

## OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

### PUBLICATION LIST

July - September 2017

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**Abbas AE**, Khoury Abdulla R, Aggrawal A, Crile J, Lester SJ and **Boura J** (2017). "A novel echocardiographic hemodynamic classification of heart failure based on stroke volume index and left atrial pressure." *Echocardiography* 34(10): 1417-1425.

[Full-Text](#)

*Department of Internal Medicine*

*Department of Biomedical Sciences (BH)*

Background and Aim: Dividing patients with heart failure (HF) based solely on ejection fraction (EF) may over simplify the hemodynamic states of these patients. We describe a novel echo-derived hemodynamic HF model based on flow (stroke volume index [SVI]) and left atrial pressure (E:E') correlates. Methods: A retrospective analysis of patients admitted with HF with both reduced (HFrEF) and preserved EF (HFpEF). Patients were subdivided into four hemodynamic groups based on echocardiographic SVI (< or ≥35 mL/m<sup>2</sup>) and E/E' (≥ or <15). Group A: normal flow and normal filling pressure, Group B: normal flow but high filling pressure, Group C: low flow and low filling pressure, and Group D: low flow and high filling pressure. Results: A total of 176 patients were enrolled, 123 patients had HFrEF and 53 patients had HFpEF. Baseline characteristics were not statistically significant in both groups. In HFrEF, most patients were in group D compared to a heterogeneous distribution in HFpEF (P<.0001). In HFrEF, there was a trend toward an increase in B-type natriuretic peptide levels with a decrease in SVI and increase in E/E' (P=.05) but not in HFpEF. There was no difference in death, major adverse cardiac events, but a higher readmissions rate in the HFpEF group at 30 days and 18 months. Conclusions: Hemodynamic subgroups differ between HFrEF and HFpEF. There is no difference in major adverse cardiovascular events between both groups with increased readmissions in HFrEF patients. Larger studies may help assess the impact of echo-derived hemodynamic state on clinical outcome.

Abbott EE, Shaffer K, Bayci A, Hothem Z, Thibodeau B, **Ahmed S, Uzieblo A, Wilson G** and **Keidan R** (2017). "Predicting lymph node positivity in melanoma patients." *Annals of Surgical Oncology* 24(1): S147-S148.

[Full-Text](#)

*Department of Family Medicine*

*Department of Pathology*

*Department of Radiation Oncology*

*Department of Surgery*

Introduction: The five-year survival of melanoma patients is dramatically decreased for those with regional disease (62.6%) compared to those with localized tumors (98.1%). Sentinel lymph node biopsy (SLNB) as a staging tool carries risk of operative morbidity and increases cost. While SLNB is only performed for lesions felt to be high-risk for nodal or distant metastasis, only 15% of patients undergoing SLNB will have positive lymph nodes. We aimed to find variations in gene expression in primary melanoma lesions and nodal tissue of patients with confirmed positive or negative lymph nodes in order to avoid unnecessary SLNB. Methods: Formalin-fixed paraffin-embedded samples of skin lesions of SLN-positive (n=1) and SLN-negative (n=2) patients as well as nodal samples [SLN-positive (n=5) and SLN-negative (n=2)] were examined. Laser capture microdissection was used to isolate pathologist-identified tumor cells. DNA was isolated and used to prepare libraries for next generation sequencing using the TruSeq Amplicon - Cancer Panel on the Illumina NextSeq 500. Software was used for alignment and variant calling based upon mutation percentage, total coverage, and balance ratio of forward and reverse reads. Further biological interpretation was performed using variant analysis software. Results: Analysis focused on genomic variation in 48 cancer-related genes. Fourteen genes were found to have variants in >70% of the positive node samples while not being present in any samples with negative nodes. These included EGFR and PDGFR. Variants in ERBB4 were present in all of the positive node samples but were not seen in any of the negative node samples. Genes such as ATM, PIK3CA, and TP53 were found to have variants in the positive node samples. These variants were not found in any of the negative node samples. Conclusion: While this is a pilot study, we are currently increasing our sample size to develop a more robust predictor of positivity. There are several gene variants seen in melanoma lesions with positive nodes that are not expressed in lesions with negative nodes. These may become useful in determining a genetic signature to predict lymph node positivity in melanoma patients. (Table presented).

Abuodeh Y, Naghavi AO, Echevarria M, DeMarco M, Tonner B, Feygelman V, **Stevens CW**, Perez BA and Dilling TJ (2017). "Quantitatively excessive normal tissue toxicity and poor target coverage in postoperative lung cancer radiotherapy meta-analysis." *Clinical Lung Cancer*: 1-8. ePub Ahead of Print.

[Full-Text](#)

*Department of Radiation Oncology*

Background: A previous meta-analysis (MA) found postoperative radiotherapy (PORT) in lung cancer patients to be detrimental in N0/N1 patients and equivocal in the N2 setting. We hypothesized that treatment plans generated using MA protocols had worse dosimetric outcomes compared to modern plans. Patients and Methods: We retrieved plans for 13 patients who received PORT with modern planning. A plan was recreated for each patient using the 8 protocols included in MA. Dosimetric values were then compared between the modern and simulated MA plans. Results: A total of 104 MA plans were generated. Median prescribed dose was 50.4 (range, 50-60) Gy in the modern plans and 53.2 (30-60) Gy in the MA protocols. Median planning volume coverage was 96% (93%-100%) in the modern plans, versus 58% (0%-100%) in the MA plans (P < .001). Internal target volume coverage was 100% (99%-100%) versus 65% (0%-100%), respectively (P < .001). Organs at risk received the following doses: spinal cord maximum dose, 36.8 (4.6-50.4) Gy versus 46.8 (2.9-74.0) Gy (P < .001); esophageal mean dose, 22.9 (5.5-35) Gy versus 30.5 (11.1-52.5) Gy (P = .003); heart V30 (percentage of volume of an organ receiving at least a dose of 30 Gy), 16% (0%-45%) versus 35% (0%-79%) (P = .047); mean lung dose, 12.4 (3.4-24.3) Gy versus 14.8 (4.1-27.4) Gy (P = .008); and lung V20, 18% (4%-34%) versus 25% (8%-67%) (P = .023). Conclusion: We quantitatively confirm the inferiority of the techniques used in the PORT MA. Our analysis showed a lower therapeutic ratio in the MA plans, which may explain the poor outcomes in the MA. The findings of the MA are not relevant in the era of modern treatment planning.

Aggrawal A, Crile J, Lester SJ, **Boura J, Sahloul E**, Salem R, Alrez W, Alkarim T, Sukari A, Maziak W and Atassi MB (2017). "Cancer care at times of crisis and war: The Syrian example." *Echocardiography* 3(4): 338-345.

[Full-Text](#)

*Department of Biomedical Sciences (BH)*

*OUWB Medical Student Author*

PURPOSE: As Syria enters its fifth year of conflict, the number of civilians killed and injured continues to rise sharply. Along with this conflict comes the rapid decline of medical care, specifically cancer care. To determine physician and equipment availability, cancer screening and management, and possible solutions relative to various major cities, a survey was distributed to physicians inside Syria through the help of the humanitarian organization Syrian American Medical Society. METHODS: Online surveys were distributed to both certified oncologists who work in cancer clinics and general physicians who work in rural and mobile clinics inside Syria. Variables assessed were physician specialty, location, population, cost, regional situation (besieged versus government controlled), and resource availability and access. Results were stratified by location and physician specialty. RESULTS: Survey results revealed a large shortage of specialized physicians and inhibited accessibility to screening and management options in besieged areas compared with government-controlled regions. Physicians within both government-controlled and besieged cities reported limited or no targeted agents, radiation therapy, clinical trials, bone marrow transplantation, positron emission tomography scans, magnetic resonance imaging, and genetic testing. CONCLUSION: The Syrian civil war has resulted in suboptimal oncology care in the majority of the region. In consideration of specific deficiencies in cancer care, we recommend several solutions that may better the level of care in Syria: patient education on medical documentation and self-examination; online consultation; and cheap, effective screening methods. The implementation of these recommendations may change the course of cancer care in a country that has deteriorated into the worst humanitarian crisis of the century.

Al-Katib S, **Shetty M, Jafri SM and Jafri SZ** (2017). "Radiologic Assessment of Native Renal Vasculature: A Multimodality Review." *Radiographics : A review publication of the Radiological Society of North America, Inc* 37(1): 136-156.

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*Department of Diagnostic Radiology and Molecular Imaging*

*Department of Urology*

A wide range of clinically important anatomic variants and pathologic conditions may affect the renal vasculature, and radiologists have a pivotal role in the diagnosis and management of these processes. Because many of these entities may not be suspected clinically, renal artery and vein assessment is an essential application of all imaging modalities. An understanding of the normal vascular anatomy is essential for recognizing clinically important anatomic variants. An understanding of the protocols used to optimize imaging modalities also is necessary. Renal artery stenosis is the most common cause of secondary hypertension and is diagnosed by using both direct ultrasonographic (US) findings at the site of stenosis and indirect US findings distal to the stenosis. Fibromuscular dysplasia, while not as common as atherosclerosis, remains an important cause of renal artery hypertension, especially among young female individuals. Fibromuscular dysplasia also predisposes individuals to renal artery aneurysms and dissection. Although most renal artery dissections are extensions of aortic dissections, on rare occasion they occur in isolation. Renal artery aneurysms often are not suspected clinically before imaging, but they can lead to catastrophic outcomes if they are overlooked. Unlike true aneurysms, pseudoaneurysms are typically iatrogenic or posttraumatic. However, multiple small pseudoaneurysms may be seen with underlying vasculitis. Arteriovenous fistulas also are commonly iatrogenic, whereas arteriovenous malformations are developmental (ie, congenital). Both of these conditions involve a prominent feeding artery and draining vein; however, arteriovenous malformations contain a nidus of tangled vessels. Nutcracker syndrome should be suspected when there is distention of the left renal vein with abrupt narrowing as it passes posterior to the superior mesenteric artery. Filling defects in a renal vein can be due to a bland or tumor thrombus. A tumor thrombus is most commonly an extension of renal cell carcinoma. When an enhancing mass is located predominantly within a renal vein, leiomyosarcoma of the renal vein should be suspected. ©RSNA, 2017.

Almradi A and **Alassi O** (2017). "Comparison of 95% alcohol immersion fixation versus spray fixation (PapFix) for thyroid fine needle aspiration regarding overall cellularity cell morphology and amount of colloid." Journal of the American Society of Cytopathology 6(5): S66-S67.

[Full-Text](#)

*Department of Pathology*

Introduction: The effect of the type of fixation, 95% alcohol immersion vs. Spray fixation (PapFix, BBC Biochemical, Mount Veron, WA) fine needle aspiration of the thyroid is not well studied. The two methods have been used widely in routine practices across the country. In this study, we intend to compare the two methods of fixation and the differences seen, if any, on the overall smear cellularity, colloid amount and character, cell morphology and architecture on all thyroid FNAs performed at our institution for 6-week duration. Materials and Methods: This is a prospective study where at least 6 passes from each case were split; The two-smear method is applied to all of the smears where 3 slides are spray fixed, 3 are air-dried, the next 3 passes; 3 fixed by immersion in 95% alcohol and 3 air-dried. All immediately fixed slides are stained with Papanicolaou stain and air-dried smears are stained with Diff-Quick stain. Results: Of the 9 cases done so far, spray fixed slides contained more and better-visualized colloid. Blood contamination was high in all samples but in spray fixed slides appeared as 'droplets' of blood separated from follicular cells, while the immersion slides had blood spread throughout the slides, and appeared hemolyzed, entrapping follicular cells. The cellularity and visualization of the cellular groups are better using the spray fixation, even in bloody smears. There was less crowding of cells in nodular goiter cases and the nuclear details were crispier and better visualized with spray fixation. Conclusion: In this limited sample numbers, we observed that spray fixation shows a slightly higher overall cellularity, more and better visualized colloid, less crowding of cells and more crisp nuclear staining when compared to the immersion of 95% alcohol fixation. Additional number of sample comparison and different diagnostic categories need to be studied. (Figure Presented).

Altawan A, Golchian D, Bazzi M, Iljas J and **Patel B** (2017). "Deep vein thrombosis post radiofrequency ablation of the saphenous and perforator veins: Is duplex ultrasound necessary within five days?" Journal for Vascular Ultrasound 41(1): 11-12.

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*Department of Internal Medicine*

Anderson M, Morris L, Tang D, Batsides G, Kirtane A, **Hanson I**, Meraj P, Kapur N and O'Neill W (2017). "Impella RP post approval study: First multi-center, prospective post market approval results for the impella RP in patients with right ventricular failure." Journal of Heart and Lung Transplantation 36(4): S64-S65.

[Full-Text](#)

*Department of Internal Medicine*

Summary of Objectives: Right Ventricular (RV) failure increases morbidity and mortality and contributes to prolonged hospital lengths of stay and higher costs of care. The primary objective for this study is to assess the outcomes of the post market approval use of the Impella RP, the first percutaneous right ventricular support FDA approved device for patients with RV failure that require hemodynamic support. Methods: The Impella RP post approval study is a prospective, single arm multi-center study planning to enroll 30 patients at 15 sites. Patients that develop acute RV failure following LVAD implantation, post myocardial infarction or post open heart surgery (including post heart transplant) and have BSA  $\geq 1.5$  m<sup>2</sup> are included in the trial. Major exclusion criteria are presence of mural thrombus into the right heart or the inferior vena cava, presence of mechanical valves, or severe stenosis or regurgitation of the tricuspid or pulmonic valves. Patient baseline and procedural characteristics, hemodynamic parameters, hospital stay data and patient outcomes to 180 days are collected. Major adverse events are adjudicated by an independent clinical events committee. Endpoints: The primary study endpoint is the survival rate at 30 days post device explant or at hospital discharge (whichever is longer). Secondary endpoints are major adverse events such as death, major bleeding, pulmonary embolism, and hemolysis. Improvement and hemodynamic parameters and use of inotropes are also evaluated. The outcome trends in the post approval study will be benchmarked against the original Recover Right study and the pooled data from all the Impella RP clinical studies will be presented at the meeting.

**Aneese AM, Yang SK and Cappell MS** (2017). "Case report of successful medical management of progressive gastric band penetration-to-perforation after band insertion at bariatric surgery: Documentation by 12 serial EGDs during 50 months of observation." Digestive Diseases and Sciences: 1-7. ePub Ahead of Print.

[Full-Text](#)

*OUWB Medical Student Author*

*Department of Internal Medicine*

Anthony GJ, Cunliffe A, Castillo R, Pham N, **Guerrero T**, Armato SG and Al-Hallaq HA (2017). "Incorporation of pre-therapy F-18-FDG uptake data with CT texture features into a radiomics model for radiation pneumonitis diagnosis." Medical Physics 44(7): 3686-3694.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: To determine whether the addition of standardized uptake value (SUV) from PET scans to CT lung texture features could improve a radiomics-based model of radiation pneumonitis (RP) diagnosis in patients undergoing radiotherapy. Methods and materials: Anonymized data from 96 esophageal cancer patients (18 RP-positive cases of Grade  $\geq 2$ ) were collected including pre-therapy PET/CT scans, pre-/post-therapy diagnostic CT scans and RP status. Twenty texture features (first-order, fractal, Laws' filter and gray-level co-occurrence matrix) were calculated from diagnostic CT scans and compared in anatomically matched regions of the lung. Classifier performance (texture, SUV, or combination) was assessed by calculating the area under the receiver operating characteristic curve (AUC). For each texture feature, logistic regression classifiers consisting of the average change in texture feature value and the pre-therapy SUV standard deviation (SUVSD) were created and compared with the texture feature as a lone classifier using ANOVA with correction for multiple comparisons ( $P < 0.0025$ ). Results: While clinical parameters (mean lung dose, smoking history, tumor location) were not significantly different among patients with and without symptomatic RP, SUV and texture parameters were significantly associated with RP status. AUC for single-texture feature classifiers alone ranged from 0.58 to 0.81 and 0.53 to 0.71 in high-dose ( $\geq 30$  Gy) and low-dose ( $< 10$  Gy) regions of the lungs, respectively. AUC for SUVSD alone was 0.69 (95% confidence interval: 0.54-0.83). Adding SUVSD into a logistic regression model significantly improved model fit for 18, 14 and 11 texture features and increased the mean AUC across features by 0.08, 0.06, and 0.04 in the low-, medium-, and high-dose regions, respectively. Conclusions: Addition of SUVSD to a single-texture feature improves classifier performance on average, but the improvement is smaller in magnitude when SUVSD is added to an already effective classifier using texture alone. These findings demonstrate the potential for more accurate assessment of RP using information from multiple imaging modalities. (C) 2017 American Association of Physicists in Medicine

Anyaiwe OED, Singh GB, **Wilson GD** and Geddes TJ (2017). "Weighted Manhattan distance classifier; SELDI data for Alzheimer's disease diagnosis." 2017 IEEE Congress on Evolutionary Computation, CEC 2017 - Proceedings. 257-262.

[Full-Text](#)

*Department of Radiation Oncology*

Bannazadeh M, Jenkins C, Forsyth A, Kramer J, Aggarwal A, Somerset AE, **Bove PG** and **Long GW** (2017). "Outcomes for concomitant common iliac artery aneurysms after endovascular abdominal aortic aneurysm repair." Journal of Vascular Surgery 66(5): 1390-1397.

[Full-Text](#)

*Department of Surgery*

Objective This study evaluated the morbidity of endovascular abdominal aortic aneurysm repair (EVAR) in patients with concomitant common iliac artery aneurysm (CCIAA). Methods This was a retrospective review of all patients who underwent elective EVAR from June 2006 through June 2012 at a single institution. Demographics, comorbidities, preoperative presentation, intraoperative details, and postoperative complications were tabulated. Patients with CCIAA were categorized into three groups according to the distal extent of their iliac limb: iliac limb extension into the external iliac artery with internal iliac artery coil

embolization (EE); flared iliac limb  $\geq 20$  mm in diameter to the iliac bifurcation (FL); and iliac limb  $\leq 20$  mm ending proximal to the CCIAA (no-FL). Results During this period, 627 consecutive patients underwent elective EVAR and preoperative computed tomographic angiograms were available for 523 patients to evaluate the presence of CCIAA. Of these, 211 patients (40.2%) had a CCIAA in at least one common iliac artery, with a total of 307 aneurysmal arteries. Of these 307 aneurysmal arteries, 62 (20.2%) were treated with EE, 132 (43.0%) were treated with FL, and 113 (36.8%) had a sufficient landing zone in the proximal common iliac artery to use an iliac limb  $\leq 20$  mm in diameter (no-FL). The overall reintervention rate was 12.4% of patients, with a higher reintervention rate between patients with CCIAA compared with those without (15.2% vs 10.9%;  $P = .039$ ). There were no significant differences in reintervention rates between the EE, FL, and no-FL techniques (4.5% vs 4.8% vs 6.2%;  $P = .802$ ) over a mean 59.8 months follow-up. The FL and EE techniques had a lower risk of distal endoleak than the no-FL technique, but the difference was not statistically significant (3.2% vs 2.3% vs 5.3% compared with 4.23% in the entire cohort). Conclusions Patients with CCIAA had a higher reintervention rate after EVAR for abdominal aortic aneurysm compared with non-CCIAA patients. Of the techniques studied (EE, FL, and no-FL), there was no significant difference in reintervention rates between the three. All three techniques remain viable options for the endovascular repair of CCIAA.

Bauer ME, Price LK, MacEachern MP, Housey M, Langen ES and **Bauer ST** (2017). "Maternal leukocytosis after antenatal corticosteroid administration: A systematic review and meta-analysis." Journal of Obstetrics and Gynaecology: 1-7. ePub Ahead of Print.

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*Department of Obstetrics and Gynecology*

Although it is known that corticosteroid administration causes leukocytosis, the magnitude and length of time this leukocytosis persists is unknown during pregnancy. This study aimed to establish the expected range of maternal leukocytosis in healthy pregnant women at risk for preterm delivery after antenatal corticosteroid administration. PubMed, Embase and ClinicalTrials.gov were searched to identify the studies in healthy women at risk for preterm delivery without signs of clinical infection that reported white blood cell values preceding and after antenatal corticosteroid administration. The inverse variance weighting technique was used to calculate the weighted means and the standard deviation from the mean for each time period. Six studies met inclusion criteria and included 524 patients and 1406 observations. Mean +/- standard deviation maternal white blood cell count values prior to antenatal corticosteroid administration and up to 24, 48, 72 and 96 hours after corticosteroid administration were 10.4 +/- 2.4, 13.6 +/- 3.6, 12.1 +/- 3.0, 11.5 +/- 2.9 and 11.1 +/- 2.5 x 10<sup>9</sup>/L, respectively. Leukocytosis in healthy, non-infected women is expected to peak 24 hours after antenatal corticosteroid administration and the magnitude of increase is small. Impact statement What is already known on this subject: While it is well known that administration of antenatal corticosteroids causes leukocytosis, it is currently unknown the magnitude and length of time the leukocytosis persists. What the results of this study add: This study establishes the expected range and the temporal progression and regression with antenatal corticosteroid administration in healthy pregnant women at risk for preterm delivery without clinical signs of infection. What the implications are of these findings for clinical practice and/or further research: Clinicians may wish to consider further investigation into the clinical cause, whether infectious or non-infectious, for absolute values and changes outside this range.

Bawa HS, **Moore DD**, Pelayo JC, Cipriani N, Mak G and Haydon RC (2017). "Pediatric chondrosarcoma of the sternum resected with thorascopic assistance." Open Orthopaedics Journal 11(Sup 3): 479-485.

[Full-Text](#)

*Department of Orthopedic Surgery*

BACKGROUND: Chondrosarcomas are a heterogeneous group of malignant neoplasms that arise from bones, cartilage or other soft tissues that produce cartilage and are commonly seen in the middle decades of life. Despite being the most common primary bone sarcoma in adults, chondrosarcomas are rare in pediatric patients. CASE REPORT: We report the case of a six-year-old child with a painless enlarging sternal mass of which biopsy was consistent with low-grade surface chondrosarcoma. This is the first reported case of a chest wall chondrosarcoma in a young child. This unusual location in a young patient presented challenges to treatment. Resection of the manubrium was performed by a multidisciplinary team of orthopaedic



oncology and pediatric general surgery. The patient underwent a wide resection of the sternal mass from an anterior approach performed by the orthopaedic oncology team using an oscillating saw under video-assisted thoracoscopic surgery to ensure adequate mass resection without injury to nearby structures. The patient was followed with quarterly physical exams and radiographs for 18 months postoperatively and did not have any pain or evidence of recurrence. **CONCLUSION:** Clinicians should consider utilizing multidisciplinary approaches to treat patients with chondrosarcomas of the chest wall.

Beall DP, Chambers MR, Thomas SM, **Easton R**, Galati S, Goodman B, Datta D, Webb JR and Linville D (2017). "EVOLVE: A prospective and multicenter evaluation of the outcomes pertaining to quality of life, pain, and activities of daily living after balloon kyphoplasty for the treatment of Medicare-eligible subjects with vertebral compression fractures." *Cardiovascular and Interventional Radiology* 40(2): S123.

[Full-Text](#)

*Department of Orthopedic Surgery*

**Purpose:** Vertebral compression fractures (VCFs) resulting from osteoporosis or cancer are common and painful. Worldwide, osteoporosis causes >8.9 million fractures annually. Quality of life is threatened, and mortality and morbidity rates increase following a VCF. Kyphoplasty is a minimally invasive procedure to stabilize a VCF, reduce pain, and improve the quality of life and mobility. **Material and methods:** In total, 354 Medicare patients with painful, acute, or subacute VCFs were prospectively enrolled at 24 sites, with 350 undergoing balloon kyphoplasty. Primary objective was to show statistically significant improvement in four co-primary endpoints (SF-36v2 PCS, EQ-5D, NRS back pain, and ODI) at 3 months. **Results:** Back pain improved from 8.7 (scale 0-10) by 5.2, 5.4, 6.0, 6.2, and 6.3 points at the 7-day and 1-, 3-, 6-, and 12-month time points, respectively ( $p < 0.001$  for each). ODI improved from 63.4 (scale 0-100) by 30.5, 35.3, 36.3, and 36.2 points at the 1-, 3-, 6-, and 12-month time points, respectively ( $p < 0.001$  for each). SF-36 PCS was 24.2 at baseline (scale 0-100) and improved by 10.7, 12.4, 13.4, and 13.8 points at 1, 3, 6, and 12 months, respectively ( $p < 0.001$  for each). EQ-5D was 0.383 points (scale 0-1) and improved by 0.316, 0.351, 0.356, and 0.358 points at 1, 3, 6, and 12 months, respectively ( $p < 0.001$  for each). **Conclusion:** Our large, prospective, multicenter study trial demonstrates that balloon kyphoplasty is a safe, very effective, and durable procedure for treating Medicare patients with VCFs due to osteoporosis or cancer.

Blankenship L, Ezekwudo D, **Jaiyesimi IA**, **Alassi O**, **Stender MJ** and **Gaikazian SS** (2017). "Discordant breast cancer: Low risk genomic, high risk pathologic." *Journal of Clinical Oncology* 35(15): Abstract No. e18160.

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*Department of Internal Medicine*

*Department of Pathology*

**Background:** Studies using the 21-gene recurrence score (RS) have shown low risk pathologic features and RS breast cancers do not benefit from systemic chemotherapy (CTx). However, data is lacking for patients with discordant risk factors and which feature, genomic or clinical, plays more of a role in determining outcomes. **Methods:** Retrospective analysis was conducted to identify breast cancer patients with discordant features, defined as low genomic/high pathologic factors, from 2011 to 2016. Patients were hormone-receptor positive with RS < 18 and had 3-2 high risk factors: tumor size  $\geq 2$ cm, lymph node (LN) positivity, or grade 2-3 disease. **Results:** There were 469 patients with low risk RS were identified of whom 118 met discordant risk criteria. Patients management is depicted in Table 1. Of the 118 discordant patients, 22 had breast cancer recurrence as either metastatic (1) or locoregional (21); 11 being ipsilateral while the remainder were contralateral. Patients with ipsilateral recurrences had partial mastectomy and radiotherapy as initial management. CTx was received in 30 patients despite low RS. Recurrences occurred in 31.8% of patients who received adjuvant CTx. The majority of recurrences occurred >5 years after initial diagnosis. **Conclusions:** Our results show both genomic and pathologic features were important in determining the need for CTx in early stage breast cancer but neither had a greater impact. Thus, we advocate a more comprehensive and individualized approach, taking into account comorbidities, genomic, and pathologic features, for addition of CTx to standard hormonal therapy. Further studies are needed to determine the proper treatment of this unique patient population.

Blankenship L, Foluso O, **Lanni TB**, Hakmeh B, **Akhtar AJ**, **Riutta J**, **Gaikazian SS**, **Anderson JM**, **Stender MJ** and **Jaiyesimi IA** (2017). "Inpatient hematology and oncology rehabilitation." Journal of Clinical Oncology 35(15): Abstract No. 6580.

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*Department of Radiation Oncology*

*Department of Internal Medicine*

*Department of Physical Medicine and Rehabilitation*

Background: Functional decline in cancer patients impacts quality of life and overall survival. Increasing attention has been focused on cancer rehabilitation in survivors, largely in the outpatient setting. Beaumont Health System has shifted its focus to include the acute setting by developing an inpatient cancer rehabilitation unit (IPCR) to improve the comprehensive care of patients. Methods: We retrospectively reviewed the patients admitted to IPCR from January 1 - December 31, 2016 for the following: demographics, length of stay (LOS), function independence measure (FIM) gain and efficiency, discharge location, and primary tumor type. Results: IPCR had 117 inpatient admissions; 98 (83.7%) were solid malignancies while 19 (16.3%) were benign hematological disorders and hematological malignancies. Of the 98 patients with solid malignancies, 22 (22.4%) patients had breast cancer, 22 (22.4%) had gastrointestinal cancers, 5 (5.1%) had gynecological cancers, 23 (23.5%) had lung cancer, 8 (8.2%) had CNS malignancies, 11 (11.2%) had other cancers, and 7 (7.2%) had prostate cancer with 81.6% of patients having metastatic disease. Among the hematological malignancies, lymphoma was diagnosed in 11 (57.9%) patients while 3 (15.9%) each had multiple myeloma and leukemia. The mean age of the patients was 68 years and 59% were female. The average LOS was 8.6 days. The mean admission total FIM was  $66.7 \pm 12.8$  and discharge total FIM was  $87.3 \pm 16.1$ . The total improvement in FIM was  $20.6 \pm 13.8$  with FIM efficiency of 2.9. There were 21 (18%) patients transferred back to acute care units for decompensation, 7 (6%) went to subacute rehabilitation, 1 (0.85%) went to hospice while 87 (74.3%) were discharge to their homes upon completion of IPCR. Conclusions: Our focused rehabilitation was able to decrease the LOS, well above the 90 percentile Center for Medicare and Medicaid Services (CMS) benchmark and other prior studies, as well as enable patients to safely return home with improved FIM. Creating an IPCR unit proved to be beneficial, allowing for more comprehensive and individualized care, even in the setting of advanced malignancies.

Blas KG, Galoforo S, Wilson TG, Krueger SA, **Grills IS**, Marples B and **Wilson GD** (2017). "Targeted inhibition of pi3k and mek in combination with radiation therapy in UT15: A murine model of head and neck squamous cell carcinoma." International Journal of Radiation Oncology Biology Physics 99(2): E578-E579.

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*Department of Radiation Oncology*

Purpose/Objective(s): To study the effectiveness of dual targeted PI3K and MEK inhibition alone and in combination with radiotherapy in HNSCC models as a novel clinical treatment strategy. Purpose/Objective(s): MTT assays were used to establish growth inhibition and schedule of RT with Buparlisib (BKM120) a pan PI3K-inhibitor. Clonogenic survival assays were used to assess the impact of BKM120 alone, Binimetnib (MEK162), a MEK1/2-inhibitor, alone, and both drugs in combination. Subcutaneous xenografts were established in female NIH III HO mice using the UT15 cell line. Tumors grew to 200-400 mm<sup>3</sup> before treatment: +BKM120 (10mg/kg oral gavage), +MEK162 (5mg/kg oral gavage), or combined +BKM120 (10mg/kg), +MEK162 (5mg/kg oral gavage) ± RT. In radiation treated cohorts, a sub-curative 45 Gy dose (3 Gy/day 5 days a week) was delivered 4 hours before drug treatment. The primary endpoint was tumor regrowth at 90 days post treatment. Results: For UT15 cell line the IC50 concentration for BKM120 was 0.5 µM and for MEK162 was above 10 µM. Delivery of BKM120 (0.5 µM) 4 hours post radiotherapy produced the greatest reduction in cell viability compared to radiation alone 100% to 70%. Clonogenic survival assay confirmed UT15 to be more sensitive to MEK162 than BKM120 with survivals of 40% at 0.1 µM versus 90% at 0.2 µM, respectively. In the UT15 flank tumor model, RT alone, (BKM120 & MEK162), RT+ BKM120, RT+ MEK162, and RT+ (BKM120 & MEK162) had slower growth rates compared to controls (p=0.004). There was no difference in growth rates between the experimental arms. The time needed to reach twice normalized volume from the start of treatment is listed in Table 1. Western analysis confirmed the targeted agents were acting as expected based on their mechanism of action. When assessing tumor regrowth past the 90 days



post-treatment it did appear that RT+ BKM120 cohort never surpasses the 3x normalized treatment volume raising the possibility of permanent change in tumor growth and viability. However, the standard error of the means (SEM) becomes increasing variable and strong conclusions cannot be drawn at this time. In previous experiments, there was a significant difference in growth rates between RT alone and RT+ MEK162 ± BKM120, primarily driven by the combination of RT and MEK162. Conclusion: In our UT15 model, radiation in combination with PI3K and/or MEK inhibition did not significant delay tumor growth rates. There was, however, a suggestion of permanent tumor change, in UT15, after 90 days in particular with PI3K blockade. This is contrary to our UT14 model where MEK inhibition produced the greatest delay in growth patterns. Further experiments with quantitative PCR and other agents are ongoing to determine if this difference is related to varying expression levels or differences in drug efficacy.

**Brisson RJ**, Dekker A, De Souza JA, Saloura V, Vokes EE and Seiwert TY (2017). "A pilot study of the pan-class I PI3K inhibitor buparlisib in combination with cetuximab in patients with recurrent/metastatic head and neck cancer." *Journal of Clinical Oncology* 35(15).

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*OUWB Medical Student Author*

Background: R/M HNC carries a poor prognosis with a median survival of 10-12 months. PI3K pathway aberrations are present in 30% of HNC. This pilot dose-escalation study assesses the safety and tolerability of the PI3K inhibitor buparlisib when given concurrently with cetuximab in R/M HNC, as well as assess efficacy in an expansion cohort. Methods: Patients (pts) with R/M HNC who were not amenable to curative intent therapy were enrolled. Pts were given oral buparlisib starting day -7 and daily thereafter. The dose of buparlisib was escalated in a 3+3 design (Level 1: 80mg daily, Level 2: 100 mg daily) followed by a dose expansion cohort. The maximum dose of buparlisib was 100 mg daily. Cetuximab (500mg/m<sup>2</sup>) was given intravenously every 14 days starting day 0. Pts continued on treatment until progression of disease. Prior cetuximab failure was allowed. Results: Of the 12 pts enrolled, 10 had at least 2 previous treatment regimens (11 with prior cetuximab). 5 pts were HPV+, 4 were HPV-, and 3 had unknown HPV status. 3 pts were treated at the 80 mg dose level while 9 were treated at the 100 mg dose level (3 + 6 patient expansion). Treatment was well tolerated with 2 pts experiencing grade 3 adverse events (AEs) (no grade 4 AEs). The most common AEs were fatigue (83.3%), maculopapular rash (50.0%), and anorexia (50.0%). 3 pts experienced grade 1 anxiety. There were no SAEs. Of the 10 pts who were evaluable for response one patient achieved a PR (10%), and 4 achieved stable disease (40%) per RECIST 1.1. Median overall survival was 280 days (HPV+: 370 days, HPV-:191 days). The study was closed early due to poor enrollment on the expansion cohort as patients opted for concurrently open immunotherapy trials. Conclusions: Based on this pilot study, buparlisib plus cetuximab proved to be well-tolerated and showed limited evidence of activity in a heavily pre-treated patient population. Further research is warranted to determine activity of buparlisib in a larger cohort of R/M HNC.

Buraimoh MA, Massie LW and **Montgomery DM** (2017). "Lateral atlantoaxial osteoarthritis: A narrative literature review." *PloS One*. ePub Ahead of Print.

