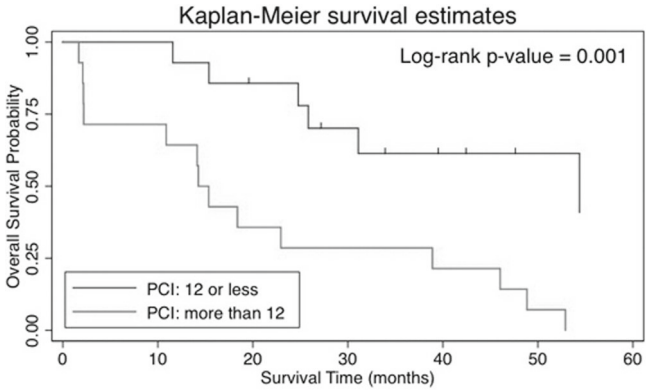


Figure. Kaplan-Meier Overall Survival estimates stratified by peritoneal cancer index.

PF25

CPNE7 as Prognostic Factor and Therapeutic Target in Colorectal Cancer M. Baek,* T. Ahn, D. Kang, D. Jeong, H. Kim. *Soonchunhyang University Hospital, Cheonan, Korea (the Republic of).*

Background: CPNE7, a member of copine family, is composed of calcium-dependent membrane-binding proteins. The encoded protein may play a role in calcium-mediated intracellular processes and membrane trafficking mainly. Although this protein was known as tumor suppressor in breast cancer, we identified the possibility as an oncogene in colorectal cancer. In this study, we performed to evaluate the oncogenic functions of CPNE7 in the colorectal cancer cell line and the clinical significance of CPNE7 expression in colorectal cancer patients. Method: The colorectal cancer cell lines (SW480, SW620, HCT116 and HT29) were transfected with siRNA for knockdown CPNE7. The oncogenic functions were identified in the transfected cell lines and compared them with CPNE7 highly expressing control cell lines. In vitro functional studies included cell proliferation assay, migration assay, invasion assay and semisolid agar colony forming assay. The clinical significance of CPNE7 expression was evaluated in 250 cases of colorectal cancer tissue by immunohistochemistry. Results: The knockdowned cell lines significantly showed lower oncogenic function (proliferation, migration, invasion and colony forming) compared to the CPNE7 highly expressing control cell lines ($p<0.05$). The overall survival rate was decreased in patients of CPNE7 high expression ($p=0.03$). Multivariate and univariate Cox-regression analysis showed that CPNE7 high expression was an independent prognostic factor in colorectal cancer (HR=1. 54, 95% CI=1. 00-2.38: p=0. 048 / HR=1. 58, 95% CI=1. 03-2.41: p=0. 032). Conclusion: This study announces that CPNE7 is a novel oncogene, an independent prognostic factor and therapeutic target in colorectal cancer. In the future, studies on in vivo assay and identifying oncogenic signal pathways of CPNE7 in colorectal cancer are necessary.

PF26

The Effect of Intravenous Iron Therapy on Long-Term Survival in Anemic Colorectal Cancer Patients: Results From a Matched Cohort Study M. Wilson,[1]* J. Dekker,[2] S. Buettner,[1] C. Verhoef,[1] J. Harlaar,[3] J. Jeekel,[1] M. Schipperus,[4] J. Zwaginga.[5] *1. Surgery, Erasmus Medical Center Rotterdam, Rotterdam, Netherlands; 2. Reinier de Graaf, Delft, Netherlands; 3. VUMC, Amsterdam, Netherlands; 4. Hagaziekenhuis, Den Haag, Netherlands; 5. LUMC, Leiden, Netherlands.*

Introduction: Intravenous iron has been shown to be advantageous in treating anemia and reducing the need for blood transfusions in colorectal cancer patients. Iron treatment, however, may also be hazardous by supporting cancer growth. Present clinical study explores, for the first time, the effect of preoperative intravenous iron therapy on tumor prognosis in anemic colorectal cancer patients. Methods: A retrospective cohort study was performed on consecutive patients who underwent surgery for colorectal cancer between 2010-2016 in a single teaching hospital. The primary outcomes were 5-year overall (OS) and disease-free survival (DFS). Survival estimates were calculated using the Kaplan-Meier method and in the intravenous iron and non-intravenous iron group patients were matched based on propensity score. Results: 320 (41.0%) of all eligible patients were anemic, of whom 102 patients received preoperative intravenous iron (31.9%). Median follow-up was 47 months. After propensity score matching 83 patients were included in both intravenous and non-intravenous iron group. The estimated 1-, 3-, and 5-year OS (91.6%, 73.1%, 64.3%) and DFS (94.5%, 86.7%, 83.4%) in the intravenous iron group were comparable with the non-intravenous iron group ($p=0.456$ and $p=0.240$, respectively). In comparing patients with an event (i.e. death or recurrence) and no event in the intravenous iron group, age was significantly increased ($p=0.009$), and with regard to iron status, a distinct trend was found for decreased transferrin in the event group (median 2.53g/L vs 2.83g/L, $p=0.052$). Conclusion: Despite a growing body of experimental studies stressing the important role of iron in cancer growth, present study illustrates that preoperative intravenous iron therapy does not impair long-term overall and disease-free survival. Therefore, the clinical implication of this study is that a dose of 1000-2000mg intravenous iron can be safely administered to preoperative anemic colorectal cancer patients. Future randomized trials are required to further investigate the predictive value of type of iron deficiency, and to establish the dose-response relationship.

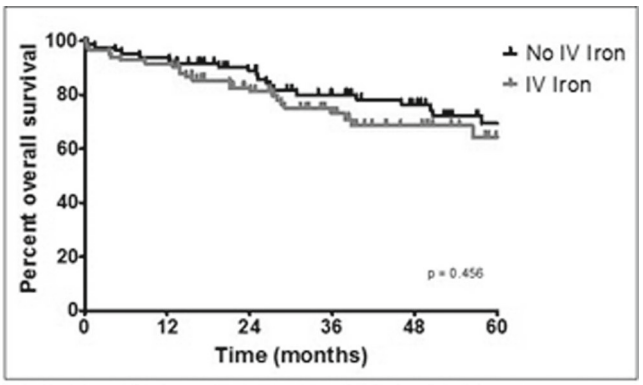


Figure 1. Overall survival stratified for intravenous iron treatment group

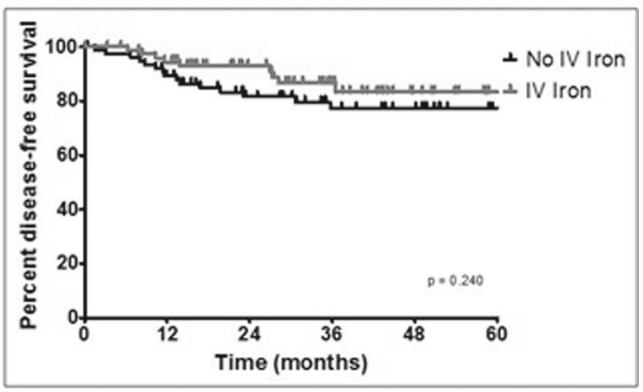


Figure 2. Disease-free survival stratified for intravenous iron treatment group

PF27

Methylomic Profiling Across Anal Squamous Neoplastic Progression in HIV-Positive Patients L. Hendrick,[1]* A. Ajidahun,[1] E.M. Siegel,[3] A. Berglund,[3] R. Putney,[3] D. Saeed-Vafa,[3] L. Balazs,[1] A. Magliocco,[3] L. Reed,[2] J. Im,[2] S. Goldstone,[2] D. Shibata.[1] *1. Surgery, University of Tennessee Health Science Center, Memphis, TN; 2. Icahn School of Medicine at Mount Sinai, New York, NY; 3. Moffitt Cancer Center, Tampa, FL.*

Background: Anal squamous cell cancer (ASCC) is an HPV-associated malignancy and is one of few cancers in the US that continue to increase in incidence. ASCC develops via progression from normal mucosa (NM) through stages of dysplasia or anal intraepithelial neoplasia (AIN). Current prevention strategies include ablation of confirmed areas of AIN3. However, most AIN3 do not progress to ASCC and thus, biomarkers to identify high-risk AIN3 requiring intervention would be valuable. We have previously identified a methylomic profile that distinguishes between NM and ASCC from

HIV- patients and segregates AIN3 lesions into "NM-like" and "ASCC-like" subtypes. We sought to examine methylomic changes across the progression of anal squamous neoplasia in HIV+ patients, a key target screening population for ASCC. Methods: Twenty-four formalin-fixed paraffin embedded (FFPE) samples (9 ASCC, 10 AIN3, 4NM) were obtained from 16 HIV+ patients. Histologic diagnoses were confirmed, tissues microdissected, DNA extracted and bisulfite-modified. Methylation status was interrogated at >850,000 CpG sites using the Illumina Methylation EPIC BeadChip array. Multi-step bioinformatics methodology was used to 1) generate principal component analysis (PCA) models, 2) model the difference between normal and tumor samples via Partial Least Squares (PLS) and examine co-applicability of our known HIV- methylomic progression signature. Results: PCA demonstrated clear 2-dimensional separation between NM and ASCC specimens with segregation of AIN3 cases into "NM-like" and "ASCC-like" cases. PLS modeling confirmed the segregation and application of the HIV- signature to HIV+ cases resulted in an identical separation of cases (Figure 1). Conclusions: We have identified methylomic alterations that may segregate AIN3 lesions into low- and high risk subtypes in HIV+ patients. Furthermore, these alterations appear to be similar to those observed in HIV- patients suggesting the underlying epigenetic basis for neoplastic progression may be the same regardless of HIV status. Our findings have implications for the identification of biomarkers for selective management of AIN3 lesions.

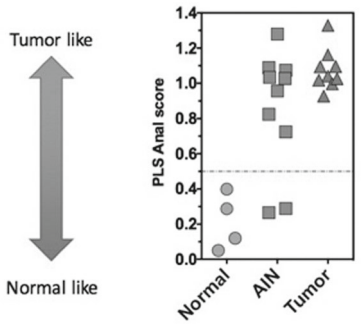


Figure1. PLS demonstrating segregation of AIN3 cases in to "NM-like" and "ASCC-like" cases

PF28

Colon Cancer and Tumor Sidedness: Does Being "Right" Matter? Results of a National Hospital Registry Cohort Study L. Sandhu,[1]* C. Hu,[1] A. Cuddy,[1] A. Francescatti,[5] Y. You,[1] K. Van Loon,[3] P. Gavin,[4] D. Schrag,[2] G. Chang.[1] *1. Department of Surgical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX; 2. Dana Farber Cancer Institute, Boston, MA; 3. Department of Medicine, Division of Hematology/Oncology, University of California, San Francisco, CA; 4. Alliance for Clinical Trials in Oncology, Chicago, IL; 5. American College of Surgeons, Chicago, IL.*

Background Tumor sidedness has recently been highlighted as an important prognostic factor among patients with advanced colon cancer. However, there is conflicting evidence regarding its impact on recurrence and survival among patients with localized disease. The objective of this study was to compare recurrence, overall survival (OS) and survival after recurrence between patients with right (R) and left (L)-sided tumors. Methods The charts of up to 10 random patients with colorectal cancer (Stage I-III, 2006-07) were abstracted for details regarding treatment and recurrence from each Commission on Cancer accredited hospital. These data were merged with records in the National Cancer Database (NCDB). Recurrence information was obtained for up to 5 years or until recurrence or death whereas survival was assessed to Dec 31, 2014. Hierarchical Cox regression models were used to compare recurrence and OS across groups. Results 8,372 patients with colon cancer from 1,190 facilities were identified (R-sided, 5,273; L-sided, 3,099). R-sided colon cancer patients were more often female (56.4 vs 48.8%, p<0.001) and older (median age 71 vs 66 years, p<0.001). R-sided tumors were more often poorly differentiated (20.3 vs 11.3%, p<0.001) and mucinous (12.7 vs 6.6%, p<0.001). Disease recurrence occurred in 1,314 patients (15.7%). There was no significant difference between groups with regard to recurrence (adjusted hazard ratio (HR) 0.94; 95% CI 0.83-1.05, p=0.32). R-sided colon cancers were associated with lower OS (adjusted HR 1.11; 95% CI 1.02-1.22, p=0.02). Among patients with recurrent disease, R-sided tumors were associated with lower OS (adjusted HR 1.43; 95% CI 1.23-1.65, p<0.001) and less frequent salvage surgery (12.2 vs 21.0%, p<0.001). Conclusion Right-sided colon cancers have a similar risk for recurrence as left-sided tumors. However, right-sided tumors that recur are associated with markedly worse survival than left-sided tumors. These data suggest that there is a strong interaction between tumor recurrence and tumor sidedness on survival. Right-sided tumors that recur are biologically more aggressive, explaining the observed differences.

Overall survival results from hierarchical Cox regression analyses

	N	Adjusted Hazard Ratio*	95% CI	p-value
All patients	8,372	1.11	1.02-1.22	0.02
Patients without recurrence	7,058	1.06	0.94-1.20	0.21
Patients with recurrence	1,314	1.43	1.23-1.65	<0.001

*Left-sided colon cancers serve as the reference group. Thus, a HR > 1.00 indicates worse survival among patients with right-sided colon cancers.

PF29

The Role of Preoperative Tumor Markers in Patients with Peritoneal Carcinomatosis from Appendiceal Cancer Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy C.A. Munoz-Zuluaga,* A. Sardi, R. MacDonald, M. Sittig, C. Nieroda, M. King, V. Gushchin. *Surgical Oncology, Mercy Medical Center, Baltimore, MD.*

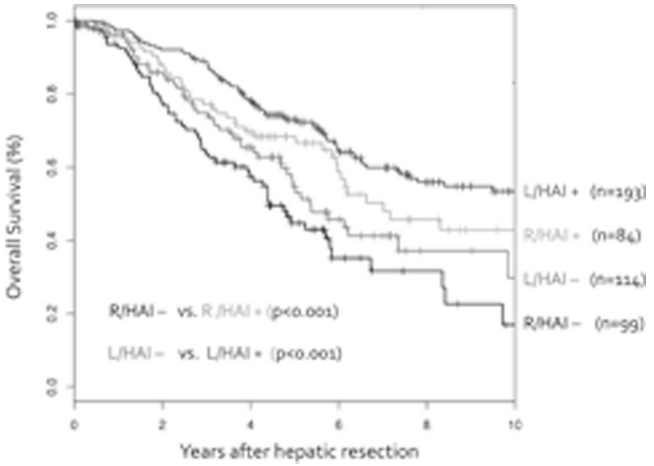
Introduction The significance of tumor markers (TM) in patients with peritoneal carcinomatosis (PC) of appendiceal origin (AO) has been variable and controversial. We analyze the role of preoperative TM in recurrence and survival after cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) in patients with PC from AO. Methods A prospective database of 267 patients with PC from AO undergoing CRS/HIPEC from 1998-2016 was reviewed. Preoperative CEA, CA 125, and CA 19-9 were compared to histopathology, Peritoneal Cancer Index (PCI), and completeness of cytoreduction (CC) using Chi-square tests. TM status was related to overall survival (OS) and time to progression (TTP) using the Kaplan-Meier method. Results Patients with all pre-operative TM (CEA, CA 125, and CA 19-9) were analyzed (n=246). Mean age at surgery was 53±12 years (65% female). CEA, CA 125, and CA 19-9 were abnormal in 36%, 29%, and 29%, respectively. Forty-nine percent had at least 1 abnormal TM; with 1, 2, or 3 elevated in 42%, 31%, and 27%, respectively. TM of high-grade (59%) vs low-grade (41%) PC from AO were associated with elevated CA 19-9 in 35% vs 19% (p=0.006) and all 3 TM were elevated in 17% vs 8% (p=0.046), respectively. Complete cytoreduction (CC 0/1) was achieved in 87%. Incomplete cytoreduction (CC 2/3) was more likely with abnormal TM (83% vs 17%, p<0.001). Median CEA was higher in CC 2/3 (46 U/mL) than in CC 0/1 (22 U/mL) (p=0.03). The number of abnormal TM correlated with higher PCI (PCI≥20) (p<0.001), incomplete cytoreduction (p<0.001), and shorter TTP (p<0.001). Patients with all 3 elevated TM had shorter survival compared to negative, 1, or 2 abnormal TM (p=0.016). OS was significantly higher with normal CA 125 or CA 19-9 compared to abnormal levels (p=0.14 and p=0.05, respectively). Cox regression analysis identified shorter TTP with elevated CEA or CA 19-9 or any abnormal TM. Conclusions The number of abnormal TM correlates with disease burden, incomplete cytoreduction, and progression. Preoperative abnormal CEA or CA 19-9 are independent predictors of disease progression.

	Time to Progression (n=215)*							
	CEA		CA-125		CA 19-9		Any TM	
	Abnormal	WNL	Abnormal	WNL	Abnormal	WNL	Abnormal	WNL
1-year (%)	83	93	87	91	88	91	87	93
3-year (%)	47	80	59	73	50	76	57	80
5-year (%)	34	68	50	58	33	64	44	66
10-year (%)	24	58	31	50	26	49	34	54
MS (years)	3	NR	4	8	3	10	4	NR
p Value	**<0.001**		0.063		**<0.001**		**0.002**	
	Overall Survival (n=246)							
	CEA		CA-125		CA 19-9		Any TM	
	Abnormal	WNL	Abnormal	WNL	Abnormal	WNL	Abnormal	WNL
1-year (%)	92	94	92	94	90	95	91	95
3-year (%)	71	78	67	80	69	78	72	79
5-year (%)	56	70	53	70	52	69	59	70
10-year (%)	45	58	38	62	41	59	46	61
MS (years)	8	12	6	NR	6	12	8	NR
p Value	0.141		**0.014**		**0.052**		0.102	
	Cox Regression Analysis							
	Abnormal CEA HR (95% CI)		Abnormal CA-125 HR (95% CI)		Abnormal CA 19-9 HR (95% CI)		Any TM Abnormal HR (95% CI)	
TTP	**2.51 (1.57-4.02) p<0.001**		1.09 (0.65-1.84) p=0.735		**1.74 (1.06-2.87) p=0.03**		**1.62 (1.01-2.64) p=0.05**	
Survival	0.77 (0.47-1.26) p=0.295		1.03 (0.62-1.73) p=0.9		0.74 (0.44-1.25) p=0.264		0.82 (0.49-1.38) p=0.455	

PF30

Adjuvant Hepatic Artery Infusion Chemotherapy After Resection of Colorectal Liver Metastases is Associated with Improved Survival in Patients with Both Right and Left-sided Primary Tumors S. Gholami,[1]* N. Kemeny,[2] M. Gönen,[2] A. Cercek,[2] P. Kingham,[2] V. Balachandran,[2] P. Allen,[2] R. DeMatteo,[3] W. Jarnagin,[2] M. D'Angelica.[2] *1. Surgery, UC Davis Medical Center, Sacramento, CA; 2. Memorial Sloan Kettering Cancer Center, New York, NY; 3. Hospital of the University of Pennsylvania, Philadelphia, PA.*

INTRODUCTION: Patients with a right-sided (R) and/or KRAS-mutated (KRAS-MUT) primary tumors have inferior outcomes compared to patients with left-sided (L) and/or KRAS-wildtype (KRAS-WT) cancers. Adjuvant hepatic artery pump infusion (HAI) chemotherapy improves overall survival (OS) in patients with colorectal liver metastases (CRLM). We investigated the impact of HAI in relation to the laterality and KRAS status of the primary tumor. METHODS: Patients with resected CRLM, with available KRAS-status, treated with and without adjuvant HAI were reviewed from a prospective institutional database. Rectal primary tumors were excluded. Correlations between adjuvant HAI, clinicopathological factors including laterality and KRAS status and OS were analyzed. Cox proportional hazard regression was used to assess survival outcomes comparing R (cecum to transverse colon, excluding appendix) vs L (splenic flexure to sigmoid) colon cancers. RESULTS: 490 patients (R, n=183; L, n=307) were evaluated between 1993-2012 with a median follow up of 6.5 years. Fifty-six percent (n=277) received adjuvant HAI. Adjuvant HAI was associated with improved median OS in both R (7.0 vs 4.4 yrs, p=0.006) and L tumors (10.5 vs 5.4 yrs, p<0.01). For patients with L tumors, HAI was correlated with significantly improved OS in KRAS-MUT (7.4 vs 3.0 yrs, p=0.01), with a trend towards prolonged OS in KRAS-WT tumors (13.6 vs 5.2 yrs, p=0.08). To the contrary, an association with improved OS outcomes was observed with HAI treatment for R/KRAS-WT (8.3 vs 4.8 yrs, p=0.013) but not for R/KRAS-MUT primary cancers (6.2 vs 4.3 yrs, p=0.15). On multivariate analysis, HAI remained associated with improved OS (HR 4.49, p=0.001) independent of primary tumor site and other clinical predictors. CONCLUSIONS: Adjuvant HAI after resection of CRLM is independently associated with improved OS regardless of laterality of primary tumor. Treatment with adjuvant HAI correlates with improved prognosis in patients with resectable L/KRAS-MUT and R/KRAS-WT tumors. The biological difference for these outcomes requires further investigation.



PF31

Neoadjuvant Pelvic Perfusion May Facilitate Resection of Pelvic Recurrent Rectal Cancer H.J. Wanebo,* G. Begossi, J. Belliveau, E. Gustafson, A.P. Mallon. *Roger Willams Medical Center, Bristol, RI.*

Introduction: Pelvic recurrence of rectal cancer is a persisting therapeutic challenge in spite of wide spread use of adjuvant/neoadjuvant chemo radiation and wide resection isolated pelvic perfusion (IPP) may facilitate pelvic resection in selected high-risk patients. Patients: IPP was done in 42 patients with locally advanced previously irradiated rectal cancer, 26 as a preoperative therapy and 16 for palliation. A comparative larger non perfused group included 63 patients with pelvic resection in selected high-risk patients. Method: Isolated pelvic perfusion (60 min) using pump oxygenation (Temp >41 C), chemo agents – 5 FU 1500mg/m^2, Cisplatin/Oxaliplatin 10 of 150mg/m^2, Mitomycin as mg/m^2, was done in 42 patients (67 IPP). Results Follow up surgery: Palliative IPP in 16 advanced rectal cancer patients in significant relief (1-4 months) of narcotic resistant pain (in 70%). Preoperative IPP in 26 locally advanced rectal cancer achieved a clinical path (CR) in 2 patients, and significant regression in 11 patients rendering them resectable. 7 had R0 pelvic resections, of 6 other patients, 4 refused surgery, 2 were medically excluded. Median survival was 24 months in 12 resectable and 30 months in resected pts (2 pts were 5 year survivors). This is compared to outcome in 63 patients amenable to having pelvic resection alone: 57% had R0 resection (median OS 36 mos), 28% had R1 resection (med OS = 15 mos) and 15% had R2 resection (med OS 21 mos). Conclusion: Neoaduvant IPP may facilitate selection of recurrent rectal cancer by identifying therapeutic responders likely to benefit from major pelvic resection and excluding non-responders most likely to benefit from non-surgical therapy. The potential to induce regression and facilitate R0 resection merits further exploration.

PF32

Validation of the COMPASS Nomogram for Colorectal Peritoneal Metastases in an Asian Population W. Loh,* D. Ng, G. Tan, C. Chia Shulyn, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: The colorectal peritoneal metastases prognostic surgical score (COMPASS) nomogram for prediction of 3-year overall survival has been developed based on patients with peritoneal metastases (PM) from colorectal cancer (CRC) treated with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS and HIPEC) in the Netherlands. We aim to evaluate the predictive accuracy of this nomogram in a cohort of patients treated at an Asian institution, which has previously not been attempted before. Materials and Methods: Patients who underwent CRS and HIPEC for PM from CRC at the National Cancer Centre Singapore (NCCS) between 2000-2015 were included in the analysis. The variables included in the nomogram included age at diagnosis, Peritoneal Carcinomatosis Index (PCI), presence of N2 disease and signet-ring histology. The nomogram was validated by assessing its extent of discrimination and level of calibration. Results: Seventy four patients were included in the analysis (29 male, 45 female), with a median age of 45 years (range 14-75). The observed 3- year Disease Specific Survival

(DSS) was 56%. The level of calibration was quantified using Harrell's concordance index. Extent of discrimination was asssesed by plotting actual survival against nomogram predicred survival. Harrell's concordance index was 0.81, which indicated that for that level of calibration, the observed correspondence between predicted and actual outcomes suggest that the nomogram predicted well for our cohort of patients, albeit under-predicting their survival. This could be attributed to differences in CRS and HIPEC protocols, patient selection, or inherent differences in tumour biology between Asian and Western patients with colorectal PM. Conclusion: The COMPASS nomogram was found to be accurate in terms of extent of discrimination.] In terms of level of calibration, it generally under-predicts survival in our cohort of patients. Modification of the COMPASS nomogram may be required for a predominantly Asian population.

PF33

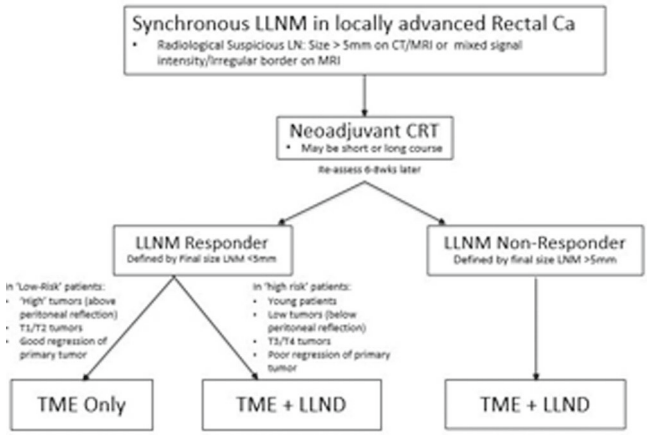
Secondary Colon Cancer in Young Adults D.W. Nelson,[1]* A. Dehal,[1] s. chang,[2] T. Fischer,[1] S.R. Steele,[3] M. Goldfarb.[1] *1. Surgical Oncology, John Wayne Cancer Institute, Santa Monica, CA; 2. Medical Data Research Center at Providence Health and Services Center, Portland, OR; 3. Cleveland Clinic, Cleveland, OH.*

Introduction: Colon cancer (CC) is no longer a malignancy of old age; the incidence is unfortunately rising substantially in younger adults <50 and can occur de novo or in patients previously treated for another cancer. The presentation and impact of secondary malignant neoplasm (SMN) status on survival has not been described for younger CC patients. Methods: All patients < 50 years with CC in the 2004-2014 National Cancer Database were identified. Patients were stratified by primary or secondary occurrence. The impact of SMN status on overall survival (OS) was evaluated with Cox proportional hazard modeling. Results: Of 41,915 patients, 2,852 (6.8%) were SMNs. Median age was similar between the groups, although more SMNs were ages 40-49 compared to primary CC (83% vs 77%, p<0.001). Secondary CCs presented at an earlier stage, with lower clinical and pathological T, N and M stages (all p<0.001). SMNs more commonly occurred in the right colon whereas primary CC had a higher prevalence for the sigmoid (p<0.001). Compared to primary CC, SMNs of the colon more frequently underwent total colectomy (17 vs 5%, p<0.001) but less frequently received adjuvant chemotherapy (53 vs 65%, p<0.001). Adjusted for demographics, tumor characteristics, treatment and stage, secondary CC was associated with a 22% decreased OS compared to primary CC (CI 1.14-1.31, p<0.001). In younger patients with a secondary CC, after adjusting for stage, lack of private insurance (HR 1.5, CI 1.28-1.77) and positive surgical margins (HR 2.14, CI 1.76-2.61) decreased OS; chemotherapy offered a 33% improved OS (CI 0.56-0.8, p<0.001). Conclusion: Secondary CC in younger patients presents at an earlier stage but is treated more aggressively surgically than primary colon cancer. In these younger patients, secondary CCs have a decreased survival stage for stage compared to primary CC and chemotherapy seems to offer a survival advantage. Further investigation is warranted to determine if these outcome disparities are due to cumulative effects of previous cancer treatment or differences in tumor biology.

PF34

Management of Lateral Pelvic Nodal Metastasis in Rectal Cancer in the Era of Neoadjuvant Chemoradiation Therapy: A Systemic Review J. Wong,* G. Tan, M. Teo. *National Cancer Centre, Singapore, Singapore.*

Introduction Lateral pelvic lymph node metastasis (LLNM) occur in up to 28% of patients with locally advanced rectal tumours. While prophylactic LLN dissection (LLND) has since been abandoned by most western institutions in the era of neoadjuvant chemoradiation therapy (CRT), the role of selective LLND in patients with enlarged LLN on pre-CRT imaging remain unclear. Some studies have shown improved survival and recurrence outcomes with LLND even in patients whose LLN show radiological 'response' to CRT. However, no management algorithm exists to differentiate treatment for 'responders' versus 'non-responders'. Methods A systemic search of PubMed and Embase databases for studies reporting on patients with synchronous radiologically suspicious LLNM (s-LLNM) in rectal cancer receiving preoperative-CRT was performed. Results Fifteen retrospective, single-centre studies were included in the final analysis. A total of 929 patients with s-LLNM were evaluated, of which 520 underwent TME alone and 409 underwent TME with selective LLND post-CRT. In the TME group, local recurrence (LR) rates range from 12.5 to 36%. 5-year disease-free survival (DFS) and overall survival (OS) range from 42 to 75% and 54 to 84% respectively. In the TME with LLND group, LR rates were 0 to 6%. 5-year DFS and OS range from 41.2 to 100% and 59 to 81% respectively. In both groups, radiological response was seen in 58% (range 35 to 72). When LLND was performed, pathologically positive LLN was found in up to 94% of non-responders versus 0 to 20% in responders. Young age, low location of rectal tumor and radiological non-response was associated with final positive LLNM and lowered DFS. Conclusion LLND confers local control in patients with s-LLNM. It should be performed in radiological non-responders given that a large majority represent true LLNM. Its role in radiological responders should be considered in the presence of tumours with high- risk features.



Flow diagram on the management of s-LLNM in rectal cancer

PF35

Preoperative Albumin and Anemia Predicts Surgical Outcome in Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy B. Koh,[1]* N.B. Shannon,[1] M. Teo.[2] *1. General Surgery, Singapore General Hospital, Singapore, Singapore; 2. National Cancer Centre, Singapore, Singapore.*

Introduction: Peritoneal metastases are generally associated with a poor prognosis. CRS-HIPEC has afforded prolonged survival in selected patients with peritoneal surface malignancies. However, it is still thought to be associated with significant morbidity. The aim of this study was to assess whether malnutrition and/or anemia, both potentially correctable pre-operative conditions, were prognostic factors for peri-operative morbidity, prolonged surgical intensive care unit (SICU) or hospitalisation stays (LOS). Methods: 137 consecutive patients with peritoneal carcinomatosis treated with CRS-HIPEC between November 2012 and November 2016 were stratified by preoperative albumin level (Alb <35g/L= malnourished), Body mass index (BMI≤18.5kg/m^2 = underweight), or haemoglobin (Hb <10.9=anemic) and compared. Univariate and multivariate analyses were performed, with p< 0.05 indicating significance. Results: 108 patients had pre- operative haemoglobin measurement of which 28 (26%) were anemic. 93 patients had albumin measurements of which 17 (18%) were found to be malnourished, and 30 (32%) had either anemia or malnourishment. 16 (17 %) patients were underweight. Pre- operative malnourishment was found to be associated with increased SICU stay (2 days vs 0 days, p < 0.0.1), LOS (16 days vs 12 days, p<0.01), whereas pre- operative anemia was associated with increased LOS (16 days vs 12 days, p=0.024). The median change in serum albumin pre- and post- operatively was -12 and was not associated with poorer surgical outcomes. BMI was not associated with prolonged LOS or peri- operative complications. A combined group of either anemic or malnourished patients (n=30, 32%) compared to patients with neither (n=63, 68%), demonstrated increase in rate of high-grade complications (27% vs 6%, p=0.016), increased duration of SICU stay (1 day vs 0 day, p=0.014) and total LOS (15 days vs 12 days, p<0.01) in the former. Conclusion: Patients who have anemia and/or low albumin prior to CRS-HIPEC have poorer surgical outcomes and should undergo pre- operative optimisation such as nutritional therapy and oral or parenteral iron supplementation.

PF36

Women with Stage IV Colorectal Cancer Live 27 Months Longer Than Men Following HIPEC for Peritoneal Carcinomatosis

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The effect of sex on outcomes for colorectal cancer (CRC) is complex, with some studies demonstrating a survival benefit for women in early stage disease. However, to our knowledge, whether sex affects outcomes in patients undergoing treatment for peritoneal carcinomatosis (PC) from CRC is less clear. Given differences in the peritoneal immune compartment between men and women, we hypothesized that women undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC) for PC from CRC would have an overall survival (OS) advantage over men. The National Surgical Quality Improvement Project (NSQIP, 2010-2015) dataset was used to assess whether there were differences in complication rates among HIPEC patients based on sex as this could have confounded differences seen in OS. We then used the NCDB colorectal public user file (2004-2014), selecting for patients who underwent HIPEC to determine whether women had longer OS as compared to men. This robust dataset allowed us to adjust for possible confounding epidemiologic variables. Univariate and multivariable statistical analyses were performed. A total of 361 patients were analyzed from NSQIP and 1578 from NCDB. There was no difference in age at diagnosis or 30 day mortality between men and women in the NSQIP or NCDB data set. There was no difference in perioperative complication rates or Charlson-Deyo scores between sexes. The median OS in months post-HIPEC was 77 for the entire group, and 64 for men vs 91 for women (p=0.0044). On multivariable analysis, male sex was independently predictive of worse OS (HR=1.344, p=0.0021) as was increasing age (HR=1.01, p=0.0138). In addition, living in a metropolitan area was predictive of improved OS (HR=0.701, p=0.0047). Women undergoing HIPEC for PC from CRC live significantly longer than men undergoing the same treatment. We found no evidence this advantage was attributable to perioperative morbidity, differences in age at treatment, Charlson-Deyo score, or urban/rural environment. Differences in the peritoneal immune response may provide an explanation for our findings.

PF37

A Predictive Model for Nodal Metastases in Patients with Appendiceal Cancers: Informing the Debate on Completion Right Hemicolectomy

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Introduction: Little is known about the propensity for different histologic subtypes of appendiceal cancer to metastasize to regional lymph nodes (LN). Methods: The National Cancer Database was queried for the years 1998 to 2012 to identify patients with primary diagnosis codes of appendiceal cancer. Univariate and multivariable logistic analysis were performed to identify predictors of node positivity and to develop a predictive model of LN metastases. Results: A total of 21,647 patients were identified. Of these, 9,079 (41.9%) had node negative disease, 4,575 (21.1%) had node positive disease, and 7,993 (36.9%) had unknown LN status. On univariate analysis, advanced age (p=0.008), high tumor grade (p<0.001), advanced T stage (p<0.001), more extensive surgical resection (p<0.001), chemotherapy (p<0.001), tumor histology (p<0.001), and combined modality treatment (p<0.001) were associated with LN positivity. On multivariable logistic regression analysis, compared to mucinous adenocarcinoma, carcinoid tumors (OR 12.78, 95% CI 9.01 – 18.12, p<0.001), signet cell (OR 2.37, 95% CI 1.96 – 2.87, p<0.001), goblet cell (OR 2.22, 95% CI 1.86 – 2.65, p<0.001), and nonmucinous adenocarcinoma (OR 1.72, 95% CI 1.53 – 1.93, p<0.001) were more likely to metastasize to LNs. Compared with T1 tumors, T2 (OR 1.69, 95% CI 1.23 – 2.32, p<0.001), T3 (OR 3.36, 95% CI 2.52 – 4.50, p<0.001), and T4 (OR 6.30, 95% CI 4.71 – 8.42, p<0.001) had a higher likelihood of lymph node metastases. Compared with G1, G2 (OR 2.13, 95% CI 1.89 – 2.44, p<0.001), G3 (OR 5.55, 95% CI 4.78 – 6.45, p<0.001), and G4 (OR 5.98, 95% CI 4.30 – 8.31, p<0.001) tumors were more likely to have LN metastases. A predictive model was then developed utilizing age, gender, tumor histology, T stage and tumor grade. Model performance was internally validated with an Area Under the Curve of 0.75 (95% CI 0.74 – 0.76) and Brier score of 0.19. Conclusion: The risk for LN metastases in patients with appendiceal cancers can be predicted with reasonable accuracy using patient age, gender, tumor histology, T stage and grade. This information can help inform decisions for extent of surgery.

Percentages of node positivity by grade and by T stage for each histology of appendiceal neoplasm

Histology	T Stage	Grade: Low			Grade: High		
		n	Number Node Positive	Percent Node Positive	n	Number Node Positive	Percent Node Positive
Carcinoid	T1	1120	111	9.91	3	1	33.33
	T2	223	97	43.50	5	4	80.00
	T3	161	57	35.40	4	3	75.00
	T4	36	18	50.00	3	1	33.33
Goblet Cell	T1	558	23	4.12	8	2	25.00
	T2	403	51	12.66	16	2	12.50
	T3	1188	169	14.23	129	40	31.01
	T4	383	177	46.21	221	129	66.52
Mucinous Adenocarcinoma	T1	340	11	3.24	11	1	9.09
	T2	371	24	6.47	13	2	15.38
	T3	1486	244	16.42	190	63	33.16
	T4	3452	524	15.18	496	205	41.33
Nonmucinous Adenocarcinoma	T1	440	25	5.68	28	8	28.57
	T2	668	72	10.78	50	8	16.00
	T3	1616	410	25.37	436	196	44.95
	T4	1195	362	30.29	591	365	61.76
Signet Cell	T1	13	0	0.00	4	1	25.00
	T2	17	0	0.00	31	4	12.90
	T3	160	46	28.75	270	120	44.44
	T4	298	118	39.60	625	394	63.04

PF38

The Role of Chemotherapy and Its Timing in Overall Survival in Malignant Peritoneal Mesothelioma

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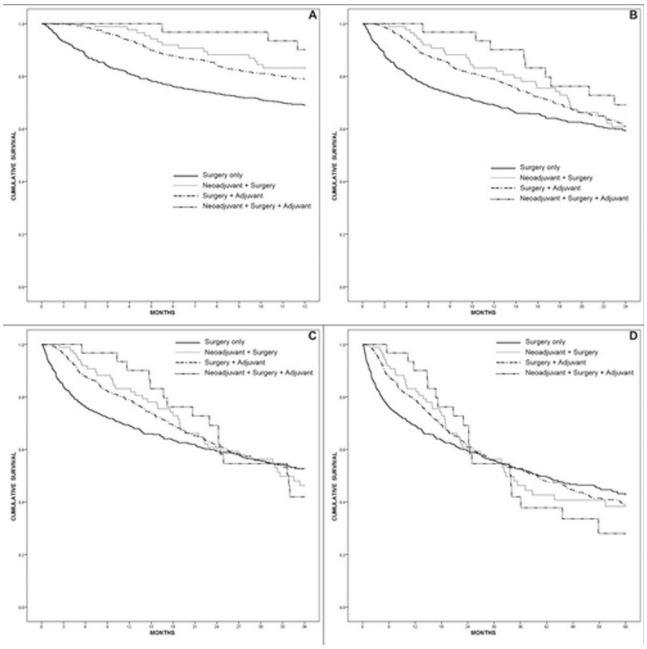
Background: Malignant Peritoneal Mesothelioma (MPM) is considered a rare serosal malignancy and comprises ~10% of all malignant mesotheliomas. The current standard of treatment for MPM is cytoreductive surgery (CRS) when the disease distribution is favorable. The role of chemotherapy as an adjunct to the surgery remains unclear. Methods: We used the National Cancer Database (NCDB) of mesothelioma to identify MPM patients diagnosed between 2004-2014. Patients were divided based on the treatment they received into: 1) chemotherapy only, 2) surgery only, 3) neoadjuvant + surgery, 4) surgery + adjuvant, and 5) neoadjuvant + surgery + adjuvant chemotherapy. We also included a negative control group of patients who did not receive either chemotherapy or surgical treatment (group 0). We used the standard inferential statistical tests to compare the study groups. Results: 2,664 patients were included. Mean age was 61.61±14.79, and 56.1% were males. The patients' distribution into the treatment groups was as follows: 620 (23.3%), 722 (27.1%), 595 (22.3%), 108 (4.1%), 582 (21.8%), and 37 (1.4%) in groups 0, 1, 2, 3, 4, and 5, respectively. Patients in the surgical groups were younger than those in group 0 or the chemotherapy-only group. Median survival in months was 3.55±0.34, 10.87±0.74, 39.51±5.32, 32.66±4.59, 39.66±3.67, and 33.84±5.65 in groups 0, 1, 2, 3, 4, and 5, respectively. The addition of chemotherapy, in any setting, to surgery provided a significantly improved survival at one year (p=0.0001). However, this survival benefit ceased at the two-, three-, and five-year checkpoints. The multivariate Cox regression analysis identified age, sarcomatoid & biphasic histologies, nodal & distant metastasis, macroscopic residual disease, and offering no treatment or chemotherapy only as poor prognostic factor for overall survival. Conclusion: Surgery remains the standard treatment for MPM. The addition of systemic chemotherapy provides a short-term survival improvement at one year only and was similar whether given in the neoadjuvant or adjuvant setting. Systemic chemotherapy, as an adjunct to surgery, did not add a survival benefit beyond the one-year time point.



Comparison of the Kaplan-Meier survival plots between MPM patients who received surgical treatment and systemic chemotherapy administered in various settings. A) one-year survival. B) two-year survival. C) three-year survival. D) 5-year survival

PF39

Effect of Increase in Radiation Dose on Postoperative Complications and Pathologic Complete Response in Rectal Cancer Patients Undergoing Neoadjuvant Chemoradiation at a Single Institution V. Zheleva,[1]* V. Satyananda,[2] Y. Chen,[1] R. Nelson,[1] S. Sentovich,[1] K. Melstrom,[1] L. Lai.[1] *1. City of Hope Medical Center, Duarte, CA; 2. Harbor-UCLA Medical Center, Torrance, CA.*

Introduction Neoadjuvant chemoradiation (CRT) improves local control and sphincter preservation for cT3-4 or cN+ rectal cancer. A pathologic complete response (pCR) after neaodjuvant CRT is noted in 15-20% of patients. Several studies have suggested that increase in radiation dose leads to improved rate of pCR, but its effect on complications is less well described. We examined the effect of increase in radiation dose (54Gy vs. ≤50.4Gy) on postoperative complications, permanent stoma rate, and pCR. Methods Defined data was abstracted from a retrospective chart review of patients with rectal adenocarcinoma treated at our institution from 2010 to 2017. Patients with metastatic disease on presentation or incomplete records were excluded. Patients treated with 54Gy of radiation were compared to those treated with ≤50.4Gy. The chi-square test was used for statistical comparison. Significance was set at p-value <0.05. Results Sixty-seven patients with cT3-4 or cN+ rectal adenocarcinoma were included in the analysis. Out of the entire cohort, 30% received 54Gy of radiation. Postoperative complications were identified in 33% of patients with 25% in the 54Gy vs. 36% in the ≤50.4Gy group, p=0.37. Ileostomy or colostomy was created in 82% (9% had undergone APR). Overall, of the patients not initially treated with an APR, 30% of patients did not have reversal of a diverting ileostomy or did have a conversion to an end colostomy resulting in a permanent stoma rate of 35% in the 54Gy vs. 30% in the ≤50.4Gy group, p=0.67. Amongst the reasons for a permanent stoma were tumor recurrence, metastatic disease, anal incontinence. The overall pCR rate was 21% -- 10% in the 54Gy vs. 26% in the ≤50.4Gy group, p=0.15. Conclusion In our cohort of rectal cancer patients undergoing neoadjuvant CRT, we did not observe an increase in pCR with escalation in radiation dose. Moreover, increasing the total radiation to 54Gy did not affect the postoperative complication or permanent stoma rate.

PF40

A Glimpse into the Future: Does Location of Primary Tumour Predict for Site of Metastases in Colorectal Cancer? J.C. Seo, W. Wang,* G. Tan, C. Chia Shulyn, J. Ong, K. Soo, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction:Rectal cancers have different biological behaviour from colon cancers. Even within colon cancers, right and left-sided tumours are embryonically distinct and present differently. There has been growing evidence to suggest that location of the primary colorectal tumour is independently associated with sites of and outcomes in metastatic cancer. In this study, we aim to investigate the role of primary colorectal tumour location in prediction of sites of metastases. Methods:Patients who had metastatic colorectal cancer between 2001 and 2015 were included. Tumours proximal to and including transverse colon were considered right-sided, while those distal to and including splenic flexure and sigmoid colon were considered left-sided. Logistic regression and Cox regression models were used to compare primary tumour location with site of distant metastases and overall survival(OS). Results:826 patients were included. 196(23.7%) had right-sided tumours, 322(39%) had left-sided tumours while the remaining 308(37.3%) had rectal tumours. 136(16.5%) patients developed only peritoneal metastases, 609(73.7%) developed only distant metastases and 81(9.8%) developed metastases in both sites. Of the patients who had only distant metastases, 418, 107 and 2 developed liver-only, lung-only, and distant nodal-only metastases respectively, whilst 79 developed metastases in 2 or more sites. Vascular invasion, location, T/N stage were found to be significantly associated with site of metastases. Left-sided tumours were more likely to develop distant compared to peritoneal metastases. Right-sided tumours were independently associated with poorer OS, even after accounting for T/N stage and other high risk factors eg. perforation, perineural and vascular invasion. Conclusion:Our study found that left-sided tumours were more likely to develop distant metastases whilst right-sided tumours had poorer OS as compared to the other 2 sites. Our results suggest that right, left-sided and rectal tumours should be considered as different disease entities and this has important clinical implications in planning of treatment, surveillance strategies and prognostication of patients.

PF41

Prognostic Pre-Operative Factors for Patients with Colorectal Peritoneal Metastases Considered for Cytoreductive Surgery (CRS) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) W. Wang,* J.C. Seo, G. Tan, C. Chia Shulyn, J. Ong, K. Soo, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: CRS and HIPEC are increasingly being accepted as a treatment option for patients with colorectal peritoneal metastases (CPM). However, even within this subgroup, treatment outcomes can differ and the challenge is selection of patients with the greatest survival benefit from this combined modality treatment. This paper aims to identify the pre-operative factors that will prognosticate for overall and disease-free survival (OS and DFS) in CPM patients undergoing CRS and HIPEC. Methods: All patients with CPM who have undergone CRS and HIPEC at our institution between January 2001 and December 2016 were included. Demographic and clinicopathological data were collected. Survival analyses were performed using Kaplan-Meier curves and cox regression proportional hazards model to identify the pre-operative factors associated with OS and DFS. Results: 77 patients were included and they were followed up for a median of 33 months. 29(37.7%) passed away and 51 (66.2%) recurred. Younger age (OS: HR: 1.036, 95% CI: 1.010 – 1.063, p=0.007; DFS HR: 0.978, 95% CI 0.959 – 0.996, p=0.021 and PLR>300 (platelet-lymphocte ratio) (OS HR: 21.57 95% CI: 2.312 – 201.21, p=0.007 and DFS: HR: 4.775 95% CI: 1.364 – 16.713, p=0.014) remained significantly associated with poorer OS and DFS on multivariate analyses, even after taking into account other known prognostic factors such as staging, histological subtype, neoadjuvant treatment and other biomarkers such as CEA. KM curves also showed PLR to be prognostic for both OS and DFS (median OS in patients with PLR <150, 150 - 300 and >300 43, 39 and 6 months respectively, p=0.004 and median DFS in patients with PLR <150, 150 - 300 and >300 were 18, 13 and 4 months respectively, p=0.033). Discussion: PLR and age are significant pre-operative prognosticators for DFS and OS in patients undergoing CRS and HIPEC for CPM and can be used to aid patient selection of those who would derive the greatest survival benefit from this procedure.

PF42

The Metastatic Profile of Colorectal Cancer: The Interplay Between the Location of Primary Tumor and KRAS Mutational Status Z. Yong, G. Tan,* M. Teo. *Division of Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore.*

Introduction Besides conferring resistance to targeted therapy, mutant KRAS tumors have been purported to metastasise differently than wild-type KRAS tumors. Similarly, the biological heterogeneity of tumors arising from different parts of the colon has been reported to affect metastasis. This study aims to characterise the metastatic profile of colorectal tumors by evaluating the interplay between the location of primary tumors and KRAS mutational status. Methods Retrospective analysis of 899 patients with metastatic colorectal cancers treated in a single institution from January 2010 to December 2014 was conducted. KRAS mutation status and location of primary tumors were correlated with location of single-site metastasis (liver, lung and peritoneum) and dual-site metastases (liver-peritoneum, liver-lung and lung-peritoneum). Patients without KRAS analyses were excluded. Results Right-sided tumors had highest frequency of peritoneal metastasis as compared to left-sided or rectal tumors (34.7% vs. 15.8% vs. 8.8%, p = 0.00) regardless of KRAS status (32.6% vs. 38.5%, p = 0.62). Left-sided tumors with wild-type KRAS had greater proportion of liver metastasis (78.6% vs. 53.5%, p = 0.00) while those with mutant KRAS had greater proportion of lung metastasis (23.3% vs. 8.7%, p = 0.02). Rectal tumors with wild-type KRAS tend to spread to the liver (81.4% vs. 48.0%, p = 0.00) and not to the peritoneum (2.3% vs. 20.0%, p = 0.01). In dual-site metastases, left-sided tumors with wild-type KRAS had more liver-peritoneal metastases (75.0% vs. 29.4%, p = 0.00) while whose with mutant KRAS had greater lung-liver metastases (64.7% vs. 20.8%, p = 0.01). Rectal tumors had the predilection for lung-liver metastases as compared to right-sided and left-sided tumors (92.3% vs. 40.0% vs. 39.0%, p = 0.00) regardless of KRAS status (100% vs. 75%, p = 0.12). Conclusions Our results have clinical implications for how personalised cancer surveillance programs may be designed based on the location of the primary tumor and KRAS mutational status.

PF44

The Impact of Indoleamine Two to Three-Dioxygenase (IDO) Expression in Colorectal Cancer T. Tokunaga,* M. Shimada, M. Nishi, K. Yoshikawa, J. Higashijima, C. Takasu, H. Kashihara, D. Ishikawa, Y. Wada, S. Ohta. *Surgery, Tokushima University, Tokushima, Japan.*

Background: Regarding the tumor microenvironment, indoleamine 2,3-dioxygenase (IDO) is known to have an important immunoregulatory role and downregulate T cell activation and is related to immune tolerance. The aim of this study is to clarify the significance of IDO expression in patients with colorectal cancer (CRC). Methods: A total of 100 patients who underwent a curative operation for stage II/III CRC were enrolled in this study. The expression of IDO was examined by the immunohistochemistry, and the relationship between each expression and clinicopathological factors. Also, expression TGF-beta, and forkhead box P3 (Foxp3) as a marker of regulatory T cell was immunohistochemically investigated. Results: The IDO expression did not correlated with any background parameters. Overall survival (OS) rate in the IDO-positive group was poorer than that in the IDO-negative group (5-year OS, 80% vs. 98%), and a multivariate analysis revealed the IDO expression as one of the independent prognostic factors in OS. Disease-free survival (DFS) in the IDO-positive group was poorer than that in the IDO-negative group (5-year DFS, 65% vs. 91%), and the IDO expression was also an independent factors in DFS. In addition, the IDO expression positively correlated with TGF-beta expression, furthermore, the TGF-beta expression positively correlated with FoxP3 expression. Conclusions: The IDO expression could be an important prognostic factor in patients with stage II/III CRC, probably due to immune tolerance by regulatory T cells. Therefore, the IDO expression may thus be a new therapeutic target for the treatment of CRC.

PF45

Primary Tumor Location Predicts Benefit from HIPEC in Colorectal Carcinomatosis A.M. Blakely,* O.S. Eng, P. ituarte, B. Lee, M. Raoof. *CIty of Hope National Medical Center, Pasadena, CA.*

Background: Recent literature suggests an association between right-sided colon cancer and worse outcomes compared to left-sided lesions. It is unknown if laterality affects clinical outcomes in patients with colorectal carcinomatosis undergoing cytoreductive surgery (CRS) with or without heated intraperitoneal chemotherapy (HIPEC). Methods: California Cancer Registry was queried for all colorectal cancer cases. Patients were selected by performance of multiple major procedures to indicate CRS and specific codes to indicate HIPEC. Right-sided lesions were defined as up to the splenic flexure. Demographics, node stage, and chemotherapy were captured. Overall survival was assessed by Cox proportional hazards model. Results: A total of 1121 CRS patients were identified, 431 (38.4%) male, 694 (61.9%) white, median age 62 years. Of these, 531 (47.4%) lesions were right-sided. HIPEC was done in 157 (14.0%). Overall, 579 (51.7%) of patients received chemotherapy; 230 (20.5%) was neoadjuvant. N-stage was negative (n=284, 25.3%), positive (n=693, 61.8%), or unknown (n=144, 12.8%). Most tumors were adenocarcinoma (n=796, 71.0%), the remainder mucinous (n=253, 22.6%), signet ring (n=57, 5.1%), or other (n=15). Patients with right- versus left-sided lesions had higher 30- and 90-day mortality (7.5% vs. 4.2%, p=0.018; 16.0% vs. 10.3%, p=0.0049, respectively). On univariate analysis, performance of HIPEC was associated with improved overall survival for both right- and left-sided lesions (HR 0.56, p<0.0001, CI 0.45-0.69). Sensitivity analysis was done using right-sided lesions without HIPEC as reference, controlling for age, chemotherapy, N stage, and histology; patients with left-sided lesions undergoing CRS and HIPEC had significantly reduced risk of mortality (HR 0.67, CI 0.50-0.88, p=0.004); this was not evident for patients with right-sided lesions undergoing HIPEC (HR 0.76, CI 0.55-1.06, p=0.11) or those with left-sided lesions not undergoing HIPEC (HR 1.07, CI 1.01-1.02, p=0.38). Conclusions: This study identifies location of primary tumor as an important determinant of long-term survival after CRS and HIPEC. Patients with left-sided tumors undergoing HIPEC have the most favorable prognosis.

Table 1: Comparison of mortality of right- versus left-sided tumors by cytoreductive surgery with or without HIPEC.

	Right-Sided	Left-Sided
Cytoreduction only	Reference	**HR 1.07** CI 1.01-1.02 ***P=0.38***
Cytoreduction with HIPEC	**HR 0.76** CI 0.55-1.06 ***P=0.11***	**HR 0.66** CI 0.50-0.88 ***P=0.004***

HR=hazards ratio; CI=95% confidence interval; HIPEC=heated intraperitoneal chemotherapy

PF46

Laparoscopic Surgery for Locally Advanced T4 Colon Cancer: Long-term Outcomes and Prognostic factors T. Yamanashi,* T. Nakamura, T. Sato, H. Miura, A. Tsutsui, M. Shimazu, M. Watanabe. *Department of Surgery, Kitasato University School of Medicine, Sagamihara, Japan.*

Purpose: The laparoscopic surgery for advanced colorectal cancer has become widely spread with demonstrated short-term benefits and long-term oncological outcomes as compared with the open surgery. For locally advanced T4 tumor, however, the safety and feasibility of laparoscopic procedures remain controversial. Therefore, this study aimed to assess retrospectively short- and long-term outcomes and prognostic factors of laparoscopic surgery for T4 colon cancer. Methods: This study group comprised 130 patients who underwent laparoscopic resection for pT4 colon and rectosigmoid cancer, excluding ones with distant metastases from January 2004 through December 2012. The clinicopathological findings, short-term outcomes, long-term outcomes, and prognostic factors in pT4 colon cancers were analyzed. Results: The median operative time was 205 minutes with a median blood loss was 10 ml. Conversion rate was 3.8 %. The median postoperative hospital stay was 7.5 days. 13 patients (10.0 %) had postoperative complications. 83 patients (63.8 %) had lymph nodes metastases. The mean harvested lymph node was 19.9. The radial resection margin was positive in 1 patient (0.8 %). The median follow-up time was 73 months. The 5-year OS and RFS were 77.2 and 63.5 %, respectively. 47 patients (36.2 %) had recurrence. The multivariate analyses revealed that male (HR 3.09, p < 0.001), lymph node ratio ≥ 0.06 (HR 2.35,

p = 0.021), tumor diameter < 38 mm (HR 2.57, p = 0.007), and right sided colon cancer (HR 2.11, p = 0.047) were significantly poor prognostic factors for OS. Conclusions: These results suggest that the laparoscopic surgery for T4 colon cancer is safe and feasible, and the oncological outcomes are acceptable. Based on these presented findings and provided expertise, the patients with locally advanced colon cancer should not be excluded from a laparoscopic surgery.