[Full-Text](#)

*Department of Orthopedic Surgery*

Lateral atlantoaxial osteoarthritis (AAOA), or C1-C2 lateral mass arthritis (LMA), is an unfamiliar degenerative cervical disease with a clinical presentation that markedly differs from subaxial spondylosis. The prevalence of LMA in the nonsurgical outpatient setting is 4%. Risk factors include age and occupation. The typical patient is between 50 and 90 years old, presents with upper cervical or occipital pain, has limited rotation, and has pain provocation during passive rotation to the affected side. Pain stems from degeneration of the lateral C1-C2 articulation and may be referred or radicular, through the greater occipital nerve. Although there is no consensus on diagnostic work-up, the disease is classically seen on the open-mouth odontoid radiograph. Computerized tomography, magnetic resonance imaging, bone scan, and diagnostic injections are also useful. Initial treatment is conservative, and upwards of two-thirds of LMA patients obtain lasting relief with noninvasive measures and injections. In patients with severe, recalcitrant pain, limited C1-C2 fusion offers satisfactory and reliable relief. The goals of this review article are to provide a synthesis of the

literature on LMA, to offer a treatment approach to LMA, and to identify problems with the current state of knowledge on LMA.

Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Nielsen JC, Curtis AB, Davies DW, Day JD, d'Avila A, de Groot NMSN, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, **Haines DE**, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ and Yamane T (2017). "2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation." Heart Rhythm 14(10): e275-e444.

[Full-Text](#)

*Department of Internal Medicine*

Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Nielsen JC, Curtis AB, Davies DW, Day JD, d'Avila A, de Groot NMSN, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, **Haines DE**, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ and Yamane T (2017). "2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary." Journal of Arrhythmia 33(5): 369-409.

[Full-Text](#)

*Department of Internal Medicine*

Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Nielsen JC, Curtis AB, Davies DW, Day JD, d'Avila A, de Groot NMSN, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, **Haines DE**, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ and Yamane T (2017). "2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary." Heart Rhythm 14(10): e445-e494.

[Full-Text](#)

*Department of Internal Medicine*

Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Nielsen JC, Curtis AB, Wyn Davies D, Day JD, d'Avila A, de Groot NMSN, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, **Haines DE**, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ and Yamane T (2017). "2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary." Journal of Interventional Cardiac Electrophysiology 50(1).

[Full-Text](#)

*Department of Internal Medicine*

Carr LK, Tu LM, Robert M, Quinlan D, Carlson KV, Jankowski R, Dmochowski R, **Chancellor M** and Herschorn S (2017). "Autologous muscle-derived cells for urinary sphincter repair in women with stress urinary incontinence: Results of a randomized, double-blind, placebo-controlled study." Canadian Urological Association Journal 11(6): S182-S183.

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*Department of Urology*

Introduction: This multicentre study assessed the effect of autologous muscle-derived cells for urinary sphincter repair (AMDC-USR) in women with stress urinary incontinence (SUI). Methods: Women with predominant SUI who presented with a mean incontinence episode frequency (IEF) of  $\geq 1$  stress leak/day were randomized 2:1 to receive intrasphincteric injection of  $150 \times 10^6$  AMDC-USR or placebo and 1:1 to receive one or two treatments. Second treatments were (Table presented) (Figure presented). administered six months after first treatments. At baseline and followup, three-day diaries, 24-hour pad tests, in-office pad tests, and Incontinence Quality of Life (IQOL) questionnaires were collected. The primary composite efficacy endpoint was the percentage of patients 12 months posttreatment with  $\geq 50\%$  IEF reduction or  $\geq 50\%$  reduction in either pad test. Patients were followed for two years, but were unblinded after 12-month visits. After unblinding, placebo patients received AMDC-USR. Results: The study treated 58% (143/246) of the planned enrollment; 99% (141/143) of patients completed 12-month visits (Table 1). Enrollment was halted early due to an unexpectedly high placebo responder rate with the composite endpoint. Baseline characteristics were similar for both AMDC-USR and placebo (Table 2). No AMDC-USR safety signals were identified. Post-hoc analyses correlated IQOL score improvement with IEF reduction to identify alternate, clinically meaningful endpoints. Patients with  $\geq 50\%$  IEF reduction had greater IQOL score improvement than those with  $< 50\%$  IEF reduction, and patients with  $\geq 75\%$  IEF reduction or  $\leq 1$  stress leak/three days had even greater IQOL improvement (Fig. 1). With alternate IEF reduction endpoints, placebo rates were reduced and a potential treatment effect was detected (Fig. 2). Conclusions: AMDC-USR is safe in women with SUI. The composite endpoint, which included pad tests, was too liberal to detect treatment differences between AMDC-USR and placebo; however, IEF reduction endpoints suggest efficacy.

Castillo E, Myziuk NK, Zhang J, Vinogradskiy Y, Castillo R and **Guerrero TM** (2017). "Radiation dose response modeling using CT-derived ventilation imaging." International Journal of Radiation Oncology Biology Physics 99(2): E644.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Computed Tomography derived ventilation imaging (CT-V) is an image processing based modality that utilizes deformable image registration (DIR) to infer local tissue volume changes, induced by respiratory motion, from inhale and exhale phases of a thoracic 4DCT image. Accordingly, radiation dose response modeling based on CT-V aims to describe temporal changes in ventilation as a function of delivered dose. However, such models have not yet achieved statistical significance due to variable patient breathing motion and uncertainty in the DIR solution. Hypothesis: In the absence of patient variability factors, the DIR spatial precision required to produce accurate CT-V dose response modeling is less than a voxel. Purpose/Objective(s): CT-V images were retrospectively generated from the simulation (treatment planning) 4DCTs of three patients who received radiotherapy (RT) for non-small cell lung cancer. The images were computed to satisfy an inhale-to-exhale contraction constraint using the transformation-based (Jacobian) CT-V method. For each patient, a linear radiation dose response model was applied to the pre-RT CT-V image to generate predicted post-RT CT-V images representing 10% (moderate), 50% (severe), and 100% (complete) functional loss responses to delivered RT dose. Finally, we solved a numerical inverse problem to compute the corresponding estimated post-RT DIR displacement fields, i.e. the DIR solutions that generate each of the three predicted post-RT CT-V images. Results: The average (std.) magnitude change (in voxels) between the pre-RT and estimated post-RT DIR displacement fields for all response levels was less  $< 0.7$  voxels, as detailed by the following Table: 

Function Loss Response	10%	50%	100%
Case 1	0.13 (0.08)	0.24 (0.12)	0.41 (0.23)
Case 2	0.26 (0.21)	0.42 (0.26)	0.68 (0.44)
Case 3	0.17 (0.15)	0.22 (0.17)	0.34 (0.24)

 Across all three cases, complete loss responses demonstrated a maximum magnitude change in DIR displacement of  $< 2.75$  voxels, despite a 100% loss in function between the corresponding pre- and estimated post-RT CT-V images. Conclusion: Using a simple linear dose response model and a numerical inverse problem formulation, we

were able to conduct a numerical experiment to assess the magnitude difference between DIR displacements corresponding to pre-and post-RT CT-V imaging, in the absence of confounding patient variability factors. The results indicate that even for unrealistically severe dose responses, as quantified by CT-V measured functional loss, the average magnitude change between the corresponding pre-and post-RT DIR solutions are <0.7 voxels. Considering that clinically acceptable DIR methods yield spatial accuracies that are only on the order of 1.0 voxels, these results suggest that current methods for computing transformation-based CT-V lack the numerical precision to accurately quantify functional responses to RT-dose. Therefore, higher precision methods are still needed.

Castillo E, Zhang J, Vinogradskiy Y, Castillo R and **Guerrero T** (2017). "Accuracy preserving normalization of deformable image registration solutions for robust CT-derived ventilation imaging." *Medical Physics* 44(6): 3168.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: To improve the robustness and reproducibility of CT-derived ventilation (CT-V) imaging. CT-V employs deformable image registration (DIR) to calculate local tissue volume changes between inhale/exhale CT pairs. Thus, CT-V quality is dependent on DIR spatial accuracy. However, subtle differences between sub-voxel accurate DIRs can cause significant variations in the corresponding CT-V images. We propose a DIR normalization strategy that reduces these variations while preserving spatial accuracy. Methods: Given a DIR solution, the accuracy-normalized solution (ANS) is defined as the "smoothest" (minimum gradient magnitude) displacement field satisfying the following c-magnitude difference condition: the maximum magnitude difference between the ANS displacement vectors and the original DIR displacement vectors is less than a scalar constant c. Every DIR solution has a unique ANS. If two DIR solutions satisfy a 2c-magnitude difference condition, then their ANS's are equivalent. In order to demonstrate the utility of ANS, we apply two DIR algorithms to the same inhale/exhale CT image pair and quantify the differences between their spatial accuracies, as measured by 300 landmarks point pairs, and their corresponding CT-V values. Results: DIR spatial accuracies for Algorithms 1 & 2 were, 1.00 (0.74) and 1.14 (0.63) respectively, while the mean difference in CT-V values was 0.07 (0.07). For Algorithm 1, the ANS spatial accuracies for  $c = 1$  and 3 were 1.35 (0.70) and 1.38 (0.71), while for Algorithm 2, they were 1.36 (0.72), and 1.38 (0.73). The mean CT-V differences were reduced to 0.02 (0.03) and 0.01 (0.01) for the  $c = 1, 3$  ANS's corresponding to Algorithms 1 and 2. Conclusion: As demonstrated by numerical experiments, the ANS approach reduces the effects of subvoxel DIR errors on the CT-V calculation, while also maintaining spatial accuracy. The results indicate that ANS reduces the variation between CT-V images computed from similarly accurate DIRs.

**Cheah C**, Dass K, **Guthrie A** and Dalal B (2017). "Angiotensin converting enzyme inhibitors-induced angioedema is causing more deaths." *Chest* 152(Sup 4): A1056.

[Full-Text](#)

*OUWB Medical Student Author*

**Chen B**, Choi H, Hirsch LJ, Katz A, Legge A, Buchsbaum R and Detyniecki K (2017). "Psychiatric and behavioral side effects of antiepileptic drugs in adults with epilepsy." *Epilepsy & Behavior* 76(Nov): 24-31.

[Full-Text](#)

*OUWB Medical Student Author*

PURPOSE: Psychiatric and behavioral side effects (PBSEs) are common, undesirable effects associated with antiepileptic drug (AED) use. The objective of the study was to compare the PBSE profiles of older and newer AEDs in a large specialty practice-based sample of patients diagnosed with epilepsy. METHODS: As part of the Columbia and Yale AED Database Project, we reviewed patient records including demographics, medical history, AED use, and side effects for 4085 adult patients (age: 18 years) newly started on an AED regimen. Psychiatric and behavioral side effects were determined by patient or physician report in the medical record, which included depressive mood, psychosis, anxiety, suicidal thoughts, irritability, aggression, and tantrum. Significant non-AED predictors of PBSE rate were first determined from 83 variables using logistic regression. Predictors were then controlled for in the comparison analysis of the rate of PBSEs and intolerable PBSEs (PBSEs that led to dosage reduction or discontinuation) between 18 AEDs. RESULTS: Psychiatric and

behavioral side effects occurred in 17.2% of patients and led to intolerability in 13.8% of patients. History of psychiatric condition(s), secondary generalized seizures, absence seizures, and intractable epilepsy were associated with increased incidence of PBSE. Levetiracetam (LEV) had the greatest PBSE rate (22.1%). This was statistically significant when compared with the aggregate of the other AEDs ( $P < 0.001$ ,  $OR = 6.87$ ). Levetiracetam was also significantly ( $P < 0.001$ ) associated with higher intolerability rate (17.7%), dose decreased rate (9.4%), and complete cessation rate (8.3%), when compared with the aggregate of the other AEDs. Zonisamide (ZNS) was also significantly associated with a higher rate of PBSE (9.7%) and IPBSE (7.9%, all  $P < 0.001$ ). On the other hand, carbamazepine (CBZ), clobazam (CLB), gabapentin (GBP), lamotrigine (LTG), oxcarbazepine (OXC), phenytoin (PHT), and valproate (VPA) were significantly associated with a decreased PBSE rates ( $P < 0.001$ ). Carbamazepine, GBP, LTG, PHT, and VPA were also associated with lower IPBSE rates when compared individually with the aggregate of other AEDs. All other AEDs were found to have intermediate rates that were not either increased or decreased compared with other AEDs. When each AED was compared to LTG, only CBZ had a significantly lower PBSE rate. The main limitations of this study were that the study design was retrospective and not blinded, and the AEDs were not randomly assigned to patients. CONCLUSIONS: Psychiatric and behavioral side effects occur more frequently in patients taking LEV and ZNS than any other AED and led to higher rates of intolerability. Lower PBSE rates were seen in patients taking CBZ, CLB, GBP, LTG, OXC, PHT, and VPA. Our findings may help facilitate the AED selection process.

**Chen PY, Wallace M, Ye H, Jawad MS, Dilworth JT, Dekhne NS, Benitez PR and Gustafson GS** (2017). "Comparative analysis of brachytherapy versus 3D conformal external beam radiation therapy in delivery of accelerated partial breast irradiation from a single institution: Determination of clinical effectiveness." International Journal of Radiation Oncology Biology Physics 99(2): E688.

[Full-Text](#)

*Department of Radiation Oncology*

*Department of Surgery*

Purpose/Objective(s): We present the results of a comparative analysis of brachytherapy (BT) vs external beam 3-D conformal radiation therapy (3-D CRT) in the delivery of accelerated partial breast irradiation (APBI) in early-stage breast cancer treated at a single institution. Purpose/Objective(s): Between 4/1993 and 8/2016, a total of 784 patients were treated with APBI; 567 received BT using either interstitial multicatheters or a balloon/strut based applicator while 217 received 3-D CRT using CT based planning without IMRT. Eligibility criteria included age  $> 40$ , infiltrating ductal carcinoma, with inclusion of invasive lobular and DCIS since 2003 (IRB addendum), margins  $\geq 2$  mm, and surgically staged axilla with  $\leq 3$  positive nodes but pN0 since 2003 (IRB modified). The multicatheter BT was either low-dose rate (LDR at 50 Gy in 96 hours) or high-dose rate (HDR at 32 Gy in 8 BID fx of 4 Gy or 34 Gy in 10 BID fx of 3.4 Gy) while the applicator BT was all HDR of 34 Gy in 10 BID fx. The 3-D CRT used 3-5 non-coplanar beams to deliver 3.85 Gy BID x 10 fractions. Results: Median age was 65 (range 39-94). The mean follow-up (FU) was 8.4 years for the 784 patients [9.0 yrs BT, 6.7 for 3-D CRT,  $p < 0.001$ ]. A higher percentage of DCIS was treated with 3-D CRT vs BT [22% vs 13%,  $p = 0.004$ ]. No statistical difference was noted in mean age, nodal status, margins, tumor size, receptor status and receipt of systemic therapy between the 2 treatment groups (Table 1). Ten year actuarial outcomes reveal no statistical difference between BT and 3-D CRT in freedom from local recurrence [95.4% vs 96.3%  $p = 0.207$ ], freedom from distant metastases [96.1% vs 98.5%  $p = 0.235$ ], freedom from contralateral breast failure [96.1% vs 95.5%  $p = 0.86$ ], DFS [92.2% vs 96.3%  $p = 0.055$ ], CSS [96.9% vs 99.0%,  $p = 0.288$ ] and OS [76.4% vs 80.3%,  $p = 0.677$ ]. Conclusion: Delivery of APBI with either BT or 3-D CRT in appropriately selected early-stage breast cancer patients results in comparable clinical outcomes in terms of local control and survival outcomes. Continued follow-up will be needed to assess the long-term effectiveness and equivalence of these two APBI modalities.

**Chen PY**, Wallace M, Ye H, **Jawad MS**, **Dilworth JT**, Wilkinson B, **Dekhne NS**, **Benitez PR** and **Gustafson GS** (2017). "Long-term clinical outcomes, late toxicities, and cosmetic results of short-course two-day brachytherapy accelerated partial breast irradiation." *International Journal of Radiation Oncology Biology Physics* 99(2): S214.

[Full-Text](#)

*Department of Radiation Oncology*

*Department of Surgery*

Purpose/Objective(s): Hypofractionated radiotherapy is increasingly being adopted for early-stage breast cancer. To assess the long-term outcome of 2-day brachytherapy accelerated partial breast irradiation [2d-APBI], we analyzed patients so treated for clinical effectiveness, late toxicity, and cosmetic results. Purpose/Objective(s): Between 3/2004 and 8/2007, 45 patients were treated with single-lumen applicator-based 2d-APBI [700 cGy BID x 4]. Updated thru 1/2017, an IRB-approved retrospective review was done. Selection criteria included age >40, ≤3.0 cm tumor size, ≤3 pathologically positive lymph nodes, and negative margins (per NSABP guidelines). Based upon the ASTRO Consensus Statement guidelines for APBI (2009) applied retrospectively, 15 were suitable (33%), 27 cautionary (60%), and 3 unsuitable (7%). Freedom from local recurrence (FFLR), regional recurrence (FFRR), distant metastasis (FFDM), contralateral breast cancer (CLBC), disease-free survival (DFS), cause-specific survival (CSS), and overall survival (OS) were assessed by Kaplan-Meier. Toxicities were scored using CTCAE v3.0. Cosmetic rating was scored via the Harvard criteria. Results: Median follow-up was 9.4 years. Fourteen patients were followed ≥ 10 yrs (31%) and 17 with follow-up of 9.0-9.9 yrs (38%). Median age was 66 yrs (48-83 yrs) with most having T1 tumors (96%) [median size 0.6cm]; all had margins with no tumor on ink. A minority (4%) had positive regional nodes. ER positivity was found in 73%. Endocrine therapy was received by 61%, while 18% had chemotherapy. Clinical outcomes revealed FFLR 97.4%, FFRR 100%, FFDM 92.9%, CLBC 97.4%, DFS 90.3%, CSS 97.6%, and OS 79.0%, all 10-year actuarial. Late toxicities analyzed included skin pigmentation, edema, and pain (all grade 1/2) along with telangiectasias, induration (Table 1), fat necrosis, seroma and rib fracture. No grade 3 or 4 toxicities were noted except for 2% grade 3 telangiectasias and 2% grade 3 induration. Fat necrosis was seen in 14% and persistent seroma in 17%. Rib fracture was seen in 3 (7%) where 160% of the prescription dose was accepted during this treatment era. Cosmesis was good/excellent in 88% at 10 years. Conclusion: With median follow-up approaching 10 years, 2-day APBI demonstrates excellent clinical effectiveness, minimal late morbidity, and good/excellent cosmesis in the majority of patients. Dose constraints such as to ribs/chest wall have been refined from these results. Short-course APBI affords appropriately selected early-stage breast cancer patients irradiation in 2 days vs several weeks of whole breast external beam treatments. Further follow-up of 2-day APBI patients will be needed to substantiate these long-term findings.

Chen S and **Yan D** (2017). "Uncertainty analysis of a FDG-PET imaging based tumor voxel dose response marker." *Medical Physics* 44(6): 2732.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: Tumor voxel dose response marker (SF2) determined from multiple FDG-PET imaging has shown a great value on predicting local tumor recurrence (LR) and ability to be used as a novel objective for dose-painting-by-number. However, uncertainties included in the SF2 construction can introduce bias in its application. This study aims to quantify the uncertainties and their impact. Methods: Tumor voxel dose response marker, SF2(v), has been constructed using pretreatment and weekly FDG-PET/CTs using the deformable image registration (DIR). SF2 of tumor voxel v was derived based on the changes of weekly SUV, within which a k-factor represents a linear relationship between the logarithm of the ratio of SUV change and the logarithm of the tumor cell survival fraction. The k-factor was determined assuming the average tumor cell size and cell density saturation in a voxel with the SUVmax at pretreatment. The SF2 uncertainty was formulated as  $\Delta SF2(v) = f(v, \Delta SUV, \Delta k)$ , where  $\Delta SUV$  was induced by PET-imaging partial-volume-effect (PVE), PET-imaging time-interval after FDG injection (TI) and weekly-to-pretreatment PET/CT DIR;  $\Delta k$  was induced by assumptions of tumor cell size, density saturation and heterogeneous FDG absorption. Perturbation analysis was performed including different time-phase PETs, DIR methods, PVE and k values to construct SF2. The SF2 uncertainty was quantified and its influence on the predictability of LR was evaluated



by receiver-operating-characteristic analysis. Results: SUV variability induced by PVE (assuming 15% SUV variability), DIR (inconsistency-vector-difference  $1.24 \pm 1.07$  mm) and TI variation (interval  $0.96 \pm 0.11$  hours) and different k values assuming tumor cell diameter range  $10 \mu\text{m}$ - $20 \mu\text{m}$  result in voxel SF2 variation of  $0.06 \pm 0.13$ . Without perturbation, area under the curves (AUC) of tumor sub-volume with SF2 > 0.9 or 1.0 is  $0.98-1$  ( $p < 0.003$ ); with perturbation induced by uncertainties results in AUC drop of  $0.04 \pm 0.02$ . Conclusion: FDG-PET imaging based tumor dose response marker (SF2) is robust respect to the uncertainties. It is reliable for early response assessment.

Chin J, Hatiboglu G, **Relle J**, Billia M, Siddiqui K, Kuru T, Popeneciu I, **Hafron J**, Roethke M, Mueller-Wolf M, Kassam Z, Harle C, Burtnyk M, Schlemmer HP and Pahernik S (2017). "24-month outcomes of a prospective, phase 1 study of magnetic resonance imaging-guided transurethral ultrasound ablation in patients with localized prostate cancer." Canadian Urological Association Journal 11(6): S260.

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*Department of Urology*

Introduction: Magnetic resonance imaging (MRI)-guided transurethral ultrasound ablation (TULSA) is a novel, minimally invasive technology for ablation of prostate tissue. The ultrasound ablation volume is shaped to patient-specific anatomy and pathology, using active MRI thermometry feedback control. Herein, we report 24-month results of the prospective, phase 1 study on safety and feasibility of TULSA for localized prostate cancer (PCa), conducted in Canada, Germany, and the U.S. Methods: 30 patients with biopsy (bx)-proven PCa were treated (T1c-T2a, prostate-specific antigen [PSA]  $\leq 10$ ng/ml, Gleason  $\leq 3 + 4$ ). TULSA was delivered with 3 mm margins at gland periphery, and expected 10% residual pericapsular viable prostate tissue. Primary endpoints were safety and feasibility (spatial ablative precision). Exploratory outcomes included PSA, quality of life, MRI, and 12-core TRUS bx. Results: Median age was 69 (interquartile range [IQR]) 67-71) years, PSA 5.8 (3.8-8.0 ng/ml). Treatment time was 36 (26-44) minutes. Spatial control of ablation was  $\pm 1.3$  mm. Adverse events (CTCAE v4) included urinary tract infection (UTI) (10 patients, Grade 2), acute retention (three patients G1, five Grade 2), and epididymitis (one patient, Grade 3). International Prostate Symptom Score (IPSS) and International Index of Erectile Function (IIEF) returned to preoperative levels and stabilized at 24 months. To date, PSA nadir is 0.5 ng/ml (0.3-0.8). Median PSA decreased 87% at one month, stable to 0.8 ng/ml at 12 months (n=30), and to 0.6 ng/ml at 24 months (n=23). Positive bx at 12 months show 61% reduction in total cancer length, clinically significant disease in 9/29 patients (31%), and any disease in 16/29 pts (55%). MRI at 12 months show 88% prostate volume reduction. Following positive bx at 12 months, four patients underwent uncomplicated salvage radical prostatectomy, one patient salvage radiation therapy, and one patient focal laser ablation. Conclusions: MRI-guided TULSA is well-tolerated in patients with localized PCa. TULSA can offer a low morbidity profile while keeping posttreatment salvage therapy options open if necessary. An international 12-centre trial in 110 patients with reduced gland periphery margins is now underway to further evaluate safety and efficacy of whole-gland TULSA.

Chopra R, **Vakharia PP**, Simpson EL, Paller AS and Silverberg JI (2017). "Severity assessments used for inclusion criteria and baseline severity evaluation in atopic dermatitis clinical trials: A systematic review." Journal of the European Academy of Dermatology and Venereology 31(11): 1890-1899.

[Full-Text](#)

*OUWB Medical Student Author*

BACKGROUND: Numerous inclusion criteria and baseline severity assessments are used in clinical trials of atopic dermatitis (AD), which may limit comparison of results. OBJECTIVE: We sought to characterize the inclusion criteria and baseline severity assessments used in randomized controlled trials (RCT) of AD internationally. METHODS: We performed a systematic review of RCT with a pharmacological intervention from 2007 to 2016. Cochrane Library, EMBASE, GREAT, LILACS, MEDLINE and Scopus were searched. Two authors independently performed study selection and data extraction. RESULTS: Overall, 212 RCT met inclusion/exclusion criteria. Target population and inclusion criteria based on AD severity were not documented in 78 (36.8%) and 25 (18.7%) studies, respectively. Thirty and 58 severity assessments were used for inclusion criteria and baseline severity, respectively, with only 60.3% concordance between their uses. Global assessments were most frequently used for both inclusion criteria and baseline severity assessment in

North America (39.5% and 32.1%), while SCORing AD (SCORAD) or objective-SCORAD index was most frequently used in Europe (23.5% and 23.0%) and Asia (34.2% and 43.5%). Minimum and maximum thresholds of severity assessments were inconsistently used between studies for inclusion criteria, even within similar target populations. SCORAD, global assessments and body surface area were most frequently used for both inclusion criteria and baseline severity assessment. IGA was particularly used in trials of topical agents. CONCLUSIONS: There were considerable variability and poor documentation of inclusion criteria and baseline severity assessments in RCT for AD. These differences may limit interpretation of a study and comparison of results between studies.

**Clark CL**, Shams AH, **Chang AM**, Fermann GF, Hiestand BC, Kea B, Mace SE, Peacock WF, **Sawyer KN**, Welker JA and **Bastani A** (2017). "52 D-dimer in hospitalized acute medically ill adults and venous thromboembolism: Analysis of the DAMIACT study by age." Annals of Emergency Medicine 70: S21-S22.

[Full-Text](#)

*Department of Emergency Medicine*

*OUIB Medical Student Author*

Cohen-Inbar O, Starke RM, Paisan G, Kano H, Huang PP, Rodriguez-Mercado R, Almodovar L, **Grills IS**, Mathieu D, Silva D, Abbassy M, Missios S, Lee JYK, Barnett GH, Kondziolka D, Lunsford LD and Sheehan JP (2017). "Early versus late arteriovenous malformation responders after stereotactic radiosurgery: An international multicenter study." Journal of Neurosurgery 127(3): 503-511.

[Request Form](#)

*Department of Radiation Oncology*

Cohen-Inbar O, Xu Z, Lee CC, Wu CC, Chytka T, Silva D, Sharma M, Radwan H, **Grills IS**, **Nguyen B**, Siddiqui Z, Mathieu D, Iorio-Morin C, Wolf A, Cifarelli CP, Cifarelli DT, Lunsford LD, Kondziolka D and Sheehan JP (2017). "Prognostic significance of corticotroph staining in radiosurgery for non-functioning pituitary adenomas: A multicenter study." Journal of Neuro-Oncology 135(1): 67-74.

[Full-Text](#)

*Department of Radiation Oncology*

*OUIB Medical Student Author*

Colvin RW, Al-Katib S and **Ebersole J** (2017). "Perforated Meckel's diverticulitis." Journal of Gastrointestinal Surgery 21(12): 2126-2128.

[Full-Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

A Meckel's diverticulum is a vestigial remnant present in approximately 2% of the population. Fewer than 10% of patients with a Meckel's diverticulum develop clinical complications, and such findings are exceedingly rare in the geriatric population. We present a case of perforated Meckel's diverticulitis with a fistulous tract involving the anterior abdominal wall in an 85-year-old male.

Comfere N, **Sundram U**, Hurley M and Swick B (2017). "Views of dermatopathologists about clonality assays in the diagnosis of cutaneous T cell and B cell lymphoproliferative disorders." Journal of Cutaneous Pathology. ePub Ahead of Print.

[Full-Text](#)

*Department of Pathology*

BACKGROUND: Appropriate use criteria have been developed for many tests using expert judgment, evidence-based practice, and clinical experience. In this context, the opinions of practitioners about clonality assays in various clinical scenarios where cutaneous lymphoma is suspected are reported. METHODS: An Appropriate Use Criteria Task Force sponsored by the American Society of Dermatopathology (ASDP) synthesized clinical scenarios for cutaneous lymphoproliferative disorders (LPD). We conducted, summarized, and presented a relevant literature search to an audience of 144 dermatopathologists with a variety of practice experiences at the 53rd Annual Meeting of the ASDP in Chicago, IL. RESULTS: 27 clinical scenarios

for lymphoproliferative disorders (13 T cell and 14 B cell) were defined. 40 relevant studies for T-cell receptor gene clonality assays and 20 relevant studies for IgH/IgK clonality assays were identified. Audience response data from participating dermatopathologists reflected a wide variety of approaches to the application of clonality assays in the evaluation of LPDs, based on practice setting, personal experience and test availability. CONCLUSIONS: Our clinical scenario analysis and literature review revealed well supported clinical scenarios and identified opportunities for additional research to further define the utility of clonality assays in some clinical scenarios.

Cvetanovich GL, Lizzio V, Meta F, Chan D, **Zaltz I**, Nho SJ and Makhni EC (2017). "Variability and comprehensiveness of North American online available physical therapy protocols following hip arthroscopy for femoroacetabular impingement and labral repair." Arthroscopy - Journal of Arthroscopic and Related Surgery 33(11): 1998-2005.

[Full-Text](#)

*Department of Orthopedic Surgery*

Daloglu I, **Espinosa M**, Sharma R and **Berman B** (2017). "Concurrence of alloimmune neutropenia and thrombocytopenia in two neonates." Pediatric Blood and Cancer 64: S92.

[Full-Text](#)

*Department of Pediatrics*

Background: Neonatal alloimmune thrombocytopenia (NAIT) and alloimmune neutropenia (NAN) are caused by transplacental passage of maternal alloantibodies against incompatible fetal platelet or neutrophil antigens, respectively. These are well-defined entities, however simultaneous occurrence of both in the same patient has been rarely described (1, 2, 3). Objectives: To describe two premature infants with extremely rare concurrence of NAIT and NAN. Design/Method: Case report. Results: Patient #1 was born at 31 weeks of gestation after an otherwise uncomplicated pregnancy to an Asian mother and Caucasian father. Shortly after birth, a complete blood count (CBC) demonstrated thrombocytopenia (60,000/ $\mu$ L), a white blood cell count of 5,300/ $\mu$ L and neutropenia (300/ $\mu$ L). The platelet count spontaneously increased and normalized by age 5 days without related complications. However, the absolute neutrophil count (ANC) fell to <100/ $\mu$ L by the second day of life and profound neutropenia persisted. Parental platelet and neutrophil antigen genotyping and antibody analysis (BloodCenter of Wisconsin, Milwaukee, USA) demonstrated maternal antibodies against HNA-1b and HPA-15b. A single dose of filgastrim (10  $\mu$ g/kg) yielded a transient rise in ANC to 3,900/ $\mu$ L. Neonatal intensive care unit (NICU) course was complicated by mild omphalitis responsive to a one-week course of intravenous antibiotics. Neutropenia gradually resolved by 13 weeks of age. Patient #2 was that of a precipitous home delivery at 32 weeks of gestation after an uncomplicated pregnancy. As with patient #1, mother was Asian and father was Caucasian. CBC at the time of hospital admission demonstrated neutropenia (600/ $\mu$ L) and moderate thrombocytopenia (96,000/ $\mu$ L). By the third day of life the ANC fell to <100/ $\mu$ L. Thrombocytopenia spontaneously resolved by age 8 days without any related complications, however profound neutropenia persisted. Parental neutrophil and platelet antigen genotyping and antibody analysis revealed alloantibodies in the mother against HNA-1b and HPA-5b. A single dose of filgastrim (10  $\mu$ g/kg) provoked a transient neutrophilic response. NICU course was uncomplicated. At the time of hospital discharge on day 23 of life, the ANC had risen to 1,300/ $\mu$ L. Conclusion: NAIT and NAN are well-described entities. Although rarely reported, their concurrence in the same patient should be considered in neonates with otherwise unexplained bicytopenia. 1. Marin, *Pediatr Allergy Immunol*, 20052. Gramatges, *Pediatric Blood Cancer*, 20093. Taaning, *Acta Paediatrica*, 2012.

David J, Jabbour S, Gresham GK, Deek M, Shant T, **Robertson JM**, **Kabolizadeh P** and Tuli R (2017). "Effect of neoadjuvant IMRT for locally advanced rectal cancer on toxicity and pathologic response." Journal of Clinical Oncology 35(4 Sup): 693.

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*Department of Radiation Oncology*

Background: Neoadjuvant chemoradiation (NeoCRT) is standard of care for the treatment of locally advanced rectal cancer (LARC). Contemporary radiation techniques may reduce dose to normal organs at risk. Our purpose was to compare clinical outcomes and acute toxicities between standard 3D conformal

(3D) and intensity modulated radiation therapy (IMRT). Methods: LARC patients (pts) treated at 4 large academic centers in the US between 2007 and 2016 were reviewed. Pts received 5FU-based NeoCRT concurrently with IMRT or 3D. Pathologic response (PR) was used as a surrogate for clinical outcome, and common terminology for adverse events version 4 was used to grade toxicities, summarized on a 1-5 scale. Toxicity rates were compared using chi-square analysis. Multivariable models were fit adjusting for age, gender, pre-tx CT to identify independent predictors of PR and toxicity. Results: 128 pts were analyzed: 60.1% male and 39.8% female, median age 57.7 years (Range 31-85). Clinical characteristics were similar across RT groups. The outcome of partial and complete PR was similar for IMRT and 3D (48.1%, 23.1% vs 32.2%, 23.7%\*), respectively. After adjusting for gender, age, and pre-RT chemotherapy type, IMRT was significantly associated with increased odds for complete and partial response (OR: 2.9, 95%CI 1.2-7.2\*). Additionally, IMRT was significantly associated with reduced rates of dehydration, dermatitis, rectal pain, rectal bleeding, diverting ostomy, and trend toward significance for decreased rates of fatigue (p = 0.07) and erythema (p = 0.06) (see table). Overall rates of grade 2 and higher toxicities were significantly reduced in IMRT vs. 3D after adjusting for confounders (OR: 0.27, 95% CI 0.08-0.87\*). Conclusions: Neoadjuvant 5FU-based IMRT for LARC leads to reduced acute toxicities and improved PR compared to 3D. Given the challenges associated with prospective validation of these data, IMRT should be considered standard treatment for LARC. (Table Presented).

David J, Yue Y, Li Q, Blas KG, **Kabolizadeh P** and Tuli R (2017). "FDG-PET correlation with active bone marrow and leukopenia during chemoradiation for anal cancer." International Journal of Radiation Oncology Biology Physics 99(Sup 1): E142-E143.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Concurrent chemoradiation (CRT) is standard of care treatment for anal cancer. CRT can result in significant hematologic toxicity leading to dose reductions and treatment delays. While nearly 60% of the bone is located within the pelvic region, not all bone marrow (BM) in this region has hematologic activity. Flurodeoxyglucose (FDG) labeled positron emission tomography (PET) avidity corresponds with BM regions with hematologic activity. We hypothesize that FDG-PET activity corresponds to active BM (ABM), predicts for treatment-related leukopenia and may allow identification of those patients who may benefit from bone-marrow sparing radiotherapy. Purpose/Objective(s): Anal cancer patients treated with 5FU, mitomycin C and intensity modulated radiation therapy between 2011-2017 were identified. Baseline characteristics including pre-treatment, weekly, and 2-week post-treatment WBC, ANC, and lymph counts were recorded. Pre-and post-treatment pelvic bones were contoured on PET-CT scan from L5 to the lesser trochanter. ABM volume was defined as the subvolume of the total BM (TBM) volume that exhibited the highest 50% of standard uptake value (SUV) for a given patient. In addition, ABM liver (ABML) was defined as the subvolume of the TBM that was greater than mean SUV of the liver. ABM/TBM was calculated pre-and post-CRT. ABM variations were calculated as the volume changes of ABM between pre-CRT and post-CRT. Pearson's coefficients and corresponding p values between SUVmax, SUVmean, SUV change, and ABML with relation to WBC, ANC, and lymphocytes were analyzed. Results: Pre-PET SUVmax and pre/post change in SUVmax correlated significantly with post-treatment WBC and ANC levels. Change in ABML identified on pre/post PET correlated with pre-and post ANC levels. There were no significant correlations with post PET SUVmax or any mean SUV pre/post/change.

Debaty G, Labarere J, Frascone RJ, Wayne MA, **Swor RA**, Mahoney BD, Domeier RM, Olinger ML, O'Neil BJ, Yannopoulos D, Aufderheide TP and Lurie KG (2017). "Long-term prognostic value of gasping during out-of-hospital cardiac arrest." Journal of the American College of Cardiology 70(12): 1467-1476.

[Full-Text](#)

*Department of Emergency Medicine*

**Dekelbab B** and Vachhani R (2017). "Severe but transient congenital hypothyroidism secondary to prenatal maternal iodine ingestion." Endocrine Reviews 38(Sup 1).

[Request Form](#)

*Department of Pediatrics*

Background: Immature fetal and neonatal thyroid gland is incapable to escape from the inhibitory Wolff-Chaikoff effect of excessive iodine levels, making newborn susceptible to hypothyroidism. Such hypothyroidism can be transient or permanent. Clinical Case: A 6-day-old full term female referred to pediatric endocrinology clinic for evaluation of abnormal newborn thyroid screen. Serum studies confirmed severe hypothyroidism with free T4 of 0.2 ng/dL and TSH of 562  $\mu$ IU/mL suggesting thyroid aplasia as the most likely etiology, but Technetium thyroid scan surprisingly showed normal thyroid gland in appropriate cervical location. Review of maternal medical history disclosed intake of daily iodine supplement using Iodoral® containing 5 mg of Iodine and 7.5 mg of Iodide [equal to 8333% of daily value], which the mother took for about two years before pregnancy and resumed around 29 weeks of gestation as recommended by holistic primary care provider. Neonatal random urine iodine level was significantly increased at 7836  $\mu$ g/L. Screening for maternal autoimmune disease was negative. The infant was started on Thyroxine at the dose of 15  $\mu$ g/kg. Over the following few weeks, Thyroxine requirements decreased and therapy was stopped around four months of age. Conclusions: Severe transient congenital hypothyroidism can be caused by excess prenatal maternal iodine intake. Differential diagnosis of hypothyroidism in newborn should include possibility of prenatal or postnatal iodine exposure. Iodine supplements package label should have clear warning of possible harmful effects of iodine intake on fetus thyroid in pregnant women.

Delgado MR, Bonikowski M, Carranza J, **Dabrowski E**, Matthews D, Russman B, Tilton A, Velez JC, Grandoulier AS and Picaut P (2017). "Safety and efficacy of repeat open-label abobotulinumtoxinA treatment in pediatric cerebral palsy." Journal of Child Neurology 32(13): 1058-1064.

[Full-Text](#)

*Department of Physical Medicine and Rehabilitation*

This was a prospective, repeat-treatment, open-label study (NCT01251380) of abobotulinumtoxinA for the management of lower limb spasticity in children who had completed a double-blind study. Children (2-17 years) received injections into the gastrocnemius-soleus complex, and other distal and proximal muscles as required (maximum total dose per injection cycle: 30 U/kg or 1000U). A total of 216 of the 241 double-blind patients entered the extension study and 207 received  $\geq 1$  open label injection into the gastrocnemius-soleus; 17-24% of patients also had injections into the hamstrings. The most frequent adverse events were related to common childhood infections and the most frequent treatment-related adverse event was injection site pain (n = 10). There was no evidence of a cumulative effect on adverse events. Sustained significant clinical improvements in muscle tone (Modified Ashworth Scale), spasticity (Tardieu Scale), overall clinical benefit (Physicians Global Assessment), and goal attainment (Goal Attainment Scale) were also observed across treatment cycles.

**Dilworth JT**, Marvin K, Gondert JM, **Grills IS**, **Chen PY**, **Krauss DJ**, **Zhou J**, **Wilson GD**, Marples B and **Chinnaiyan P** (2017). "Pulsed partial brain irradiation for newly diagnosed glioblastoma." International Journal of Radiation Oncology Biology Physics 99(2): E71.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): We report an analysis of a prospective, single-arm clinical trial investigating pulsed radiation therapy (PRT) in the treatment of newly diagnosed glioblastoma. Purpose/Objective(s): Patients with a WHO performance status of  $\leq 2$  diagnosed with primary glioblastoma without brainstem involvement or multicentricity per magnetic resonance imaging were eligible for this study. Patients received 60 Gy PRT utilizing volumetric modulated arc radiation therapy (VMAT) with concurrent temozolomide (TMZ), followed by maintenance TMZ. Each daily 2-Gy fraction comprised ten 0.2-Gy pulses. Each pulse was delivered with the same arc, covered the entire planning target volume (PTV), and was separated by 3-minute "beam-off" intervals. The initial PTV (FLAIR+2 cm) received 46 Gy; the boost PTV (T1+2.5 cm) received 14 Gy. Daily cone beam CT performed prior to the first and sixth pulses were used to make inter-fraction and inter-pulse

adjustments in patient position. Brain MRI and neurocognitive, quality of life, and toxicity assessments were performed at baseline and at regular intervals. Toxicities were graded per CTCAEv4. Clinical outcomes were estimated using Kaplan-Meier analysis. Results: Sixteen patients were enrolled and treated with PRT with concurrent TMZ; all but one completed at least 6 months of maintenance TMZ. The mean age was 54 yrs (27-71 yrs). One (6%), 6 (38%), 4 (25%), and 5 (31%) patients underwent biopsy only, subtotal resection, near total resection, and gross total resection, respectively. Four (25%) patients had hypermethylated MGMT promoter status; the remaining patients had unmethylated MGMT promoter status. Three (19%) patients received alternating electrical field treatment using the Optune® device during the maintenance phase of TMZ. The mean follow-up was 17 mos (3-34 mos). The mean progression-free survival (PFS) was 11 mos. The 1-yr and 2-yr actuarial PFS rates were 37% and 12%, respectively. Salvage treatments for the 10 patients who recurred included second-line chemotherapy (5 patients), re-resection (3 patients), fractionated stereotactic radiosurgery (1 patient), vaccine trial (1 patient), and re-irradiation with external beam treatment (1 patient). The mean overall survival (OS) was 16.8 mos. The 1-yr and 2-yr actuarial overall survival rates were 85% and 54%, respectively. The median time from progression until death was 10.8 mos. There was no grade 3 or higher treatment related toxicity. Conclusion: This study is the first to evaluate the efficacy of PRT in the treatment of newly diagnosed glioblastoma. PRT appears well tolerated and confers promising preliminary tumor control and overall survival rates.

Ding D, Starke RM, Kano H, Mathieu D, Huang PP, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Almodovar L, **Grills IS**, Silva D, Abbassy M, Missios S, Barnett GH, Lunsford LD and Sheehan JP (2017). "Stereotactic radiosurgery for ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations)-eligible Spetzler-Martin grade I and II arteriovenous malformations: A multicenter study." World Neurosurgery 102(Jun): 507-517.

[Full-Text](#)

*Department of Radiation Oncology*

OBJECTIVE: ARUBA (A Randomized Trial of Unruptured Brain Arteriovenous Malformations) found better short-term outcomes after conservative management compared with intervention for unruptured arteriovenous malformations (AVMs). However, because Spetzler-Martin (SM) grade IeII AVMs have the lowest treatment morbidity, sufficient follow-up of these lesions may show a long-term benefit from intervention. The aim of this multicenter, retrospective cohort study is to assess the outcomes after stereotactic radiosurgery (SRS) for ARUBA-eligible SM grade IeII AVMs. METHODS: We pooled SRS data for patients with AVM from 7 institutions and selected ARUBA-eligible SM grade IeII AVMs with  $\geq 12$  months follow-up for analysis. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes. RESULTS: The ARUBA-eligible SM grade IeII AVM cohort comprised 232 patients (mean age, 42 years). The mean nidus volume, SRS margin dose, and follow-up duration were 2.1 cm<sup>3</sup>, 22.5 Gy, and 90.5 months, respectively. The actuarial obliteration rates at 5 and 10 years were 72% and 87%, respectively; annual post-SRS hemorrhage rate was 1.0%; symptomatic and permanent radiation-induced changes occurred in 8% and 1%, respectively; and favorable outcome was achieved in 76%. Favorable outcome was significantly more likely in patients treated with a margin dose  $>20$  Gy (83%) versus  $\geq 20$  Gy (62%;  $P < 0.001$ ). Stroke or death occurred in 10% after SRS. CONCLUSIONS: For ARUBA-eligible SM grade IeII AVMs, long-term SRS outcomes compare favorably with the natural history. SRS should be considered for adult patients harboring unruptured, previously untreated low-grade AVMs with a minimum life expectancy of a decade.

Ding X, Li X, **Qin A, Zhou J, Yan D, Stevens C, Krauss D** and Kabolizadeh P (2017). "Have we reached proton beam therapy dosimetric limitations? – A novel robust, delivery-efficient and continuous Spot-Scanning Proton Arc (SPArc) therapy is to improve the dosimetric outcome in treating prostate cancer." Acta Oncologica: 1-3. ePub Ahead of Print.

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*Department of Radiation Oncology*



Ding X, **Qin A**, Li X, **Zhou J**, **Stevens C**, **Krauss D**, **Kabolizadeh P** and **Yan D** (2017). "Improve the dosimetric outcome in treating bilateral head and neck cancer treatment using a novel robust and delivery efficient spot scanning proton ARC therapy: A feasibility study." *Medical Physics* 44(6): 3277.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: Spot-scanning proton arc therapy (SPArc) is a novel planning and treatment technique which has the potential to deliver a robust proton beam therapy through arc trajectories continuously and efficiently. This is the first study to evaluate its feasibility to improve the dosimetric outcome in treating bilateral head and neck cancer (HNC) patients over the traditional robust optimized intensity modulated proton therapy (ro-IMPT) with limited beam angles. Methods: Ten HNC patients were retrospectively included in this study. Both SPArc and ro-IMPT plans were generated using robust optimization with  $\pm 3.5\%$  range and 3mm setup uncertainties in which SPArc plans utilize a full arc with 2.5 degree sampling frequency and ro-IMPT plans utilize three beam angles. The prescription dose is 7000cGy for high-risk clinical target volume (CTV1) and 6000cGy for lymph nodes (CTV2-nodes). Dosimetric parameters were extracted and compared between the two groups. Root-mean-square deviation doses (RMSDs) Volume Histogram, or RVH, and worst-case-scenario perturbed dose volume histogram were used for plan robustness evaluation. Total beam delivery time was compared based on a full gantry rotation with 1RPM, 2ms spot switching time simulating different proton systems with energy-layer-switching-time (ELST) from 0.1 to 5 seconds. Results: SPArc had demonstrated significant dosimetric improvements over ro-IMPT plans by reducing 28.0%, 30.8% and 35.5% of mean dose to the ipsilateral parotid ( $p < 0.001$ ), contralateral parotid ( $p < 0.001$ ), and oral cavity ( $p < 0.001$ ) respectively. The D1 of brain stem also reduced by a factor of 22.5% ( $p = 0.004$ ). RVH and perturbed DVH analysis shows that plan robustness of SPArc is comparable to ro-IMPT in OARs and target coverage. The average total estimated beam delivery of SPArc plans could potentially achieve less than 500s in the modern proton machine with ELST less than 1s. Conclusion: This study demonstrated that SPArc could significantly reduce dose to the critical organ dose and has the potential to be implemented in routine clinic.

Ding X, **Zhou J**, Blas K, Li X, Wang Y, **Qin A**, **Stevens C**, **Yan D**, **Grills I** and **Kabolizadeh P** (2017). "A novel robust and delivery-efficient spot scanning arc therapy to spare hippocampus and cochlea in whole brain radiotherapy." *Medical Physics* 44(6): 2742-2743.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: Recently, there have been significant interests towards whole-brain radiotherapy (WBRT) with hippocampal and cochlea avoidance. Herein, we present a novel robust, continuous and delivery-efficient spot-scanning proton arc therapy technique (SPArc) to improve dosimetric outcome. Methods: Eight whole brain patients were used to evaluate the feasibility of using SPArc for hippocampal and cochlea avoidance WBRT. Both SPArc and robust optimized Intensity Modulated Proton Therapy (ro-IMPT) plans were generated using the robust optimization with  $\pm 3.5\%$  range and 3 mm setup uncertainties compared to the Volumetric Modulated Arc Therapy (VMAT). Root-mean-square deviation doses (RMSDs) Volume Histogram, or RVH, was used for plan robustness evaluation. Total delivery time was compared based on a full gantry rotation with 1 RPM, 2 ms spot switching time, 0.01 minimum spot monitor unit, and energy-layer-switching-time (ELST) from 0.1 to 5 seconds. Results: SPArc plans showed significant dosimetric improvements in terms of reduction of the mean dose to the hippocampus 6.20 Gy[RBE] compared to VMAT 10.89 Gy[RBE] ( $p < 0.001$ ) and ro-IMPT 9.38 Gy[RBE] ( $p < 0.001$ ); D100% to the hippocampus is reduced to 4.50 Gy[RBE] compared to VMAT 9.16 Gy[RBE] ( $p = 0.001$ ) and ro-IMPT 7.02 Gy[RBE] ( $p = 0.002$ ); cochlear mean dose is reduced to 7.75 Gy[RBE] compared to VMAT 11.52 Gy[RBE] ( $p = 0.018$ ) and ro-IMPT 10.15 Gy [RBE], ( $p = 0.037$ ); Skin maximum dose is reduced to 33.84 Gy[RBE] compared to ro-IMPT 36.37 Gy[RBE]. RVH shows SPArc is more robust in Organ-at-risks (OARs) sparing e.g. hippocampus, cochlea, lens and eyes. The average total estimated delivery time was 412 s, 627 s, 1694 s based on ELST of 0.2 s, 1 s, and 5 s for SPArc plans, compared with the respective values of 547s ( $p < 0.001$ ), 626 s ( $p = 0.484$ ), and 1025 s ( $p = 0.002$ ) for ro-IMPT plans. Hence, SPArc plans could potentially achieve similar or faster delivery time in the modern proton machine with ELST less than 1 s. Conclusion: SPArc could significantly reduce the dose delivered to the hippocampus and cochlea in patients treated with WBRT.

Ellis J, **Dekhne N**, DeLaere A and Pople B (2017). "Experience with a nurse navigator-led, risk-based breast cancer survivorship care clinic." Journal of Clinical Oncology 35(5): Abstract No. 52.

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*Department of Surgery*

Background: Our tertiary care hospital addressed recent survivorship care initiatives by implementing a Nurse Practitioner (NP)-led Breast Care Survivorship Clinic (BCSC). The monthly, NP-led multidisciplinary clinic (MDC) integrated the unique needs of Breast Cancer Survivors (BCS). After 14 months, an internal evaluation prompted three significant changes to the NP-led BCSC. First, the new BCBS would become a Nurse Navigator (NN)-led riskbased model that would allow survivorship care to be individually tailored to each BCS's needs. Secondly, patients would not meet with rest of MDC team (i.e. social work, nutrition, physical therapy) during this visit. Patients were instead referred to the Survivorship Care Workshop Series (SCWS), a bi-monthly educational program developed to complement the NN-led BCSC and address common BCS needs; needs falling outside of the SCWS content were handled individually by MDC referrals. Lastly, the NN-led BCSC was conducted at follow-up visit with surgeon to avoid an additional appointment. The NN administers a questionnaire that addresses medical and psychosocial concerns, refers BCS to relevant SCWS lecture and/or MDC referrals based on questionnaire results, and finally, delivers the SCP. Methods: A comparison of the NP-led versus the NN-led BCSC was performed on the following factors: average total time and effort (TandE) for preparation and delivery of SCPs; number of actual SCPs delivered to BCS; and cost analysis of each model. Results: There were 58 SCPs completed, and 37/58 were successfully delivered to patients during the NP-led BCSC (9/2014-10/2015). There were 95 SCPs completed, and 91/95 were successfully delivered during the NN-led BCSC (2/2016-7/2016). The average total time spent by NP was two hours (n = 37) per patient compared to the average total time of 45 minutes spent by NN (n = 91) for preparation and delivery of SCPs. The estimated annual cost of the NP-led model includes TandE for NP and MDC team, is \$273,946 compared to cost of the NN-model, which includes NN TandE as well a full-time SCWS program coordinator, is \$86,651. Conclusions: The NN-led risk-based BCSC model is less resource-intensive, less expensive and allows for increased delivery of SCPs to BCS.

Ezekwudo DE, **Ifabiyi T**, Gbadamosi B, Haberichter K, Yu Z, **Amin M**, **Shaheen K**, **Stender M** and **Jaiyesimi I** (2017). "Breast implant-associated anaplastic large cell lymphoma: A case report and review of the literature." Case Reports in Oncological Medicine 2017(Article ID 6478467): 6.

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*OUWB Medical Student Author*

*Department of Pathology*

*Department of Surgery*

*Department of Internal Medicine*

**Faia LJ** and **Drenser KA** (2017). "Pediatric uveitis: Challenging for ophthalmologists, patients, and parents." Retina Today 2017(October): 62-71.

[Request Form](#)

*Department of Ophthalmology*

Faught A, Schubert L, Olsen L, Zhang J, Castillo E, Castillo R, **Guerrero T** and Vinogradskiy Y (2017). "Functional-guided radiotherapy using knowledge-based planning." Medical Physics 44(6): 2764-2765.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: 4DCT-ventilation is being used to calculate lung ventilation and novel implementations of functional-guided radiotherapy. The incorporation of functional information into the treatment planning process allows for preferential sparing of high-functioning lung with the goal of reducing toxicity events. There are two significant challenges when implementing functional radiotherapy: 1) the lack of knowledge of realistic patient specific dosimetric goals for functional lung sparing and 2) ensuring consistent treatment plans across multiple centers involved in clinical trials. Knowledge-based planning (KBP) is uniquely

positioned to address these concerns by estimating achievable dose reductions to functional lung and improving plan quality and consistency. The purpose of our study was to develop a pilot KBP model to test the feasibility of use in functional-guided radiotherapy. Methods: Using Varian's knowledge-based planning package, RapidPlan, a model was created from 31 previously planned functional-guided lung patients. In addition to standard critical structures in lung radiotherapy, a functional contour delineating areas of high ventilation was included. The RapidPlan model was validated by comparing V20 Gy and mean dose within the functional contour from 5 independent cases that were planned with and without RapidPlan. Absolute differences in the dose-function metrics are reported. Results: A comparison of the average V20 Gy and mean dose to the functional contour in the validation set demonstrated respective values of 14.9% and 9.8 Gy for the non-RapidPlan plans and 14.1% and 9.5 Gy for the plans using Rapid- Plan. Both dose-function metrics demonstrated a small improvement for plans utilizing RapidPlan. Conclusion: Knowledge-based planning is especially valuable to new and emerging treatment planning strategies such as functional-guided radiotherapy. The dose predictions can guide treatment plan optimization with respect to areas of high function. KBP can improve plan quality and consistency within a department and even more so in ongoing multi-institutional clinical trials where consistent quality is of added importance.

Folbe AJ, Calkins H, Hindricks G, Cappato R, Kim YH, Saad EB, Aguinaga L, Akar JG, Badhwar V, Brugada J, Camm J, Chen PS, Chen SA, Chung MK, Nielsen JC, Curtis AB, Davies DW, Day JD, d'Avila A, de Groot N, Di Biase L, Duytschaever M, Edgerton JR, Ellenbogen KA, Ellinor PT, Ernst S, Fenelon G, Gerstenfeld EP, **Haines DE**, Haissaguerre M, Helm RH, Hylek E, Jackman WM, Jalife J, Kalman JM, Kautzner J, Kottkamp H, Kuck KH, Kumagai K, Lee R, Lewalter T, Lindsay BD, Macle L, Mansour M, Marchlinski FE, Michaud GF, Nakagawa H, Natale A, Nattel S, Okumura K, Packer D, Pokushalov E, Reynolds MR, Sanders P, Scanavacca M, Schilling R, Tondo C, Tsao HM, Verma A, Wilber DJ and Yamane T (2017). "2017 HRS/EHRA/ECAS/APHRS/SOLAECE expert consensus statement on catheter and surgical ablation of atrial fibrillation: Executive summary." *International Forum of Allergy & Rhinology* 33(5): 369-409.

[Full-Text](#)

*Department of Internal Medicine*

Folbe AJ, Francis JH, Kim J, Lin A, **Folberg R**, Iyer S and Abramson DH (2017). "Growth of uveal melanoma following intravitreal bevacizumab." *International Forum of Allergy & Rhinology* 3(2): 117-121.

[Full-Text](#)

*Administration*

**PURPOSE:** Typically treatment of large melanomas (by Collaborative Ocular Melanoma Study criteria) is restricted to enucleation, due to size constraints for plaque brachytherapy. Because primary and metastatic uveal melanoma cells are inhibited by bevacizumab (an anti-vascular endothelial growth factor), this prospective study evaluated the impact of intravitreal bevacizumab on large uveal melanomas that were destined for enucleation. Size reduction by bevacizumab would potentially salvage these eyes by making them eligible for treatment with plaque brachytherapy. **PROCEDURES:** Two patients with large uveal melanoma were each treated with one intravitreal injection of bevacizumab (1.25 mg/0.05 mL). **RESULTS:** Both tumors displayed paradoxical growth 1 week following the injection, with confirmed growth 1 week later (increase from baseline of 1.1 mm in one eye and 3.1 mm in the other eye). Both eyes were enucleated and monosomy 3 and vasculogenic mimicry patterns were identified in both tumors. At 9 years follow-up, both patients were alive and metastasis free. **CONCLUSION:** These patients demonstrate that neoadjuvant intravitreal bevacizumab does not decrease the size of large uveal melanomas and may, in fact, result in their paradoxical growth. This observation supports a cautious approach in the use of intravitreal bevacizumab for uveal melanoma, particularly in the neoadjuvant setting.

**Fortunato JT, Wasserman JA and Menkes DL** (2017). "When respecting autonomy is harmful: A clinically useful approach to the nocebo effect." [American Journal of Bioethics](#) 17(6): 36-42.

[Full-Text](#)

*OUWB Medical Student Author*

*Department of Biomedical Sciences (OU)*

*Department of Neurology*

Nocebo effects occur when an adverse effect on the patient arises from the patient's own negative expectations. In accordance with informed consent, providers often disclose information that results in unintended adverse outcomes for the patient. While this may adhere to the principle of autonomy, it violates the doctrine of "primum non nocere," given that side-effect disclosure may cause those side effects. In this article we build off previous work, particularly by Wells and Kaptchuk (2012) and by Cohen (2013), to suggest ethical guidelines that permit nondisclosure in the case when a nocebo effect is likely to occur on the basis of nonmaleficence. We accept that that autonomy vis-à-vis informed consent must be forestalled, but salvage much of its role by elaborating a practical clinical approach to postencounter follow-up. In doing so, we reconcile a clinically practicable process of determining conditions of disclosure with long-standing ethical commitments to patients.

**Foster LM, Wallace M, Dilworth JT, Firestone M, Ye H, Chen PY, Gustafson GS and Jawad MS** (2017). "Toxicity profiles following whole breast irradiation plus sequential boost using hypofractionated or conventionally fractionated treatment." [International Journal of Radiation Oncology Biology Physics](#) 99(Sup 1): E15.

[Full-Text](#)

*OUWB Medical Student Author*

*Department of Radiation Oncology*

Purpose/Objective(s): To compare toxicity and cosmesis in women with early-stage breast cancer treated with conventionally fractionated (C-WB) or hypofractionated (H-WB) whole breast irradiation with sequential boost. Purpose/Objective(s): We performed a matched-pair analysis to compare patients treated with C-WB or H-WB as part of BCT at a single institution from 2008-2016. 240 patients (120 pairs) were matched by age (+/-3 y), T-stage, chemotherapy (y/n), and endocrine therapy (y/n). Acute ( $\leq 6$  mos post-WB) and chronic ( $> 6$  mos post-WB) toxicities were graded according to CTCAEv3.0. Cosmesis was evaluated using the Harvard cosmesis scale. Outcomes were analyzed using t-tests for continuous variables,  $\chi^2$  for categorical variables, and Kaplan-Meier estimates. P-values  $< 0.05$  were considered significant. Results: Median whole breast dose was 42.56 Gy (39.9-41.72) in 2.66 Gy fractions for H-WB and 45 Gy (45-50.4) in 1.8-2 Gy fractions for C-WB. Median boost dose was 10.64 Gy (2.66-14) in 2.50-2.66 Gy fractions for H-WB and 16 Gy (6-22.5) in 2-2.5 Gy fractions for C-WB. Median follow up for all patients was 2.6y (0.1-28.1); 1.1 and 6.3y for H-WB and C-WB, respectively ( $p < 0.001$ ). Median age at diagnosis was 61 (44-88). 84% and 12% of patients received anti-hormone and chemotherapy, respectively. There were no differences in race, menopausal status, histology, or grade. The H-WB group had more close margins ( $< 2$  mm; 32 v 4%,  $p < 0.001$ ). There were no differences in acute toxicity between H-WB and C-WB. Rates of grade 2/3 acute toxicity were  $< 10\%$  overall, with the exception of hyperpigmentation (15%). Rates of chronic toxicity (Table 1) were similar, with low rates of grade 2/3 toxicities ( $< 12\%$ ). Cosmesis was good/excellent in 93% of patients, with no differences in the acute period. There were more H-WB patients with fair/poor chronic cosmesis (13 v 3%,  $p = 0.026$ ). Clinical outcomes were excellent at 3 years and similar between H-WB and C-WB. Conclusion: Patients had favorable toxicity profiles regardless of fractionation schedule used. In light of recently published data supporting favorable toxicity and cosmesis with hypofractionated regimens, we are evaluating specific dosimetric or patient related features that may contribute to the small difference in chronic cosmetic outcomes when comparing groups.

Francis JH, Kim J, Lin A, **Folberg R**, Iyer S and Abramson DH (2017). "Growth of uveal melanoma following intravitreal bevacizumab." [Ocular Oncology and Pathology](#) 3(2): 117-121.

[Request Form](#)

*Administration*

Purpose: Typically treatment of large melanomas (by Collaborative Ocular Melanoma Study criteria) is

restricted to enucleation, due to size constraints for plaque brachytherapy. Because primary and metastatic uveal melanoma cells are inhibited by bevacizumab (an anti-vascular endothelial growth factor), this prospective study evaluated the impact of intravitreal bevacizumab on large uveal melanomas that were destined for enucleation. Size reduction by bevacizumab would potentially salvage these eyes by making them eligible for treatment with plaque brachytherapy. Procedures: Two patients with large uveal melanoma were each treated with one intravitreal injection of bevacizumab (1.25 mg/0.05 mL). Results: Both tumors displayed paradoxical growth 1 week following the injection, with confirmed growth 1 week later (increase from baseline of 1.1 mm in one eye and 3.1 mm in the other eye). Both eyes were enucleated and monosomy 3 and vasculogenic mimicry patterns were identified in both tumors. At 9 years follow-up, both patients were alive and metastasis free. Conclusion: These patients demonstrate that neoadjuvant intravitreal bevacizumab does not decrease the size of large uveal melanomas and may, in fact, result in their paradoxical growth. This observation supports a cautious approach in the use of intravitreal bevacizumab for uveal melanoma, particularly in the neoadjuvant setting. (C) 2016 S. Karger AG, Basel

Gbadamosi B, Bastola S, Ye H, Ezekwudo D, Ogunleye F, Yu Z, **Fennell T**, Mora E, Hart B, **Gaikazian S** and **Jaiyesimi I** (2017). "Treatment outcomes in adults with Acute Myeloid Leukemia (AML) using standard induction "3+7", hypomethylating agents or best supportive care: A single institution experience." Clinical Lymphoma, Myeloma & Leukemia 17(Sup 2): S283.

[Full-Text](#)

*Department of Pathology*

*Department of Internal Medicine*

Gebhard C, Buechel RR, Stahli BE, Gransar H, Achenbach S, Berman DS, Budoff MJ, Canister TQ, Chow B, Dunning A, Al-Mallah MH, Cademartiri F, **Chinnaiyan K**, Rubinshtein R, Marques H, DeLago A, Villines TC, Hadamitzky M, Hausleiter J, Shaw LJ, Cury RC, Feuchtner G, Kim YJ, Maffei E, **Raff G**, Pontone G, Andreini D, Chang HJ, Leipsic J, Minn JK and Kaufmann PA (2017). "Impact of age and sex on left ventricular function determined by coronary computed tomographic angiography: results from the prospective multicentre CONFIRM study." European Heart Journal- Cardiovascular Imaging 18(9): 990-1000.

[Full-Text](#)

*Department of Internal Medicine*

Background Left ventricular (LV) volumetric and functional parameters measured with cardiac computed tomography (cardiac CT) augment risk prediction and discrimination for future mortality. Gender- and age-specific standard values for LV dimensions and systolic function obtained by 64-slice cardiac CT are lacking. Methods and results 1155 patients from the Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter registry (54.5% males, mean age 53.1 +/- 12.4 years, range: 18-92 years) without known coronary artery disease (CAD), structural heart disease, diabetes, or hypertension who underwent cardiac CT for various indications were categorized according to age and sex. A cardiac CT data acquisition protocol was used that allowed volumetric measuring of LV function. Image interpretation was performed at each site. Patients with significant CAD (> 50% stenosis) on cardiac CT were excluded from the analysis. Overall, mean left ventricular ejection fraction (LVEF) was higher in women when compared with men (66.6 +/- 7.7% vs. 64.6 +/- 8.1%, P < 0.001). This gender-difference in overall LVEF was caused by a significantly higher LVEF in women >= 70 years when compared with men >= 70 years (69.95 +/- 8.89% vs. 65.50 +/- 9.42%, P = 0.004). Accordingly, a significant increase in LVEF was observed with age (P = 0.005 for males and P, 0.001 for females), which was more pronounced in females (5.21%) than in males (2.6%). LV end-diastolic volume decreased in females from 122.48 +/- 27.87 (< 40 years) to 95.56 +/- 23.17 (>= 70 years; P < 0.001) and in males from 155.22 +/- 35.07 (< 40 years) to 130.26 +/- 27.18 (>70 years; P < 0.001). Conclusion Our findings indicate that the LV undergoes a lifelong remodelling and highlight the need for age and gender adjusted reference values.

Glaser A, Kotzen L, Weissman H, **Singer L** and **Grysiwicz R** (2017). "Efficacy of a comprehensive stroke clinic model on reducing readmissions after ischemic stroke." *Stroke* 48(Sup 1): AWMP93.

[Full-Text](#)

*OUWB Medical Student Author*

*Department of Neurology*

Background: Stroke is a leading cause of hospital admissions among the elderly, and reducing readmission rates has become a primary goal of healthcare reform. Hospitals are now being held financially responsible for 30 day readmission rates exceeding their expected rate [1]. Our aim was to determine if patients seen in the comprehensive stroke discharge clinic had reduced 30 day readmissions compared to standard hospital follow up after ischemic stroke. Methods: Patients with a discharge diagnosis of ischemic stroke receive a phone call from the neurology office staff within 3 business days of hospital discharge to schedule an appointment with a mid-level provider in the comprehensive stroke discharge clinic within 1-3 weeks. Eligibility for the clinic includes patients  $\geq 18$  years of age that are either discharged to home directly or discharged to home from inpatient rehabilitation. We performed a retrospective stroke database search of patients meeting this criteria from May 2015 to June 2016. Patients were excluded from the search if they had an inpatient stroke event. Results: Of the 526 patients reviewed, 116 patients (22.1%) were seen in the comprehensive stroke discharge clinic. The average age of patients seen in clinic was 67 years and the average age of patients in the non-clinic group was 69 years. Approximately 12% of patients in each group received acute reperfusion therapy. There was only one 30 day related readmission in the clinic group, and fourteen 30 day related readmissions in the non-clinic group (0.86% versus 3.41%; 95% CI 0.12-4.99%). There were eight 30 day all cause readmissions in the clinic group, and forty-two 30 day all cause readmissions in the non-clinic group (6.90% versus 10.24%; 95% CI-2.12-8.81%). Conclusion: The comprehensive stroke clinic model may reduce 30 day related readmissions for patients discharged to home. However, there were limitations to this study. The percentage of patients seen in the comprehensive stroke clinic was low. The goal is to improve the clinic follow up rate over the course of the next year. In addition, patients were excluded from the clinic if they were discharged to a skilled nursing facility, which is often associated with a higher readmission rate.

Glode LM, Tangen CM, Hussain M, Swanson GP, **Wood DP**, Sakr W, Dawson NA, Haas NB, Flaig TW, Dorff TB, Lin DW, Crawford ED, Quinn DI, Vogelzang NJ and Thompson IM (2017). "Adjuvant androgen deprivation (ADT) versus mitoxantrone plus prednisone (MP) plus ADT in high-risk prostate cancer (PCa) patients following radical prostatectomy: A phase III intergroup trial (SWOG S9921) NCT00004124." *Journal of Clinical Oncology* 35(6): Abstract No. 2.

[Request Form](#)

*Department of Urology*

Background: High risk localized Pca patients are more likely to relapse and suffer morbidity/mortality from metastatic disease after prostatectomy. Adjuvant ADT can reduce this risk. We hypothesized that MP in addition to two years of ADT could further reduce mortality from PCa. Methods: Participants with clinically localized (T1-T3, N0, M0) PCa received radical prostatectomy. Eligibility required  $\geq 1$  high risk criteria defined as Gleason sum  $\geq 8$ ; pT3b or pT4 or N1; Gleason 7 with positive margin; any one of these preoperative findings: PSA  $>15$ ng/ml, biopsy Gleason  $>7$ , biopsy Gleason  $>6$  with PSA  $>10$ . ADT arm consisted of bicalutamide and goserelin for 2 years. ADT+MP arm received ADT plus 6 cycles of M 12mg/m<sup>2</sup>+ P 5mg BID. Primary endpoint was survival (OS). Median OS was anticipated to be 10 years in ADT arm requiring 680 patients/arm to detect a hazard ratio of 1.30 with 92% power and one-sided  $\alpha=0.05$ . Results: S9921 enrolled patients from 10/99 to 1/07 when the DSMC recommended stopping due to increased incidence of leukemia in the ADT+MP arm. Of 983 patients randomized, 22 ineligible. 481 eligible on ADT and 480 on ADT+MP. Patients were stratified by stage ( $\leq$ pT2,  $\geq$ pT3, N0 or N+), Gleason score, and intent to receive adjuvant radiation (RT) (Y/N). Median age was 60 years, 84% were white, presurgical PSA was 7.6 ng/ml, 16% had positive nodes, 26% intended to receive RT, 63% had positive margins. 11 ADT and 20 ADT+ MP received no protocol treatment. Median follow-up is 11.2 years. Conclusions: Survival was greater than anticipated in both arms. MP increases the risk of leukemia. There is no evidence that MP improves PCa specific survival when added to 2 years of adjuvant ADT.