PF47

Salvage Abdominoperineal Resection for Squamous Cell Anal Cancer: A 30-Year Single Institution Experience J.A. Hagemans,[1]* S.E. Blinde,[2] J.J. Nuyttens,[2] W.G. Morshuis,[2] M.A. Mureau,[2] J. Rothbarth,[1] C. Verhoef,[1] J.W. Burger.[1] *1. Surgical Oncology, Erasmus MC Cancer Institute, Rotterdam, Netherlands; 2. Erasmus MC, Rotterdam, Netherlands.*

Background: If chemoradiotherapy (CRT) for anal squamous cell carcinoma (SCC) fails, it results in persistent or recurrent anal SCC. Treatment with salvage abdominoperineal resection (APR) can potentially reach cure. The aims of this study were to analyze oncological and surgical outcomes of 30-year experience with salvage APR for anal SCC after failed CRT and identify prognostic factors for overall survival (OS). Methods: All consecutive patients, who underwent salvage APR between 1988 and 2016 for histologically confirmed persistent or recurrent anal SCC after failed CRT, were retrospectively analyzed. Results: Fifty patients underwent salvage APR for either persistent (n=24) or recurrent SCC (n=26). Median OS was 41 months [95%CI 9.3;72.7] and 5-year survival was 41.4%, which did not differ significantly between persistent or recurrent disease (p=0.753). Radical resection was achieved in 41 patients (82%). None of the patients died within 30 days. The majority of patients (n=36; 72%) experienced no or minor complications (Dindo-Clavien ≤2) and 14 patients (28%) developed major complications (Dindo-Clavien ≥3). Advanced pathological tumor stage (p=0.002), lymph node involvement (p=0.017) and irradical resection (p=0.011) were associated with impaired hazard for OS in multivariable analysis. Twenty patients developed local recurrence after salvage APR, of whom eight underwent repeat salvage surgery, 10 received palliative treatment and in two patients treatment was unknown. Median OS was 9 months [95%CI 7.2;10.8] after repeat salvage surgery and 4 months [95%CI 3.1;4.9] following palliative treatment (p=0.134). Conclusion: Salvage APR for anal SCC after failed CRT resulted in adequate survival, with 5-year survival of 41.4%. Negative prognostic factors for survival were advanced tumor stage, lymph node involvement and irradical resection. Patients with recurrent anal SCC after salvage APR had a poor prognosis, irrespective of performance of repeat salvage surgery, which never resulted in cure.

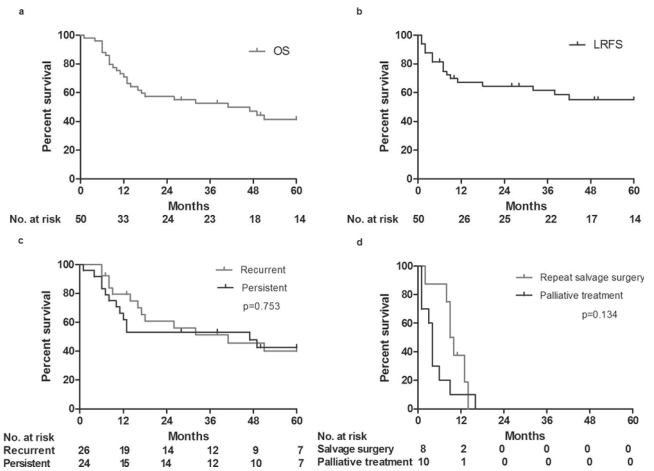


Figure 1. a Overall survival (OS). b Local recurrence free survial (LRFS). c OS for persistent and recurrent disease d OS for local recurrence after salvage APR; repeat salvage surgery and palliative treatment.

PF48

Trans-Perineal Minimally Invasive Surgery During Laparoscopic Abdominal Resection for Low Rectal Cancer D. Yasukawa,* T. Hori, T. Kitano, Y. Takamatsu, Y. Kimura, Y. Aisu, S. Kato, T. Ito, Y. Kadokawa, T. Machimoto, T. Yoshimura. *Digestive Surgery, Tenriyorozusoudanjyo Hospital, Tenri, Japan.*

Background Laparoscopic abdominoperineal resection (APR) for low rectal cancer (LRC) is performed worldwide. However, APR involves technical difficulties, and often causes intractable perineal complications. Therefore, a novel and secure technique during APR is required to overcome these critical issues. Although the usefulness of the endoscopic trans-anal approach has already been documented, no series of the endoscopic trans-perineal approach during laparoscopic APR for LRC has been reported. Methods In our institution, from April 2014, trans-perineal minimally invasive surgery (TpMIS) has been used during laparoscopic APR. TpMIS is defined as an endoscopic trans-perineal approach using a single-port device and laparoscopic instruments. This study retrospectively evaluated 50 consecutive patients with LRC who underwent laparoscopic APR with or without TpMIS at our institution from February 2011 to June 2017. We divided this population into two groups based on surgical procedures: laparoscopic APR with the endoscopic trans-perineal approach (TpMIS group, n = 21) and laparoscopic APR with the conventional trans-perineal approach (conventional group, n = 29). We investigated our experiences of TpMIS in detail, and the safety and utility of TpMIS for patients with LRC were evaluated. Moreover, major features and difficulties of TpMIS were also examined from a surgical viewpoint. Results Intraoperative blood loss and severe perineal wound infection (Clavien–Dindo grade 3) were significantly lower in the TpMIS group than in the conventional group. This occurred because magnified visualization via endoscopy provided more accurate dissection and less blood loss during surgery, and minimal skin incisions enabled a reduction in postoperative perineal complications in the TpMIS group. TpMIS led to a shortened hospital stay, and neither mortality nor conversion to open surgery was observed. Therefore, short-term postoperative outcomes of TpMIS during laparoscopic APR were considered reasonable. Conclusions TpMIS during laparoscopic APR is safe and beneficial for patients with LRC.

PF49

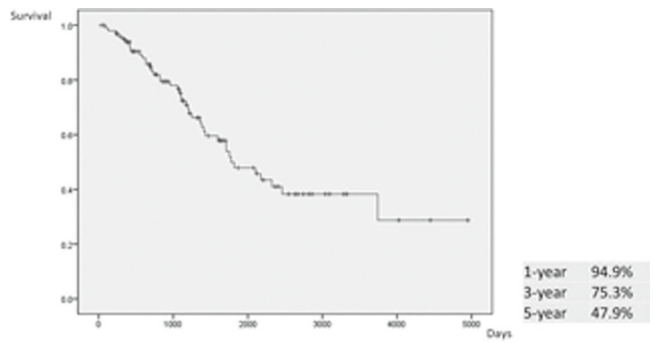
Activation of Mesothelial Cells by Paracrine Signalling Promotes Metastatic Colonisation in Colorectal Peritoneal Carcinomatosis H. Lim,* J. Hendrikson, W. Ng, Q. Tan, N. Shannon, J.W. Tan, C. Chia Shulyn, G. Tan, O. Kon, J. Ong, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction Tumour microenvironment has shown to play a key role in the pathogenesis of various malignancies. To date, the role of activated stroma in colorectal peritoneal carcinomatosis (PC) remains unclear. The aim of this study is to investigate the tumour-stroma interaction that hinges on ascites-mediated paracrine signalling in the pathogenesis of colorectal PC. Methods Malignant ascites was collected from 3 colorectal cancer patients during cytoreductive surgery. 4 stromal cell lines, consisting of 1 colorectal normal fibroblast (NF), 1 colorectal cancer fibroblast (CAF) and 2 benign mesothelial cells (HM3-TERT and LP9-TERT), were treated with cell-free ascites. Gene expression profiling of treated cells coupled with gene set enrichment analysis were performed to identify upregulated genes and pathways induced by ascites. In-vitro co-culture model of colorectal cancer cell lines and various stroma feeder layers were utilized to study the metastatic colonization of cancer cells on activated stroma. Results Treatment of NF with cell-free ascites led to upregulation of several cytokines and growth factors, including TGFB (Running Enrichment Score (RES)=0.21), VEGFs (RES=0.14) and MCT4/SLC16A3 (RES=0.122). Overexpression of these cytokines is often noted in cancer associated fibroblasts suggesting that paracrine signalling induced by cell-free ascites on NF led to the transformation of a CAF-like phenotype. Significantly enriched signatures in CAF, HM3 and LP9 upon treatment with ascites included hypoxia (Normalised Enrichment Score (NES)=1.35-1.44, $p<0.05$) and Epithelial-Mesenchymal-Transition (NES=1.42-1.49, $p<0.05$), suggesting that paracrine signalling induced by ascites promotes cellular plasticity to support metastasis and tumour survival in stroma cells. Validation performed in a unique co-culture model of stroma and cancer cells in the presence of ascites showed 70% increase in metastatic colonies ($p<0.05$). Conclusion We have shown that paracrine signalling induced by ascites promotes a favourable tumour microenvironment in promoting metastatic colonization. This provides a potential therapeutic option in colorectal PC.

PF50

Combination of Liver Resection and Perioperative Chemotherapy Prolonged the Survival of Patients with Colorectal Liver Metastases T. Ochiai,* S. iida, S. Yamazaki. *Surgery, Ohta Nishinouchi General Hospital, Kohriyama, Japan.*

Introduction: Advances in chemotherapy have expanded the resectability of colorectal cancer with liver metastases (CRLM). We studied treatment results in the patients with CRLM since molecular target-based agent was approved in Japan. Methodology: Based on data collected retrospectively, we analyzed the demographics, clinical data, operative findings, chemotherapy, and outcomes of 266 consecutive CRLM patients treated between 2008 and 2016. To investigate the correlation between resectability and survival, we devided the observation periods into 2 periods, 2008-2010 and 2011-2016. Results: The 1-, 3-, and 5-year overall survival rates for the entire CRLM patient were 80.6%, 46.9%, and 25.9%, respectively. The 1-, 3-, and 5-year overall survival rates of 101 patients who underwent liver resection, were 94.9%, 75.3%, and 47.9%, and 165 who did not underwent liver resection, were 71.1%, 23.8%, and 8.4%, respectively. We studied the patients who underwent hepatectomy and age, gender, synchronous/metachronous, neo-adjuvant and adjuvant chemotherapy, repeat liver resection were analyzed. Only perioperative chemotherapy revealed significant difference. The total resectability of CRLM was 38.0%, and 46.2% in 2008-2010, and 32.5% in 2011-2016. The 1-, 3-, and 5-year overall survival rates for the entire CRLM patient and the patients who underwent hepatectomy in 2008-2010 were 74.8%, 48.4%, and 31.1%, and 93.7%, 80.7%, and 52.9% respectively. The 1-, 3-, and 5-year overall survival rates for the entire CRLM patient and the patients who underwent hepatectomy in 2011-2016 were 84.8%, 42.3%, and 16.8%, and 96.0%, 66.9%, and 38.6%, respectively. Conclusions: Although development of various molecular target-based agents has improved short-term survival of CRLM patients, liver resection is still the key of long-survival. The combination of liver resection and chemotherapy prolonged the survival of patients with CRLM.



Overall survival of 101 patients who underwent liver resection

PF51

Risk Factors for Early Recurrence After Repeat Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Appendiceal Primary Neoplasms M.M. Garland,* F. Hsu, K.C. Perry, P. Shen. *Wake Forest University School of Medicine, Winston-Salem, NC.*

Introduction: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is a well-established treatment for peritoneal surface disease from appendiceal neoplasms. Previous research has shown that repeat CRS/HIPEC in selected patients produces results similar to the original surgery if complete cytoreduction can be achieved. Given the substantial morbidity associated with this procedure, we examined our experience to determine significant predictors of early recurrence after repeat CRS/HIPEC to assist with patient selection. Methods: Patients who underwent CRS and HIPEC for appendiceal tumors were identified from a prospectively maintained database from 1995-September 2017. Clinicopathologic factors associated with the original surgery were examined to determine risks for early recurrence and death after repeat surgery using logistic regression analysis. Results: Seventy-three patients were included in this study. Of these, 62.7% were men. Median age at repeat surgery was 49.5 years. Of these 28 (38.9%) were R0/R1 resections, 22 (30.6%)were R2a, 16 (22.2%) were R2b, and 6 (8.3%) were R2c. Independent predictors of mortality after repeat HIPEC were tumor grade (p=0.003), time to recurrence (p=0.020), resection status (p<0.001) and Clavien-Dindo IV at first surgery (p<0.001). Peritoneal carcinomatosis index (PCI) and pre- and post-operative chemotherapy use were not predictive of mortality. Independent predictors of recurrence after repeat HIPEC were tumor grade (p=0.04) and Clavien-Dindo IV (p<0.001) at first surgery. Time to recurrence was the only predictor of change from low to high grade at repeat surgery. Conclusions: Early recurrence after repeat CRS/HIPEC is likely due to many factors, including poor tumor biology. While PCI has been shown previously to affect outcomes at first HIPEC, it does not appear to affect recurrence or mortality at repeat surgery. Patients with Clavien-Dindo IV complications at first surgery and high tumor grade are poor candidates for repeat HIPEC.

PF52

Predictors of Post-operative Outcomes in Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy for Recurrent Colorectal Cancer with Peritoneal Carcinomatosis K. Chin,* G. Tan, C. Chia Shulyn, J. Ong, M. Teo. *Department of Surgical Oncology, Singapore General Hospital, Singapore, Singapore.*

Background: The combination of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) has significantly improved prognosis of patients with peritoneal carcinomatosis (PC), a diagnosis once deemed to have few therapeutic options. Patient selection is key to improved survival outcomes. We aimed to identify pre- and peri-operative parameters with predictive value for post-CRS-HIPEC disease-free and overall survivals in patients with recurrent colorectal cancer and PC. Methods: A single-institution review of prospectively collected data from all patients who underwent CRS-HIPEC between Oct 2005-Oct 2017 was conducted. Pre- and peri-operative parameters (e.g. age, nodal status, neoadjuvant chemoradiotherapy, carcinoembryonic antigen (CEA), peritoneal cancer index (PCI), pre-operative disease free interval (DFI: time between primary tumour resection and peritoneal disease recurrence)) were assessed and analyzed for their predictive value of post-CRS-HIPEC disease-free survival (DFS) and overall survival (OS). Univariate and multivariate analyses were used to identify significant predictors and ROC curves to identify cutoffs most significantly associated with DFS and OS. Results: 278 patients underwent CRS-HIPEC, of which 62 for recurrent colorectal cancers. DFI (p=0.03) and PCI (p=0.04) were independent predictors of 3-year OS. PCI was an independent predictor of 5-year OS (p=0.047) and DFS (p<0.01). DFI greater than 15.5 months (p<0.01; sensitivity and specificity of 86% and 89%) and PCI lesser than 13 (p=0.012; sensitivity and specificity of 78% and 77%) were significantly predictive of 3-year OS. DFI greater than 7 months (p<0.01; sensitivity and specificity of 99% and 58%) and PCI lesser than 12 (p<0.01; sensitivity and specificity of 98% and 95%) were significantly predictive of 5-year OS. CEA was not significantly associated with DFS or OS. Conclusion: PCI and DFI have significant predictive value for post-CRS-HIPEC survival in patients with PC from recurrent colorectal cancer. Consideration of these parameters could allow for more prudent patient selection.

PF53

Prognostic Relevance of Tumor Laterality in Stage IV Colon Cancer Patients with Peritoneal Metastases Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy C. Ihemelandu.* *Surgical Oncology, Medstar Washington Hospital, Washington, DC.*

Introduction: - Tumor laterality is associated with survival outcome in colon cancer. Our aim was to analyze the prognostic relevance of tumor laterality, right colon cancer (RCC) vs. left colon cancer (LCC) in stage IV colon cancer patients with peritoneal metastases treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Methods: - Retrospective analysis of a prospectively maintained database of patients treated for peritoneal metastases of a colonic origin from January 2000- April 2015. Results: - Of 150 patients in our study there were 84(56.0%) males vs. 66(44.0%) females. Mean age at presentation was 48.8 vs. 50.3 years respectively for LCC and RCC. Median survival for RCC was 20.1 vs. 41.8 months for LCC (p=0.017). Three and 5 year survival was 39% and 25% vs. 27% and 20% respectively for LCC and RCC. The mean peritoneal carcinomatosis index was 14.2 vs. 18.6 respectively for LCC and RCC (p=0.017). There were no differences in the completeness of cytoreduction (CC) score achieved for both sides (p=0.130). RCC was significantly associated with a higher CA19-9 level 665.37 vs. 94.2 for LCC (p=0.007). There was no significant difference in CEA

level expression between the two sides 95.3 vs. 167.6 respectively for RCC and LCC (p=0.495). Significant independent predictors of survival in multivariate analysis included: CC score, PCI, elevated tumor makers CA19-9, tumor laterality with RCC being an independent predictor of a shorter overall survival (HR 2.2, 95% CI 1.0-4.9, p=0.036). Conclusion: - Right tumor laterality in stage IV colon cancer patients with peritoneal metastases treated with CRS and HIPEC is associated with a worse prognosis compared to left sided tumors.

PF54

Mutation Patterns and Overall Survival in Colorectal Cancer with Lymphovascular Invasion. F. Lambreton,* G. Gauvin, J. Purchla, S. Reddy, N. Nweze, E. Sigurdson, J. Farma. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Introduction: Lymphovascular invasion (LVI) has been shown to predict a worse prognosis in patients with colorectal cancer (CRC). However, the nature of the relationship between LVI and prognosis is not completely elucidated in studies. This study aims to define the patterns in mutation status in patients with CRC whose tumors display LVI. Methods: Patients who underwent molecular profiling (MP) while undergoing treatment for CRC at Fox Chase Cancer Center were retrospectively reviewed. MP was tested with an in-house next-generation sequencing targeted cancer panel, Foundation One or Caris. Relevant clinical and pathological data was collected. Comparisons were made using t-test, chi-squared, or Mann-Whitney tests as appropriate. Results: 69 patients were included. Mean age was 61 years. Twenty-eight (40%) patients presented at stage III, and 36 (52%) were stage IV. Mutation in KRAS was identified in 27 (39%) patients, in P53 in 37 (53%), APC in 31 (44%). BRAF mutation was detected in 11 (16%) of patients. KRAS mutation was present in 7 (25%) of stage III patients, and in 18 (50%) of stage IV patients. BRAF was mutated in 6 (21%) of Stage III patients and in 4 (11%) of Stage IV patients. For patients with and without KRAS mutation, overall survival (OS) was 36 vs 22 months (p=0.02), and patients with BRAF mutation had an OS of 15 vs 30 months (p=0.070) for patients with no BRAF mutation. In Stage III patients, OS for those with and without KRAS mutation was 37 vs 27 months (p=NS), and those with BRAF mutation had an OS of 11 vs 29 months for those without BRAF mutation (p=0.042). In stage IV patients, OS for those with and without KRAS mutation was 34 vs 26 months (p=NS), while those with and without BRAF mutation had OS of 18 vs 28 months (p=NS). Conclusions: Patients with KRAS mutations appear to have an improved OS. Patients who present with BRAF mutations trended toward a worse prognosis, but we will need to evaluate a larger dataset. Patients with LVI in stage III with BRAF mutations showed a statistically worse prognosis. Patients with LVI and stage IV had similar OS regardless of KRAS or BRAF mutations. A study of greater power is required to confirm these results.

PF55

Identification of a Distinct Subset of Patients with Intermediate-Grade Mucinous Appendiceal Neoplasm L.M. Knab,[1]* H. Choudry,[1] S. Perkins,[1] L. Totin,[1] M. holtzman,[1] S. Ahrendt,[2] A. Zureikat,[1] M. Hogg,[1] H. Zeh,[1] D. Bartlett,[1] J. Pingpank.[1] *1. University of Pittsburgh Medical Center, Pittsburgh, PA; 2. University of Colorado, Aurora, CO.*

Introduction: Pathologic assessment of appendiceal mucinous neoplasms has traditionally been challenging, and a recent study has separated these neoplasms into three morphologically defined grades (G1- G3) with prognostic significance. Grades are based on tumor cellularity, cytologic grade, invasion, and a signet ring cell component. Five-year overall survival for G1, G2, and G3 is 91%, 61%, and 23%, respectively. We hypothesized that within the intermediate group (G2) there is significant heterogeneity leading to a subgroup of patients that do significantly worse and behave more like the G3 group. Methods: We analyzed the perioperative outcomes, as well as the clinicopathologic and molecular features of patients in a prospectively maintained database with G2, intermediate grade, mucinous appendiceal neoplasm who underwent CRS/HIPEC between 2008 and 2017. Wilcoxon rank-sum and Kaplan-Meier were used as appropriate for statistical analyses. Results: The average age and BMI at first HIPEC of 52 patients with G2 pathology were 52 yo and 29.2 kg/m2, respectively. The average number of months to progression after first HIPEC was 19.5, and 5-year overall survival (OS) was 65%. When patients were divided into early progression (less than 12 months) and late progression (greater than or equal to 12 months), the risk of death was significantly decreased in those with late progression (hazard ratio 0.2, p=0.005). In the early progression group, pre-op CEA, peritoneal carcinomatosis index (PCI), completeness of cytoreduction (CC), length of stay (LOS), and number of positive lymph nodes were are significantly increased compared to the late progression group (Table). Five-year OS in the early group was 35% (compared to 23% OS in the G3 group from prior study), and in the late group it was 85%. Conclusions: There is a distinct subset of patients within the G2 mucinous appendiceal neoplasm group who have a worse prognosis indicated by early progression in less than 12 months from first HIPEC. In this group there is an increased risk of death (5-year OS approaching G3 survival data) as well as several significant clinicopathologic factors associated with early progression.

Clinicopathologic factors of patients with intermediate grade, mucinous appendiceal neoplasm

Progression (months)	Pre-op CEA* (med)	Pre-op CA 19-9 (med)	Pre-op CA 125 (med)	PCI* (med)	CC* Score (mean)	LOS* (med days)	LN (mean)	+LN* (mean)	LOH (mean)	KRAS (mean)
<12	12.3	116.5	21.8	26	0.5	16	9.1	2	12.8	0.58
>=12	4.1	17.2	19.7	12	0.1	12	14	0.17	9.4	0.42

PCI: peritoneal carcinomatosis index; CC: completeness of cytoreduction; LOS: length of stay; LN: lymph node; LOH: loss of heterozygosity; *indicates significant difference p<0.05

PF56

Is Routine High Ligation of the IMA in Rectal Cancer Necessary? A.M. Covelli,[1]* S.A. Chadi,[2] F.A. Quereshy.[3] *1. University of Toronto, Toronto, ON, Canada; 2. University Health Network, University of Toronto, Toronto, ON, Canada; 3. Princess Margaret Cancer Centre, University Health Network, University of Toronto, Toronto, ON, Canada.*

Introduction High ligation of the Inferior Mesenteric Artery (IMA) for rectal and sigmoid cancers is the standard of care. Little data exists about the rate of lymph node (LN) positivity of the apical LNs at the root of the IMA. Study objectives were to determine: 1.feasibility of separately harvesting apical IMA LNs and low ligation 2. the rate of involved apical LNs 3. characteristics associated with positive apical LNs. Methods A prospective chart review was completed of patients with rectal or sigmoid cancer treated at a tertiary center by a single high-volume surgical oncologist. Surgery was curative intent via laparotomy, laparoscopy or robot-assisted. Low ligation of the IMA and separate harvesting of the apical IMA LNs was planned in advance of the proposed surgery. Results 86 patients underwent surgery between August 2012 and July 2015. 72% were laparoscopic low anterior (LAR) or abdominal perineal resection (APR), 16% were robotic-assisted LAR/APR and 12% were open LAR/APR. Low ligation and harvesting of the apical IMA LNs was feasible in 82 patients (95%). 98% of all patients had ≥12 LNs removed. Of those who underwent low ligation 95% had ≥12 LNs identified within the rectosigmoid specimen alone. 40% of patients with <12 LNs received neoadjuvant therapy. 38% of patients had LN positive disease. 2 patients (2.4%) who underwent low ligation had positive apical IMA LNs. All patients with a positive apical LN had pathological T3 disease, yet only 4.8% of all T3 patients had a positive apical LN. No patients with T4 nor synchronous M1a disease had positive apical LNs. The presence of positive apical LNs did not increase pathological N stage. 7 patients recurred with local or distant disease. All patients who recurred had negative apical lymph nodes but node positive disease in the rectosigmoid specimen. Conclusion Low ligation and harvesting of apical IMA lymph nodes is frequently achievable. Positive apical LNs were rare and did not provide further oncologic information. Given the potential for compromised blood supply and injury to the hypogastric nerves, low ligation may be preferred in the correct clinical context. Further studies are necessary to clarify the utility of routine high IMA ligation.

PF57

Ovarian Metastasis Predicts Worse Outcomes in Cytoreductive Surgery and HIPEC M. Kuncewitch,* K. Chouliaras, L. Enomoto, K.C. Perry, G. Russell, P. Shen, E.A. Levine, K. Votanopoulos. *Wake Forest School of Medicine, Winston-Salem, NC.*

Introduction: Ovarian metastasis can be difficult to ascertain during cytoreductive surgery (CRS) with heated intraperitoneal chemotherapy (HIPEC) for non-gynecologic malignancies. We identified the incidence of ovarian metastasis (OM), impact of OM on survival, and correlation between

peritoneal carcinomatosis index (PCI) and the rate of pathologically confirmed OM. Methods: A prospectively maintained database of 1424 CRS-HIPEC was analyzed. Gynecologic malignancies were excluded. Median survival and 1-, 3-, and 5-year survival rates were calculated. The relationship between OM and extent of cytoreduction was evaluated. PCI was arranged by quartile with corresponding OM rates calculated. Results:Two-hundred and one patients met criteria. Appendiceal tumors comprised the majority of indications for oophorectomy (63.7%), with colorectal cancer, mesothelioma, gastric cancer, and small bowel tumors at 26.3%, 7%, 2%, and 1%, respectively. The overall rate of OM to either or both ovaries was 72.6%. No significant difference in OM rate by primary tumor was observed. When R0/R1 resection was achieved the OM rate was 63.8%, rising to 85.2% for R2a (p=0.0075). Rates of 1-, 3-, and 5-year survival for patients with and without OM were 79 vs. 91.6%, 48.7 vs. 72.2%, and 29.8 vs. 65.6%, respectively (p=0.0003). Median survival for women with OM was 2.9 years, rising to 3.6 years with R0/R1 resection. Median survival was not reached for women without ovarian involvement and an R0/R1 resection. Women without OM had a lower PCI compared to those with OM (7.2 vs. 15.9, p<0.0001). The 25th, 50th, and 75th percentiles for PCI were 6.0, 13.1, and 17.0, with corresponding OM rates of 26.5%, 73.5%, and 88.9%, respectively (p=0.0002; odds ratio 7.12 between 25th and 50th percentile). Conclusion: Nearly 3 in 4 women undergoing CRS and HIPEC for non-gynecologic malignancies will have ovarian metastasis. This is associated with a decreased likelihood that a complete cytoreduction will be possible and represents a negative prognostic indicator for long-term survival. A PCI > 6 dramatically increases the odds of ovarian involvement and merits strong consideration for bilateral oophorectomy during CRS-HIPEC.

PF58

Indication of Extended Lateral Lymph Node Dissection for Patients with Lower Rectal Cancer S. Yamauchi,* A. Takaoka, R. Seki, Y. Matsumiya, F. Orita, M. Sasaki, T. Miura, A. Kikuchi, T. Matsuyama, M. Ishiguro, T. Ishikawa, H. Uetake, M. Yasuno, Y. Kinugasa, K. Sugihara. *Digestive and General Surgery, Tokyo Medical and Dental University, Tokyo, Japan.*

Background Total mesorectal excision (TME) with lateral lymph node dissection (LLND) for lower rectal cancers (RCs) is the standard surgical procedure in Japan, while preoperative chemo-radiotherapy followed by TME is applied in Western countries. We previously reported that TME without LLND for lower RCs is an independent risk factor for RFS and OS by retrospective study which analyzed clinical data of 4269 lower RC patients (Hazard ratio 0.83, 0.83, respectively). In this study, we analyzed the same cohort in order to extract subsequent cohort which TME with LLND can extend the prognosis. Methods A total of 4269 patients with pathological stage I-III lower RC who underwent curative surgical resection with or without LLND (LLND group or non-LLND group) on during the period from 1997 to 2008 at 23 institutions of the Japanese Study Group for Postoperative Follow-up of Colorectal Cancer (JFUP-CRC) were retrospectively collected. The association between LLND and clinico-pathological factors was analyzed statistically. Results The median age of this cohort was 63 years (range, 19-96), and the median follow-up time was 73 months (range, 1-179). A total of 1807 patients (42%) underwent TME with LLND and 2462 patients (58%) underwent curative resection without LLND. LLND group were younger, more often male, higher preoperative CEA and CA19-9, had more often high grade histological status, more often T3/T4 tumor and more often vascular invasion than non-LLND group(all P<0.05). There is a tendency that adjuvant chemotherapy is more often applied for LLND group (P<0.001). Patients regardless of gender, or of high and low CA19-9 received prognostic benefits from LLND. In the cohort which tumor with differentiated tumor, with venous invasion and which patients without adjuvant therapy, LLND group had better RFS and OS than non-LLND group (all P<0.001). Conclusion Although there are limitations that this is a retrospective study and the indication for LLND differs from each institutions and surgeons, this study suggests that patients with lower RC which tumor is differentiated type and has venous invasion receive prognostic benefit.

PF59

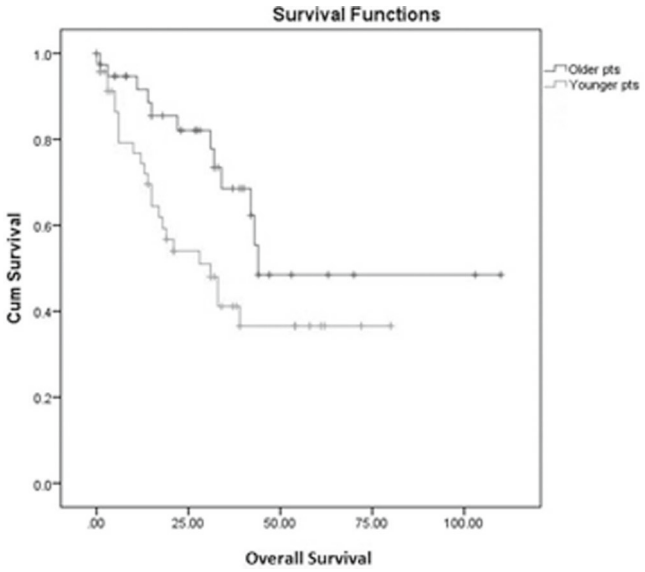
Melphalan versus Mitomycin-C: Similar Survival with More Neutropenia in Patients with Disseminated Colorectal Cancer Treated with Hyperthermic Intraperitoneal Chemotherapy Agent A. Sardi, A. Sipok,* C. Nieroda, M. Sittig, V. Gushchin. *Surgical Oncology, Mercy Medical Center, Baltimore, MD.*

Introduction: Search continues for an optimal hyperthermic intraperitoneal chemotherapy (HIPEC) agent for peritoneal dissemination of colorectal cancer (CRC). Melphalan has been used in recurrent/resistant ovarian cancer. We compare patient outcomes and survival obtained using melphalan vs mitomycin-C (MMC) as the chemotherapeutic agent in HIPEC. Methods: Sixty CRC patients were identified by retrospective review of a prospective database. Nineteen patients underwent CRS/HIPEC with melphalan (group I) and 41 with MMC (group II). Tumor site, peritoneal cancer index (PCI), cytoreduction scores (CC), and lymph node (LN) involvement were compared. Disease free survival (DFS) and overall survival (OS) were estimated with Kaplan-Meier survival analysis. Results: Median age at CRS/HIPEC was 53 years (range: 19-72). Right-sided primary lesions were in 19/60(32%) and left-sided in 40/60(67%), and 1(2%) was unknown (p=1). Median PCI was 17 (range: 3-35) vs 24 (range: 3-39) in groups I and II, respectively (p=0.5). All patients had complete cytoreduction (CC 0-1) in group I and 85% in group II (p=0.16). Positive lymph nodes were identified in 8/19 (42%) vs. 16/41(39%), respectively (p=1). Postoperative complications grade II/III/IV were observed in 6/4/0 patients in group I and 6/2/4 in group II, respectively (p=0.2). Hematologic complications occurred in 9/19 (47%) patients in group I and 3/41 (7%) in group II (p<0.001). Median follow-up was 23 months (range: 3-66). Median disease-free survival in groups I and II was 15 months (95% CI: 11-19) and 32 months (95% CI: 11-54), respectively (p=0.03). Median OS since CRS/HIPEC was 30 months (95% CI: 13-46) and 24 months (95% CI: 16-31), respectively (p>0.05). Of the 15 patients alive, 6 (40%) are alive with disease; 5 in group I and 1 in group II. Conclusions: No therapeutic advantage of melphalan over MMC was found in patients with PC from CRC, while more hematologic complications occurred. Further studies correlating chemotherapeutic perfusion agents to outcomes are needed.

PF60

More Advanced Disease but Longer Survival in Younger Patients with Carcinomatosis from Colorectal Cancer Following Cytoredcutive Surgery and Hyperthermic Intraperitoneal Chemotherapy D. Solomon,* N.L. Leigh, D. Feingold, D.R. Magge, B.J. Golas, D.M. Labow, U. Sarpel. *Surgical Oncology, Icahn School of Medicine at Mount Sinai, New York, NY.*

Background: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is an effective treatment in select patients with peritoneal carcinomatosis (PC) from colorectal cancer (CRC). Current guidelines recommend beginning screening colonoscopy at age 50. However, CRC rates are increasing in the prescreening population. Methods: Data collected from a prospectively maintained database of CRC patients undergoing CRS/HIPEC from 2007 to 2017 were retrospectively analyzed. A pre-screening cohort included patients <50 years at diagnosis; patients ≥50 years were compared as controls. We also analyzed age distribution for all patients undergoing colon resection, liver metastasectomy, and CRS/HIPEC from 1993 to 2013 in order to determine whether age varied with aggressiveness of surgery. Results: 103 patients underwent CRS/HIPEC, of which 45 (44%) belonged to the younger group. Younger patients were more likely to present with stage IV disease at diagnosis (p=0.033), yet survived longer after CRS/HIPEC (p=0.046). Charlson Comorbidity Index and ECOG score were similar for both groups (p=NS). Tumor grade was similar (p=NS). There was no difference in time from diagnosis to CRS/HIPEC or receipt of neoadjuvant and adjuvant chemotherapy (p=NS). Peritoneal Carcinomatosis Index (PCI), number of organs resected and anastomoses created were comparable (p=NS). Major Clavien-Dindo morbidity (3-4) and LOS were similar (p=NS). A non-significant trend towards higher rates of CC>1 in the older group was noted (p=0.071). Comparison of demographic data from colectomies (n=225), liver metastasectomies (n=233) and CRS/HIPEC showed that age <50 years was increasingly common with more aggressive procedures (9%, 14% and 44%, respectively). Conclusions: Younger patients with CRC presented with more advanced disease but demonstrated longer OS than older patients after CRS/HIPEC despite similar perioperative features. Our data also suggests that younger patients with CRC are more likely to undergo aggressive surgical treatment, which may explain this finding.



Kaplan Meier curves of overall survival for younger and older patients

PF61

C6 Ceramide (C6-Cer) to Induce Sensitivity to Cetuximab (Cet) in KRAS Mutant Colorectal Cancer (Crc) A. Menendez,[1] A.P. Mallon,[2] D. Curzake,[1] G. Haidemenos,[1] L. Luo,[1] H.J. Wanebo.[1]* *1. Roger Williams Medical Center, Bristol, RI; 2. Chemoenhanced LLC, Bristol, RI.*

BACKGROUND: Cet is beneficial for patients with metastatic KRAS Wild type (WT) CRC. C6 Cer can act synergistically with chemotherapy to induce apoptosis The aim was to compare growth inhibition percentage (GIP) of cytostatics 5 FU, Oxaliplatin (OX) and Cet with or without C6 Cer in DRAS WT and KRAS mutant (KRAS Mut) CRC cell lines (SW48 and SW480, respectively). METHODS: Cells were incubated with IC50 (0.8μM for OX 25 ug/ml for Cet and C6 Cer concentrations ranged from 5 to 10 μM). Cell survival was assessed 72 h after using 0.4% Trypan Blue. RESULTS: C6-Cer's GIP was 78.3% for SW-480 (vs. 33.33% for SW – 48). Addition of C6-Cer increased GIP with an 75% Addition of 5 and 7 μM resulted in 75% and 86.25% respectively vs 32.5% of 5-FU + Ox + Cet alone The greatest effect was seen when 10μM of C6-Cer was added (92.5%). Same concentration of drugs increased GIP for SW-48 to 93.5%. CONCLUSION: C6-Cer appears to have direct inhibitory properties, especially on KRAS Mut cells. When added to Ox, 5-FU and CET, C6-Cer reversed the apparent insensitivity of KRAS Mut to Cet. Also the study showed C6 Cer can provide additional synergism to their sytostatic properties in RAS WT CRC cell lines. The effect of isolated C6-Cer on KRAS Mut raises possibility of a different pathway bypass WFGR pathway.

PF62

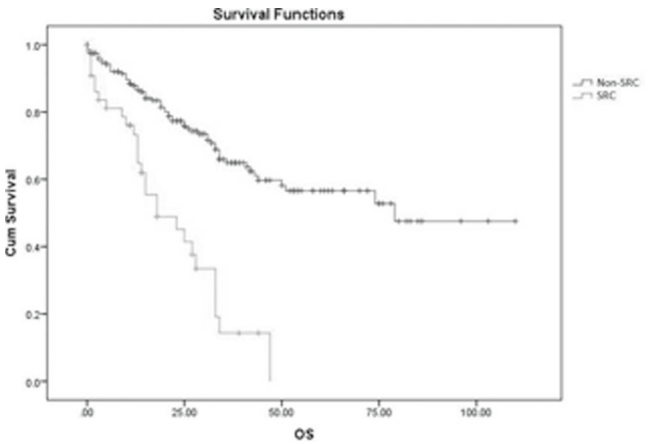
The ACA has No Impact on Surgically Resectable Colorectal Cancer Cases: A Population-Level Assessment of 2004-2014 A. Ramirez,* R. Balkrishnan, T.L. Hedrick, M. Williams. *University of Virginia, Charlottesville, VA.*

Objective: Following the enactment of the ACA's elimination of cost-sharing fees for preventative cancer screening, national screening rates for colonoscopy increased. The purpose of this study is to examine the link between changes in screening patterns and receipt of surgical treatment. We hypothesized that higher screening resulted in detection of earlier stage cancers increasing the likelihood of receiving surgical intervention. Methods: 416,056 cases aged 18-85 diagnosed with colorectal cancer (CRC) between 2004-2014 were identified using the SEER Registry. Patient demographic, cancer-related staging, and ICD-10-CP surgical management were collected. Segmented logistic regression analysis comparing a seven-year period before and four-year period after the ACA preventive service provision was performed. Results were stratified by stage at time of diagnosis and socio-demographic factors, controlling for secular trends and available confounders. Results: The ACA had no measureable impact on overall incidence rate of colorectal cancer (49.7 pre-ACA versus 38.9 post-ACA per 100,000) when slopes compared p>0.05. The policy was not associated with changing trends of stage at time of diagnosis except for a decrease in stage I cancer incidence, Wald X^2 6.9, p=0.008. The overall proportion of patients receiving curative-intent surgery for CRC decreased from 87.5% pre-ACA provision to 81.5% post-ACA provision, Wald X^2 1.6, p=0.21. Unexpected findings included an increase in stage III and IV over the study period. Additionally, there has been a 19.6% decrease in surgeries for stage IV CRC, which parallels an increase in recommendations for less surgical intervention from 9.1% to 15.4%, p<0.001. We also observed that the gap in racial disparities between Caucasians and African-Americans has decreased for receipt of surgery, 3.86% Pre-ACA versus 3.06% Post-ACA p<0.001. Conclusion: This is the first study to evaluate the impact of ACA-related coverage expansion on the surgical treatment of colorectal cancer. Elimination of cost-sharing fees for colorectal cancer was not associated with earlier stage diagnosis or rates of surgical intervention.

PF63

Signet Ring Cell Carcinoma with Peritoneal Carcinomatosis in Patients Undergoing Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy is Associated with Poor Overall Survival D. Solomon,* N.L. Leigh, D. Feingold, P.H. Liu, B.J. Golas, D.M. Labow, U. Sarpel, D.R. Magge. *Surgical Oncology, Icahn School of Medicine at Mount Sinai, New York, NY.*

Background: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS/HIPEC) is an effective treatment in select patients with peritoneal carcinomatosis (PC). Signet ring cell (SRC) pathology is rare but associated with poor prognosis; the role of CRS/HIPEC in this population is unclear. Methods: Patients with PC from appendiceal, colorectal and gastric cancer (AC, CRC, GC) who underwent CRS/HIPEC between 2007 and 2016 were included from a prospectively maintained database. Clinical outcomes of patients with and without SRC were compared. Results: A total of 253 patients underwent CRS/HIPEC: 130 (51.3%) with PC from AC, 103 (40.7%) from CRC and 20 (7.9%) from GC. GC patients had higher rates of SRC pathology than AC and CRC: 14 (70%), 17 (13.1%), and 13 (12.6%), respectively. Overall, 1 and 2-year survival were 73.2% and 48.9% for the SRC group and 87.8% and 75.9% for the non-SRC group (p<0.0001). Among the AC group, non-SRC patients demonstrated better survival than SRC patients; the median survival for SRC patients was 27 months, while at a median follow-up of 25 months, median survival was not yet reached in non-SRC patients (p=0.001). CRC patients with SRC had lower median survival than non-SRC (18 vs 44mos, p=0.009). In the GC group, all non-SRC patients had poorly differentiated histology; median survival between cohorts was similar (p=NS) and 1-year survival for the SRC group was 45.7%. Overall, SRC patients received more neoadjuvant chemotherapy prior to CRS/HIPEC (p<0.0001); PCI and CC-scores were comparable between cohorts (p=NS). In multivariate analysis, SRC (p<0.0001), PCI>20 (p=0.002) and CC>1(p=0.049) were independent predictors of poor OS. Conclusions: Survival in SRC carcinoma of GI origin with PC is dismal, particularly when associated with CRC and GC. CRS/HIPEC in this population provides only marginal clinical benefit and its role remains controversial.



Kaplan Meier Curves of Survival for SRC and non-SRC patients of GI origin undergoing CRS/HIPEC

PF64

Younger Patients have a Higher Incidence of Advanced Stage Rectal Adenocarcinoma at Time of Diagnosis S. Sujatha-Bhaskar,* A. Dosch, S. Mills, J.C. Carmichael, A. Pigazzi, M.J. Stamos, M.D. Jafari. *University of California Irvine Medical Center, Orange, CA.*

Background: Recent studies have highlighted the growing incidence of rectal cancer in younger patient demographics (age < 50). Due to the absence of standardized screening modalities for younger age groups, we hypothesize that these patients are at a higher risk for advanced disease at time of diagnosis. Methods: The National Cancer Database from 2006-2014 was reviewed for this study. Inclusion criteria consisted of patients diagnosed with rectal adenocarcinoma who underwent neoadjuvant chemoradiation, surgical resection, and adjuvant chemotherapy. Study cohorts were stratified by age into the following groups: < 35 years, 35-49, 50-64, and > 65 years. Pathological outcomes were reviewed in each cohort using multivariate analysis with Cox proportional hazard modeling and Kaplan-Meier curves to estimate overall survival. Results: Of 13,808 patients were identified who met our inclusion criteria, 2.6% (365) were in the < 35 year group, 22.5% (3,119) in the 35-49 group, 48% (6,597) in the 50-64 group, and 27% (3,727) in the > 65 group. Pathological Stage III disease was present in 41% of the < 35, 37% of the 35-49 group, 32% of the 50-64 group, and 32% of the > 65 group. Incidence of Stage III disease was significantly higher in the < 35 group and 35-49 group when compared to the > 65 group, P <0.01. Younger age groups had a higher incidence of pathological N2 disease with the < 35 at 18%, 35-49 at 13%, 50-64 at 9.4%, and >65 at 9.5%. An R0 resection was obtained in 88% of the < 35 group, 91% of the 35-49 group, 93% of the 50-64 group, and 92% of the > 65 group. Multivariate analysis demonstrated significantly low rates of overall negative margin for the < 35 group compared to 50-64 group (OR 0.52, 95 % CI 0.41-0.95, P = 0.02). Conclusion: Younger patients with rectal adenocarcinoma have higher rates of nodal involvement and are diagnosed at a later stage. Given a quarter of patients diagnosed with rectal cancer in our study are under 50 years, further investigation should be performed into expanding screening criteria for younger patients at risk.

Clinical and Pathological Characteristics of Age Groups

	< 35 years N = 365	35-49 years N = 3,119	50-64 years N = 6,597	> 65 N=3,727
Pathological T-Stage, %				
pT0	9.6	10	10	11
pT1	6.6	5.1	5.4	4.6
pT2	21	24	25	26
pT3	48	46	43	44
pT4	4.1	3.9	4.3	2.8
Pathological N-Stage, %				
pN0	51	52	56	56
PN1	24	25	24	24
pN2	18	13	9.4	9.5
Overall Pathological Stage, %				
Stage 1	18	19	21	21
Stage 2	19	21	23	23
Stage 3	41	37	32	32
Overall Clinical Stage, %				
Stage 1	2.5	4	3.9	5
Stage 2	25	30	35	38
Stage 3	59	55	50	44

PF65

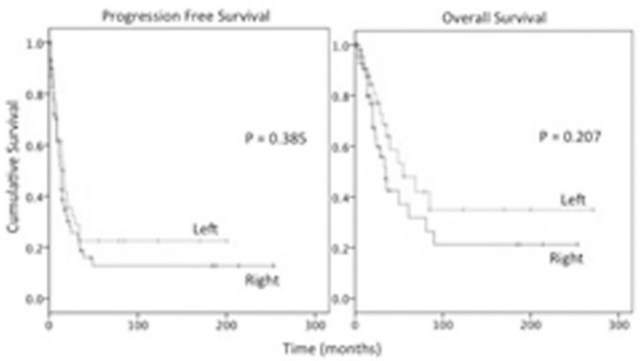
SMAD4 Gene Mutation is Associated with Higher Incidence of Peritoneal Involvement in Unresectable Metastatic Colorectal Cancer D. Vicente,* T. Mizuno, A. Loehrer, P. Limani, R.E. Royal, K. Fournier, Y. Chun, C. Conrad, C. Tzeng, S. Kopetz, T. Aloia, J. Vauthey. *Surgical Oncology, MD Anderson Cancer Center, HOUSTON, TX.*

Introduction: Drosophilia protein, mothers against decapentaplegic homolog 4 (SMAD4) is involved in TGF- β and Bone Morphogenic Protein (BMP) signaling pathways. Dysregulation in these signaling pathways is associated with carcinogenesis and poor prognosis in colorectal cancer (CRC). The aim of this study was to evaluate whether SMAD4 mutation was associated with peritoneal metastasis. Methods: Patients from a single institution with next generation sequencing of 50 cancer related genes and unresectable metastatic CRC were identified from a prospectively maintained medical oncology department database. Clinicopathological variables, metastatic sites, and genetic mutations were compared between SMAD4 mutant and SMAD4 wild type patients. Multivariable analysis was performed to evaluate for factors associated with peritoneal involvement. Results: Among 324 total patients with unresectable metastatic CRC who met inclusion criteria, 36 (11%) were SMAD4 mutants. Clinicopathological variables and additional cancer-related gene mutations were similar between SMAD4 mutant and wild type patients. Patients with SMAD4 mutations were more likely to present with peritoneal disease (50% vs. 24%, p = 0.002). Metastatic rates to the lungs, distant lymph nodes, and multiple metastatic sites at presentation were similar between the two groups. In patients with metachronous metastatic disease (n=131), SMAD4 mutation patients demonstrated a trend towards shorter interval to metastatic recurrence (12 vs. 23 months, p=0.059). During a median follow up of 26 months, SMAD4 mutation patients were more likely to develop peritoneal involvement at either presentation or in progression of disease (58 vs. 35%, p = 0.010). Multivariable analysis showed that compared to other mutations, only the SMAD4 mutation was associated with a higher risk of peritoneal metastasis (OR 2.5, 95% CI 1.2-5.6, p = 0.025). Conclusion: In patients with unresectable metastatic CRC, SMAD4 mutation is independently associated with peritoneal metastasis. Identification of this mutation may heighten awareness for peritoneal disease on staging scans and may inform decisions on treatment strategies.

PF66

Does Side Matter in Patients with Metastatic Colon Cancer Treated with Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy? M. Alsayednasser,[1]* R.M. Barone,[2] J. Veerapong,[1] J. Baumgartner,[1] A. Lowy,[1] K.J. Kelly.[1] *1. Surgery, UCSD, La Jolla, CA; 2. Sharp Memorial Hospital, San Diego, CA.*

Introduction: Primary tumor location has been shown to be prognostic of overall survival in patients (pts) with metastatic colorectal cancer treated with systemic chemotherapy. The impact of sidedness on prognosis has not been evaluated in the setting of peritoneal-based metastatic disease treated with cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC). Methods: A retrospective review of prospectively maintained databases of pts with peritoneal surface malignancy undergoing CRS/HIPEC from two high-volume centers was performed. Results: A total of 110 pts with metastatic colorectal cancer to the peritoneum who underwent CRS/HIPEC with mitomycin C were identified. Forty-seven patients (43%) had left-sided, and 63 (57%) had right-sided primary tumors. Pts with right-sided tumors were more likely to be male (49% vs 25%, p=0.012) and were more likely to have signet ring cell histology (18% vs 2%, p=0.011). There were no differences in age, peritoneal carcinomatosis index (PCI), completeness of cytoreduction (CC) score, differentiation, mucinous histology, lymph node involvement, or receipt of prior or adjuvant systemic chemotherapy between the two groups. The median follow-up was 19 months. Pts with left-sided tumors had a median progression free (PFS) and overall survival (OS) of 17 (95% CI 12.9 – 21.1) and 55 months (95% CI 18.9 – 91.0); respectively, versus 14 (95% CI 11.0 – 17.0) and 35 months (95% CI 25.3 – 44.7) for those with right sided primary tumors (p=0.207, 0.385; respectively) (Figure). On multivariate analysis accounting for PCI, CC-score, and lymph node involvement, CC-score was the only independent predictor of PFS or OS. Conclusions: It is known that right and left sided primary colorectal tumors are biologically different. There was a clinically, but not statistically, significant difference in OS between right and left sided tumors in this study. The impact of sidedness on survival following CRS/HIPEC warrants further investigation.

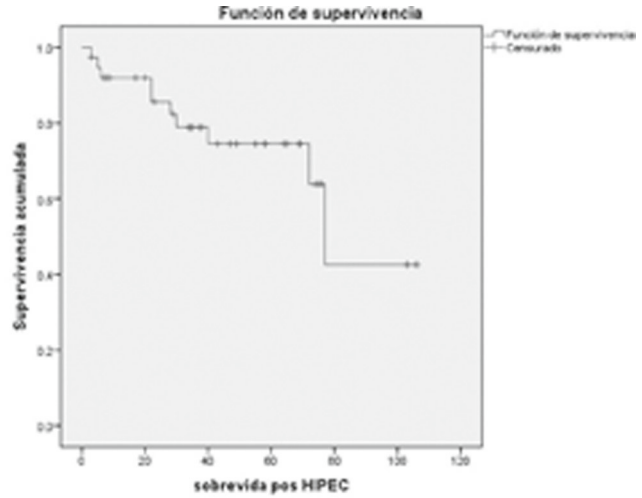


Kaplan-Meier plots demonstrating progression free and overall survival for pts with metastatic colorectal cancer to the peritoneum following CRS/HIPEC based on primary tumor side.

PF68

HIPEC in Epithelial Ovarian Cancer: First Prospective, Multicenter and Observational Report in Mexico with a 10-Year Follow-up J.M. Medina.* *ISSEMyM, Toluca, Mexico.*

Objective: The aim of the study is to demonstrate clinical and surgical features, overall survival and disease-free interval (DFI) of patients with advanced or recurrent EOC undergoing CRS +HIPEC at three Mexican cancer centers during a follow-up of 10 years. Methods: During the period from August 2007 to March 2017, 38 patients with EOC with peritoneal carcinomatosis treated with CRS+HIPEC were analyzed in a prospective, observational study at three Oncology Institutions of national patient reference. Results: The mean patient age was 51.71 years, The mean peritoneal carcinomatosis index-(PCI) was 8,. Complete cytorreduction (CC0) was performed in 33 patients (86.8%) and optimal (with residual of less than 1 cm) in 5 patients (17.2%). Pathologically, a complete microscopic resection (RR0) was achieved in 26 patients (68.4%). The mean surgical time was 6.57 hours. The average ICU length of stay was 3.4, days and the average length of hospital stay was 9.9, days. No intraoperative deathsoccurred; one perioperative death secondary to acute heart attack was presented. Only 5 patients (13.2%) required intestinal anastomosis. Regarding intraoperative bleeding, the mean blood loss was 1488. cc. Five patients (13.2%) required re-interventions due to bleeding, anastomotic dehiscence or eventration. Severe complications occurred in 10 patients (26.3%). The most frequent were pneumoniaand acute renal failure. Regarding preoperative chemotherapy, 31 patients (81.57%) received at least one first line therapy. About postoperative chemotherapy, 21 patients (55.3%) received treatment. During the 10-year follow-up, 39.4% of recurrences (15patients) were found, changing the pattern of peritoneal recurrence to systemic disease in 51.7%. In relation to cancer mortality, 10 patients died because cancer (26.31%) during the 10-year follow-up period. The disease-free interval was 35.5 months and the overall survival at 10 years was 74.6 months. Conclusion: CRS+HIPEC for advanced or recurrent EOC are feasible with acceptable morbidity and mortality providing adequate cancer control at 10 years. Keywords: Ovarian cancer, Cytoreduction, HIPEC, prospective study.



PF69

Long-term Survival Results of a Single-Institution Program of Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy for Peritoneal Malignancies S. Rodriguez-Qizilbash,[1]* K. Garbis,[2] R. Loungnarath,[1] M.L. Soucisse,[3] M. Alfayiz,[1] R. Younan.[1] *1. Department of Surgery, Centre Hospitalier de l'Université de Montréal, Montreal, QC, Canada; 2. University of Montreal, Montreal, QC, Canada; 3. Hôpital Maisonneuve-Rosemont, Montreal, QC, Canada.*

Introduction: Cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy (CRS + HIPEC) is a technique used to treat peritoneal carcinomatosis. This study's objective is to assess the long-term survival results from our single-institution program located in Canada. Methods: This is a retrospective study of a prospectively gathered database of 130 patients treated by two surgical oncologists from 2005 to 2017. Palliative and repeat procedures were excluded. Post-intervention survival rates at 5 years and 10 years were estimated using the Kaplan-Meier method. Complications were assessed using the Common Terminology Criteria for Adverse Events (CTCAE). Results: The average age of our patients was 54 years old. The most common tumor origins were colorectal (54 patients), appendiceal (disseminated peritoneal adenomucinosis (DPAM) (12 patients) and peritoneal mucinous carcinomatosis (PMCA) (38 patients)), peritoneal (11 patients) and ovarian (7 patients). The 5-year and 10-year overall survival (OS) rates were of 57% and 43%, respectively, whereas the disease-free survival rates were of 44% and 39%, respectively. 5-year OS by tumour origin were 30% for colorectal, 100% for DPAM, 77% for PMCA, 68% for peritoneal and 60% for ovarian. The average peritoneal cancer index (PCI) of our patients was 15. The 5-year OS rates per PCI category were as follows: 65% for a PCI between 0-10, 61% for a PCI between 11-20 and 34% for a PCI over 20. Ten-year OS results according to PCI were as follows: 59% for a PCI between 0-10, 53% for a PCI between 11-20 and 29% for a PCI over 20. The 5-year OS was of 57%, 51% and 38% for patients with a CCR of 0, 1 and 2, respectively. Severe complications (CTCAE grade 3 or 4) occurred in 25% of patients. One or more anastomoses were performed on 59% of patients. There was no 30-day mortality. Conclusions: CRS + HIPEC is an effective treatment option for patients with peritoneal carcinomatosis. Our 5-year and 10-year survival rates have shown to be comparable to those in the recent literature.

Grade 3 and 4 adverse events (CTCAE classification)

Grade 3 adverse events	Events	Grade 4 adverse events	Events
Catheter-related infection	5%	Anastomosis leak	2%
Clostridium difficile	4%	Bleeding splenic pedicle and intrahepatic vascular trauma requiring 7 returns to OR	1%
Fistula (enterocutaneous and at mesh)	3%	Delirium with threats to self and others	1%
Abscess (drained)	2%	Pneumonia requiring intubation	1%
Delirium (including one patient refusing to feed himself)	2%	Respiratory depression secondary to medication requiring admission to ICU	1%
Bowel obstruction	2%	Sepsis	1%
Wound dehiscence	2%	Septic shock	1%
Wound infection	2%		
Acute myocardial infarction	1%		
Anemia <80 g/L	1%		
Arterial thrombosis requiring fem-fem bypass	1%		
Bladder laceration fixed perioperatively	1%		
Catheter candidemia with ophthalmic extension	1%		
Fungemia	1%		
Hydronephrosis	1%		
Hypercapnia secondary to epidural migration	1%		
Liver abscess (rehospitalized and drained)	1%		
Operative bleeding requiring transfusion	1%		
Pelvic hematoma causing anemia requiring 7 transfusions and rehospitalization	1%		
Pneumonia (IV antibiotics)	1%		
Pulmonary embolus	1%		
QTc over 500 ms	1%		
Thrombosis of SVC	1%		
Unstable AF	1%		
Vertigo (rehospitalized)	1%		

PF70

Prognostic Impact of Nodal Status and Number of Positive Lymph Node in Right versus Left Colon Cancer: National Cancer Database 2004 -2014 S. Saha,[1]* S. Ramanathan,[2] D. Livert,[2] S. Mukkamala,[2] s. barola,[1] D. Wiese,[1] M. Arora.[1] *1. McLaren Regional Medical Center, Flint, MI; 2. Easton Hospital, Easton, PA.*

Introduction: Colon cancer (Cca) patients (pts) are treated according to the TNM staging rather than the location of the primary tumor. Hence, we wanted to analyze the prognostic impact of Right (Rt) versus Left (Lt) Cca in regard to Lymph node (LNs) status as well as no. of positive(+ve) LNs on survival. Methods: Data was obtained from the National Cancer Database (NCDB) from 2004-14. All Cca located to the cecum, ascending colon and hepatic flexure were designated as Rt(Group A) and splenic flexure with descending colon as Lt (Group B). Tumors of transverse colon, overlapping or not otherwise specified were excluded. Clinical characteristics were calculated with Pearson chi square testing. Overall survival(OS) analysis was performed based on LN status and no. of +ve LN using Kaplan Meier method. Results: A total of 232,691 pts were identified with 197,430 in Rt(GpA) and 35,261 cases in Lt(GpB) side. Rt sided Cca had a higher median age and female preponderance. Average no. of LNs examined and +ve LNs were 18.9/1.6 vs 16.7/1.4 respectively. Overall, there were more Stage I&II pts for GpA vs GpB. Five-year OS among Rt vs Lt was 74.6% vs 75.7% for Stage I & II and 42.6% vs 47.6% for Stage III & IV respectively.(Tab.1) Pts with LN -ve disease had a similar survival for both groups and correspondingly had the best survival. Comparing 5 yrs OS between Rt vs Lt, all LN +ve was 43.4% vs 49.1%. For 1+ve LN the OS was similar but for 2 or more LN +ve pts the 5 yr OS was significantly worse for Rt vs Lt. All p-values for survival analysis were significant.(Tab 1). Conclusion: This largest data from NCDB for comparing Rt vs Lt Cca suggests that eventhough more LNs were examined and more earlier stages were found in Rt vs Lt, OS for LN-ve and LN+ve pts were much worse for Rt vs Lt Cca. Further works related to the different molecular markers between the two sites might explain such differences.

TABLE 1a. Characteristics of Right and Left colon cancer. n = 232,691

	Right (Group A) (197,430)	Left (Group B) (35,261)	p-value
Age (Median)	73	68	<001
Sex- Male Female	 44% 55%	 53% 47%	<001
Grade - Well Moderately Poorly Undifferentiated	 10.9% 65.6% 21.2% 2.4%	 10.9% 73.1% 14.5% 1.4%	<001
Mean no. of LN Examined	18.9	16.7	<001
Mean no. of LN Positive	1.6	1.4	<001
Stage I	27.2%	23.0%	<001
Stage II	37.3%	39.8%	<001
Stage III	24.8%	25.3%	<001
Stage IV	10.8%	11.9%	<001
Five year Survival between Right and Left by Colon cancer by Stage and Number of positive Lymph nodes.			
	Right	Left	p-value
Stage I and II	74.6%	75.7%	<001
Stage III and IV	42.6%	47.6%	<001
Node negative	73.5%	73.7%	<001
All Node positive	43.4%	49.1%	<001
1 +ve LN	59.6%	59.5%	<001
2+ve LN	52.3%	55.2%	<001
3+ve LN	46.1%	53.3%	<001
> 4+ve LN	29.7%	36.1%	<001
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PF71

Should Neoadjuvant Chemoradiotherapy be Eliminated in the Elderly? A Review of NCDB A. Allard-Picou,* S. Mukkamalla, J.C. Hardaway, R. Rathore, J. Espat, P. Somasundar. *Roger Williams Medical Center, Providence, RI.*

Introduction: Standard of care for locally advanced rectal cancer (T3-4 or N1-2) includes neoadjuvant chemoradiotherapy (CRT) and surgical resection. In the elderly (≥65 years), it is often difficult to tolerate. Elderly patients comprise majority of new rectal cancer patients but many are unable to complete neoadjuvant CRT resulting in low compliance rates. Grade III/IV toxicities cause significant morbidity resulting in delays to surgical resection. The purpose of this study is to evaluate the impact of neoadjuvant CRT on elderly rectal cancer patients. Methods: A review of NCDB of all patients with rectal cancer who underwent surgical resection from 2006 to 2009 was performed. Patients receiving preoperative CRT were compared to those receiving postoperative CRT and those receiving surgery alone. Subgroup analyses were performed on elderly and very elderly groups (≥75 years). The primary outcome was overall survival (OS). The effect of radiation on outcomes in elderly was investigated. Statistical analyses performed using Pearson Chi-square test and multivariate logistic regression. Results: We identified 8,656 patients with rectal cancer who met criteria (52.2% elderly, 26% very elderly). Overall, 64.6% patients received chemotherapy (58.1% received multi-drug regimen), 32.7% of patients received radiotherapy. Very elderly patients exhibited worse OS compared to elderly (HR 0.58), and to patients 18-64 years (HR 0.36), p<0.0001. Patients who underwent treatment with systemic chemotherapy (single/multi-agent) demonstrated better OS compared to surgery alone patients (HR multi-agent: 0.64, p=0.002; single agent: 0.69, p=0.01). On multivariate analysis, elderly patients who received preoperative CRT exhibited worse OS compared to those who received post-operative CRT (HR 0.64, p<0.0001) (Figure 1). Additionally, radiation did not have a significant survival impact in the elderly (HR 0.98, p.32). Conclusion: Elderly patients receiving neoadjuvant CRT demonstrate worse OS compared to patients who received adjuvant CRT, irrespective of surgical resection. Consideration should be given to eliminating neoadjuvant CRT in the elderly and when administered, should be done with caution.

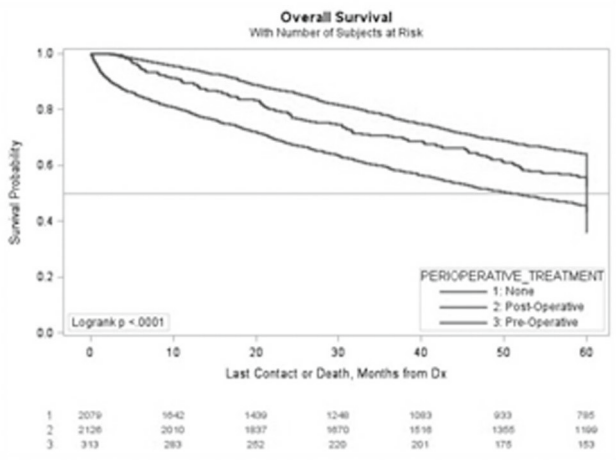


Figure 1. Effect of Preoperative vs Postoperative CRT on Overall Survival in Elderly Patients

PF72

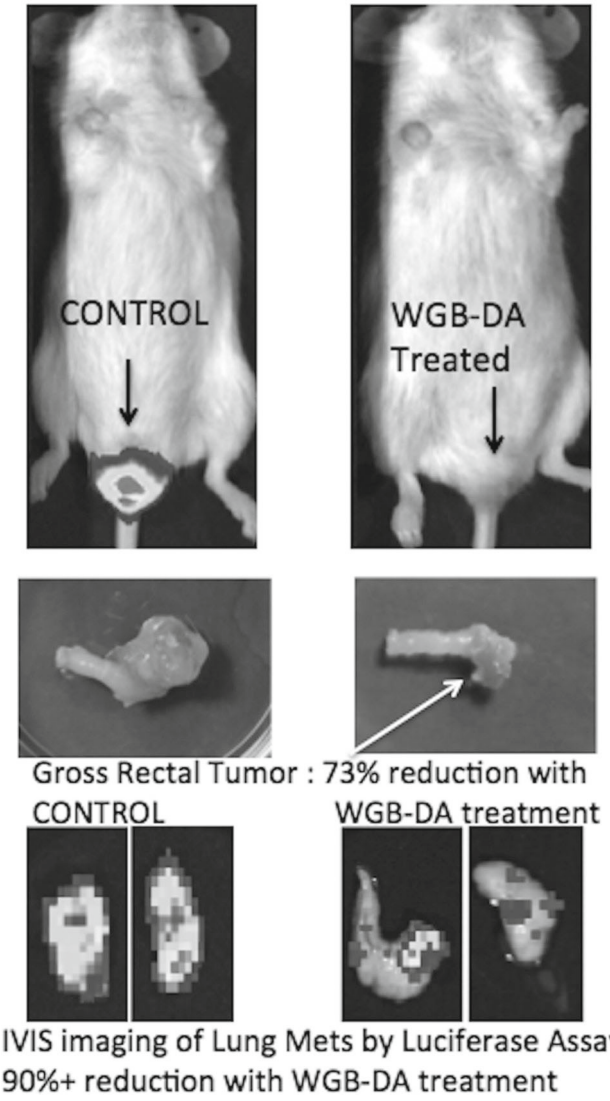
Neoadjuvant Strategies Leading to a Complete Clinical Response and Non-Operative Management for Rectal Cancer: A Single Institution Experience M. Strode,[1]* R. Shah,[1] C. Mangieri,[2] A. Saunders,[1] K. Atwood,[1] V. Francescutti,[1] S. Nurkin.[1] *1. Roswell Park Cancer Institute, Buffalo, NY; 2. Eisenhower Army Medical Center, Evans, GA.*

Introduction: Non-operative management (NOM) strategies have emerged as an option for patients with rectal cancer experiencing a complete clinic response (cCR) after neoadjuvant therapy. Methods: We performed a retrospective review of a prospectively collected database for patients with rectal cancer treated from 2012-2016. We identified patients that had elected for NOM after receiving neoadjuvant therapy and achieving documented cCR. Patients were followed on a strict surveillance schedule that included physical exam, laboratory testing, endoscopy and imaging. Results: A total of 33 patients (54% female, 46% male) elected to undergo NOM. Mean patient age was 70.8 years. Twenty-three patients (69%) had low tumors (≤ 7cm from anal verge) and 42% of patients were treated with total neoadjuvant therapy (induction or consolidation, and long course chemoradiation). During a median follow-up of 22 months, there were 5 (15.1%) recurrences (1 local, 1 local and distant, and 3 distant). Two of the isolated distant recurrences were to the lung or liver and were amenable to metastasectomy. Another patient experienced a synchronous distant liver and local recurrence treated with resection of the primary tumor and liver metastasectomy. One patient experienced a local recurrence alone and was also successfully salvaged with surgery. Of the 5 total recurrences, 4 (80%) were salvaged. There was 1 mortality, due an unrelated cause. Conclusion: Neoadjuvant treatment strategies may facilitate greater rates of cCR. Durable responses after these treatments may enable more patients to undergo NOM. More research is required to identify the appropriate patient population. For those patients experiencing recurrence, surgical salvage is often possible.

PF73

Novel Safe Withanolide Inhibits Orthotopic and Metastatic Colorectal Cancer Growth In Vivo Through Wnt Blockade C. Subramanian,[1]* L. Hellmers,[3] E. Brandes,[1] J. Sanchez,[1] K. Kovatch,[1] G. Maresh,[3] N. Hite,[3] D. Margolin,[3] B.N. Timmermann,[2] L. Li,[3] M.S. Cohen.[1] *1. Department of Surgery, University of Michigan, Ann Arbor, MI; 2. University of Kansas, Lawrence, KS; 3. Ochsner Clinic, New Orleans, LA.*

Introduction: Colorectal cancer (CRC) claims 600,000 deaths each year worldwide with 93% of cases having an altered Wnt signaling pathway. Based on our findings in other cancers, we hypothesize that the novel withanolide, Withalongolide B 4,19 Diacetate (WBD) prevents CRC tumor growth in vitro and in vivo through Wnt signaling blockade. Methods: Validated CRC lines (SW48, SW480 and HT29) were grown in 2D culture. Wnt signaling pathway proteins were evaluated by Western Blot (WB) for changes after withaferinA (WA) or WGB-DA treatment. Apoptosis was measured by flow cytometry(FC) and confirmed by WB. β-catenin pathway was evaluated by Luciferase reporter assay (LRA). For our orthotropic CRC model, NOD/SCID mice were injected with luciferase tagged HT29 cells in combination with lymph node stromal HK cells into the sub-mucosal rectum and treated i.p. after day14 with 8mg/kg WA, 6mg/kg WGB-DA, or saline control daily x 28days and imaged for luciferase activity to determine tumor growth using IVIS spectrum. Necroscopy assessed tumor weight, liver/lung metastasis and organ toxicity. Results: Phosphorylated GSK-3β was significantly enhanced with 500 nM withanolide treatment($p<0.01$ vs control) while total levels of GSK-3β remained constant. LRA revealed 60-80% down regulation of β-catenin activity ($p<0.001$) and significant modulation of its down stream effectors, such as axin, cyclinD1, TCF1 and LEF1(all $p<0.05$) at 1μM withanolide. FC and WB confirmed significant increase in apoptosis (Cleavage of PARP and Caspase 3) at 500nM withanolide treatment. In vivo, only WGB-DA signifcsntly inhibited orthotopic tumor growth by over 70% ($p<0.001$vs control) Figure 1. 100% of controls developed liver/lung mets vs. 10% with WGB-DA ($p<0.0001$) while no organ toxicity was observed with treatment. Conclusion: The novel withanolide WGB-DA significantly inhibits CRC growth through blockade of Wnt signaling in vitro and in an orthotopic in vivo model. In vivo it lacks toxicity and potently inhibits tumor growth while preventing metastatic spread to the liver and lungs and warrants further translational evaluation to support its clinical development.

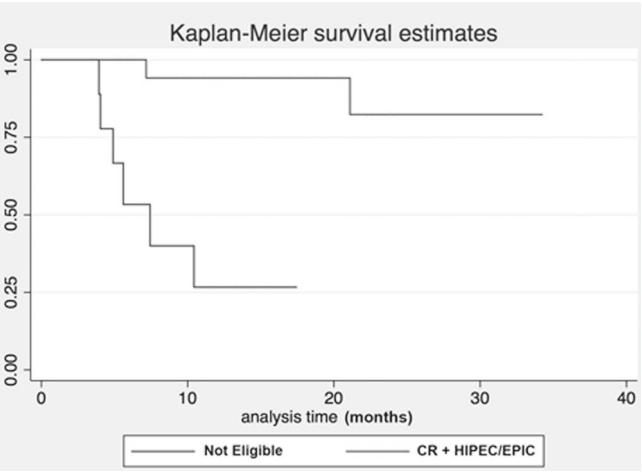


In vivo comparison of orthotopic CRC tumor control (Left) with WGB-DA treated mouse (Right) showing significant tumor volume reduction on IVIS luciferase assay whole body imaging (upper photographs) as well >70% tumor reduction grossly (middle photos). Additionally WGB-DA reduced lung metasases by > 90% vs. controls as shown on representative IVIS organ Luciferase imaging from necropsy.

PF74

Starting a Peritoneal Carcinomatosis Treatment Program in a Developing Country J. Gajardo,* N. Devaud, S. Hoefler, R. Charles, J. Butte. *Surgical Oncology, Fundacion Arturo Lopez Perez, Santiago, Chile.*

Introduction. Citoreduction (CR) plus hiperthermic intraperitoneal chemotherapy (HIPEC) has become the standard treatment for selected patients with peritoneal carcinomatosis derived from primary peritoneal or gastrointestinal tumours. The aim of this study is to evaluate the perioperative and mid-term results of this evolving procedure at our institution. Materials and Methods. A prospectively maintained database for all patients undergoing exploratory surgery for peritoneal carcinomatosis was reviewed. Eligible patients for CR and HIPEC were selected using the peritoneal cancer index (PCI) in correlation with the primary tumor origin. After the achievement of a complete citorreduction (CC-0), patients underwent HIPEC using Mitomycin-C for 90 minutes at 42 celcius using a closed technique. Clinical data and post-operative results were evaluated and analyzed using Stata 14. Results. Thirty-three patients underwent exploratory surgery with curative intent between October 2014 and August 2017. Most patients were male (58%) with a median age of 59 years [range 25-83]. The treatment included CC-0 and HIPEC in 19 patients and CC-0 and EPIC in 3 patients. Eleven patients were considered unresectable. The most frequent primary tumor site was colorectal in 12 patients, followed by appendix (n=8), gastric (n=6), peritoneal (n=5) and others (n=2). Median PCI was 10.5 (range 2 – 39) and median length of surgery was 539 minutes. The median number of resected organs was 4 (range 1 – 8), with a mean blood loss of 200cc. In 5 patients (26%) a diverting ileostomy was required. The median length of hospital stay was 8 days, with a median intermediate care unit length of stay of 3 days (range 1 – 7). Postoperative surgical morbidity included 31% Clavien-Dindo II and III complications. Ninety-day mortality was 0%. Eighteen patients (94%) who underwent CC-0 and HIPEC were alive by the end of this study. Conclusion. The peritoneal carcinomatosis treatment program at our institution has been established in a safe manner, with low morbidity and adequate patient selection resulting in prolonged survival.



Kaplan Meier survival estimates of CC-0 plus HIPEC/EPIC treatment versus not eligible patients.

PF75

Primary Tumor Location Predicts Colorectal Carcinomatosis Burden in Patients Undergoing Cytoreductive Surgery K.J. Lafaro,* A.M. Blakely, O.S. Eng, M. Raoof, B. Lee. *Surgery, City of Hope, Pasadena, CA.*

Background: Primary tumor location is prognostic for metastatic colorectal cancer including patients with peritoneal carcinomatosis (PM). Further it predicts response to first-line chemotherapy. However it is not known if primary tumor location is associated with the burden of disease at the time of cytoreductive surgery (CRS) or completeness of cytoreduction (CCR) Methods: A retrospective review of a prospectively maintained institutional database of all patients undergoing CRS with or without heated intraperitoneal chemotherapy (CRS/HIPEC) from 1/2009-8/2016 was performed to examine demographics, primary tumor characteristics, peritoneal carcinomatosis index (PCI) and CCR in patients who underwent CRS and HIPEC for colorectal adenocarcinomas. Patients with appendiceal tumors were excluded. Cut-off for right and left-sided tumors was defined as… Results: A total of 55 patients underwent CRS with or without HIPEC for colorectal cancer with PM. Majority were left-sided (n=32, 58%) and the remainder were right-sided (n=23, 42%). The median age was 53 and majority were female (29, 52.7, %). Median PCI for all patients was 9 (2-34). HIPEC was performed for 43 patients. On univariate analysis there was no difference in median age, sex, histology between the right and left-sided tumors. However, patients who underwent CRS/HIPEC for right sided colon primary had a significantly higher median PCI than those with a left sided colon or rectal primary (14.80 [95% CI 9.90-19.70] vs. 8.625 [95%CI 6.5-10.73], p=0.008). This finding persisted after adjusting for patient demographic and tumor characteristics. Similarly patients with right-sided tumors were more likely to have incomplete cytoreduction compared to those with the left sided tumors after adjusting or covariates (5.78, 95% CI 4.21-7.35, p<0.001). Conclusions: Primary tumor location is correlated with burden of carcinomatosis and ability to achieve complete cytoreduction.

PF76

Evaluation of Prognostic Factors Affecting Length of Hospital Stay (LOS) Post Cytoreductive Surgery(CRS) and Hyperthermic Intraperitonal Chemotherapy(HIPEC) B. Koh, N. Shannon,* M. Teo. *Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: Peritoneal carcinomatosis has historically been considered a terminal condition treated with palliation. A paradigm shift occurred when aggressive locoregional therapy with cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) afforded long-term survival and cure in selected patients. However, it is still viewed with skepticism as a highly morbid procedure with prolonged hospital stays. Our objective was to assess factors associated with prolonged hospital stays, in an attempt at better patient selection. Methods: 137 consecutive patients with peritoneal carcinomatosis treated with CRS-HIPEC between November 2012 and November 2016 were stratified by whether they had prolonged hospital stay (≥ the median of 12 days) and compared. Factors assessed consisted of pre-operative factors such as patient demographics, intra-operative factors such as tumour histology, peritoneal cancer index (PCI) and types of surgical procedures performed. Results: 78 (57%) patients who underwent CRS-HIPEC, had a prolonged hospital stay and typically had more extensive disease (median PCI score 12 vs 6, p<0.01). Although mucinous tumours were found to have higher burden of peritoneal disease as compared to adenocarcinoma or serous adenocarcinoma (median PCI 17 vs 7.5, 10 respectively, p<0.01) this was not prognostic for length of stay (p=0.13). There was no association with patient demographics or other peri-operative factors assessed. Prolonged length of stay was predicted following operations requiring multivisceral resection (p<0.01), and right hemicolectomy (44% vs 20%, p<0.01). Only right hemicolectomy was significant in multivariable analysis. Conclusion: Higher PCI score, multivisceral resection and right hemicolectomy performed during CRS-HIPEC were prognostic factors leading to prolonged LOS. While LOS may have multiple etiologies, we hypothesize that right-sided colectomy procedures result in a protracted recovery due to slower return of bowel function and higher incidence of post-operative ileus, however, more in-depth studies need to be done.

PF77

Factors Affecting Requirement for SICU Admission After CRS and HIPEC N. Shannon,* G. Tan, C. Chia Shulyn, K. Soo, M. Teo. *Surgical Oncology, National Cancer Centre Singapore, Singapore, Singapore.*

Introduction: Cytoreductive surgery (CRS) with hyperthermic intraperitoneal chemotherapy (HIPEC) is used to treat selected patients with peritoneal carcinomatosis, but can be associated with prolonged hospital stay, significant morbidity and mortality. Our objective was to assess factors associated with SICU admission after CRS/HIPEC. Methods: 241 consecutive patients undergoing CRS/HIPEC between 2001 and 2016 were stratified by post-operative SICU stay as none, overnight (1 day) or extended (≥2 days) and compared. Variables assessed consisted of demographics, preoperative haemoglobin and albumin, and intraoperative factors. Variables significant on univariate analysis were combined into a multivariable model with continuous variables binarised by Youden's index. Results: SICU stay was as follows: 87 none (36.1%), 71 overnight (29.4%), and 83 extended (34.4%) and was not associated with demographic factors aside from diabetes (12% vs 3.4% p=0.039) and low pre-operative albumin (22% vs 6.9%, p=0.022). SICU admission was associated with higher median PCI score, multivisceral resection, chest tube insertion, stoma creation, and blood loss (p<0.01) although only PCI score remained significant for predicting extended stay. SICU admission was associated with duration of CRS/HIPEC (9 vs 6 hours, p<0.01) and later median end time of operation (7pm vs 5pm, p<0.01). In multivariable analysis, for SICU admission: chest tube insertion, estimated blood loss ≥ 750ml, duration of surgery ≥ 7.5 hours and end time of surgery ≥ 6pm were independently prognostic, of these chest tube insertion and end time had the highest weightage. For predicting extended SICU stay, only multivisceral resection and duration of surgery ≥ 10.5 hours were independently prognostic. Conclusion: Need for SICU admission after CRS/HIPEC is driven by intraoperative factors. Extended stay is associated with prolonged operation time (≥ 10 hours) and multivisceral resection. However, overnight stay is associated with chest tube insertion and end-time after 6pm. Perhaps patients in the latter group may be better served by a period of observation in the post-operative care unit, rather than requiring admission directly to SICU.

PF78

Does Sentinel Lymph Node Status have Prognostic Significance in Patients with Acral Lentiginous Melanoma? S.N. Pavri,* G. Han, S.A. Khan, D. Han. *Surgery, Yale University, New Haven, CT.*

Introduction: Sentinel lymph node biopsy (SLNB) is indicated in patients with localized melanoma and provides important staging data. However, the prognostic benefit of performing SLNB and factors predictive of survival in patients with acral lentiginous melanoma (ALM) are unknown. We evaluated for factors predictive of SLN metastasis and of survival in patients with ALM. Methods: The Surveillance, Epidemiology, and End Results database was queried for ALM cases that had a SLNB from 1998 to 2013. Clinicopathologic factors were correlated with SLN status, overall survival (OS), and melanoma-specific survival (MSS). Results: There were 753 ALM patients who had a SLNB. Overall median age was 65 years; 51.8% of cases were female while 26.8% of cases were non-Caucasian. The majority of ALM were on the leg (83.0%), and the overall median Breslow thickness was 2 mm. Ulceration was seen in 59.0% of cases, while SLN metastases were detected in 188 of 753 cases (25.0%). Multivariable analysis showed that only Breslow thickness significantly predicted for a positive SLNB (OR: 1.38, 95% CI: 1.22-1.60; P<0.0001). Overall median follow up was 44 months. ALM patients who had a positive SLN had significantly worse OS and MSS compared with negative SLN patients (both P<0.0001). Overall 5-year OS and MSS were 70.7% and 80.8%, respectively. For positive SLN patients, 5-year OS and MSS were 48.1% and 58.9%, respectively, while for negative SLN patients, 5-year OS and MSS were 78.7% and 88.5%, respectively. On multivariable analyses, older age, increasing Breslow thickness, presence of ulceration, and a positive SLNB significantly predicted for worse OS and MSS (all P<0.05). Conclusions: This study is the largest report evaluating SLNB in ALM patients and confirms the important role of SLNB in this specific population. SLN metastases are seen in 25% of ALM cases, and SLNB provides significant prognostic information in ALM patients, with worse survival seen in positive SLN compared with negative SLN patients. In addition, similar to what is seen in other forms of melanoma, thickness, ulceration status and SLNB status significantly predict for survival in ALM.

PF79

Age-related Changes in Lymphatic Permeability Promote Visceral Melanoma Metastasis B. Ecker,[1]* A. Kaur,[1] M.G. Neuwirth,[1] A.J. Sinnamon,[1] X. Xu,[1] G. Karakousis,[1] A. Weeraratna.[2] *1. Surgery, University of Pennsylvania, Philadelphia, PA; 2. Wistar Institute, Philadelphia, PA.*

Older age identifies a high-risk cohort of melanoma patients, with increased risk of distant metastases and inferior survival. While clinical observation supports the lymphatic systemic as the predominant pathway of melanoma dissemination, older patients have lower rates of sentinel lymph node metastases yet paradoxically have inferior disease-specific survival. We examined whether age-related changes in lymphatic permeability may account for melanoma progression from the lymphatic system to distant visceral sites. In melanoma patients undergoing sentinel lymph node biopsy, patient age correlated with retention of Technetium radiotracer as well as the lymphatic expression of collagen crosslinking protein HAPLN1, supporting the age-dependent role of the extracellular matrix (ECM) in maintaining lymphatic endothelial integrity. The addition of rHAPLN1 to aged fibroblast ECMs in vitro was sufficient to reduce endothelial permeability, whereas endothelial permeability was increased following HAPLN1 knockdown. Such differences in permeability were mediated by changes in endothelial adherens junctions, where the treatment of aged fibroblasts with rHAPLN1 rescued endothelial VE-cadherin signaling to that observed in the context of young fibroblasts. VE-cadherin staining of lymphatic endothelium correlated with patient age in human lymph node specimens, and the treatment of aged murine lymph nodes with rHAPLN1 restored VE-cadherin signaling. Lymphatic HAPLN1 expression was prognostic of long-term patient survival in a multivariate Cox proportional hazards model adjusting for disease stage and patient age. The role of the extracellular matrix in mediating endothelial permeability and melanoma tumor progression will be important for cancer surveillance and treatment in an aging population.

PF80

Is the Number of Sentinel Lymph Nodes Important for Head and Neck Melanoma Staging? C.J. Puza,[1]* S. Josyula,[2] D.M. Agnese,[2] J. Howard,[2] A.M. Terando,[2] P.J. Mosca,[1] W.T. Lee,[1] G. Beasley.[1] *1. Duke University, Department of Surgery, Durham, NC; 2. Ohio State University, Division of Surgical Oncology, Columbus, OH.*

Background: Head and neck (HN) cutaneous melanoma is associated with worse disease-free survival compared to non-HN cutaneous melanoma. Sentinel lymph node biopsy (SLNB) for HN melanoma has been reported to have lower rates of SLNB positivity and higher false negative (FN) rates compared to SLNB for non-HN cutaneous melanoma. This suggests inadequate staging may contribute to worse disease-free survival for HN melanoma. We aim to determine if a higher yield of SLNs affected rates of SLNB positivity. Methods: Data from 2 centers Cancer Registries were used to identify 333 patients who underwent SLNB for HN melanoma from 2009 to 2016. A FN was defined by nodal recurrence after a negative SLNB. FN rate was calculated by the number of FN SLNs divided by the sum of FN and true negative SLNs. Results: Of 333 patients who underwent SLNB for HN melanoma, 20% (n=69) had a positive SLN with a FN rate of 6.3%. Group 1 was defined as patients with 1 or 2 LNs harvested, and Group 2 was defined as having 3 or more LNs harvested druing SLNB. Group 2 had a higher rate of SLN positivity (23.8% vs. 16.4%), a lower FN rate (5.8% vs. 9.6%), higher sensitivity (83.3% vs. 65.7%), and a higher negative predictive value (94.1% vs. 90.4%) compared to Group 1. These differences occurred despite similar median Breslow depths (1.5 mm Group 1 vs. 1.6 mm Group 2) and a similar percentage of tumors with ulceration (35% Group 1 vs 33% Group 2). Of patients in Group 1 with a positive SLN who underwent completion lymph node dissection (CLND) (20/23), 47% had one or more positive non-sentinel nodes compared to 29% of patients in Group 2 with positive non-sentinel nodes who underwent CLND (42/46) after a positive SLN. Although not statistically significant, the median survival for patients in Group 1 was 5.84 years compared to 7.05 years for those in Group 2. Conclusion: In HN melanoma cases in which lymphoscintigraphy identifies multiple nodes, diligent efforts should be made to harvest all SLNs to adequately stage patients, especially given SLNB may now be the only therapeutic surgical procedure performed for the LN basin.

Table 1

Group	Positive SLN	False Negative	True Negative	False Negative Rate	Sensitivity	Negative Predictable Value
All (n=333)	20.7% (n=69)	6.3% (n=21)	77.8% (n=259)	7.5%	76.4%	92.5%
1 or 2 SLN (n=140)	16.4% (n=23)	8.6% (n=12)	80.7% (n=113)	9.6%	65.7%	90.4%
3 or more SLN (n=193)	23.8% (n=46)	4.6% (n=9)	75.6% (n=146)	5.8%	83.3%	94.1%

PF81

Surgical Management and Immunotherapy in the Treatment of Anorectal Melanoma B.D. Babcock,* D. Kearns, M. Rodrigues, J. Lee, N. Solomon, C.A. Garberoglio, M. Senthil, S.S. Lum, M.E. Reeves, J.P. Namm. *Surgery, Loma Linda University Medical Center, Loma Linda, CA.*

Introduction: Anorectal melanoma (ARM) is a rare clinical entity representing <2% of all melanomas. A diagnosis of ARM carries a poor prognosis with a five-year survival ranging from 12-18%. Currently, there are no established guidelines for surgical resection or adjuvant therapy in the setting of this rare disease. Objective: To determine whether overall survival (OS) is affected by surgical approach or immunotherapy in patients diagnosed with ARM without distant metastatic disease. Methods: The National Cancer Database (NCDB) was used to identify all patients diagnosed with ARM without distant metastatic disease between 2012-2014 post-FDA approval of adjuvant immunotherapy for treatment in melanoma. Univariate and multivariate analyses were performed to determine the significance of surgical approach (local excision vs. segmental resection) and adjuvant immunotherapy with regards to overall survival. Results: 257 patients were identified within the NCDB with ARM between 2012-2014 without evidence of metastatic disease at diagnosis. Of these patients, 27 received immunotherapy. Median OS of all patients was 20 months. Median OS of patients receiving immunotherapy was 17 months. Neither immunotherapy (HR=1.51, p=0.352) nor surgical approach (local excision HR=0.75, p=0.309) was significant in respect to OS. On multivariate analysis only male gender (HR=1.68, p=0.03), Charlson-Deyo ≤1(HR=0.44, p=0.05), and age <50 years (HR=0.25, p=0.01) were significantly associated with survival hazards. Conclusions: This study supports the surgical literature in that local excision for ARM is the preferred surgical approach due to decreased morbidity and no difference in overall survival compared to segmental rectal resection. Females, younger age, and limited comorbidities are associated with improved prognosis in ARM. Furthermore, the addition of immunotherapy in these patients may not offer a significant survival advantage, however, these results must be interpreted with caution due limited adoption and abbreviated follow up.

Survival Hazards for Anorectal Melanoma

Variable	HR	p-value
Male gender	1.68	0.032
Age <50yrs	0.25	0.013
Age 50-70yrs	0.74	0.206
Academic facility	1.43	0.127
White race	1.10	0.737
Charlson-Deyo ≤1	0.44	0.049
Immunotherapy received	1.51	0.352
Local excision of tumor	0.75	0.309

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National Practice Patterns of Completion Lymph Node Dissection for Sentinel Node-Positive Melanoma B. Hewitt,[1]* R. Merkow,[1] J. DeLancey,[1] J. Wayne,[1] C. Balch,[2] K. Bilimoria.[1] *1. Surgical Outcomes and Quality Improvement Center - Northwestern University, Chicago, IL; 2. MD Anderson Cancer Center, Houston, TX.*

Background: Current recommended management of a positive sentinel lymph node (SLN) for regionally metastatic melanoma is to consider completion lymph node dissection (CLND). However, two recent trials and several retrospective studies suggest close observation may be an appropriate alternative to CLND for selected patient populations. Our objectives were to examine current practice patterns and factors associated with the utilization of CLND in patients with sentinel node-positive melanoma. Methods: Using the National Cancer Database, we examined the use of CLND in SLN positive patients diagnosed with clinically node-negative Stage III melanoma in 2013-2014. Logistic regression models were developed to assess the patient, tumor, and hospital factors associated with CLND utilization after positive SLN biopsy. Results: Of 57,951 patients identified with stage I-III melanoma, 24,927 (43.1%) underwent SLN biopsy, and 2,469 (9.9%) had a SLN with metastatic disease. Of these patients, 1,795 (72.7%) had only one positive SLN with metastatic melanoma, and 923 (51.4%) of these patients underwent CLND. Among 674 patients with >1 positive SLN, 507 (75.2%) underwent CLND (P<0.001). Patients were less likely to undergo CLND if the primary tumor was located on the lower extremity (i.e., needing inguinal lymphadenectomy; Odds Ratio [OR] 0.60 95% Confidence Interval [CI] 0.47-0.77; p<0.001), were older (p<0.001), or were treated at a hospital with lower melanoma surgical volume (<20 cases per year: OR 0.57 95% CI 0.44-0.75; p<0.001 and 20-49 cases per year: OR 0.68 95% CI 0.52-0.88; p=0.004). Patients with >1 positive SLN were more likely to undergo CLND (OR=2.91; 95% CI 2.36-3.57; p<0.001). Conclusions: CLND performance varied significantly based on the number of positive SLNs. As growing evidence supports close observation in selected patient populations with low SLN disease burden, monitoring is needed to ensure that CLND is performed in appropriate patient populations.

Table: Factors associated with CLND (compared with no additional intervention) in 2,469 patients with metastatic melanoma on SLN biopsy

Factor	All patients with positive SLN: Proportion undergoing CLND (%)	Odds Ratio (95% Confidence Interval)	P-value[1]
Total cohort	57.9		
Age, y			
≤55	65.1	1.0 (Referent)	
56-65	60.9	0.82 (0.65-1.02)	0.08
66-75	54.0	0.60 (0.48-0.76)	<0.001
≥76	40.1	0.36 (0.28-0.47)	<0.001
Tumor location			
Upper extremity	56.9	1.0 (Referent)	
Head and neck	60.6	1.04 (0.78-1.38)	0.80
Trunk	63.8	1.10 (0.88-1.39)	0.40
Lower extremity	48.8	0.60 (0.47-0.77)	<0.001
Hospital volume quintile			
Highest	63.4	1.0 (Referent)	
High	59.6	0.85 (0.66-1.09)	0.19
Moderate	60.2	0.91 (0.70-1.18)	0.47
Low	53.7	0.68 (0.52-0.88)	0.004
Lowest	49.4	0.57 (0.44-0.75)	<0.001
Number of positive LNs			
1	51.4	1.0 (Referent)	
>1	75.2	2.91 (2.36-3.57)	<0.001

[1]P value from multivariable logistic regression model. Factors not statistically significant include sex, race, ulceration, lymphovascular invasion, Breslow thickness, income, Charlson-Deyo index, and year of diagnosis.

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Completion Lymphadenectomy for a Positive Sentinel Node Biopsy in Melanoma Patients is Not Associated with a Survival Benefit N.D. Klemen,[1]* G. Han,[2] S.P.L. Leong,[3] M. Kashani-Sabet,[3] J.T. Vetto,[4] R.L. White,[5] S. Schneebaum,[6] B.A. Pockaj,[7] N. Mozzillo,[8] K.J. Charney,[9] H. Hoekstra,[10] V.K. Sondak,[11] J.L. Messina,[11] J.S. Zager,[11] D. Han.[1] *1. Yale University, New Haven, CT; 2. Texas A&M University, Bryan, TX; 3. California Pacific Medical Center Research Institute, San Francisco, CA; 4. Oregon Health and Sciences University, Portland, OR; 5. Carolinas HealthCare, Charlotte, NC; 6. Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel; 7. Mayo Clinic, Phoenix, AZ; 8. Istituto Tumori Napoli Fondazione G. Pascale, Napoli, Italy; 9. St. Joseph Hospital Of Orange, Orange, CA; 10. University of Groningen, Groningen, Netherlands; 11. Moffitt Cancer Center, Tampa, FL.*

Introduction: Completion lymph node dissection (CLND) for a positive sentinel lymph node (SLN) biopsy in melanoma patients improves regional disease control and provides prognostic data, but studies have not shown a survival benefit. We evaluated the impact of CLND on survival and assessed for factors predictive of non-SLN metastases (positive CLND). Methods: Retrospective review of the Sentinel Lymph Node Working Group database from 1994 to 2016 identified 847 positive SLN melanoma patients. Clinicopathologic factors were correlated with a positive CLND, overall survival (OS), and melanoma-specific survival (MSS). Results: Median follow-up was 28.7 months. CLND was performed in 742 of 847 positive SLN patients (87.6%); 125 of 742 CLND cases (16.8%) had a positive CLND. Significantly worse OS and MSS were seen in positive CLND versus negative CLND patients (P<0.01). CLND was not performed (No CLND) in 105 of 847 positive SLN cases (12.4%) with follow up data available in 91 of 105 patients. In 15 of 91 No CLND cases (16.5%), a clinically-detected nodal recurrence (NR) developed at a median of 11 months. No significant differences in OS and MSS were seen comparing CLND with No CLND cases (P=0.07, P=0.15, respectively) and comparing positive CLND with the 15 No CLND cases that had a NR (P=0.48, P=0.82, respectively). Performance of CLND was not correlated with OS or MSS, but the number of positive sentinel nodes or a positive CLND significantly predicted OS and MSS on multivariable analyses (P<0.01). Significant predictors of a positive CLND on multivariable analysis included increasing age, female gender, head/neck or leg primary site, ulceration, lymphovascular invasion and increasing number of positive sentinel nodes (P<0.05). Conclusions: Our retrospective study supports the MSLT-II trial results and shows that CLND for a positive SLN is not associated with a survival benefit, although it does provide additional prognostic information. Furthermore, positive SLN patients may represent a heterogeneous group, and the challenge remains to identify high-risk patients with micrometastatic nodal disease who could potentially benefit from CLND.

Descriptive Statistics

Variable	All Patients n=847	Positive CLND n=125	Negative CLND n=617	No CLND n=105	P-value
Age (years; median, [IQR])	54, [42.1, 65.9]	56.4, [44.1, 67.8]	52.9, [40.7, 63.2]	62.3, [47.5, 72.9]	<0.001
Gender: Female (n, %)	332 (39%)	60 (48%)	238 (39%)	34 (32%)	0.04
Gender: Male (n, %)	515 (61%)	65 (52%)	379 (61%)	71 (68%)	
Primary Site: Head/Neck (n, %)	106 (13%)	21 (17%)	69 (11%)	16 (15%)	<0.001
Primary Site: Leg (n, %)	254 (30%)	58 (46%)	167 (27%)	29 (28%)	
Primary Site: Trunk (n, %)	364 (43%)	37 (30%)	283 (46%)	44 (42%)	
Primary Site: Arm (n, %)	121 (14%)	9 (7%)	97 (16%)	15 (14%)	
Thickness (mm; median, [IQR])	2.5, [1.4, 4.2]	3.3, [2.3, 5.7]	2.3, [1.4, 3.9]	2.4, [1.3, 4.6]	<0.001
Ulceration: Yes (n, %)	316 (38%)	69 (55%)	207 (34%)	40 (38%)	<0.001
Ulceration: No (n, %)	414 (49%)	43 (34%)	318 (52%)	53 (51%)	
Ulceration: Unknown (n, %)	112 (13%)	13 (10%)	88 (14%)	11 (11%)	
LVI: Yes (n, %)	105 (12%)	30 (24%)	62 (10%)	13 (13%)	<0.001
LVI: No (n, %)	383 (45%)	49 (39%)	282 (46%)	52 (50%)	
LVI: Unknown (n, %)	354 (42%)	46 (37%)	269 (44%)	39 (38%)	
Mitotic Rate: <1/mm2 (n, %)	2 (1%)		2 (1%)		0.01
Mitotic Rate: 1-5/mm2 (n, %)	206 (64%)	25 (45%)	152 (68%)	29 (67%)	
Mitotic Rate: >5-10/mm2 (n, %)	74 (23%)	17 (30%)	46 (21%)	11 (26%)	
Mitotic Rate: >10/mm2 (n, %)	40 (12%)	14 (25%)	23 (10%)	3 (7%)	
SLNB Site: Axilla (n, %)	371 (44%)	40 (32%)	288 (47%)	43 (41%)	0.05
SLNB Site: Head/Neck (n, %)	154 (18%)	26 (21%)	109 (18%)	19 (18%)	
SLNB Site: Inguinal (n, %)	267 (32%)	53 (42%)	182 (29%)	32 (30%)	
SLNB Site: Other (n, %)	48 (6%)	6 (5%)	32 (5%)	10 (10%)	
SLNB Site: Unknown (n, %)	7 (1%)		6 (1%)	1 (1%)	
Total positive SLN (n; median, [IQR])	1, [1, 2]	1, [1, 2]	1, [1, 1]	1, [1, 1]	<0.001
Reason for No CLND: Surgeon choice (n, %)				11 (10%)	
Reason for No CLND: Clinical Trial (n, %)				15 (14%)	
Reason for No CLND: Technical (n, %)				3 (3%)	
Reason for No CLND: Patient refusal (n, %)				12 (11%)	
Reason for No CLND: Unknown (n, %)				64 (61%)	

IQR: interquartile range. LVI: lymphovascular invasion. SLNB: sentinel lymph node biopsy. CLND: completion lymph node dissection.

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Molecular Profiling in Melanomas That are Non-Recurrent or Recurrent within Two Years of Diagnosis M. Renzetti,* I.A. Soliman, K. Loo, J. D'Souza, E. Handorf, H. Wu, B. Luo, H. Liu, A. Olszanski, S. Movva, M. Lango, S. Reddy, J. Farma. *Fox Chase Cancer Center, Philadelphia, PA.*

INTRODUCTION: Commercial Gene expression profiles (GEP) have offered potential for better prognostic testing for patients with malignant melanoma (MM). However, they only determine overall recurrence risk, and do not distinguish between risk of recurrence with metastasis and other recurrence types. Here we examine the use of molecular profiling of patients who did not recur (NRM) compared those who recurred (RM) within 2 years of diagnosis. METHODS: Patients with MM diagnosis were included. Using NGS, we analyzed tissue for mutations in targeted regions of 50 cancer-related genes. Clinical and pathologic data were collected. RESULTS: We performed NGS on 179 patients with MM. 97 were nonrecurrent (NRM) without progression and 66 were recurrent (RM) within 2 years. Median age at diagnosis was 65 (range 22-81). 67% were male. 16 were stage I, 58 were stage II, 77 were stage III, and 13 were stage IV. 58% of tested tissue (n=91) was from a primary tumor. In NRM, 116 total mutations were identified over 45 unique genes. In RM 118 mutations were identified over 45 genes. The median number of mutations in both was 2 (range 0-9). Most frequently identified NRM mutations included BRAF (42%), NRAS (30%), TP53 (16%), and CDKN2A (9%). The most frequently identified RM mutations included NRAS (40%), TP53 (32%), BRAF (22%), and CDKN2A (13%). BRAF mutation was predictive for no recurrence within 2 years (p=0.032). RM were divided into non-metastatic (NMR, n=24), and lymph node or solid organ metastasis (MR, n=42). In NMR 57 mutations were identified over 37 genes. In MR 74 mutations were identified over 40 genes. Median number of mutations in NMR was 2 (range 0-9), and MR median was 1 (range 0-5). The most frequently identified NMR mutations included NRAS (54%), TP53 (42%), CDKN2A (13%), and FLT3 (13%). The most frequently identified MR mutations were NRAS (33%), BRAF (29%), TP53 (26%), and CDKN2A (12%). No predictive mutation was identified. CONCLUSIONS: We found that BRAF was predictive for NRM. NMR appeared to have more NRAS and TP53 instances, while MR seemed to have more BRAF mutations. These trends warrant further study with larger sample size to identify more predictive genes.

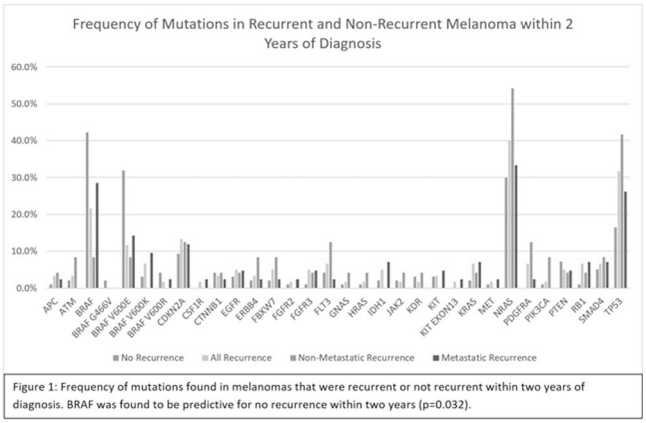

Figure 1: Frequency of mutations found in melanomas that were recurrent or not recurrent within two years of diagnosis. BRAF was found to be predictive for no recurrence within two years (p=0.032).

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Re-Biopsy of Partially-Sampled Thin Melanoma Impacts Sentinel Lymph Node Sampling as Well As Surgical Margins E. Weitman,* D. Lee, M.C. Perez, V.K. Sondak, A.A. Sarnaik, R. Gonzalez, C. Cruse, J.L. Messina, J.S. Zager. *Moffitt Cancer Center, Tampa, FL.*

Background: Cutaneous thin melanoma (defined as ≤ 1.0 mm in depth) is typically treated by wide excision alone with sentinel node biopsy (SLNB) for melanomas >0.75 mm. In some cases, the final surgical pathology may identify a thicker primary than noted on initial biopsy. We sought to assess the impact of additional biopsy of residual pigment and its role in changing surgical management of the primary tumor. Methods: All patients with residual pigment after a diagnosis of atypical melanocytic proliferation (AMP), melanoma in-situ (MMIS), or invasive melanoma ≤0.75mm who underwent additional biopsy prior to definitive resection were reviewed. Clinico-pathologic outcomes were reviewed. Results: Seventy-five patients were identified who met the search criteria. Fifty patients (66.7%) presented with a thin melanoma on initial biopsy and twenty-five patients (33.3%) presented with either AMP or MMIS on initial biopsy. The mean age of patients was 62.6 years old (51% male). The median number of additional biopsies was one. Initial biopsies were most commonly performed as a shave biopsy (62.7%) whereas re-biopsies were most commonly performed as a punch biopsy (86.7%). Primary melanomas were most commonly found on the extremities (62.78%), followed by the trunk (26.7%) and head and neck (10.7%). Of the seventy-five total patients with a melanoma ≤ 0.75mm on initial biopsy, twelve patients (16%) had a final depth >0.75mm on re-biopsy and subsequently underwent SLNB at the time of wide excision. One of these patients (1.3%) had a positive node identified on SLNB. Six patients (8.0%) had a change in surgical margins during wide excision due to re-biopsy upstaging the AMP, MMIS or melanoma. Five of these patients (6.7%) were identified as either AMP or MMIS on initial biopsy and on re-biopsy had thin melanomas. Sixty-five patients (86. 7%) did not demonstrate a greater depth on final pathology as compared to preoperative biopsy. Conclusion: Re-biopsy of thin melanoma can impact both the decision to perform a SLNB as well as the extent of surgical margins. Additionally, re-biopsy of a partially-sampled melanoma is a strong indicator of final tumor depth.

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Melanoma Incidence Among Ethnic Minority Populations M. Huyser,[1]* A.L. Chang,[2] K. Yang,[2] C. Chang.[2] *1. UCSF East Bay, Oakland, CA; 2. Kaiser Permanente, Oakland, CA.*

Introduction: Melanoma incidence continues to increase in Caucasian populations, but less is known about the incidence in ethnic minority populations. The purpose of this study was to characterize the incidence and prognosis of cutaneous melanoma among the non-Caucasian population in Northern California. Methods: A retrospective chart review was performed to identify patients with thin melanoma treated in Northern California between January 1996 and December 2015. This identified 15,157 Caucasian, 138 Asian, 51 African American, and 335 Hispanic cases. Univariate and multivariate analyses of predictive factors were evaluated with the log-rank test and Cox regression. In addition chi-square test of relevant clinicopathologic factors determined which factors were predictive of overall survival. Results: Mean ages at diagnosis were 54 year old for Asian and Hispanics, while African-American were older at 59 years old, followed by Caucasian at 61 years old (p<.001). Asian and African-American tended to have a higher percentage of females at 59% and 55% respectively. Among histologic types, Caucasians were least likely to be diagnosed with acral lentiginous melanoma (0.4%) and Asians most likely (5.1%). Asians were also most likely to have Desmoplastic type (2.9%). African Americans were least likely to be diagnosed with superficial spreading or nodular types (9.8% and 2.0%) with Hispanics most likely to have superficial spreading (23.3%) and Asians most likely to have nodular types (6.5%). Hispanics had similar rates of localized and distant disease compared with Caucasians, but were more likely to have regional extension as well as nodal involvement (2.7% and 9.6%) than Caucasians (1.6% and 3.1%). Asian and African Americans were more likely to present with nodal involvement (13.8% and 11.8%) and distant disease (8.7% and 7.8%) than Caucasians (4.3% and 3.1%). Additionally, African Americans had a poorer survival than all other races. Conclusions: Differences exist among ethnic groups and genders in terms of melanoma stage, histological type, and overall survival. Recognizing these differences may promote earlier detection and decrease melanoma related mortality among patients.

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Priming with IL: 7/15 to Generate CD8+ T Cells Metabolically Fit in the Tumor Microenvironment T. Hoki, T. Yamauchi, S. Patel, K.A. Collins, J.V. Welch, J. DiTursi, C. Eppolito, A.J. Francois, K. Odunsi, F. Ito.* *Roswell Park Cancer Institute, Buffalo, NY.*

Current approaches to adoptive T cell therapy are limited by the difficulty of obtaining sufficient numbers of T cells against targeted antigens with effective in vivo characteristics. Whereas interleukin (IL)-2 has been widely used for generation of antitumor T cells in vitro clinically, dose-dependent effects of IL-2 on differentiation of T cells are associated with decreased proliferative and self-renewal capacity in vivo. Accumulating evidence largely from examining hematological malignancies indicates that the combined use of another common γ chain cytokines, IL-7 and IL-15 (IL-7/15) can produce T cells that confer superior antitumor immunity in vivo. However, antitumor efficacy of IL-7/15-primed T cells in an orthotopic tumor model has not been rigorously evaluated. To this end, we used Pmel-1 T-cell receptor transgenic $CD8^+$ T cells activated with the cognate antigen gp100 expressed on B16 melanoma in IL-2 or IL-7/15. Cell expansion was significantly higher when T cells were activated in IL-7/15. IL-7/15-primed T cells secreted significantly more IL-2 against the target antigen compared to IL-2-primed T cells while both had comparable effector function in vitro. Furthermore, IL-7/15-primed T cells had higher mitochondrial spare respiratory capacity than IL-2-primed T cells under low glucose condition even with an inhibitor of fatty acid oxidation and glutaminase, suggesting that IL-7/15-primed T cells have capacity to produce more ATP in case of a sudden increase in energy demand. In line with this, adoptively-transferred IL-7/15-primed T cells expressed significantly higher Ki67 than IL-2-primed T cells in the tumor microenvironment. Significantly delayed tumor growth and improved survival were observed in mice treated with IL-7/15-primed T cells compared to IL-2-primed T cells. Taken together, our studies suggest that IL-7/15 modulates the metabolic programming of T cells to promote more robust and efficient $CD8^+$ T cells that can proliferate in the TME. In particular, IL-7/15-primed T cells have higher self-renewal and spare respiratory capacity with potent effector function that correspond to significantly improved survival in an orthotopic tumor model.

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Genome Editing of Tumor Specific T Cell-Derived Induced Pluripotent Stem Cells T. Yamauchi,[1] H. Saito,[2] T. Hoki,[1] F. Ito.[1]* *1. Roswell Park Cancer Institute, Buffalo, NY; 2. Kanazawa Medical University, Kanazawa, Japan.*

Induced pluripotent stem cells (iPSCs) derived from somatic cells of patients hold great promise for autologous cell therapies. One of the possible applications of iPSCs is to use them as a cell source for producing autologous lymphocytes for cell-based therapy against cancer. We and others have shown that iPSC-derived regenerated T cells have potent antitumor efficacy in vitro and in vivo. The potential of iPSCs can be further enhanced by genome engineering and then used to study individual gene function, track cells or endogenous proteins with a knock-in reporter, and correct genetic defects for gene therapy. We reprogrammed T-cell receptor (TCR) transgenic melanoma-specific T cells into pluripotency, and established a syngeneic mouse model for evaluating antitumor reactivity of regenerated T cells from iPSCs bearing a

rearranged TCR of known antigen specificity. Pluripotency of T cell-derived iPSCs (TiPSCs) was confirmed with immunostaining of embryonic stem cell (ESC) markers, RT-PCR analysis of pluripotency-associated transcription factors, and microarray analysis demonstrated a high degree of similarity in their gene expression patterns with ESCs, but distinct from parental T cells. Cytogenetic analysis revealed the TiPSCs maintained normal karyotype. The TiPSCs differentiated to embryoid bodies in vitro, and upregulation of marker genes for all three germ layers was detected by immunostaining. Their differentiation capacity was further confirmed by teratoma formation in immune-deficient mice in vivo. Moreover, we confirmed that the TiPSCs retained the same rearranged configuration of TCR chain genes as the original TCR transgenic T cells. TiPSCs were, then, subjected to the lentivirus-mediated transduction of tetracycline-inducible Cas9 vectors. The transduction efficacy was confirmed by the mCherry fluorescence and the RT-PCR against the Cas9 sequence. In conclusion, we found successful reprogramming of antigen-specific T cells and lentiviral-mediated transduction of tetracycline-inducible Cas9 vectors into TiPSCs, which will allow us to generate an unlimited number of phenotypically defined, functional and expandable genome-edited autologous antigen-specific T cells.

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Intratumoral CD8+ T-Cell Heterogeneity Defined by the Chemokine Receptor, CX3CR1 T. Yamauchi, T. Hoki, C. Eppolito, A.J. Francois, K. Odunsi, F. Ito.* *Department of Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Although a significant subset of cancer patients benefit from immune checkpoint inhibitors such as anti-PD-1/PD-L1, many fail to have clinical responses. A better understanding of the mechanisms that regulate $CD8^+$ T-cell responses in the tumor microenvironment is required to improve immunotherapies that restore function in exhausted $CD8^+$ T cells. Heterogeneity of $CD8^+$ T cells in the tumor microenvironment (TME) has been recognized; however, their functions and roles are ill-defined. We have evaluated phenotypical and functional heterogeneity of tumor-infiltrating lymphocytes (TILs) after adoptive transfer of ex vivo primed Pmel-1 T-cell receptor transgenic $CD8^+$ T cells specific for the gp100 melanocyte differentiation antigen expressed on B16 melanoma. We found that the chemokine receptor, CX3CR1 identified three distinct effector $CD8^+$ T-cell subsets, CX3CR1 negative (-), intermediate (int), and high (hi) in the TME. A $CX3CR1^{hi}$ subset contained terminally-differentiated $CD8^+$ T cells that expressed higher levels of killer-cell lectin like receptor G1 (KLRG1), TNF-related apoptosis-inducing ligand (TRAIL), perforin, and granzyme. Significantly more $CX3CR1^{int}$ $CD8^+$ T cells expressed CD25 compared to the other subsets, suggesting this is the subset that rapidly proliferates and preferentially generates terminally-differentiated T cells. Unexpectedly, despite their terminally differentiated status, a $CX3CR1^{hi}$ $CD8^+$ T-cell subset expressed significantly lower levels of co-inhibitory receptors, PD-1, LAG3, and TIGIT compared to $CX3CR1^-$ and $CX3CR1^{int}$ $CD8^+$ T-cell subsets in the TME. In line with this, proliferation and cytokine production of $CX3CR1^-$ and $CX3CR1^{int}$ $CD8^+$ T-cell subsets were significantly decreased in the TME compared to $CX3CR1^{hi}$ $CD8^+$ T-cell subset. Importantly, PD-1/PD-L1 blockade significantly improved effector functions of $CX3CR1^-$ and $CX3CR1^{int}$ $CD8^+$ T-cell subsets in the TME. In conclusion, the chemokine receptor, CX3CR1 defines distinct effector $CD8^+$ T-cell subsets in the TME. Tumor-infiltrating $CX3CR1^-$ and $CX3CR1^{int}$ $CD8^+$ T-cell subsets express high levels of co-inhibitory receptors, PD-1, LAG3, and TIGIT, and their effector functions are improved by PD-1/PD-L1 blockade.