**Graham SF**, Turkoglu O, Kumar P, Yilmaz A, Bjorndahl TC, Han B, Mandal R, Wishart DS and **Bahado-Singh RO** (2017). "Targeted metabolic profiling of post-mortem brain from infants who died from sudden infant death syndrome." Journal of Proteome Research 16(7): 2587-2596.

[Request Form](#)

*Department of Obstetrics and Gynecology*

Currently little is known about the underlying pathophysiology associated with SIDS, and no objective biomarkers exist for the accurate identification of those at greatest risk of dying from SIDS. Using targeted metabolomics, we aim to profile the medulla oblongata of infants who have died from SIDS (n = 16) and directly compare their biochemical profile with age matched controls. Combining data acquired using 111 NMR and targeted DI-LC-MS/MS, we have identified fatty acid oxidation as a pivotal biochemical pathway perturbed in the brains of those infants who have from SIDS (p = 0:0016). Further we have identified a potential central biomarker with an AUC (95% CI) = 0.933 (0.845-1.000) having high sensitivity (0.933) and specificity (0.875) values for discriminating between control and SIDS brains. This is the first reported study to use targeted metabolomics for the study of PM brain from infants who have died from SIDS. We have identified pathways associated with the disease and central biomarkers for early screening/diagnosis.

**Grills IS**, Lee KC, Belderbos J, Hope AJ, Giuliani ME, Guckenberger M, Mantel F, Werner-Wasik M, Peulen HM, Sonke JJ, **Yan D**, Hymas RV, Caruso A, Abro N, Johnson MC, Abbott E, Ye H and **Welsh R** (2017). "International collaborative propensity-based matched pair analysis of operable early stage lung cancer patients treated with stereotactic body radiation therapy compared to resection: Differences in recurrence and survival with prolonged follow-up." International Journal of Radiation Oncology Biology Physics 99(2): E456-E457.

[Full-Text](#)

*Department of Radiation Oncology*

*Department of Surgery*

Purpose/Objective(s): Compare outcomes for operable patients treated with SBRT to resection.

Purpose/Objective(s): An international collaborative pooled 1298 T1-T2N0 NSCLC lung cancers from 5 centers treated with SBRT to a median PTV dose of 54 Gy/3 fractions (40-60Gy/1-8fx) using cone-beam CT IGRT. 133 were defined as Operable by the treating center from 2006-2015 and compared to 308 who underwent Resection (R) at 1/5 centers (Lobectomy=222; Wedge=86). A propensity match using the following was applied: age, gender, tumor size, T stage, prior/synchronous tumor, baseline SUV max and PFT. This yielded 36 pairs well-balanced for all characteristics except histology and baseline DLCO. 37% (20% matched (M)) SBRT had no biopsy (varied by center). For the entire group (SBRT v R), median age was 73 v 70y, tumor size 2.2 v 2.0cm, max baseline SUV 5.8 v 5.3, 49% v 61% female, 79% v 71% T1, 21% v 28% T2, median FEV1 1.59L v 1.88L (%pred 71% v 77%), median DLCO 54% v 80% for SBRT v R, respectively. For the M group, there were no statistical differences in age for SBRT v R (70 v 69y), tumor size (2.1 v 2.0cm), baseline SUV max (5.1 v 5.8), gender (60% female both), T stage (81% T1 v 76% T1), prior/synchronous tumor, FEV1 (2.0L/73% predicted v 1.8L/77%). Actual DLCO was similar, but %pred lower for SBRT (50% v 68%). 8% v 11% (p=NS) had chemo. LN sampling (any form) was 14% SBRT v 100% R. Survival/recurrence outcomes were calculated using Kaplan Meier. Results: With a mean follow-up of 5.6y, local recurrence (LR), regional recurrence (RR), distant metastasis (DM), clinical failure (CF = any LR, RR, DM), cause-specific survival (CSS), and overall survival (OS) are shown in Table 1. Rates of LR were similar for SBRT v R for all patients and M. RR, DM, CF and DFS were statistically worse for SBRT not only for all patients but also M. For the M group, lower CSS for SBRT had a p-value of 0.11 (CSS 97% R v 84% SBRT). OS was higher for R, all cases and M. 1y OS for R was 98.4% for all cases and 100% for M cases (30d mortality of 0%). UVA and MVA for recurrence/survival will be presented. Conclusion: With prolonged follow-up, RR, DM, CF progressively increased and were higher after SBRT with poorer survival than R in an operable population and may be related to multiple factors including: institutional selection, lack of biopsy, lack of surgical staging limiting micrometastasis detection, or undetected LR in regions of RT fibrosis. Alternatively, the higher locoregional control with R may lead to superior outcomes. All factors should be considered; results support enrollment of operable patients in clinical trials.

**Grills IS**, Lee KC, Hymas RV, Ye H, Sura K, Johnson MC, Abro N, Caruso A, Abbott E, Deraniyagala RL, **Stevens CW** and **Welsh R** (2017). "Operable stage I non-small cell lung cancer treated with stereotactic radiotherapy (SBRT) compared to surgical lobectomy: Failure patterns and implications for management." International Journal of Radiation Oncology Biology Physics 99(2): S17-S18.

[Full-Text](#)

*Department of Radiation Oncology*

*Department of Surgery*

Purpose/Objective(s): Compare outcomes for biopsy-proven operable NSCLC treated with SBRT or standard of care lobectomy. Purpose/Objective(s): Two hundred fifty-four patients with Stage I T1-2N0M0 NSCLC medically operable for resection underwent cone-beam CT image-guided SBRT to a median dose of 48 Gy/4 fractions (48-60 Gy; 3-5) (n = 32), 29/32 on a prospective clinical trial allowing patients refusing surgery (n = 32) OR Lobectomy (L) (n = 222) at a single institution. Median age was 73y for SBRT v 69 for L (P = 0.002). The following were similar between groups for SBRT vs L: median tumor size 2.2 vs 2.2 cm, median baseline max SUV 5.3 vs 6.0, gender 63% vs 59% female, T stage 75% vs 69% T1, synchronous lung cancer 6% vs 7%, smoking history 88% v 86%, and receipt of chemotherapy 9% v 16% (P = NS). SBRT group had more squamous cell ca (32% vs 5%, P<0.001), more prior lung cancer (25% v 1%, P<0.001), and lower PFT (median FEV1 1.4L vs 1.9L, %predFEV1 52% vs 79%, DLCO 10.6 vs 16.3, %pred DLCO 37% vs 72%, P<0.01). Mediastinoscopy was done in 19% of SBRT cases; all L cases had nodal staging. From these, a propensity match was performed using: age, gender, tumor size, prior/synchronous lung cancer, baseline SUV, and FEV1 yielding 14 pairs. Imbalanced factors remained %pred DLCO (46% vs 62%, P = 0.018), LN sampling (30% for SBRT) and histology. Survival/recurrence was calculated according to Kaplan Meier. Median follow-up time was 5.8 years for all cases. Results: The 2-year, 3-year, and 5-year outcomes in Table 1. SBRT had higher rates of regional recurrence (RR), and clinical failure (CF). SBRT and L had similar local recurrence (LR) and distant metastasis (DM). L had higher overall survival (OS) and disease-free survival (DFS), with a P = 0.012 for cause-specific survival. For the matched group, SBRT had higher CF, lower DFS, and OS, with 5y LR (11% v 7%), RR 16% v 8%, and DM 21% v 15%. Baseline SUV, squamous histology, and metachronous ca predicted LR on UVA; all 3 remained significant on MVA (squamous histology HR 12.2). Significant factors predicting RR on UVA were squamous histology (P = 0.017, Hazard Ratio 6.1) and L v SBRT (P = 0.01, L HR 0.26) with the latter true on MVA. Tumor max dimension and baseline SUV were highly correlated and predicted DM, along with chemotherapy. SUV and chemo remained on MVA. Conclusion: SBRT in this operable population had similar rates of LR but higher rates of RR and CF and lower DFS and OS compared to lobectomy. Although operable, SBRT served as a second curative therapy for a new lung cancer in 25% of the applied population. Squamous histology serves as a predictor of not only LR but RR after SBRT, implying employment of more rigorous staging and further radiobiological evaluation.

Gupta P, Ehlert M, **Bartley J**, **Gilleran J**, **Killinger KA**, **Boura JA**, **Nagaraju P** and **Fischer M** (2017). "Perioperative outcomes, complications, and efficacy of robotic-assisted prolapse repair: A single institution study of 196 patients." Female Pelvic Medicine & Reconstructive Surgery. ePub Ahead of Print.

[Full-Text](#)

*Department of Urology*

*Department of Biomedical Sciences (BH)*

Abdominal pelvic organ prolapse repair is efficacious for uterovaginal and apical prolapse. We describe the safety and efficacy of robotic prolapse repair in a large teaching institution. METHODS: Consecutive robotic-assisted prolapse repairs at a single institution between 2006 and 2014 were retrospectively reviewed for patient characteristics, operative information, and outcomes. RESULTS: A total of 196 women (mean age, 61 +/- 9 years) underwent robotic prolapse repair (189 sacrocolpopexy, 6 sacrohysteropexy, 1 enterocele repair). Concomitant procedures included hysterectomy (88), midurethral sling (84), and/or Burch colposuspension (7). Mean odds ratio time was 242 +/- 69.9 minutes, and median length of stay was 1 day. Intraoperative complications were as follows: cystotomy (4), vaginotomy (4), conversion to open (2), bowel injury/aborted (1), adhesions/aborted (1), and ureteral injury (1). Women with complications had greater blood loss than those without complications (P = 0.0015). Immediate (<30 days) postoperative complications were rare: port-site hernia (2), discitis (1), ileus (1), and ulnar neuropraxia (3). At median follow-up of 9

months (range, 0-85 months), 14 women had recurrent grade 3 prolapse, and 4 had grade 2 apical prolapse. Nine of 14 women had additional prolapse repair at a mean of 9.5 +/- 6.3 months. Vaginal mesh exposure was detected in 12 (6.3%) of 192 women. There were 6 procedures for mesh exposure and 2 procedures for exposed sutures. One mesh erosion into the bladder required open excision. CONCLUSIONS: In this large series of robotic prolapse repair, complications are infrequent. Short-term apical outcomes are excellent. Few women required additional compartment repairs within 1 year with 6% rate of mesh exposure.

Gurm HS and **Dixon S** (2017). "Hydration and contrast-induced kidney injury." Lancet 390(10093): 452-453.

[Full-Text](#)

*Department of Internal Medicine*

Haberichter KL, **Johnson PC, Chittick PJ, Millward P, Robinson-Dunn B and Boyanton BL** (2017). "The brief case: False-positive rapid malaria antigen test result in a returned traveler." Journal of Clinical Microbiology 55(8): 2294-2297.

[Full-Text](#)

*Department of Internal Medicine*

*Department of Pathology*

Haberichter KL, **Johnson PC, Chittick PJ, Millward P, Robinson-Dunn B and Boyanton BL** (2017). "Closing the brief case: False-positive rapid malaria antigen test result in a returned traveler." Journal of Clinical Microbiology 55(8): 2560-2561.

[Full-Text](#)

*Department of Internal Medicine*

*Department of Pathology*

Haggart J, Newton MD, Hartner S, Ho A, **Baker KC, Kurdziel MD and Wiater JM** (2017). "Neer Award 2017: Wear rates of 32-mm and 40-mm glenospheres in a reverse total shoulder arthroplasty wear simulation model." Journal of Shoulder and Elbow Surgery 26(11): 2029-2037.

[Full-Text](#)

*Department of Orthopedic Surgery*

Hakim S, Reddy SRR, **Batke M, Polidori G and Cappell MS** (2017). "Two case reports of acute upper gastrointestinal bleeding from duodenal ulcers after Roux-en-Y gastric bypass surgery: Endoscopic diagnosis and therapy by single balloon or push enteroscopy after missed diagnosis by standard esophagogastroduodenoscopy." Case Reports in Surgery 9(10): 521-528.

[Full-Text](#)

*Department of Internal Medicine*

The diagnosis and opportunity for endoscopic therapy of gastric or duodenal lesions may be missed at esophagogastroduodenoscopy (EGD) because of technical difficulty in intubating at EGD the postoperatively excluded stomach and proximal duodenum in patients status post Roux-en-Y gastric bypass (RYGB). Two cases are reported of acute upper gastrointestinal bleeding 10 or 11 years status post RYGB, performed for morbid obesity, in which the EGD was non-diagnostic due to failure to intubate the excluded stomach and proximal duodenum, whereas subsequent push enteroscopy or single balloon enteroscopy were diagnostic and revealed 4-cm-wide or 5-mm-wide bulbar ulcers and even permitted application of endoscopic therapy. These case reports suggest consideration of push enteroscopy, or single balloon enteroscopy, where available, in the endoscopic evaluation of acute UGI bleeding in patients status post RYGB surgery when the EGD was non-diagnostic because of failure to intubate these excluded segments.

Hall WA, Bergom C, Thompson RF, Baschnagel AM, Vijayakumar S, Willers H, Li XA, Schultz CJ, **Wilson GD**, West CML, Capala J, Coleman CN, Torres-Roca JF, Weidhaas J and Feng FY (2017). "Precision oncology and genomically guided radiation therapy: A report from the American Society for Radiation Oncology/American Association of Physicists in Medicine/National Cancer Institute Precision Medicine Conference." International Journal of Radiation Oncology Biology Physics. ePub Ahead of Print.

[Full-Text](#)

*Department of Radiation Oncology*

Han D, Hartaigh BO, Gransar H, Lee JH, Rizvi A, Baskaran L, Schulman-Marcus J, Dunning A, Achenbach S, Al-Mallah MH, Berman DS, Budoff MJ, Cademartiri F, Maffei E, Callister TQ, **Chinnaiyan K**, Chow BJW, DeLago A, Hadamitzky M, Hausleiter J, Kaufmann PA, **Raff G**, Shaw LJ, Villines TC, Kim YJ, Leipsic J, Feuchtner G, Cury RC, Pontone G, Andreini D, Marques H, Rubinshtein R, Hindoyan N, Jones EC, Gomez M, Lin FY, Chang HJ and Min JK (2017). "Incremental prognostic value of coronary computed tomography angiography over coronary calcium scoring for major adverse cardiac events in elderly asymptomatic individuals." European Heart Journal Cardiovascular Imaging. ePub Ahead of Print.

[Full-Text](#)

*Department of Internal Medicine*

Aims: Coronary computed tomography angiography (CCTA) and coronary artery calcium score (CACs) have prognostic value for coronary artery disease (CAD) events beyond traditional risk assessment. Age is a risk factor with very high weight and little is known regarding the incremental value of CCTA over CAC for predicting cardiac events in older adults. Methods and results: Of 27 125 individuals undergoing CCTA, a total of 3145 asymptomatic adults were identified. This study sample was categorized according to tertiles of age (cut-off points: 52 and 62 years). CAD severity was classified as 0, 1-49, and  $\geq 50\%$  maximal stenosis in CCTA, and further categorized according to number of vessels  $\geq 50\%$  stenosis. The Framingham 10-year risk score (FRS) and CACS were employed as major covariates. Major adverse cardiovascular events (MACE) were defined as a composite of all-cause death or non-fatal MI. During a median follow-up of 26 months (interquartile range: 18-41 months), 59 (1.9%) MACE occurred. For patients in the top age tertile, CCTA improved discrimination beyond a model included FRS and CACS (C-statistic: 0.75 vs. 0.70, P-value = 0.015). Likewise, the addition of CCTA improved category-free net reclassification (cNRI) of MACE in patients within the highest age tertile (e.g. cNRI = 0.75; proportion of events/non-events reclassified were 50 and 25%, respectively; P-value <0.05, all). CCTA displayed no incremental benefit beyond FRS and CACS for prediction of MACE in the lower age tertiles. Conclusion: CCTA provides added prognostic value beyond cardiac risk factors and CACS for the prediction of MACE in asymptomatic older adults.

Hanba C, Svider PF, **Lai W**, Raza SN, Sheyn A, Eloy JA and Folbe AJ (2017). "An investigation of operative outcomes: Pediatric invasive fungal sinusitis." International Journal of Pediatric Otorhinolaryngology 102(2017): 142-147.

[Full-Text](#)

*OUWB Medical Student Author*

Hanna N, Johnson D, Temin S, Baker S, Brahmer J, Ellis PM, Giaccone G, Hesketh PJ, **Jaiyesimi I**, Leighl NB, Riely GJ, Schiller JH, Schneider BJ, Smith TJ, Tashbar J, Biermann WA and Masters G (2017). "Systemic therapy for stage IV non-small-cell lung cancer: American Society of Clinical Oncology clinical practice guideline update." Journal of Clinical Oncology 35(30): 3484-3515.

[Request Form](#)

*Department of Internal Medicine*

Hauck CR, **Qin A**, Liang J, Ye H, **Krauss DJ**, **Grills IS**, **Chen PY** and **Yan D** (2017). "Factors associated with organ geometric and treatment dose variations identified during PET-CT-based adaptive head and neck cancer radiation therapy." International Journal of Radiation Oncology Biology Physics 99(2): E179.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Adaptive radiotherapy can be employed to maximize conformality throughout a

course of treatment, as well as to reduce radiation dose to normal structures and thereby reduce toxicity; however the degree of this reduction is difficult to predict. The purpose of this study was to determine if there are factors which predict for increased benefit from adaptive radiotherapy treatment for head and neck squamous cell carcinoma (HNSCC). Purpose/Objective(s): Between 2012 and 2015, while enrolled on a prospective protocol, 20 patients with primary HNSCC underwent adaptive radiotherapy. Each patient was treated with intensity modulated radiation therapy to a dose of 70 Gy in 35 fractions, with 3 cycles of concurrent Cisplatin. PET-CT imaging with immobilization was performed weekly. In addition to the initial planning PET-CT, those obtained after fractions 12 and 24 were used to edit region of interest (ROI) contours to account for changes in anatomy. Cone beam computed tomography (CBCT) scans were performed daily. ROI contours from the initial treatment plan were propagated onto each CBCT, and edited individually by a single physician. Actual treatment dose delivered to each ROI was constructed following the deformable CBCT image registration. Patient and tumor characteristics including initial tumor volume, grade, stage, P16 status, and tobacco and alcohol use, were correlated with changes in geometric and dosimetric data of all ROIs using Pearson Correlation and 2-tailed t-test. Results: All tumors decreased in volume from initial to final fraction. The average GTV decrease was 22.3% (4.6-49.0%). The center of each tumor shifted by an average of 0.4 cm (0.2-0.8 cm) during treatment. There was no correlation between tumor grade, stage, alcohol use or P16 status and change in tumor volume or position. The initial GTV volume significantly correlated with tumor position change during treatment, but not with percent volume reduction. The reduction in mean dose to the ipsilateral parotid gland achieved by using 2 plan modifications correlated weakly with the relative decrease in patient weight during therapy ( $R = -0.34$ ,  $P = 0.15$ ). A history of tobacco-smoking correlated with less decrease in constrictor muscle mean dose ( $R = -0.57$ ,  $P = 0.01$ ) and ipsilateral parotid V26 ( $R = -0.49$ ,  $P = 0.03$ ) when adaptive planning was performed compared to non-smoking. In non-smokers, the mean reduction in constrictor muscle mean dose was 3.1%, and the mean reduction in ipsilateral parotid gland V26 was 15.9%. In smokers, the mean reductions in these parameters were 0.7% and 3.1%, respectively. Conclusion: Knowledge of ROI volumetric and geometric changes during radiotherapy will assist in better selecting patients who will benefit from adaptive planning. Non-smokers may derive a greater benefit from adaptive radiotherapy than smokers, as the dose to the constrictor muscles and ipsilateral parotid gland in these patients were found to decrease by a greater margin when using adaptive planning compared to the initial plan.

Hauck CR, Thibodeau BJ, **Ahmed S**, Johnson MD and **Wilson GD** (2017). "Targeted DNA sequencing of non-small cell lung cancer identifies mutations associated with brain metastases." [International Journal of Radiation Oncology Biology Physics](#) 99(2): S199-S200.

[Full-Text](#)

*Department of Family Medicine*

Purpose/Objective(s): The ability to predict at the time of diagnosis which patients with primary non-small cell lung cancer (NSCLC) are likely to experience metastasis to the CNS could be exploited clinically to rationally offer prophylactic cranial irradiation or a targeted agent based on the mutational landscape. We selected NSCLC patients with and without brain metastases (BM), and performed next generation DNA sequencing of a panel of 160 cancer-associated genes in order to identify mutation signatures which distinguish patients who develop BM from those who do not. Purpose/Objective(s): This retrospective study was approved by the Institutional Review Board under expedited review. Forty eight archival formalin-fixed paraffin-embedded (FFPE) tumor samples with the diagnosis of NSCLC were obtained from the Department of Pathology. Four groups of samples were selected: 1) NSCLC from patients with no evidence of metastases within 5 years of surgery ( $n = 10$ ), 2) NSCLC from patients with metastatic disease but not CNS involvement ( $n = 16$ ), 3) NSCLC of patients who developed BM after diagnosis ( $n = 6$ ), 4) BM from NSCLC patients who developed BM after diagnosis ( $n = 6$ ), and 5) BM from patients with simultaneous diagnosis of NSCLC and BM ( $n = 10$ ). Tissue sections underwent DNA isolation, library preparation of the 160 genes, sequencing, alignment, and mutation analysis. Results: Analysis identified 167 variants in 34 genes that differed in primary NSCLC specimens between patients with interval BM compared to patients with elsewhere metastases or no metastases. Eight genes, TP53, BCL6, ABL1, NOTCH2, CREBBP, BRCA2, ERCC5, and CDK12, had variants in  $\geq 50\%$  of the BM patients and this panel was able to discriminate all patients with BM from

those without BMs. In addition, when brain metastases specimens were compared to primary lung cancers, we identified 458 variants in 33 genes that were present in the BMs including 5 genes (TP53, CDK12, BRCA1, BUB1B, and RET) that had variants in  $\geq 50\%$  of the BMs. Pathway analysis revealed "HER-2 Signaling in Breast Cancer" and "PI3K/AKT Signaling" as the top two deregulated pathways in the BMs. Conclusion: We have identified a mutation signature that discriminated NSCLC patients that develop subsequent BM. The future strategy will be to develop a predictive test in a blinded independent larger set of specimens using the same methods where we will use increasing number of genes in the classifier and categorize the blinded specimens as NSCLC with BMs or NSCLC without BMs. Receiver operating characteristic analysis will be used to assess the performance of the classifiers with increasing number of genes. In addition, we have identified the EGFR/RAS/RAF/MEK/ERK and PI3K/PTEN/AKT signaling cascades as potential targets in NSCLC BMs. Future work will develop an intracranial orthotopic NSCLC model using cell lines screened to match the mutational profile developed in the primary NSCLCs that metastasized to the brain and to study the effects of molecular targeted agents in combination with radiation.

Herbst MO, **Price MD** and **Soto RG** (2017). "Pain related readmissions/revisits following same-day surgery: Have they decreased over a decade?" Journal of Clinical Anesthesia 42(2017): 15.

[Full-Text](#)

*Department of Anesthesiology*

Hohenwarter EJ, Stone JR, O'Moore PV, Smith SJ, Selby JB, Lewandowski RJ, Samuels S, Kiproff PM, Trost DW, Madoff DC, **Handel J**, Gandras EJ, Vlahos A and Rilling WS (2017). "Multicenter trial of the VenaTech convertible vena cava filter." Journal of Vascular and Interventional Radiology 28(10): 1353-1362.

[Full-Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Hothem Z, Simon R, Barnes W, Mohammad A, Sevak S, **Ziegler K**, **Iacco A** and **Janczyk R** (2017). "Effects of repealing the motorcycle helmet law in Michigan." American Journal of Surgery 214(3): 407-412.

[Full-Text](#)

*Department of Surgery*

Background In 2012, Michigan repealed its universal helmet law. Our study assessed the clinical impact of this repeal. Methods Our trauma database was queried retrospectively for 2 motorcycle riding seasons before and 3 seasons after repeal. On-scene death data was obtained from the Medical Examiner. Results Helmet use in hospitalized patients decreased after the helmet law repeal. Non-helmeted patients had a significant increased rate of head injury. Non-helmeted patients were more likely to die during hospitalization. While, helmet use and drugs/alcohol status significantly affected the risk for head injury, only drug/alcohol had a significant effect on overall mortality. Conclusions Following helmet law repeal, helmet use has decreased. Helmet status and drug/alcohol use was found to significantly increase risk of head injury. Although overall mortality was only affected by drug/alcohol use, non-helmeted patients did have a higher inpatient mortality. These findings deserve furthermore study and may provide a basis for reinstating the universal helmet law.

**Huang N**, Lee WA, Rivera S and Montezuma SR (2017). "Ruptured retinal arterial macroaneurysm secondary to toxoplasmic kyrieleis arteriolitis: A case report." Case Reports in Ophthalmology 8(2): 390-395.

[Full-Text](#)

*OUIWB Medical Student Author*

Purpose: The aim of this report was to describe multimodal ocular imaging findings in a patient who presented with a ruptured retinal arterial macroaneurysm (RAM) associated with toxoplasmic Kyrieleis arteriolitis. Methods: We report the case of a 64-year-old man with a history of systemic hypertension and dense amblyopia of the left eye who presented with decreased vision and new floaters in the left eye. Color fundus photography, spectral-domain optical coherence tomography, fluorescein angiography, and indocyanine green angiography were used as diagnostic imaging tools. Results: No signs of hypertensive retinopathy were noted in the right eye. Multiple chorioretinal scars characteristic of previous toxoplasmosis



were revealed in the left eye, with one covering most of the macula. Periarterial plaques or Kyrieleis arteriolitis were observed in retinal arteries surrounding the toxoplasmic retinal scars. Multiple RAMs were observed in these vessels, one of which was acutely ruptured. A perivenular plaque associated with a chronic branch retinal vein occlusion (BRVO) was noted along the same arcade at the arteriovenous crossing. Conclusion: RAM formation and BRVO can present as possible long-term complications of toxoplasmic Kyrieleis arteriolitis. This is the first reported case demonstrating an association between toxoplasmic Kyrieleis arteriolitis and RAM formation.

Hussain M, Tangen CM, Thompson IM, Swanson GP, **Wood DP**, Sakr W, Ann Dawson N, Haas NB, Flaig TW, Dorff TB, Lin DW, Crawford ED, Quinn DI, Vogelzang NJ and Glode LM (2017). "Adjuvant Androgen Deprivation (AD) +/- Mitoxantrone + Prednisone (MP) in patients with high-risk Prostate Cancer (PC) post radical prostatectomy (RP): Phase III Intergroup Trial S9921." *Journal of Clinical Oncology* 35(Sup 1): Abstract No. 5019.

[Request Form](#)

*Department of Urology*

Background: Patients (pts) with high-risk PC post RP are at risk of systemic relapse with related morbidity/mortality. Adjuvant AD can reduce this risk. In 1999, based on available data, we hypothesized that adjuvant MP + 2 years (ys) of AD can further reduce mortality. Methods: Eligible pts had cT1-T3, N0 PC with post RP > = 1 high risk factors defined as Gleason sum (GS) ≥ 8, pT3b, pT4, pN+, GS 7 + positive margin or any of these preoperative findings (in pts with neoadjuvant AD): preoperative PSA of > 15 ng/ml, bx GS score > 7, or PSA of > 10 ng/ml + bx GS > 6. Pts had to have post RP PSA = < 0.2 ng/ml, were stratified by T, N, GS, and adjuvant radiation plan and randomized: Arm 1 AD (bicalutamide + goserelin for 2 ys) or Arm 2 AD + 6 cycles m 12 mg/m + P 5mg BID. Primary endpoint: overall survival (OS). Median OS was estimated to be 10 ys in AD arm requiring 680 pts/arm to detect a hazard ratio (HR) of 1.30 with 92% power and one-sided  $\alpha = 0.05$ . Results: 983 pts (961 eligible intent to treat) with median age 60 ys and median PSA 7.6 ng/ml were randomized to AD or AD + MP from 10/99 -1/07 when the DSMC recommended stopping accrual due to higher leukemia rate in Arm 2. 16% had N1 (Group "Gr" 1), 61% GS ≥8 or pT3b (Gr 2), 23% other risk factors (Gr 3). Median time to testosterone recovery was 9.5 months. Median follow-up (f/u) 11.2 ys. Conclusions: OS was higher than anticipated in both arms; MP did not improve OS and increased other malignancy risk. These data illustrate that systemic therapy benefit cannot be extrapolated from different disease stages and the importance of adequate f/u in adjuvant PCa trials. The remarkable DFS and 10 y OS, irrespective of risk extent, may be result of risk definition, and/or 2 ys AD. Pending definitive data 2 ys adjuvant AD for high-risk PCa post RP is a reasonable option to consider. (Table Presented).

Indik JH, Patton KK, Beardsall M, Chen-Scarabelli CA, Cohen MI, Dickfeld TML, **Haines DE**, Helm RH, Krishnan K, Nielsen JC, Rickard J, Sapp JL and Chung M (2017). "HRS clinical document development methodology manual and policies: Executive summary." *Heart Rhythm* 14(10): e495-e500.

[Full-Text](#)

*Department of Internal Medicine*

Ippolito JE, Yim AKY, Luo JQ, **Chinnaiyan P** and Rubin JB (2017). "Sexual dimorphism in glioma glycolysis underlies sex differences in survival." *JCI Insight* 2(15): 1-16.

[Full-Text](#)

*Department of Radiation Oncology*

The molecular bases for sex differences in cancer remain undefined and how to incorporate them into risk stratification remains undetermined. Given sex differences in metabolism and the inverse correlation between fluorodeoxyglucose (FDG) uptake and survival, we hypothesized that glycolytic phenotyping would improve glioma subtyping. Using retrospectively acquired lower-grade glioma (LGG) transcriptome data from The Cancer Genome Atlas (TCGA), we discovered male-specific decreased survival resulting from glycolytic gene overexpression. Patients within this high-glycolytic group showed significant differences in the presence of key genomic alterations (i.e., 1p/19q codeletion, CIC, EGFR, NF1, PTEN, FUBP1, and IDH mutations) compared with the low-glycolytic group. Although glycolytic stratification defined poor prognostic males independent of grade, histology, TP53, and ATRX mutation status, we unexpectedly found

that females with high-glycolytic gene expression and wild-type IDH survived longer than all other wild-type patients. Validation with an independent metabolomics dataset from grade 2 gliomas determined that glycolytic metabolites selectively stratified males and also uncovered a potential sexual dimorphism in pyruvate metabolism. These findings identify a potential synergy between patient sex, tumor metabolism, and genomic alterations in determining outcome for glioma patients.

James CA, **Gonzalez I**, **Khandhar P** and **Freij BJ** (2017). "Severe mitral regurgitation in a child with Henoch-Schonlein Purpura and pulmonary hemorrhage." Global Pediatric Health 4(Sep): 1-4.

[Full-Text](#)

*Department of Pediatrics*

Introduction: Henoch-Schonlein purpura (HSP) is the most common vasculitis of childhood. The classic triad of HSP consists of nonthrombocytopenic purpura, arthritis/arthralgia, and gastrointestinal complaints. Pulmonary hemorrhage and cardiac involvement are rare complications of HSP. Case Report: We report the case of a 10-year-old girl with HSP complicated by both severe mitral regurgitation and pulmonary hemorrhage. Discussion: HSP is typically a self-limited illness with an excellent prognosis in children. Pulmonary hemorrhage is a rare complication that increases morbidity and mortality; it generally indicates the presence of severe vasculitis. Cardiac involvement in HSP is extremely rare and associated with a poor prognosis. Conclusion: Cardiac involvement in HSP may be more common than believed. Because of the increased morbidity and mortality associated with HSP complicated by pulmonary hemorrhage and cardiac involvement, it is important for clinicians to be aware of these potential complications.

**Jawad MS**, Shah C, Wilkinson JB, Wallace M, Mitchell CK, Wobb J, **Gustafson GS**, Brabbins DS, **Grills IS** and **Chen PY** (2017). "Seven-year outcomes following accelerated partial breast irradiation stratified by ASTRO consensus groupings." American Journal of Clinical Oncology: Cancer Clinical Trials 40(5): 483-489.

[Full-Text](#)

*Department of Radiation Oncology*

Jayaschandran V, Mertens AN, **Patel VK** and **Dalal B** (2017). "Life-threatening massive hemoptysis after cryoablation for atrial fibrillation." Liver International. ePub Ahead of Print.

[Full-Text](#)

*Department of Internal Medicine*

A 59-year-old man developed massive hemoptysis, 1 month after undergoing cryoablation procedure for atrial fibrillation. He underwent emergent bronchoscopy that revealed massive, active bleeding with clots requiring repeated suctioning, epinephrine, and cold saline injection. The source of bleeding was identified in a follow-up bronchoscopy performed few days later—a 2x3 cm area of ulceration of the left main stem bronchus which was missed in the initial bronchoscopy owing to blood obscuring the field of vision. Considering the timeline, the ulcer most likely resulted from cryoablation-induced bronchial injury. Patient remained asymptomatic after stabilization and 2 months following discharge, another bronchoscopy was performed which showed the ulcer to be healing. Hemoptysis following cryoablation is quite rare with a reported incidence <2%. The cases of hemoptysis reported thus far have all been mild and self-limiting and manifesting within hours to days following the procedure. To our knowledge, this is the first reported case of massive hemoptysis associated with cryoballoon ablation, presenting 1 month after procedure.

Jensen ET, van der Burg JW, O'Shea TM, Joseph RM, Allred EN, Heeren T, Leviton A, Kuban KCK, Shah B, Singh R, Smith A, Klein D, McQuiston S, Rollins J, Douglass L, Ware J, Coster T, Henson B, Wilson R, McGhee K, Lee P, Asgarian A, Sadhwani A, Perrin E, Neger E, Mattern K, Walkowiak J, Barron S, Frazier J, Venuti L, Powers B, Foley A, Dessureau B, Wood M, Damon-Minow J, Ehrenkranz R, Benjamin J, Romano E, Tsatsanis K, Chawarska K, Kim S, Dieterich S, Bearrs K, O'Shea TM, Peters N, Brown P, Anusinha E, Waldrep E, Friedman J, Hounshell G, Allred D, Engelke SC, Darden-Saad N, Stainback G, Warner D, Wereszczak J, Bernhardt J, McKeeman J, Meyer E, Pastyrnak S, Burdo-Hartman W, Rathbun J, Nota S, Crumb T, Lenski M, Weiland D, Lloyd M, Hunter S, Msall M, Ramoskaite R, Wiggins S, Washington K, Martin R, Prendergast B, Scott M, **Klarr J**, Kring B, DeRidder J and Vogt K (2017). "The relationship of maternal prepregnancy body mass index and pregnancy weight gain to neurocognitive function at age 10 years among children born extremely preterm." Journal of Pediatrics 187(Aug): 50-57.e53.