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CD40 Signaling for Generation and Expansion of Cytotoxic CX3CR1+CD8+ T Cells T. Yamauchi, T. Hoki, C. Eppolito, A.J. Francois, K. Odunsi, F. Ito.* *Department of Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Successful immunotherapeutic treatment of cancer requires generation and expansion of tumor-specific cytotoxic $CD8^+$ T cells. Recently, the chemokine receptor, CX3CR1 was found to identify distinct populations of pathogen-specific effector $CD8^+$ T cells in periphery in infectious models of vaccinia and lymphocytic choriomeningitis virus (LCMV) where $CX3CR1^+CD8^+$ T cells were the progeny of $CX3CR1^-CD8^+$ T cells. Although $CX3CR1^+CD8^+$ T cells were found to exhibit robust cytotoxicity, their role in the context of tumor immunity remains unknown. To this end, we used ex vivo primed Pmel-1 T cell receptor (TCR) transgenic $CD8^+$ T cells specific for the gp100 melanocyte differentiation antigen expressed on B16 melanoma. Although in vitro activation with gp100 generates $CX3CR1^-CD8^+$ T cells that have potent effector function against B16, secreting IFNγ, TNFα, and IL-2 with enhanced cytotoxicity against target antigen in vitro, they failed to mediate anti-tumor efficacy against large established tumor in vivo. Interestingly, combined CD40 antibody and toll-like receptor (TLR) (CD40/TLR) stimulation not only expanded adoptively transferred T cells but also induced differentiation of $CX3CR1^-CD8^+$ T cells to express CX3CR1 in vivo. $CX3CR1^+CD8^+$ T cells were found to express higher levels of killer-cell lectin like receptor G1 (KLRG1), perforin, and granzyme, suggesting a terminally-differentiated subset. The generation of $CX3CR1^+CD8^+$ T cells was greatly facilitated by CD40 antibody while TLR agonist increases the expansion of total number of adoptively transferred antigen-specific $CD8^+$T cells. Importantly, total number and frequency of $CX3CR1^+CD8^+$ T cells after adoptive transfer and vaccination were significantly decreased in tumor-bearing CD40 knockout (KO) mice, indicating that host expression of CD40 is required for generation and expansion of $CX3CR1^+CD8^+$ T cells. In conclusion, effective vaccination with the cognate antigen and CD40/TLR accompanies generation of adoptively-transferred tumor-specific terminally-differentiated $CX3CR1^+CD8^+$ T cells, which is dependent on CD40 signaling.

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Diphencyprone (DPCP) versus Isolated Limb Infusion (ILI): Management of In-Transit Metastasis (ITMs) in Melanoma M. Lo,* D. Morgan Jones, J. Garioch, M.D. Moncrieff. *Norfolk & Norwich University Hospital, Norwich, United Kingdom.*

Objectives ITMs in melanoma are associated with a poor prognosis, however a significant proportion of patients with ITMs survive for extended periods without further disease progression. Locoregional treatment strategies such as DPCP, a topical immunotherapy agent, and ILI are used as long-term palliation. The aim of this study was to attempt to identify correct sequencing of these therapies based on disease burden and progression. Method Retrospective evaluation of all melanoma patients with ITMs treated with DPCP, ILI or both between 2010 and 2017 at a University hospital tertiary melanoma referral center, was performed. Patients were initially assessed in a multidisciplinary setting and empirically prescribed DPCP for low disease burden and ILI for high disease burden. Patient demographics, tumor characteristics, response to therapy and ITM progression were analyzed. Patient outcomes were recorded. Results 78 patients with ITMs (M:F, 30:48), aged 47-95 years (median 74) treated with DPCP, ILI or both (n=44, 24, 13 respectively) were identified. Progression-free survival (PFS) was significantly increased in patients who demonstrated a response to either DPCP or ILI as the initial treatment. In general, there was no significant difference in PFS between ILI and DPCP only groups. Patients who fail to respond to DPCP and were subsequently treated with ILI had a significantly increased PFS compared to DPCP alone (HR = 0.48; p=0.026). This was not the case with patients who were subsequently treated with DPCP following a failed ILI. In all categories, patients who failed to respond to the initial therapy progressed within 6 months. Discussion/ Conclusion Our study shows that careful stratification ITM patients according to disease burden is fundamental to producing optimal patient outcomes. Those with high disease burden benefit from initial ILI, whereas those with low disease burden can be trialed with DPCP. ILI can be considered in DPCP patients who fail early but the increased limb morbidity associated with ILI should not be disregarded. Systemic therapy should be considered when locoregional therapies fail after 12 months or after rapid relapse following ILI.

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Predictors for Melanoma Recurrence and the Impact of Local Recurrence on Outcomes After a Negative Sentinel Node Biopsy

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Introduction: Factors that predict for melanoma recurrence after a negative sentinel lymph node biopsy (SLNB) are not well defined. We evaluated melanoma recurrence patterns, factors prognostic for recurrence, and the impact of disease recurrence on outcomes for negative SLN patients (pts). Materials and Methods: The Sentinel Lymph Node Working Group database was evaluated from 1996 to 2016 for negative SLNB melanoma pts. Clinicopathologic characteristics were correlated with recurrence type (LR-local recurrence, NR-nodal recurrence, ITR-in-transit recurrence, DR-distant recurrence), overall survival (OS), and melanoma-specific survival (MSS). Results: Median follow-up was 32.1 months. Recurrences developed in 558 of 5,351 negative SLN pts (10.4%). First site of recurrence included a LR in 146 cases (2.7%), NR in 109 cases (2%), ITR in 75 cases (1.4%), DR in 220 cases (4.1%), and an unknown site in 8 cases (0.2%). On multivariable analysis, age ≥80 years, depth >3 mm, head/neck or leg primary and microsatellitosis significantly predicted for a LR as first site (all P<0.05). Having a LR as first site significantly predicted for a subsequent NR (OR: 3.0, 95% CI: 1.6-5.5) and DR (OR: 2.7, 95% CI: 1.6-4.5) on multivariable analyses and significantly predicted for worse OS and MSS (all P<0.05). Multivariable analyses also showed that depth >2 mm and head/neck or leg primary significantly predicted for a NR as first site and that a prior LR or ITR significantly predicted for a subsequent NR (all P<0.05). Factors significantly predictive for DR included depth >2 mm, head/neck or trunk primary, ulceration and lymphovascular invasion. Pts with any type of locoregional recurrence were all at higher risk for DR compared with pts who never had locoregional recurrences (P<0.05), with pts with ITR having the highest risk of a subsequent DR (OR 4.1, 95% CI 2.2-7.5). Conclusion: Recurrences occur in 10.4% of negative SLN pts, with DR being the most common (39.4% of all recurrences). Importantly, our data show that having a LR significantly predicts for a subsequent NR and DR and that having a LR negatively affects survival in melanoma pts after a negative SLNB.

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Ki-67 Expression Correlates with Other Pathological Features and is a Prognostic Factor for Sentinel Node Positivity in Invasive Melanomas

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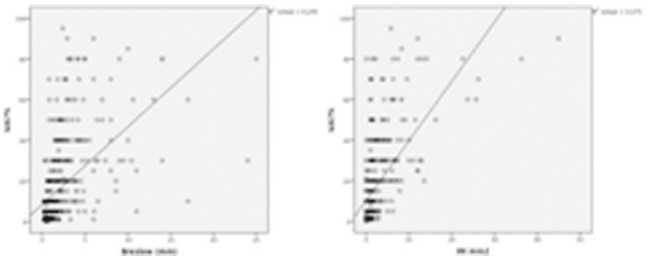
Background: ki 67 is a proliferative index assessed in the invasive component of melanomas, but its role in the clinical setting remains unclear. Objectives: Correlate ki 67 expression to other histopathological features of primary melanoma lesions, and access its impact in nodal disease, either regarding sentinel node biopsy (SNB) positivity as for non-sentinel node (NSN) positivity after completion node dissection in these patients. Material and methods: Retrospective analysis of melanoma patients treated in a single institution between years 2011 and 2016. Primary lesions were either biopsied or had the slides reviewed by experienced pathologists to assess ki 67 proliferation index by immunohistochemistry. Correlation between ki 67 and other pathological features was tested by nonparametric Spearman's (ρs) test. Comparison between groups was done by nonparametric Mann-Whitney test and ROC-Curve was done to establish a cut-off value. Results: Among 488 patients, there were 258 (52,9%) male patients and mean age was 53,32 years. There was a weak positive correlation between age and and ki 67 (ρs: 0,251; p < 0,0001); a mild positive correlation between ki 67 expression and Breslow thickness (ρs: 0,533; p < 0,0001), as well as between ki 67 and mitotic index (ρs: 0,659; p < 0,0001). Regarding prognosis, ki 67 expression was statistically different according to SNB positivity (p < 0,002) but it was not observed for NSN positivity (p: 0,12). With a cut-off value established, ki 67 > 10% was associated to SNB positivity (OR 3,665 [CI 95% 1,811 – 7,419], p < 0,0001] in single logistic regression. In a multiple logistic regression model, Breslow thickness (p 0,003) and ki 67 > 10% (p 0,004) were statistically associated to SNB positivity. Conclusions: In our data, there was correlation between ki 67 proliferative index and both Breslow thickness and mitotic index. Ki 67 expression > 10% was a risk factor for SNB positivity. This study shows that KI-67 positivity brings important information regarding melanoma behavior and so is a potential marker to be incorporated in routine pathology reports for melanoma patients.



Correlation between (A) ki 67 and Breslow thickness and (B) ki 67 and mitotic index

PF94

Correlation Between Surgical and Histologic Margins in Melanoma

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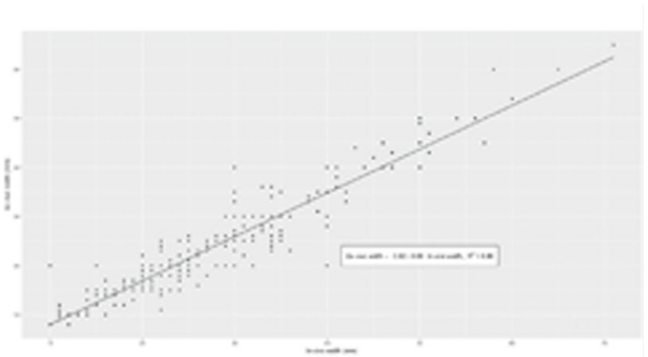
Background: Wide surgical excision is the mainstay of treatment for localized primary melanomas. There is an increased risk of local recurrence with a narrow histologic margin. Few data exist in relation to the adequacy of surgical margins at a histologic level. Methods: We performed a quality assurance audit to 1) examine the degree of shrinkage of formalin-fixed specimens and 2) use a precisely measured surgical margin in vivo to linearily predict the corresponding histologic margin. The effects of patient characteristics, including age, sex, and body mass index (BMI), anatomic site, tumor type (melanoma in situ, invasive melanoma, or non-melanoma skin cancer) and presence of visible tumor in predicting histological margin were also assessed. Results: When compared to in-vivo measured width, measurement of the width of the formalin-fixed specimen showed a mean shrinkage rate of 11% (R^2=0.89, Figure 1), regardless of patient age, sex, BMI or anatomic site of the lesion. The measured surgical margin did not appear to be a strong predictor of histologic margin, with a high degree of variability seen upon histologic assessment (R^2=0.55). The variability was not associated with patient factors, tumor type or presence of visible tumor at the time of excision (p>0.05). Conclusion: An 11% correction factor will account for fixation and shrinkage of cutaneous excision specimens. This is constant across all patients and all sites of excision. Excision margins measured by the surgeon are a poor predictor of the histologic margins measured by the pathologist.



Correlation between measured in-vivo width of planned excision and ex-vivo width of formalin- fixed specimen

PF95

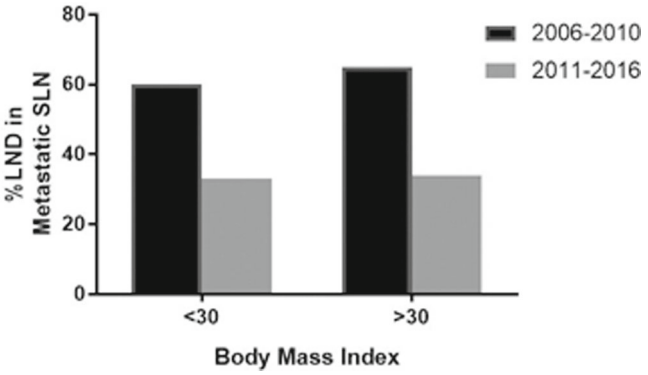
Talimogene Laherparepvec for the Treatment of Advanced Melanoma : A Single Institution Experience M. Perez,* J. Miura, S.H. Naqvi, Y. Kim, A. Holstein, D. Lee, A.A. Sarnaik, J.S. Zager. *Moffitt Cancer Center, Tampa, FL.*

Intro Talimogene laherparepvec (TVEC) is an oncolytic herpes virus used as intralesional therapy for patients with unresectable cutaneous, subcutaneous, and nodal metastatic melanoma (Stage IIIB, IIIC and IVA). We sought to review the standard of care treatment of TVEC at a single institution. Methods All patients treated with TVEC for unresectable advanced melanoma were retrospectively evaluated from 2015-2017. Patient demographics, clinicopathologic characteristics, treatment response, and toxicity were reviewed. Results 23 patients underwent therapy with TVEC. Median age was 75 years, 61% of patients were female. 15 (65.2%) patients underwent injections in the lower extremity, 3 (13%) in the upper extremity, 4 (17.4%) in the head and neck and 1 (4.4%) on the trunk. 3 (13%) patients previously underwent systemic immunotherapy, 4 (17.4%) patients previously had an isolated limb infusion (ILI), and 2 (8.7%) patients previously underwent both immunotherapy and ILI. Median number of injections was 5. 19 patients had at least 8 weeks follow-up and were included in response analysis with a median follow-up of 7.52 months. 7 (36.8 %) patients experienced a complete response (CR), 3 (15.8 %) patients experienced a partial response, and 4 (21.1%) patients had stable disease for an overall response rate of 52.6% (CR+PR) and a disease control rate of 73.7%. A CR was achieved in 54.5% of patients who had all their lesions injected. Median time to response was 2.56 months. In-field and out-of-field progression free survival (PFS) estimates at 12 months were 62.7% and 55%, respectively. Adverse events were mostly limited to mild constitutional symptoms within 48 hours of injection. 2 patients developed cellulitis treated with oral antibiotics, and 1 patient underwent excision of a lesion for ulceration and bleeding during therapy. Conclusion TVEC is an effective and well-tolerated intralesional therapy for patients with unresectable stage IIIB, IIIC or IVA melanoma. A CR can be achieved in over 1/3 of patients treated and in over 50% of patients where all lesions can be injected. Disease control is seen in the vast majority.

PF96

Tumor Factors and Not Patient Body Mass Index (BMI) Determine Surgical Treatment of Melanoma Patients Z.L. Gentry,* S. Reddy, J. Richman, C.M. Contreras, T. Wang. *Surgery, University of Alabama at Birmingham, Birmingham, AL.*

Introduction: MSLT-II showed that completion lymph node dissection (LND) did not increase melanoma disease-specific survival among patients with sentinel lymph node (SLN) metastasis. The first interim analysis was published in 2011. The decision to perform a LND may not solely be determined by evidence-based clinical factors but also influenced by patient co-morbidities and the anticipated outcomes of MSLT-II. Due to perceived biases that obese patients have higher incidences of postoperative complication, we hypothesized that patients with higher BMI were less likely to have a LND after a positive SLN than patients with normal BMI. Methods: We retrospectively reviewed all melanoma patients who underwent a SLN biopsy over an eleven-year period (2006-2016) at a single institution. Bivariate analyses and adjusted logistic regressions were used to evaluate BMI, number of positive SLNs, size of micrometastases, and year of diagnosis in patients undergoing LND vs. no LND. Results: Among the 1169 patients who underwent SLN biopsies, 290 patients had a positive SLN. 122 (42%) patients underwent a LND. Patients undergoing a LND had a comparable mean BMI to those who did not undergo a LND (mean: 29.4 ± 5.5 and 29.5 ± 5.9, respectively, p=0.87). Patients undergoing LND had more positive nodes (mean = 1.37 ± 0.61 vs. 1.17 ± 0.41, p=0.045) and larger tumor size (mean 3.23 ± 5.19 vs. 1.76 ± 3.96 mm, p=0.018). These factors remained significant in adjusted analyses: OR 1.83 (1.01- 3.3) per positive node (p=0.045) and OR 1.19 (1.10- 1.3) per tumor size (p<0.001). Patients diagnosed from 2006 to 2010 were more likely to have a LND (61.2 vs. 33.8%, p<0.0001). Both obese and non-obese patients had similar trends in LND rates between each time interval (see figure, p=0.88). Conclusions: Our data show that the year of diagnosis was the most important predictor of whether a patient underwent LND after a positive SLN. In addition, our analysis provides evidence against a disparity in LND rates in obese melanoma patients. The decision to do a LND is based on objective tumor factors and the anticipated results of MSLT-II.



PF98

Reexamining the Role of Pelvic Lymphadenectomy for Melanoma in the Era of Effective Systemic Therapy: A Multi-Institutional Experience C.R. Farley,[1]* M. Perez,[2] J.S. Zager,[2] A. Lee,[3] R. Berman,[3] J. Hyngstrom,[4] K. Delman,[1] M. Lowe.[1] *1. Emory University School of Medicine, Atlanta, GA; 2. Moffitt Cancer Center, Tampa, FL; 3. New York University School of Medicine, New York, NY; 4. Huntsman Cancer Institute-University of Utah, Salt Lake City, UT.*

Background: Pelvic lymph node disease has been associated with systemic relapse and death from melanoma. There are conflicting opinions as to the utility of pelvic lymphadenectomy (pLND) in an era of effective immune and targeted therapy. Outcomes following pLND were reviewed to determine if access to systemic therapy should affect the decision to perform pLND. Methods: Patients with melanoma who underwent pLND from 2013 to 2016 were included from 3 centers. Demographics, clinicopathologic characteristics and outcomes were reviewed. Results: Forty-six patients underwent pLND. Median age was 64 (21-78); 23 (50%) were male. Median time from excision to pLND was 7 months (0-101). Median of 9.5 nodes (4-26) were removed. Indications for pLND were positive inguinal SLN with drainage to the pelvis on lympho (n=6), clinically positive inguinal LN (n=11) and radiographically suspicious pelvic LN (n=29). For all indications, the median number of positive nodes was 1 (0-19). Seven (15.2%) patients received neoadjuvant therapy, 13 (28.3%) adjuvant radiation, 8 (17.4%) adjuvant systemic therapy. Of the 46 patients who underwent pLND, 17 (37.0%) patients recurred distantly at a median time of 10 months (1-24); 12 (70.6%) initially had radiographically positive pelvic disease, 4 (23.5%) clinically positive inguinal LN and 1 (5.9%) positive SLN with pelvic drainage. Twelve (70.6%) pts who recurred with distant disease were treated with systemic therapy, 2 (11.8%) surgery, 1 (5.9%) tumor infiltrating lymphocytes, and 2 (11.8%) unknown or none. Demographics, clinicopathologic characteristics and indication for pLND did not impact recurrence or time to recurrence. At last follow up (median 15.5 months, 0-45), 41/46 (89.1%) patients were alive; 21 (51.2%) were NED, 20 (48.8%) AWD. Conclusion: Patients who undergo pLND are at high risk for recurrence; however, it appears that in the era of effective systemic therapy, melanoma-specific survival is also high. The role and timing of pLND should be reexamined in the current treatment paradigm. A prospective trial of systemic therapy alone versus surgery and systemic therapy should be considered.

PF99

Resection Margins in Merkel Cell Carcinoma: Is a 1 cm Margin Wide Enough? M. Perez,* F. de Pinho, A. Holstein, E. Burke, S.H. Naqvi, Y. Kim, J.L. Messina, R. Gonzalez, A.A. Sarnaik, C. Cruse, L.B. Harrison, V.K. Sondak, J.S. Zager. *Moffitt Cancer Center, Tampa, FL.*

Background Due to the rarity of the disease, therapeutic guidelines regarding resection margins are not well established for primary Merkel cell carcinoma (MCC). Current NCCN guidelines recommend 1-2 cm resection margins. We sought to determine if margin width had an impact on local recurrence (LR), disease-specific survival (DSS), overall survival (OS) and type of wound closure. Methods All patients who underwent resection of primary MCC at a single institution were reviewed from 2000-2015. Patients without clearly identified resection margin width in the operative report were excluded. Patient demographics, clinicopathologic characteristics, treatments,

and outcomes were reviewed. Results We identified 240 patients who underwent resection of their primary MCC. Median age was 76 years, and 65.8% were male. Eighty-five (35.4%) patients had tumors of the head and neck, 140 (58.3%) of the extremity and 15 (6.3%) of the trunk. Sixty-nine (28.8%) patients had a 1 cm margin, 36 (15%) patients had between a 1.1-1.9 cm margin and 135 (56.2%) patients had a ≥ 2 cm margin. Median follow-up for all patients was 21.0 months. LR was 2.9%, 2.8%, and 5.2% for 1 cm, 1.1-1.9 cm and ≥ 2 cm margins, respectively (p=0.670). Five-year DSS was 80.3%, 66.2% and 91.8% for 1 cm, 1.1-1.9 cm and ≥ 2 cm margins, respectively (p=0.283). Five-year OS was 63.6%, 59.7% and 70.7% for 1 cm, 1.1-1.9 cm and ≥ 2 cm margins, respectively (p=0.582). Primary tumor site, depth of tumor, presence of lymphovascular invasion, use of adjuvant radiation to the primary site, and margin status did not significantly predict local recurrence on multivariate analysis. 43.5%, 50%, and 65.9% of patients required a graft or flap for wound closure with a 1 cm margin, 1.1-1.9 cm margin and ≥ 2 cm margin, respectively (p= 0.006). Conclusions A 1 cm resection margin did not increase the risk of LR. No significant difference was observed in DSS and OS with margin width. Larger resection margins may increase the need for a graft or flap closure.

PF100

Management of Intussusception Secondary to Metastatic Melanoma M. Perez,[1]* C.R. Farley,[2] D. Han,[3] A. Sun,[3] D. Narayan,[3] M. Lowe,[2] K. Delman,[2] J.L. Messina,[1] R. Gonzalez,[1] V.K. Sondak,[1] N.I. Khushalani,[1] J.S. Zager.[1] *1. Moffitt Cancer Center, Tampa, FL; 2. Emory University, Atlanta, GA; 3. Yale University, New Haven, CT.*

Background Melanoma is the most common metastatic tumor to cause enteric intussusception in adults, and resection is indicated in symptomatic patients. With the routine use of cross-sectional imaging for surveillance in metastatic melanoma, asymptomatic intussusception is increasingly encountered. We review the experience of managing intussusception in both asymptomatic and symptomatic patients at three high-volume cancer centers. Methods Patients with a history of metastatic melanoma and imaging findings consistent with intussusception were identified. Patient demographics, clinicopathologic characteristics and outcomes were retrospectively reviewed. Results 84 patients had findings of intussusception identified on imaging. Median age was 54.5 years, 71.4% were male. 92.9% of initial imaging was performed with computed tomography (CT). Patients were divided into 3 groups: 1) asymptomatic patients with no current evidence of disease (NED, n=16), 2) asymptomatic patients with known metastatic melanoma (n=39), and 3) patients with symptomatic intussusception (n=29). Of 16 asymptomatic NED patients, 14 (88%) resolved spontaneously on subsequent imaging, and 2 patients underwent an elective (preemptive) operation. 25 of 39 asymptomatic patients with known metastases were observed, 7 underwent an elective operation, 5 were transitioned to hospice care and 2 were lost to follow-up. Of the 25 asymptomatic patients with known metastatic melanoma who were observed, 16 (64%) resolved on subsequent imaging while 9 developed symptoms requiring operation. 25 of 29 initially symptomatic patients underwent surgery, while 4 were transitioned to hospice care. 7 of 9 asymptomatic patients and 33 of 34 symptomatic patients who underwent surgery had intussusception identified at operation and/or melanoma in the resected small bowel. Discussion Imaging findings consistent with intussusception spontaneously resolve in the majority of asymptomatic patients, especially in those with NED, and can be managed expectantly, with surgery reserved for the development of symptoms. Intussusception and/or intestinal melanoma was confirmed intraoperatively in the majority of those who underwent surgery with known metastatic disease.

PF101

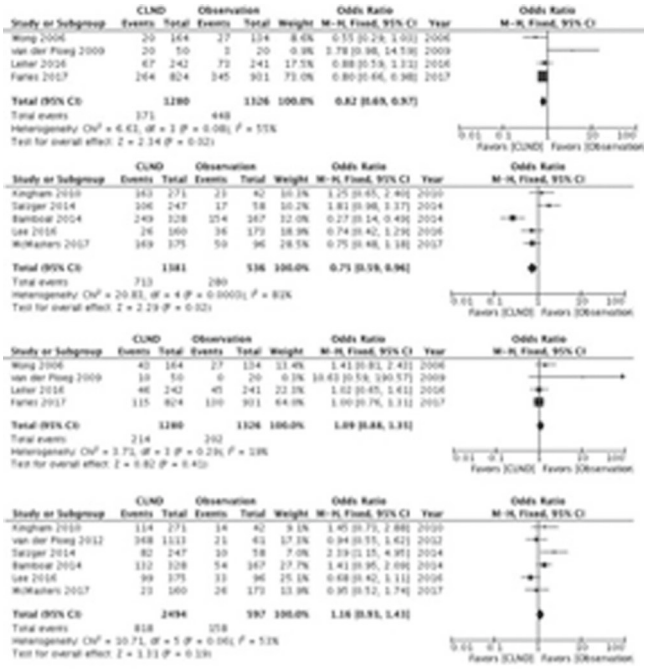
Assessment of Quality of Life in Patients with Locally Advanced Cutaneous Melanoma Using Patient-Reported Outcomes E. Weitman,[1]* M.C. Perez,[1] J.F. Thompson,[2] R. Andtbacka,[3] J. Dalton,[2] M. Martin,[4] T. Miller,[4] C. Gwaltney,[5] D. Sarson,[6] E. Wachter,[7] J.S. Zager.[1] *1. Moffitt Cancer Center, Tampa, FL; 2. melanoma institute australia, Wollstonecraft, NSW, Australia; 3. Huntsman Cancer Institute, Salt Lake City, UT; 4. Health Research Associates, Mountlake Terrace, WA; 5. ERT, Philadelphia, PA; 6. Delpharm Consultants, Sydney, NSW, Australia; 7. Provectus Biopharmaceuticals, Knoxville, TN.*

Background: Patients with locally advanced cutaneous melanoma often experience a significant deterioration in their quality of life. However, this detrimental impact has not been well-characterized. This study utilized a patient-reported outcome approach with qualitative interviews to better define the changes in quality of life due to advanced melanoma. Methods: Adults with AJCC (7th edition) Stage IIIB, IIIC or IV (M1a) cutaneous melanoma were recruited from two cancer centers in the US and one in Australia. Patient-reported outcomes were elicited during telephone interviews to assess the impact of locoregionally advanced cutaneous melanoma on quality of life metrics. Data from these interviews was coded for qualitative analysis. Results: Interviews were conducted on twenty-two patients with locally advanced melanoma, including stage IIIB (36%), stage IIIC (59%) and stage IV M1a (5%). Emotional health/self-perception issues, such as worry, concern, embarrassment and self-consciousness, were the most commonly identified patient impact expressions (41%). Limitations of lifestyle and activities, including leisure and social activities, physical functioning and general functioning, were also commonly identified (28%). Approximately 20% of patient impact expressions focused on coping strategies such as modified clothing choices, increased use of pain and/or anti-inflammatory medications, and avoidance/protection from the sun. The impact on quality of life was rated on an 11-point Numerical Rating Scale (mean 5.7, SD 2.9). Conclusion: Quality of life is dramatically impacted in patients with locally advanced cutaneous melanoma. These impacts can be well-characterized with qualitative interviews to define patient-reported outcomes.

PF102

The Role of Completion Lymphadenectomy in Positive Regional Lymph Nodes in Melanoma: A Meta-Analysis F. Macedo,* R.A. Fayne, B. Azab, D. Yakoub, M. Moller. *Sylvester Comprehensive Cancer Center, Jackson Memorial Hospital, University of Miami School of Medicine, Miami, FL.*

BACKGROUND: The optimal management of melanoma with positive sentinel lymph node (SLN) remains unclear. Completion lymph node dissection (CLND) is currently advocated in positive SLN tumors, however only yields additional positive non-SLN in 20% of cases. METHODS: An online database search of MEDLINE was performed; key bibliographies were reviewed. Studies comparing outcomes after CLND versus observation were included. Odds ratios with the corresponding 95% confidence intervals (CI) by random fixed effects models of pooled data were calculated. The primary endpoints were disease-free survival (DFS), melanoma-specific survival (MSS) and overall survival (OS). Study quality was assessed using STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) criteria. RESULTS: Search strategy yielded 117 publications. Twelve studies were selected for inclusion, comprising 7,966 SLN-positive patients. Among these patients, 5,306 subjects underwent CLND and 2,660 patients were observed. Median Breslow thickness and ulceration were similar between groups (2.8 ± 0.6 vs. 2.5 ± 0.8, p=0.721; and 38.8% vs. 37.2%, p=0.136, for CLND and observation groups, respectively). CLND was associated with statistically significant improved 3-year (71.0% vs. 66.2%, OR 0.82, 95% CI 0.69-0.97, p=0.02) and 5-year DFS (48.3% vs. 47.8%, OR 0.75, 95% CI 0.59-0.96, p=0.02) as compared to observation. However, no difference was demonstrated in 3-year (83.7% vs. 84.7%, OR 1.09, 95% CI 0.88-1.35, p=0.41), 5-year MSS (68.4% vs. 69.8%, OR 1.02, 95% CI 0.88-1.19, p=0.78) or OS (68.2% vs. 78.9%, OR 0.93, 95% CI 0.55-1.57, p=0.78). CONCLUSION: Based on this worldwide large-scale analysis, CLND improved both 3-and 5-year DFS, possibly due to increased rates of local control, however this did not translate in improved MSS or OS. Efforts toward the identification of molecular markers associated with poor outcomes in patients who undergo observation are warranted.



PF103

Ratio of Tumor Thickness to Adjacent Dermal Thickness: A Novel Prognostic Factor for Cutaneous Melanoma P.H. Rambhia,[1]* S. Somach,[2] R.Z. Conic,[1] A. Funovits,[2] D. Crowe,[2] B. Li,[2] N. Joseph,[2] S.M. Sharpe,[2] B.J. Averbook.[2] *1. Case Western Reserve University School of Medicine, Cleveland, OH; 2. MetroHealth Medical Center, Cleveland, OH.*

Background: Melanoma tumor thickness is a strong prognostic factor for cutaneous melanoma survival. We hypothesized that further prognostic precision could be obtained by adjusting tumor thickness relative to specific skin site dermal thickness. This pilot study aimed to demonstrate that a ratio of melanoma thickness to mean, site-specific dermal thickness would be a strong prognostic factor. Methods: The IRB approved MetroHealth Medical Center Melanoma Registry was reviewed for demographic information, tumor characteristics and survival. From 1976 to 2016, 2294 cutaneous melanomas were evaluated. Melanomas were grouped into 5 anatomical locations and mean dermal thickness was calculated from review of 153 slides by a single dermatopathologist. Melanoma to dermal ratios (M-D ratios) were calculated from tumor thickness divided by mean site specific dermal thickness: upper (n=498), and lower(n=482) extremity, upper(n=725) and lower(n=203) trunk, and head and neck (n=386). Cox proportional hazards model was used to evaluate overall survival (OS). Results: Mean dermal thickness values used included: 2.86mm-head and neck, 2.50mm-lower extremity, 3.17mm-upper extremity, 4.85mm-lower trunk, and 5.21mm-upper trunk. Compared to patients with a 0-0.24 M-D ratio, OS with a ratio of 0.25-0.49 was 38% worse (HR 1.38, 95%CI 1.14-1.78, p=0.001), 131% worse for those between 0.50-0.74 (HR 2.31, 95%CI 1.83-2.93, p<0.001), and 216% worse over 0.75 (HR 3.16, 95%CI 2.63-3.8, p<0.001). After adjusting for age, sex, site, melanoma type, ulceration and sentinel lymph node biopsy positivity, OS was 37% worse in ratios 0.25-0.49 (HR 1.37, 95%CI 1.11-1.7, p=0.004), 75% in ratios 0.5-0.74 (HR 1.75, 95%CI 1.31-2.3, p<0.001) and 96% in ratios 0.75 or greater (HR 1.96, 95%CI 1.49-2.58, p<0.001). Discussion: M-D ratios may be a stronger predictor of OS for melanoma patients. Future study will need to compare M-D ratios to thickness in predicting survival. Melanoma staging may be improved by using this novel prognostic factor.

PF104

Degree of Mitotic Activity Predicts Risk of Recurrence and Survival in Melanoma Patients Independent of Sentinel Node Status A. Allard-Picou,* D. George, J.C. Hardaway, A. Saied-Calvino, J. Koness, J. Espat, S.C. Katz. *Roger Williams Medical Center, Providence, RI.*

Introduction: The presence of mitotic activity is known to be a significant predictor of outcomes in patients with melanoma. However, there is little data on the relationship between the extent of mitotic activity and outcomes in melanoma. Our goal was to evaluate the correlation between mitotic rate (MR) and recurrence-free (RFS) and overall survival (OS) for stage I to III patients, irrespective of sentinel node status. Methods: We conducted a retrospective review of patients diagnosed with primary cutaneous melanoma between January 2010 and December 2015 at our institution. Primary outcome measures were RFS, OS, and disease specific survival (DSS). We correlated OS, RFS and DSS with various subgroups of MR (mitotic figures/mm^2: < 1, 1-5, 5-10 and >10). Outcomes for SLN negative (SLN-) patients with MR>10 were compared with those for SLN positive (SLN+) patients with MR<10. Results: There were 309 patients who met criteria. Of these, 53% had mitotically active primary tumors (MR 1-5: 34.6%; 6-10: 9.7% and >10: 8.7%). Overall recurrence rate was 10.7%, with higher recurrences in patients with MR>10 (67.8%), compared to MR<1, 1-5 or 5-10 (0%, 6.6%, 26.7% respectively). Patients with MR>10 were significantly more likely to recur compared to MR<10 (OR 15.4, p<0.001). Most recurrences were distant (53%) and patients with MR>10 exhibited a trend toward more distant recurrences compared to those with MR<10 (57.9% % vs 46.7, p=0.296). Patients with MR>10 demonstrated worse RFS compared to other groups (MR<1: 39.5 months; 1-5: 34.9 months; 6-10: 31.6 months and >10: 22 months, p<0.001). Compared to SLN+ patients with MR <10, SLN- patients with MR>10 demonstrated a trend toward higher recurrence rates (38.5% vs 25.0%; DFS 28.1 months vs 30.7 months, p=0.47) and worse OS (32.4 vs 37.4 months, p=0.60). Conclusion: This study demonstrates that the extent of mitotic activity may enable refined risk stratification in melanoma patients. Patients who were SLN- with MR>10 exhibited similar outcomes compared to SLN+ patients with MR<10. Node negative patients with MR>10 may be considered to be in a similar high-risk category as those with nodal metastases.

PF105

Safety and Efficacy of Liposomal Bupivacaine in Patients Undergoing Lymph Node Dissection for Melanoma N. Narula,* J.E. Gershenwald, V.N.R. Gottumukkala, B.J. Kim, C.H. Davis, R.E. Royal, J. Wargo, A. Lucci, J. Cormier, J.E. Lee, M.I. Ross, T. Aloia. *Surgical Oncology, The University of Texas MD Anderson Cancer Center, Brookline, MA.*

Introduction Liposomal bupivacaine (LB; Exparel®) is a non-narcotic, long-acting, local analgesic wound infiltration agent. Despite its increasing use in surgery, there are no prior studies specifically reporting on associated outcomes in patients (pts) with melanoma and/or in pts undergoing lymph node dissection (LND). Methods Consecutive pts who underwent axillary or inguinal LND for melanoma at a single quaternary cancer center from 2013 to 2016 were identified in institutional databases by Current Procedural Terminology codes. After stratification by receipt of LB, pain scores, cardiac complications, length of stay (LOS), and readmissions were compared for all pts and oral morphine equivalent (OME) dosing during the hospital stay was compared for the most recently treated subset of 100 pts (50 pts in each group). Results Five hundred and twenty-five pts were included in the analysis: 57.5% had axillary LND, 43.4% had inguinal LND, 43.4% were female, the mean age was 55.4 years, 56.8% received LB, and 26.7% were preoperatively taking narcotic pain medications. Pts who received LB had lower median pain scores, lower in-hospital OME use and shorter LOS (all p<0.05) with no increase in 30-day readmission rate (11.5% non-LB vs. 5.8% LB, p=0.080). Additionally, for patients having inguinal LND, LB use was associated with lower incidence of severe postoperative pain (any pain score >=7; 36.4% non-LB vs. 21.7% LB, p=0.015). The inguinal LND patients treated with LB were more likely to be discharged without traditional oral narcotics (7.6% non-LB vs. 19.8% LB, p=0.012). Extensive review of all postoperative EKG records identified no arrhythmias or other cardiac complications potentially related to “lidocaine” toxicity. Conclusion In pts with melanoma undergoing axillary and inguinal LND, LB was associated with zero toxicity, lower pain scores, decreased use of narcotics and decreased LOS without increase in readmissions. The drug cost of LB (US$265) appears to be offset by improved patient experience, reduced

need for narcotics to achieve adequate pain control, and the cost savings attributable to shorter admissions (average national inpatient per diem, US$2,271).

PF106

Initial Results of a Phase I andII: A trial of Tumor Lysate Particle Loaded Dendritic Cell (TLPLDC) Vaccine Combined with Checkpoint Inhibitors in Metastatic Melanoma J.W. Myers,[1]* G.T. Clifton,[1] T.J. Vreeland,[2] T.A. Brown,[1] K.M. Peace,[1] J.M. Greene,[1] D.O. Jackson,[1] D.F. Hale,[1] J.S. Berry,[3] S.J. O'Day,[4] G.E. Peoples.[5] *1. General Surgery, San Antonio Military Medical Center, San Antonio, TX; 2. University of Texas MD Anderson Cancer Center, Houston, TX; 3. Womack Army Medical Center, Fort Bragg, NC; 4. John Wayne Cancer Institute, Santa Monica, CA; 5. Cancer Vaccine Development Program, Metis Foundation, San Antonio, TX.*

BACKGROUND Checkpoint inhibitors, a standard first-line treatment for metastatic melanoma, work through making existing anti-tumor immune responses more effective. Not all patients will respond, in some cases because of a lack of endogenous immune response to the tumor. T-cell eliciting vaccines hold the potential to work synergistically with checkpoint inhibitors (CPI). We have developed a novel technique for ex-vivo loading of autologous tumor lysate into dendritic cells using yeast cell wall particles (YCWP). Here we report the trial design and initial patient safety and efficacy data. METHODS The TLPLDC vaccine is created by loading autologous tumor lysate into prepared yeast cell wall particles, then introduced ex vivo to the patient's own dendritic cells for phagocytosis. $1x10^6$ TLPLDCs are given via intradermal injection monthly x 4 followed by boosters at 6 and 9 months to patients with metastatic melanoma with progression on checkpoint inhibitor therapy as determined by the patient's treatment team. Primary endpoints are to determine the safety of adding the TLPLDC vaccine to standard of care checkpoint inhibition, and to determine tumor response per RECIST and iRECIST criteria. RESULTS 10 patients have been consented, 6 have vaccines in creation, and 3 have been treated with the vaccine. In the initial 3 treated, a single toxicity >grade 2 (grade 3 Clostridium difficile infection) occurred resulting in hospitalization but was unrelated to the study drug. One patient withdrew prior to completing the vaccine series. One patient who progressed on nivolumab demonstrated stable disease with the addition of TLPLDC on 9 month imaging. One patient who progressed on pembrolizumab demonstrated a partial response with near complete resolution of measurable disease after the addition of TLPLDC at 3 month follow up. CONCLUSION Preliminary TLPLDC vaccine data demonstrates that the combination of TLPLDC vaccination with checkpoint inhibition is safe and can lead to clinical benefit in patients who previously progressed on checkpoint inhibition alone.

PF108

Improved Survival Among Patients with Melanoma Residing in Geographic Regions with High Frequency of Diagnosis N. Goel,* A.S. Moten, M. Lango. *Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA.*

Background Incidence of melanoma varies substantially by geographic region, corresponding with different rates of diagnosis. It is unclear how regional variation in rates of diagnosis relates to guideline-based care and patient outcomes. Methods Data on first primary melanoma patients (2004-2013) was obtained using the Surveillance, Epidemiology, and End Results database. Counties were ranked into quartiles of diagnostic rates, defined as the number of new melanoma patients diagnosed per 100,000. Chi-square and Cox regression analyses tested the effect of regional diagnostic rates on patient and clinical factors as well as cancer-specific survival. Results The analytic cohort was 74,635 patients. Crude rates of diagnosis (range 0-94.8 per 100,000) over 596 counties increased with increased median age, percent non-Hispanic white, median income, and percent college-educated. Rates decreased with percent African American and Medicaid-eligible population. Patients in the highest quartile of diagnosis (Q4) presented with earlier stage disease compared to those in the lowest quartile (Q1). Wide local excision (WLE) for stage IA melanoma was performed more often in Q1 than Q4 (27% vs 19%). For stage IB, sentinel lymph node biopsy (SLNB) was performed in 50% of Q4 versus 45% of Q1 patients ($p<0.001$), while WLE and SLNB was similar (24% in Q1 vs 25% in Q4). For stage 2, SLNB was performed in 62% of Q4 and 54% of Q1 patients ($p<0.001$), while WLE and SNLB was performed in 34% of Q4 and 31% of Q1 patients. Compared with Q1, residence in Q4 significantly decreased the risk of death from melanoma, even after adjusting for age, sex, race, histology, stage, treatment, and socioeconomic variables (HR:0.877;95%CI:0.801-0.961). Conclusion Guideline-based treatment such as WLE and SLNB are more commonly employed in thick melanomas in regions with higher rates of melanoma diagnosis, but are generally underutilized. Cancer-specific survival for patients in regions with higher diagnostic rates is significantly better, even after accounting for other variables. Reasons for improved survival of melanoma patients from regions with higher rates of diagnosis merit further study.

Patient Demographic and Socioeconomic Factors by Quartiles of Diagnostic Rates.

	All, n (%)	Quartile 1 n (%)	Quartile 2 n (%)	Quartile 3 n (%)	Quartile 4 n (%)	P-value
Total	74, 635 (100)	18,646 (25.0)	18,101 (24.3)	18,907 (25.3)	18,981 (25.4)	
Mean (SD) Age (years)	59.7 (16.2)	59.8 (16.4)	59.8 (16.3)	59.0 (16.3)	60.2 (15.7)	< 0.001
Age (years)						< 0.001
15 – 24	1,310 (1.8)	353 (1.9)	290 (1.6)	366 (1.9)	301 (1.6)	
25 – 34	4,360 (5.8)	1,146 (6.2)	1,050 (5.8)	1,191 (6.3)	973 (5.1)	
35 – 44	7,551 (10.1)	1,885 (10.0)	1,863 (10.3)	2,016 (10.7)	1,817 (9.6)	
45 – 54	13,397 (18.8)	3,412 (18.3)	3,510 (19.4)	3,664 (19.4)	3,411 (18.0)	
55 – 64	17,525 (23.5)	4,338 (23.3)	4,108 (22.7)	4,494 (23.8)	4,585 (24.2)	
65 – 74	15,296 (20.5)	3,760 (20.2)	3,605 (19.9)	3,658 (19.4)	4,273 (22.5)	
75 – 84	10,204 (13.7)	2,614 (14.0)	2,527 (14.0)	2,441 (12.9)	2,622 (13.8)	
≥ 85	4,392 (5.9)	1,168 (6.3)	1,148 (6.3)	1,077 (5.7)	999 (5.3)	
Sex						< 0.001
Male	42,118 (56.5)	10,662 (57.2)	10,161 (56.2)	10,517 (55.6)	10,778 (56.8)	
Female	32,492 (43.6)	7,975 (42.8)	7,932 (43.8)	8,384 (44.4)	8,201 (43.2)	
Race						< 0.001
White	67,140 (90.0)	16,176 (86.8)	16,568 (91.5)	16,899 (89.4)	17,497 (92.2)	
Black	335 (0.5)	176 (0.9)	86 (0.5)	40 (0.2)	33 (0.2)	
Hispanic	2,313 (3.1)	1,017 (5.5)	511 (2.8)	487 (2.6)	298 (1.6)	
Asian	346 (0.5)	134 (0.7)	87 (0.5)	82 (0.4)	43 (0.2)	
Other/Unknown	4,501 (6.0)	1,143 (6.1)	849 (4.7)	1,399 (7.4)	1,110 (5.9)	
Insurance						< 0.001
Uninsured	1,542 (2.1)	456 (2.5)	354 (2.0)	355 (1.9)	277 (2.0)	
Medicaid	2,328 (3.1)	855 (4.6)	550 (3.0)	483 (2.6)	440 (2.3)	
Private or Medicare	53,390 (71.6)	13,594 (72.9)	13,291 (73.5)	13,602 (72.0)	12,903 (68.0)	
Unknown	17,350 (23.3)	3,732 (20.0)	3,898 (21.5)	4,461 (23.6)	5,259 (27.7)	
Mean (SD) Proportion with < High School Education	13.6 (5.8)	19.2 (6.0)	13.0 (4.5)	11.8 (4.0)	10.7 (4.3)	< 0.001
Mean (SD) Proportion Below Poverty Level	14.6 (5.2)	19.1 (5.1)	14.3 (4.5)	12.7 (3.8)	12.4 (4.4)	< 0.001
Mean (SD) Proportion Unemployed	8.8 (2.4)	10.3 (2.7)	9.2 (2.1)	7.8 (1.7)	7.8 (2.1)	< 0.001
Median (IQR) Household Income ($1,000)	$60.3 ($20.8)	$53.4 ($11.0)	$59.9 ($13.2)	$70.7 ($14.8)	$62.9 ($19.8)	< 0.001

PF109

Association Between Indoor Tanning State Regulation in Minors and Melanoma Trends G. Gauvin,[1]* F. Lambreton,[1] S. Lynch,[1] K. Henry,[2] C. Heckman,[1] J. Farma.[1] *1. Surgical Oncology, Fox Chase Cancer Center, Philadelphia, PA; 2. Temple University, Philadelphia, PA.*

Introduction:The FDA recently published a consumer update on the dangers of indoor tanning. Despite this, the legislation on indoor tanning in minors is still highly variable across the country. In this study, we explore the current trend in melanoma incidence rate (IR) at a national level and the restrictiveness of the legislation per state. Methods: We interrogated the National Cancer Institute SEER+NPCR database and included all 50 states, 1 district and 1 territory for which data are documented. We reviewed the melanoma IR, the 5-year trend for all ages, sexes and races as well as white non-Hispanic females <50 years of age, who have the highest rates of indoor tanning. We then reviewed the legislation in all states regarding indoor tanning restrictions for minors. States were separated into 4 categories: 16 had a ban for all minors, 13 had age-specific bans (between 14 and 17), 15 required parental permission, and 8 had no restriction. Results: In patients of all ages, sexes and races from 2009-2013 (n=71,035) the IR of melanoma was 20.7 per 100,000, and the 5-year melanoma IR trend across the US was rising, at 1.8. The rising IR was different in the 4 different subgroups. When looking at all-comers, the average 5-year IR trend is 1.05 in states restricting all minors, 0.75 in states with age-specific bans, 2.49 in those requiring parental permission and 2.89 in those without restriction. White non-Hispanic females <50 (n=7,656), had an

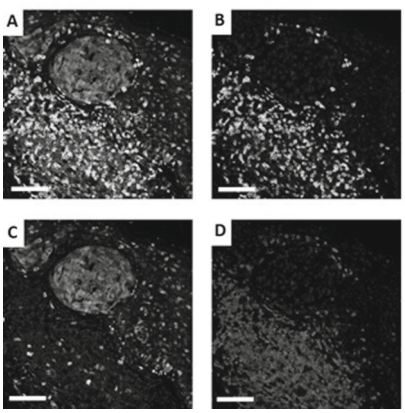
overall stable 5-year IR trend of -0.3 across the country. This trend is falling at -4.38 in states restricting all minors, stable at 0.12 for age-specific bans and 0.13 for states requiring parental permission, and rising at 1.86 for states with no restrictions. Conclusions: While a causative relationship between melanoma and UV beds has already clearly established, we have yet to see significant legislation applied to this practice. These preliminary observations will guide future investigations focused on the relationship between legislation of tanning salon use and melanoma. In future analyses, we plan to consider when legislation went into effect and other related risk factors, including adjustments for UV index.

PF110

An Automated Multiplexed Immunofluorescence Platform Quantifies CD3+/CD8+ T-Cells within Melanoma with Prognostic Significance B. Schmidt,[1]* D.W. Ollila,[1] B.R. Midkiff,[2] Y. Tsai,[2] J. Frank,[1] J.S. Parker,[2] N.N. Feinberg,[2] N.E. Thomas.[2] *1. Surgical Oncology, University of North Carolina, Chapel Hill, NC; 2. University of North Carolina, Chapel Hill, NC.*

The importance of the immune response to melanoma has long been understood, as the subjective observation of tumor infiltrating lymphocytes (TILs) typically correlates with improved recurrence-free (RFS) and overall survival (OS). Quantification of CD3+/CD8+ T-cells is prognostically superior to visual scoring of TILs in breast and colon cancer, but the algorithms are proprietary and no such model exists for melanoma. We sought to develop a platform for the quantification of CD3+/CD8+ cell density in melanoma and correlate this score with RFS and OS. A pilot set of 71 formalin fixed paraffin embedded primary melanomas, evenly distributed across T stage, was stained with a newly developed automated multiplexed immunofluorescence (MIF) protocol allowing for simultaneous identification of florescent labels for CD3, CD8, S100 and a nuclear counterstain with electronic scanning of slide images (Figure 1). Commercially available software (Definiens Tissue Studio) was used to define regions of interest (ROI), contouring the tumor based on S100 staining. We quantified the cell density of cytotoxic T lymphocytes as defined by counts of co-localized CD3+/CD8+ cells with intact nuclei per square mm within the ROI. Tumors were classified into two groups: CD3/CD8-high and CD3/CD8-low using the median measured CD3+/CD8+ cell density as a cutoff point. CD3/CD8-low melanomas display shorter relapse free survival (5-year RFS = 41.5%) than CD3/CD8-high melanomas (5-year RFS = 73.3%; p = 0.01). Similarly, CD3/CD8-low melanomas display shorter overall survival (5-year OS = 49.2%) than CD3/CD8-high melanomas (5-year OS = 76.6%; p = 0.05). Our automated MIF platform quantified the density of CD3+/CD8+ cells in relation to melanoma tumor cells. This score strongly correlates with RFS and OS. While further validation of our methodology is necessary, our automated methods will allow for consistent comparison between samples in large melanoma datasets.

Figure 1: Multiplex Immunofluorescence Quantification of CD3+/CD8+ Cells in Melanoma



(A) CD8 in green (Alexa488), S100 in cyan (Cy3), CD3 in red (Cy5) **(B)** CD8 in green (Alexa488) **(C)** S100 in cyan (Cy3), **(D)** CD3 in red (Cy5) **(A-D)** Hoechst 33258 nuclear counterstain in dark blue.

Scale bars = 100 µm.

PF111

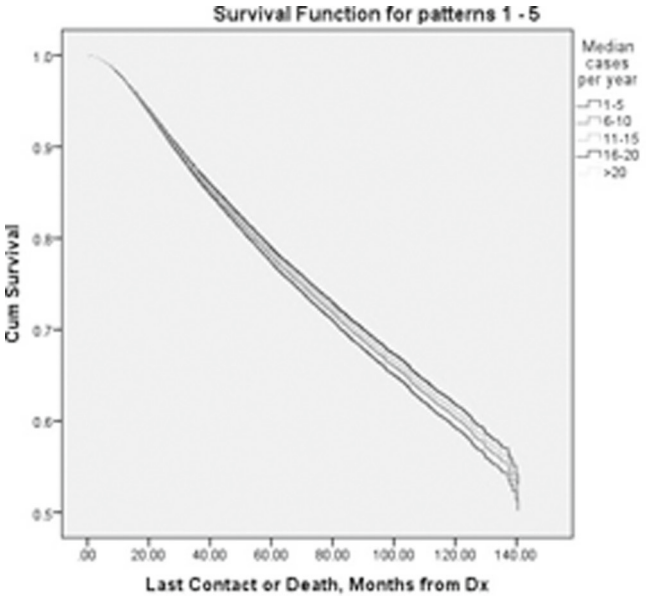
Neoadjuvant Vismodegib for the Treatment of Periocular Basal Cell Carcinoma A. Gonzalez.* *Alexander Fleming, Martinez, Argentina.*

Introduction: Locally advanced basal cell carcinoma (LA-BCC) of the periocular region is the most frequent cause for orbital exenteration (OE). Vismodegib has shown consistent response rates in LA-BCC. Mohs surgery (MS) provides high cure rates and sparing of normal tissue that make it the treatment of choice for periocular BCC. We decided to combine Vismodegib as neodjuvant (neoV) followed by MS for the treatment of periocular LA-BCC. Patients and methods: Between 6/2014 and 12/2016, six patients with periocular LA-BCC were treated with neoV (150mg /day) + MS. Male/female ratio was 1:1. Median age 74.7 years. Site: inner canthus 5(83.3%) and lower eyelid 1(16.7%). Histology: nodular 3(50%), infiltrative 2(33.3%) and micronodular 1(16.7%). Mean size: 2.2cm (range 1-3.5). tthree cases (50%) were recurrent after surgery. Five out of six patients were candidates for OE. Results: Mean time of neoV was: 5.8 months (range 4-8). Adverse events: all patients experienced muscle spasms and taste loss, 3(50%) weight loss between 5-12kg. Three patients developed alopecia. Only one 88 years old patient, suspended treatment after 4 months because of muscle cramps. Five patients had a complete clinical response (CR). MS showed 4(66.7%) complete histological responses (CHR) and in 1(16.7%) residual tumor was found. The 5 patients had a reconstructive procedure, successful both from functional and cosmetic point of view. One (16.7%) patient progressed during neoV and an OE was performed. Conclusions: In this short series, 6 cases of periocular LA-BCC treated with NeoV + MS we observed 4(66.7%) CHR and 1(16.7%) PR. This allowed eye preservation with a satisfactory cosmetic and functional result in 5 out of 6 patients. We consider this option should be tested in a large prospective trial to prove it's real value.

PF112

Surgical Volume Impacts Long-term Survival in Patients Undergoing Curative Intent Melanoma Resection with Nodal Staging K. McCoy,* J. Clarke, T. Wasser, S. Rose, C. Gajdos. *Stamford Hospital, Stamford, CT.*

Over 85,000 cases of melanoma will be diagnosed in 2017, according to the American Cancer Society. The objective of our study was to evaluate if a survival advantage exists for patients who underwent a curative intent melanoma resection with nodal staging at high volume institutions. To our knowledge, this concept has not been examined in operations with less surgical complexity like melanoma resections in a large sample size with long-term follow-up. Utilizing the National Cancer Data Base, the data for patients who underwent a curative intent melanoma resection with nodal staging between 2004 and 2014 were pulled. A multivariable Cox regression analysis was applied to estimate the Odds ratio of predictors of survival in the aforementioned patient population. Survival curves were then created using the Kaplan-Meier Method for volume using Wald Chi-square values to compare rates and assess the relative importance of each covariate. 54,047 patients, who underwent surgery between 2004 and 2014, were included in this study. Of this population: 6969 (12.89%) patients had surgery at institutions that reported an AMMS between 1 and 5 cases. Breakdown for other volume categories were as follows: 6-10 annual cases: 7358 (13.61%), 11-15 cases: 6431 (11.9%), 16-20 cases: 4462 (8.26%), over 20 cases: 28827 (53.34%). The three most important predictors of overall survival in multivariable analysis were: nodal status, Breslow depth and age. Patients who underwent a melanoma excision at a high volume center had a significantly improved overall 12-year survival rate compared to patients treated at lower volume centers: 12.2% ($P<0.001$) vs 1-5 AMMS; 8.4% ($p=0.003$) vs 6-10 AMMS, 3.8% ($p=0.038$); 16-20 AMMS ($p=0.317$) at 12 years of follow-up. Patients undergoing melanoma resection with nodal staging at higher volume programs had an overall improved 12-year survival rate compared to patients who underwent treatment at a lower volume center. Regionalizing curative intent melanoma surgeries to centers with an annual median volume of more than 15 cases may improve long-term outcome. .



PF113

Age and Gender Influence Tumor Site and Locoregional Recurrence in Head and Neck Melanoma R. Torphy,[1]* A. Gleisner,[1] B. Chapman,[1] M. McCarter,[1] W. Robinson,[2] N. Kounalakis.[1]
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2. University of Colorado, Department of Medicine, Denver, CO.

Head and neck melanomas (H&NM) account for 10-15% of all cutaneous melanomas and tend to have worse outcomes when compared to other locations. Scalp melanomas are the most aggressive tumors in this cohort. We aimed to evaluate how age and gender influence tumor location and oncologic outcomes in H&NM. Patients with H&NM undergoing wide local excision and sentinel lymph node biopsy at the University of Colorado from 1998 to 2017 were retrospectively reviewed. We analyzed demographic and pathologic variables of patients with distinct head and neck tumor locations. Multinomial logistic regression was performed to evaluate the effect of age and gender on H&NM location and stage. A Cox proportional hazard model was used to evaluate for prognostic variables. Among the 306 patients with H&NM included in the analysis, 75% were male and 67.8 % were > 50 years of age. Overall, face location was most common site (41%), followed by scalp (32.3%), ear (17.6%), and neck (8.5%). Age of diagnosis varied by tumor location with scalp melanomas being diagnosed at the oldest age (mean 60.9) and neck at the youngest (48.1) (p=0.007). For patients ≤50 yo, face melanoma was the most common tumor site. Patients ≤50 yo are more likely to develop face (relative risk ratio (RR) 2.4, p=0.005), ear (RR 3.0, p=0.005), and neck melanomas (RR 4.4, p=0.002) than scalp melanomas when compared to patients >50 yo. Face melanoma was the most common tumor site for both males and females. Female patients are less likely to develop ear melanomas (RR 0.35, p=0.033) when compared to males but there is no significant difference in scalp, face or neck location by gender. Age and gender did not impact tumor stage. Age ≤50 yo (HR 0.37, p=0.001) and female gender (HR 0.58, p=0.047) were independently associated with improved locoregional recurrence free survival (Overall mean follow-up=40 months). Among patients with H&NM, younger patients rarely develop scalp tumors whereas for the >50 yo patients, the scalp represents a common primary location. Younger age and female gender are independently associated with improved locoregional recurrence free survival. Younger age is also associated with an improved overall survival.

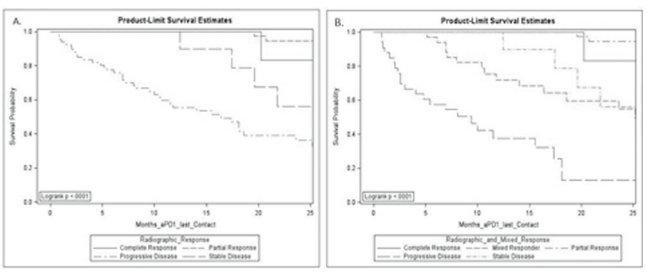
	≤50 years of age (n = 99)	>50 years of age (n=207)	P-value*	Male (n=230)	Female (n=76)	P-value*
Location						
Scalp	28.6%	29.6%	Ref	32.0%	32.9%	Ref
Face	49.0%	33.0%	0.005	38.5%	51.3%	0.541
Ear	13.3%	27.3%	0.006	20.8%	7.9%	0.030
Neck	9.2%	10.2%	0.002	8.7%	23.1%	0.665
T Stage						
T1	28.6%	29.6%	Ref	27.8%	32.9%	Ref
T2	49.0%	33.0%	0.062	38.3%	38.2%	0.576
T3	13.3%	27.3%	0.208	23.0%	22.4%	0.678
T4	9.2%	10.2%	0.495	10.9%	6.6%	0.220
N Stage						
N0	82.7%	84.5%	Ref	85.3%	80.3%	Ref
≥N1	32.1%	15.5%	0.363	14.7%	19.7%	0.341
Locoregional Recurrence (% yes)						
At 1 year	5.1%	14.1%	0.001	12.6%	6.6%	0.047
Overall	9.2%	23.2%		21.3%	11.8%	
Distant Recurrence (% yes)						
At 1 year	3.1%	8.7%	0.002	7.8%	4.0%	0.227
Overall	11.2%	21.7%		19.1%	15.8%	
Overall Survival (% death)						
At 1 year	0%	3.4%	0.001	3.4%	0%	0.364
Overall	9.1%	23.8%		20.0%	15.8%	

* Reported P-values from multinomial logistic regression and Cox proportional hazard model (Ref=Reference Population).

PF115

Evaluation of Clinical and Radiographic Response in Patients with Metastatic Melanoma Treated with Immunotherapy A. Chawla,* M.M. Kim, G.G. Kasumova, D.T. Frederick, G.M. Boland.
Massachusetts General Hospital, BOSTON, MA.

Background: Melanoma patients undergoing immunotherapy (IT) demonstrate a wide range of treatment responses. While immune-related response criteria (irRC) have been introduced, it has yet to become as broadly utilized as Response Evaluation Criteria in Solid Tumors (RECIST). Oncologists also utilize clinical designations to describe tumors with atypical responses. We compared the relationship between radiographic response, clinical response, and overall survival (OS). **Methods:** Patients treated with IT targeting programed cell death 1 receptor (aPD-1) with or without combination cytotoxic T-lymphocyte-associated protein 4 (aCTLA-4) therapy were identified. The best responses while on IT were collected. For radiologic response, if RECIST staging was not available, radiology reports were reviewed to characterize response. Clinical response was derived from review of oncology reports. OS was calculated from start of treatment and analyzed using the Kaplan-Meier method. Prognostic performance was assessed using the Akaike information criterion (AIC) from univariate Cox proportional hazard analysis. **Results:** 146 patients with metastatic melanoma were included. 69.9% were male and 77.3% had cutaneous melanoma, with median age of 65.5 (IQR: 54-73). 23.3% of patients who were characterized clinically as having mixed response were categorized as having progressive disease radiologically. There was a significant difference in OS between groups when stratified by radiographic response (complete, partial, progressive and stable disease; Figure 1A), as well as clinical response (responders, mixed responders, and non-responders) (p<0.0001). Furthermore, separating out mixed responders from those deemed to have progressive disease radiographically, demonstrated a survival benefit in mixed responders (log-rank p<0.0001; Figure 1B). The AIC was similar for both clinical and radiographic staging. **Conclusions:** These results suggest that the survival of mixed responders may be underestimated by using traditional radiographic response and may be better classified using clinical criteria as a cost-effective and timely surrogate for irRC response.



PF116

Evaluation of Chest Radiographs in Workup for Low-Risk Melanomas W.C. Brooks, K. Votanopoulos, P. Shen, E.A. Levine.* *Surgical Oncology, Wake Forest Baptist Health, Winston-Salem, NC.*

Background: Chest radiographs (CR) have historically been captured as a part of low-risk melanoma (clinical stage I/II) workup. Current guidelines do not recommend imaging for these patients. However, there is still debate on whether this imaging should be included in routine evaluation. This study evaluates the utility of CR during the staging of clinical stage 1 and 2 melanoma patients. Methods: This study was approved by the internal review board at Wake Forest University. A prospective database of sentinel lymph node biopsies performed for clinical stage 1 and 2 melanoma was used to identify early stage melanoma patients. The medical records of patients with melanoma were retrospectively reviewed and preoperative workup procedures were recorded. Results: 189 patients were reviewed. 112 patients had preoperative CR. 50 had pathologic stage I disease, 44 stage II, and 18 stage III. The median age of subjects was 58, with 42.3% female. Of 112 preoperative CR obtained, none (0%) correctly identified metastatic melanoma. 11 patients' imaging reports suspected melanoma. Two of these patients subsequently recurred. One had local failure at the excision site one year post excision; the other had progression after 6 years to an inguinal node. Conclusion: No patients were found to have metastatic melanoma by screening with CR during preoperative workup. Frequently, other imaging techniques were utilized that made the CR irrelevant. The cost and anxiety caused by false positives results gives ample support to recommend not conducting CR as part of routine workup for early stage melanoma patients.

PF117

Exosomal PD-L1 Protein Expression Correlates with Targeted Therapy Resistance in Melanoma G.G. Kasumova,[1]* M.M. Kim,[1] A. Shi,[2] I. Chien,[1] D.T. Frederick,[1] R. Alpatov,[1] W.A. Michaud,[1] D. Plana,[1] D. Panka,[3] R.B. Corcoran,[1] K.T. Flaherty,[1] R.J. Sullivan,[1] M. Kellis,[2] G.M. Boland.[1] *1. Surgical Oncology, Massachusetts General Hospital, Boston, MA; 2. Massachusetts Institute of Technology, Cambridge, MA; 3. Beth Israel Deaconess Medical Center, Boston, MA.*

Background: PD-L1 expression on tumor cells correlates with poorer outcomes and functional modulation of the PD-1/PD-L1 axis remains of critical importance. Exosomes are circulating microvesicles that contain a subtranscriptome/subproteome of their cell of origin and are known to regulate the activation status of T cells. We noted an increase in exosomal PD-L1 protein concentration in exosomes from melanoma cell lines, more pronounced in targeted therapy resistant cells. Therefore, we sought to evaluate exosomal PD-L1 expression and exosome-mediated immune changes in melanoma. Methods: Melanoma cell lines (BRAFi sensitive and resistant) and patient plasma were used for analysis. Exosomal vesicles were isolated using serial centrifugation. Functional proteomics by reverse phase protein array (RPPA) were performed in cell lines and exosomes treated with control (DMSO) and BRAFi (PLX-4720). ELISA was used to assess exosomal PD-L1 expression prior to and after initiation of therapy in patient with metastatic melanoma. The role of exosomal PD-L1 high and low cell lines on T cell function are currently being assessed. Results: Proteomic analysis revealed PD-L1 protein on cell lines with several fold higher expression on paired exosomes. This enrichment of exosomal PD-L1 protein was significantly higher in resistant lines and increased upon treatment with BRAFi. Melanoma patient-derived exosomes also revealed PD-L1 protein with higher baseline exosomal PD-L1 expression in BRAF mutant tumors. In several patients, treatment with BRAFi resulted in increased exosomal PD-L1 expression. We are currently investigating the effects of tumor derived exosomes on T cell activation and exhaustion states in vitro. Conclusions: Exosomes express PD-L1 at variable levels, which can be modulated by targeted therapy and increase at the time of therapy resistance. Soluble exosomal PD-L1 protein may be a potential mechanism for exosome mediated immune evasion and functional studies are underway. We are currently monitoring exosomal PD-L1 protein levels in patients treated with combination targeted therapy and immunotherapy as a potential predictor of response.

PF118

Examining the Incidence of Melanoma and Non-Melanoma Skin Cancers Among Solid Organ Transplant Recipients H. Khadra,* J. Crowther, A.S. Paramesh, E. Kandil, J.F. Buell, H. Jeon, M.T. Killackey, J. Hamner. *Department of Surgery, Tulane University School of Medicine, New Orleans, LA.*

Background Numerous studies have documented the increased risk of non-melanoma skin cancers in solid organ transplant recipients. However, studies have not been in agreement regarding whether the incidence of melanoma is increased in solid organ transplant patients. Methods We examined the incidence of melanoma and non-melanoma skin cancers among all solid organ transplant recipients from 1989-2015 using the United Network for Organ Sharing (UNOS) registry. The types of transplants included: intestinal, kidney, pancreatic, kidney + pancreatic, liver, heart, lung, and heart + lung. Results There were 624,985 patients who underwent solid organ transplants with a median follow up of 5.5 years that were included in our analysis. There were 37,294 patients who developed skin cancer of any type during follow up, with 751 of these cases being a recurrence of a skin cancer treated prior to transplant surgery. We first analyzed whether there was a significant difference in the rate of de novo skin cancer development for the different transplant types, which was significant ($c^2(7) = 9114$, $p < 0.001$). Significant results were found both for combined squamous and basal ($c^2(7) = 8937$, $p < 0.001$) and for melanoma ($c^2(7) = 360$, $p < 0.001$). Similar results were found for the rate of recurrent skin cancers for both squamous and basal combined ($c^2(7) = 84$, $p < 0.001$) and melanoma ($c^2(7) = 30$, $p < 0.001$). Thoracic organ transplants were associated with higher rates for all types of skin cancer. Conclusion The current registry study demonstrates that solid organ transplant recipients are at an increased risk of developing melanoma. This increased risk suggests more intense screening should be considered for both melanoma and non-melanoma skin cancers in the post-transplant setting.

Incidence of Skin Cancer in Solid Organ Transplant Recipients (per 100,000 patients)

Type of Transplant	Recurrence Non-Melanoma Skin Cancer	Recurrence of Melanoma	De Novo Squamous Skin Cancer	De Novo Basal Skin Cancer	De Novo Melanoma
Intestinal	0 (0)	0 (0)	907 (21)	345 (8)	43 (1)
Kidney	122 (458)	10 (37)	3014 (11335)	1688 (6348)	245 (921)
Pancreas	101 (16)	0 (0)	1949 (310)	1081 (172)	182 (29)
Kidney-Pancreas	32 (6)	11 (2)	3170 (599)	1789 (338)	270 (51)
Liver	57 (72)	8 (10)	2694 (3404)	1609 (2034)	237 (299)
Heart	135 (75)	30 (17)	7654 (4266)	3992 (2225)	606 (338)
Lung	194 (56)	7 (2)	9734 (2814)	3003 (868)	336 (97)
Heart + Lung	0 (0)	0 (0)	5915 (43)	2338 (17)	688 (5)

PF119

Partially Exhausted T Lymphocyte Directed Neoadjuvant Treatment in Operable Stage III Melanoma J. Lin, K. Mahuron, K. Tsai, A. Algazi, M. Rosenblum, a. daud, M. Alvarado.* *Surgery, UCSF, San Rafael, CA.*

Background: We have previously demonstrated that the partially exhausted cytotoxic T lymphocytes (peCTL) frequency predicts response to anti–PD-1 monotherapy and combination CTLA4/PD-1 blockade in metastatic melanoma. However, the utility of this assay in the neoadjuvant setting has not been established. In the current study, 7 patients with operable Stage III Melanoma were assessed for response to neoadjuvant anti-PD-1 or anti-PD-1/CTLA-4 inhibition as assigned by peCTL frequency. Materials and methods: Pretreatment tumor samples from 7 patients with locally advanced melanoma underwent multiparameter flow cytometric analysis. Patients received neoadjuvant anti–PD-1 monotherapy or combination therapy followed by surgical resection. Patients with low peCTL burden (<20%) received anti-PD-1/CTLA-4 inhibitors whereas those with high peCTL (>20%) were assigned to anti-PD-1 monotherapy. Patients with documented follow up history and evaluable immunophenotype were included in efficacy and safety analysis. Results: Patients were 57% male with mean age of 58 years. Six patients had Stage III disease with LDH<ULN, and 5 BRAF WT. Prior therapy included CTLA-4 monotherapy in 2 of 7 patients. Five patients received anti-PD-1 monotherapy and 2 received CTLA-4/PD-1 blockade and were evaluable at time of analysis. Six out of 7 patients achieved complete pathologic response. Responses were durable. At a median follow-up of 21 months only the patient who did not achieve pCR had disease progression. Toxicity profile was consistent with previously reported studies with grade 1/2 diarrhea, pruritus, arthralgia, and

hypothyroidism most frequently reported. Grade 3/4 adverse effects included isolated cases of gastritis and anaphylaxis. Conclusion: Our results suggest the efficacy of peCTL directed neoadjuvant treatment in operable Stage III melanoma with the large predominance of patients achieving complete pathologic response with acceptable toxicity profile. These promising data from this pilot study merit further investigation with a larger cohort validation study.

PF120

Development of a Comprehensive Prognostic Survival Model for Cutaneous Melanoma D.J. Winchester, G. Ajmani,* C. Wang.
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Introduction Traditional TNM staging provides limited precision in estimates of prognosis, leading to the development of quantitative models or calculators. For cutaneous melanoma, several such models have been published, but these are limited by use of outdated data and or in datasets which exclude nodal or distant metastases. Methods Using the National Cancer Data Base (NCDB), we developed a prognostic model for melanoma inclusive of patients diagnosed from 2010-2013 with all stages of disease. Patients were separated into training and testing cohorts. Bootstrapped parametric survival regression was used to compute estimates of 3-year overall survival. Variables used in the model included age, Breslow thickness, site, ulceration, mitotic index, number of positive lymph nodes, ratio of positive nodes, and distant metastases. Model prognostic performance was assessed in the NCDB testing cohort and using the Surveillance, Epidemiology, and End Results (SEER) database. Results 76,213 patients in the NCDB were randomly divided into a training (n=53,350) and testing (n=22,863) cohort. Thee model was also applied to 33,555 patients in SEER. Across all levels of each covariate, the model demonstrated good fit within the NCDB training cohort, with concordance correlation coefficients (rc) ranging from 0.98-1.00. We then computed a variable including all possible combinations of binary versions of each variable and found a concordance correlation coefficient of 0.87. When weighting for the number of patients within each combination of factors (rc_{wt}) this increased to 0.97. For all combinations of factors within the NCDB testing cohort we found rc 0.82 and rc_{wt} 0.96, and within the SEER cohort rc 0.78 and rc_{wt} 0.95. The c-statistic (equivalent to an AUC for survival analysis) was: 0.85 in the NCDB training, 0.85 in the NCDB testing, and 0.88 in SEER cohorts. Conclusions We developed a prognostic model for cutaneous melanoma in a large, contemporary cohort of patients in the U.S. with strong internal NCDB and external SEER validation. This equation may be used to define accurate prognostic information for patients with cutaneous melanoma.

PF121

Evaluation of Short Term Complication Rate After Melanoma Surgery in the Italian Central National Melanoma Registry A. Sommariva,[1]* A. Vecchiato,[1] P. Del Fiore,[1] C. Panzano,[2] C. Rossi.[1]
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2. Clinical Research Technology, Salerno, Italy.

INTRODUCTION: There is increasing interest for monitoring quality of surgical treatment of melanoma. Morbidity risk is poorly investigated and remains an important factor in patient counseling before surgery and for monitoring quality of surgical treatment. Aim of the study is to identify the complications rate after surgery among the Institutions afferent to the Italian Melanoma Intergroup (IMI) METHOD: The Central National Melanoma Registry (CNMR) is a prospectively maintained national data collection for melanoma treatment promoted by the IMI in 43 melanoma centers in Italy. Only patients with invasive, non-metastatic melanoma were identified. The following short term (<30 days after surgery) complications were investigated: infection, dehiscence, skin necrosis after wide excision (WE), infection, dehiscence and seroma after sentinel lymph node biopsy (SLNB) and radical lymphadenectomy (LA). Values are expressed as percentage. Centers have been divided according to the 50th percentile of the median number of procedures performed. Chi-square test was used to analyze centers volume associated with complications. RESULTS: a total of 6922 melanoma patients surgically treated during the period 2011-2016 (59% WE, 32% SLNB and 9% LA) were included. Low volume centers are correlated with an higher wound infections rate after WE (p=0,00002) and SLNB (p=0,0009), and seroma after SLNB (p=0,0001). Values are summarized in table 1. CONCLUSION: Values with relative benchmark of short term morbidity have been identified in Italy. These parameters can now be used for promoting QA programs for surgical treatment of melanoma through a continuous feedback of performance of these values to the Italian centers performing melanoma surgery.

Table 1

Procedures	(N)	Complications	Rate (%)	10th-90th percentile
EA	4099	Infection	1,5	0,4-6,1
		Dehiscence	6,1	0,6-31,8
		Skin necrosis	0,3	0-0,7
SLNB	2210	Infection	1,2	0-3,3
		Dehiscence	1,8	0-7,5
		Seroma	5,7	0,1-15,7
LA	613	Infection	3,1	0-10,9
		Dehiscence	4,0	0-11,1
		Seroma	13,0	2,1-36,4

PF122

Patients' Preference for the Use of Photographs Versus Graphics in a Patient Information Booklet J. Li, B. Heller,* N. Hodgson.
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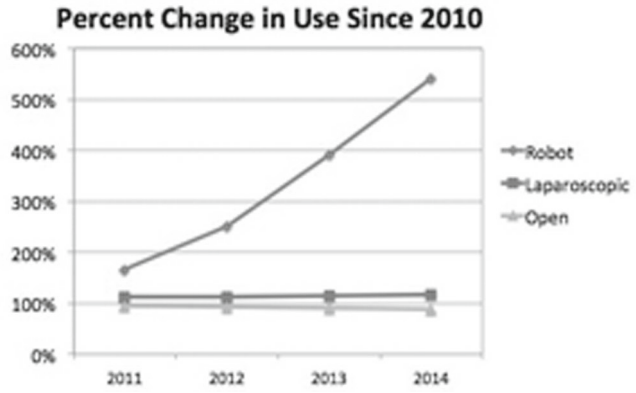
Introduction Breast cancer is the most common cancer among women and often involves a complex sequence of treatments. As a part of quality assurance, a patient information booklet is being developed at our centre to provide patients with information on their post-operative wounds, dressings and drains. While a sizable body of literature support the use of images to enhance patient understanding, no studies have assessed patients' preference of photographs vs. graphics. Method Eighty sequentially treated breast cancer patients were surveyed in the perioperative setting to determine whether they felt they received enough information about their surgery, if they had sought additional information online, and if they felt wound information best be presented with graphics or real photographs. Result 92.5% (74/80) of patients felt they had obtained sufficient information prior to surgery. Of these 56.8% (42/74) had searched images online to see how post-operative wounds would appear. All patients reported preference for a pre-op information sheet with images (graphics or photographs) for the wounds, dressing and drains. 77.5% (62/80) of patients preferred actual photographs of the wounds versus 22.5% (18/80) who preferred graphics. All patients who preferred wound graphics cited that they felt real photographs may be too disturbing. For the dressings and drains, all patients preferred photographs over graphics so that they would have realistic expectations. Conclusion Most patients preferred realistic photographs of post-op wounds. However, those patients who preferred graphics felt strongly that photographs would be disturbing. These results will be reflected in a patient information booklet currently under production.

PF123

Here to Stay – Robotic Surgery Trends in General Surgical Oncology from the National Inpatient Sample C. Stewart,* P. ituarte, K. Melstrom, S. Warner, L.G. Melstrom, L. Lai, Y. Fong, Y. Woo.
Surgery, City of Hope, Altadena, CA.

Introduction: Robotic surgery has demonstrated oncologic safety and similar outcomes to laparoscopy in skilled hands. The extent of robotic surgery use, however, is poorly defined. We analyzed the National Inpatient Sample (NIS) to test our hypothesis that robotic surgery is outpacing laparoscopy in general surgical oncology, with decreasing complications and in patients with more comorbidities over time. Methods: We queried the NIS 2010-2014 databases for patients who had esophageal, gastric, small bowel, pancreas, liver, and colorectal operations for malignancies. Operations were considered robotic if any robotic code was used. Results: We identified 147,259 patients who had 3,676 esophageal, 7,103 gastric, 7,698 small bowel, 11,016 pancreas, 6,730 liver, and 111,035 colorectal operations. In 2010, only 1.1% of all cancer operations were performed using a robotic approach, compared to 23.5% laparoscopic, and 75.3% open. Over the 5-year study period, there was a 540% increase in robotic surgery, 117% increase in laparoscopy, and 114% decrease in open operations (<0.001, figure). Adjusting for age and comorbidities, the odds of having a robotic operation increased by 1.11 per quarter (p<0.001). There was a weak, but significant trend towards more robotic operations in patients with comorbidities (r=0.07, p<0.001). Conversion to open was lower in robotic (5-7%) compared to laparoscopic surgery (17-19%, p<0.001). Rate of other surgical complications varied by year in robotic (35-55%), and laparoscopic groups (24-47%); both were lower compared to the open group (50-82%, p<0.001). Length of stay was also similar between robotic (6.9 ± 6.5

days) and laparoscopic groups (7.0 ± 6.5 days, p=0.52), but shorter than the open group (10.6 ± 9.3 days, p=<0.001), which was stable time. Conclusion: Robotic surgery for patients with cancer has steadily increased over time, and is increasing at a faster rate than laparoscopic surgery. This trend occurred for all surgical sites and persisted after adjustment for age and comorbidities. These data suggest robotic surgery will be an important part of general surgical oncology in the future.



PF124

Development and Implementation of a Peri-Operative Clinical Pathway for Cytoreductive Surgery and Heated Intraperitoneal Chemotherapy Improves Resource Utilization J.S. Peng,* J. LaPiano, A. Maciver, K. Attwood, J. Skitzki, J.M. Kane, V. Francescutti. *Surgical Oncology, Roswell Park Cancer Institute, Buffalo, NY.*

Introduction: Cytoreductive surgery and heated intraperitoneal chemotherapy (CS/HIPEC) is performed for peritoneal metastases and can be associated with significant morbidity and length of stay. Clinical pathways (CPW) have been applied for a variety of clinical indications, resulting in decreased complications without negatively impacting the length of stay or readmission rate. A CPW was implemented at our institution in June 2016 for patients undergoing CS/HIPEC and outcomes for this transition were evaluated. Methods: The CPW was developed through evidence based literature review of best practices. The hospitalization was conceptualized into the acute postoperative period, gastrointestinal recovery, clinical stabilization, and discharge, with multi-disciplinary roles defined at each phase. Components of the CPW included admitting location, intravenous fluids, analgesia, ulcer and venous thromboembolism prophylaxis, and activity. Demographics, operative details, and postoperative course were compared for all patients who underwent CS/HIPEC after the implementation of the CPW and an equal number of sequential patients prior to the transition. Results: Eighty patients were included for analysis including 40 patients prior to the CPW (pre-CPW) and 40 patients after CPW implementation, with results and statistical analyses detailed in Table 1. The two groups were comparable with regard to age, gender, diagnosis, indication for surgery, and prior therapy. Operative procedures and completeness of cytoreduction was similar. The CPW groups required fewer days in a monitor step-down unit (median 1 day for CPW vs 2 days pre-CPW, p = 0.002), but overall length of stay and 90-day complication rates were comparable. Conclusions: CS/HIPEC can be a highly variable surgical procedure, resulting in a heterogeneous patient population. However, these variations can be captured using a milestone-based care pathway which provides flexibility and improved resource utilization. The implementation of a CPW at our institution demonstrated a reduction in high acuity care, without compromising clinical outcomes.

Table 1. CS/HIPEC Demographics, Operative and Post-Operative Outcomes

	Total n = 80	Pre-CPW n = 40	CPW n = 40	p-value
Age (years)	58.2	58.5	57.9	0.85
Gender				0.65
Male	37 (46)	20 (50)	17 (43)	
Female	43 (54)	20 (50)	23 (58)	
Diagnosis				0.15
Appendiceal low grade mucinous neoplasm	22 (28)	9 (23)	13 (33)	
Colorectal adenocarcinoma	20 (25)	10 (25)	10 (25)	
Appendiceal adenocarcinoma	19 (24)	14 (35)	5 (13)	
Appendiceal goblet cell	6 (8)	1 (3)	5 (13)	
Ovarian cancer	5 (6)	2 (5)	3 (8)	
Mesothelioma	4 (5)	1 (3)	3 (8)	
Indication				0.56
Primary resection	23 (29)	13 (33)	10 (25)	
Residual disease after primary resection	32 (40)	17 (43)	15 (38)	
Peritoneal recurrence	25 (31)	10 (25)	15 (38)	
Prior therapy				
Chemotherapy	37 (46)	18 (45)	19 (48)	1.00
Resection or debulking	69 (85)	32 (80)	37 (93)	0.19
Operation				
Laparoscopic/hand-assisted	8 (10)	1 (3)	7 (18)	0.06
Colorectal resection	40 (50)	20 (50)	20 (50)	1.00
Small bowel resection	14 (18)	5 (13)	9 (23)	0.38
Diaphragm stripping	26 (33)	11 (28)	15 (38)	0.47
Splenectomy	12 (15)	6 (15)	6 (15)	1.00
Stoma	9 (11)	2 (5)	7 (18)	1.00
Complete cytoreduction	50/60 (83)	28/35 (80)	22/25 (88)	0.50
Estimated blood loss (mL)	120	135	100	0.63
Length of stay (days)				
ICU	0	0	0	0.41
Monitored step-down	2	2	1	0.002*
Overall	9	9	9	0.20
Complications (90-day)				
Any complication	40 (50)	18 (45)	22 (55)	0.50
Clavien-Dindo grade 3-4	18 (23)	8 (20)	10 (25)	0.79
Anastomotic leak	6/54 (11)	3/26 (12)	3/28 (11)	1.00
Surgical site infection	15 (19)	6 (15)	9 (23)	0.57
Pulmonary	2 (3)	0	2 (5)	0.49
Cardiac	3 (4)	1 (3)	2 (5)	1.00
Reoperation	7 (9)	3 (8)	4 (10)	1.00
90-day readmission	19 (24)	8 (20)	11 (28)	0.60
90-day mortality	0	0	0	

Reported as median or number (%). CPW, clinical pathway.

PF125

Returns to the OR After Breast Operations: A Learning Opportunity for Quality Improvement B.L. Murphy,* A.E. Glasgow, E.B. Habermann, T.J. Hieken. *Surgery, Mayo Clinic, Rochester, MN.*

Background: Returns to the operating room (ROR) after breast surgery increase costs, may delay adjuvant therapy and compromise reconstruction. Better understanding causes and patients at highest risk RORs may spur practice improvements. Our aim was to determine ROR frequency and indications after breast surgery at a tertiary care center. Methods: Using CPT codes we identified all patients ≥ age 18 undergoing breast surgery at our institution from 1/1/14-1/13/17. We queried an institution-specific database to identify ROR within 45 days of the index operation. RORs were categorized as staged procedures (further oncologic surgery) or complications (bleeding, tissue necrosis, infection, implant or wound issues, seroma). Student's t-tests, Chi-square and Fisher's exact tests compared patient, diagnosis and procedural variables between patients who had an ROR and those who did not. Results: 2,914 patients underwent breast surgery during the study period. 117 patients (4.2%) had 121 RORs within 45 days of the index surgery. Patients who had a ROR were slightly younger than those who did not (55.5±11.9 vs 57.8±13.7, p=0.04). ROR was more common after mastectomy (vs lumpectomy) and immediate breast reconstruction (vs no immediate reconstruction), p<0.01 and p=0.01 respectively (Table). Staged procedures accounted for 44 of RORs (36.3%), while complications accounted for 77 (63.7%). Further oncologic surgery included sentinel lymph node surgery in 5 patients (11.6%), axillary dissection in 8 (18.6%), and reexcision of close or positive margins in 30 (69.8%). Among ROR for complications, hematoma evacuation was most frequent (30;24.8%), followed by flap necrosis (17;14.0%), other related to reconstruction (12;9.9%), and infection (9;7.4%), other wound complication (5;4.2%) and seroma (4;3.4%). Conclusion: RORs following breast surgery occurred in ~4% of patients: one-third were cancer-related while the remainder were for complications. These data provide baseline measures for clinical prac-

tice improvement initiatives, and justify efforts to decrease hematoma and flap necrosis rates to reduce costs, while improving patient care and satisfaction.

Patient and Treatment Variables with Association to Return to Operating Room (ROR)

	Overall	No ROR	ROR	P-Value
N	2914	2797	117	
Age				0.04
Mean (standard deviation)	57.7 (13.7)	57.8 (13.7)	55.5 (11.9)	
Gender				0.21
Female	2893 (99.3%)	2778 (99.3%)	115 (98.3%)	
Male	21 (0.7%)	19 (0.7%)	2 (1.7%)	
Diabetes				0.30
No	2681 (92.0%)	2570 (91.9%)	111 (94.9%)	
Yes	233 (8.0%)	227 (8.1%)	6 (5.1%)	
Body Mass Index				0.15
Mean (standard deviation)	28.7 (6.6)	28.6 (6.6)	29.1 (6.1)	
Smoking Status				0.64
Current	182 (6.2%)	173 (6.2%)	9 (7.7%)	
Former	805 (27.6%)	770 (27.5%)	35 (29.9%)	
Never	1927 (66.1%)	1854 (66.3%)	73 (62.4%)	
Type of Surgery				<0.01
Lumpectomy	1570 (53.9%)	1532 (54.8%)	38 (32.5%)	
Mastectomy	1344 (46.1%)	1265 (45.2%)	79 (67.5%)	
Reconstruction				0.01
No	1386 (47.6%)	1344 (48.1%)	42 (35.9%)	
Yes	1528 (52.4%)	1453 (51.9%)	75 (64.1%)	

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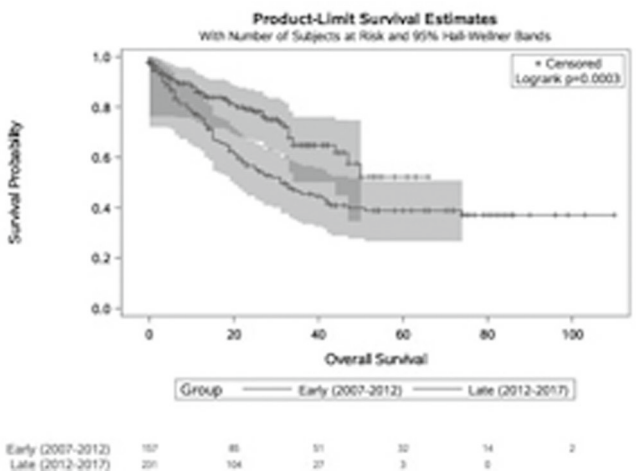
Improved Survival with Experience: A Ten Year Learning Curve in Hyperthermic Intraperitoneal Chemotherapy and Cytoreductive Surgery N.L. Leigh,* D. Solomon, D. Feingold, D.R. Magge, B.J. Golas, U. Sarpel, D.M. Labow. *Icahn School of Medicine Mt. Sinai, New York, NY.*

Objective: Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) is an aggressive treatment for select patients with peritoneal carcinomatosis (PC) and is only offered at specialized institutions. Multiple studies demonstrate that experience affects outcomes for these complex surgical procedures. Methods: We retrospectively analyzed all patients who underwent attempted CRS/HIPEC for various malignancies with PC at our institution from 2007 to 2017. We compared clinicopathologic, perioperative, and oncologic outcomes of early (2007-2012) and late (2012-2017) cohorts. Results: Over a 10-year period, 441 patients underwent attempted CRS/HIPEC. 388 were completed; 157 and 231 in the early and late cohorts, respectively. The early cohort had higher EBL (400 vs.150 ccs, p<0.0001), longer operations (341 vs. 273 mins, p<0.001), more ICU admissions (55% vs. 13%, p<0.0001), longer LOS (8 vs. 6 days, p=0.0134), and a trend towards higher major postoperative morbidity (Clavien III-V, 24% vs. 18%, p=0.1264). While completeness of cytoreduction (CC-0/CC-1) was similar between the two cohorts (119 vs. 178, p=0.7737), the late cohort had a lower PCI (10 vs. 16, p<0.0001) and more aborted procedures (47 vs. 6, p<0.0001). Median follow-up time was 19 months. Median PFS (11 vs. 13 months, p=0.0086), 1-year OS (76% vs. 86%) and 3-year OS (45% vs 65%, p=0.0003) were all significantly longer in the late cohort. On multivariate analysis, early cohort, higher PCI and tumor recurrence were significant predictors of poor OS (p<0.05). Conclusions: At our center, with increased volume and experience over time, there has been a significant improvement in perioperative and survival outcomes for patients undergoing CRS/HIPEC for PC.



Kaplan-Meier curves of overall survival for early and late cohorts

PF127

Predictive Factors for Severe Morbidity Following Cytoreductive Surgery and Hyperthermic Intraperitoneal Chemotherapy J.W. Tan,* N. Shannon, C. Chia Shulyn, G. Tan, J. Ong, M. Teo. *National Cancer Centre Singapore, Singapore, Singapore.*

Introduction Peritoneal carcinomatosis (PC) occurs in 15% of colorectal cancer and up to 60% in ovarian cancer, and was associated with a poor prognosis of 6–12 months survival. Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) has led to improved survival. Despite decreasing morbidity, there remain concerns regarding the procedure. This study examines predictive factors for severe morbidity. Methods Data was prospectively collected for consecutive cases of patients with PC treated with CRS and HIPEC from January 2001 to December 2016. Patients were grouped into those with and without severe morbidity, defined as grade 3 or more as per Clavien-Dindo classification. Risk factors were identified using a logistic regression model, and optimum cutoff determined by Youden's index. Results 52 out of 244 patients (21.3%) experienced severe morbidity. A multivariate model was constructed using pre-operative factors (age, elevated tumour markers, malnourishment, anaemia, race, gender, BMI, ASA, ECOG, prior surgical score, co-morbidities, primary tumour, histology of tumour, T, N, M stage, recent smoking and drinking history, CT evidence of ascites, omentum thickening and small bowel), and intra-operative factors (PCI, duration of surgery, estimated blood loss, intra- and post-operative blood transfusions, CC score, number of peritoneal, visceral and total resections, HIPEC regime, presence of chest tubes and stoma). Multivisceral resections (p<0.01) and duration of surgery of 470 minutes or more (p=0.0197) independently predicted occurrence of severe morbidity. PCI, commonly associated with extent of surgery, did not independently predict severe morbidity, despite showing significance in the univariate analysis. CT evidence of omentum thickening was close to significance (p=0.0535). ASA score demonstrated an inverse relationship with severe morbidity. Conclusion Severe morbidity was predicted by factors pertaining to extent of surgery. Improvements in pre-operative imaging that would enable better estimation of extent of disease would be most useful amongst all pre-operative considerations when planning for CRS and HIPEC.

PF128

Effect of Paravertebral Blocks on Cost of Hospitalization in Breast Cancer Patients Undergoing Mastectomy with Implant Based Reconstruction E.L. Siegel,* R.F. Alban, K. Anand, L. Ozcan, K.A. Carlson, H. Sax, A. Chung, A. Giuliano, F. Amersi. *Surgery, Cedars Sinai Medical Center, Los Angeles, CA.*

Introduction: Inadequate pain control frequently extends length of stay (LOS) and therefore cost of hospitalization for patients undergoing mastectomy with implant based reconstruction (IBR). Paravertebral blocks (PVB) have been shown to improve pain management and early mobilization. Therefore, we sought to determine if use of PVB affects cost of hospitalization in patients undergoing mastectomy with IBR. Methods: Prospective database review of 129 patients undergoing mastectomy with IBR between January 2013 and

January 2017 was performed. We compared LOS, total and direct cost, and payer information in patients who had and did not have PVB. Statistics are reported as median (interquartile range) or mean ± standard deviation. Results: Of 129 patients, 38 (29.5%) received a PVB. Both groups had similar rates of bilateral mastectomies and axillary procedures (76.3% PVB and 82.4% no-PVB group, p=0.47 and 86.9% PVB vs. and 82.0% no PVB, p=0.83, respectively). Insurance coverage in the majority of patients was private PPO or HMO (82.2%), followed by Medicare (10.9%) and Medicaid (6.2%). The PVB group had a higher case mix index (CMI) (1.27 (1.18-1.62) PVB vs 1.18 (1.06-1.36) no-PVB, p<0.01) and lower LOS (1.92± 1.22 PVB vs 2.92±1.51, p<0.01) and cost associated with LOS ($5734±3631 PVB vs $8725±4499 no-PVB, p<0.01). Despite decreased LOS, total cost of hospitalization was increased in the PVB group ($27533 (23026-31252) PVB vs $23136 (18721-28272) no-PVB, p=0.01). The direct cost to patients of hospitalization was also increased in the PVB group ($15720 (12545-17759) PVB vs $12200 (9587-15825 no-PVB, p<0.01). Conclusions: Although use of PVB in patients undergoing mastectomy with IBR decreases length of stay, it is associated with increased total and direct cost of hospitalization.

PF129

Developing New Patient-Centered Measures of Cancer Surgery Recovery: Feasibility of Digital Phenotyping in a Breast Cancer Cohort I. Solsky,[1]* P. Staples,[2] I. Barnett,[3] M.A. Gadd,[4] M.C. Specht,[4] J. Onnela,[2] A.B. Haynes.[1] *1. Ariadne Labs (Brigham and Women's Hospital; Harvard T.H. Chan School of Public Health), Boston, MA; 2. Harvard T.H. Chan School of Public Health, Boston, MA; 3. University of Pennsylvania, Philadelphia, PA; 4. Massachusetts General Hospital, Boston, MA.*

INTRO: Digital phenotyping—the quantification of individual behavior from digital devices such as smartphones—may provide a more nuanced understanding of recovery from cancer surgery. This pilot study assesses the feasibility of digital phenotyping methods in a breast cancer cohort. METHODS: Breast cancer surgery patients downloaded the Beiwe smartphone app, which continuously collected pre- / post-op passive data including GPS (1 min of every 11) and accelerometry (10 sec of every 20), providing proxy measures of daily physical activity like number of steps taken. They also received daily 5 item surveys taken from the RAND-36 (R36), which taps health domains such as physical functioning (active data). Mean percentages of passive data collected and surveys completed were calculated. A linear mixed model predicting R36 physical functioning score (0-100) from the proxy measures was used to determine the correlation between this score derived from active data with that modeled from passive data. The mean difference between model fits and survey responses was calculated. RESULTS: Four patients undergoing breast-conserving therapy were followed for a mean of 72.5 days. Data was collected on 97.7% of study days on average. On average, 78.8% of expected GPS data points were collected, 93.8% of expected accelerometer data points were collected, and 49.3% of surveys were completed. Each subject had a unique recovery signature based on passive and active data (Figure 1). The correlation between model fits and R36 survey responses for physical functioning was 0.67. The mean average difference between self-reported physical functioning and model fits was 14.5. CONCLUSION: Digital phenotyping is feasible in this cohort and provides nuanced behavioral data. High percentages of passive data collected and strong correlation between active and passive physical activity measures indicate that passive data may be a satisfactory and reliable marker of recovery. Further research is needed to validate these methods in a larger cohort so detailed recovery arcs can be established for all cancer patients undergoing different treatment.

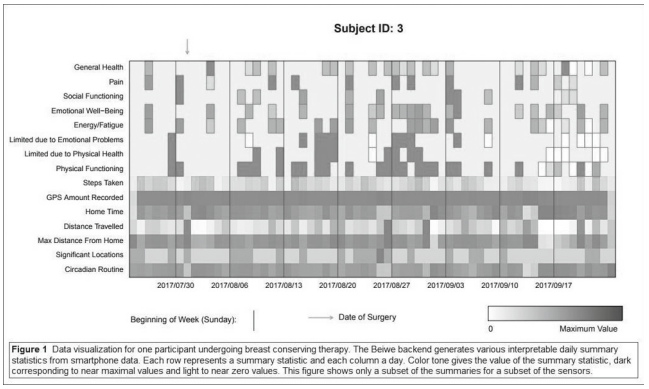


Figure 1 Data visualization for one participant undergoing breast conserving therapy. The Beiwe backend generates various interpretable daily summary statistics from smartphone data. Each row represents a summary statistic and each column a day. Color tone gives the value of the summary statistic, dark corresponding to near maximal values and light to near zero values. This figure shows only a subset of the summaries for a subset of the sensors.

PF130

Academic Surgical Oncologists' H-Indices are a Better Predictor of Academic Productivity and Professorial Rank than Total Publications or Citations V. Nguyen,[1]* R.A. Marmor,[2] J. Sicklick.[3] *1. University of California, San Diego School of Medicine, La Jolla, CA; 2. University of California, San Diego, Department of Surgery, La Jolla, CA; 3. University of California, San Diego, Division of Surgical Oncology, Department of Surgery, La Jolla, CA.*

Introduction An individual's h-index is defined as the number of h papers published, each with ≥h citations. We hypothesized that the h-index is a stronger predictor of surgical oncologists' academic rank than total publication or citation counts. Methods We identified National Cancer Institute (NCI)-designated Comprehensive Cancer Centers (CCC) and used Doximity to identify the 50 highest-ranked general surgery residency programs with surgical oncology divisions. Data for academic surgical oncologists were collected from departmental websites, Grantome, and Web of Science. Results We identified 544 surgical oncologists from 64 programs with a mean h-index of 21±17. Increased h-index was correlated with academic rank (p<0.001), male gender (p<0.001), number of NIH grants funded (p<0.001), and NCI CCC designation (p=0.018), but not number of additional degrees earned (p=0.661) or general surgery program rank (p=0.102); (Table). H-index was a stronger bibliometric predictor of academic rank (r=0.648) than total publications (r=0.585) or citations (r=0.450). Conclusions This is the first report to assess the h-index within academic surgical oncology. H-index is a stronger bibliometric predictor of academic rank than total publications or citations. Moreover, both personal (gender and number of NIH grants funded) and institutional (NCI CCC designation) factors also correlate with h-index. Further studies are needed to evaluate the h-index threshold as a new variable to consider for academic promotion.

Demographic Variable			H-index			
			Mean±SD	Median	Range	p-value
Personal	Academic Rank	Assistant Professor (n=186)	7.9±5.5	7	0-34	<0.001
		Associate Professor (n=128)	18±8.9	17	3-52	
		Professor (n=142)	32±18	28	2-107	
		Division Chief (n=68)	33±17	29	7-84	
		Department Chair (n=20)	48±26	42	8-111	
	Gender	Male (n=331)	26±19	21	0-111	<0.001
		Female (n=213)	13±11	11	0-78	
	Additional Degrees	0 (n=412)	22±18	17	0-111	0.661
		1 (n=122)	18±13	15	1-65	
		2 (n=9)	31±18	28	4-63	
		3 (n=1)	33	33	33	
	NIH grants	0 (n=369)	15±12	12	0-84	<0.001
		1-5 (n=152)	32±20	28	2-111	
		6-10 (n=14)	43±20	37	24-97	
		>10 (n=9)	48±11	47	27-67	
Institutional	NCI-designated Comprehensive Cancer Center	Yes (n=438)	22±18	17	0-107	0.018
		No (n=106)	17±17	13	0-111	
	Doximity General Surgery Residency Program Rank	1-10 (n=114)	22±18	17	0-107	0.102
		11-20 (n=104)	22±18	18	0-111	
		21-30 (n=77)	20±18	16	0-83	
		31-40 (n=73)	17±14	16	0-86	
		41-50 (n=63)	20±16	15	0-64	

Table. H-index distribution of U.S. surgical oncologists by personal and institutional demographic variables.

PF131

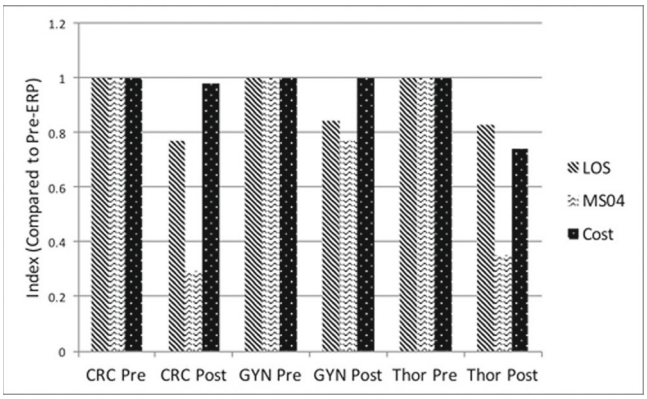
Balancing the Benefits of Success Against the Burden of Recovery: Considering the Surgical Treatment of Gastric Outlet Obstruction from Advanced Cancer B.A. Potz,* V.L. Garcia, K.P. Charpentier, W.G. Cioffi, T.J. Miner. *Surgical Oncology, The Warren Alpert Medical School of Brown University, Providence, RI.*

INTRO: Palliative (PAL) operations are offered to cancer patients (pts) with the intent of relieving symptoms of gastric outlet obstruction (GOO), especially when endoscopic approaches are not possible. To ensure appropriate selection and counseling, the individual pt's quality and expectancy of life, symptom severity, and the chance of both complications and potential success must be considered. MET: Pts undergoing a PAL operation for GOO caused by advanced cancer between 2008-2015 were identified from an institutional PAL surgery database. Pts were observed for >90 days or until death. RES: PAL operations for GOO were performed in 65 pts (median age 66 yrs) for symptoms caused by incurable pancreatic (45%), gastric (23%), and other metastatic cancers (32%). Pre-operative symptoms included early satiety (100%), nausea (63%), vomiting (57%), weight loss (57%), pain (47%), poor PO tolerance (38%), and fatigue (13%) and were associated with GOO scores of: 0 (45%), 1 (6%), 2 (3%) and 3 (45%). Symptom improvement was noted by 90% pts and was not associated with operation type. All-cause mortality (12%) and morbidity (28%) was recorded at 30 days. Median length of hospital stay was 11 days. There was no difference in major complications based on GOO score or type of procedure performed. A nasogastric tube was present postoperatively in 95% (median 4 days (range 1-26)) with 18% requiring reinsertion (range 1-4). Additional treatment of delayed gastric emptying symptoms was required in 23%. TPN was used in 40% (median of 13 dys). 32% of pts had recurrence of GOO symptoms requiring intervention prior to death. Overall survival was greater in pts presenting with less severe symptoms (GOO score 0; 410 days vs GOO score >1; 134 days, p=0.02). CON: Although overall symptom improvement following PAL operations for GOO is often noted, delayed gastric emptying and limited procedure durability are frequently encountered. Beyond morbidity and mortality, the burden of recovery following this PAL operation must be appreciated in order to ensure appropriate counseling, clinical decision making, and optimal postoperative management.

PF132

Perioperative Impact of Widespread Implementation of an Enhanced Recovery Protocol on Short-term Outcomes in Cancer Patients A.N. Martin,* T. Hassinger, K. Lynch, C. Friel, R.H. Thiele, T.L. Hedrick. *Surgery, University of Virginia, Charlottesville, VA.*

Introduction: Enhanced recovery (ER) protocols have been shown to improve short-term outcomes in many surgical subspecialties, including colorectal and gynecologic cancer surgery. Based on the growing body of literature, an institutional ER Program (ERP) was implemented in 2014 with the objective of improving perioperative outcomes and lowering health care costs through widespread implementation of ERP. Methods: Based on the success of ERP in colorectal surgery, an official ERP with institutional support was initiated in 2014 at a single institution. The program was led by an RN, surgeon and anesthesia champion triad with the goal of maintaining success in colorectal surgery and expanding ERP to various other surgical specialties. A pre-ER/post-ER study design was undertaken comparing consecutive patients with colorectal, gynecologic, and thoracic neoplasms between August 2012 and August 2017 before and after establishment of the ERP. Results: In total, 994 patients underwent surgery within the ER protocol compared to 483 consecutive historical controls. When comparing pre-ER to post-ER outcomes for colorectal surgery, there were significant reductions in mean length of stay (LOS) (6.4 vs 4.9 days, p=0.02) and mean administered total ins/outs (total IO) (3.4L vs 113mL, p<0.001). Significant reductions in gynecologic surgery included mean LOS (2.2 vs 1.9, p=0.002), mean morphine equivalents (ME) (27 vs. 21, p=0.001), and mean total IO (1.6L vs 136mL, p<0.001). Patients with thoracic neoplasms saw significant reductions in mean ME (210 vs 73, p=0.003), mean total IO (1.2L vs -558mL, p=0.005), and mean total hospital costs ($29,651 vs $21,992, p=0.01, see Figure). Conclusions: Establishment of an institutional ERP was associated with significant improvements in short-term surgical outcomes in patients with colorectal, gynecologic, and thoracic neoplasm. These data demonstrate the utility of institutional involvement in establishment of ERPs. Further study is warranted to discern whether improvements in short-term outcomes translate into improved oncologic results.

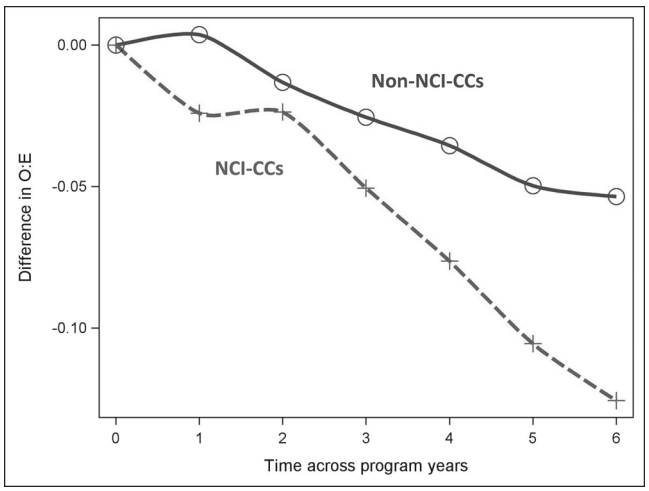


PF133

Trends in Perioperative Outcomes of Hospitals Performing Major Cancer Surgery J. Liu,[1]* J.R. Berian,[2] Y. Liu,[1] C.Y. Ko,[1] S. Weber.[3] *1. American College of Surgeons, Chicago, IL; 2. University of Chicago Medicine, Chicago, IL; 3. University of Wisconsin Madison, Madison, WI.*

Introduction: Studies have demonstrated hospital-level variation in perioperative outcomes after major cancer surgery at National Cancer Institute-designated Cancer Centers (NCI-CC). Following the establishment of the Oncology NSQIP NCI-designated Cancer Center (ONNCC) Collaborative, we sought to assess whether improvements were achieved. Methods: Patients who underwent colectomy, esophagectomy, hepatectomy, pancreatectomy, and proctectomy for cancer between January 1, 2010 and December 31, 2016 were identified in the American College of Surgeons' National Surgical Quality Improvement Program (ACS NSQIP) registry. Observed-to-expected (O:E) ratios were computed for each hospital and for year of first participation (hospital cohort) from hierarchical regression models predicting a composite death or serious morbidity (DSM) measure. Within-hospital trends in logged O:E ratios over time (slope) were assessed to evaluate improvement, stratified on

NCI-CC status. Variation in NCI-CC performance on DSM in 2016 was also assessed. Results: Of 204,732 patients who underwent their cancer operation at 754 hospitals, DSM occurred in 38,488 (18.8%). At the 54 NCI-CCs included, the DSM rate was 19.9% (12,116/60,903). Hospital-average log O:E ratios were generally negative, denoting improving performance over time irrespective of NCI-CC status (Figure). From these data, we estimate 2.7% average annual reductions in DSM at NCI-CCs compared to 0.6% at non-NCI-CCs. A greater proportion of NCI-CCs compared to non-NCI-CCs improved (85.2% vs. 58.4%; p<0.001), and this improvement persisted after adjusting for years in the ACS NSQIP (relative risk 2.84; 95% confidence interval 1.33-6.06). Variation in NCI-CC performance on DSM in 2016 was detected to be statistically significant (p=0.006). Conclusions: In this cohort of ACS NSQIP hospitals, NCI-CCs were detected to have significantly improved over a contemporary seven-year period. However, variability in hospital-level perioperative outcomes at NCI-CCs remains, warranting continued quality assurance and improvement efforts targeting cancer-specific operations.



Mean differences in O:E ratios as a function of years in the ACS NSQIP stratified by NCI-CC status for the death or serious morbidity composite measure. Downward direction indicates improvement.

PF134

Can International Expertise be Leveraged for Multidisciplinary Cancer Care in LMICs? A. Saunders,[1]* C. Gaudioso,[1] M. Jimoh,[2] U. Ajoku,[2] S. George,[1] T. O'Connor,[1] C. Nwogu.[1] *1. Roswell Park Cancer Institute, Buffalo, NY; 2. Lakeshore Cancer Center, Lagos, Nigeria.*

Background Cancer care in high-income countries (HICs) is characterized by coordination of multimodal treatment at a multidisciplinary conference (MDC). However, among disparities encountered by cancer care providers in low- and middle-income countries (LMICs) is lack of access to specialized expertise. Modern communication technologies offer an opportunity for remote MDCs; reports of this are limited and have described logistical barriers. Methods We reviewed the single-institution experience of a cancer center in Lagos, Nigeria, connecting with multidisciplinary expertise in the United States (US). Multidisciplinary consultations were reviewed and descriptive data were generated for their characteristics, outcomes, and limitations. Results Cancer types seen at the study location as of June 2016 were 38% breast, 12% prostate, 8% colorectal, and 6% cervical, while the remainder were a combination of other gynecological, gastrointestinal, CNS, hematologic, and renal cancers. Over the two-year period reviewed, 27 cases were referred for multidisciplinary consultation. Of these, 21 (78%) were referred to a team at Roswell Park Cancer Institute in Buffalo, NY, and 6 (22%) were referred to specialists at other US institutions. All but one of the cases (26, 97%) were referred using email, while one case was discussed via videoconference. The reason for consultation was uncertainty about management in 10 patients (37%), the need for validation of treatment plans in 14 patients (52%) and unusual clinical scenarios in 3 patients (11%). Limitations included incomplete communication of treatment recommendations in 5 patients (18.5%), unavailable diagnostic testing services in 7 patients (26%), and unavailable therapies in 3 patients (11%). All cases (100%) received treatment recommendations. The time required to receive final recommendations ranged from 1 to 14 days, with a median of 3 days. Conclusion This early experience demonstrates both feasibility of sharing expertise to benefit providers and patients in LMICs, and limitations of the approach and technologies. Future directions include using more sophisticated software and organization to maximize the benefits of this concept.