[Full-Text](#)

*Department of Pediatrics*

Kaufman CS, Cross MJ, Goyal S, Barone J, Devisetty K, **Dekhne NS**, Edmonson D, Gass J, Graham C, Hong RL, Patton B, Phillips R, Schonholz SM, Smith LA, Tafra L, Smith A and Dilworth J (2017). "Registry study of 337 bio-absorbable 3-D implants marking lumpectomy cavity benefit cosmesis while targeting radiation." Annals of Surgical Oncology 24(1): S63.

[Full-Text](#)

*Department of Surgery*

Introduction: Oncoplastic procedures at the time of lumpectomy have become commonplace. A 3-D bioabsorbable implant placed during lumpectomy may deliver solutions to three common problems; providing a dependable tumor bed target for radiation, providing a scaffold for oncoplastic closure resulting in better cosmesis and identifying re-excision sites after tissue rearrangement. An IRB-approved Registry started in 2012 collected 337 cases to assess these issues. Methods: A bioabsorbable 3-D implant was sutured to the tumor excision site during lumpectomy and was utilized for planning and targeting breast irradiation. Data includes patient demographics, breast size, tumor characteristics, surgical and radiotherapy techniques, cosmesis and follow-up. Results: As of September 2016, there are 337 patients from 14 centers involving 17 physicians from 12 States enrolled in the implant registry. Tumor characteristics are similar to other reports involving early breast cancer regarding patient age, size, location, tumor histology, prognostic indicators, node positivity (12%), and location (upper outer 48%). Cancers were T-1 (56%), T-2 (18%) and DCIS (20%). In most cases, implant sizes mirrored the size of the original tumor, 2X2cm (39%) and 2X3cm (33%). The radiation oncologist verified implant as "easily seen" on CT in 92% of cases and 96% found "improved accuracy" in boost targeting and set up. Oncoplastic procedures were used in 90% of patients with 41% 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 (94%, 97%, 90%) and by patients (95%, 94%, 87%). The device contributed to the cosmetic benefit for each time period (78%, 80%, and 80%). (See Figure). Conclusion: An IRB approved Registry reports the benefits of a 3-D bioabsorbable implant placed during lumpectomy to provide a dependable target for radiation, a scaffold for oncoplastic tissue rearrangement and to enhance cosmesis over time. This report of 337 patients describes early evidence that this device may achieve multiple goals. Further collection of data over time will validate these early impressions. (Figure presented).

Kaur H, Muhleman M, Gupta A and **Balon H** (2017). "Applications of Tc-99m Sestamibi: Cardiac imaging and beyond." Journal of Nuclear Medicine 58(Sup 1): 970.

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*Department of Diagnostic Radiology and Molecular Imaging*

Educational objectives: 1. Learn the mechanism of Tc-99m sestamibi localization in tissue. 2. Learn the major indications of Tc-99m sestamibi imaging. 3. Be aware and recognize patterns of various incidental findings on Tc-99m sestamibi scintigraphy. Technetium-99m sestamibi myocardial perfusion imaging (most often employing the 1-day rest/stress protocol) is a commonly used non-invasive test for evaluation and risk stratification of patients with known or suspected coronary artery disease. Another well-established indication for Tc-99m sestamibi is parathyroid imaging for pre-operative localization of parathyroid

adenomas or ectopic parathyroid tissue in patients with hyperparathyroidism. Breast specific gamma imaging (BSGI)/scintimammography is yet another indication where Tc-99m sestamibi (under the brand name Miraluma™) may be helpful in certain patients as supplemental breast imaging (for example in patients with dense breasts, with a lump at previous surgical site, with breast implants, indeterminate mammograms, or when multiple tumors are suspected). Often, unsuspected or incidental findings on these images may be seen and can be important in the clinical course and management of the patients. We will present multiple case examples of sestamibi scintigraphy along with correlative images from other modalities, as well as histopathology. We will discuss the subcellular mechanism of sestamibi uptake that may explain its localization in some of the pathologic conditions. These will include myocardial perfusion imaging, parathyroid imaging, BSGI, thyroid cancer (especially Hurthle cell) and a variety of incidental extracardiac findings (e.g., breast ca, hibernoma, hiatal hernia). Some of these diagnoses were unexpected and had an impact on patient management, therefore, timely communication of even some incidental findings to the referring physician is essential.

Kaur H, Muhleman M, **Seitz J** and **Qing F** (2017). "Aortic root abscess clearly shown on In-111 leukocyte scan but less obvious on transesophageal echocardiogram." Journal of Nuclear Medicine 58(Sup 1): 971.

[Request Form](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Kaur H, Muhleman M and **Wu DF** (2017). "Non-invasive diagnosis of acute interstitial nephritis using planar and SPECT Gallium-67 imaging." Journal of Nuclear Medicine 58(Sup 1): 972.

[Request Form](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Keeney S and **Halalau A** (2017). "Anchoring bias in a case of recurrent abdominal pain." BMJ Case Reports 2017. ePub Ahead of Print.

[Request Form](#)

*Department of Internal Medicine*

Kennedy A, Cohn M, Coldwell DM, Drooz A, Ehrenwald E, Kaiser A, Nutting CW, Rose SC, Wang EA and **Savin MA** (2017). "Updated survival outcomes and analysis of long-term survivors from the MORE study on safety and efficacy of radioembolization in patients with unresectable colorectal cancer liver metastases." Journal of Gastrointestinal Oncology 8(4): 614-624.

[Full-Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Background: The Metastatic colorectal cancer liver metastases Outcomes after RadioEmbolization (MORE) study was a retrospective analysis of 606 patients with unresectable colorectal liver metastases treated with radioembolization (RE) using 90Y-labeled resin microspheres. The first analysis of this study was completed with a last patient follow-up of 77.7 months. We now provide an updated survival analysis through September 15, 2016, with a last patient follow-up of 125 months. Methods: 90Y-RE was considered for patients with advanced liver-only or liver-dominant metastatic colorectal cancer which was deemed not suitable for surgery, ablation, or systemic therapy, and which had progressed or become refractory to at least one line of systemic therapy. All patients with a diagnosis of metastatic colorectal cancer who had received at least 1 RE treatment and 1 follow-up visit were included in the analysis. Patients were treated between July 2002 and December 2011 at one of 11 U.S. tertiary care centers. Data were collected at baseline, on the day of the first 90Y-RE treatment (day 0), and at all subsequent visits or until death. Patient medical charts and/or public records were accessed to obtain dates of death. Results: Dates of death were obtained for 574 out of a total of 606 patients, and overall survival (OS) data analyzed. Updated median OS was 10.0 months (95% CI: 9.2-11.8 months) at a median follow-up of 9.5 months versus the originally reported median OS of 9.6 months (95% CI: 9.0-11.1 months) at a follow-up of 8.6 months in the first MORE analysis. Patients received a median (range) of 2 (0 to 6) lines of chemotherapy. Baseline characteristics and factors significantly associated with patient survival ( $P < 0.01$ ) are consistent with those reported in the first safety analysis of the

MORE study. These factors include poor ECOG performance status, markers of advanced disease such as increased extent of tumor-to-target liver involvement, poor baseline liver function, pre-treatment anemia, lung shunt fraction, and number of lines of prior chemotherapy. Patient age did not significantly affect survival outcomes. Conclusions: Long-term follow-up confirms that 90Y-RE treatment offers favorable survival benefits for patients with unresectable metastatic colorectal cancer, even among patients who received 3 or more prior lines of chemotherapy. Our analysis also supports earlier reported prognostic factors for survival after 90Y-RE. Overall, our updated analysis confirms that 90Y-RE treatment provided a meaningful response and survival advantage for MORE patients across all ages and across diverse community and academic centers in the U.S.

Kennedy AS, Cohn M, Coldwell DM, Drooz A, Ehrenwald E, Kaiser A, Nutting CW, Rose SC, Wang E and **Savin M** (2017). "Unresectable colorectal cancer liver metastases treated with radioembolization: Updated survival analysis of the MORE study." Journal of Clinical Oncology 35(4): Abstract No. 666.

[Request Form](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Background: In December 2011, the Metastatic Colorectal Cancer Liver Metastases Outcomes after Radioembolization (MORE) study retrospectively analyzed 606 patients with unresectable colorectal liver metastases treated with radioembolization using Y-90 resin microspheres. At a median follow-up of 8.6 months, 503 of these patients had died. Here, we summarize survival outcomes from extended follow-up of the remaining patients through September 1, 2016. Methods: Extended survival surveillance was abstracted from patient charts and public records. Survival time was compared for prognostic variables using Kaplan-Meier estimates. Results: Survival data were analyzed for 574 of 606 patients with median follow-up of 9.5 months (IQR 12.9 months). Patients received a median (range) of 2 (0 to 6) lines of chemotherapy. Additional death dates were obtained on 71 patients, and median survival was 10.0 months (95% CI 9.2-11.8) -versus 9.6 (95% CI 9.0-11.1) months originally reported. Data confirm ECOG PS, disease stage, extent of liver involvement, liver function, metachronous metastasis, and prior chemotherapy as predictors of post-radioembolization survival. Conclusions: Long-term follow-up confirms the originally reported prognostic factors for survival and that radioembolization offers a favorable survival benefit for patients with unresectable colorectal cancer liver metastases, even among those who already received 3 or more lines of chemotherapy. (Table Presented).

Kesarwani P, Kumar P, Kant S, **Prabhu A, Wilson GD, Graham S** and **Chinnaiyan P** (2017). "GDC-0919 modulates tryptophan metabolism in glioblastoma and enhances radiation response." International Journal of Radiation Oncology Biology Physics 99(2): E601.

[Full-Text](#)

*Department of Pediatrics*

*Department of Radiation Oncology*

*Department of Obstetrics and Gynecology*

Purpose/Objective(s): Glioblastoma (GBM) is an aggressive tumor and despite multi-modality therapy, including high dose ionizing radiation (RT), inevitably recurs. Immune checkpoint inhibitors designed to revert tumor-induced immune suppression have emerged as potent anti-cancer therapies. The potential of RT to stimulate an immune response and work synergistically with immune checkpoint agents offers strong promise in enhancing therapeutic response. Tryptophan metabolism represents an important immune checkpoint with particular relevance to GBM and targeting this pathway's rate limiting enzyme indoleamine 2,3-dioxygenase (IDO) is actively being investigated. In this study, we evaluated tryptophan metabolism in patient-derived glioma specimens and the activity of the novel, potent, IDO inhibitor GDC-0919 (Genentech), both alone and in combination with RT, in a panel of GBM preclinical models. Purpose/Objective(s): LC/GC-MS was used for metabolomic analyses of patient-derived glioma. Western blot and kynurenine (metabolite of the tryptophan pathway) production were used to analyze IDO pathway activation in GBM cell lines at baseline and following IDO inhibition. Pharmacodynamic studies were performed to evaluate blood brain barrier (BBB) penetrance of GDC-0919 using LC-MS. The immune consequences and antitumor activity of GDC-0919 were evaluated using an immune competent murine model both alone and in combination with

RT. Results: Global metabolomic profiling of over 200 patient-derived gliomas in two independent studies identified accumulation of several intermediaries of tryptophan metabolism in GBM. These findings were recapitulated in a panel of GBM cell lines, demonstrating that activation of the IDO pathway is induced by the inflammatory cytokine IFN $\gamma$ . GDC-0919 demonstrated potent inhibition of tryptophan metabolism, resulting in reduced kynurenine production. We also demonstrated this inhibitor can effectively cross the BBB at biologically relevant concentrations. Initial studies using an immune competent murine model demonstrated that GDC-0919 reduced levels of immune suppressive cells at the tumor site. Although GDC-0919 alone did not influence tumor growth, it did demonstrate the capacity to significantly enhance RT response. Conclusion: Our study demonstrates that tryptophan metabolism is significantly upregulated in GBM. The IDO inhibitor GDC-0919 is able to modulate tryptophan metabolism, cross the BBB, and attenuate tumor-mediated immune suppression. Although GDC-0919 alone does not appear to effect tumor growth in GBM, it demonstrates strong potential for enhancing RT response, and therefore, warrants further investigation.

Khoury Abdulla R, Kheder E, **Yeow R**, Ginoya Meka S, **Yaldo O** and **Abbas AE** (2017). "The impact of statin therapy on survival for in-hospital cardiac arrest." Journal of Investigative Medicine 65(7): e4.

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*OUIB Medical Student Author*

*Department of Internal Medicine*

**Killinger KA, Fergus J**, Edwards L, **Boura JA, Bartley J**, Gupta P, Tomakowsky J, **Gilliran J** and **Peters KM** (2017). "Coexisting depressive symptoms do not limit the benefits of chronic neuromodulation: A study of over 200 patients." Neurourology and Urodynamics. ePub Ahead of Print.

[Full-Text](#)

*Department of Urology*

*OUIB Medical Student Author*

*Department of Biomedical Sciences (BH)*

Aims: To examine the relationship between coexisting depressive symptoms and outcomes after staged neuromodulation procedures for refractory urological symptoms. Methods: Adults who enrolled in a prospective database and completed a Personal Health Questionnaire Depression Scale (PHQ-8) at baseline were reviewed. The PHQ-8 and Generalized Anxiety Disorder (GAD-7) assessed depressive/anxiety symptoms pre and 6 months post device implant. Urological symptoms were assessed with The Interstitial Cystitis Symptom Index/Problem Index (ICSI-PI) and Overactive Bladder Questionnaire (OAB-q) at baseline, 3 and 6 months, and Global Response Assessments (GRA) post implant. Subjects, grouped by PHQ<10 and PHQ  $\geq$ 10, were compared with Pearson's Chi-square, Fisher's Exact or Wilcoxon rank test, and Spearman's correlations. Results: In 117 PHQ <10 and 84 PHQ  $\geq$ 10 patients, age differed (mean 59 vs 52 years; P=0.001), and PHQ <10 had lower GAD-7, ICSI-PI, and OAB-q scores at baseline (P<0.0001, P=0.0003, and P<0.0008, respectively). Implantation rates were similar between groups. Reoperation and complication rates within the first 6 months did not differ, similar proportions (majority) were improved on the GRA at each time point, and ICSI-PI and OAB-q scores improved significantly. PHQ scores only improved significantly for those with baseline PHQ  $\geq$ 10. Baseline PHQ strongly correlated with GAD-7 at baseline and 6 months, and baseline ICSI-PI. Change in PHQ positively correlated with the change in GAD-7, 6 month ICSI-PI, and change in ICSI-PI from baseline to 6 months. Conclusions: Coexisting depressive symptoms do not limit the efficacy of neuromodulation and PHQ improvements correlate with improved anxiety and bladder symptoms.

Kim EL, Thanos A, Yonekawa Y, Todorich B, **Wolfe J, Randhawa S** and **Faia LJ** (2017). "Optical coherence tomography angiography findings in punctate inner choroidopathy." Ophthalmic Surgery Lasers and Imaging Retina 48(10): 786-792.

[Request Form](#)

*Department of Ophthalmology*

Background and Objective: Punctate inner choroidopathy (PIC) is an inflammatory chorioretinopathy characterized by multiple punctate, hypopigmented fundus lesions. Optical coherence tomography



angiography (OCTA) is an emerging imaging modality that enables high-resolution visualization of the retinal and choroidal vasculature. The objective of this study is to examine the OCTA findings in PIC. PATIENTS AND METHODS: Observational, retrospective review of five patients with PIC. RESULTS: OCTA revealed several features in PIC lesions: distinctly visible choroidal neovascular membranes when present, as well as flow voids within the choroid and choriocapillaris layers that correspond with hypofluorescent lesions on indocyanine green angiography. CONCLUSION: OCTA may serve as a useful adjunctive imaging modality in diagnosing and monitoring patients with PIC.

Kogachi K, **Wolfe JD** and Kashani AH (2017). "Surgically induced focal retinal detachment does not cause detectable SD-OCT retinal changes in normal human retina." *Investigative Ophthalmology and Visual Science* 58(12): 5270-5279.

[Full-Text](#)

*Department of Ophthalmology*

PURPOSE. Induction of focal retinal detachment (RD) for subretinal delivery of stem cells and gene therapy is increasingly common. In order to determine if this procedure has an adverse impact on the retina, we use spectral-domain optical coherence tomography (SD-OCT) to evaluate the pre- and postoperative retinal anatomy of the incidentally detached normal retina surrounding large submacular hemorrhages (SMH) during surgical displacement procedures. METHODS. Retrospective, observational study of human subjects with monocular SMH evaluated before and after surgical displacement using clinical exam, fundus photography, and SD-OCT. Manual measurements of the inner retinal thickness (IRT), outer retinal thickness (ORT), and full retinal thickness (FRT) were made in regions involving the SMH and surrounding normal retina. Comparison of retinal thickness measurements was made using the Wilcoxon signed-rank test. RESULTS. Seven eyes were included in this study. All eyes successfully underwent surgical displacement of SMH. Visual acuity improved in 6/7 subjects and was unchanged in the remaining subject. Incidental RD of the normal retinal regions surrounding the SMH did not cause any significant change in IRT, ORT, or FRT that was detectable by SD-OCT. In contrast, mean FRT overlying regions with SMH was significantly greater before surgery compared to after displacement of SMH or normal adjacent retina. CONCLUSIONS. Surgically induced focal RD does not cause detectable retinal changes in the incidentally detached normal retina surrounding large SMH. Therefore, surgical induction of focal RD should not be considered to have the same adverse impact on the retina as pathologic RD.

Lack D, **Chen PY, Dilworth JT, Jawad MS, Gustafson GS** and Liu Q (2017). "Biological effective dose of two accelerated partial breast irradiation techniques used in RTOG 0413/NSABP B-39." *International Journal of Radiation Oncology Biology Physics* 99(2): E26-E27.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): MammoSite brachytherapy (BT) and 3D conformal EBRT are APBI techniques in the B-39/RTOG 0413 protocol. The doses used are 3.4 Gy x 10 for BT and 3.85 Gy x 10 for EBRT, delivered BID with a > 6 hour inter-fraction interval. These were setup to be equivalent to 45 Gy given in 25 fx using a  $\alpha/\beta = 10$  Gy. While preliminary data suggests comparable efficacy, the adverse toxicity associated with EBRT has raised concerns. We hypothesize the increased toxicity is due to the higher biological effective doses delivered to a larger volume than is seen with BT. We test this by retrospectively modeling the biological dose for both modalities for patients treated at our institution. Purpose/Objective(s): Eight patients treated with MammoSite BT were randomly chosen for evaluation. Each had 2 CTs, acquired before and after balloon implantation. These CTs were taken within 1 week of each other and used the same patient setup. Target/normal tissue delineation and planning for BT and EBRT plans followed protocol guidelines. BED calculations in the form of EQD2 (equivalent dose in 2 Gy fx) were performed for each voxel in MATLAB and considered the increased fractionation sensitivity of breast cancer ( $\alpha/\beta = 4$ Gy) and late reacting normal breast tissue ( $\alpha/\beta = 3$ Gy). A limitation of the simple LQ model is that it ignores intra-fraction repair and assumes full inter-fraction repair. Given the BID nature of APBI, a general model that accounts for repair kinetics of tumors (mono-exponential repair) and normal tissue (double-exponential repair) was used. For each patient, the EQD2 dose distribution and DVH were compared for BT and EBRT. For the target, PTV-EVAL, a generalized equivalent uniform dose (gEU-EQD2) was also calculated. Results: All plans met protocol

dosimetric criteria. Comparatively, the EBRT PTV-EVAL is on average 2.8x larger than the BT PTV-EVAL due to an additional CTV-PTV margin required by the protocol for EBRT. For targets, the mean gEU-EQD2 values are 51.3 (48.4-56.3) Gy for BT and 51.0 (50.4-51.8) Gy for EBRT. A larger range in values is seen for BT due to greater heterogeneity in target coverage. For normal breast, BT provides greater sparing up to 60 Gy with small volumes receiving 65-90 Gy in the overlapping PTV-EVAL. Due to the slower repair kinetics of normal tissue and the larger target volumes irradiated in EBRT, the normal breast volume receiving 50-60 Gy may be 2-5x greater than BT. Conclusion: Biological modeling of MammoSite BT and EBRT plans showed these techniques have similar gEU-EQD2 values, suggesting the minimum biological doses to target volumes are equally effective. From our analysis, the larger normal breast volumes (approaching > 400cc for EBRT vs. 80cc for BT) that receive biological doses of 55-60Gy in the overlapping PTV-EVAL may be linked to the poorer cosmesis results reported. While BT delivers higher biological doses of 65-90 Gy, these are to a much smaller volume of 28-82 cc.

Lack D, Liang J, Benedetti L, Knill C and **Yan D** (2017). "Advanced detection of potential errors during patient treatment planning." Medical Physics 44(6): 3162-3163.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: Data errors caught late in the planning process require time to correct, resulting in treatment delays of up to 1 weeks' time. In this work we identify causes of potential data errors in the planning process and develop a software tool that automatically detects these errors in advance. Methods: There are 2 major categories of data errors which require user intervention. These can be classified as 1) data transfer errors, 2) TPS errors. Using root analyses, the causes of these potential data errors were determined. For data transfer errors, the main causes identified were: incorrect patient identifier entry, image slice missing from dataset, and incorrect DICOM tag generated at CT console. For TPS errors, the main causes identified were: incorrect CTdensity table application and image file imported to incorrect patient. This information was incorporated into a windows-based software tool developed using SQL and FTP services that is scheduled to run daily. The SQL service accesses the unix-based TPS's Postgres database and windows-based Mosaik MSSQL databases, and the read-only FTP service scans the TPS unix file system for potential data errors. Detected errors are automatically sent to a physicist for review and once confirmed, the responsible clinician is notified to correct the error and educated to prevent errors in the future. Results: The software tool has been running automatically since 2015. In 2016, 84 planning errors were detected within which the most frequent errors were the incorrect patient identifier entry (35 occurrences) followed by the incorrect CT-density table application (17 occurrences) and image slice missing (16 occurrences). Conclusion: The planning error tracking tool successfully detects errors during the planning process, improving the accuracy and efficiency of clinical treatment. This important QA tool will focus our efforts on the areas in the clinical treatment planning process that need the most improvement.

**Lamb LE**, Janicki JJ, Bartolone SN, **Peters KM** and **Chancellor MB** (2017). "Development of an interstitial cystitis risk score for bladder permeability." PloS One 12(10): 1-15.

[Full-Text](#)

*Department of Urology*

**Lanni T**, **Stevens CW**, **Welsh R**, **Keena D**, **Akhtar A** and **Mezwa D** (2017). "The effect of positive lung-rads results in a lung cancer screening program: The Beaumont Health experience." International Journal of Radiation Oncology Biology Physics 99(2): E204.

[Full-Text](#)

*Department of Radiation Oncology*

*Department of Surgery*

*Department of Internal Medicine*

*Department of Diagnostic Radiology and Molecular Imaging*

Purpose/Objective(s): To evaluate the initial outcomes and cost effectiveness of who received a positive screening result and were diagnosed with lung cancer. Purpose/Objective(s): Three thousand four hundred

sixty-eight patients were screened from January 2014 to December 2016. These patients were screened on a low-dose CT screening protocol at Beaumont Health System. The ACR Lung Imaging Reporting and Data System (Lung-RADS™) were used to assign the score for each patient. Screening eligibility criteria were based on the CMS guidelines and follow up was based on Lung-RADS guidelines. Costs were calculated using patient data from internal financial systems. The expected costs quality adjusted life years (QALY) were calculated with a cost-effectiveness between \$100,000 to \$150,000 QALY. Results: Six hundred twenty-four patients were categorized with a positive Lung-RADS score (3 or 4). The median age, packs per day and pack years smoked for all patients was 65, 1.0 and 40.0 years respectively. The Lung-RADS score for these patients was 55.6% (3), 22.2% (4A), and 17.1% (4B). Lung cancer diagnosis rates for each score was 0.9% (3), 8.6% (4A) and 30.8% (4B) with 49 lung cancers diagnosed. Median follow up was 1.2 years with 5 deaths in cohort. We found that screening for this high risk population would cost \$92,132 per QALY, therefore making it cost effective. Conclusion: The establishment of a low-dose CT lung cancer screening program improved the ability to screen patients as demonstrated by the number of patients screened and those diagnosed with a malignancy. These findings were also consistent with the findings from the National Lung Screening Trial study and reiterates the need for a coordinated screening program.

**Lee YA** (2017). "White matter injury of prematurity: Its mechanisms and clinical features." Journal of Pathology and Translational Medicine 51(5): 449-455.

[Full-Text](#)

*Department of Pediatrics*

A developing central nervous system is vulnerable to various insults such as infection and ischemia. While increased understanding of the dynamic nature of brain development allows a deeper insight into the pathophysiology of perinatal brain injury, the precise nature of specific fetal and neonatal brain injuries and their short- and long-term clinical consequences need special attention and further elucidation. The current review will describe the pathophysiological aspects and clinical significance of white matter injury of prematurity, a main form of perinatal brain injury in premature newborns, with a particular emphasis on its potential antenatal components.

**Li X, Kabolizadeh P, Zhou J, Qin A, Yan D, Guerrero T, Grills I, Stevens C** and Ding X (2017). "Mitigation of interplay effects using a novel robust, delivery-efficient and continuous spot scanning proton arc therapy for lung cancer." Medical Physics 44(6): 2993.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: Spot scanning proton arc therapy (SPArc) is a novel planning and treatment technique with potential to deliver proton therapy via continuous arc trajectories efficiently. We hypothesize that SPArc can result in diminishing the negative dosimetric impacts of respiratory tumor motion in lung cancer treatment compared to traditional intensity modulated proton therapy (IMPT) with limited number of beam angles. Methods: Six lung patients with average internal target volume (ITV) of 331 cc (range 77-735 cc) and average tumor motion of 0.82 cm (range: 0.53-1.35 cm) were planned. Both SPArc and IMPT plans were developed on the average phase scan of 4D CT scan using robust optimization with same uncertainty parameters to achieve an optimal coverage to 99% of the ITV with 66 Gy (RBE) in 33 fractions. To evaluate the interplay effect, ten scenarios of single-fraction 4D dynamic doses via different starting breathing phases were calculated using spot switching time of 0.2 ms and energy layer switching time of 0.9s without repainting. The doses encompassing 95% (D95%) and 1% (D1%) of ITV were compared for both plans. Results: SPArc significantly improved the target coverage D95% ( $p < 0.01$ ) and reduced target volume hotspots D1% ( $p = 0.01$ ). More specifically, for all patients planned in SPArc group, the median D95% reached at least 95% of prescription and the median D1% were less than 115% of prescription. In contrast, only 50% of the patients in the IMPT group maintained at least 95% of prescription coverage or hotspots less than 115% of prescribed dose. Conclusion: SPArc maintained 95% ITV of prescription coverage for 100% of the evaluated plans, even using a single fraction delivery simulation, compared to multi-field IMPT which achieved this only 50% of the time. SPArc has the potential to be implemented into clinical practice to treat lung cancer.

Liang J, **Zhou J**, Zhou D, **Qin A** and **Yan D** (2017). "Assess tumor intrafraction motion and dose variation by using intrafraction KV projection streaming." Medical Physics 44(6): 2735.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: Using intrafraction KV imaging to track real-time tumor motion and treatment dose variation. Methods: Real-time projection images are acquired by Elekta-XVI5 during the treatment delivery and simultaneously transferred to a client computer. Diaphragm at KV image is used as surrogate to predict tumor position. Prior to treatment, diaphragm templates on 2D projection images are created using pre-treatment 4DCT. On treatment day, from pre-treatment KV images, diaphragm positions are detected on 2D projections while tumor positions are obtained from 10 phase reconstructed CBCT. A daily tumor-diaphragm motion correlation model is created. Diaphragm motion is converted into tumor motion and serves as reference. During VMAT delivery, diaphragm positions are detected at each intrafraction projection and subsequently converted into tumor positions. The tumor motion is compared with the daily reference for online correction if necessary. The 4D dose constructed using the pre-treatment 4D-CBCT and the intrafraction 4D-CBCT will be compared to evaluate the intrafraction variation. To date, intrafraction tumor motion of 2 hypolung treatments (4 fractions/treatment) has been monitored using our intrafraction motion tracking system. Results: Diaphragm position detecting took about 70-90 milliseconds per projection, well within the image acquisition interval of 182 milliseconds. Difference of diaphragm position between auto-tracking and manual-tracking were within 1 pixel for 84.2% and 78.1% of projections for KV-only and KVMV scans respectively. The largest uncertainties were mostly located at the KV-source angles of 70°-110° and 250°-290° where the projections of the right and left lungs overlapped. A tumor baseline shift of  $-0.2 \pm 1.3$  mm was observed. The target dose D99 constructed using the intrafraction 4D CBCT was reduced up to 1.7% relative to the dose constructed using the pretreatment 4D CBCT. Conclusion: Real-time tumor position could be tracked in given time interval with high accuracy. Target dose coverage could be improved if necessary online correction is performed.

Lin HYD, Limbacher A, Wallace M, Ye H, **Dilworth JT**, **Grills IS**, Mathews M and **Chen PY** (2017). "Acute and chronic toxicities from multilumen versus single lumen brachytherapy: Correlating clinical outcome with dosimetry."

International Journal of Radiation Oncology Biology Physics 99(2): E31-E32.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Prior studies have shown improved dosimetry with lower skin doses using multi-lumen (ML) catheter brachytherapy compared to single lumen (SL) devices for accelerated partial breast irradiation (APBI). However, there are no long-term clinical data to correlate the improved dosimetry with less early and late toxicities. We hypothesized that ML APBI had a more favorable side effect profile and dosimetry compared to SL APBI. Purpose/Objective(s): A total of 191 patients were treated between 6/30/2000 and 2/22/2013 using either SL MammoSite (N=129; single or multi-dwell), ML MammoSite (N=22), or ML Contura applicators (N=40). All patients were treated with 34 Gy prescribed to a depth of 1 cm from the applicator in 10 twice daily fractions. Only patients with more than 3 years of follow-up data were included in this study. The median follow-up was 8 years. Toxicities including dermatitis, hyperpigmentation, hypopigmentation, breast pain, breast edema, telangiectasia, and induration were assessed at each follow-up visit using the CTCAE (v3.0) criteria. Acute toxicity was defined as <6 months from the date of radiotherapy completion, and chronic toxicity was defined as >6 months. Skin spacing and maximum skin dose were measured for each patient. Differences in acute and chronic toxicities were compared using chi-square and log-rank tests. Mean maximum skin doses were compared using a t-test. Results: Patients treated with ML applicators had significantly less acute dermatitis (grade 1-4: ML 42.4%/SL 66.7%,  $P=0.003$ ; grade 2-4: ML 8.5%/SL 9.4%,  $P=0.785$ ), chronic dermatitis (grade 1-4: ML 14.5%/SL 30.5%,  $P=0.018$ ; grade 2-4: ML 0%/SL 3.9%,  $P=0.135$ ), and chronic telangiectasia (grade 1-4: ML 19.4%/SL 34.6%,  $P=0.031$ ; grade 2-4: ML 14.6%/SL 17.3%,  $P=0.681$ ) compared to SL MammoSite. There were no significant differences between ML and SL in the rates of acute or chronic hyperpigmentation, hypopigmentation, breast pain, breast edema, and induration. Using a log-rank test, patients treated with ML applicators had less chronic dermatitis compared to SL MammoSite ( $P=0.05$ ). The mean maximum skin dose was significantly lower for ML (34.1 Gy)

compared to SL (36.3 Gy) when the skin spacing was between 6-11 mm (P=0.038). However, the mean maximum skin dose was not significantly different between ML and SL when skin spacing was <6 mm (P=0.086) or >12 mm (P=0.419). Regardless of skin spacing, the median maximum skin doses were 32.2 Gy for ML and 33.7 Gy for SL. Conclusion: ML applicators resulted in less acute and chronic toxicities compared to SL MammoSite. ML devices also had significantly lower mean maximum skin doses when skin spacing was between 6-11 mm.

Lin HYD, Ye H and **Krauss DJ** (2017). "Muscle invasive bladder cancer survival after radical cystectomy or definitive chemoradiation: A national cancer database matched pair analysis." International Journal of Radiation Oncology Biology Physics 99(2): E252.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Radical cystectomy or definitive chemoradiation (chemoRT) are both treatments for muscle invasive bladder cancer, but there has not been a prospective randomized phase III trial directly comparing the two. Retrospective comparisons are confounded by differences in patients' performance status or characteristics. We hypothesized that treatment with radical cystectomy and chemotherapy (cystectomy/chemo) versus chemoRT would have similar survival when patient variables were balanced in a matched pair analysis. Purpose/Objective(s): A total of 125879 patients with stage II-IV, M0 bladder cancer diagnosed between 2004 to 2014 without a second primary malignancy were identified from the National Cancer Data Base. Patients who received no treatment, cystectomy only, chemotherapy only, radiation only, radiation and cystectomy, or trimodality therapy were excluded from the analysis. There were 9834 patients treated with cystectomy/chemo, and 4399 patients were treated with chemoRT ( $\geq 60$  Gy to the bladder). Univariate analyses using Cox regressions were used to investigate for variables that correlated with overall survival (OS). OS was compared between cystectomy/chemo versus chemoRT both before and after a matched pair analysis using a log-rank test. Results: Age (P<0.001), sex (P<0.001), race (P<0.001), Charlson/Deyo Comorbidity Score (CDCS; P<0.001), insurance status (P<0.001), type of facility (P<0.001), income (P=0.05), and stage (P=0.005) were significantly correlated with overall survival on univariate analyses. Prior to a matched pair analysis, patients treated with cystectomy/chemo were younger (mean: cystectomy/chemo 63.6 vs. chemoRT 73.7, P<0.001), had better CDCS performance status (CDCS 0: cystectomy/chemo 74.2% vs. chemoRT 68.5%, P<0.001), privately insured (cystectomy/chemo 42.8% vs. chemoRT 19.9%, P<0.001), and were more likely female (cystectomy/chemo 32.7% vs. chemoRT 28.4%, P<0.001). Before a matched pair analysis, OS was significantly better when treated with cystectomy/chemo (3 yr 50.9% and 5 yr 41.4%) compared to chemoRT (3 yr 40.6% and 5 yr 28.4%)(P<0.001). A matched pair analysis matching age ( $\pm 2$  yr), sex, race, CDCS, insurance status, income, and stage produced 722 pairs (N=1444). After the matched pair analysis, OS was no longer significantly different between cystectomy/chemo (3 yr 47.3% and 5 yr 37.8%) versus chemoRT (3 yr 45.7% and 5 yr 32%)(P=0.119). Conclusion: Patients treated with cystectomy/chemo were significantly younger and had better performance status compared to ones who had chemoRT. Prior to a matched pair analysis, OS was significantly better with cystectomy/chemo than chemoRT. OS became similar between cystectomy/chemo and chemoRT after matching age, sex, race, CDCS, insurance status, income, and stage.