PF135

Prospective Implementation of a Standardized Screening Protocol for Deep Venous Thrombosis (DVT) in Abdominal Surgical Oncology Patients A.J. Sinnamon,* J. Tong, E.A. Bailey, L. Colbert-Mack, S. Murray, B.M. Jackson, R. Roses. *Surgery, Hospital of the University of Pennsylvania, Philadelphia, PA.*

Introduction Despite broad implementation of aggressive perioperative prophylaxis, venous thromboembolism (VTE) remains a major cause of perioperative morbidity and mortality. We sought to identify the incidence of and risk factors for occult DVT following abdominal surgery for cancer after prospective implementation of a standardized postoperative screening protocol. Methods Patients undergoing abdominal surgery lasting >2 hours for malignant indication were screened on postoperative 4 (+/-1) with lower extremity (LE) duplex to identify DVT. All patients received pre-induction and postoperative subcutaneous heparin prophylaxis in accordance with clinical guidelines. Patients with known pre-existing DVT or DVT identified preoperatively were excluded from primary analysis. Clinical and pathologic factors associated with DVT were identified using univariate and multivariable logistic regression. Results Among 252 consecutive cases meeting study criteria, 21 patients were found to have occult LE DVT on routine postoperative screening and 1 patient presented with symptomatic upper extremity DVT for an overall DVT rate of 8.7%. Patients found to have DVT were not significantly different in age (median 66 vs 60 years, p=0.17) or BMI (median 28.5 vs 27.0, p=0.14). Operative time was significantly longer for patients found to have DVT versus not (median 341 vs 234 minutes, p=0.02). Prior history of VTE was significantly associated with postoperative DVT (OR 2.2, p=0.001). There were 3 pulmonary emboli (1.2%); 2 following negative duplex screen and 1 following a screen positive for a unilateral soleal DVT for which the patient not therapeutically anticoagulated due to contraindication. There was 1 bleeding event (rectus sheath hematoma) following initiation of therapeutic anticoagulation for occult DVT. Conclusion Despite prophylaxis in accordance with consensus recommendations, the incidence of postoperative DVT is substantial. Standardized postoperative screening duplex is effective at identifying these events and can guide further management. The absolute impact of such screening on the rate of subsequent symptomatic VTE is uncertain.

PF136

Simple Office-based Tool for Predicting Facility Discharge in Older Patients After Major Gastrointestinal Cancer Surgery R. Ramanathan,[1]* T. Mason,[2] L. Wolfe,[2] B.J. Kaplan.[2] *1. Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA; 2. Virginia Commonwealth University Medical Center, Richmond, VA.*

Background: Discharge to acute care, skilled nursing or rehabilitation facilities after major gastrointestinal oncologic surgery is an important patient-centered quality outcome. This study reports a simple office-based tool that can be used for counselling older patients on their likelihood of discharge to a facility after major gastrointestinal cancer surgery. Methods: Patients undergoing surgery for malignancies of the esophagus, stomach, pancreas, liver, colon/rectum between 2011 and 2015 were analyzed using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. Associations between facility discharge and age, gender, BMI, malnutrition (>10% weight loss or albumin <3g/dL) and frailty were investigated. Frailty was quantified using a simple 5-point abbreviated modified frailty index (amFI). The amFI assigns one point each for the presence of congestive heart failure, hypertension, diabetes, chronic obstructive pulmonary disease and non-independent functional status. Results: There were 61,683 surgeries during this study period with the following anatomic distribution: 4,252 esophagus, 3,258 stomach, 12,956 pancreas, 12,352 liver and 28,865 colon/rectum. Patients discharged to a facility were older (72.3 vs. 61.4 years, p<0.01), had more malnutrition (37.7% vs. 30.1%, p<0.01), and had higher amFI (1.13 vs. 0.71, p<0.01). Adjusting for age, each point increase in amFI was associated with 1.5 times increased odds of discharge to a facility. Adjusting for amFI, age over 60 years was associated with a 4.4 times increased risk

of facility discharge. For those aged over 60 years, amFI had an acceptable area under the receiver operating curve (AUROC) of 0.71. The overall probability of facility discharge was 8.5% for 0 amFI, 13.0% for 1 amFI, 17.4% for 2 amFI, 14.4% for 3 amFI and 58.5% for 4 amFI. The table describes the predicted facility discharge rates by amFI for each anatomic area. Conclusions: The amFI is a simple tool that can be used in the office-setting to help counsel older patients on their likelihood of discharge to a facility after major gastrointestinal oncologic surgery.

Probablity of facility discharge by amFI

	amFI score 0	amFI score 1	amFI score 2	amFI score 3	amFI score 4
Esophagus	11.1%	16.3%	20.4%	32.0%	100%
Stomach	9.5%	14.3%	19.1%	26.3%	20.0%
Pancreas	10.7%	17.3%	20.3%	41.4%	33.3%
Liver	6.2%	8.4%	12.0%	27.8%	100%
Colon/Rectum	7.7%	12.1%	17.1%	34.7%	66.7%

PF137

Pain and Opioid Prescriptions Vary by Procedure, Age, and Diagnosis After Breast Surgery B.L. Murphy,* K.T. hanson, D.S. Ubl, E.B. Habermann. *Surgery, Mayo Clinic, Rochester, MN.*

Introduction: In light of the growing opioid epidemic in the United States, evaluating opioid prescribing patterns is essential. While postoperative pain following many surgical procedures has been studied, opioid requirements in cancer surgery patients are less understood. We sought to evaluate the opioids provided at discharge following breast surgery. Methods: We retrospectively identified patients ≥18 years of age who underwent a breast surgery at our academic institution 1/2010-12/2016. Pain scores and prescription data converted into oral morphine equivalents (OME) were compared across various breast surgeries and patient factors by univariate analysis. Results: Of 10,752 patients, 10,011 (93%) received an opioid prescription; 99% of patients were female. Mean (±SD) age was 58.7±13.9 years. Median OMEs were similar across all procedure groups (medians ranging 225-300). Median pain scores ranged from 1-3 across procedure groups, with bilateral mastectomy (BM)+immediate breast reconstruction(IBR)+axillary node procedure (LN) patients having the greatest pain scores. Within lumpectomy (BCS) patients, slightly higher median pain scores were observed for patients with LN vs without (2 vs 1, p<0.01). Median OME was the same (225 for each), but Q1 and Q3 were higher among +LN (IQR 180-300 for +LN, 150-225 -LN) and more +LN patients received an opioid refill. Pain scores decreased as age increased, within both BCS (median 0 for age ≥80 vs 1-2 <80, p<0.01) and BCS+LN (median 3 for age <30 vs 1.5-2 for ≥30, p=0.03). Among BCS patients, those with DCIS or invasive cancer received more OMEs than patients with benign conditions (median 225 vs 200, p<0.01), but there was no difference in their pain scores (medians 1, p=0.14). Within patients undergoing BM+IBR, similar OMEs were prescribed for benign and malignant (p=0.89), even though patients with benign conditions reported greater pain (median 4 vs 3, p=0.04). Conclusion: Pain following breast surgery varied by procedure and with patient age while OMEs varied for patients undergoing BCS depending on their diagnoses. Pain scores and OME needs are important to consider when prescribing opioids in surgical oncology patients.

Pain and Opioids Prescribed for Patients with Benign Versus Malignant Conditions

	Lumpectomy				Bilateral Mastectomy + Immediate Breast Reconstruction			
Number	Total (N=3169)	Benign (N=1963)	Invasive/Ductal Carcinoma In Situ (N=1206)	p-value	Total (N=318)	Benign (N=249)	Invasive/Ductal Carcinoma In Situ (N=69)	p-value
Last pain score before discharge				0.14				0.04
N	2601	1517	1084		313	245	68	
Mean (Standard Deviation)	1.5 (1.6)	1.5 (1.7)	1.6 (1.6)		3.6 (1.8)	3.7 (1.8)	3.2 (1.8)	
Median	1	1	1		3	4	3	
Q1, Q3	0.0, 3.0	0.0, 3.0	0.0, 3.0		2.0, 5.0	2.0, 5.0	2.0, 4.0	
Discharge opioid prescription				<0.001				0.59
No	344 (10.9%)	262 (13.3%)	82 (6.8%)		18 (5.7%)	15 (6.0%)	3 (4.3%)	
Yes	2825 (89.1%)	1701 (86.7%)	1124 (93.2%)		300 (94.3%)	234 (94.0%)	66 (95.7%)	
Oral morphine equivalents (OME)			<0.001					0.89
N	3169	1963	1206		318	249	69	
Mean (Standard Deviation)	207.6 (239.4)	194.0 (172.9)	229.7 (318.1)		325.6 (178.8)	325.8 (177.2)	325.0 (185.7)	
Median	225	200	225		300	300	300	
Q1, Q3	150.0, 225.0	112.5, 225.0	150.0, 225.0		225.0, 375.0	225.0, 375.0	225.0, 375.0	
Range	(0.0-9000.0)	(0.0-2175.0)	(0.0-9000.0)		(0.0-1125.0)	(0.0-1050.0)	(0.0-1125.0)	
Had opioid refill*				0.99				0.79
No	2813 (96.4%)	1841 (96.4%)	972 (96.4%)		178 (62.9%)	140 (62.5%)	38 (64.4%)	
Yes	104 (3.6%)	68 (3.6%)	36 (3.6%)		105 (37.1%)	84 (37.5%)	21 (35.6%)	

*Opioid refills were assessed for patients who did not undergo another surgery within 30 days following discharge.

PF138

Identifying Variability in Cost of Breast Conservation Surgery at Different Hospitals within an Academic Health System D.A. Quintana,* M. Habibi, J. Canner, D.M. Euhus, L.K. Jacobs. *Johns Hopkins University, Baltimore, MD.*

INTRODUCTION: The cost of health care in the United States has increasingly become an important policy focus. This study examines the drivers of variability of cost per case for the most common breast surgical procedures done at the 5 hospitals affiliated with our system. METHODS: Data was obtained from the QLIK PeriOperative Dashboard for women who had breast conservation surgery over a 12-month period 2016-2017. We looked at disposables and length of surgery as indicators of cost. The analysis compared the cost per case among facilities for patients by age, race, payment type, procedure length, ASA class, surgeon volume, and hospital volume. RESULTS: We found significant differences in cost of disposables per case among the hospitals as well as within a given hospital. The most costly hospital (#1) was 78% greater than the least expensive hospital (#4). Across all hospitals, the cost for Medicaid patients was significantly greater than Medicare, private insurance or self pay. ASA class alone did not appear to result in longer surgeries or increased cost and was constant across all facilities. The cost per case of surgery for Asian women was significantly greater as compared to White and Black women. While there was a trend toward increase in cost for longer case times, this did not entirely account for the discrepancy. Surgeons with the highest volume had the shortest OR times and those at facilities with trainees tended to have the longest OR times. Although the case load was similar between hospital #3 and #4, the cost of disposables was 32% less at hospital #4. CONCLUSIONS: We found there is significant variability in cost of disposables per case among hospitals in the same health care system. A more thorough analysis of the variability could inform strategies to standardize this procedure across the system and reduce costs. Further study is necessary to determine why costs for Medicaid and Asian patients are greater. This study provides insight into OR cost per case and provides information for health systems to determine best practices.

	Hospital 1	Hospital 2	Hospital 3	Hospital 4	Hospital 5
Mean Cost of OR Disposables	$278.68	$208.03	$231.40	$156.44	$177.26
Mean Age (years)	60.65	61.02	56.68	61.35	55.02
ASA					
1	7 (9.09%)	13 (7.60%)	12 (3.5%)	24 (12.06%)	4 (12.50%)
2	37 (48%)	101 (59.06%)	247 (72.01%)	144 (72.36%)	15 (46.88%)
3	30 (38.96%)	56 (32.75%)	78 (22.74%)	30 (15.08%)	13 (40.63%)
4	3 (3.9%)	1 (0.58%)	6 (1.75%)	1 (0.50%)	0 (0%)
Payor					
Medicare	28 (35.44%)	60 (34.68%)	98 (28.08%)	77 (36.49%)	10 (29.41%)
Medicaid	9 (11.39%)	4 (2.31%)	24 (6.88%)	0 (0%)	7 (20.59%)
Private	40 (50.63%)	107 (61.85%)	224 (64.18%)	130 (61.61%)	16 (47.06%)
Self	2 (2.53%)	2 (1.16%)	3 (0.86%)	4 (1.90%)	1 (2.94%)
Mean OR Time (min)	89.26	90.70	98.47	67.88	80.58
Frequency by Hospital	79 (8.14)	173 (17.82)	349 (35.94)	336 (34.60)	34 (3.50)
High Volume Surgeon Cases/Total	79/79 (100%)	90/173 (52%)	101/349 (28.9%)	119/211 (56.4%)	24/34 (48.8%)

CHART OF PATIENT DATA BY HOSPITAL

PF139

Disparities in Refusing Offered Surgical Treatment in Gastrointestinal Malignancies O. Moaven,* J. Richman, S. Reddy, T. Wang, M.J. Heslin, C.M. Contreras. *Surgery, University of Alabama at Birmingham, Birmingham, AL.*

Introduction: When indicated, Tumor resection provides the greatest survival benefit to patients with gastrointestinal (GI) malignancies. The aim of this study was to evaluate clinical and socioeconomic factors in patients with GI malignancies associated with accepting or refusing surgery. Methods: We retrospectively analyzed patients with primary GI cancers (esophageal, gastric, colorectal and pancreatic cancer) in National Cancer Database of the American College of Surgeons, years 2004-2014. Unadjusted chi-square, student's t-tests and multivariate logistic regression were used to identify patient and tumor characteristics that differed between patients who underwent surgery vs. those who refused. Results: Surgical resection was offered to 787,447 patients as a treatment option. Overall, 13,609 patients (1.73%) refused the offered surgical treatment (5.2% of esophageal, 3.6% of gastric, 1.1% of colon, 2.6% of rectal and 1.0% of pancreatic cancer). Refusal of surgery was associated with patient characteristics including age (OR=1.08; 95%CI 1.08-1.09), male gender (OR=1.13; 95%CI 1.09-1.17), increasing income quartile (OR=0.91; 95%CI 0.89-0.94), comorbidities by Charlson/Dayo score (OR=1.10; 95%CI 1.07-1.13), black race (OR=2.08; 95% CI 1.97-2.20), lack of insurance (OR= 2.64; 95% CI 2.36-2.95) and clinical stages 3 (OR= 1.13; 95% CI 1.05-1.22) and 4 (OR=2.68; 95% CI 2.51-2.86). Academic centers were associated with lower refusal rate (OR= 0.88; 95% CI 0.84-0.92). Refusing surgical treatment was also associated with geographic location; versus East North Central, refusal is higher in the New England region (OR= 1.33; 95% CI 1.24-1.44), while southern centers are associated with lower refusal rate (OR, 95% CI: west south 0.63,0.58-0.69; south Atlantic 0.70,0.66-0.74; southeast 0.59,0.54-0.64) and other regions had similar rate of refusal. The trends were generally preserved across the included primary tumor sites. Conclusion: Racial, socioeconomic and geographic disparities are associated with refusal of surgical therapy. Identifying barriers to provide and receive equal care may facilitate future efforts to minimize these observed disparities.

PF140

Feasibility of Implementing a Comprehensive Approach to Bowel Dysfunction After Low Anterior Resection for Rectal Cancer A. Nadler,[1]* S. Koller,[2] N. Goel,[1] J. Kozempel,[1] L. Peters,[1] K. Vincek,[1] E. Sigurdson,[1] C. Denlinger,[1] J. Meyer,[1] C. Fang,[1] E. Handorf,[1] J. Farma.[1] *1. Fox Chase Cancer Center, Philadelphia, PA; 2. Temple University, Philadelphia, PA.*

INTRODUCTION Patients undergoing low anterior resection (LAR) for rectal cancer are at risk of bowel dysfunction and LAR syndrome (LARS). Evidence suggests that pelvic floor muscle exercises (PFME), dietary changes, and medications may be helpful, however integrated programs to manage and improve LARS have not been developed. METHODS A pilot feasibility study was undertaken at a tertiary care cancer center to assess the implementation of a comprehensive, multi-disciplinary program to improve bowel dysfunction following LAR. Patients were recruited from surgical oncology clinics at the time of consideration for stoma reversal. Patients were eligible if they had undergone a LAR with diverting stoma and were current candidates for stoma reversal. Additional criteria for inclusion were completion of a pre-operative questionnaire, and completion of pre-operative consultations with physical therapy for PFME and nutrition for dietary advice. Bowel dysfunction was assessed using the LARS score. The Mann-Whitney U Test was used to compare medians. RESULTS Of 14 patients who consented to the study, 9 met inclusion criteria, of which 7 (78%) remained in the study to date. At the first post-operative visit following stoma reversal, 86% of patients met the criteria for major LARS (score of ≥30 out of 42) with a median score of 35. Two of these patients improved to meet the criteria for minor LARS (score of 21-29) within 3 months. All patients had improvement or stability in their LARS score by 3 months, with a median score of 30 (p=0.06, compared to baseline). Over 70% of patients found PFME helpful, and over 50% found both medications and dietary counselling helpful. Over 50% of patients found the overall program somewhat or quite a bit helpful. CONCLUSIONS Our findings suggest that rectal cancer patients are interested in participating in an integrated program for bowel dysfunction. Preliminary data suggest early improvement in LARS, but long-term follow-up and a larger sample size are needed to see if results are maintained.

PF141

Daikenchuto for Postoperative Bowel Dysfunction After Open Abdominal Surgery: A Pooled Analysis of Three Randomized Controlled Trials M. Nishi,[1]* M. Shimada,[1] T. Kono,[2] Y. morine,[1] K. Yoshikawa,[1] H. Katsuno,[3] K. Maeda,[4] K. Koeda,[5] S. Morita,[6] M. Watanabe,[7] M. Kusano,[8] J. Sakamoto,[9] S. Saji,[10] H. Sokuoka,[10] Y. Ohtake,[10] Y. Sato,[11] T. Kanematsu,[12] M. Kitajima.[13] *1. Department of Surgery, Tokushima University, Tokushima, Japan; 2. Advanced Surgery Center, Sapporo Higashi Tokushukai Hospital, Sapporo, Japan; 3. Department of Surgery, Fujita Health University, School of Medicine, Toyoake, Japan; 4. International Medical Center Fujita Health University Hospital, Toyoake, Japan; 5. Department of Surgery, Iwate Medical University, School of Medicine, Morioka, Japan; 6. Department of Biomedical Statistics and Bioinformatics, Kyoto University Graduate School of Medicine, Kyoto, Japan; 7. Department of Surgery, Kitasato University School of Medicine, Sagamihara, Japan; 8. Seiwa Memorial Hospital, Sapporo, Japan; 9. Tokai Central Hospital, Kakamihara, Japan; 10. Public Interest Incorporated Foundation, Japanese Foundation for Multidisciplinary Treatment of Cancer, Tokyo, Japan; 11. Department of Public Health, Tokyo Women's Medical University, Tokyo, Japan; 12. Nagasaki City Hospital Organization, Nagasaki, Japan; 13. International University of Health and Welfare, Tokyo, Japan.*

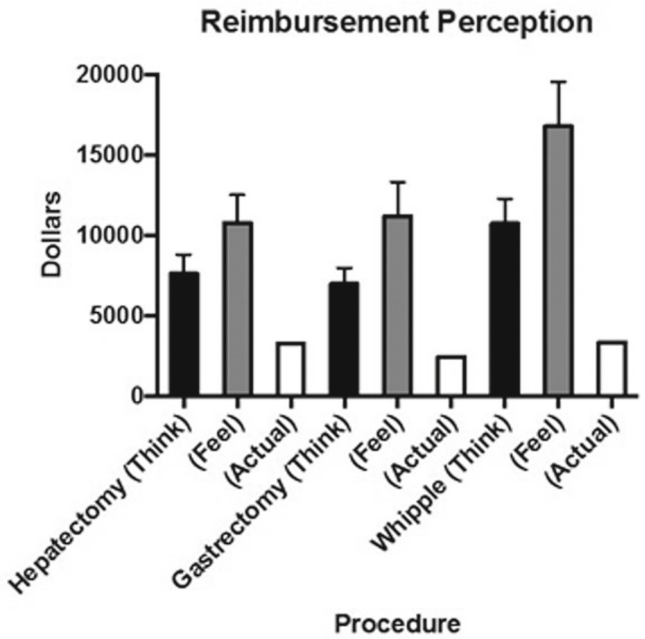
Background:The present study aims to elucidate whether daikenchuto (DKT), a traditional Japanese prescribed medicine, accelerates the recovery of postoperative bowel dysfunction (PBD) after scheduled open abdominal surgery (OAS). In three exploratory randomized controlled trials (RCT), DKT has been shown to stimulate the neurogenic pathway peripherally and reduce PBD. From the pharmacokinetic study of DKT (not published while the three RCTs were ongoing), the blood concentration of the active ingredient was positively correlated with the dose. Methods:We conducted a pooled analysis of OAS patients with colon, liver, or gastric cancer in DKT RCTs, which were supported by the Japanese Foundation for Multidisciplinary Treatment of Cancer (JFMC). Of all patients enrolled and randomized in the three RCTs (JFMC project numbers 39-0902, 40-1001, and 42-1002), 740 patients were eligible for efficacy analysis. The modified intent-to-treat population comprised 410 patients, who did not have their bowel movement before the first meal; these patients were administered either 5 g DKT (n = 214) or placebo (n = 196) orally, thrice a day for up to 12 days. The primary endpoint of each trial was the time from the end of the surgery to the first bowel movement, which was evaluated using survival analysis. In addition, we conducted sensitivity analysis for age, BMI, and dosage as subgroup analyses. Results:Compared with the placebo group, the time from the end of the surgery to the first bowel movement was accelerated in the DKT group (P = 0.004; hazard ratio, 1.337; 95% CI: 1.096–1.631), with a difference of median 14.8 h. Furthermore, subset analyses that provided age < 75 years, BMI < 30 kg/m^2, or dosage ≥ 10 g/day had a shorter time from the end of the surgery to the first bowel movement. The tolerability profiles were similar in both the groups. Conclusions:Our study

concludes that compared with the placebo group, DKT was well-tolerated, and significantly accelerated PBD recovery. Patients who can benefit from DKT may be those younger than 75 years, with BMI less than 30, or a daily dosage of 10 g or more.

PF142

Perception of Reimbursement for Complex General Surgical Oncology D.M. Urban,* S.T. Levi, E.C. Alberto, N.J. Petrelli, G. Tiesi. *Christiana Care Health Systems, Newark, DE.*

Introduction: Perception of physician reimbursement for surgical procedures is not well studied and primarily has focused on plastic and orthopedic procedures. These studies show patients believe compensation is much higher than it actually is. No studies have examined perception of reimbursement for surgical oncology procedures. Our study aimed to examine healthcare workers' perception as they should have a better understanding of the procedures and their reimbursements. Methods: An online survey was distributed to employees of a cancer center. Three index procedures: hepatic lobectomy, total gastrectomy and Whipple procedure were chosen. Brief descriptions were provided. Participants were asked to guess what the Medicare fee is and what they felt it should be. Participants were asked about their perception of overall surgeon compensation before and after revealing the Medicare fee schedule. Results: 153 individuals completed the survey. The majority were physicians (45%) followed by nurses (25%). When blinded to reimbursement, the majority of respondents felt that reimbursements were likely too low for a hepatectomy (66%), total gastrectomy (61%) and Whipple procedure (64%). 58% felt surgeons are overall undercompensated and only 5% felt surgeons are overcompensated. How much participants think surgeons receive, feel they should receive and the actual Medicare fee schedule (Figure 1) were very discordant. After revealing the Medicare fee schedules, more felt that surgeons are overcompensated (8%) and less felt they are undercompensated (54%) despite feeling Medicare reimbursement should be around 300 – 500% higher than it actually is. Conclusions: Even among healthcare workers, there was a large discrepancy between perceived reimbursement and actual reimbursement. Despite feeling that surgeons are undercompensated for each procedure and overall, revealing that the actual reimbursements were markedly lower did not change participant perception on overall surgeon compensation.



PF143

Fragmentation of Cancer Care Does Not Lead to Worse Survival Among Commission on Cancer (CoC) Accredited Centers S. Zafar,[1]* M. Neville,[2] E.B. Habermann,[3] D. Etzioni,[3] N. Wasif.[2] *1. Surgery, University of Maryland, Baltimore, MD; 2. Mayo Clinic Arizona, Scotsdale, AZ; 3. Mayo Clinic Rochester, Rochester, MN.*

Introduction Patients receiving surgery, chemotherapy and radiation at separate institutions risk interruptions and delays in care with potentially worse outcomes. The aim of this study is to determine the effect of such care fragmentation on long term survival for complex gastrointestinal cancers. Methods Patients diagnosed between 2003 and 2006 and undergoing surgery for esophageal, liver, pancreas, or colon cancer were selected from the National Cancer Data Base. Patients with AJCC stage IV disease and those who received no adjuvant treatment were excluded. Patients were categorized in two groups. The coordinated care (CC) group included patients who underwent surgery plus all elements of adjuvant therapy at the same institution. The fragmented care (FC) group consisted of patients for whom radiation and/or chemotherapy was performed at an institution other than that where surgery was performed. Multivariable logistic regression analyses were used to determine associations with FC (table 1). Kaplan Meier curves and multivariable Cox proportional hazard models were used to test to differences in 5-year survival between the two groups. Results Care fragmentation occurred between 17.4% (liver) and 55.2% (esophageal) of the 45,396 patients included. Patients receiving FC were more likely to be white (OR 1.3 [1.22, 1.39]), further from the surgical locations (every 50 miles OR 1.001 [1.001, 1.002]), older (OR 1.122, [1.04, 1.21]) (age 65-80 compared to younger than 50), and were insured vs not insured (OR 2.46 [1.79, 2.20]). Patients' odds of receiving FC after undergoing surgery at community comprehensive cancer centers were 84.7% higher than if they had surgery at academic centers (OR 1.76 [1.67, 1.84]). When compared with colon cancer, patients with esophageal cancer were more likely to received fragmented care (OR 1.26 [1.17, 1.36]). There was no statistically significant difference in 5 -year survival between the two groups for any of the cancer subtypes. Conclusions Although fragmentation of cancer care occurs frequently among patients receiving surgery at CoC accredited institutions, this does not adversely affect survival outcomes.

Variable	Category	Odds Ratio	95% Confidence Interval	P value
Race	Other Vs Black	1.21	1.08, 1.36	0.288
	White Vs Black	1.30	1.22, 1.39	<0.001
Gender	Female Vs Male	1.02	0.98, 1.07	0.265
Age (years)	50–64 Vs <50 years old	1.03	0.97, 1.09	0.053
	65-79 Vs <50 years old	1.12	1.04, 1.21	0.039
	80+ Vs. <50 years old	1.15	1.03, 1.28	0.039
Distance	Every 50 miles from surgical facility	1.001	1.001,1.002	<0.001
Insurance	Medicaid Vs Private Insurance	0.62	0.56, 0.69	0.005
	Medicare/Govt Vs Private Insurance	0.95	0.89, 1.01	<0.001
	Not Insured Vs Private Insurance	0.41	0.36, 0.46	<0.001
Location	Metro Vs Urban	1.25	1.18, 1.33	0.004
	Rural Vs Urban	1.23	1.06, 1.43	0.207
Hospital type	Community Cancer Program Vs Academic/Research Program	1.52	1.42, 1.63	<0.001
	Comprehensive Community Cancer Program Vs Academic/Research Program	1.73	1.65, 1.82	0.003
	Other specified types of cancer programs Vs Academic/Research Program	9.56	4.88, 18.73	<0.001
Income	$30,000-$45,999 Vs <$30,000	0.97	0.91, 1.04	0.155
	$46,000+ Vs <$30,000	1.01	0.93, 1.10	0.467
Cancer site	Esophageal Vs Colon	1.26	1.17, 1.36	<0.001
	Liver Vs Colon	0.21	0.17, 0.25	<0.001
	Pancreas Vs Colon	0.92	0.85, 0.99	<0.001

urther adjusted for education and state of residence

Table 1: Independent factors associated with care fragmentation.

PF144

Squamous Cell Carcinoma with Regional Metastasis to Axilla or Groin Lymph Nodes: An Analysis of Outcomes G. Pang,[1]* N. Look Hong,[3] G. Paull,[2] S. Kupper,[4] D. Kagedan,[3] C. Nessim,[2] M. Quan,[4] F. Wright.[3] *1. Western University, London, ON, Canada; 2. University of Ottawa, Ottawa, ON, Canada; 3. University of Toronto, Toronto, ON, Canada; 4. University of Calgary, Calgary, AB, Canada.*

BACKGROUND Cutaneous squamous cell carcinoma (cSCC) is increasing in incidence worldwide. cSCC of the trunk and extremities with regional metastasis is uncommon but presents a significant clinical challenge. Treatment patterns and outcomes are poorly described and limited to small single center studies. METHODS Patients diagnosed with cSCC who developed

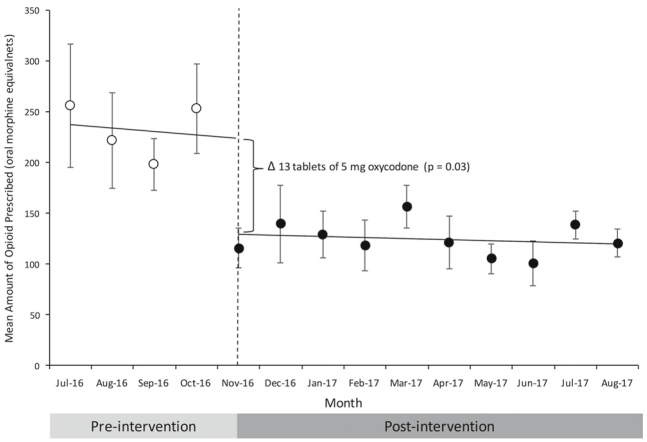
axilla or groin lymph node metastasis and underwent curative-intent nodal surgery between 2004 and 2016 were identified at 3 Canadian academic cancer centers. Demographics, tumor characteristics, mortality, treatment patterns and recurrence rates were described. Overall survival (OS) and disease-free survival (DFS) were calculated using Kaplan-Meier analysis. RESULTS Of the 41 patients identified, 28 (68%) were male with a median age of 74. Median follow-up was 38 months. Median primary lesion size was 30mm and median time to nodal metastasis was 11.3 months. 29 patients had nodal metastasis to the axilla, of whom 6 (21%) underwent level I-II dissections and 23 (79%) underwent level I-III dissections. 12 patients had groin metastasis, of whom 7 (58%) underwent superficial dissection, and 5 (42%) underwent a combined superficial and deep dissection. 29 (71%) patients received adjuvant nodal radiotherapy; 3 (7%) received neoadjuvant nodal radiotherapy, and 1 (2%) received adjuvant systemic chemotherapy. Following nodal surgery, 9 (22%) patients developed disease recurrence: 5 (12%) had nodal recurrence alone, 2 (5%) developed nodal and distant metastasis, 1 (2%) developed distant metastasis alone, 1 (2%) developed local, nodal and distant metastasis. Crude mortality rate was 37% at median follow up of 38 months. Mean OS was 5.6 years (95% CI 4.10 – 7.07) and DFS was 5.0 years (95% CI 1.80 – 8.71). Five-year OS was 58%, and five-year DFS was 52%. CONCLUSION Contemporary outcomes remain poor for patients with nodal metastases from cSCC, pointing to a need for a continued multi-disciplinary approach and integration of new systemic agents.

PF145

Education and Guidelines Reduce Opioid Prescribing for Common Surgical Oncology Procedures J.S. Lee,[1]* M.P. Klueh,[1] R.A. Howard,[1] M.J. Englesbe,[1] C.M. Brummett,[2] J.F. Waljee,[1] H. Nathan,[1] W.R. Burns,[1] L.A. Dossett,[1] M.S. Sabel.[1] *1. Department of Surgery, University of Michigan Comprehensive Cancer Center, Ann Arbor, MI; 2. Department of Anesthesiology, University of Michigan, Ann Arbor, MI.*

INTRODUCTION: Excessive opioid prescribing is common in surgical oncology with 72% of prescribed opioids going unused after curative-intent surgery. In this study, we sought to reduce opioid prescribing after common surgical oncology procedures by designing and implementing an intervention focused on education and prescribing guidelines. We then evaluated the impact of this intervention. METHODS: We designed an intervention targeting factors identified in qualitative interviews. We then compared opioid prescribing before and after the intervention (7/2016 – 8/2017). Interrupted time-series analysis was used to evaluate changes in the amount of opioid prescribed. We also evaluated the relative frequency of opioid prescription refills. RESULTS: Initial qualitative work identified lack of knowledge and guidelines as key determinants of prescribing behavior. Based on these findings, we designed an intervention with education conferences for prescribers, patient education (emphasizing scheduled acetaminophen with opioids only for breakthrough pain), and evidence-based prescribing guidelines. Guidelines were based on prior studies and included: 1) 20 tablets of 5 mg oxycodone for mastectomy or melanoma wide local excision (WLE) with or without sentinel lymph node biopsy (±SLN); and 2) 10 tablets of 5 mg oxycodone for lumpectomy ± SLN. During the study, 804 patients received opioid prescriptions from 56 prescribers. For mastectomy or WLE, the amount prescribed immediately decreased by 42% after the intervention (p=0.03), equivalent to 13 tablets of 5 mg oxycodone. This reduction was sustained for the remaining 10 months of the study (Figure 1). For lumpectomy, prescribing declined by 50% or 12 tablets of 5 mg oxycodone (p=0.07). In addition, there was no change in the percentage of patients obtaining opioid prescription refills (2.3% vs. 2.0%, p=0.9). CONCLUSIONS: Education and prescribing guidelines reduced opioid prescribing for common surgical oncology procedures without increasing the need for refills. This suggests further reductions in opioid prescribing may be possible, and provides rationale for implementing similar interventions for other procedures and practice settings.

Figure 1. Amount of Opioid Prescribed Before and After Intervention
Mastectomy or Wide Local Excision of Melanoma with or without Sentinal Lymph Node Biopsy



PF146

The Impact of Race and Socioeconomic Status on the Management and Outcomes for Gastric Cancer in an Urban Setting M. Tsao,* O. Delozier, Z.E. Stiles, W. Lynn, N. Goins, J.L. Deneve, E.S. Glazer, M. Fleming, D. Shibata, S. Behrman, P. Dickson. *University of Tennessee Health Science Center, Memphis, TN.*

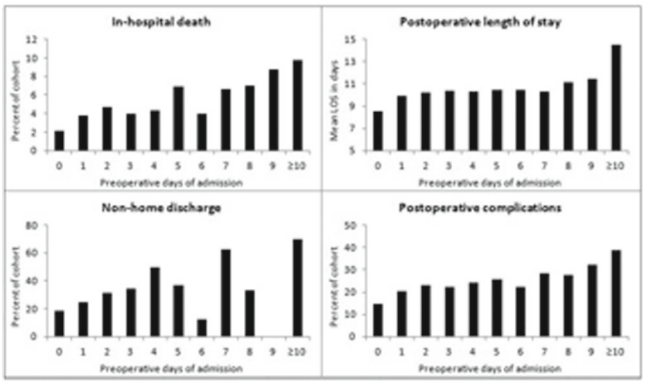
Background Socioeconomic disparities may limit access to cancer care and lead to inferior oncologic outcomes. We evaluated treatment and survival for patients with gastric cancer (GC) in a low-income urban setting with a large African American population. Methods Retrospective analysis of patients with GC (2003-2017) across a multi-hospital healthcare system was performed. Associations between demographic, socioeconomic, and clinicopathologic data with treatments received and overall survival (OS) were examined. Results Of 327 patients, 238 (73%) were African American and 89 (23%) Caucasian. African Americans were more likely to present at a younger age (63.5 vs 74, p<0.001) and with stage III/IV disease (65.9% vs 51.8%, p=0.025) than Caucasians. In addition, African Americans were more likely to have state sponsored or no insurance (21% vs 3.4%, p=0.003) and reside within areas of the lowest quartile for median income (31.9% vs 5.7%, p=<0.001). Stage-specific 5-year OS was similar between groups and there was no difference in the proportion of patients receiving curative intent resection (54.5 vs 60.5%, p=0.356). Race, income, and insurance status did not influence receipt of multi-modality therapy. Among patients who underwent curative intent resection (n=157, median f/u 19mos), median OS was lower for patients with age ≥66 (30 vs 71mos, p=0.030), Charlson Comorbidity Index ≥4 (34 vs 124mos, p=0.020), AJCC T3/4 class (28 vs 95mos, p=0.015), node positivity (22 vs 148mos, p<0.001), and grade 3/4 complications (13 vs 65mos, p<0.001), but not impacted by race, insurance or income. On multivariable analysis, perineural invasion (HR 3.3) and grade 3/4 (HR 3.3) complications remained significant predictors of worse OS. Conclusion Despite socioeconomic disparities, African Americans and Caucasians with GC had similar treatment and outcomes within our healthcare system. African Americans presented at a younger age and with more advanced disease, warranting further investigation into potential differences in risk factors and tumor biology.

PF147

Preoperative Hospital Length of Stay Associated with Adverse Outcomes Following Elective Oncologic Resection E.A. O'Halloran,[1]* S.A. Brownlee,[2] A.N. Cobb,[1] S.G. Pappas,[3] T.J. Saclarides,[3] G.J. Abood,[1] P.C. Kuo,[4] A.N. Kothari.[1] *1. Loyola University Medical Center, Maywood, IL; 2. Loyola University Chicago, Chicago, IL; 3. Rush University Medical Center, Chicago, IL; 4. USF Department of Surgery, Tampa, FL.*

INTRODUCTION: Patients undergoing elective oncologic resection are often hospitalized prior to their scheduled procedure. We aimed to investigate whether increased preoperative length of stay (PLOS) places patients at increased risk for adverse postoperative events. METHODS: The Healthcare Cost and Utilization Project (HCUP) State Inpatient Databses for California,

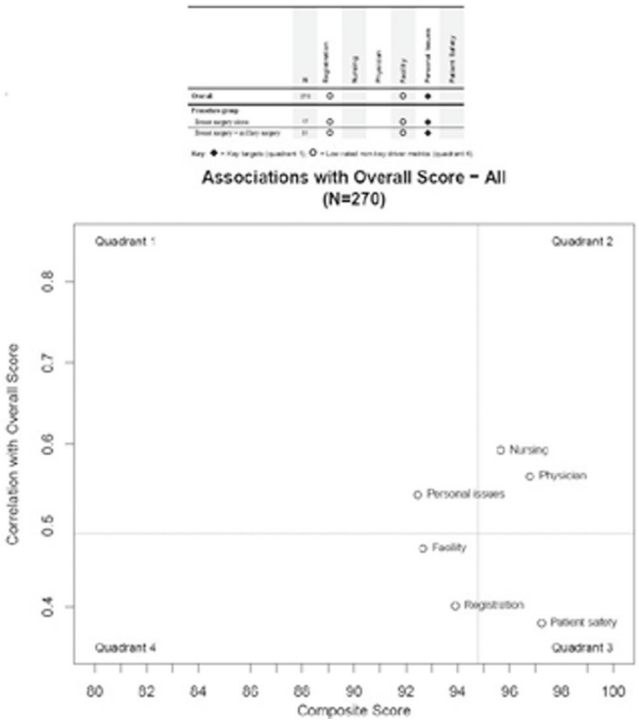
Florida, Iowa, and New York were linked. Using ICD-9-CM codes, patients that underwent colectomy, esophagectomy, hepatectomy, or pancreatectomy with a corresponding oncologic diagnosis were identified and included. The primary exposure variable was PLOS, defined as time elapsed between admission date and operative date. Outcomes included inpatient mortality, major morbidity, and location of discharge. Multiple variable logistic and linear regressions were performed. RESULTS: The cohort included 16,208 patients with a median age of 68 years. Of these, 5,981 (36.9%) were admitted prior to the day of operation. On adjusted analysis, the odds of inpatient mortality increased with each PLOS day (aOR 1.07, 95% C.I. [1.06 - 1.09]). Risk of non-home discharge (aOR 1.12, 95% C.I. [1.04 - 1.20]) and developing any postoperative complication (aOR 1.08, 95% C.I. [1.07 -1.09]) also were increased with each additional PLOS day. Increasing PLOS was significantly associated with surgical site infection (P<.001), urinary tract infection (P<.001), pneumonia (P<.001), sepsis (P<.001), DVT/PE (P<.001), and myocardial infarction (P<.001). Additionally, postoperative length of stay increased by 1.31 days (1.28 – 1.35, P<.001) with each additional inpatient day prior to surgery. CONCLUSIONS: Preoperative hospitalization is associated with poorer outcomes and longer postoperative recovery in patients undergoing elective oncologic resections. This risk increases for each additional preoperative day prior to surgery. Efforts to improve preoperative inpatient care may provide an important quality improvement target.



PF148

Factors Associated with Good Patient Experience after Outpatient Breast Surgery B.L. Murphy,* K.T. hanson, E.B. Habermann. *Surgery, Mayo Clinic, Rochester, MN.*

Background: With the growing number of healthcare options available and emphasis on patient-centered care, patient satisfaction is ever more important. We sought to determine factors that contribute to good patient experience in patients undergoing outpatient breast procedures at a tertiary medical center. Methods: We retrospectively identified all patients ≥18 years of age who underwent a breast surgical procedure 7/2015-12/2016 and responded to a survey about their outpatient experience. Univariate analyses evaluated associations of top box survey measures (registration, nursing, surgeon, facility, personal issues, patient safety, and overall assessment) with patient factors. Key driver analysis identified top priority survey measures for improving the overall assessment measure. Results: Of 270 patients, 99% were female. Mean age (± SD) was 61.7±12.3 years. No significant differences in top box scores were observed between patients who underwent a breast procedure alone (40%) versus breast and axillary surgery (60%) (all p>0.05). In comparing patients who did or did not give a top box surgeon score, patients who gave a top box surgeon score were older (mean 62.5 vs 58.6 years, p=0.048). While the median pain score was 0 for both groups, those reporting top box where more likely to report a pain score of 0 before discharge (87% vs 68%, p<0.01). In review of overall hospital ratings, patients who gave a top box surgeon rating were 30.8 times more likely to give a top box overall rating to the hospital and 22.9 times more likely to give a top box rating for likelihood to recommend the surgery center, compared to those with a low surgeon score (both p<0.01). Key driver analysis showed that personal issues, including pain control, responsiveness to needs, and inclusion in treatment decisions, should be top priorities for improvement in overall assessment score. Conclusion: Patient age and minimum pain score were associated with giving a high surgeon score, and surgeon score was related to overall hospital score. The personal issues measure was a key driver of the overall score. Efforts for improvement should be focused on these areas to advance the overall patient experience.



Correlation of Survey Variables with Overall Satisfaction Score

PF149

Financial Burden and Distress Among Patients Undergoing Surgical Oncology Care D. Levy,[2] J. Carr,[1] N. Allcott,[3] A. Millan,[1] K. Stitzenberg.[1]* *1. Surgery, UNC, Chapel Hill, NC; 2. UCLA, Los Angeles, CA; 3. Campbell University, Buies Creek, NC.*

Recent studies have brought to light substantial financial burden and toxicity experienced by cancer patients. However, these studies have focused on patients receiving chemotherapy. Very little is known about financial burden amongst cancer patients who do not require chemotherapy. We hypothesize that a substantial portion of cancer patients experience financial toxicity, even when treated with surgery alone. METHODS: A questionnaire was administered to a convenience sample of surgical oncology patients at a single institution. Cancer patients ≥18 years who were 6-18 months post curative intent surgery were eligible. Patients who received cytotoxic chemotherapy or immunotherapy were excluded. Survey items collected information regarding the effects of costs of care on treatment decisions and on financial well-being. RESULTS: Of 109 participants, 57.8% were female. Average age was 62 years. 36.1% had melanoma, 47.2% DCIS/breast cancer and the remainder sarcoma, colorectal, appendiceal or thyroid cancer. 35.8% were employed full-time, 11.9% part-time; and 42.2% retired. Most (97.1%) had continuous insurance coverage, yet cost was an important factor when deciding whether to have surgery for 10 (9.3%); what type of surgery to have for 9 (8.3%); when to have surgery for 13 (12.3%) and where to have surgery for 11 (10.5%). Participants reported gas (22.0%), parking (18.3%), hotel (9.2%), time away from work (21.1%), meals away from home (11.9%) and insurance copay (25.7%) impacted decisions about treatment. 24 (23.5%) reported significant ongoing debt related to the costs of surgery. 36 (33.0%) did not feel they had adequate access to the information needed to calculate costs prior to surgery; 36 (33.0%) were not aware that resources existed to help understand costs; and 38 (34.9%) felt they were not adequately informed about the costs of surgery and recovery before making treatment decisions. CONCLUSION: Even for insured patients, cost is an important factor when making decisions about surgical care. Many patients feel ill-equipped to make those decisions. Even without chemotherapy, a substantial portion of patients incur sustained medical debt related to cancer care.

PF150

Disparities in Mucinous Appendiceal Cancer Treatment and Survival I. Konstantinidis,* M. Raoof, P. ituarte, V. Trisal, I.B. Paz, B. Lee. *Surgery, City of Hope National Cancer Center, Duarte, CA.*

Introduction: Aggressive surgical resection represents the best treatment for mucinous appendiceal cancer. We investigated whether there are disparities in the overall survival of patients with mucinous appendiceal cancer. Methods: A population-based analysis of National Cancer Data Base (NCDB) for stage IV mucinous appendiceal cancer diagnosed between 2004-2014 in patients 18-90 years of age who underwent colectomy (partial, subtotal or total) with or without continuous organ resection was performed. Results: A total of 2017 patients who underwent resection at 585 institutions were identified. The vast majority of patients (94.5%) were treated in institutions who treated less than 10 patients during the study period (low volume) whereas 5% of institutions treated 10-50 patients (medium volume) and 0.5% treated more than 50 patients (high volume). Female patients with less comorbidities had a better survival (female:73.3mo vs male:49.8mo; p<0.001 and Charlson Comorbidity Index (CCI): CCI0: 63.5mo vs CCI1:49.4mo vs CCI2:29.3mo; p<0.001). White and black race patients had similar survival (57.6mo vs 52.4mo;p=0.3). Resections with negative margins and well differentiated tumors were associated with the best OS (R0:86.9mo vs R1:37.8mo vs R2:37.2mo vs positive margins NOS 42.6mo; p<0.001) (Grade:Well:95.9mo vs moderate:45.3mo vs Poor/undifferentiated: 19.7mo; p<0.001). Patients who were in the highest median income quartile and privately insured had the best outcome (highest income quartile:82.5mo vs 47-58.2mo for the others;p<0.001 and private insurance:75.6mo vs 38.8mo for medicare, 52.4mo for medicaid and 58.6 for uninsured;p<0.001). The volume of cases correlate with survival (low volume: 49.3mo vs medium volume:73.3mo vs high volume:117.9mo;p<0.001). Conclusions: The vast majority of mucinous appendiceal cancer patients are treated in centers with limited experience with worse outcome compared to high volume centers. Disparities in socioeconomic status may lead to limited access to specialized centers and merit further investigation.

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Predictors of Disease-Free and Overall Survival in Retroperitoneal Sarcomas: A modern 16 year Multi-Institutional Study from the United States Sarcoma Collaboration (USSC) P.B. Schwartz,[1]* K. Vande Walle,[1] E.R. Winslow,[1] C.G. Ethun,[2] G. Poultsides,[3] K.K. Roggin,[4] V.P. Grignol,[5] J.H. Howard,[5] J. Davidson,[6] R. Fields,[6] H. Mogal,[7] C.N. Clarke,[7] K. Votanopoulos,[8] K. Cardona,[2] D. Abbott.[1] *1. Surgery, University of Wisconsin Hospitals and Clinics, Madison, WI; 2. Emory University School of Medicine, Atlanta, GA; 3. Stanford University, Stanford, CA; 4. University of Chicago, Chicago, IL; 5. The Ohio State University, Columbus, OH; 6. Washington University, St. Louis, MO; 7. Medical College of Wisconsin, Milwaukee, WI; 8. Wake Forest, Salem, NC.*

Background: Retroperitoneal sarcomas (RPS) comprise approximately 15% of all soft-tissue sarcomas, frequently associated with significant morbidity and as little as 30% 5-year survival. Here we provide a large, contemporary, and multi-institutional experience to determine which tumor, patient and treatment characteristics are associated with long-term cancer-specific outcomes in RPS. Methods: 577 patients with primary RPS were identified from the United States Sarcoma Collaboration (USSC). RPS patients who underwent resection from January 2000-April 2016 were included with patient, tumor and treatment-specific variables investigated as independent predictors of survival. Survival analyses for disease-free (DFS) and overall survival (OS) were conducted using Kaplan Meier and Cox Proportional Hazards model methods; p≤0.05 was defined as significant. Results: The study cohort was 55% female, with a median age of 59 years (IQR 48.4-70.0). The most common tumor histiotypes were liposarcoma (32%) and leiomyosarcoma (27%). Median follow up was 30.6 months (IQR 11.2-60.4). Median DFS was 35.9 months (95% CI 27.8-44.0), with multi-variate predictors of poorer DFS including higher grade tumors, node-positive disease and multivisceral resection (Table 1). The 1-, 3-, and 5-year survival was 86%, 73% and 67% respectively. On multivariate analysis, predictors of shorter OS included older age, higher grade tumors, node positive and multifocal disease, larger tumor size (>20 cm) and grossly positive margins (R2) following resection. Conclusions: Our analyses demonstrate that the strongest predictors of DFS and OS are tumor-specific characteristics, while surgical factors are less impactful. Non-surgical therapies are not associated with improved outcomes. Identifying patients with early stage disease should be the primary goal in optimizing outcomes for RPS patients.

Table 1: Predictors of Disease-Free and Overall Survival

	Disease-Free Survival			Overall Survival		
Demographic/tumor characteristics	*Univariate p-value*	*Multivariate p-value*	*Hazard Ratio (95% CI)*	*Univariate p-value*	*Multivariate p-value*	*Hazard Ratio (95% CI)*
Patient age > 65	0.27			**<0.01**	**0.02**	1.40 (1.06-1.86)
Sex	0.26			0.87		
Race	0.65			0.37		
Smoking Status	0.95			0.43		
Prior Radiation Exposure	0.68			0.76		
Known Genetic Syndrome	0.16			**0.02**	0.13	0.22 (0.03-1.57)
Tumor Histology	0.10			0.36		
Tumor Grade	**<0.01**			**<0.01**		
Low Grade						
High Grade		**<0.01**	2.67 (1.89-3.78)		**<0.01**	3.06 (1.99-4.72)
Nodal Disease	**<0.01**	**<0.01**	2.09 (1.23-3.54)	**<0.01**	**<0.01**	2.52 (1.47-4.31)
Multifocal Disease	0.11			**<0.01**	**<0.01**	2.83 (1.48-5.43)
Size of Tumor	**<0.01**			**0.02**		
< 10 cm						
10-20 cm		0.06	1.34 (0.72-1.42)		0.73	1.06 (0.76-1.49)
> 20 cm		0.06	1.40 (0.98-2.07)		**0.04**	1.48 (1.02-2.16)
Organs Resected	**<0.01**			**0.03**		
0						
1-2		0.63	0.92 (0.66-1.29)		0.60	1.11 (0.76-1.63)
3-4		**0.04**	1.55 (1.02-2.36)		0.10	1.50 (0.92-2.44)
≥5		0.12	1.53 (0.89-2.64)		0.29	1.43 (0.74-2.74)
Neoadjuvant Therapy	**0.01**	0.21	0.82 (0.59-1.12)	0.10		
Adjuvant Therapy	**<0.01**	0.22	0.81 (0.58-1.13)	**<0.01**	0.61	1.11 (0.75-1.64)
Margin Status	**<0.01**			**<0.01**		
R0						
R1		0.62	0.92 (0.99-1.69)		0.18	1.24 (0.91-1.68)
R2		0.89	1.55 (0.53-1.76)		**<0.01**	3.00 (1.92-4.74)

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Histopathologic Tumor Response Following Neoadjuvant Hyperthermic Isolated Limb Perfusion in Extremity Soft Tissue Sarcomas, the Prognostic Value of the European Organization for Research and Treatment of Cancer: Soft Tissue and Bone Sarcoma Group (EORTC-STBSG) Response Score M.G. Stevenson,[1]* H. Hoekstra,[1] W. Song,[2] L.B. Been,[1] A.J. Suurmeijer.[2] *1. University of Groningen, University Medical Center Groningen, Department of Surgical Oncology, Groningen, Netherlands; 2. University of Groningen, University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, Netherlands.*

Introduction: The increased use of neoadjuvant treatment strategies i.e. hyperthermic isolated limb perfusion (HILP), preoperative radiotherapy and neoadjuvant chemotherapy in soft tissue sarcomas (STS) led to a standardized approach of the histopathologic examination of pretreated STS by the European Organization for Research and Treatment of Cancer-Soft Tissue and Bone Sarcoma Group (EORTC-STBSG). This protocol includes a STS response score based on the percentage of stainable tumor cells. This study aims to determine the prognostic value of this response score in extremity soft tissue sarcoma (ESTS) patients treated with neoadjuvant HILP and delayed surgical resection. Methods: Patients treated between 1991 and 2016 were analyzed. All resection specimens were re-analyzed and the histopathologic tumor response was established in accordance with the EORTC STS response score. Local recurrence free survival (LRFS), distant metastases free survival (DMFS), disease-specific survival (DSS) and overall survival (OS) were determined for patients. Results: Ninety-one patients were included. Eleven patients had a Grade A (12.1%), ten patients a Grade B (11.0%), 15 patients a Grade C (16.5%), 22 patients a Grade D (24.2%) and 33 patients a Grade E (36.3%) histopathologic response. Median follow-up was 65.0 (18.0-157.0) months. No differences in LRFS (p=0.540), DMFS (p=0.758), DSS (p=0.655) and OS (p=0.282) were found among the five histopathologic response grades. Conclusions: The percentage stainable tumor cells following neoadjuvant HILP and surgical resection has no prognostic value considering oncological outcome in locally advanced ESTS. Further prospective studies considering the prognostic value of the histopathologic response score in pretreated STS are warranted.

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Long-term Outcomes Among Patients with Gastrointestinal Stromal Tumors: An Analysis of the National Cancer Database

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Introduction: Gastrointestinal stromal tumors (GISTs) are the most common sarcoma that arises from the gastrointestinal tract. Data regarding long-term prognosis based on tumor location (stomach vs. small intestine) are mixed. We aimed to analyze the outcomes of gastric and small intestine GISTs using a large national oncology database. Methods: The National Cancer Database (NCDB) was queried for cases of gastric and small intestine GIST between the years 2004 and 2014. Survival analysis was performed using the Kaplan-Meier method and factors related to survival were compared using the Cox proportional hazards model. Results: A total of 18,900 patients were identified with either gastric (n=13,217, 69.9%) or small intestine (n=5,683, 30.1%) GIST during the study period. The incidence of GIST increased over time (2004: n=999 vs. 2014: n=2,349; P<0.001). The overwhelming majority of patients (n=16,049, 84.9%) underwent surgical resection with nearly one-half (n=7,160, 42.9%) receiving chemotherapy. Patients with small intestine GIST had larger median tumor size (gastric: 5.0 cm, IQR: 3.0, 9.0 vs. small intestine: 6.2 cm, IQR: 3.8, 10.0; P<0.001) and a higher incidence of tumors with ≥5 mitoses/high power field (gastric: n=1,598, 24.2% vs. small intestine: n=848, 29.3%; P<0.001). Unadjusted median overall survival (OS) was longer for patients with gastric GIST (10.3 years) as compared to small intestine GIST (9.4 years) (P=0.01). After controlling for all factors, however, OS did not differ between gastric and small intestine GIST (HR 1.19, 95% CI 0.88-1.61; P=0.26). Conclusion: Patients with small intestine GIST more commonly have larger tumors and tumors with higher mitotic rates as compared to patients with gastric GIST. Despite possessing worse pathologic and prognostic features, tumor location did not independently impact overall survival.

Multivariate Survival Analysis of Factors associated with Overall Survival in Patients with Gastrointestinal Stromal Tumor from the National Cancer Database (n=18,900)

Variables	Median Survival (Years)	P Value	Hazard Ratio	95% CI	P Value
Age			1.04	1.02-1.06	<0.001
Sex		<0.001			
Male	8.8		Ref	-	
Female	11.4		0.62	0.46-0.84	0.002
Race		<0.001			
White	9.9		Ref	-	
Black	10.2		1.06	0.71-1.59	0.78
Asian	Not Reached		0.91	0.45-1.81	0.78
Tumor Size		<0.001			
<5 cm	Not Reached		Ref	-	
≥5 cm	9.6		1.42	0.99-2.06	0.06
Lymph Node Involvement		<0.001			
No	10.2		Ref	-	
Yes	7.0		0.75	0.41-1.36	0.34
Metastatic Disease		<0.001			
No	Not Reached		Ref	-	
Yes	4.5		2.75	1.79-4.22	<0.001
Mitoses		<0.001			
<5/HPF	Not Reached		Ref	-	
≥5/HPF	10.2		1.30	0.96-1.78	0.10
Tumor Location		0.01			
Stomach	10.3		Ref	-	
Small Intestine	9.4		1.19	0.88-1.61	0.26
Surgery		<0.001			
Yes	11.3		Ref	-	
No	3.6		3.78	1.15-12.33	0.03
Chemotherapy		<0.001			
Yes	9.5		Ref		
No	10.5		1.55	1.11-2.15	0.01

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Low Local Recurrence with Tailored Multi-Visceral Resection and Combination Therapy for Retroperitoneal Sarcoma: A Long Term Institutional Follow-up

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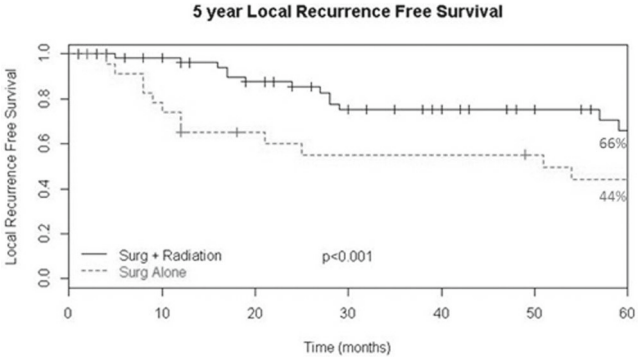
Introduction Recently there has been a shift in the treatment of retroperitoneal sarcoma (RPS) toward a multidisciplinary approach to reduce local recurrence (LR). We have previously reported excellent local recurrence free survival (LRFS) using a tailored multi-visceral resection in combination with neoadjuvant external beam radiation therapy and intraoperative radiation therapy (SRT). This is our update with longer term follow up. Methods Retrospective review of 83 consecutive patients with RPS undergoing R0 or R1 resections from 1993-2016. Bivariate analyses were performed to identify differences between patients undergoing surgery alone vs SRT. A multivariable analysis using logistic regression was performed to determine predictors of LR. Estimates for LRFS and overall survival were derived by Kaplan–Meier analysis with the log–rank test. Results 59 patients (71%) underwent SRT and 24 (29%) underwent surgery alone. Median follow-up was 39 months (range 0-246 months). 63% of tumors were high-grade and 33% were locally recurrent at time of initial treatment. R0 resection was completed in 75% of patients and R1 in 25%. Patients receiving SRT were younger (median age 61 vs 72 years old, p=0.002) and had more organs resected (2.0 vs 1.5, p=0.056). 20% of SRT patients had LR vs 42% with surgery alone (p=0.046). 5-year LRFS was 66% with SRT vs 44% with surgery alone (p<0.001). Factors associated with LR were LR at presentation to our institution, surgical intervention alone, and longer length of follow up. Margin status and number of organs resected were not significantly associated with LR. On multivariate analysis, SRT was the only variable associated with lower risk of LR (OR 0.161, CI 0.04-0.644, p=0.01). 5 year overall survival for both groups was 59.5%. Conclusion Combination of preoperative radiation, tailored multi-visceral surgical resection, and intraoperative radiation produces excellent local disease control for RPS. Combination therapy was associated with improved LRFS but not overall survival at 5 years.



PF155

Determining the Optimal Sampling Regimen for Soft Tissue Sarcoma Biopsies

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Objective: Fine needle aspirates (FNAs) and core biopsies are both used to diagnose sarcomas, but variable diagnostic performance of FNAs compared to core biopsies has been reported. Additionally, the diagnostic performance of repeat core biopsy after an inconclusive first biopsy is unclear. The goal of this study was to delineate the optimal sampling regimen by comparing diagnostic performance of FNAs and core biopsies and determining the outcome of a repeat core biopsy. Methods: We analyzed a cohort of adult patients with soft tissue sarcomas (n=407) who underwent at least one diagnostic core biopsy or FNA. The accuracy of FNAs and core biopsies was determined by concordance with their corresponding surgical specimens for the parameters of sarcoma diagnosis, classification of sarcoma type, and tumor grade. FNAs and core biopsies were then independently compared in each parameter in their ability to yield accurate diagnoses. A subset of cases (n=22) with repeat core biopsies was also analyzed to see if it could provide additional clinical data. Results: In cases with conclusive diagnoses for core biopsies, FNAs, and operative excisions, there was a statistically significant association between biopsy type and accurate diagnosis (p<0.001). Core biopsies (95.9%) were more likely than FNAs (79.4%) to produce diagnoses that were concordant with their surgical specimen. There was also a statistically significant association between biopsy type and correct classification (p<0.001) and grade (p<0.001), with core biopsies more likely than FNAs to provide accurate classifications (71.8% v. 32.8%)

and grades (75.4% v. 55.9%). In a subset of cases with repeat core biopsies, we found that repeat biopsies were associated with successful sarcoma diagnoses (86.7%, $p<0.01$) and histopathological classifications (53.3%, $p<0.05$), even after a failed or incomplete first biopsy. Conclusion: FNAs were statistically inferior to core biopsies in providing accurate diagnostic information; however, FNAs might be useful for other ancillary analyses. Repeat core biopsies were able to provide diagnostic information, indicating that a failed or incomplete first biopsy does not preclude the success of a second one.

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Managing Extremity Sarcomas: When and Why to Delay Definitive Reconstruction A.N. Goldin,[1]* G.A. Mackert,[2] A. Kulidjian,[1] M.K. Dobke.[1] *1. Orthopaedic Surgery, University of California San Diego, San Diego, CA; 2. University of Heidelberg, Ludwigshafen, Germany.*

Introduction: Delaying definitive reconstruction after extremity sarcoma resection is appropriate when the diagnosis or adequacy of margins is not clear, molecular typing needs time, or the focus is on sparing the extremity rather than survival. Indications for delayed reconstruction can be related to systemic, donor site, and recipient site considerations. We set to analyze a joint team of orthopaedic and plastic surgeons' experiences, and evaluate the rationale behind the choice of immediate versus delayed reconstruction. We introduce a Choice Determining Points (CDP) system to determine if a score-based system could be used to justify timing of reconstruction in the decision-making process. Methods: A retrospective review was performed on patients with extremity sarcomas from 2011 to 2015 for evaluation of timing of definitive reconstruction. Chats were reviewed for patient age, sex, tumor site, symptoms, previous treatment, initial diagnosis, local recurrences, metastases, prognosis, and outcome. For each case treatment planning was reviewed. Choice Determining Points (CDPs) were determined by commonly quoted predictors of margin status to develop a score-based approach for guidelines on when to use immediate versus delayed reconstruction. Results: Of 81 patients identified, definitive reconstruction was performed in 58 (72%) and delayed in 23 (28%). Factors leading to delay included inadequacy of frozen material for assessment, sampling error from heterogeneity, multicentricity, infection, and non-appositional growth. In the 23 cases of delayed reconstruction, 16 were because of diagnostic uncertainty, six were because of infection, and in one the intraoperative histology necessitated a change of plans. Only one of the delayed cases met 11 of the 12 CDPs, and the remaining 22 patients had a maximum of 9 CDPs (average 7) (Table 1). Conclusions: The pivotal factor for reconstructive planning and CDPs are surgical margins, and the majority of reconstructive dilemmas evolve from diagnosis and/or issues related to the margins. As increased knowledge about sarcomas leads to personalized management plans, CDPs may become a useful, evidence based tool for planning timing of reconstruction.

Choice Determining Point Data of Patients Undergoing Delayed Reconstruction

CPD	Number of Patients (Percent)
Non-established diagnosis (which includes cases of changing diagnosis)	2 (9%)
Lack of certainty regarding appropriate margins	16 (70%)
High local or general risk for major procedure, significant comorbidities	8 (35%)
Technical inability to perform reconstruction as a single stage procedure	2 (9%)
Non-completion of neo-adjuvant treatment	2 (9%)
Concern about delaying adjuvant treatment	2 (9%)
Tumor size greater than 5cm	2 (9%)
Patient greater than 50 years old	2 (9%)
Recurrent tumor and need to rule out satellite tumors, regional and distal metastatic lesions	4 (17%)
Presence of evidence of metastatic disease	3 (13%)

Factors characterizing patients who underwent the delayed definitive reconstruction, as they were known prior to ablative surgery. All but one of the 23 patients in these groups were characterized by more than one CDP (Choice Determining Point).

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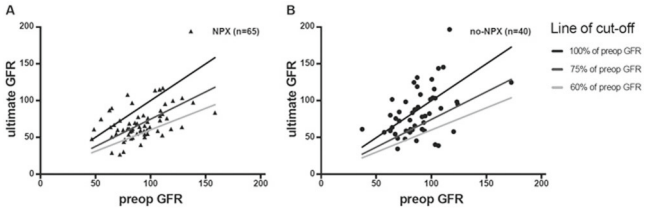
Clinical Benefit and Residual Kidney Function of En Bloc Nephrectomy for Perirenal Retroperitoneal Sarcoma J. Rhu,* C. Cho, S. Kim. *Surgery, Samsung Medical Center, Seoul, Korea (the Republic of).*

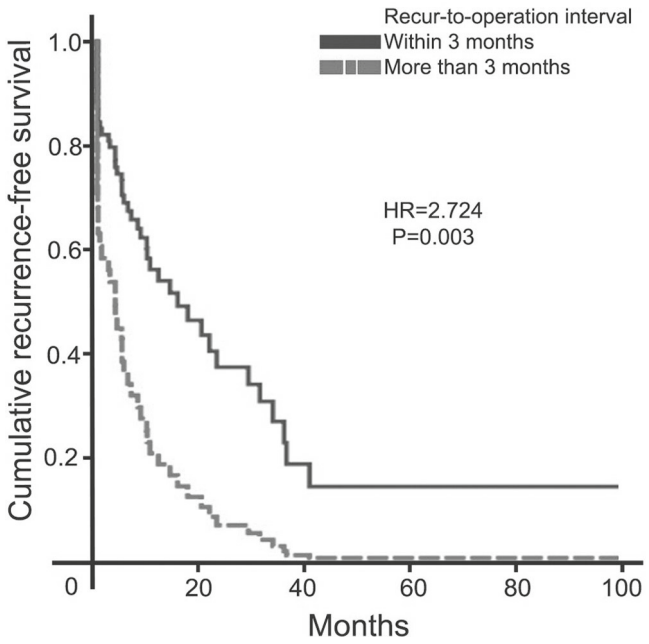
Aim: The purpose of this study was to evaluate the efficacy of en bloc nephrectomy for perirenal retroperitoneal sarcoma (RPS) with respect to postoperative kidney function and oncological benefits. Methods: We performed a comparative study of 114 patients undergoing surgery for primary RPS, classifying cases as nephrectomy (NPX, N = 65) versus no nephrectomy (no-NPX, N = 49). The Δ and % change between preoperative and postoperative estimated glomerulus filtration rate (eGFR) were analyzed to compare renal function changes after surgery. Kaplan-Meier analysis was performed to verify the incidence of local relapse between the two groups. Results: During a median follow up of 29 months, median postoperative GFR of 65 patients in the NPX group decreased to 73.5% of preoperative eGFR. Although 38 patients (58%) in the NPX group experienced a progression in CKD stage after nephrectomy, no patients progressed to end-stage renal disease (ESRD). In FNCLCC grade 2, the NPX group had statistically significant local control benefits, compared with the no-NPX group (P = 0.048). Conclusions: Residual renal function after en bloc nephrectomy was stabilized without progression to ESRD. Moreover, en bloc nephrectomy for perirenal RPS might secure a complete resection margin for local tumor control.



PF158

Optimal Maximum Duration for Delaying Salvage Operation when Recurrence of Retroperitoneal Liposarcoma is Suspected: A Single-Center Study J. Rhu,* S. Kim. *Surgery, Samsung Medical Center, Seoul, Korea (the Republic of).*

Background: This study was designed to identify the optimal maximum duration for delaying salvage operation when recurrence of retroperitoneal liposarcoma (LPS) is suspected. Methods: Patients who underwent salvage operation at Samsung Medical Center for recurrent retroperitoneal LPS from January 2000 to December 2015 were reviewed. The time interval between recurrence and operation for recurrence was divided by 1, 2 or 3 months. A Cox proportional-hazards model was used to analyze factors related to disease-free survival along with recurrence-to-operation interval divided by 1, 2 or 3 months. Results: The 1-, 3-, and 5-year disease-free survival rates were 43.2%, 15.6% and 13.4%, respectively. FNCLCC grade ($p=0.023$) and recurrence-to-operation interval divided by 3 months ($p=0.003$) were significant factors associated with recurrence. FNCLCC grade 2 (HR=1.940, CI=0.935-4.026, $p=0.238$) and grade 3 (HR=4.049, CI=1.767-9.281, $p=0.007$) showed increased risk compared to grade 1. Patients who underwent salvage operation more than 3 months after recurrence showed significantly increased risk of recurrence compared to patients within 3 months (HR=2.724, CI=1.391-5.337, $p=0.003$). Conclusions: Based on our analysis of recurrence-free survival, salvage operation can be delayed for less than 3 months when recurrence is suspected. A short-term follow-up imaging study should be performed within this period.



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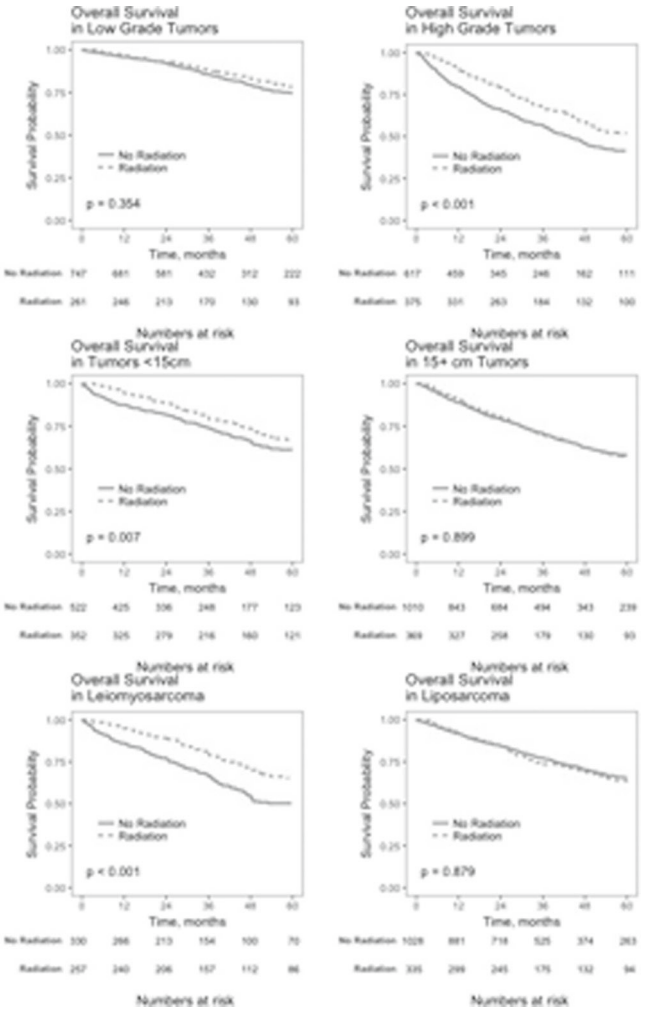
Radiation Therapy for Retroperitoneal Sarcoma: Influences of Histology, Grade, and Size J. Bergquist,[1] J. Leiting,[1]* M. Hernandez,[1] K. Merrell,[2] M. Truty,[1] T.E. Grotz.[1] *1. Mayo Clinic - Department of Surgery, Rochester, MN; 2. Mayo Clinic - Department of Radiation Oncology, Rochester, MN.*

Background: Although radiation therapy has been associated with reduced local recurrence in extremity sarcoma, the influence of tumor grade, histology and tumor size on the applicability of radiation therapy in RPS remains unclear. We hypothesized that peri-operative radiation therapy would be associated with improved outcomes in RPS and this association would be impacted by grade, tumor size, and histologic type. Methods: The National Cancer Data Base (NCDB) 2004-2012 was reviewed for patients diagnosed with non-metastatic RPS undergoing curative intent resection. Tumor size was dichotomized at 15cm based on 8th ed AJCC staging. Patients with highest comorbidity score were excluded. Unadjusted Kaplan-Meier and adjusted Cox Proportional Hazards modeling analyzed overall survival (OS). Multivariable logistic regression modeled margin positivity. Results: 2264 patients were included. 727 (32.1%) were treated with radiation, 203 (8.9%) of these pre-operatively. Median [IQR] tumor size was 17.5 [11.0-27.0] cm. 1048 (43.7%) patients had high grade tumors. Multivariable analysis revealed that treatment with radiation was independently associated with decreased mortality hazard (HR 0.70, 95% CI 0.60-0.81, p<0.001), and pre-operative radiation was associated with reduced margin positivity (HR 0.71, 95% CI 0.52-0.97, p=0.03). Stratified survival analysis showed that, compared to untreated patients, those treated with radiation had prolonged median OS when tumors were high grade (64.3 vs. 43.6 months, p<0.001), small size (104.1 vs. 84.2 months, p<0.007), and Leiomyosarcomatous (104.8 vs. 61.8 months, p<0.001 - Figure). Conclusion: A minority of patients who present with curative-intent resection for RPS will be treated with radiation therapy, less than 10% being treated pre-operatively. Radiation therapy is independently associated with decreased mortality hazard in patients with high grade, small size, and Leiomyosarcomatous tumors. Pre-operative radiation is independently associated with margin negative resection. These data support the conclusion that management of RPS should be multidisciplinary in nature and consideration should be given to pre-operative radiation.



Stratified Kaplan-Meier overall survival analysis of Patients who were or were not treated with peri-operative radiation therapy.

PF160

Predictors of Early versus Late Death in Resected Retroperitoneal Sarcoma (RPS): An 8-Institution Study from the U.S. Sarcoma Collaborative B.A. Krasnick,[1]* D.R. Cullinan,[1] M. Roubakha,[1] M. McGilvray,[1] D. Coble,[1] C.G. Ethun,[2] T.B. Tran,[3] G. Poultsides,[3] V.P. Grignol,[4] J.H. Howard,[4] M. Hembrook,[5] T.C. Gamblin,[5] J. Tseng,[6] K.K. Roggin,[6] K. Chouliaras,[7] K. Votanopoulos,[7] E.R. Winslow,[8] D. Abbott,[8] W. Hawkins,[1] K. Cardona,[2] R. Fields.[1] *1. Washington University School of Medicine, St. Louis, MO; 2. Emory University Winship Cancer Institute, Atlanta, GA; 3. Stanford University, Stanford, CA; 4. The Ohio State University Medical School, Columbus, OH; 5. Medical College of Wisonsin, Milwaukee, WI; 6. University of Chicago, Chicago, IL; 7. Wake Forest University, Winston-Salem, NC; 8. University of Wisconsin, Madison, WI.*

Introduction: RPS accounts for 15% of soft tissue sarcomas. We sought to determine predictors of early vs. late mortality in patients undergoing resection of localized RPS. Methods: Utilizing data from the 8 institution U.S. Sarcoma Collaborative, all patient undergoing surgery with curative intent for localized RPS were identified. Patients were categorized into 3 groups: alive, death <90 days postoperatively, and death >90 days postoperatively. Univariate multi-group analysis was done to establish the effect of multiple preoperative, operative, and pathological variables. Only variables that were coded in >85% of patients were included in this analysis. All factors found to have a p value of <0.05 were included in a multinomial logit regression model. All data was analyzed using SAS 9.4. Results: Of the 817 patients

identified, 495 are still alive (60.6%), 28 (3.4%) died <90 days postoperatively and 294 (36.0%) died >90 days postoperatively. On univariate analysis, age (p<0.01), HTN (p<0.0001), DM (p<0.05), recurrent tumor status (p<0.0001), duodenal resection (p<0.05), intraoperative PRBCs (p<0.0001), postoperative PRBCs (p<0.05), positive margin (p<0.01), tumor grade (p<0.0001), other organ tumor involvement (p<0.0001), neoadjuvant chemotherapy (p<0.0144), operative blood loss (p<0.0001), and tumor size (p<0.0001) all had a significant association between groups. These were all used to create our multinomial model. In this model, predictors of early death vs. alive status were high grade tumor, while predictors of late death versus alive were high grade tumor and positive tumor margin (Table). Although non-significant, factors predictive of early death over late death approaching significance were, postoperative PRBC transfusion (OR 9.98, p=0.084), and concomitant duodenal resection (OR 9.985, p=0.092). Conclusions: In a multinomial model looking at patients with resected localized RPS, high grade tumors are predictive of both early and late mortality. Positive pathologic margin is a predictor of late mortality only.

Multinomial Model for Resected Localized RPS

Variable	OR (95% CI)
Early Death vs. Alive	
High Grade	7.56 (1.75-32.66)
Late Death vs. Alive	
High Grade	3.26 (2.10-5.06)
Positive Path Margin (R1 or R2)	1.55 (1.02-2.37)

RPS, retroperitoneal sarcoma.

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Perioperative Outcomes and Survival of Octogenarians Undergoing Curative Resection for Esophagogastric Cancer E. Chen,[2]* Z. Senders,[1] J. Hardacre,[1] J. Kim,[1] J. Ammori.[1] *1. Surgery, University Hospitals Cleveland Medical Center, Cleveland, OH; 2. Case Western Reserve University School of Medicine, Cleveland, OH.*

Introduction Curative resection is routinely performed for selected octogenarians with esophagogastric cancer, however data conflicts as to whether perioperative outcomes and survival are comparable to younger patients. This study aims to compare perioperative outcomes and survival of patients 80 or older with younger patients undergoing curative resection for esophagogastric cancer at our institution. Methods Retrospective data was collected on 190 patients who underwent resection with curative intent for esophagogastric cancer from 2004-2015 at a single institution. Results Of the 190 patients, 34 (18%) were ≥80 years old. Octogenarians were more likely to have chronic kidney disease, however, the incidence of other comorbidities was comparable. Octogenarians were less likely to have received neoadjuvant chemotherapy. Pathological findings including tumor stage, size, grade, histology, margin status, and lymph node involvement were similar between groups. Tumors of octogenarians were more likely to be located in the gastric body while younger patients were more likely to have esophagogastric junction tumors. Length of stay was comparable between groups, however, octogenarians were significantly more likely to be discharged to a location other than home. Both groups had a single death during index admission. Incidence of 90-day post-operative complications and accordion severity grading score were not significantly different between groups. There was no difference in overall 30-day, 90-day, 1-year, or median survival. Conclusion Perioperative outcomes and survival of octogenarians undergoing curative resection for esophagogastric cancer are comparable to younger patients at our institution.

Table 1: Clinicopathologic characteristics and postoperative outcomes

	≥80 (n=34) (17.9%)	<80 (n=156) (82.1%)	p value
Race	*Number (%)*		0.46
White	25 (75.8)	116 (75.3)	
Black	7 (21.2)	37 (24.0)	
Sex			0.17
Male	18 (52.9)	103 (66.0)	
Female	16 (47.1)	53 (34.0)	
Comorbidities			
Diabetes mellitus	3 (8.82)	35 (22.6)	0.10
COPD	3 (8.82)	19 (12.3)	0.77
Chronic heart failure	6 (17.7)	13 (8.39)	0.12
Coronary artery disease	11 (32.4)	35 (22.6)	0.27
Myocardial infarction	3 (8.82)	7 (4.52)	0.39
Peripheral vascular disease	7 (20.6)	16 (10.3)	0.14
Chronic kidney disease	5 (14.7)	7 (4.52)	**0.04**
Stroke	3 (8.82)	9 (5.81)	0.46
Operative Features			
Staging laparoscopy	9 (27.3)	42 (27.1)	1.00
Open (vs Lap)	30 (88.2)	131 (85.1)	0.79
Resection type			**0.001**
Total	7 (20.6)	55 (35.3)	0.11
Partial	22 (64.7)	47 (30.1)	**<0.001**
Esophagectomy	5 (14.7)	54 (34.6)	**0.02**
Pathology	*Median (IQR)*		
Size in cm	4.15 (2.5-6)	3.55 (2.15-5.5)	0.50
Location	*Number (%)*		**0.04**
Antrum	9 (26.5)	28 (18.0)	0.34
Body	18 (52.9)	47 (30.1)	**0.02**
Cardia	1 (2.94)	10 (6.41)	0.69
EGJ	5 (14.7)	61 (39.1)	**0.01**
Fundus	1 (2.94)	7 (4.49)	1.00
Pylorus	0 (0)	3 (1.92)	1.00
AJCC Stage			0.27
Stage 0	0 (0)	11 (7.10)	
Stage 1	15 (44.1)	46 (29.7)	
Stage 2	8 (23.5)	33 (21.3)	
Stage 3	9 (26.5)	57 (36.8)	
Stage 4	2 (5.88)	8 (5.16)	
Grade			0.38
Poorly	18 (54.6)	95 (66.9)	
Moderately	14 (42.4)	45 (31.7)	
Well	1 (3.03)	2 (1.41)	
Histology			0.17
Signet ring	5 (14.7)	46 (29.5)	0.09
Adenocarcinoma	26 (76.5)	104 (66.7)	0.31
Mucinous	3 (8.82)	5 (3.21)	0.15
R1 resection margin	0 (0)	11 (7.19)	0.36
	Mean (Lower 95% - Upper 95%)		
Nodes examined	20.2 (16.3-24.0)	20.8 (19.1-22.6)	0.74
Metastatic Lymph Node Ratio	0.19 (0.09-0.29)	0.19 (0.14-0.23)	0.94
	Mean days (range)		
Length of stay	13.7 (4-61)	10.6 (5-61)	0.19
Discharge destination	*Number (%)*		**<0.001**
Home	6 (18.2)	67 (47.2)	**0.003**
Home w/ Home Care	8 (24.2)	52 (36.6)	0.22
LTAC	3 (9.09)	0 (0)	**0.01**
SNF	15 (45.5)	22 (15.5)	**0.001**
In-hospital death	1 (3.03)	1 (0.70)	0.34
	Average (SD)		
Accordion Score	1.79 (1.6)	2.05 (1.6)	0.40
90-Day post-op occurences	*Number (%)*		
Superficial surgical site infection	4 (11.8)	23 (14.7)	0.79
Deep organ space infection	2 (5.88)	10 (6.41)	1.00
Wound dehiscence	2 (5.88)	11 (7.05)	1.00
Pneumonia	4 (11.8)	20 (12.8)	1.00
Respiratory failure	4 (11.8)	18 (11.5)	1.00
Pulmonary embolism	1 (2.94)	5 (3.21)	1.00
Deep vein thrombosis	2 (5.88)	5 (3.21)	0.61
Post-op ventilator requirement	3 (8.82)	6 (3.85)	0.20
Urinary tract infection	2 (5.88)	7 (4.49)	0.66
Stroke	0 (0)	1 (0.64)	1.00
Myocardial infarction	1 (2.94)	3 (1.92)	0.55
Sepsis	2 (5.88)	7 (4.49)	0.66
Neoadjuvant therapy	5 (14.7)	65 (42.5)	**<0.001**
Adjuvant therapy	9 (29.0)	70 (46.7)	0.08
Overall Survival	*% (SE)*		
30-Day	100 (0)	99 (0.01)	0.64
90-Day	91 (0.05)	96 (0.02)	0.20
1-Year	78 (0.07)	82 (0.03)	0.60
	Months (IQR)		
Median	38.5 (13 - 66)	40.4 (16 - 131)	0.49

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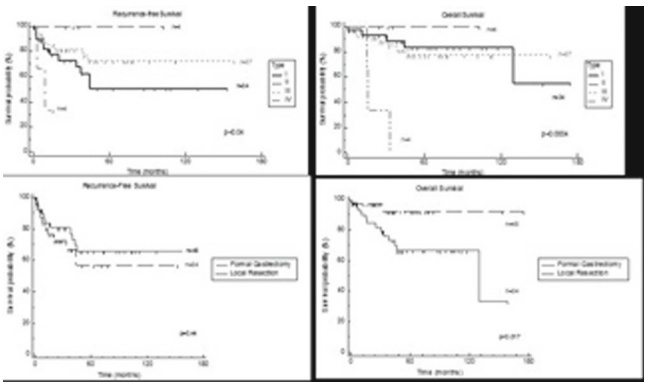
Gastric Carcinoids: Does Type of Surgery or Tumor Affect Survival? A. Crown,[1]* Z.S. Kanji,[1] A.G. Lopez-Aguiar,[2] M. Dillhoff,[3] E.W. Beal,[3] G. Poultsides,[4] E.A. Makris,[4] K. Idrees,[5] P. Marincola Smith,[5] H. Nathan,[6] M. Beems,[6] S. Weber,[7] A. Fisher,[7] R. Fields,[8] J. Davidson,[8] S.K. Maithel,[2] F.G. Rocha.[1] *1. General, Thoracic and Vascular Surgery, Virginia Mason Medical Center, Seattle, WA; 2. Emory, Atlanta, GA; 3. Ohio State University, Columbus, OH; 4. Stanford, Palo Alto, CA; 5. Vanderbilt, Nashville, TN; 6. University of Michigan, Ann Arbor, MI; 7. University of Wisconsin, Madison, WI; 8. Washington University, St. Louis, MO.*

Background: Gastric carcinoids are rare neuroendocrine tumors of the GI tract. They are typically managed according to their etiology. However, there is little known about the impact of surgical strategy on the long-term outcomes of these patients. Methods: All patients who underwent resection of gastric carcinoids at 8 institutions from 2000-2016 were analyzed retrospectively. Tumors were stratified according to subtype (I, II, III, IV) and resection type (local resection LR or formal gastrectomy FG). Clinicopathological parameters, recurrence-free (RFS) and overall survival (OS) were compared between groups. Results: Of 79 patients identified with gastric carcinoids, 34 had type I lesions associated with atrophic gastritis, 4 had type II lesions associated with a gastrinoma, 37 had type III sporadic lesions, and 4 had type IV poorly-differentiated lesions. The mean age of presentation was 56 years in predominantly Caucasian (77%) and female (63%) patients. Mean tumor size was 2.4 cm and multifocal tumors were found in 24 (30%) of patients with the majority occurring in those with type I tumors. Lymph node positive tumors were seen in 15 (19%) patients and 7 (8%) had M1 disease; both most often in type IV followed by type III tumors. R0 resection was achieved in 56 (71%) patients while 15 (19%) had R1 resections and 6 (8%) R2 resections. Patients with type I and III tumors were equally likely to have a LR (50% and 43% respectively) compared to FG while those with type II and IV all had FG with one exception. Type IV tumors had the poorest RFS and OS while Type II tumors had the most favorable RFS and OS ($p<0.04$ and $p<0.0004$, respectively). While there was no difference in RFS in those patients undergoing FG versus LR, OS was worse in the FG group ($p<0.017$). This trend persisted when type II and type IV groups were excluded ($p<0.045$). Conclusion: Gastric carcinoid treatment should be tailored to tumor type, as biologic behavior rather than resection technique is the more important factor contributing to long-term outcomes.



PF164

A Pilot Case Control Study: Could a Gastric Cancer Risk Screening Tool Help Identify High Risk Patients for Endoscopic Screening in the U.S.? H. In,[1]* M. Langdon-Embry,[1] C. Schechter,[2] L. Gordon,[1] J. Wylie-Rosett,[2] P. Castle,[2] M. Kemeny,[3] B. Rapkin.[2] *1. Montefiore Medical Center/Albert Einstein College of Medicine, Bronx, NY; 2. Albert Einstein College of Medicine, Bronx, NY; 3. Queens Cancer Center of Queens Hospital, Queens, NY.*

Background Gastric cancer incidence varies greatly among US racial/ethnic groups. Few studies have examined ethnicity, birth country, immigration and cultural diet as gastric cancer risk factors in the US. These factors, in combination with known risk factors may narrow a target population for gastric cancer screening. Methods Two racially diverse hospital systems were used to recruit gastric cancer cases using the cancer registry, and primary care (PC) controls from waiting rooms or phone. Community controls were recruited at community gatherings. Participants were eligible if 40-85 years old, not under endoscopic surveillance and without genetic syndromes. The survey items (n=227) included conventional risk factors, plus items about ethnicity, birth country, acculturation, and ethnic diet. Results Of 150 participants, 39 cases, 41 PC-controls and 44 community controls were eligible for analysis. PC-controls generally completed phone interviews (72% vs 28%), while community controls generally completed paper surveys (92% vs 8%). Gastric cancer cases were more likely to be foreign born (85% vs. 49%, $p=<0.01$), from a country with gastric cancer incidence >5 per 100,000: (62% vs. 30%, $p=<0.01$) and report daily consumption of cultural food at ages 15 to 18 (69% vs. 35%, $p=<0.01$) compared to controls. Cases were also older, male, Hispanic, and had stronger family history of gastric cancer. Cases and controls had similar frequency of alcohol consumption, smoking, acculturation, and barbequed food consumption. In multivariate analysis, increased age (per year, aOR 1.4, 95%CI 1.07-1.21), daily consumption of cultural foods at ages 15 to 18 (aOR 19.58, 95%CI 1.54-248.99), having less than high school education (aOR 7.24, 95%CI 1.49-35.10), and being foreign born (aOR 11.81, 95%CI 1.69-82.64) were associated with case status. Conclusions A risk assessment tool that addresses awareness of gastric cancer risk factors, ethnicity, cultural habits and immigration patterns has potential to identify high-risk persons from multicultural areas within the US, who might benefit from endoscopic screening for gastric cancer. (Support: UG1CA189823)

PF165

Minimally-Invasive Gastrectomy for Gastric Cancer is Safe for Octogenarians: A Western Population-based Study L.M. Pak,* T. Yang, J. Wang. *Brigham and Women's Hospital, Boston, MA.*

INTRODUCTION: Gastric cancer is the fifth most common cancer worldwide and is rising in incidence among the elderly as life expectancies increase. The safety of minimally-invasive gastrectomy (MIG) in the elderly has been demonstrated in several international studies but has not been evaluated in the context of a large, Western population. The objective of this study was the evaluate the use of MIG among octogenarians in the United States. METHODS: The National Cancer Database was queried from 2010 to 2014 for patients with gastric adenocarcinoma who underwent gastrectomy with curative intent by open (OG) or minimally-invasive approach. Disease and treatment characteristics were compared across three age groups (<65 years, 65-79 years, ≥80 years). Treatment outcomes among octogenarians were compared by surgical approach. Multivariable regression analysis was used to identify risk factors associated with 90-day mortality in octogenarians undergoing minimally-invasive gastrectomy. RESULTS: 17,070 patients were identified who met study inclusion criteria, of which 2,428 patients (14%) were aged ≥80 years. Octogenarians tended to present with larger, well- or moderately-differentiated tumors of higher pathologic stage (all $p<0.001$). They were also more likely to undergo subtotal/partial resections compared to younger patients, and were less likely to receive neoadjuvant or adjuvant chemoradiation (all $p<0.001$). Among these elderly patients, MIG was associated with decreased length of stay (10.0 vs 11.6 days, $p<0.001$) compared to OG; however, there was no difference in the rate of margin-positive resections ($p=0.27$), adequate lymph node sampling ($p=0.08$), readmissions ($p=0.32$), 30- or 90-day mortality ($p=0.75$, $p=0.82$), or overall survival ($p=0.77$) [Figure]. On multivariable analysis, N2 disease and increased length of stay were associated with increased risk of 90-day mortality, while female gender and adjuvant chemotherapy were associated with decreased risk. CONCLUSION: MIG is a safe and effective technique for octogenarians. In this Western population-based study, we report comparable oncologic and post-operative outcomes between MIG and OG.

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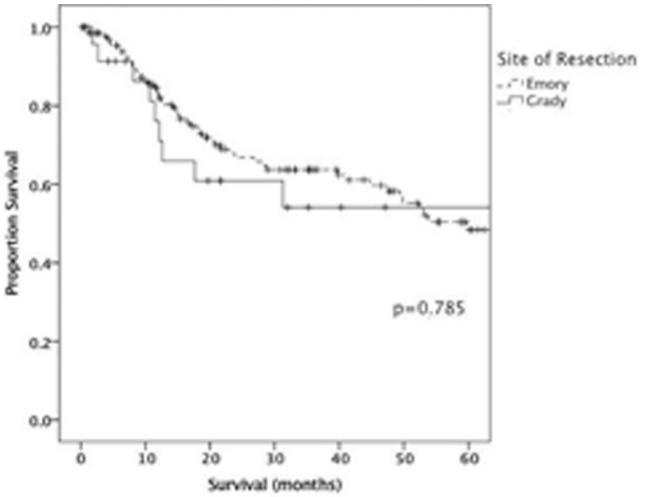
Identifying the Barriers to Cancer Care at Safety-Net Hospitals: A Novel Comparison of a Safety-Net Hospital to a Neighboring Quaternary Referral Academic Institution in the Same Healthcare System M.Y. Zaidi,* J.M. Rappaport, C.G. Ethun, T. Gillespie, N. Hawk, S. Chawla, K. Cardona, S.K. Maithel, M.C. Russell. *Surgery, Emory University, Atlanta, GA.*

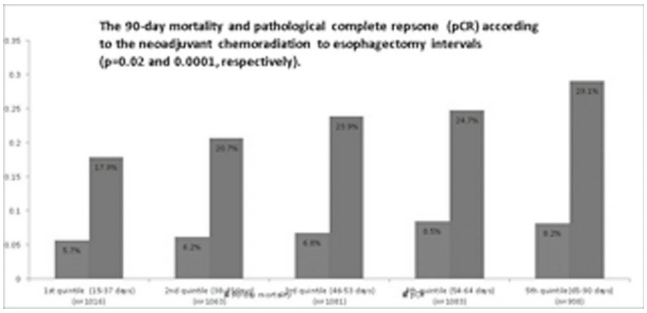
Background: The three-delays model for vulnerable and minority populations to obtain care include delays in seeking, reaching, and receiving care. The dominant delay for vulnerable patients with gastric adenocarcinoma (GAC) is not known. Our aim was to define those patients with GAC who reached care at our regional safety-net hospital compared to academic centers from the National Cancer Database (NCDB). We also aimed to compare survival outcomes of patients who received curative-intent resection at our safety-net hospital to those in a nearby quaternary referral hospital. Methods: Grady-Memorial-Hospital (GMH), a safety-net hospital and Emory-University-Hospital (EUH), a quaternary referral hospital, are within the same healthcare-system. Clinicopathologic data of patients at presentation from NCDB-participating academic centers were compared with GMH from 2004-2014. Patients undergoing curative-intent resection of GAC at GMH were compared to those at EUH during a similar time period. Primary outcome for the latter was overall survival (OS). Results: At presentation, compared to NCDB-participating academic centers (n=69,662), GMH patients (n=154) were more likely to be black (85.1 vs 17.2%; p<0.001), uninsured (30.5 vs 4.7%; p<0.001), have stage IV disease (43.5 vs 30.1%; p=0.017), and receive no treatment (40.3 vs 18.4%; p<0.001). When only comparing those who underwent curative-intent resection at GMH (n=23) to EUH (n=137), median OS was similar between both groups (GMH: median not reached; EUH: 59.8mos; p=0.785; Figure). Conclusion: Patients with gastric cancer who reached care at our safety-net hospital are more likely to be uninsured, have stage IV disease, and receive no treatment compared to academic centers. When they receive curative-intent resection, however, overall survival is similar. Efforts must be made to identify and overcome the barriers in seeking and reaching care for this vulnerable patient population, as it appears that outcomes are acceptable in those who receive care.



PF167

The Impact of the Chemo-radiation to Surgery Interval on Pathological Complete Response, Short and Long-term Overall Survival in Esophageal Cancer Patients B. Azab,* J. Amundson, O. Picado, F. Macedo, C. Ripat, A.S. Livingstone, D. Franceschi, D. Yakoub. *University of Miami Leonard M. Miller School of Medicine, Miami, FL.*

Background: The association of the interval between neoadjuvant chemo-radiation and surgery (CRT-S), and cancer outcomes in patients with esophageal cancer is not clear. We aimed to determine the relationship between CRT-S interval and pathological complete response rate (pCR), short and long overall survival (OS). Methods: Patients listed on the National Cancer Data Base from 2004 to 2013 were studied. We included patients with CRT followed by surgery in 15-90 days. All patients had reported pT, pN cancer stages and survival status. CRT-S interval was studied as continuous (weeks) and categorical variables (quintiles). Results: A total of 5181 patients were included; 81% were adenocarcinomas, 84% were males and mean age was 62 years. They were divided into CRT-S interval quintiles (15 to 37, 38 to 45, 46 to 53, 54 to 64 and 65 to 90 days) (n=1016, 1063, 1081, 1083 and 938 patients), respectively. There was a significant increase of pCR rate across the CRT-S quintiles (18%, 21%, 24%, 25% and 29%, p<0.001). This advantage persisted when CRT-S was measured as continuous variable in weeks (OR: 1.11, 95% CI=1.078-1.143, p<0.001). However, 90-day mortality significantly increased as CRT-S increased across quintiles (5.7%, 6.2%, 6.8%, 8.5% and 8.2%, p=0.02) and through weeks (OR=1.05, 95%CI= 1.005-1.106, p=0.03). Mean OS across CRT-S quintiles was 59.2, 58.8, 55.4, 56.6 and 51.5 months, respectively. Multivariate Cox regression showed significantly worse OS per week increase in CRT-S interval (HR 1.02, 95% 1.003-1.037, p=0.02), especially among the last quintile (CRT-S=65-90 days: HR 1.2, 95% CI 1.04-1.32, p=0.009). Those with no-pCR had worse OS as time to surgery increased (p<0.001), while pCR group had similar OS across CTR-S intervals. Conclusion: Despite higher pCR rate as CRT-S interval increasing, surgery is preferred to be done in less than 65 days after CRT to avoid worse 90-day mortality and achieve better OS. Further randomized studies are needed to consolidate our findings.

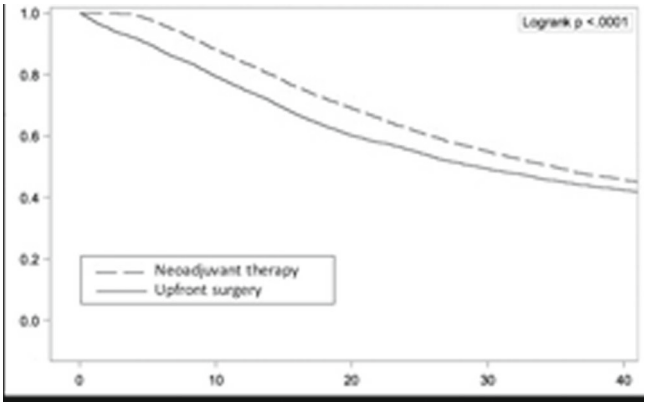


The 90-day mortality and pathological complete repsone (pCR) rates according to the neoadjuvant chemoradiation-surgery intervals in esophageal cancer patients.

PF168

Multimodality Therapy for Gastric Cancer: A Population-Level Propensity-Score Matched Study S.W.L. de Geus,* G.G. Kasumova, O. Akintorin, T.E. Sachs, S. Ng, D. McAneny, J.F. Tseng. *Surgery, Boston University School of Medicine, Boston, MA.*

Introduction: Combined modality therapy represents the standard of care for locally advanced gastric cancer across Western countries; however, the best sequence remains a matter of debate. Practices still vary widely; neoadjuvant chemoradiotherapy constitutes the standard of care in Europe, while adjuvant chemoradiotherapy remains the most common treatment strategy throughout North America. The present study investigates the survival impact and optimal timing of chemo(radio)therapy for locally advanced non-metastatic gastric cancer. Methods: Patients with stage II-III resected non-metastatic gastric adenocarcinoma that received neoadjuvant chemo(radio)therapy or upfront surgery with or without adjuvant chemo(radio)therapy between 2006-2013 were identified from the National Cancer Data Base. Propensity score matching was used to account for potential selection bias between patients undergoing neoadjuvant chemo(radio)therapy and upfront surgery. Survival analysis was performed using the Kaplan-Meier method. Results: 9,874 patients underwent upfront surgery and 4,864 patients received neoadjuvant therapy succeeded by surgery. Unadjusted, neoadjuvant therapy was associated with age £ 65 years (58.6% vs. 38.3%, p<0.0001), white race (79.8 vs. 58.7%, p<0.0001), academic treatment center (60.0% vs. 39.0%, p<0.0001), inadequate lymphadenectomy (< 15 nodes resected: 46.4% vs. 44.1%, p=0.0074) and total gastrectomy (42.0% vs. 30.2%, p<0.0001). After matching, covariates were well balanced with 4,221 each group. Neoadjuvant therapy was associated with decreased R1/2-resection rate (11.6% vs. 20.4%; p<0.0001) and 30-day mortality (2.9% vs. 4.3%; p=0.0004), but not with readmission (6.4% vs. 7.0%; p=02770), or hospital stay (>9 days: 47.3% vs. 45.3%; p=0.0700). In resected patients, neoadjuvant therapy demonstrated significant survival benefit compared to upfront surgery before (median survival, 35.4 vs. 26.3 months) and after (median survival, 34.8 vs. 29.3 months) matching. Conclusions: Although non-randomized, the results of this study suggest that neoadjuvant therapy improves surgical outcomes and may positively impact overall survival for locally advanced gastric cancer patients.

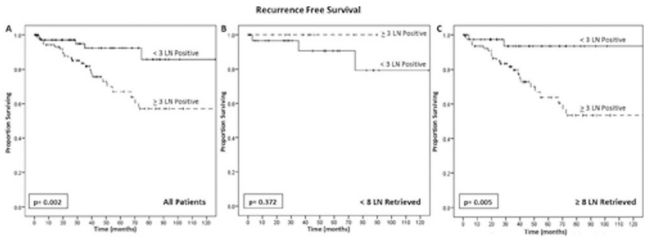


Kaplan-Meier survival curve comparing neoadjuvant chemo(radio) therapy to upfront surgery in locally advanced gastric cancer patients after matching.

PF169

Defining the Number of Lymph Nodes Needed to Accurately Stage Small Bowel Neuroendocrine Tumors: An Eight-Institution Study from the U.S. Neuroendocrine Tumor Study Group M.Y. Zaidi,[1]* A.G. Lopez-Aguiar,[1] M. Dillhoff,[2] E.W. Beal,[2] G. Poultsides,[3] E.A. Makris,[3] F.G. Rocha,[4] A. Crown,[4] K. Idrees,[5] P.M. Smith,[5] H. Nathan,[6] M. Beems,[6] D. Abbott,[7] J.R. Barrett,[7] R.C. Fields,[8] J. Davidson,[8] K. Cardona,[1] S.K. Maithel.[1] *1. Surgery, Emory University, Atlanta, GA; 2. The Ohio State University Comprehensive Cancer Center, Columbus, OH; 3. Stanford University Medical Center, Stanford, CA; 4. Virginia Mason Medical Center, Seattle, WA; 5. Vanderbilt University Medical Center, Nashville, TN; 6. University of Michigan, Ann Arbor, MI; 7. University of Wisconsin School of Medicine and Public Health, Madison, WI; 8. Washington University School of Medicine, St. Louis, MO.*

Background: Small bowel neuroendocrine tumors (SB-NETs) frequently involve regional lymph nodes (LNs). The prognostic value of LN positivity on recurrence of disease is not well defined. The number of LNs needed to accurately stage patients is unknown. Methods: All patients with primary SB-NETs who underwent curative-intent resection at 8 institutions in the US Neuroendocrine Tumor Study Group between 2000 and 2016 were identified. Patients with distant metastatic disease were excluded. The association of LN positivity with recurrence of disease and the extent of lymphadenectomy required were analyzed. Results: Of 2182 pts with resected NETs, 203 had SB-NETs. Median age was 60 yrs, 56% were male, and median follow-up was 39 months. 83.5% of patients (n=157) had LN positive disease. There was no difference in 3-yr recurrence free survival (3-yr RFS) among patients with 1 or 2 positive LNs compared to patients with negative LNs (p=0.63). Patients who had 3 or more positive LNs had a worse 3-yr RFS compared to those with 0, 1, or 2 positive LNs (n=92 vs n=73; 3-yr RFS 82%vs92%; p =0.002;Fig1a). Retrieval of 8 or more LNs was associated with a higher positive LN count compared to less than 8 LNs (4.6 vs 1.6; p<0.001). However, an increasing LN ratio was not associated with 3-yr RFS. When examining patients who had less than 8 LNs retrieved, there was no difference in 3-yr RFS in those patients with 3 or more positive LNs compared to those with 0, 1, or 2 positive LNs (3-yr RFS: 100% vs 91%; p=0.37;Fig1b). Retrieval of more than 8 lymph nodes, however, accurately discriminated patients with 3 or more positive LNs compared to those with 0, 1, or 2 positive LNs (3-yr RFS: 79.7% vs 93.5%; p=0.005;Fig1c). Conclusions: For patients undergoing curative-intent resection of small bowel NETs, accurate lymph node staging requires a minimum of 8 lymph nodes for examination. 3 or more positive LNs is associated with decreased 3-yr RFS compared to 0, 1, or 2 positive lymph nodes. A thorough regional lymphadenectomy is critical for accurate staging and management of patients with small bowel neuroendocrine tumors.



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A Comparison of Two-Step Retrogastric Lymphadenectomy Versus En Bloc Dissection During Resection for Gastroesophageal Malignancy M.J. Minarich,* U. von Holzen, R.E. Schwarz. *Goshen Center for Cancer Care, Goshen, IN.*

Objective: Extended lymph node dissection (ELND) remains an important component of curative intent resection of mid-stage gastric cancer (GC). Benefits include enhanced staging accuracy, extending regional disease control and optimizing potential curability. Methods: A traditional en bloc ELND was modified to facilitate greater ease of dissection with better exposure. The resulting 2-step technique includes a similar initial gastrectomy extent with resection of perigastric LNs, followed by transection of the left gastric lymphovascular pedicle. After completion of the gastrectomy component, retrogastric nodes are dissected in a separate, contiguous specimen. Data related to this technique were collected in an academic oncology practice and compared to outcomes obtained with en bloc resection. Results: Of 179 consecutive patients undergoing gastrectomy for a spectrum of neoplastic conditions (n=148) and some benign indications (n=31), 129 underwent an ELND (73%). There were 97 men and 32 women, with a median age of 64 years (range: 24-98). Resections included distal/subtotal (n=53, 41%), total (n=48, 37%) and proximal gastrectomies (including esophagogastric resections, n=28, 22%). The median total LN count was 25 (3-86). Two-step LND (n=35, compared to 94 en bloc LNDs) was performed predominantly in the second half of the study period. The two-step dissection yielded an average of 18.3 (+/- 8.5 S.D.) perigastric and 12.1 (+/- 5.8) retrogastric nodes. Two-step LND was associated with lower estimated blood loss (265 vs. 448 ml, p=0.0005), lower transfusion requirements (3 vs. 28%, p=0.002), greater mean total LN counts (30 vs. 26, p=0.01), a greater rate of obtaining at least 15 or 20 LNs (91 vs. 77% and 83 vs. 65%, p=0.05), and fewer R1 or R2 resections (9 vs. 23%, p=0.05). Conclusions: The 2-step LND technique was found to be associated with favorable operative and postoperative outcome parameters without compromising LN yield. It can be recommended for standard ELND indications in the absence of macroscopically abnormal LNs.

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Association Between Surgeon Specialty and Surgical Outcomes Following Esophagectomy A.H. Bui,* A. Ninh, M. Leitman. *Medical Education, Icahn School of Medicine at Mount Sinai, New York, NY.*

Introduction Esophagectomy is a complex procedure with a high risk for adverse postoperative outcomes. The purpose of this study is to assess whether surgical outcomes following esophagectomy are associated with surgeon specialty. Methods The American College of Surgeons National Surgical Quality Improvement Program database was queried for this study. All total and partial esophagectomies performed by general and thoracic surgeons from 2012-2015 were evaluated. Chi-square tests were performed to evaluate the association between surgeon specialty and postoperative outcomes. Multivariate analyses (logistic and linear regressions) were performed to adjust for relevant preoperative demographic and clinical variables. Results There were 4,879 esophagectomies, of which 2,716 (55.7%) were performed by general surgeons and 2,163 (44.3%) by thoracic surgeons. Of the esophagectomies performed by general surgeons, 1,271 (46.8%) were total and 1,445 (53.2%) partial; for thoracic surgeons, 781 (36.1%) were total and 1,382 (63.9%) partial (p<.0001). Return to operating room (OR) rates following esophagectomy were 11.8% for general vs. 18.4% for thoracic surgeons (p<.0001); esophagectomies performed by thoracic surgeons had 1.75 times increased odds of return to OR compared to general surgeons (95% CI=1.49-2.06). Postoperative myocardial infarction (MI) rates were 1.5% for general vs. 0.6% for thoracic surgeons (p=0.003); esophagectomies performed by thoracic surgeons were 0.37 times less likely to result in postoperative MI (95% CI=0.19-0.69). Rates of bleeding requiring transfusion were 16.0% for general vs. 20.5% for thoracic surgeons (p<.0001); total esophagectomies performed by thoracic surgeons were 2.1 times more likely to result in bleeding requiring transfusion (95% CI=1.70-2.71). Length of stay following total esophagectomy was on average 1.5 days longer when performed by a thoracic surgeon compared to a general surgeon (95% CI=0.51-2.44). Conclusion Outcomes following esophagectomy may vary according to the surgeon's specialty training. These approaches should be further evaluated to identify techniques and management protocols that may decrease risk of adverse outcomes in these patients.

PF172

Laparoscopic Hyperthermic Intraperitoneal Chemotherapy is Safe for Patients with Peritoneal Metastases from Gastric Cancer and May Lead to Gastrectomy T. Newhook,* A. Agnes, M. Blum, J. Estrella, S.R. Chowdhuri, A. Matamoros, P. Das, L. Ho, J. Ajani, B. Badgwell. *Surgery, MD Anderson Cancer Center, Houston, TX.*

Introduction: Laparoscopic hyperthermic intraoperitoneal chemotherapy (HIPEC) is a novel strategy for patients with gastric adenocarcinoma (GA) metastatic to the peritoneum. We aimed to evaluate the safety profile of laparoscopic HIPEC for patients with positive peritoneal cytology or carcinomatosis from GA. Methods: Outcomes were reviewed of patients with stage IV GA with peritoneal involvement who received laparoscopic HIPEC from June 2014 to January 2017 at The University of Texas MD Anderson Cancer Center. Laparoscopic HIPEC included a 60-minute perfusion of mitomycin C (30 mg) and cisplatin (220 mg) at an inflow temperature of 41-42°C and outflow temperature of 39-40°C. Results: A total of 71 HIPEC procedures were performed in 44 patients (1-5 HIPEC per patient; median 1). At diagnosis, 68% (n=30) had peritoneal carcinomatosis and 32% (n=14) had isolated positive peritoneal cytology. Three patients (7%) underwent laparoscopic HIPEC for palliative indications. All patients had initially received systemic chemotherapy, and 20 patients (45%) had received pre-procedural chemoradiotherapy. The median number of HIPEC procedures performed per patient was 1 (range 1-5 procedures). There were no conversions to open surgery, 2 outflow catheter obstructions, and 1 major (Clavien-Dingo grade III) surgical complication within 30 days. A total of 7 postoperative adverse hematologic events (>CTCAE 2) were observed in 5 total patients (11%), without any major renal or gastrointestinal adverse events within 30 days. 25% (n=11) of patients went on undergo secondary gastrectomy following resolution of peritoneal disease. The median overall length of hospital stay after laparoscopic HIPEC was 2 days (range 2-11 days). Conclusions: Laparoscopic HIPEC is a safe procedure and may be repeated in patients with peritoneal metastases from gastric cancer. Future studies are required to determine the optimal HIPEC regimen and timing relative to systemic therapy in order to best minimize morbidity.

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A Clinical Risk Score for Post-Operative Morbidity and Mortality in Young and Elderly Gastric Cancer Patients S. Nelen,[1] K. Bosscha,[2] V. Lemmens,[5] H. Hartgrink,[4] R. Verhoeven,[3] H. de Wilt.[1]* *1. Surgical Oncology, Radboud University Medical Center, Nijmegen, Netherlands; 2. Jeroen Bosch Hospital, 's-Hertogenbosch, Netherlands; 3. Netherlands Comprehensive Cancer Organization (IKNL), Utrecht, Netherlands; 4. Leiden University Medical Center, Leiden, Netherlands; 5. Erasmus University Medical Center, Rotterdam, Netherlands.*

Introduction: This study investigates age-related differences in surgically treated gastric cancer patients and aims to identify factors which predict outcome in order to create a clinical risk score. Methods: Data from the Dutch Upper gastrointestinal Cancer Audit were used. All patients with non-cardia gastric cancer between 2011-2015 were selected. Patients were divided and analyzed per age group(<70 vs. ≥70 years). Descriptive statistics were used to characterize both age groups. Multivariable logistic regression was used for both age groups to examine the influence of different clinicopathological factors on morbidity and mortality. The factors significantly associated with post-operative outcome were used to create a clinical risk score. Results: A total of 1,109 young and 1,206 elderly gastric cancer patients were included. Elderly patients had significantly more post-operative complications (41% vs. 33%, p<0.01), higher failure to rescue rates (7.7% vs. 1.7% p<0.01) and higher 30-day mortality rates compared to young patients (8.0% vs. 3.2%, p<0.01). In multivariable analysis, older age was associated with the occurrence of more complications (OR 1.29, 95% C.I. 1.05-1.59). Post-operative

mortality and failure to rescue were not significantly associated with age. Post-operative morbidity and mortality were most influenced by ASA-score, the ability to undergo neo-adjuvant chemotherapy and type of resection for both young and elderly patients. Discussion: ASA-score, the ability to undergo neo-adjuvant chemotherapy and type of resection are best overall predictors for post-operative morbidity and mortality in both young and elderly gastric cancer patients. Based on this a clinical risk score was made to aid pre-operative decision making.