Loeffler JW, Obara H, Fujimura N, **Bove P**, Newton DH, Zettervall SL, van Petersen AS, Geelkerken RH, Charlton-Ouw KM, Shalhub S, Singh N, Roussel A, Glebova NO, Harlander-Locke MP, Gasper WJ, Humphries MD and Lawrence PF (2017). "Medical therapy and intervention do not improve uncomplicated isolated mesenteric artery dissection outcomes over observation alone." Journal of Vascular Surgery 66(1): 202-208.

[Full-Text](#)

*Department of Surgery*

Objective: Isolated dissection of the mesenteric vessels is rare but increasingly recognized. This study aimed to evaluate patient characteristics, primary treatment, and subsequent outcomes of mesenteric dissection using multi-institutional data. Methods: All patients at participant hospitals between January 2003 and December 2015 with dissection of the celiac artery (or its branches) or dissection of the superior mesenteric artery (SMA) were included. Patients with an aortic dissection were excluded. Demographic, treatment, and

follow-up data were collected. The primary outcomes included late vessel thrombosis (LVT) and aneurysmal degeneration (AD). Results: Twelve institutions identified 227 patients (220 with complete treatment records) with a mean age of 55.6 ± 12.5 years. Median time to last follow up was 15 months (interquartile range, 3.8-32). Most patients were men (82% vs 18% women) and symptomatic at presentation (162 vs 65 asymptomatic). Isolated SMA dissection was more common than celiac artery dissection (n = 158 and 81, respectively). Concomitant dissection of both arteries was rare (n = 12). The mean dissection length was significantly longer in symptomatic patients than in asymptomatic patients in both the celiac artery (27 vs 18 mm; P = .01) and the SMA (64 vs 40 mm; P < .001). Primary treatment was medical in 146 patients with oral anticoagulation or antiplatelet therapy (n = 76 and 70, respectively), whereas 56 patients were observed. LVT occurred in six patients, and 16 patients developed AD (3% and 8%, respectively). For symptomatic patients without evidence of ischemia (n = 134), there was no difference in occurrence of LVT with medical therapy compared with observation alone (9% vs 0%; P = .35). No asymptomatic patient (n = 64) had an episode of LVT at 5 years. AD rates did not differ among symptomatic patients without ischemia treated with medical therapy or observed (9% vs 5%; P = .95). Surgical or endovascular intervention was performed in 18 patients (3 ischemia, 13 pain, 1 AD, 1 asymptomatic). Excluding the patients treated for ischemia, there was no difference in LVT with surgical intervention vs medical management (one vs five; P = .57). Conclusions: Asymptomatic patients with isolated mesenteric artery dissection may be observed and followed up with intermittent imaging. Symptomatic patients tend to have longer dissections than asymptomatic patients. Symptomatic isolated mesenteric artery dissection without evidence of ischemia does not require anticoagulation and may be treated with antiplatelet therapy or observation alone.

Lohani S, Golenbiewski J, **Swami A** and **Halalau A** (2017). "A unique case of nephrogenic systemic fibrosis from gadolinium exposure in a patient with normal EGFR." BMJ Case Reports 2017(Oct): bcr-2017-221016.

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*Department of Internal Medicine*

Lohasammakul S, Turbpaiboon C, Ratanalekha R, Lohsiriwat V, **Chaiyasate K**, Roham A and Chuangsuwanich A (2017). "Anatomy of superficial inferior epigastric vessels: Revival of Superficial Inferior Epigastric (SIEA) flap." European Journal of Plastic Surgery: 1-8. ePub Ahead of Print.

[Full-Text](#)

*Department of Surgery*

Majima T, Tyagi P, Dogishi K, Kashyap M, Funahashi Y, Gotoh M, **Chancellor MB** and Yoshimura N (2017). "Effect of intravesical liposome-based nerve growth factor antisense therapy on bladder overactivity and nociception in a rat model of cystitis induced by hydrogen peroxide." Human Gene Therapy 28(7): 598-609.

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*Department of Urology*

The aim of this study was to evaluate whether liposome-based local suppression of nerve growth factor (NGF) in the bladder has effects on bladder hypersensitivity in a rat cystitis model induced by intravesical instillation of hydrogen peroxide (HP). HP (1.5%) was intravesically administered to adult female Sprague-Dawley rats. Liposomes complexed with NGF antisense oligonucleotide (OND) labeled with TYE563 fluorescent tag were intravesically instilled on day 2. Red fluorescence from the TYE 563 tag was observed with fluorescent microscopy on day 3. Four separate groups of rats were used in the following experiments: (a) sham-liposome group, (b) sham-OND group, (c) cystitis-liposome group, and (d) cystitis-OND group. Saline or 1.5% HP was intravesically administered on day 0. Empty liposomes or liposomes-antisense OND were instilled into the bladder on day 2. The following experiments were conducted to evaluate the effect of NGF antisense treatment on day 7: (a) continuous cystometry was performed in an awake condition; (b) pain behavior induced by instillation of resiniferatoxin into the bladder, including licking behavior (lower abdominal licking) and freezing behavior (motionless head-turning toward lower abdomen), was observed; (c) immunohistochemical staining of the bladder and L6 DRG for NGF was performed; (d) the expression of several genes in the bladder was analyzed by reverse transcription polymerase chain reaction (RT-PCR); and (e) after Fast Blue was injected into the bladder wall, Fast Blue-positive or -negative cells in DRG neurons



were separately collected by using a laser-capture microdissection method 7 days later. RT-PCR was performed to evaluate gene expressions in captured neuronal cells. The expression of TYE563 was identified only in the urothelial layer. In cystometric investigation, intercontraction intervals (ICI) were significantly ( $p = 0.001$ ) shorter in the cystitis-liposome group in comparison to the sham-liposome group. ICI was significantly ( $p = 0.007$ ) longer in the cystitis-OND group compared to the cystitis-liposome group. Comparisons of the sham-liposome and the sham-OND groups showed no significant difference in ICI ( $p = 0.56$ ). Licking events did not significantly differ among the four groups. In contrast, the cystitis-liposome group showed significantly more freezing events than the sham-liposome group did ( $p = 0.002$ ). A significant reduction in the number of freezing events was observed in the cystitis-OND group compared to the cystitis-liposome group ( $p = 0.04$ ). Immunofluorescence staining demonstrated that NGF expression in the mucosa ( $p = 0.02$ ) and L6 DRG ( $p = 0.01$ ) was significantly higher in the cystitis-liposome group than it was in the sham-liposome group. The expression of NGF was significantly lower in the mucosa ( $p = 0.002$ ) and L6 DRG ( $p = 0.01$ ) in the cystitis-OND group compared to the cystitis-liposome group. RT-PCR showed that the expression of NGF and TRPV1 mRNA in the mucosa was significantly higher in the cystitis-liposome group than it was in the sham-liposome group ( $p = 0.001$  and  $0.03$ , respectively). On the other hand, these gene expressions were significantly lower in the cystitis-OND group than they were in the cystitis-liposome group ( $p = 0.007$  and  $0.02$ , respectively). The cystitis-liposome group showed significantly higher expression of TRPA1, P2X3, and BDNF mRNA in labeled bladder afferent neurons than the sham-liposome group did ( $p = 0.03$ ,  $0.01$ , and  $0.001$ , respectively). These gene expressions were significantly lower in the cystitis-OND group compared to the cystitis-liposome group ( $p = 0.04$ ,  $0.006$ , and  $0.03$ , respectively). The study indicated that intravesical application of liposome-NGF antisense OND significantly improved bladder hypersensitivity induced by chemical cystitis in rats. Intravesical treatment with liposome-OND conjugates could be a novel local therapy of hypersensitive bladder disorders such as bladder pain syndrome/interstitial cystitis.

May T, Stewart JM, Bernardini MQ, Ferguson SE, Laframboise S, Jiang H and **Rosen B** (2017). "The prognostic value of perioperative, pre-systemic therapy CA125 levels in patients with high-grade serous ovarian cancer." International Journal of Gynaecology and Obstetrics. ePub Ahead of Print.

[Full-Text](#)

*Department of Obstetrics and Gynecology*

OBJECTIVE: To investigate the ability of preoperative CA125 and post-surgical CA125 changes to predict outcomes among patients with high-grade serous ovarian cancer (HGSC). METHODS: The present retrospective cohort study included patients with HGSC who underwent surgery between January 1, 2003, and December 31, 2011 at Princess Margaret Cancer Center, Toronto, ON, Canada. CA125 was measured at diagnosis and following surgery, and the CA125 ratio was calculated (preoperative CA125/postoperative CA125). Optimal CA125 cutoff levels were identified using the point with the most significant log-rank-test result. Univariate and multivariate analyses with Cox proportional hazard modeling was used to study overall survival. RESULTS: Among 212 patients, an optimal baseline CA125 cutoff value of 174 U/mL and a seven-fold decrease in CA125 after surgery were positive prognostic indicators. A 10-fold increase in baseline CA125 was associated with decreased overall survival (univariate hazard ratio 1.55, 95% confidence interval [CI] 1.17-2.06;  $P=0.002$ ; multivariate hazard ratio 1.72, 95% CI 1.21-2.44;  $P=0.002$ ). An increase in the CA125 ratio ( $\log_{10}$  [preoperative CA125/postoperative CA125]) was associated with improved overall survival (univariate hazard ratio 0.63, 95% CI 0.43-0.90;  $P=0.012$ ; multivariate hazard ratio 0.41, 95% CI 0.24-0.70,  $P<0.001$ ). CONCLUSION: CA125 demonstrated prognostic value for HGSC; baseline CA125 of 174 U/mL or lower and a post-surgical decline of seven-fold or greater were associated with improved overall survival. This article is protected by copyright. All rights reserved.

McCuaig JM, Noor A, **Rosen B**, Casper RF, Mitri F, Colgan T and Kim RH (2017). "Case report: Use of tumor and germline y chromosomal analysis to guide surgical management in a 46, XX female presenting with gonadoblastoma with dysgerminoma." International Journal of Gynecological Pathology 36(5): 466-470.

[Full-Text](#)

*Department of Obstetrics and Gynecology*

Gonadoblastomas are rare mixed gonadal tumors that are almost always found in individuals with 46, XY

karyotype or some other form of Y chromosome mosaicism. It is extremely rare to diagnose gonadoblastoma in phenotypically normal 46, XX females. Herein, we present a 20-year-old 46, XX female diagnosed with gonadoblastoma and dysgerminoma. Use of cytogenetic and molecular analyses to identify the presence of Y chromosome material in peripheral blood, gonadal, and tumor tissue can exclude mosaicism to provide reassurance to undertake conservative surgical management and preserve fertility.

McLaughlin PW, Liss AL, Nguyen PL, Assimos DG, D'Amico AV, Gottschalk AR, **Gustafson GS**, Keole SR, Liauw SL, Lloyd S, Movsas B, Prestidge BR, Showalter TN, Taira AV, Vapiwala N and Davis BJ (2017). "ACR Appropriateness Criteria® locally advanced, high-risk prostate cancer." *American Journal of Clinical Oncology: Cancer Clinical Trials* 40(1): 1-10.

[Full-Text](#)

*Department of Radiation Oncology*

Merchan-Del Hierro X and **Halalau A** (2017). "Cytomegalovirus-related transverse myelitis in an immunocompetent host: A subacute onset of an immune-mediated disease?" *BMJ Case Reports* 2017.

[Request Form](#)

*Department of Internal Medicine*

We report a case of transverse myelitis in an immunocompetent host with an atypical long onset of symptoms. A 56-year-old man was admitted to the hospital reporting 5 months of progressive ascending lower extremity weakness and numbness, inability to walk, bowel incontinence, urinary retention and several episodes of nausea and vomiting. MRI showed moderate spinal swelling and multiple hyperintense signal changes on cervical levels C2-C5 and thoracic levels T1-T3. Cerebrospinal fluid (CSF) showed pleocytosis and was positive for anti-cytomegalovirus (CMV) IgG intrathecal antibodies, but the CSF PCR for CMV was negative. The diagnosis of immune-mediated CMV-related transverse myelitis was established and the patient was treated with methylprednisolone and valgancyclovir. The patient had poor recovery and remained paraplegic at discharge.

Milling TJ, **Clark CL**, Feronti C, Song SS, Torbati SS, Fermann GJ, Weiss J and Patel D (2017). "Management of Factor Xa inhibitor-associated life-threatening major hemorrhage: A retrospective multi-center analysis." *American Journal of Emergency Medicine*. ePub Ahead of Print.

[Full-Text](#)

*Department of Emergency Medicine*

Background: Factor Xa (FXa) inhibitors, used for stroke prevention in atrial fibrillation and venous thromboembolism treatment and prevention, are the dominant non-Vitamin K oral anticoagulants on the market. While major bleeding may be less common with these agents compared to warfarin, it is always a risk, and little has been published on the most serious bleeding scenarios. This study describes a cohort of patients with FXa inhibitor-associated life-threatening bleeding events, their clinical characteristics, interventions and outcomes. Methods: We performed a retrospective, 5-center review of FXa inhibitor-treated major bleeding patients. Investigators identified potential cases by cross-referencing ICD-9/10 codes for hemorrhage with medication lists. Investigators selected cases they deemed to require immediate reversal of coagulopathy, and reviewed charts for characteristics, reversal strategies and other interventions, and outcomes. Results: A total of 56 charts met the inclusion criteria for the retrospective cohort, including 29 (52%) gastrointestinal bleeds (GIB), 19 (34%) intracranial hemorrhages (ICH) and 8 (14%) others. Twenty-four (43%) patients received various factor or plasma products, and the remainder received supportive care. Thirty-day mortality was 21% (n = 12). Re-anticoagulation within 30-days occurred in 23 (41%) patients. Thromboembolic events (TEEs) occurred in 6 (11%) patients. No differences were observed in outcomes by treatment strategy. Conclusions: This cohort of FXa inhibitor-associated major bleeding scenarios deemed appropriate for acute anticoagulant reversal illustrates the variable approaches in the absence of a specific reversal agent.

**Millward PA**, Ma A, Hay SN, Brecher ME and Bandarenko N (2017). "Management of Gardner-Diamond syndrome with therapeutic plasma exchange." *Journal of Clinical Apheresis* 32(4): 273.

[Full-Text](#)

*Department of Pathology*

Morace R, Kumar T, **Tantisattamo E**, Gibson J, Britton S, **Li W**, **Kanaan HD**, **Cohn SR**, **Samarapungavan D**, **Zhang PL** and **Boyanton BL** (2017). "Feasibility of BK virus real-time PCR testing in renal graft biopsies with negative SV40 staining." *Transplantation Proceedings* 49(6): 1294-1300.

[Full-Text](#)

*Department of Internal Medicine*

*Department of Pathology*

*Department of Surgery*

Background. BK virus (BKV)-associated nephropathy (BKVAN) is often associated with renal graft dysfunction. When renal transplant recipients present with high clinical suspicion for BKVAN (high serum and urine BKV titer with graft dysfunction) but their graft biopsies stain negatively for BKV, non-correlated situations between the two tests often lead to a dilemma about how to treat them. Methods. This retrospective investigation was conducted to determine how real-time quantitative PCR (qPCR) for BKV, routinely applied to serum and urine, could be helpful in identifying the existing BKV in biopsy tissue stained negatively for BKV. Results. DNA was extracted from each specimen through the use of five 10- $\mu$ m curls from the tissue block with use of the QIAamp DNA FFPE Tissue Kit (Qiagen), followed by BKV qPCR to determine copies of BKV/ $\mu$ g of biopsy tissue DNA. Group 1 (11 negative renal controls for BKV) demonstrated 0 to 9 BKV copies/ $\mu$ g DNA. Except for 3 focally staining cases showing low BKV, the remaining 10 positive renal controls in group 2 (13 positive transplant biopsies staining positively) demonstrated elevated BKV up to 160 million copies/ $\mu$ g DNA. Group 3 transplants (13 uncertain transplants with negative BKV staining but positive liquid BKV) were negative for BKV (0-12 copies/ $\mu$ g) in 4 of 13, had low BKV copies (36-346 copies/ $\mu$ g) in 5 of 13, and had high BKV copies (17,240-526,945 copies/ $\mu$ g) in 4 of 13 cases, through the use of qPCR. Conclusions. The data indicate that qPCR from paraffin-embedded tissue as a backup test is sensitive for ruling in/out BKV infection in renal transplant biopsies, particularly in uncertain cases.

Mortada I, Leone A, Gerges Geagea A, Mortada R, Matar C, Rizzo M, **Hajj Hussein I**, Massaad-Massade L and Jurjus A (2017). "Oral manifestations of inflammatory bowel disease." *Journal of Biological Regulators and Homeostatic Agents* 31(3): 817-821.

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*Department of Biomedical Sciences (OU)*

Inflammatory bowel diseases (IBD), including Crohn's disease and ulcerative colitis, have important extraintestinal manifestations, notably in the oral cavity. These oral manifestations can constitute important clinical clues in the diagnosis and management of IBD, and include changes at the immune and bacterial levels. Aphthous ulcers, pyostomatitis vegetans, cobblestoning and gingivitis are important oral findings frequently observed in IBD patients. Their presentations vary considerably and might be well diagnosed and distinguished from other oral lesions. Infections, drug side effects, deficiencies in some nutrients and many other diseases involved with oral manifestations should also be taken into account. This article discusses the most recent findings on the oral manifestations of IBD with a focus on bacterial modulations and immune changes. It also includes an overview on options for management of the oral lesions of IBD.

Muhleman M, Kaur H and **Palka J** (2017). "The value of Tc99m-MDP bone scan and SPECT/CT in the diagnosis of metastatic carcinoid rectal cancer with hypoglossal nerve palsy." *Journal of Nuclear Medicine* 58(Sup 1): 998.

[Request Form](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Muhleman M, Kaur H, Patel M and **Rydberg J** (2017). "The value of F-18 FDG PET-CT scan in the diagnosis of infection of unknown origin in a patient with aortic valve replacement. In the diagnosis of infection of unknown origin in a patient with aortic valve replacement. value of F-18 FDG PET/CT scan in the diagnosis of infection of unknown origin in a patient with aortic valve replacement." Journal of Nuclear Medicine 58(Sup 1): 985.

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*Department of Diagnostic Radiology and Molecular Imaging*

Mukherjee D, Coffey M and **Maisels MJ** (2017). "How many babies in the NICU receive phototherapy and for how long?" Acta Paediatrica, International Journal of Paediatrics 106(Sup): 19-20.

[Full-Text](#)

*Department of Pediatrics*

Background: Although published data have documented the number of infants receiving phototherapy (PT) in wellbaby nurseries in the US, no similar information exists for NICU infants in the US. A preliminary study documenting the frequency of PT in Norwegian NICUs (E-PAS2015: 1579.582) prompted us to examine this question. Objective: (1) To document the use of PT at different gestations in 2 level III NICUs and (2) to compare the use of PT in 3 time periods during which different guidelines for phototherapy thresholds were in use. Design/Methods: From an electronic medical record database we identified all 2505 infants with gestational age (GA) from 23 0/7-34 6/7 weeks, admitted to the NICU between January 2009-September 2015 and the proportion of those infants who received PT. Each infant receiving PT was counted only once, but we summed all PT episodes per infant to calculate total duration. Results: The table displays frequency and duration of PT use. Overall 2023 (80.8%) received PT and the usage was similar for girls (79.6%) and boys (81.8%). PT was more frequent in the shorter GA groups and did not vary across time periods in the 23-27 6/7 week group. In the other two GA groups, PT use increased over the time periods. The median duration (interquartile range) of PT for all infants was 50.4 (27.0-84.5) hours and in the lowest GA group was 72.7 (41.1-110.9) hours. Conclusions: Some 81% of infants  $\leq 34$  6/7 weeks and 88% of those  $< 28$  weeks in our NICUs receive PT for median durations of 50 and 73 hours respectively, and the number receiving PT increased when the latest guidelines were followed. In Norway, 69% of infants  $< 32$  weeks receive PT vs 81% in our units. These population-based data from a single institution cannot be generalized but, in view of the known complications associated with PT and the potential increase in mortality in ELBW infants receiving PT (NEJM 2008;359:1885), it is reasonable to ask whether PT exposure can be reduced, perhaps by using cycled (intermittent) PT (E-PAS 2015.1582.605). Frequency of phototherapy by gestation and time period. (Table Presented).

Myziuk NK, **Guerrero TM**, Castillo E, Solis D, Zhang J, **Sakthivel G** and Guerra R (2017). "Pulmonary blood mass dynamics during tidal breathing measured from 4DCT." International Journal of Radiation Oncology Biology Physics 99(2): E701-E702.

[Full-Text](#)

*Department of Radiation Oncology*

*OUWB Medical Student Author*

Purpose/Objective(s): We previously reported a variation in the lung mass with phase in four-dimensional computed tomography (4DCT) for 3 cases. We hypothesize this variation corresponds to the physiologic change in pulmonary perfusion with normal tidal breathing and should be present in every breathing patient. In this study we characterize and quantify the respiratory induced blood mass variation in 89 cases. Purpose/Objective(s): Helical 4DCT image volumes of 89 individual patients, obtained for use in radiotherapy treatment planning, have been retrospectively obtained for this study. Each volume consists of 10 breath phases, equally divided in time, during the respiratory cycle. For all 89 cases; the lung parenchyma was identified, and appropriate contours were drawn to include only the area of interest, e.g., removal of trachea, bronchi, bone and/or muscle tissue. Conversion from Hounsfield Units (HU) to density and mass per voxel was made using the density calibration curve over the volume of the masked region. Results: Averaged CT numbers within the lung parenchyma region are calculated as -712.9 and -704.5 HU for inhale and exhale phases respectively. This results in an observed difference of 8.4 HU, whereas expected CT number difference, i.e., if mass were constant throughout respiration, is calculated to be 19.5 HU, showing a deviation

of 11.1 HU representing missing mass at the exhale phase. Pulmonary blood mass (PBM) calculations for maximum and minimum respiratory phases show ranges (374 g-1835 g), and (331-1676 g), with calculated mean values of 769g and 715g, respectively. A resultant trend of successively decreasing PBM during expiration is observed for nearly all cases. Tidal volume calculations over the masked regions have similar behavior, with ranges of (1753mL-7687mL) and (1523mL-6576mL), and resultant mean values of 3745mL and 3413mL, for the maximum and minimum respiratory phases respectively. PBM differences, measured between inhale and exhale phases, for all 89 patients, therefore exhibit a mean value of 55g over a range of (6g-229g), associated with a mean tidal volume of 341mL over a range of (27mL-1111mL). A strong trend for increasing PBM discrepancy with increasing tidal volume was found. Linear regression between PBM discrepancy and tidal volume has an R2 value of 0.51 over the patient pool. Conclusion: 4DCT imaging was found to be capable of measuring changes in pulmonary perfusion due to respiration. A difference in PBM with respiration was found in all cases; we've found that the PBM increased with inhalation, and decreased with exhalation. There was a correlation between PBM loss and tidal volume found. The 4DCT derived respiratory induced PBM signal will provide a new window to investigate pulmonary circulation in health and diseases (e.g. pulmonary emboli).

Navin MC and **Wasserman JA** (2017). "Harm and parental permission: A response to our critics...McDougall, R. 2017. Can families have interests?". *American Journal of Bioethics* 17 (11):27–29." [American Journal of Bioethics](#) 17(11): W1-W4.

[Full-Text](#)

*Department of Biomedical Sciences (OU)*

Navin MC and **Wasserman JA** (2017). "Reasons to amplify the role of parental permission in pediatric treatment." [American Journal of Bioethics](#) 17(11): 6-14.

[Full-Text](#)

*Department of Biomedical Sciences (OU)*

Two new documents from the Committee on Bioethics of the American Academy of Pediatrics (AAP) expand the terrain for parental decision making, suggesting that pediatricians may override only those parental requests that cross a harm threshold. These new documents introduce a broader set of considerations in favor of parental authority in pediatric care than previous AAP documents have embraced. While we find this to be a positive move, we argue that the 2016 AAP positions actually understate the importance of informed and voluntary parental involvement in pediatric decision making. This article provides a more expansive account of the value of parental permission. In particular, we suggest that an expansive role for parental permission may (1) reveal facts and values relevant to their child's treatment, (2) encourage resistance to suboptimal default practices, (3) improve adherence to treatment, (4) nurture children's autonomy, and (5) promote the interests of other family members.

Newman D, **Diokno A**, Low L, Goode P, Burgio K, Griebing T, **Maddens M**, Sampsel C, Subak L, Raghunathan T and McIntyre D (2017). "A multi-site prospective randomized controlled trial of groupadministered behavioral treatment in reducing urinary incontinence in older adult women." [Neurourology and Urodynamics](#) 36(Sup 3): S390-S391.

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*Department of Urology*

*Department of Internal Medicine*

Hypothesis/aims of study This innovative clinical trial enrolled adult women, > 55 years from diverse backgrounds who reported stress, urgency, or mixed urinary incontinence (UI) and who had never been treated for UI. The study aim was to compare the effectiveness of a novel group-administered behavioral treatment class, the Group Behavioral Treatment (GBT), to no treatment. Study design, materials and methods A multi-site, prospective randomized, controlled trial to assess the efficacy of a face-to-face 2-hour GBT compared to a no care control. A reactive mass mailing recruitment was used, with enriched sampling for representation to achieve oversampling in urban and African American communities through zip code indicators for each study site. Mailings were sent to communitydwelling adult women 55 years and older. Responders were screened centrally for incontinence frequency and severity and to insure that potential

participants were naïve to UI treatment. Potentially eligible women were referred to their local clinical sites for screening and random assigned to one of two treatment arms: 1) Group Behavioral Treatment or 2) No treatment. Inclusion/exclusion criteria included women 55 years and older, International Consultation on Incontinence Questionnaire (ICIQ UI-SF), score of at least 3 (1 for frequency, 2 for severity), report of UI for at least 3-months duration, no prior UI treatment, no symptomatic prolapse, and no previous bladder surgery or pelvic cancer. Primary outcome: ICIQ UI-SF. Secondary outcomes: 3-day voiding diary, paper towel test, 24-hr pad weight, Brink test, Incontinence Quality of Life Questionnaire (I-QOL) and Patient Global Impression of Improvement (PGI-I). GBT group received a one-time 2-hour bladder health class whereas the control group received no treatment. Both received a behavioral education brochure, were monitored every 3 months for 12-months with clinic visits at 3 & 12 months and mailed questionnaires at 6 & 9 months. Results This study was able to recruit 463 women with a mean age of 64+/-7.3 years, age range 55 to 91 years, mean BMI >30 in 52%, 46% African American; 1% Hispanic; 13% high school education or less, 30% employed full time. 232 subjects were randomized to GBT and 231 to no treatment control; 34 withdrew (GBT=22 & Control =12). Demographics were not significantly different between groups. Outcomes at 3, 6, 9 & 12 months showed significant differences in favor of GBT over control including ICIQ-UI SF ( $p<0.0001$ ) (Table 1), average number of voids/day ( $p<0.0002$ ) and average number of leaks/day ( $p=0.0002$ ) on a voiding diary (Table 2), paper towel test ( $p=0.0008$ ), 24-hr pad weights ( $p=0.0007$ ), Medical, Epidemiologic & Social aspects of Aging questionnaire (MESA) ( $p<0.0001$ ), Incontinence Quality of Life (IQOL) ( $p<0.0001$ ) & PGI-I ( $p<0.0001$ ) but not the Brink test for pelvic floor strength ( $p=0.09$ ). No significant adverse events or serious events were encountered in either group. Interpretation of results This novel group learning intervention safely and effectively reduced incontinence frequency, severity, and bother, while improving incontinence-related quality of life as measured by multiple validated instruments. Improvement was maintained for 12 months after the 2-hour, one time intervention. Behavioral interventions are recommended in most treatment guidelines as first line therapy for UI. The study recruitment methodology of mailed letters with a toll-free response telephone number was able to yield a group of treatment-naïve older adult women who were very accepting of a group behavioral intervention. The potential of using a group learning intervention as an initial treatment strategy for adult women with urinary incontinence may be less-costly for this very burdensome condition that affects 1 in 3 older women. Concluding message This bladder health education program delivered in a group setting was safe and effective in reducing UI frequency, severity and bother and improving quality of life for community-dwelling older adult women with UI. This easily scale intervention increases opportunity to reach larger populations beyond medical practices and into community settings.

Nguyen LN, Gaines N, Gurney-McMaster A, **Killinger K, Fischer M, Gilleran J, Peters K and Sirls L** (2017). "Do surgeon factors predict outcomes after AdVance male sling?" Canadian Urological Association Journal 11(6): S236-S237.

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*Department of Urology*

Introduction: The AdVance male sling is used to treat male post-prostatectomy stress urinary incontinence (SUI). We evaluated patient selection criteria, surgical technique, and surgeon volume and experience on patient-reported outcomes. Methods: We conducted a retrospective review of patients undergoing AdVance male sling placement from January 2006-May 2016 at a large-volume institution. Cure was defined as no pads/day or one pad for safety only, or report of 100% dry. Improvement was defined as 1-2 pads/day and >50% improvement in leakage. Failure was defined as >2 pads/day or <50% improvement in leakage. Results: 175 men were identified. Mean age was 68 years. Operative data was available on 152 patients. 128/152 (84%) of patients were cured or improved after surgery. 12 surgeons placed AdVance slings. Surgeon volume was not associated with cure/improvement (five highest-volume surgeons 112/132 [85%] vs. five lowest-volume surgeons 16/20 [80%];  $p=0.77$ ). The first five years of surgical experience (76/95 [80%] cure/ improved) was not different than most recent five years of experience (52/57 [91%] cure/improved;  $p=0.17$ ). 37/175 (21%) of men had preoperative 24-hour pad weight testing, with complete data available on 32 men. Mean pad weight was 206.8 mL (range 11-739). Men who underwent pad weight testing had better outcomes than men who did not. 13/32 (41%) men were cured and 17/32 (53%) improved with pad (Figure



presented). weight testing vs. 66/120 (55%) cured and 32/120 (27%) improved with no pad weight testing ( $p=0.012$ ). 147 men had data available on intraoperative sling tunneling and outcomes. 69/147 patients had no sling tunneling and 78 had sling tunneling. Tunneling was not associated with cure or improvement ( $p=0.36$ ). Conclusions: AdVance male sling is effective with 84% of men reporting cure or improvement. Surgeon volume, surgeon experience, and sling tunneling were not associated with outcome; however, having had pad weight testing were associated with higher rates of cure/improvement.

Nguyen LN, Gaines N, **Sirls L, Gruner M, Killinger K** and **Peters K** (2017). "Outcomes in the first year following transvaginal and abdominal pelvic organ prolapse repair." Canadian Urological Association Journal 11(6): S189.

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*Department of Urology*

*OUWB Medical Student Author*

Introduction: We evaluated satisfaction, quality of life (QOL), and additional treatments after transvaginal (TV) and abdominal (ABD) pelvic organ prolapse (POP) repair. Methods: Adult women enrolled in a prospective POP database were reviewed. Baseline and outcomes data one year after surgery were collected from validated Pelvic Floor Distress Inventory (PFDI) and mailed surveys, and analyzed with descriptive statistics, Fishers exact, and two sample t-tests. Results: 222 patients were identified; 147 (66%) had TV and 75 (34%) had ABD repair. TV patients were older (mean 64.1 vs. 59.7 years;  $p=0.003$ ), but no differences in other characteristics were identified. Preoperative mean anterior (TV 2.7 vs. ABD 3.1;  $p=0.003$ ) and apical (TV 2.1 vs. ABD 3.1;  $p<0.001$ ) POP grades were more severe in the ABD patients compared to the TV patients. Baseline PFDI scores, however, were similar between groups (TV 115.8 vs. ABD 111.6;  $p=0.605$ ). One-year PFDI scores were improved in both groups, though were significantly higher in the TV group (45.6 vs. 32.6;  $p=0.032$ ). Absolute score improvement did not differ (TV-67.6 vs. ABD-76.1;  $p=0.353$ ). The majority of patients in both groups reported moderately or markedly improved overall symptoms (TV 79/101 [78%] and ABD 51/59 [86%];  $p=0.199$ ) and QOL (80/101 [79%] and 51/59 [87%];  $p=0.252$ ). Similar proportions of patients (TV 52/109 [48%] vs. ABD 21/62 [34%];  $p=0.108$ ) had additional POP treatments, including pelvic floor physical therapy, coping strategies, and surgical procedures. There was no difference in rates of additional surgical treatments for prolapse between groups (TV 32/109 [29%] vs. ABD 10/62 [11%];  $p=0.053$ ). Most TV and ABD patients were satisfied (68/101 [68%] and 48/59 [81%];  $p=0.055$ , respectively) and would recommend to a friend (85/99 [86%] and 55/57 [96%];  $p=0.052$ ). Conclusions: Although symptoms, satisfaction, and QOL improve after both TV and ABD prolapse repair, women seek additional treatments as early as the first year after surgery.

Nguyen LN, Gaines N, **Sirls L, Henrichsen J, Bartley J**, Gupta P, **Killinger K, Gilleran J, Petrossian R** and **Peters K** (2017). "Pelvic floor physical therapy improves validated pelvic floor questionnaires and pelvic pain." Canadian Urological Association Journal 11(6): S236.

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*Department of Urology*

*OUWB Medical Student Author*

Introduction: Pelvic floor physical therapy (PFPT) is crucial in managing many pelvic floor disorders. We evaluated changes in validated symptom scores at intake and discharge in women undergoing PFPT at a multidisciplinary women's urology centre. Methods: Retrospective chart review was performed of women presenting to a women's urology centre for PFPT. Pelvic floor physical therapists performed individualized interventions, including external and internal (vaginal) manual therapies, neuromuscular reeducation, and teaching home exercises and self-care. We collected pertinent history, demographic information, Pelvic Floor Distress Inventory Questionnaire (PFDI) total and domain scores (Pelvic Organ Prolapse Distress Inventory [POPDI]; Urogenital Distress Inventory [UDI]; Colorectal-Anal Distress Inventory [CRADI]), Pelvic Floor Impact Questionnaire (PFIQ), and pain levels on a 0-10 visual analog scale (VAS) scores at both intake and discharge. Results: Of 200 women, 178 had complete information available (Table 1). Mean age was 50.3 years (standard deviation [SD] 16; range 18-83). The most common indications for PFPT were pelvic pain (95/178 [53.4%]), urinary urgency (19/178 [10.7%]), urge incontinence (16/178 [9%]), and dyspareunia (15/178 [8.4%]). Mean number of visits was  $8.8 \pm 5.6$  and mean pain level decreased from 3.43 at the first visit to 2.09 by the

last visit ( $p < 0.0001$ ). Pre- and post-treatment PFDI and PFIQ questionnaires were completed by 100/178 (56%) and 93/178 (52%) women, respectively. PFDI scores significantly improved, but did not meet the minimally important difference (MID); UDI scores significantly improved and did meet the MID. Although POPDI and CRADI did not significantly improve, CRADI met the MID. PFIQ scores improved significantly. Conclusions: PFPT is an excellent tool for patient with a variety of pelvic floor complaints. Patients report improvement with pelvic pain, pelvic floor distress, and pelvic floor symptom quality of life (Table presented).