PF174

Adjuvant Chemotherapy in the Treatment of Duodenal Adenocarcinoma S. Narayanan,* K. Attwood, S. Hochwald, B. Kuvshinoff, M. Kukar. *Roswell Park Cancer Institute, Buffalo, NY.*

Background: Duodenal adenocarcinoma is a rare and aggressive gastrointestinal cancer without standardized adjuvant chemotherapy treatment. We aimed to assess clinicopathologic and survival differences between patients who received adjuvant chemotherapy (AC) and those who received no chemotherapy (NC) at our institution. Methods: A database of patients with resected duodenal adenocarcinoma from 2000 to 2016 at Roswell Park Cancer Institute was created and divided into AC and NC groups. Survival outcomes (Overall survival- OS, Disease Specific Survival- DSS and Recurrence Free Survival-RFS) were summarized by cohort using standard Kaplan-Meier methods. Results: Of 41 patients identified, 20 were in the AC and 21 in NC groups. AC patients were younger with a mean age of 62.5 vs. 71.1 (p= 0.019). There were no differences in sex, race, co-morbidities, surgical procedure (pancreaticoduodenectomy vs. partial duodenectomy), tumor grade or pathologic T-stage between the 2 groups. There was also no difference in margin positivity, lymphovascular or perineural invasion, post-operative complications or length of stay. However, the NC had higher 30-day re-admission (23.8% vs. 0%, p= 0.049). The AC group had larger tumors (5.9 vs. 4.1cm, p= 0.039), more node positive patients (80% vs. 35%, p=0.003) and higher pathologic stage (stage II- 15% vs. 31.6% and stage III- 75% vs. 26.3%, p=0.001) than NC patients. Only 15.4% of patients of patients were treated with adjuvant radiation and all were in the AC group. Median OS was longer for NC compared to AC but was not statistically significant (79.8 vs. 49.4 months, p= 0.69). 3-year OS (68% vs. 74%, p=0.69), DSS (73% vs. 84%, p=0.13) and RFS (51% vs. 79%, p=0.12) trended towards inferior survival in AC vs. NC patients, without statistical significance. Conclusions: In this evaluation of patients who received AC after duodenal resection, we found that AC patients had bulkier, more node positive and higher stage tumors. These patients were likely selectively chosen to receive chemotherapy due to their tumors' biologic aggressiveness and thus trended towards having poorer survival. A larger cohort is needed to better evaluate the role of adjuvant therapy.

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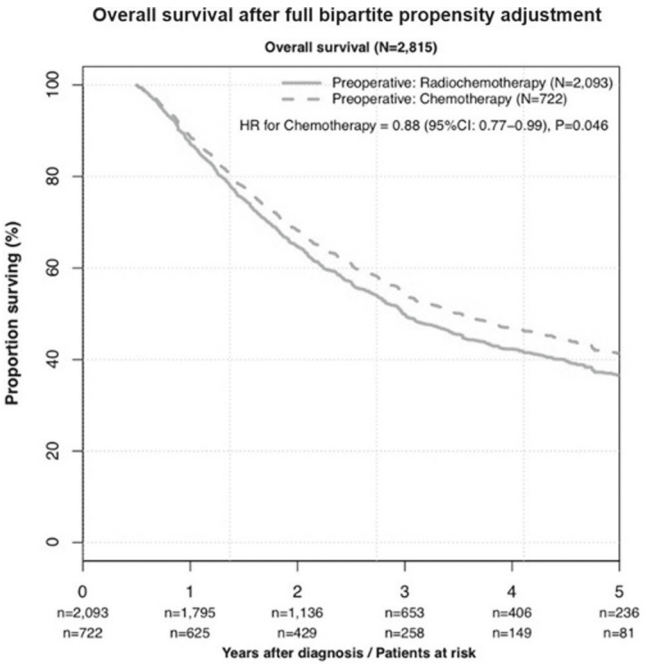
Neo-adjuvant Chemotherapy Improves Survival Compared to Neo-adjuvant Radio-Chemotherapy Among Gastric Cardia Cancer Patients C. Tsai,[1] A. Müller,[1] R. Warschkow,[2] D.P. Nussbaum,[3] S. Bruno,[2] B. Gloor,[1] D.G. Blazer,[3] M. Worni.[1]* *1. Department of Visceral and Transplantation Surgery, Inselspital, Bern University Hospital, University of Bern, Switzerland, Bern, Switzerland; 2. Department of Surgery, Kantonsspital St. Gallen, 9007, St. Gallen, Switzerland, Bern, Switzerland; 3. Department of Surgery, Duke University Medical Center, Duke University, Durham, NC, USA, Durham, NC.*

Background: Surgery is an integral part in treatment algorithms of cardia cancer in potentially curative settings. Both neo-adjuvant chemo-radiotherapy (neo_chemo_XRT) and neo-adjuvant chemotherapy (neo_chemo) have proven to be superior to surgery alone. However, whether one regimen is more beneficial than the other is unknown given no head-to-head comparison exists. The primary aim of this study was to assess whether neo_chemo_XRT or neo_chemo is superior concerning overall survival (OS) on a population-based level. Methods: The National Cancer Data Base was reviewed from 2006 to 2012 to identify non-metastatic adult cardia cancer patients who underwent surgical resection and were treated with 1) neo_chemo_XRT or 2) neo_chemo. OS was assessed using Cox proportional hazard regression analyses before and after exact weighted propensity score adjustment. Results: Of the 4033 patients included, 3041 (75.4%) underwent neo_chemo_XRT and 992 (24.6%) underwent neo_chemo. Most patients were male (n=3374, 83.7%), mean age was 61 years (SD 10.2). Patients who received neo_chemo_XRT more often had an R0 resection compared to neo_chemo (90.8% vs. 85.3%, p<0.001, respectively), while comorbidities were similar between the two groups. Treatment strategies did not differ over time. Unadjusted 2-year OS rates were 65.8% (95%CI: 64.0-67.5) for neo_chemo_XRT and 69.1% (66.2-72.1) for neo_chemo (p=0.16). In multivariable adjusted analyses, patients treated with neo_chemo had better overall survival compared to neo_chemo_XRT (HR: 0.88, 95%CI: 0.79-0.98, p=0.02). Patients with G3/4 tumors, positive resection margins, more comorbidities, and older patients (>65 years) had worse OS compared to their counterparts. The survival difference favoring neo_chemo persisted even after exact weighted propensity score adjustment (HR: 0.88, 95%CI: 0.77-0.99, p=0.046). Conclusion: The results of this study support the use of neo_chemo over neo_chemo_XRT among patients with cardia cancer. The wide use of neo_chemo_XRT in the United States should be reconsidered and further evaluated with a direct comparison of the two regimens by a prospective randomized controlled trial.



Kaplan-Meier survival curve of overall survival after full bipartite propensity adjustment comparing neo-adjuvant chemo-radiotherapy and neo-adjuvant chemotherapy.

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The Influence of Helicobacter Pylori on Regulatory T Cells in Gastric Cancer S. Urakawa,* K. Nishida, R. Kato, M. Mori, Y. Doki, H. Wada. *Gastroenterological Surgery, Osaka University, Osaka, Japan.*

<Background and Aim> Regulatory T cells (Tregs) have a suppressive role in antitumor immunity. Effector Tregs (eTregs), which have highly suppressive functions, are located in a subpopulation of $Foxp3^+$ $CD4^+$ Tregs. We have reported that ICOS has the potential as a novel prognostic biomarker for patients with gastric cancer as well as a marker for eTregs. Because $ICOS^+$ eTregs were abundant in gastric cancer, we speculate that H. pylori(HP) infection may influence the infiltration of $ICOS^+$ eTregs into gastric cancer. In this study, we try to investigate the induction of $ICOS^+$ eTregs <Materials and Methods> Tissue-infiltrating mononuclear cells were extracted from fresh gastric cancer tissues with the gentleMACS Dissociator. First, the expression of % ICOS-L in plasmacytoid dendritic cells (pDCs) and % ICOS in $Foxp3^+$ cells were analyzed by flow cytometry. Second, the involvement of HP infection in the expression of ICOS in Tregs was analyzed by flow cytometry and by multicolor immunohistochemistry. Finally, we investigated the effect of eradicating therapy for HP on $ICOS^+$ eTregs. <Result> % ICOS-L in pDCs was closely related to % ICOS in $Foxp3^+$ cells (r^2=0.52, p<0.001). In vitro assay, $ICOS^+$ eTregs were efficiently induced from naïve $CD4^+$ T cells with the agonistic ICOS-L protein under a stimulation with TGF-β and CD3/CD28 mAbs. % TLR9 and % ICOS-L in pDCs were significantly higher in patients

with the H. pylori antibody (HP-Ab) than without the HP-Ab (p=0.001 and p=0.042, respectively.). Furthermore, $ICOS^+$ eTregs were significantly higher in patients with HP-Ab than without the HP-Ab (p=0.020). In multicolor immunohistochemistry, a large number of $ICOS^+$ cells showed the co-expression of Foxp3 (p=0.007). $ICOS^+$ eTregs were significantly lower in patients who underwent eradication therapy for HP than in those with HP <Conclusion> The expression of $ICOS^+$ eTregs was closely related to pDCs. Our results demonstrate the potential of eradicating therapy for HP as an indirect immune therapy for gastric cancer.

PF177

Robotic Versus Laparoscopic Gastrectomy for Gastric Adenocarcinoma: Propensity Matched Analysis of the National Cancer Database S.P. Ryan,[1]* A. Tameron,[1] A. Murphy,[1] L. Hussein,[1] E. Dunki-Jacobs,[2] D.Y. Lee.[2] *1. TriHealth, Good Samaritan Hospital Residency Program, Cincinnati, OH; 2. Trihealth Cancer Institute, Cincinnati, OH.*

Background There has been increased adoption of robotic technology in gastrointestinal surgical oncology. We compared the outcomes of laparoscopic (LG) and robotic gastrectomies (RG) performed for gastric adenocarcinoma (GA) in the National Cancer Database (NCDB). Methods The NCDB database was queried for patients ≥ 18 years old with stage I-III GA who underwent LG or RG. Propensity matching was performed between the two groups with regards to clinical staging, adjuvant treatment, demographics, and the extent of surgery. Results A cohort of 1893 (1262-LG, 631-RG) patients was identified in a 2:1 propensity match. Demographics and co-morbidities were similar between the groups. Clinical staging and extent of surgery were well matched. The rate of negative margins, 30-day and 90-day mortality was similar between the two groups. Outcomes with respect to readmission and length of stay were also similar (Table 1). Long-term survival was not significantly different between the two cohorts with a median survival of 49 months in the LG group and 56.1 months in the RG group (p=0.405). Also, lymph node (LN) positivity was similar between the two groups (40.1 % vs 42.8%, p= 0.278). However, the average number of LNs sampled was significantly higher in the RG group compared to the LG group (19.6 vs 17.4, p<0.001). Similarly, the percentage of surgeries in which ≥15 LNs were sampled was greater in the RG group compared to the LG group (63.9% vs 57.6%, p=0.010). Conclusion A greater number of patients in the RG group achieved the NCCN guideline goal of harvesting ≥15 lymph nodes for more accurate staging. RG may allow a greater harvest of lymph nodes without increasing short term adverse outcomes compared to LG. Long term outcomes in this well matched cohort appears comparable for both approaches.

Table 1- Baseline demographics, tumor characteristics, treatment details and short-term outcomes

Characteristics	Robotic Gastrectomies (n=)	Laparoscopic Gastrectomies (n=)	p value
Age	64.5 ± 11.9	65.1 ± 11.8	0.359
Gender			0.889
Male	449 (71.2%)	906 (71.8%)	
Female	182 (28.8%)	356 (28.2%)	
AJCC Clinical Staging			1.000
1	217 (34.4%)	434 (34.4%)	
2	241 (38.2%)	482 (38.2%)	
3	173 (27.4%)	346 (27.4%)	
Charlson Comorbidity Score			0.263
0	421 (66.7%)	845 (67.0%)	
1	165 (26.1%)	331 (26.2%)	
≥2	45 (7.1%)	86 (6.8%)	
Extent of Surgery			0.885
Total Gastrectomy	174 (27.6%)	352 (27.9%)	
Subtotal Gastrectomy	457 (72.4%)	910 (72.1%)	
Chemotherapy			0.162
None	452 (71.6%)	829 (65.7%)	
Single-agent	22 (3.5%)	56 (4.4%)	
Multi-agent	157 (24.9%)	355 (28.1%)	
Unknown type	2 (0.3%)	22 (1.7%)	
Radiation			0.945
No	424 (67.2%)	850 (67.4%)	
Yes	207 (32.8%)	412 (32.6%)	
Length of Stay (Median)	8 days	8 days	0.145
Readmission	44 (7.0%)	85 (6.9%)	0.932
30-day Mortality	19 (4.5%)	26 (2.7%)	0.101
90-day Mortality	34 (8.2%)	54 (5.8%)	0.109
Negative Margins	574 (91.7%)	1133 (90.9%)	0.549

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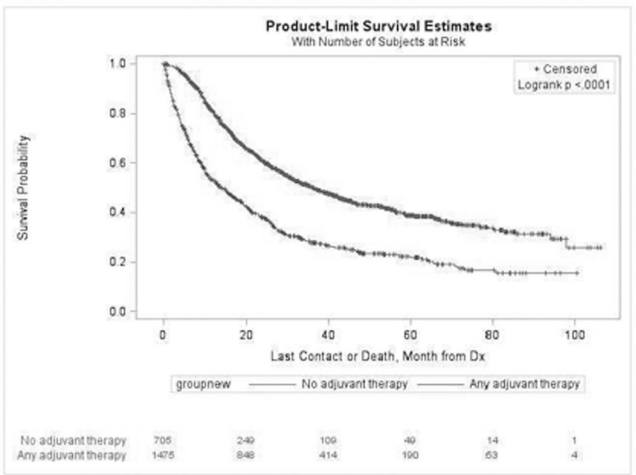
Clinical Impact of Underutilization of Adjuvant Therapy in Node Positive Gastric Adenocarcinoma R. Zhu,* F. Liu, G. Grisotti, J. Perez Irizarry, R. Salem, C. Cha, K. Johung, D. Boffa, Y. Zhang, S.A. Khan. *Surgery, Yale University School of Medicine, New Haven, CT.*

Introduction: Adjuvant therapy in the treatment of gastric adenocarcinoma has been demonstrated to provide a survival advantage, though it may be underutilized. The purpose of this study is to examine how infrequently adjuvant therapy is administered with curative intent gastrectomy for node positive gastric cancer and the long-term effects to patients. Methods: The National Cancer Database was queried from 2006-2013 for patients with node positive gastric adenocarcinoma who underwent a potentially curative gastrectomy. Patients who received adjuvant chemotherapy or chemoradiation were compared to those who did not. Overall survival was compared after adjusting for demographics and tumor related factors. Results: Of 2,565 patients, 793 (30.9%) patients did not receive any adjuvant chemotherapy or radiation therapy, while 147 (5.7%) received peri-operative chemotherapy and 748 (28.2%) received post-operative chemoradiation. From 2006-2013, the percentage of patients receiving peri-operative chemotherapy rose from 1.1% to 9.9%, while those receiving post-operative chemoradiation decreased from 39.7% to 21.6%. Peri-operative chemotherapy was associated with higher rate of R0 resections (90.7% vs 77.9%, p<0.0001). The adjusted restricted mean survival time over 5 years for patients who did not receive any adjuvant therapy was 27.8 months, who received peri-operative chemotherapy was 39.6 months, and who received post-operative chemoradiation was 37.7 months (p<0.0001). Conclusion: Approximately one third of patients treated for node positive gastric cancer undergo surgical resection without adjuvant therapy. This is associated with poorer survival compared to patients receiving adjuvant therapy, highlighting the need for improvement in multimodality care across the United States to improve cancer outcomes.



Kaplan Meier curve depicting overall survival by administration of any adjuvant therapy.

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To Evaluate the Outcomes of Physical Activity in Patients Who Have Undergone Thoracic Esophageal Cancer Surgery H. Sato,* Y. Miyawaki, M. Aikawa, K. Okamoto, S. Sakuramoto, S. Yamaguchi, I. Koyama. *Gastroenterological Surgery, International Medical Center Saitama Medical University, Hidaka, Japan.*

Introduction: Cardiopulmonary exercise testing (CPX) and Shuttle walking test (SWT) are non-invasive, objective methods of assessing integrated response of the heart, lungs, and musculoskeletal system to incremental exercise. This study aimed to evaluate the impact of physical activity using CPX or SWT in patients who underwent a transthoracic esophagectomy. Methods: 34 patients who underwent a transthoracic esophagectomy were enrolled into the Enhanced recovery after surgery (ERAS) program that included early post-operative enteral nutrition and mobilization. Each patient was evaluated using CPX on both the day of an admission day (pre) and day of discharge (post). On the other hand, 22 patients were enrolled into this program using SWT. The

program was started on the first postoperative day (POD 1). Routine postoperative bronchoscopy for toileting sputum and mechanical bowel preparation (MBP) before surgery were only performed when considered to be necessary. Outcome metrics comprised peakVO2, peak workload, and anaerobic threshold (AT) in CPX, the distance in SWT. Results: In CPX, PeakVO2 (mL/kg/min) was 21.9 ± 4.4 (pre) and 17.0 ± 3.7 (post) ($p<0.01$). Peak workload (watt) was 101.8 ± 23.5 (pre) and 76.5 ± 22.0 (post) ($p<0.01$). AT(mL/kg/min) was 12.6 ± 2.2 (pre) and 11.3 ± 1.7 (post) ($p<0.01$). The rates of decrease for peak VO2 and workload were 26.4% and 24.9%, respectively. In SWT, 521.4m in preoperative status, 477.1m in postoperative month 6 (POM 6), and 491.4m in POM 12. Conclusions: Physical activity on the day of discharge decreased by approximately 25% and 4.9 METS which was calculated based on peakVO2. This level is not limited in daily usual life, but not enough to keep quality of life. The data of SWT indicated about 94% in POM12 compared with preoperative status.

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Disparate Utilization of Staging Laparoscopy for Gastric Cancer in the U.S. E.M. Groh,* L. Enewold, Z. Brown, R.T. Ripley, J.M. Hernandez, J.L. Davis. *Surgical Oncology Section, TGIB, National Cancer Institute, Bethesda, MD.*

Introduction: Staging laparoscopy (SL) for gastric adenocarcinoma is recommended to identify radiographically occult metastatic disease and prevent unnecessary laparotomy. The goal of this study was to characterize population-based utilization of SL for gastric adenocarcinoma and identify factors related to its use. Methods: Surveillance, Epidemiology and End Results (SEER)-Medicare linked data from 2004-2013 were used to identify patients aged 65 or older diagnosed with gastric adenocarcinoma. Patients who underwent gastric cancer-related surgery (laparoscopy, laparotomy, gastric bypass or gastrectomy) were characterized further. Laparoscopy that occurred from 30 days pre-diagnosis to 3 months post-diagnosis, and occurred before or on the same day as laparotomy or therapeutic surgery, was considered SL. Annual rates of SL were determined and logistic regression analysis was performed to identify factors associated with utilization of SL. Results: During the study period, 5,610 patients underwent surgery related to gastric adenocarcinoma. SL was carried out in 733 patients (13%), of whom 258 (35%) underwent no additional surgical procedures. Of the 4,877 patients (87%) that did not undergo SL, 463 (9%) underwent laparotomy with no gastrectomy or gastric bypass suggesting an unnecessary laparotomy. Patients with unnecessary laparotomy had significantly increased length of stay and in-hospital mortality compared to patients who underwent SL without gastrectomy ($p<0.01$). Multivariate results indicated that undergoing SL was more likely among females and in the Northeast and was less likely among Hispanics and patients who were not married ($p\leq0.02$). The annual rate of staging laparoscopy increased significantly throughout the study period ($p<0.01$). Conclusion: Utilization of staging laparoscopy in the management of gastric cancer is steadily increasing in the U.S. However, procedure rates vary by patient characteristics and geographic region suggesting irregular application of clinical practice guidelines. Laparoscopy should continue to be used to prevent unnecessary laparotomy and improve detection of occult metastatic disease.

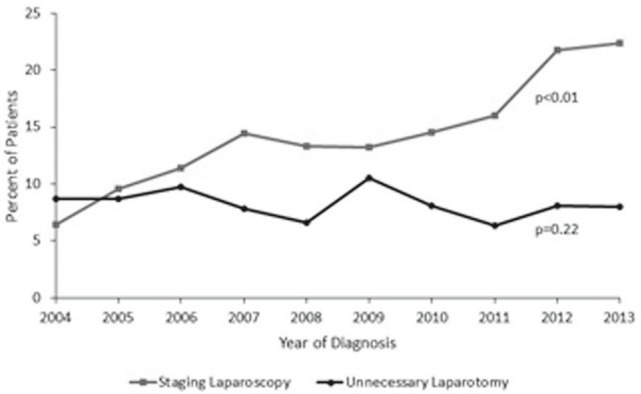

Figure 1. Temporal Trends of Staging Laparoscopy and Unnecessary Laparotomy among individuals who underwent operation for gastric cancer diagnosed between 2004 and 2013, SEER-Medicare (n=5,610)

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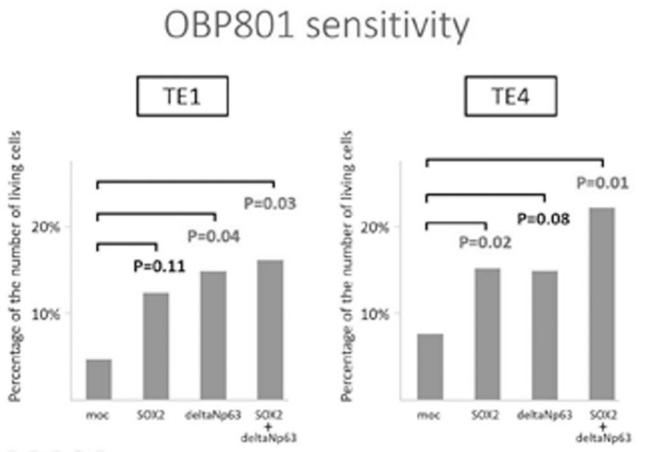
Identification the Molecular Mechanisms that Explain a Novel Histone Deacetylase Inhibitor OBP-801 Sensitivity in Human Cancer Y. Ooizumi,* K. Yamashita, y. kazuko, K. Igarashi, K. Kojima, H. Katoh, T. Yamanashi, T. Sato, T. Nakamura, M. Watanabe. *Kitasato University School of Medicine, Sagamihara-shi, Japan.*

<Introduction⟩ OBP-801, a novel histone deacetylase (HDAC) inhibitor, is currently under a phase I trial by the U.S. Food and Drug Administration. In this study, we clarified the effects of OBP-801 in human cancer cell lines, and identify the predictive biomarkers to OBP-801 chemo therapy. <Methods⟩ OBP-801 sensitivity was assessed in 36 strains of human cancer cell lines. To explore the molecular profiles determining of OBP-801 sensitivity, expression microarrays (harboring 54675 genes) were performed. 5-Aza-2′-deoxycytidine (5-Aza-dC) and trichostatin A (TSA) treatments were done to evaluate whether epigenetic factors regulate the gene candidates. OBP-801 resistant gene candidates were selected and transfected into OBP-801 sensitive cell lines. OBP-801 sensitivity, cell count assay, cell proliferation assay were done after transfections. <Results⟩ (1) OBP-801 inhibits cell proliferations in all of 36 cell lines by dose-dependent manner. Only 6 cell lines could be viable over 50% at a concentration of 10nM OBP-801. Esophageal squamous cell carcinoma (ESCC) cell lines has both of the sensitive strains (TE1. TE4) and the resistant strains (TE6. TE10. TE11). (2) Using expression microarray, 20 genes were selected as resistant gene candidates, and 5 genes were selected as sensitive gene candidates. The expressions of SOX2 and deltaNp63 showed strong correlation with OBP-801 resistance. (3) 5-Aza-dC and TSA treatment showed robust downregulation of both SOX2 and deltaNp63 overexpressed in OBP-801 resistant ESCC cell lines. (4) SOX2 and deltaNp63 expressed independently. (5) Transfections both SOX2 and deltaNp63 enhanced proliferative ability in TE1 ($p=0.0005$) and TE4 ($P=0.02$), and OBP-801 resistivity in TE1 ($P=0.03$) and TE4 ($P=0.01$). <Conclusions⟩ We narrowed down candidate genes to SOX2 and deltaNp63. Both genes have been recently focused on in the context of stem cell signatures of SCC. And we revealed the overexpression of both candidate genes are tightly regulated by an epigenetic manner. We predict that those representing stem cell signatures as the predictive biomarkers to OBP-801 chemo therapy in ESCC cells.



Percentage of the number of living cells transfected with SOX2 and deltaNp63 after OBP-801 administration.

PF182

Examining National Trends of Endoscopic Resection and Gastrectomy for Gastric Cancer F.S. Dahdaleh,* A. Benjamin, S.K. Sherman, M. Posner, K. Turaga. *Surgery, Section of General Surgery/Surgical Oncology, University of Chicago Medicine, Chicago, IL.*

Background: The staging and management of early gastric cancer (EGC) has been enhanced by the use of endoscopic ultrasound and resection (ER). We hypothesized that ER is less likely to represent a curative surgical strategy for Western patients with EGC. Methods: The NCDB was queried for patients diagnosed with clinical T1N0 gastric adenocarcinoma who underwent definitive surgical therapy. Trends in procedure type over time were analyzed using

Chi-squared trend analysis. Propensity score matching was performed against age, margin status, Charlson-Deyo comorbidity (CD) score and histology. Cox regression identified covariates associated with overall survival (OS) after propensity matching. Results: Between 2004 and 2012, 4258 patients with EGC were included; 1034 underwent ER. Median follow-up was 35.6 months. Over that period, the use of ER increased from 11 to 34% (P<0.001). Patients were more likely to undergo ER if they were >75 years old (41.3% vs 28.1%, P<0.001), had lower CD scores (CD0: 73.8% vs 63.8%, P <0.001) or were treated at an academic program (65.0% vs 45.0%, P<0.001). R1 margins were more common in the ER group (9.6% vs 1.5%, P<0.001), and upstaging occurred in 14.3% of the gastrectomy group. All upstaged patients received adjuvant radiation, and 53 (5.1%) of ER patients as well as 360 (11.2%) of gastrectomy patients received adjuvant chemotherapy. On multivariate analysis, and after propensity matching, ER did not affect OS (HR: 0.88, 95% CI: 0.73-1.07; P=0.19). Conclusions: Despite a paucity of level I evidence to support the utility of ER in EGC in Western countries, its use increased over time in this nationwide cohort. While ER presents as an attractive and less invasive option for the treatment of EGC, pathologic upstaging after gastrectomy and inadequate margins contest its oncologic adequacy. This was not reflected as a significant difference in OS in this study, which is potentially due to limited follow-up time and selection bias.

Patient and Tumor Characteristics for Early Gastric Cancer Treated by Endoscopic Resection (ER) Versus Gastrectomy

	ER	Gastrectomy	P-Value
Number of patients	1034 (24.3%)	3224 (75.7%)	<0.001
Stage	.	.	<0.001
I	578 (55.9%)	2443 (75.8%)	
IA	347 (33.6%)	419 (13.0%)	
IB	109 (10.4%)	362 (11.2%)	
Age (years)	.	.	<0.001
>75	427 (41.3%)	907 (28.1%)	
66-75	313 (30.3%)	1013 (31.4%)	
56-65	198 (19.1%)	815 (25.3%)	
18-55	96 (9.3%)	489 (15.2%)	
Male	747 (72.2%)	2263 (70.2%)	0.207
Race	.	.	<0.001
Caucasian	916 (88.5%)	2579 (80.0%)	
Black	53 (5.1%)	343 (10.6%)	
Other	65 (6.3%)	302 (9.4%)	
Margin Status	.	.	<0.001
R0	658 (63.6%)	3010 (93.4%)	
R1	99 (9.6%)	47 (1.5%)	
R2	5 (0.5%)	3 (0.1%)	
Unknown	272 (26.3%)	164 (5.1%)	
Histology	.	.	<0.001
Well differentiated	169 (16.3%)	465 (14.4%)	
Moderately differentiated	354 (34.2%)	1365 (42.3%)	
Poorly differentiated	144 (13.9%)	1070 (33.1%)	
Undifferentiated	8 (0.8%)	23 (0.7%)	
Not determined	359 (34.7%)	301 (9.3%)	
Size, mean (SD) (cm)	6.4 (1.76)	5.4 (1.50)	0.100
Charlson-Deyo Score	.	.	<0.001
0	763 (73.8%)	2058 (63.8%)	
1	176 (17.0%)	853 (26.4%)	
2	95 (9.2%)	313 (9.7%)	
Adjuvant Radiation	68 (6.6%)	278 (8.6%)	0.036

PF183

Changes in Patterns of Care and Patient Outcomes After Adoption of Perioperative Chemotherapy in the Treatment of Esophagogastric Cancer Z. Senders,[1]* E. Chen,[2] J. Hardacre,[1] J. Kim,[1] J. Ammori.[1] *1. Surgery, University Hospitals Cleveland Medical Center, Cleveland, OH; 2. Case Western Reserve University School of Medicine, Cleveland, OH.*

Introduction: Results of the MAGIC trial were published in 2006 and support the use of perioperative chemotherapy in the treatment of resectable esophagogastric (EG) cancer. The purpose of this study is to assess changes in the patterns of care and compare patient outcomes before and after the adoption of peri-operative chemotherapy in the treatment of EG cancer at our institution. Methods: Retrospective data was collected on 190 patients who underwent resection with curative intent for EG cancer from 2004-2015 at a single institution. Results: Patients were significantly more likely to receive neoadjuvant therapy beginning after 2008. Patients treated after 2008 were significantly younger, had higher BMI, and were more likely to be white. Other demographics and the incidence of co-morbidities were similar between groups. Patients in the later group had lower stage at surgery, had significantly smaller tumors, and were more likely to have tumors located at the EG junction. There was no difference in histologic grade. Patients were significantly more likely to receive a laparoscopic procedure, esophagectomy, total vs partial gastrectomy, and D2 vs D1 lymphadenectomy after 2008. Accordion severity scores were similar between groups. There was no significant difference in overall or recurrence free survival. After 2008, non-white patients were less likely to receive any chemotherapy compared to white patients, and those who received chemotherapy were more likely to receive adjuvant versus neoadjuvant or perioperative treatment, though stage was similar (p=.35). There were no significant differences in therapy by race in the earlier group. Conclusion: Changes in treatment of EG cancer based on the results of the MAGIC trial were adopted at our institution after 2008, with no statistically significant increase in survival. Improvements in stage and tumor size after 2008 could be attributed to changes in therapy, however differences in demographics and disease presentation confound this explanation. Racial disparities were introduced with changes in treatment after 2008, the causes of which require further examination.

Table 1. Clinicopathologic features and treatment details

	2004-2008 (n=63)	After 2008 (n=128)	p
	Median (IQR)		
Age (years)	74 (63-82)	68 (59-76)	0.05
Race	*n (%)*		**0.02**
White	39 (64%)	102 (80%)	
Non-white	22 (36%)	26 (20%)	
Gender			0.3
Male	37 (59%)	85 (66%)	
Female	26 (41%)	43 (34%)	
Tobacco use	41 (73%)	87 (71%)	0.73
Co-morbidities			
Coronary artery disease	15 (25%)	31 (24%)	0.98
Diabetes mellitus	9 (15%)	29 (23%)	0.19
COPD	7 (11%)	15 (12%)	0.93
Peripheral vascular disease	7 (11%)	16 (13%)	0.81
Chronic kidney disease	6 (10%)	6 (5%)	0.19
Heart failure	5 (8%)	14 (11%)	0.54
Stroke	5 (8%)	8 (6%)	0.63
Myocardial infarction	4 (7%)	6 (5%)	0.6
Stage			**0.01**
0	1 (2%)	10 (8%)	
1	21 (33%)	41 (32%)	
2	13 (21%)	28 (22%)	
3	20 (32%)	46 (36%)	
4	8 (13%)	2 (2%)	
Type of surgery			**<0.001**
Laparoscopic	0 (0%)	27 (21%)	
Open	61 (97%)	101 (79%)	
Resection type			**<0.001**
Total gastrectomy	17 (27%)	46 (36%)	
Partial gastrectomy	38 (60%)	32 (25%)	
Esophagectomy	8 (13%)	49 (39%)	
Lymphadenectomy			**<0.001**
D1	38 (60%)	52 (41%)	
D2	17 (27%)	72 (56%)	
Other	8 (13%)	4 (3%)	
Length of stay (days)	9 (7-11)	8 (7-10)	0.43
	Mean (SE)		
Accordion Grade	1.9 (.21)	2.1 (.14)	0.58
Lesion size	5.58 (0.44)	4.06 (0.33)	**<0.01**
Metastatic Lymph Node Ratio	0.24 (0.04)	0.16 (0.02)	0.07
Nodes Examined	19.1 (1.4)	21.3 (1.0)	0.19
Tumor grade	*n (%)*		0.96
Well differentiated	1 (2%)	2 (2%)	
Moderately differentiated	21 (35%)	38 (33%)	
Poorly differentiated	38 (63%)	76 (66%)	
Chemotherapy regimen			**<0.001**
None	26 (41%)	38 (30%)	0.14
Adjuvant	28 (44%)	29 (23%)	**0.002**
Neoadjuvant	7 (11%)	40 (31%)	**0.001**
Peri-operative	2 (3%)	21 (16%)	**0.004**
5-year overall survival	37%	38%	0.53
5-year recurrence free survival	34%	32%	0.81

	Non-white (n=22)	White (n=39)	p
2004-2008			
Any chemotherapy	10 (45%)	27 (69%)	0.07
Adjuvant	9 (90%)	19 (70%)	0.18
Neoadjuvant	1 (10%)	6 (22%)	0.37
Peri-operative	0 (0%)	2 (7%)	0.25
	Non-white	**White**	
After 2008	**(n=26)**	**(n= 102)**	**p**
Any chemotherapy	14 (54%)	76 (75%)	**0.03**
Adjuvant	8 (57%)	21 (27%)	**0.03**
Neoadjuvant	3 (21%)	37 (49%)	**0.05**
Peri-operative	3 (21%)	18 (24%)	0.85

PF184

Moffitt Cancer Center Experience with Esophageal Cancer in Hispanics in the U.S.: Under-Diagnosed or Different Biology?

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PURPOSE: To compare the characteristics of Hispanic vs Caucasian patients with esophageal cancer, their disease, and their treatments using an institutional database at a high-volume cancer center over a 26 year period. METHODS: Data for esophageal cancer patients was prospectively collected in an IRB approved database at Moffitt Cancer Center from 1991-2017. 1027 patients received surgical intervention of which 903 had complete clinical data and were included. All histologies of esophageal cancers were reviewed. Demographics, risk factors, tumor characteristics, and treatment course were analyzed between Hispanic and Caucasian patients. RESULTS: 877 Caucasian and 26 Hispanic patients were included in this review. The clinical stage at diagnosis of Hispanics vs Caucasians was not significantly different between the groups (p=0.505). Histology of tumors were 78% vs 86% Adenocarcinoma, 15% vs 12% Squamous Cell Carcinoma, 0% vs 1% Adenosquamous Carcinoma, and 7% vs 1% other pathologies for Hispanics vs Caucasians, respectively. (p=0.027) Similar anatomic locations were noted with ~90% of tumors in the lower third and GE junction. No difference was seen in gender, tobacco or alcohol use, response to therapies, post-operative complications, or recurrence of disease. Hispanic patients trended toward higher use of neoadjuvant treatments (81% vs 66%, p=0.09), and did receive more adjuvant therapies (25% vs 15%, p=0.02) than Caucasian patients. For Hispanics vs Caucasians, the average time from onset of symptoms to diagnosis was 6.6 vs 8.4 months, the average time from diagnosis to surgery was 5.1 months for both groups, and the average time from surgery to recurrence was 24.6 vs 14.9 months. CONCLUSION: Esophageal cancer in surgically treated Hispanic patients is rarely seen at Moffitt Cancer Center. The low incidence in our population suggests the disease may be either under-identified or may have a different biology in Hispanics vs Caucasians. Our comparison noted lower rates of adenocarcinomas and a higher rate of adjuvant therapy usage for Hispanics. Epidemiologic studies as well as genomic comparisons of tumors are indicated for future pursuit.

PF185

Perioperative and Oncologic Results After Multimodal Treatment for Gastric Cancer in a High Volume Institution in Chile

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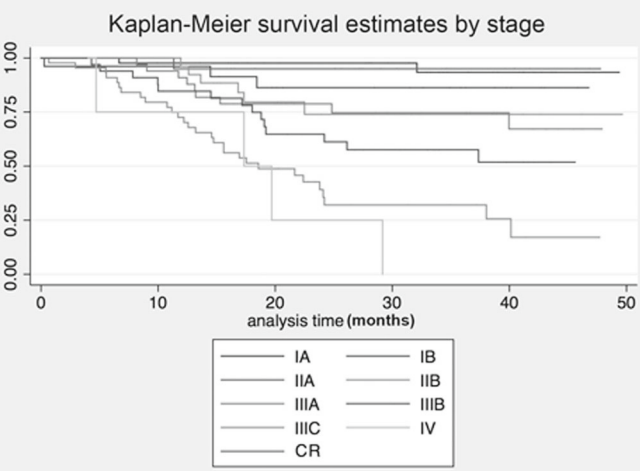
Introduction: Chile is among countries with the highest incidence of Gastric Cancer (GC) in the world. Multimodal treatment has proven to be the best treatment compared to surgery only, however standard treatment and timing is still a matter of debate. The study aim is to analyze perioperative and oncologic results after multimodal treatment for GC in a high volume center in Chile with evolving standards of neoadjuvant and adjuvant treatment. Methods: All patients with biopsy proven gastric adenocarcinoma and fit for curative intent treatment were included in a prospective data base between August 2013 - 2017. Data included perioperative results, pathology and oncologic results. Operative variables included type of surgery, blood loss, hospital stay, post operative morbidity and mortality 90 days post surgery. Pathology data included tumor differentiation, surgical margins and lymphnode retrieval. Oncologic results were analyzed based on median survival and pTNM stage survival (8th Edition). Results: 255 patients were treated for Gastric Adenocarcinoma with curative intent, Median age was 65 years (range 28-89). 56% were indicated perioperative or adjuvant chemotherapy. 85%(n=217) underwent a total gastrectomy with D2 lymphadenectomy. Median blood loss was 200ml (range 50-1500), with a lenght of hospital stay = 8 days (range 6-188). Post operative morbidity (Clavien>III) was 10%(n=26) with 90 day mortality = 0.8%(n=2) and in hospital mortality = 1.1%(n=3). Post operative pathology showed 63% poorly differentiated tumors with 34% signet cell carcinoma. R0 margins = 99%(n=254), median node retrieval = 47(range 18-103). pTNM was stage I= 29.5%, stage II= 21.9%, stage III= 46.8%, IV= 1.7%. Median follow up was 24 months with overall 3 and 4 year survival of 54% and 22% respectively. 3 year stage survival was 84%(stage I), 65%(stageII), 35%(stageIII) and 0%(stage IV) (p<0.001) Conclusion: Gastric Cancer proves an agressive biology in Chile although good 3 year survival after multimodal treatment and adequate oncologic surgery



PF186

Regional Variation in the Costs of Treating Curatively Resected Gastric Cancer Y. Jeong,[1]* A. Mahar,[3] B. Zagorski,[2] N. Coburn.[1] *1. Surgery, University of Toronto, Toronto, ON, Canada; 2. Institute of Health Policy, Management and Evaluation, Toronto, ON, Canada; 3. Sunnybrook Research Institute, Toronto, ON, Canada.*

Gastric cancer (GC) is highly morbid and fatal. While the clinical challenge with GC is widely described, little is known about its economic burden. Many guidelines outline the curative treatment for GC and in a universal healthcare system, equal access and uniform healthcare delivery is predicted. Yet, regional variation in practice exists and may result in increased healthcare costs. We therefore aimed to describe the costs of treating curatively resected GC, explore regional variation in costs, and identify the factors driving costs. We conducted a patient-level cost analysis of curative-intent, resected stage I-III GC diagnosed between 2005 and 2008. A universal healthcare system's perspective and a 26-month time horizon were used. Clinical and stage data were abstracted from a provincial chart review. Costs associated with physician billings, same day surgery, hospitalization, drug benefits, emergency department visits, continuing care, and long-term care were derived using administrative healthcare databases and compared among healthcare regions. Costs were inflated to 2017 United States dollars (USD). We used a linear regression model with log-transformed cost data to identify predictors of cost. We identified 722 patients with resected Stage I-III GC. Mean costs per region ranged from $55,650 - $92,852 USD across fourteen health regions. Hospital admissions were the largest contributors to cost and long-term care contributed the least. A laparoscopic approach predicted lower costs, while age over 70 years and death at one year from diagnosis predicted higher costs. Regional variation in the cost of treating curatively resected GC exists, despite guidelines directing appropriate care and healthcare delivery in a universal healthcare system. This variation may reflect different disease symptoms and biology but could also reflect practice pattern variation and differential healthcare accessibility. Quality control metrics and further investigation are necessary to identify any inefficiencies in care and/or adverse outcomes as a result of lack of access to appropriate care to ensure optimal and sustainable curative GC care.

PF187

Impact of Enteral Feeding Access on Outcomes in Esophagectomy: An Analysis of SEER-Medicare P.D. Lorimer,[1]* B.M. Motz,[1] Y. Han,[1] R.S. Prabhu,[2] J.S. Hill,[1] J.C. Salo.[1] *1. Surgical Oncology, Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC; 2. Southeast Radiation Oncology, Charlotte, NC.*

Background Optimal nutrition in esophagectomy patients is challenging due to alterations in the physiology of eating resultant from the operation. Enteral nutrition via a surgically placed feeding tube is commonly used to augment nutrition. The present study utilizes a large national dataset to further understand the impact of feeding tube use on outcomes in this population. Methods SEER-Medicare was queried for patients with esophageal cancer (1998-2013) who underwent esophagectomy. Patients who had a feeding tube placed were identified using claims data. Chi square and T tests were used to compare categorical and continuous variables. Generalized linear modeling with stepwise selection was used for multivariable categorical analyses. Time trend analyses were performed with Cochran-Armitage. Survival was analyzed using log rank analysis. Results 2495 patients met inclusion criteria. 71% had feeding tubes placed. Rate of feeding tube placement varied by anastomotic site: cervical 81.4%, thoracic 61.1% and abdominal 51.5%. Feeding tube placement increased over time ($p<0.01$). There was no difference in feeding tube utilization based on demographics or comorbidities. Mortality in patients who received a feeding tube was lower at 30 days (5.4% vs. 8.4%), 60 days (9.0% vs. 13.0%), and 90 days (12.2% vs. 15.8%). On multivariable analysis patients who received feeding tubes had improved survival at 30 days (OR 0.65, 95% CI [0.46, 0.93]), 60 days (OR 0.64, [0.49, 0.85]) and 90 days (OR 0.70, [0.54, 0.90]). No difference in survival was observed at 6 months with respect to feeding tube use. No difference in length of stay or discharge destination was noted between those who received a feeding tube and those who did not. Conclusions Placement of feeding tubes in patients undergoing esophagectomy resulted in an increase in survival in our cohort out to 90 days. Feeding tube placement was not associated with a higher rate of non-home discharges or with an increased length of stay. Given the association of feeding tube utilization and survival improvement seen in the short term, we recommend providers consider placement of a feeding tubes in patients undergoing esophagectomy.

PF188

Prognostic Factors of Recurrence and Survival of Gastrointestinal Stromal Tumors: Adjuvant Therapy is Needed? First Multicentric Study of Mexico R.M. Guzman.* *National Medical Center, IMSS, Mexico City, Mexico.*

Background: Gastrointestinal stromal tumors are mesenchymal lesions arising from the interstitial cells of Cajal. In GIST the location, size, number of mitosis and risk group are accepted as prognostic factors; some factors in which there are still controversies about their value as prognostic factors include male gender, tumor cellularity, the margins of resection,. The most effective treatment for primary localized disease is surgery; with the use of imatinib as adyuvant therapy in high-risk lesions the 5-year survival has improved significantly about 70% The OBJECTIVE: is to analyze the prognostic factors and recurrence-free survival in GIST and the impact of adyuvant therapy. METHODS: Observational, retrospective and longitudinal study. Patients admitted of 1991 to April 30, 2012, with surgical treatment of the primary lesion. Univariate and multivariate analysis, survival analysis Kaplan-Meier (log rank test) was performed with SPSS- 20 RESULTS:We identified 384 patients, the mean follow-up time was 55.86 months, the mean age was 58 years, 80.3% had symptoms and only 4.54% the finding was incidental. Were expressed mainly by abdominal pain (39.39%) and less frequently gastrointestinal bleeding (30.30%) The most common comorbidity was hypertension (25.75%). The most common site was the stomach (66.6%), followed by small intestine (28.7%) and colon (1.54%). The 7.57% had metastases at diagnosis, 4.5 in liver and 3.03% in the peritoneum., intestinal obstruction in 1.5%; some of the specific symptoms were abdominal distension, weight loss and constipation.;. CONCLUTIONS:The tumor location, size, number of mitosis, the risk group and adjuvant treatment with Imatinib were statistically significant prognostic factors for disease recurrence. The location of the lesion was the only factor that showed statistical significance as a predictor of overall survival. Although the adjuvant treatment was significant in RFS. This study did not report better results than surgical management. It is necessary a debate and updating of guides in Mexico on GIST.

PF189

Optimal Timing to Esophagectomy Following Neoadjuvant Therapy for Esophageal Cancer: A Study of The National Cancer Database E. Efiong,* S.H. Slipak, M. Fluck, M. Hunsinger, M. Shabahang, J. Wild, T. Arora, J. Blansfield. *Department of Surgery, Geisinger Medical Center, Danville, PA.*

BACKGROUND: Resection for esophageal cancer offers the best opportunity for cure. However, 5-year survival remains low. Randomized trials have shown neoadjuvant chemoradiation leads to a survival benefit compared to surgery alone but timing of treatment is controversial. Some clinical trials have stipulated that surgery be performed within 3–8 weeks, however other studies suggest a longer interval between radiation and surgery may be better. The goal of this study was to explore the optimal timing of esophagectomy following

neoadjuvant chemoradiation using the National Cancer Database (NCDB). STUDY DESIGN: A retrospective study from the NCDB was performed for patients diagnosed with esophageal cancer and who underwent neoadjuvant chemoradiation and esophagectomy between the years 2004-2014. Restricted cubic spline regression was performed to determine the optimal timing to maximize the (log) odds of a negative surgical margin, and to maximize tumor and nodal downstaging. Study cohorts were created based on these timeframes. RESULTS: A total of 4979 patients were included in this study. Multivariate regression modeling with restricted cubic splines was used to evaluate the adjusted association between time to surgery and primary endpoints. This model demonstrated a critical threshold at 50 days after chemoradiation for both margin positivity and downstaging. Our data revealed that as time elapsed passed 50 days, the risk of positive margins increased. Additionally, as time elapsed, there was a linear increase in likelihood of downstaging. However, after 50 days, further postponement of surgery did not confer greater benefit. There were no differences in the demographics of the two groups except for the short interval being more likely to be privately insured (54%). Facility type did not affect the interval. CONCLUSIONS: This study determined the optimal time for esophagectomy following neoadjuvant chemoradiation based on completeness of resection and tumor and nodal downstaging is 50 days. Prolonging the duration between completion of neoadjuvant therapy and surgery beyond 50 days is associated with worse outcomes.

PF190

Gastric Cancer Disparity in the United States: What's to Blame?
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Background Previous studies have demonstrated disparate gastric cancer (GC) survival among racial groups in the US, however, the cause for these differences is not fully explored. Methods Patients with GC in the 2004–2013 NCDB were identified and categorized into 4 racial groups: white, black, Asian, and Hispanic. Potential sources of disparity including patient-related, socioeconomic, and treatment-related factors were examined for their impact on overall survival (OS). Results Among 63,010 patients identified, 69% were white, 14.1% black, 10.3% Hispanic, and 6.6% Asian. Median age at diagnosis was 66, however, black and Hispanic patients were significantly younger at 64 and 60, respectively ($p<0.001$). In addition, blacks (52.9%) and Hispanics (55.9%) were more likely to present with stage IV disease than whites (45.8%) and Asians (43.8%) ($p<0.001$). Black (85.9%) and Hispanic (52.7%) patients were more likely to reside in lower income areas than whites (38%) and Asians (24%) ($p<0.001$). Blacks (7.3%), Hispanics (15.4%) and Asians (7.6%) were more likely uninsured than whites (2.9%) ($p<0.001$). Among patients with stage I-III disease, blacks (61.8%) were less likely to undergo resection than whites (63.7%), Hispanics (68.0%) and Asians (74.7%) ($p<0.001$). For stage IV disease, blacks (54.6%) were less likely to receive chemotherapy than whites (62.5%), Hispanics (61.4%), and Asians (59.8%). As shown in table 1, black patients experienced significantly lower stage-specific OS relative to other races. On multivariable analysis, the greatest predictor of OS was surgical resection (HR 0.28) although predictably, for stage IV this was surpassed by receipt of chemotherapy (HR 0.34 vs 0.52). Lack of insurance and residing in a lower income area were also associated with greater risk of mortality (both HR 1.15). Conclusion Analysis of the NCDB demonstrated significant differences in age and stage at presentation, socioeconomic status, and treatment among GC patients in the US as stratified by race. Disparity in GC is likely multifactorial, but warrants further study of its root causes including differences in tumor biology, along with strategies aimed at improving care for disadvantaged populations.

Stage-specific median overall survival by racial group

Clinical Stage	White	Black	Asian	Hispanic
Stage 0-I	43.2 months	33.4 months	118.1 months	68.1 months
Stage II	26.6 months	23.9 months	57.0 months	34.9 months
Stage III	17.8 months	14.9 months	19.8 months	19.3 months
Stage IV	5.6 months	4.8 months	6.6 months	5.6 months

PF191

Survival Benefit of Gastric Resection in the Setting of Metastatic Gastric Cancer
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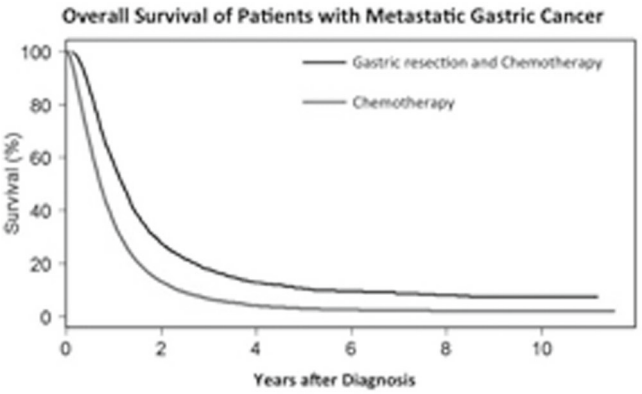
Introduction: Prognosis remains poor for metastatic gastric cancer. Several studies have indicated that gastric resection in addition to standard chemotherapy treatment in the setting of Stage IV gastric cancer can not only be palliative, but may also increase survival. The objective of this study is to determine using the National Cancer Database (NCDB) whether there was an increase in overall survival in patients diagnosed with metastatic cancer who underwent a gastrectomy in addition to chemotherapy. Methods: The NCDB was queried between 2004-2014 for patients with metastatic gastric cancer (adenocarcinoma, mucinous adenocarcinoma, or signet ring carcinoma) who had chemotherapy. Kaplan-Meier analysis and multivariate Cox proportional hazards regression analysis was done using SAS software. Results: A total of 20,599 patients met inclusion criteria. A minority of these patients (2,508; 12.2%) underwent gastric resection in addition to chemotherapy. The median overall survival for those who underwent gastrectomy was 14.1 months compared to 8.6 months for chemotherapy alone ($p<0.0001$). Other factors influencing survival included age, race, Charlson-Deyo score, year of diagnosis, primary tumor site, grade, and metastasis to multiple organs. Following multivariate analysis, patients who underwent gastrectomy and chemotherapy had a 36% lower risk of death compared to patients that had only chemotherapy (HR 0.64, 95% CI 0.48–0.80, $P<0.0001$). Conclusions: Only a small proportion of patients with metastatic gastric cancer undergo gastric resection in the United States. Gastrectomy should be considered for patients who are surgical candidates since it provides a survival benefit in addition to palliation of symptoms.



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Patient-Level Costs of Treating Metastatic Gastric Cancer by Treatment Strategy
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Half of gastric cancer patients in North America present with metastatic disease. The appropriate management of these patients is complex and few guidelines exist to definitively guide treatment; as a result, practice variation exists. This variation may lead to care inefficiencies and/or adverse outcomes. We therefore aimed to conduct a patient-level exploration of metastatic gastric cancer management costs, by treatment strategy, and to identify predictors of cost. We conducted a patient-level cost analysis of metastatic gastric cancer patients diagnosed between 2005 and 2008. A 26-month time horizon and the healthcare system's perspective was used. Clinical data was collected through a provincial chart review. Costs associated with supportive care, radiation only, chemotherapy only, chemoradiation, gastrectomy, and gastrectomy with chemotherapy +/- radiotherapy were collected using administrative data in a single payer system. Costs were inflated to 2017 United States dollars (USD). Linear regression with log-transformed costs was used to identify predictors of cost. We identified 1,285 patients with metastatic gastric cancer. The absolute mean costs of metastatic gastric cancer management increased with increasing level of intervention and ranged from $34,002 to $72,778 (USD); supportive care was associated with the lowest costs and gastrectomy with chemotherapy

+/- radiotherapy was associated with the highest costs. Age over 70 and lower Charlson Comorbidity Index were predictors of lower costs while supportive care, radiotherapy, chemoradiation, and gastrectomy were associated with higher costs. Practice variation in the management of metastatic gastric cancer has economic implications. Variation may be necessary and reflect differences in disease biology or symptoms. Variation in costs may also be explained by dissimilar resource availability between health regions, as well as differential access to palliative care, which may be intervenable. This information may be used to plan resource allocation and direct financial support to institutions treating these patients.

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Comparison of Perioperative Chemotherapy Versus Postoperative Chemoradiation Therapy for Distal Gastric Cancer: An Analysis of the National Cancer Database M.M. Shah,[1]* R. NeMoyer,[2] S.H. Greco,[1] Y. Lin,[3] M.S. Grandhi,[1] D.R. Carpizo,[1] P. Javidian,[2] S.K. Jabbour,[1] D.A. August,[1] S. Libutti,[1] T.J. Kennedy.[1] *1. Surgical Oncology, Rutgers Cancer Institute of New Jersey, New Brunswick, NJ; 2. Robertwood Johnson Medical School, New Brunswick, NJ; 3. Rutgers School of Public Health, Piscataway, NJ.*

Introduction Perioperative chemotherapy (PEC) and postoperative chemoradiation therapy (POCR) are considered standard of care for patients with resectable gastric adenocarcinoma (GC) based on level 1 evidence. However, no significant evidence exists directly comparing PEC and POCR for distal GC. The purpose of this study was to compare these treatment modalities in patients with surgically resectable distal gastric cancer, and evaluate the impact on overall survival (OS). Methods A retrospective review of patients undergoing definitive surgery for GC was performed using the National Cancer Database (2004-2014). Patients with gastric cardia as the primary tumor site were excluded. The difference in OS in patients who received PEC or POCR was compared. A second analysis identified patients who received optimal therapy, defined as - negative surgical margins, radiation doses between 4500-5040cGy, radiation to the stomach only, and chemotherapy started within 90 days of surgery. We utilized Cox proportional hazard model for our multivariate analysis. Results We identified 62,931 patients who underwent definitive surgery for GC. 7,166 patients underwent PEC or POCR. Here, PEC was statistically significantly associated with improved OS compared to POCR (p=0.015; HR 0.855). The median OS for patients who received PEC was 56 months vs. 41.5 months for POCR. However, when we selected patients who received optimal therapy (n = 3,425), the difference in the treatment modalities did not reach statistical significance (p=0.432; HR 0.94). The median OS was 63.5 months for all patients (PEC 85 months, POCR 61.9 months). In addition to treatment (PEC and POCR), race, age, grade, Charlson score and primary site were statistically significant predictors of overall survival. Conclusion PEC is associated with improved OS compared to POCR after adjusting for covariates in patients who underwent definitive surgery for distal GC. However, this benefit loses statistical significance after selecting patients who received optimal therapy. The median OS is superior in patients receiving optimal therapy, regardless of treatment type.

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