Nguyen LN, Jafri M, Gaines N, Lavin J, **Killinger K** and **Sirls L** (2017). "Urinary function after robotic-assisted laparoscopic vs. radical perineal prostatectomy for low-risk prostate cancer." Canadian Urological Association Journal 11(6): S255.

[Request Form](#)

*Department of Urology*

Introduction: Robotic-assisted laparoscopic prostatectomy (RALP) has largely replaced open radical prostatectomy in many markets. Radical perineal prostatectomy (RPP) is another less invasive alternative approach to open radical that has not been widely adopted. RPP offers excellent exposure of the urinary sphincter and bladder neck, yet surgeons differ on the ability to spare the cavernosal nerves. We evaluate the recovery of urinary function between RALP and RPP. Methods: Retrospective review of a prospective radical prostatectomy database was performed. Urinary modules from the Expanded Prostate Cancer Index Composite-Urinary Function (EPIC-UF) questionnaire were used to determine preoperative baseline urinary symptom summary score and subscale scores of urinary incontinence, bother, irritative or obstructive symptoms, and function and six, 12, 18, and 24 months after surgery. Results: 753 men underwent RALP ( $n=623$ ) or RPP ( $n=130$ ). There were no demographic or clinical differences between groups; however, a significantly (Table presented) higher number of patients undergoing RALP than RPP had pelvic lymph node dissection (20.2% vs. 0%;  $p < 0.0001$ ) and sparing of cavernosal neurovascular bundles (79.2% vs. 68.4%;  $p < 0.0001$ ). 508 patients had complete EPIC-UF data. Overall urinary symptom score recovery was greater for RALP than RPP at six months ( $p=0.028$ ). Urinary incontinence and function were also more improved after RALP compared to RPP but only at six months ( $p=0.021$ ,  $p=0.006$ ). There were no differences in overall, urinary incontinence, or urinary function scores at 12, 18, or 24 months. There was no difference between RALP and RPP for urinary bother or irritative or obstructive symptoms at any time point (Table 1). Conclusions: RALP had statistically significantly more rapid recovery of EPIC-UF data at six months vs. RPP, although clinical significance is unclear; however, at 12-24 months, RALP and RPP had similar recovery of urinary function in all urinary subdomains.

**Nojkov B**, **Amin M**, **Ghaith G** and **Cappell MS** (2017). "A statistically significant association between esophageal granular cell tumors and eosinophilic esophagitis: A 16-year analysis at two large hospitals of 167,434 EGDs." Digestive Diseases and Sciences: 1-8. ePub Ahead of Print.

[Full-Text](#)

*Department of Internal Medicine*

*Department of Pathology*

Ogunleye F, Blankenship L, Millisor V, **Anderson J** and **Jaiyesimi I** (2017). "Programmed cell death-1/Programmed cell death ligand-1(PD-1/PD-L1) inhibitors, heralding a new era of immunotherapy in the management of advanced Non-Small Cell Lung Cancer (NSCLC)." Cancer Treatment and Research Communications 12(2017): 6-13.

[Full-Text](#)

*Department of Internal Medicine*

Ogunleye FN, Sura KT, Blankenship L, Ezekwudo D, Gbadamosi B, **Jaiyesimi IA** and **Kabolizadeh P** (2017). "Treatment patterns for resected gastric cancer using the National Cancer Database." Journal of Clinical Oncology 35(15): Abstract No. 4061.

[Request Form](#)

*Department of Internal Medicine*

*Department of Radiation Oncology*

Background: The optimal management of patients with resected gastric cancer remains a therapeutic challenge. Although the benefit of peri-operative chemotherapy or adjuvant concurrent chemoradiotherapy for these patients is clearly established, recurrence and mortality rates remain high despite aggressive treatment. The goal of this study was to characterize the treatment patterns employed for patients with resected gastric cancer using the National Cancer Database (NCDB). Methods: The NCDB was queried between 2004-2013 for patients with invasive resected gastric cancer and negative margins, excluding those with metastatic disease. Results: We identified a total of 21,156 cases. The median age was 67 (range 55-79). A majority of patients were white (74%) followed by black (14%) and other (12%). Most patients had either insurance through the government (58%) or private insurance (37%). 47% of patients had surgery alone with approximately 53% of these patients diagnosed with stage I gastric cancer. The remainder of the patients had radiation alone (1.4%), chemotherapy alone (15.2%), or combined chemotherapy and radiation (36.7%). Table 1 includes the further breakdown of treatment. Conclusions: A majority of patients with resected gastric cancer had treatment with either radiation, chemotherapy, or a combination of both. However, it is interesting to note that in patients receiving adjuvant or neoadjuvant treatment, only a portion of the patients received treatment options with level 1 evidence such as the MAGIC or McDonald regimens. (Table presented).

**Ogunyemi D**, Boulet JR and Sobolewski P (2017). "International medical graduate obstetrician-gynecologists in United States healthcare: Practice patterns and board certification." Journal of Reproductive Medicine 62(4): 413-420.

[Request Form](#)

*Department of Obstetrics and Gynecology*

OBJECTIVE: To describe, based on current data, the practice patterns and board certification of international medical graduate (IMG) obstetrician-gynecologists (OBGYNs) who provide patient care in the U.S. STUDY DESIGN: Physician data from the Educational Commission for Foreign Medical Graduates, American Medical Association, and American Board of Medical Specialties were combined. Descriptive statistics provided overview demographics and practice profiles of U.S. citizen IMGs (USIMGs), non-USIMGs, and U.S. medical graduate (USMG) OBGYNs. RESULTS: IMGs comprise 15% of the practicing OBGYN workforce as compared to 24% for all physicians. US MD OBGYNs (mean age=46.0) are, on average, younger than IMG OBGYNs (mean age=52.1). 63% of all OBGYNs are office-based, with the lowest rate in non-USIMGs (56%). USIMGs have the highest percentage in residency (15%), with the lowest rate in non-USIMGs (6%). One in 3 OBGYN physicians in New York and New Jersey, and 1 in 5 in Florida, Michigan, and California, are IMGs. Board certification was attained by 81% of USMG OBGYNs, with lower rates for non-USIMGs (71%) and US-IMGs (60%). CONCLUSION: IMG OBGYNs play an important role in the U.S. healthcare system. Given their numbers and propensity to practice in areas where USMGs do not, further efforts to monitor their practice patterns and qualities are warranted.

Otoupalova E, Meka SG, **Dogra S** and **Dalal B** (2017). "Recurrent chylothorax: A clinical mystery." BMJ Case Reports 2017.

[Request Form](#)

*Department of Internal Medicine*

Pangrazzi GJ, **Baker EA**, Shaheen PJ, Okeagu CN and **Fortin PT** (2017). "Single-surgeon experience and complications of a fixed-bearing total ankle arthroplasty." Foot and Ankle International: 1-13. ePub Ahead of Print.

[Full-Text](#)

*Department of Orthopedic Surgery*

BACKGROUND: Total ankle arthroplasty (TAA) has historically resulted in inferior survivorship rates compared

with total hip and knee arthroplasty, because of technical issues unique to ankle anatomy. In this study, a single-surgeon series of intra- and postoperative complications as well as resultant reoperations/revisions of the Tornier Salto Talaris, a fixed-bearing TAA prosthesis, were reviewed. METHODS: Medical records from index procedure to latest follow-up of primary TAA were reviewed. Complications were categorized according to the Glazebrook classification; additional complications were documented. Concurrent procedures were recorded, and radiographs were analyzed for alignment, subsidence, and cyst formation. Time to complication onset and learning curve analyses were performed. One hundred four Salto Talaris TAA prostheses (96 patients), with an average follow-up of 46 months, were included. RESULTS: Thirty-five complications were identified in 32 ankles with a 34% complication rate, resulting in 11 reoperations (5 TAA revisions). Technical error (n = 12), wound healing (n = 9), and aseptic loosening (n = 4) were the most common complications, and there were no statistically significant differences in demographics or follow-up duration between cases with versus without complications. In both the cohorts with and without complications, there were moderate, negative correlations between radiographically observed keel osteopenia and lucency ( $\rho = -0.548$ ,  $P = .00125$ , and  $\rho = -0.416$ ,  $P = .000303$ , respectively); also, in the complication cohort, a weak, positive correlation between subsidence and lucency ( $\rho = 0.357$ ,  $P = .0450$ ) was found. CONCLUSION: Salto Talaris TAA survivorship and reoperation rates in our series were comparable with previous reports, using either the same or similar mobile-bearing prostheses; new information regarding complication, radiographic, and learning curve analyses was presented. LEVEL OF EVIDENCE: Level IV, retrospective case series.

Paximadis P, Schipper M, Matuszak M, Feng M, Jolly S, Boike T, **Grills I**, Kestin L, Movsas B, Griffith K, **Gustafson G**, Moran J, Nurushev T, Radawski J, Pierce L and Hayman J (2017). "Dosimetric predictors for acute esophagitis during radiation therapy for lung cancer: Results of a large statewide observational study." Practical Radiation Oncology. ePub Ahead of Print.

[Request Form](#)

*Department of Radiation Oncology*

**Peters K**, Johnston MA, Small S, Taylor R, **Killinger K** and **Sirls L** (2017). ""Kegels in a bottle": Preliminary results of a selective androgen receptor modulator (GTx-024) for the treatment of stress urinary incontinence in post-menopausal women." Neurourology and Urodynamics 36(Sup 3): S55-S56.

[Request Form](#)

*Department of Urology*

Hypothesis/aims of study There are no effective oral therapies available in the US for women with stress urinary incontinence (SUI). The pelvic floor and urinary sphincter are androgen receptor (AR) rich and can be modulated by androgenic agents. GTx-024 is a novel selective AR modulator (SARM) that has been shown to be well tolerated in clinical trials of more than 1,500 patients for other disease processes. The purpose of this pilot study is to assess the efficacy and safety of GTx-024 for the management of SUI. Study design, materials and methods In this Phase 2 study, 3 mg of GTx-024 was given daily for 12 weeks to post-menopausal women. Inclusion criteria were predominant SUI, SUI symptoms for  $\geq 6$  months, 24 hour pad weights  $>3$  grams, 3-15 SUI episodes per day averaged over three days, and a positive bladder stress test. The primary endpoint is the number of stress incontinence episodes per day on the 3-day voiding diary. Secondary endpoints include: pad weights, bladder stress test, and quality of life instruments including the Female Sexual Function Index (FSFI) and Patient Global Impression of improvement (PGI-I). Results This study is ongoing and the preliminary findings are presented on the first seven patients completing 12 weeks of treatment. Mean stress leaks decreased by 80.9% (Figure) and all patients saw at least a 65% reduction in leaking episodes. Stress leaks decreased from a mean number per day of 5.7 at baseline, to 1.1 at 12 weeks. Patients are being followed for durability of response post treatment and are demonstrating continued improvement up to 5 months. Patients pad weights decreased from a mean of 29.6 g at baseline, to 13.9 g at 12 weeks. FSFI scores increased from a mean of 16.8 at baseline, to 20.3 at 12 weeks, with 5/7 patients showing improvement. In all seven patients, PGI-I scores were improved at 12 weeks. Adverse events were minimal with none above a Grade I. Interpretation of results Both animal and human studies have demonstrated that a Selective Androgen Receptor Modulator can result in enhancement of muscle mass.

The pelvic floor muscles are rich in androgen-receptors [1]. The role of the pelvic floor in maintaining the continence mechanism in women has been well established and is the basis of Kegel exercises and pelvic floor physical therapy. The integrity of the pelvic muscle support can be compromised by physical insults such as vaginal childbirth, atrophy associated with aging and changes in the hormone milieu. This is the first study to assess the role of a SARM in the management of SUI. The early results of this study showed an excellent safety profile with a profound effect on reducing incontinence episodes per day, improving quality of life and enhancing female sexual function. Interestingly, the improvements in symptom were sustained well beyond stopping the study drug. Although the results have been very impressive in this pilot study, the small sample size is a recognized limitation. A placebo-controlled trial is in development to further study the effect of GTx-024 in SUI. Concluding message These early results suggest GTx-024 substantially improves stress incontinence in women with associated reductions in pad weight and improvements in quality of life measurements. The safety profile has been excellent. Additional patients will be studied as part of this ongoing study.

**Peters KM** (2017). "Editorial comment." *Urology* 108(Oct): 57-58.

[Full-Text](#)

*Department of Urology*

**Qin A, Liang J and Yan D** (2017). "A clinical treatment dose monitoring system based on CBCT." *Medical Physics* 44(6): 3245.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: To monitor delivered dose and trigger plan adaptation when necessary, an automatic treatment dose (Tx-dose) reconstruction system based on CBCT was developed and evaluated on various cancer sites. Methods: An in-house system was developed which includes three modules: Treatment Schedule Monitoring module (TSM), Pseudo-CT Generating Module (PCM) and Treatment Dose Reconstruction module (TDR). The workflow is as following: the image specialist, who conducts daily CBCT evaluation, requests Tx-dose when significant anatomic or motion variation is observed. TSM will watch the treatment progress in MOSAIQ and trigger PCM when CBCTs are available. PCM will perform pre-treatment CT to CBCT deformable registration (DIR), and map the CT intensity to CBCT to generate Pseudo-CT. A novel phase-matching DIR were developed to generate 4D-Pseudo-CT for lung cancer treatment. TDR module is then started to create Pinnacle scripts to reconstruct Tx-dose on Pseudo-CT. Finally, the Tx-doses are warped to plan-CT and accumulated through all delivered fractions as cumulative dose via DIR. For lung patients, the 4D-dose is calculated on both 4DCT and 4DPseudo-CT and warped to the end of inhale phase of the plan-CT. To minimize extra clinical workload, the system is designed to run mostly automatic with few user interactions. Eight recent treated patients (five SBRT-lung, two head&neck, one breast) were retrospectively evaluated. Clinical relevant dosimetric parameters were extracted from the final cumulative Tx-dose and compared with the planned ones. Results: For 5 Lung patients, D99 of the final cumulative dose of GTV is  $95.9 \pm 2.5\%$  (93.6-100.1%) of that of originally planned. One of two head & neck patient had 3% decrease in CTV D99 and 11.5% increase of ipsilateral-parotid mean dose due to weight loss. The D99 of the breast patient CTV decreased to 93.5%. Conclusion: We have demonstrated the feasibility and effectiveness of a treatment dose verification system on various cancer sites in our clinical setting.

Quindry JC and **Franklin BA** (2017). "Cardioprotective exercise and pharmacologic interventions: Complementary antidotes to cardiovascular disease?" *Exercise and Sport Sciences Reviews*. ePub Ahead of Print.

[Full-Text](#)

*Department of Internal Medicine*

Exercise and pharmacologic therapies to prevent and treat cardiovascular disease have largely advanced through independent efforts. Understanding of first line drug therapies, findings from preclinical animal studies, and the need for research initiatives related to complementary cardioprotective exercise-pharma interventions are reviewed from the premise that contemporary cardioprotective therapies must include adjunctive exercise and lifestyle interventions in addition to pharmacologic agents.

Quinn TJ, Galoforo S, Wilson TG, Ahmed S and **Wilson GD** (2017). "Dual EGFR and PI3K/MTOR targeting of head and neck cancer in combination with radiation therapy." International Journal of Radiation Oncology Biology Physics 99(2): E614-E615.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Previous research has identified the PI3K/Akt/mTOR and the EGFR/Ras/Raf/MAPK as key pathways that are dysregulated in head and neck cancer (HNSCC). In this study we describe the use of two novel small molecular agents, Dacomitinib and Gedatolisib, in combination with radiation treatment (RT) to target EGFR and PI3K as novel clinical treatment strategy in a murine xenograft model of human HNSCC. Purpose/Objective(s): Dacomitinib, an oral once-daily, irreversible pan-HER inhibitor and Gedatolisib, a highly potent dual inhibitor of PI3K $\alpha$ , PI3K $\gamma$  and mTOR administered by intravenous infusion were provided by Pfizer. The drugs were studied alone and in combination with radiation in a panel of low passage HNSCC cell lines in vitro and in vivo using MTT assays, clonogenic assays, western blotting, RT-PCR and tumor growth delay using a 3 week fractionated schedule of daily doses of 2 Gy. Results: There is a close relationship between EGFR overexpression and sensitivity to Dacomitinib with UT-SCC-14 and UT-SCC-16A being more sensitive than UT-SCC-15 and UT-SCC-24A, which do not overexpress EGFR. Gedatolisib showed a classical dose response in both the UT-SCC-14 and UT-SCC-15 cell lines with an IC50 of 0.075 $\mu$ M and 0.2 $\mu$ M, respectively. Gedatolisib was effective at reducing phosphorylation of PI3K, mTOR and AKT in both cell lines. In tumor growth delay experiments with the UT-SCC-14 cell line, Gedatolisib caused a 15 day growth delay to double the tumor volume while Dacomitinib delayed tumor doubling time by 32 days; the combination of the two drugs was similar to Dacomitinib alone. Gedatolisib and radiation delays were similar to radiation alone while combinations involving Dacomitinib and radiation caused profound growth delay and complete cure of 60% of tumors in ongoing studies. Conclusion: Dacomitinib is an extremely potent EGFR targeting agent in the UT-SCC-14 tumor model while Gedatolisib was less effective. Further research is ongoing to establish whether the relationship between EGFR expression levels and Dacomitinib activity is observed in vivo. If this relationship can be established, then a Phase I study using EGFR expression to stratify patients to Dacomitinib treatment would be warranted.

Rafique Z, Kosiborod M, **Clark CL**, Singer AJ, Miller J, Lagina A, Caterino JM, Sindh B, Char D and Peacock WF (2017). "61 Electrocardiogram changes are not reliably associated with hyperkalemia or its severity." Annals of Emergency Medicine 70(Sup): S25-S26.

[Full-Text](#)

*Department of Emergency Medicine*

Rafique Z, Kosiborod M, **Clark CL**, Singer AJ, Miller J, Lagina A, Caterino JM, Singh B, Char D and Peacock WF (2017). "60 Electrocardiogram changes in patients with acute and chronic hyperkalemia." Annals of Emergency Medicine 70(Sup): S24-S25.

[Full-Text](#)

*Department of Emergency Medicine*

Rafique Z, Kosiborod M, **Clark CL**, Singer AJ, Turner S, Miller J, Char D and Peacock WF (2017). "Study design of Real World Evidence for Treatment of Hyperkalemia in the Emergency Department (REVEAL-ED): a multicenter, prospective, observational study." Clinical and Experimental Emergency Medicine 4(3): 154-159.

[Full-Text](#)

*Department of Emergency Medicine*

OBJECTIVE: Hyperkalemia affects up to 10% of hospitalized patients and, if left untreated, can lead to serious cardiac arrhythmias or death. Although hyperkalemia is frequently encountered in the emergency department (ED), and is potentially life-threatening, standard of care for the treatment is poorly defined, with little supporting evidence. The main objectives of this observational study are to define the overall burden of hyperkalemia in the ED setting, describe its causes, the variability in treatment patterns and characterize the effectiveness and safety of ED standard of care therapies used in the United States. METHODS: This is an



observational study evaluating the management of hyperkalemia in the ED. Two hundred and three patients who presented to the ED with a potassium value  $\geq 5.5$  mmol/L were enrolled in the study at 14 sites across the United States. Patients were treated per standard of care practices at the discretion of the patient's physician. In patients who received a treatment for hyperkalemia, blood samples were drawn at pre-specified time points and serum potassium values were recorded. The change in potassium over 4 hours and the adverse events after standard of care treatment were analyzed. RESULTS AND CONCLUSION: This article describes the background, rationale, study design, and methodology of the REVEAL-ED (Real World Evidence for Treatment of Hyperkalemia in the Emergency Department) trial, a multicenter, prospective, observational study evaluating contemporary management of patients admitted to the ED with hyperkalemia.

Ramsey T, **Lai W**, Svider PF, Hojjat H, Eloy JA and Folbe AJ (2017). "Allergen immunotherapy: Exploring areas for further inquiry." International Forum of Allergy and Rhinology. ePub Ahead of Print.

[Full-Text](#)

*OUWB Medical Student Author*

Randall TC, Chuang L, Orang'o E, **Rosen B**, Uwinkindi F, Rebbeck T and Trimble EL (2017). "Strengthening care and research for women's cancers in Sub-Saharan Africa." Gynecologic Oncology Reports 21(2017): 109-113.

[Full-Text](#)

*Department of Obstetrics and Gynecology*

Roesch J, Cho JBC, **Fahim DK**, Gerszten PC, Flickinger JC, **Grills IS**, **Jawad M**, Kersh R, Letourneau D, Mantel F, Sahgal A, Shin JH, Winey B and Guckenberger M (2017). "Risk for surgical complications after previous stereotactic body radiotherapy of the spine." Radiation Oncology 12(1): Article No. 153.

[Full-Text](#)

*Department of Neurosurgery*

*Department of Radiation Oncology*

**Rosen B**, Itsura P, Tonui P, Covens A, van Lonkhuijzen L and Orang'o EO (2017). "Development of a comprehensive and sustainable gynecologic oncology training program in western Kenya, a low resource setting." Gynecologic Oncology Reports 21(2017): 122-127.

[Full-Text](#)

*Department of Obstetrics and Gynecology*

To provide information on the development of a gynecologic oncology training program in a low-resource setting in Kenya. This is a review of a collaboration between Kenyan and North American physicians who worked together to develop a gynecologic oncology training in Kenya. We review the published data on the increase of cancer incidence in sub-Saharan Africa and outline the steps that were taken to develop this program. The incidence of cervical cancer in Kenya is very high and is the leading cause of cancer mortality in Kenya. WHO identifies cancer as a new epidemic affecting countries in sub-Saharan Africa. In Kenya, a country of 45 million, there is limited resources to diagnose and treat cancer. In 2009 in western Kenya, at Moi University there was no strategy to manage oncology in the Reproductive Health department. There was only 1 gynecologic oncologists in Kenya in 2009. A collaboration between Canadian and Kenya physicians resulted in development of a gynecologic oncology clinical program and initiation of fellowship training in Kenya. In the past 4 years, five fellows have graduated from a 2 year fellowship training program. Integration of data collection on all the patients as part of this program provided opportunities to do clinical research and to acquire peer reviewed grants. This is the first recognized fellowship training program in sub-Saharan Africa outside of South Africa. It is an example of a collaborative effort to improve women's health in a low-resource country. This is a Kenyan managed program through Moi University. These subspecialty trained doctors will also provide advice that will shape health care policy and provide sustainable expertise for women diagnosed with a gynecologic cancer.

**Safian RD** (2017). "Current approaches to retroperitoneal hemorrhage: Too little, too late." Catheterization and Cardiovascular Interventions 90(1): 112-113.

[Full-Text](#)

*Department of Internal Medicine*

**Safian RD** (2017). "Improving outcomes after CABG and PCI." Catheterization and Cardiovascular Interventions 90(2): 194-195.

[Full-Text](#)

*Department of Internal Medicine*

Saloura V, Fatima A, Zewde M, Kiyotani K, **Brisson RJ**, Park JH, Ikeda Y, Vougiouklakis T, Bao R, Seiwert TY, Cipriani N, Lingen MW, Vokes EE and Nakamura Y (2017). "Characterization of the T-cell receptor repertoire and immune microenvironment in patients with locoregionally advanced squamous cell carcinoma of the head and neck." Journal of Clinical Oncology 35(15): Abstract No. 3080.

[Request Form](#)

*OUIB Medical Student Author*

Background: Immunotherapy with checkpoint blockade was recently approved for patients with recurrent/metastatic SCCHN, however it has not been investigated in the curative-intent setting yet. In this study, we investigated the T-cell receptor repertoire and the immune microenvironment in tumor tissues of SCCHN patients with locoregionally advanced disease. Methods: T-cell receptor sequencing and polymerase chain reaction for immune-related genes of tumor tissues from 44 patients with locoregionally advanced SCCHN prior to treatment with definitive chemoradiotherapy were conducted. T-cell receptor clonality and the mRNA expression levels of immune-related genes were correlated with various clinicopathological parameters. Results: In patients with locoregionally advanced SCCHN, tumor infiltrating T-cells clonally expand and GRZB mRNA levels were associated significantly with longer progression-free survival (PFS) ( $p = 0.003$ ) independent of HPV status, tumor and nodal stage. The TCR- $\beta$  DI was significantly lower in HPV-negative compared to HPV-positive tumors ( $p = 0.002$ ), signifying more clonal T-cell expansion in HPV-negative tumors. A higher percentage of HPV-negative tumors expressed HLA-A protein compared to HPV-positive tumors ( $p = 0.049$ ), suggesting that the greater T-cell clonal expansion might be due to more robust antigen presentation by HPV-negative tumors. Conclusions: This study suggests the pre-existence of clonally expanded T-cells in patients with locoregionally advanced SCCHN prior to treatment, and provides rationale to introduce immunotherapy in the curative-intent setting. The association of high GRZB mRNA levels with favorable PFS independent of HPV-status, tumor and nodal stage supports that the pre-existence of an intrinsically inflamed microenvironment enhances chemoradiotherapy effects. Finally, in HPV-positive tumors, the T-cell infiltrate seemed to be more diverse which could be secondary to virally-induced defective expression of HLA class I molecules.

Sandler KA, Cook RR, Ciezki JP, Shaikh T, Stock RG, Merrick GS, Demanes DJ, Spratt DE, Abu-Isa EI, Wedde T, Lilleby W, **Krauss DJ**, Song D, Alam R, Reddy CA, Nickols N, Steinberg ML, Horwitz EM, King CR and Kishan AU (2017). "Clinical outcomes for patients with Gleason score 10 prostate adenocarcinoma: Results from a multi-institutional consortium study." International Journal of Radiation Oncology Biology Physics 99(2): S132-S133.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Gleason score (GS) 10 disease is the most aggressive form of clinically localized prostate adenocarcinoma (PCa). The long-term clinical outcomes and overall prognosis for patients presenting with GS10 PCa are largely unknown due to its rarity. We interrogated a large, multi-institutional consortium of patients with biopsy GS 9-10 disease to identify those with GS 10 PCa and obtain benchmark clinical outcomes data for patients treated with definitive intent. Purpose/Objective(s): Ninety-eight patients with biopsy GS 10 PCa who received definitive treatment with radical prostatectomy (RP,  $n = 22$ ), external beam radiotherapy (EBRT,  $n = 38$ ), and EBRT with a brachytherapy boost (EBRT+BT,  $n = 38$ ) between 2000 and 2013 were included. Overall survival (OS), cancer-specific survival (CSS), distant metastasis-free survival (DMFS), and biochemical recurrence-free survival (bRFS) were estimated with the Kaplan-Meier method.

Results: The median follow-up was 4.9 years. The median age was 67. The T stage distribution was 32 (33%) T1c, 14 (14%) T2a, 13 (13%) T2b, 6 (6%) T2c, 18 (18%) T3a, 5 (5%) T3b, 10 (10%) T4. The median initial prostate-specific antigen was 7.9 (range, 0.4–219). Six patients (27%) who underwent RP received neoadjuvant systemic therapy (mainly androgen deprivation therapy [ADT]), 5% received adjuvant radiotherapy, and 32% received salvage radiotherapy. All patients undergoing EBRT or EBRT+BT received ADT, with median durations of 24 and 22 months, respectively. Systemic salvage therapy rates were 23% among RP patients, 13% among EBRT patients, and 3% among EBRT+BT patients. For the entire cohort, the 5-year and 10-year OS, CSS, DMFS, and bRFS were 77% and 53%, 86% and 69%, 74% and 66%, and 77% and 52%, respectively. Outcomes stratified by treatment type are presented in Table 1. Conclusion: To our knowledge, this is the largest series ever reported on the clinical outcomes of patients with biopsy GS 10 PCa. These data provide useful prognostic benchmark information for physicians and patients. Biopsy GS 10 PCas follow a very aggressive natural history with nearly 30% of patients dying of this disease at 10 years. Nonetheless, aggressive therapy with curative intent is warranted, as >50% of patients remain free of systemic disease five years following treatment.

Sandler KA, Cook RR, Ciezki JP, Shaikh T, Stock RG, Merrick GS, Demanes DJ, Spratt DE, Abu-Isa EI, Wedde T, Lilleby W, **Krauss DJ**, Song D, Alam R, Reddy CA, Nickols N, Steinberg ML, Horwitz EM, King CR and Kishan AU (2017). "Whole pelvis radiation therapy does not significantly improve prostate-cancer specific survival in patients with Gleason score 9-10 prostate adenocarcinoma: An analysis of 942 patients treated in the modern era." International Journal of Radiation Oncology Biology Physics 99(2): E263.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): To assess the effect on clinical outcomes of the addition of whole pelvis radiation (WPRT) to definitive prostate external beam radiation therapy (EBRT) or external beam radiation therapy plus brachytherapy boost (EBRT-BT) for patients with Gleason Score (GS) 9-10 prostate cancer (PCa), who are at high risk of having occult nodal metastases. Purpose/Objective(s): Nine-hundred-forty-two patients with biopsy-proven GS 9-10 PCa treated between 2000 and 2013 at 10 institutions (506 with EBRT and 436 with EBRT+BT) were included. 299 EBRT patients (59%) and 320 EBRT+BT patients (73.4%) received WPRT. A cohort of surgically-treated patients from the same multi-institutional database had a pathologic node positivity rate of 17%. Biochemical recurrence-free survival (bRFS), distant metastasis-free survival (DMFS), and prostate cancer-specific mortality (PCSM) were compared between groups using Cox proportional hazards models with propensity score adjustment. Propensity scores were calculated as the conditional probability of receiving WPRT given age, tumor stage, GS, and initial PSA. Results: The median follow-up was 5.6 years. The median doses were isoeffective to 81 Gy and 96 Gy in 1.8 Gy fractions in the EBRT and EBRT-BT groups, respectively. The median WPRT dose was isoeffective to 50.4 Gy in 1.8 Gy fractions. In the EBRT group 94% of patients receiving WPRT and 96% of patients not receiving WPRT received ADT (median duration 23 months), and in the EBRT-BT group, 80% of patients receiving WPRT received ADT, and 98% not receiving WPRT received ADT (median duration 12 months). WPRT did not significantly improve PCSM in the EBRT group (HR = 0.76, 95% CI 0.45-1.3, p = .3), though it trended towards improvement in the EBRT-BT group (HR 0.46, 0.19-1.11, p = .08). Similar results were seen in a competing risks regression model, treating other cause mortality as a competing risk. WPRT improved bRFS among patients treated with EBRT-BT (HR = 0.4, 95% CI 0.29-0.54, p <.001) but not in those treated with EBRT (HR 1.1, 95% CI 0.67-1.68, p = 0.8). There was borderline improvement in DMFS in the EBRT-BT group (HR 0.64, 95% CI .40-1.03, p = .065), but not the EBRT group (HR = 1.21, 95% CI 0.76-1.93, p = .4). Conclusion: WPRT offered a trend towards improved DMFS and PCSM in this large cohort of patients with biopsy GS 9-10 PCa, but only in those treated with EBRT+BT. This trend did not reach statistical significance. WPRT did significantly improve bRFS, but again only in patients treated with EBRT+BT. These results are hypothesis-generating in suggesting that a long-term clinical benefit to WPRT, if present, might only be seen in the setting of extreme dose-escalation to the prostate itself.

Schreiber T, Htun WW, Kaki A, **Dixon S**, Blank N, Meraj P, Grines C and O'Neill W (2017). "Despite higher morbidity and mortality risk women had similar outcomes and improvement in heart failure as men in complex PCI with impella hemodynamic support." *Journal of Cardiac Failure* 23(8): S67-S68.

[Full-Text](#)

*Department of Internal Medicine*

Background: Sex effect on outcomes in patients undergoing complex high risk percutaneous coronary intervention (PCI) with percutaneous hemodynamic support is not well known. Methods: We studied the sex differences in the cVAD Registry, the largest data set to date of patients undergoing complex PCI with the aid of Impella percutaneous assist devices. Patients without cardiogenic shock who underwent elective or urgent intervention were included. Results: A total of 1053 patients were included in this analysis, 24.8% of which were women. Women were older ( $72 \pm 12$  vs.  $69 \pm 11$ ,  $P < .001$ ), had more diabetes (59% vs 49%,  $P = .005$ ), renal insufficiency (35%vs 27%,  $p = 0,018$ ), valve disease (18% vs 11%,  $P=.016$ ) and higher STS score ( $8.21 \pm 8$  vs  $5 \pm 6$ ,  $P < .001$ ). Women had less prior CABG than men (19% vs33%,  $P < .001$ ) and had higher LVEF ( $33 \pm 17$ vs. $28 \pm 15$ ,  $P < .001$ ). There was more left main disease in women and more graft occlusion in men. Women were more likely to undergo multivessel revascularization than men. In hospital mortality, myocardial infarction, stroke and repeat revascularization rates were similar between groups. Both men and women improved their EF (28% to 33%,  $P < .0001$  and NYHA class post PCI (71%NYHA Class III and IV to 51% Class IIIand IV, $P < .001$ ). Vascular complications were also similar. Women had more bleeding requiring transfusion than men. Conclusion: Women are underrepresented in the overall population undergoing complex supported PCI suggesting that women may encounter a barrier to access to highly specialized medical care. Despite being older and sicker women have similar favorable outcomes as men, suggesting a mitigating effect of the Impella hemodynamic support during PCI.

Secemsky EA, Yeh RW, Kereiakes DJ, Cutlip DE, **Cohen DJ**, Steg PG, Cannon CP, Apruzzese PK, D'Agostino RB, Massaro JM, Mauri L, Kaplan A, Ahmed A, Ahmed AH, Albirini A, Moreyra A, Rabinowitz A, Shroff A, Moak A, Jacobs A, Kabour A, Gupta A, Irimpen A, Rosenthal A, Taussig A, Ferraro A, Chhabra A, Pucillo A, Spaedy A, White A, Pratsos A, Shakir A, Ghitis A, Agarwal A, Jain A, Chawla A, Tang A, Barker B, Bertolet B, Uretsky B, Erickson B, Rama B, McLaurin B, Dearing B, Negus B, Price B, Brott B, Bhambi B, Bowers B, Watt B, Donohue B, Hassel CD, Croft C, Lambert C, O'Shaughnessy C, Shoults C, Kim C, Caputo C, Nielson C, Scott C, Wolfe C, McKenzie C, Brachfeld C, Thieling C, Fisher D, Lee D, Simon D, Churchill D, Dobies D, Eich D, Goldberg D, Griffin D, Henderson D, Kandzari D, Lee D, Lewis D, Mego D, Paniagua D, Rizik D, Roberts D, Safley D, Abbott D, Shaw D, Temizer D, Canaday D, Myears D, Westerhausen D, Ebersole D, Netz D, Baldwin D, Letts D, Harlamert E, Kosinski E, Portnay E, Mahmud E, Korban E, Hockstad E, Rivera E, Shawl F, Shamoan F, Kiernan F, Aycock GR, Schaer G, Kunz G, Kichura G, Myers G, Pilcher G, Tadros G, Kaddissi GI, Ramadurai G, Eaton G, Elsner G, Mishkel G, Simonian G, Piegari G, Chen H, Liberman H, Aronow H, Tamboli HP, Dotani I, Marin J, Fleischhauer JF, Hopkins J, Leggett J, Mills J, Phillips J, Revenaugh J, Mann JT, Wilson J, Pattanayak J, Aji J, Strain J, Patel J, Carr J, Moses J, Chen JC, Williams J, Greenberg J, Cohn J, Douglas J, Gordon J, Griffin J, Hawkins J, Katopodis J, Lopez J, Marshall J, Wang J, Waltman J, Saucedo J, Galichia J, McClure M, Kozina J, Stella J, Tuma J, Kieval J, Giri K, Ramanathan K, Allen K, Atassi K, Baran K, Khaw K, Clayton K, Croce K, Skelding K, Patel K, Garratt K, Harjai K, Chandrasekhar K, Kalapatapu K, Lin L, Dean L, Barr L, MacDonald L, Cannon L, Satler L, Gruberg L, Tami L, Bikkina M, Shah M, Atieh M, Chauhan M, Litt M, Unterman M, Lechin M, Zughuib M, Fisch M, Grabarczyk M, Greenberg M, Lurie M, Rothenberg M, Stewart M, Purvis M, Hook M, Leesar M, Buchbinder M, Weiss M, Guerrero M, Abu-Fadel M, Ball M, Chang M, Cunningham M, Del Core M, Jones M, Kelberman M, Lim M, Ragosta M, Rinaldi M, Rosenberg M, Savage M, Tamberella M, Kellett M, Vidovich M, Effat M, Mirza MA, Khan M, Dib N, Laufer N, Kleiman N, Farhat N, Amjadi N, Schechtman N, Bladuell N, Quintana O, Gigliotti O, Best P, Flaherty P, Hall P, Gordon P, Gurbel P, Ho P, Luetmer P, Mahoney P, Mullen P, Teirstein P, Tolerico P, Ramanathan P, Kerwin P, Lee PV, **Kraft P**, Wyman RM, Gonzalez R, Kamineni R, Dave R, Sharma R, Prashad R, Aycock R, Quesada R, Goodroe R, Magorien R, Randolph R, Bach R, Kettelkamp R, Paulus R, Waters R, Zelman R, Ganim R, Bashir R, Applegate R, Feldman R, Frankel R, Hibbard R, Jobe R, Jumper R, Maholic R, Siegel R, Smith R, Stoler R, Watson R, Wheatley R, Gammon R, Hill R, Sundrani R, Caputo R, Jenkins R, Stella R, Germanwala S, Hadeed S, Ledford S, Dube S, Gupta S, Davis S, Martin S, Waxman S, **Dixon S**, Naidu S, Potluri S, Cook S, Crowley S, Kirkland S, McIntyre S, Thew S, Lin S, Marshalko S, Guidera S, Hearne S, Karas S, Manoukian S, Rowe S, Yakubov S, Pollock S, Banerjee S, Allaqaband S, Choi S, Mulukutla S, Papadakos S, Bajwa T, Addo T, Schreiber T, Haldis T, Mathew T, McGarry T, Nygaard T, Pow T, Larkin T, Caulfield T, Stys T, Lee T, Mansouri V,

Srinivas V, Gupta V, Marquardt W, Ballard W, Bachinsky W, Colyer W, Dillon W, Felten W, French W, Kuehl W, Nicholas W, Nicholson W, Phillips W, Khatib Y, Al-Saghir Y, Hawa Z, Masud Z, Jafar Z, Muller D, Meredith I, Rankin J, Worthley M, Jepson N, Thompson P, Hendriks R, Whitbourn R, Duffy S, Stasek J, Novobilsky K, Naplava R, Coufal Z, Vaquette B, Bressollette E, Teiger E, Coste P, Rihani R, Darius H, Bergmann MW, Radke P, Sebastian P, Strasser R, Hoffmann S, Behrens S, Moebius-Winkler S, Rutsch W, Lupkovics G, Horvath I, Kancz S, Forster T, Koszegi Z, Devlin G, Hart H, Elliott J, Ormiston J, Abernathy M, Fisher N, Kay P, Harding S, Jaffe W, Hoffmann A, Sosnowski C, Trebacz J, Buszman P, Dobrzycki S, Kornacewicz-Jach Z, Iancu AC, Ginghina CD, Matei C, Dobreanu D, Bolohan FR, Dorobantu M, Jacques A, Jain A, Bakhai A, Gershlick A, Adamson D, Newby D, Felmeden D, Purcell I, Edmond J, Irving J, De Belder M, Pitt M, Kelly P, O'Kane P, Clifford P and Suresh V (2017). "Mortality following cardiovascular and bleeding events occurring beyond 1 year after coronary stenting: A secondary analysis of the Dual Antiplatelet Therapy (DAPT) Study." JAMA Cardiology 2(5): 478-487.

[Full-Text](#)

*Department of Anesthesiology*

*Department of Internal Medicine*

**Seltzer M, Menoch M** and Chen C (2017). "Opportunistic screening for exposure to bullying in the pediatric emergency department." Global Pediatric Health 4(Jun): 1-6.

[Full-Text](#)

*Department of Obstetrics and Gynecology*

*Department of Emergency Medicine*

To assess opportunistic screening for exposure to bullying in the pediatric emergency department (ED), an anonymous survey inquiring about exposure to physical, verbal, social, and cyber bullying behaviors was given to ED patients 5 to 18 years old. The survey asked about being the recipient, perpetrator, and/or witness of bullying; the frequency of exposure; liking school; missing school; and presenting complaint. Either the child or parent could complete the survey. A total of 909 surveys were analyzed. Exposure was 78.7%. A greater proportion of females reported being victims and witnesses. Youth who reported being both victims and witnesses represented the largest group, with witness-only the second largest. Parents reported less cyber-bullying and witness status to all types of bullying. For children who did not like school, there was a significant difference in exposure versus nonexposure. There was no association with presenting complaint. Opportunistic screening for bullying exposure in pediatric ED patients warrants consideration as it may increase detection of preclinical status and clinical sequelae.

Selvam N, **Doshi SK, Patel Z** and **Nall C** (2017). "Fundamentals of ultrasound imaging of common musculoskeletal injuries in the emergency setting." Emergency Radiology 24(5): 458-459.

[Full-Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

*OUIWB Medical Student Author*

Learning Objectives: 1) Familiarize the radiologist with the ultrasound equipment and techniques for imaging of common musculoskeletal injuries 2) Demonstrate typical and atypical ultrasound appearances and imaging characteristics of common musculoskeletal injuries 3) Discuss the utility of ultrasound for the accurate and efficient diagnosis of common musculoskeletal injuries in the emergency setting Background: There has been a consistent rise in patients of all age groups presenting to emergency rooms for musculoskeletal injuries. Accurately and efficiently diagnosing musculoskeletal injuries in the emergency setting can be challenging for the radiologist. Advanced cross sectional imaging modalities such as CT and MRI may not play a role in the emergency setting. Relative to other advanced cross sectional imaging modalities such as CT and MRI, ultrasound is less costly, more readily available, allows for efficient and dynamic evaluation, and permits comparison with the contralateral or unaffected areas without concern for exposure to ionizing radiation. Content: Ultrasound is very useful for the evaluation of musculoskeletal injuries involving the upper and lower extremities as well as the thoracic and body wall. Evaluation of the soft tissues including muscles and tendons is the primary utility of ultrasound in the evaluation of musculoskeletal injuries. However, assessment of ligaments, fluid collections, and a few intracapsular structures is possible with ultrasound. We will demonstrate various imaging appearances and characteristics

for musculoskeletal injuries involving the biceps and triceps tendons, common tendons of the elbow, rotator cuff of the shoulder, extensor mechanism of the knee, Achilles tendon, joint effusions and bursitis, as well as body wall and groin hernias. Summary: Ultrasound can play a critical role in the efficient and accurate diagnosis of common musculoskeletal injuries in the emergency setting. Familiarizing the radiologist with ultrasound equipment and technique as well as educating the radiologist on the imaging characteristics and appearances of common musculoskeletal injuries may allow for a more comprehensive evaluation and effective diagnosis in hopes of improved patient outcomes.

Sevak S, **Akay B** and **Bloom DA** (2017). "Anomalous pancreatic ductal system allowing distal bowel gas with duodenal atresia." Journal of Pediatric Surgery Case Reports 26(Nov): 7-10.

[Full-Text](#)

*Department of Surgery*

*Department of Diagnostic Radiology and Molecular Imaging*

A twelve-day-old male presented with non-bilious, non-bloody emesis 2 hours after feeding since two-days-old, with flatus and light stools since birth. An upper gastrointestinal series (UGI) at an outside institution was reported as normal. Abdominal radiographs demonstrated distal bowel gas with proximal duodenal dilation. Abdominal ultrasound demonstrated gas in the main pancreatic duct and a dilated, fluid-filled duodenum. An UGI revealed duodenal atresia with enteric bypass by congenital anomaly of the pancreaticobiliary system. At thirteen days old the patient underwent uncomplicated duodenoduodenostomy. The post-operative course was uneventful and the patient subsequently tolerated oral feeds. Bypass of the atretic duodenal segment through an anomalous pancreatic ductal system is a rare anomaly described in the literature in only a handful of cases. This case report highlights the importance of considering duodenal atresia and pancreaticobiliary enteric bypass in the differential diagnosis of neonates presenting with partial duodenal obstruction. On ultrasound, the presence of gas in the biliary tree or pancreatic duct should alert the physician to the possibility of duodenal atresia with congenital pancreaticobiliary duct anomalies that allow for bypass of enteric contents, including air, into more distal bowel, thereby creating a gas pattern aptly described as double bubble with distal gas.

Shaffer K, Abbott EE, Hothem Z, Thibodeau B and **Keidan R** (2017). "Predicting cancer risk in patients with atypical ductal hyperplasia at the genomic level." Annals of Surgical Oncology 24(1): S19.

[Full-Text](#)

*Department of Surgery*

Background: The current treatment of atypical ductal hyperplasia (ADH) diagnosed on core needle biopsy (CNB) is excisional breast biopsy due to the risk of finding invasive cancer or in situ disease. Upstaging of ADH may occur 10-20% of the time, meaning unnecessary surgical procedures are performed in up to 90% of patients. Several studies have examined clinical features to distinguish those patients more likely to benefit from excision, but few studies describe variation within oncologic genes. The purpose of this study was to identify genetic variation associated with the risk of upstaging in patients with ADH on CNB. Methods: 35 samples total, 21 ADH and 14 DCIS were examined, comparing samples with ADH on both CNB and excision with ADH on CNB but DCIS on excision. DNA was isolated and libraries made for next generation sequencing using the TruSeq Amplicon-Cancer Panel on the Illumina NextSeq 500. NextGENe and Ingenuity Variant Analysis software was used for alignment and variant calling. This was also used to determine the Overall Mutation score to estimate the likelihood the mutation is real. Results: Genetic analysis studied 160 oncologic genes. Five tumor-specific variants were found in > 50% of DCIS patients. Unfortunately, these variants were also found in more than half of the ADH samples. At the gene level, two genes had variants in > 50% of the DCIS group, ATRX and KMT2D. Again these variants were seen in the ADH group as well. Genes containing variants occurring in at least 5 of the DCIS patients but no more than one ADH patient included APC, BRCA1, and CDK12, and all of these variants have some evidence of being deleterious. The BRCA1 variant at position 41,246,401 using genome build GRCh37 was present in 80% of the DCIS patients containing any BRCA1 variation and also has evidence of being deleterious. Conclusion: On analyzing 160 different oncologic genes for variation between ADH on both CNB and excisional biopsy, versus ADH on CNB and DCIS on excisional biopsy, no genetic variants were found to be unique to the DCIS



group. Consequently, in patients with ADH on CNB, surgical excision remains a reasonable treatment.

**Sharma J, Bastani A and Jones S** (2017). "50 Cost benefit analysis of physician-in-triage model at community hospital emergency department." Annals of Emergency Medicine 70(Sup): S20.

[Full-Text](#)

*OUWB Medical Student Author*

*Department of Emergency Medicine*

Siddiqui ZA, Thibodeau BJ, **Ahmed S, Dekhne NS, Benitez PR, Amin MB, Grills IS**, Wobb JL and **Wilson GD** (2017). "Mutational landscape of radiation-induced angiosarcoma in breast cancer patients." International Journal of Radiation Oncology Biology Physics 99(2): S55.

[Full-Text](#)

*Department of Family Medicine*

*Department of Surgery*

*Department of Pathology*

*Department of Radiation Oncology*

Purpose/Objective(s): Angiosarcomas are rare but aggressive tumors of endothelial origin representing approximately 1% of all soft tissue sarcomas. Radiation-induced angiosarcomas (RAAs) are a recognized complication of radiation therapy, and approximately 40% of all RAAs occur after adjuvant radiotherapy for breast cancer. The incidence of breast RAA has increased over the years due to the more common use of adjuvant radiotherapy as part of breast-conserving treatment. Radiation-induced breast angiosarcomas have poor prognosis, and relatively little is known about what cellular pathways are involved. In this study, we use targeted next generation DNA sequencing (NGS) to determine whether there is a specific radiation-induced mutation signature and to determine the key genes and pathways altered in breast RAA.

Purpose/Objective(s): The institutional database was reviewed and the clinical information about those with angiosarcomas of the breast was recorded. H&E stained sections of each tumor were reviewed by a pathologist to confirm the diagnosis of angiosarcoma. The diagnosis of RAA was made with the classic criteria: history of radiotherapy, asymptomatic latent period of several years, the occurrence of a sarcoma within a previously irradiated field, and histological confirmation of the sarcomatous nature of the post-irradiation lesion. NGS was carried out on 13 unique RAA samples and 3 sporadic angiosarcomas using a panel of 160 cancer-related genes comprising 7,951 amplicons. Tissue sections underwent pathologist-guided laser capture microdissection to isolate regions of sarcoma followed by DNA isolation, library preparation of the 160 genes, sequencing, alignment, and mutation analysis. Results: Thirty-two variants were found in 27 genes in  $\geq 53\%$  of the RAAs. Of these genes, 5 were found in all 13 cases including EPCAM, NP1, TNFA1P3, EP300, and ATRX. Five other missense variants were predicted to be deleterious including MTOR in 8 cases, MAP3K1 in 12 cases, two separate BRAF mutations in 12 cases and a BUB1B mutation in 11 cases. At the gene level, ERBB4, APC, EP300, MTOR ROS1, SETD2, FANCA, KDM6A, ATRX, KMT2D, CREBBP, and ARID1A had variants in  $\geq 11$  cases. These genes highlighted three major cellular pathways that were deregulated in RAA including "Role of BRCA1 in DNA damage response," "DNA double-strand break repair by homologous recombination," and "cell cycle: G2/M DNA damage checkpoint regulation." From this analysis, several potential drug targets were identified including BRCA1, DNA-PK, CHEK2, CDC2, and PLK1. Conclusion: RAAs share common genetic changes associated with DNA repair and cell cycle control that differ from sporadic angiosarcomas, which suggests new opportunities for molecular targeted treatments. The DNA sequence context of the mutational events is currently under study.

Siljander M, Vara AD, Koueiter DM, Gandhi S, Quigley M, **Wiater B** and **Wiater P** (2017). "Plate osteosynthesis of patella fractures-a video case report." Journal of Orthopaedic Trauma 31(Sup 3): S26-s27.

[Request Form](#)

*Department of Orthopedic Surgery*

Operative management of patella fractures continues to be associated with poor outcomes and high reoperation rates. Traditionally, tension band fixation has been used for more simple fracture patterns; however, fixation remains a challenge particularly for comminuted fractures. More recently, various types of

plate fixation have been used and reported in the literature. Earlier mobilization after plate osteosynthesis of patella fractures is possible because of a more robust construct, with the potential for decreased knee stiffness and improved functional outcomes. We present a video case of a 79-year-old man who sustained a displaced patella fracture treated with an anterior mesh plate.

Siljander MP, Sobh AH, **Baker KC, Baker EA** and **Kaplan LM** (2017). "Multidrug-resistant organisms in the setting of periprosthetic joint infection-diagnosis, prevention, and treatment." Journal of Arthroplasty. ePub Ahead of Print.

[Full-Text](#)

*Department of Orthopedic Surgery*

Smith TJ, Hanna N, Johnson D, Baker S, Jr., Biermann WA, Brahmer J, Ellis PM, Giaccone G, Hesketh PJ, **Jaiyesimi I**, Leighl NB, Riely GJ, Schiller JH, Schneider BJ, Tashbar J, Temin S and Masters G (2017). "Case for stopping targeted therapy when lung cancer progresses on treatment in hospice-eligible patients." Journal of Oncology Practice: 1-5. ePub Ahead of Print.

[Request Form](#)

*Department of Internal Medicine*

Sobh AH, Siljander MP, **Mells AJ**, Koueiter DM, **Moore DD** and Karadsheh MS (2017). "Cost analysis, complications, and discharge disposition associated with simultaneous vs staged bilateral total knee arthroplasty." Journal of Arthroplasty. ePub Ahead of Print.

[Full-Text](#)

*OUIWB Medical Student Author*

*Department of Orthopedic Surgery*

Speyer CL, **Bukhsh MA**, Jafry WS, Sexton RE, Bandyopadhyay S and Gorski DH (2017). "Riluzole synergizes with paclitaxel to inhibit cell growth and induce apoptosis in triple-negative breast cancer." Breast Cancer Research and Treatment 166(2): 407-419.

[Full-Text](#)

*OUIWB Medical Student Author*

Purpose: One in eight women will develop breast cancer, 15–20% of whom will have triple-negative breast cancer (TNBC), an aggressive breast cancer with no current targeted therapy. We have demonstrated that riluzole, an FDA-approved drug for treating amyotrophic lateral sclerosis, inhibits growth of TNBC. In this study, we explore potential synergism between riluzole and paclitaxel, a chemotherapeutic agent commonly used to treat TNBC, in regulating TNBC proliferation, cell cycle arrest, and apoptosis. Methods: TNBC cells were treated with paclitaxel and/or riluzole and synergistic effects on cell proliferation were quantified via MTT assay and CompuSyn analysis. Apoptosis was observed morphologically and by measuring cleaved PARP/caspase three products. Microarray analysis was performed using MDA-MB-231 cells to examine cell cycle genes regulated by riluzole and any enhanced effects on paclitaxel-mediated cell cycle arrest, determined by FACS analysis. These results were confirmed in vivo using a MDA-MB-231 xenograft model. Results: Strong enhanced or synergistic effects of riluzole on paclitaxel regulation of cell cycle progression and apoptosis was demonstrated in all TNBC cells tested as well as in the xenograft model. The MDA-MB-231, SUM149, and SUM229 cells, which are resistant to paclitaxel treatment, demonstrated the strongest synergistic or enhanced effect. Key protein kinases were shown to be upregulated in this study by riluzole as well as downstream cell cycle genes regulated by these kinases. Conclusions: All TNBC cells tested responded synergistically to riluzole and paclitaxel strongly suggesting the usefulness of this combinatorial treatment strategy in TNBC, especially for patients whose tumors are relatively resistant to paclitaxel.

Stam B, **Grills IS**, Kwint M, Guckenberger M, Mantel F, Hope AJ, Giuliani ME, Werner-Wasik M, Sonke JJ and Belderbos J (2017). "SBRT for central tumors in early stage NSCLC patients." International Journal of Radiation Oncology Biology Physics 99(2): S17.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): For NSCLC patients treated with SBRT, we investigated if proximity to the proximal bronchial tree is associated with non-cancer death. Purpose/Objective(s): From 2006-2013 patients with a single early stage NSCLC tumors were irradiated with CBCT guided SBRT (median dose 54 Gy in 3 fractions) in 5 institutes. Patients with progressive disease, metastases, or second cancers at the time of death were scored as death from cancer; all other deceased patients were scored as non-cancer death. Treatment plans were collected, and the main and lobar bronchi were automatically delineated using atlas based segmentation. For each patient the shortest distance from the edge of the GTV to the proximal bronchial tree (PBT) was determined. Patients were stratified into 3 groups; GTV  $\geq 2$  cm from the PBT (peripheral (A); RTOG 0236), GTV  $\geq 1$  cm and  $< 2$  cm from the PBT (B), and GTV  $< 1$  cm from the PBT (C). Actuarial non-cancer survival at 1y, 2y and 5y were determined (i.e., death from cancer was censored). Association between the stratified distance of the GTV to the PBT and non-cancer death were evaluated using univariate Cox regression (at the  $P < 0.05$  level), and compared to the association with cause specific survival to test for competing mortality risk. Finally, the stratified distance was included in a multivariate Cox analysis, also including; age, gender, performance status, comorbidity index, lung-function FEV1, Mean Lung Dose, tumor diameter, and smoking history. Results: Seven hundred sixty-nine patients were identified with a median age of 75 y. Median Biologically Equivalent Dose (a/b = 10 Gy) was 126 Gy, 180 Gy and 227 Gy for group C, B, and A, respectively, with 33, 71 and 665 patients per group. Median GTV diameter was 4.1 cm (1.1-7.0), 2.7 cm (0.9-5.7) and 2.2 cm (0.7-6.5) for groups C, B, and A, respectively. Survival rates were lower for patients in group C (Table 1) with a Hazard ratio (HR) of 2.91 ( $P < 0.001$ ). Patients in group B had a lower, non-significant HR of 0.87 ( $P = 0.554$ ). The association with cause specific survival showed a significantly higher HR (2.45,  $P = 0.036$ ) for patients in group C with respect to A, but not B. In the multivariate Cox analysis, the stratified distance from the GTV to PBT was significantly associated with non-cancer death (group C:  $P < 0.001$ , HR = 3.56, group B:  $P = 0.319$ , HR = 0.79), as well as age ( $P = 0.001$ , HR = 1.03), performance status ( $P < 0.001$ , HR = 0.30) and lung-function FEV1 ( $P = 0.004$ , HR = 0.99). Conclusion: Patients with a tumor  $< 1$  cm from the proximal bronchial tree had 3.56 fold higher risk of non-cancer death than patients with a peripheral tumor. Delivered dose distributions will be further studied.

Stam B, Peulen H, Guckenberger M, Mantel F, Hope A, Werner-Wasik M, Belderbos J, **Grills I**, O'Connell N and Sonke JJ (2017). "Dose to heart substructures is associated with non-cancer death after SBRT in stage I-II NSCLC patients." Radiotherapy and Oncology 123(3): 370-375.

[Full-Text](#)

*Department of Radiation Oncology*

Background and purpose: To investigate potential associations between dose to heart (sub)structures and non-cancer death, in early stage non-small cell lung cancer (NSCLC) patients treated with stereotactic body radiation therapy (SBRT). Methods: 803 patients with early stage NSCLC received SBRT with predominant schedules of 3 x 18 Gy (59%) or 4 x 12 Gy (19%). All patients were registered to an average anatomy, their planned dose deformed accordingly, and dosimetric parameters for heart substructures were obtained. Multivariate Cox regression and a sensitivity analysis were used to identify doses to heart substructures or heart region with a significant association with non-cancer death respectively. Results: Median follow-up was 34.8 months. Two year Kaplan-Meier overall survival rate was 67%. Of the deceased patients, 26.8% died of cancer. Multivariate analysis showed that the maximum dose on the left atrium (median 6.5 Gy EQD2, range = 0.009-197, HR = 1.005, p-value = 0.035), and the dose to 90% of the superior vena cava (median 0.59 Gy EQD2, range = 0.003-70, HR = 1.025, p-value = 0.008) were significantly associated with non-cancer death. Sensitivity analysis identified the upper region of the heart (atria + vessels) to be significantly associated with non-cancer death. Conclusions: Doses to mainly the upper region of the heart were significantly associated with non-cancer death. Consequently, dose sparing in particular of the upper region of the heart could potentially improve outcome, and should be further studied. (C) 2017 Elsevier B.V. All rights reserved.

Stanhope C, Liang J, Drake D and **Yan D** (2017). "Anatomically-based log file QA using Monte Carlo as an alternative patient-specific QA technique." *Medical Physics* 44(6): 2893.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: To investigate the feasibility of a Log File (LF)/Monte Carlo(MC)- based QA system. Methods: 23 clinical VMAT cases [46 arcs] previously planned in Pinnacle, calculated using Convolution-Superposition (CS), treated using an Elekta Agility MLC, and QA'ed using ArcCHECK were selected. Log files were converted into DCMRT plan format with one control point per useful log file sample. Elekta's Log File Converter R3.2 records linac delivery parameters (dose rate, gantry angle, leaf position) every 40 ms. Dose was calculated on the patient's anatomy for the original plan and log file plan using ScientificRT's SciMoCa MC algorithm. Doses were labeled Plan-MC and LF-MC respectively. Three dose comparisons were made: (a) LF-MC vs Plan-MC isolates delivery error; (b) Plan-MC vs Plan-CS isolates calculation algorithm; (c) LF-MC vs Plan-CS combines the first two. 2%/ 2 mm per-beam gamma pass rates were calculated for each comparison using 10% and 85% dose thresholds. Per-beam percent differences in OAR mean dose, PTV D1, and PTV D99 were calculated for each comparison. Results: Plan-CS vs. ArcCHECK 2%/2 mm pass rates were  $97.2 \pm 2.2\%$  (standard 10% threshold) and  $91.1 \pm 18\%$  (85% target threshold). Pass rates for comparisons a-c were  $99.9 \pm 0.2\%$ ,  $92.5 \pm 2.9\%$ , and  $92.3 \pm 3.0\%$  for the 10% threshold. Using an 85% threshold, pass rates decreased to  $99.8 \pm 0.1\%$ ,  $80.0 \pm 11.7\%$ , and  $83.7 \pm 16.1\%$ . Mean OAR doses were consistently within 1%, 3%, and 3%. Change in PTV D1 was  $-0.2 \pm 0.3\%$ ,  $-0.1 \pm 1.3\%$ , and  $-0.3 \pm 1.3\%$ . Change in PTV D99 was  $0.1 \pm 0.4\%$ ,  $-4.2 \pm 2.9\%$ , and  $-4.1 \pm 2.8\%$ . Conclusion: LF QA dose difference was largely due to calculation algorithm and minimally due to log file-determined delivery error. Increasing the gamma dose threshold yielded decreased passing rates for both QA techniques. However, whereas ArcCHECK consistently yielded passing (> 90%) results, LF QA recorded worrisome target coverage (gamma 85% and D99).

Steffens C, **Clement B**, Fales W, Chegade AEH, Putman K and **Swor R** (2017). "Evaluating the cost and utility of mandating schools to stock epinephrine auto-injectors." *Prehospital Emergency Care* 21(5): 563-566.

[Full-Text](#)

*OUWB Medical Student Author*

*Department of Emergency Medicine*

Background: The Michigan Legislature mandated that all public schools stock epinephrine auto-injectors (EAI's). A minimal amount is known regarding the incremental value of EAI's in schools. Our primary objective was to describe the frequency of administration of epinephrine for EMS patients with acute allergic reactions in public schools. Our secondary objective was to estimate the cost of mandating public schools to stock EAI's. Methods: We performed a retrospective cohort study of EMS cases with an impression of allergic reaction and who received epinephrine recorded in the 2014 Michigan EMS Information System (MI-EMSIS). We abstracted patient demographics, incident location by address to identify public schools, source of epinephrine given, and suspected allergen if known. We calculated advanced life support (ALS) response times to assess temporal impact of school EAI's in communities with ALS systems. We estimated the unsubsidized annual procurement cost of this mandate for Michigan public schools (N = 4,039), using range of costs for the required 2 EAI's (adult and pediatric) as estimated by the legislature (\$140/each) and recently reported costs for commercial sources (\$1,200). Training costs were not included. Descriptive statistics are reported. Results: During this period, there were 1,550,009 EMS cases in the state with 631 receiving non-cardiac arrest epinephrine for presumed anaphylaxis, of which 23 cases were in public schools. Reported allergens were most often food 12 (51.2%), insect stings 4(22.2%) or unknown 7(30.4%). Among these patients, the source for epinephrine used was from the student, 7 (30.4%), EMS 7 (30.4%), school 7(30.4%), and unknown 2(8.7%). A majority (21, 91.3%) of the public school cases occurred in communities with ALS systems and ALS response was relatively rapid (median response 6 minutes, 90 percentile, 13 minutes). The unsubsidized annual cost of Michigan public schools to stock EAI's ranges from \$565,460 to \$4,846,800. Conclusion: In this study, few public school patients received epinephrine for anaphylaxis and the vast majority occurred in communities with rapid ALS response. The direct annual supply cost of the school EAI mandate is substantial.

Sukul D, Seth M, **Dixon SR**, Khandelwal A, Lalonde TA and Gurm HS (2017). "Contemporary trends and outcomes associated with the preprocedural use of oral P2Y12 inhibitors in patients undergoing percutaneous coronary intervention: Insights from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2)." Journal of Invasive Cardiology 29(10): 340-351.

[Request Form](#)

*Department of Internal Medicine*

Sukul D, Seth M, **Dixon SR**, Zainea M, Slocum NK, Pielsticker EJ and Gurm HS (2017). "Clinical outcomes of percutaneous coronary intervention in patients turned down for surgical revascularization." Catheterization and Cardiovascular Interventions 90(1): 94-101.

[Full-Text](#)

*Department of Internal Medicine*

**Objectives**We examined clinical outcomes following percutaneous coronary intervention (PCI) in patients turned down for surgical revascularization across a broad population. **Background**Prior studies suggest that surgical ineligibility is associated with increased mortality in patients with unprotected left main or multivessel coronary artery disease undergoing PCI. **Methods**This study included consecutive patients who underwent PCI in a multicenter registry in Michigan from January 2010 to December 2014. Surgical ineligibility required documentation indicating that a cardiac surgeon deemed the patient ineligible for surgery. In-hospital outcomes included mortality (primary outcome), cardiogenic shock, cerebrovascular accident, contrast-induced nephropathy (CIN), and a new requirement for dialysis (NRD). **Results**Of 99,370 patients at 33 hospitals with on-site surgical backup, 1,922 (1.9%) were surgically ineligible. The rate of ineligibility did not vary by hospital (range: 1.5-2.5%; P=0.79). Overall, there were no major differences in baseline characteristics or outcomes between surgically ineligible patients and the rest (i.e., nonineligible patients): mortality (0.52% vs. 0.52%; P>0.5), cardiogenic shock (0.68% vs. 0.73%; P>0.5), cerebrovascular accident (0.05% vs. 0.19%; P=0.28), NRD (0.16% vs. 0.19%; P>0.5), CIN (2.7% vs. 2.3%; P=0.27). Among 1,074 patients who underwent unprotected left main PCI, 20 (1.9%) were surgically ineligible and experienced increased rates of mortality (20.0% vs. 5.3%; P=0.022; adjusted OR=7.38; P<0.001) and other complications as compared to the remainder. **Conclusions**PCI in a broad population of surgically ineligible patients is generally safe. However, among patients who underwent unprotected left main PCI, those deemed surgically ineligible experienced significantly worse outcomes as compared to the rest. (c) 2016 Wiley Periodicals, Inc.

Sura K, **Grills IS**, **Kabolizadeh P**, **Zhou J**, Li X, **Yan D**, **Krauss DJ**, **Chinnaiyan P** and Ding X (2017). "Feasibility of spot-scanning proton ARC fractionated radiosurgery to the post-operative cavity for brain metastases." International Journal of Radiation Oncology Biology Physics 99(2): E725.

[Full-Text](#)

*Department of Radiation Oncology*

**Purpose/Objective(s):** To determine dosimetric outcomes of Spot-Scanning Proton ARC (SPArc) fractionated radiosurgery to the post-operative cavity in brain metastases when compared to intensity modulated radiation therapy (IMRT) and intensity modulated proton therapy (IMPT) techniques. **Purpose/Objective(s):** A previously treated post-operative brain metastasis cavity was re-planned using 3-field robust optimized IMPT and SPArc techniques. 5-field IMRT was planned according to institutional standards with a frameless setup. Robust optimization parameters were set to  $\pm 3.5\%$  range and  $\pm 1\text{mm}$  setup uncertainties in x,y,z directions (21 worst-case-scenarios optimization). The treatment volume was prescribed to 25 Gy [RBE] in 5 fractions to 100% of volume for all plans. Multiple parameters were used to compare the plans including conformity index (CI) [total volume covered by 25Gy/target volume covered by 25Gy], gradient index (GI) [V50%RX/V100%RX], mean brain dose, V1Gy, V2Gy, V5Gy and V12Gy. **Results:** The volume of the post-operative cavity was 73.12 cc. IMPT was superior to IMRT in all metrics except CI. SPArc had a similar CI as IMRT and was superior in all other metrics. When compared to IMPT, SPArc demonstrated an improved V12 and mean brain dose, consistent with a lower GI achieved with this technique, although did result in a higher low dose volume. A breakdown of the dosimetric parameters is located in Table 1. **Conclusion:** Proton therapy offered better dosimetric outcomes when compared to IMRT in treatment of post-operative cavity

of brain metastases using fractionated radiosurgery. SPArc offered additional advantages of improved CI and GI.

Sura K, Wilson LD and **Grills IS** (2017). "Comparison of self-reported data on student doctor network to objective data of the National Resident Matching Program for individuals applying to radiation oncology." International Journal of Radiation Oncology Biology Physics 99(2): E129.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): To compare matching outcomes between self-reporting on Student Doctor Network (SDN) and objective data from the National Resident Matching Program (NRMP). Purpose/Objective(s): Data was collected from SDN starting in the 2010-2011 academic year to 2015-2016 academic year. A total of 193 radiation oncology (RO) applicants had reported data during the period. A total of 4 applicants (2.1%) did not match and were excluded from the analysis. Applicants were compared to the NRMP charting outcomes of 2011, 2014, and 2016. Results: US allopathic seniors comprised a majority of those reporting on SDN (95.2%). The majority of applicants (58.2%), self-reported in the later years between 2014 and 2016. Those reporting on SDN were more likely to be members of Alpha Omega Alpha (AOA) (39.7% on SDN versus 27.5% in 2016 NRMP, 23.6% in 2014 NRMP, and 31.2% in 2011 NRMP) and had higher mean USMLE step 1 (248 on SDN versus 247 in 2016 NRMP, 241 in 2014 NRMP, and 240 in 2011 NRMP), and mean USMLE step 2 scores (254 in SDN versus 251 in 2016 NRMP, 248 in 2014 NRMP, and 244 in 2011 NRMP). 81% of the applicants matched within their top 3 ranked residencies on their match list. Common themes associated with reasons for their successful match included research experience, letters of recommendation, and away rotations. Common themes associated with advice given to future applicants were the importance of research, personality, and away rotations. Conclusion: Self-reporting on SDN does have a bias toward more successful RO applicants compared to the objective NRMP data. However, if self-reporting increases, SDN may serve as a reasonably accurate source of information for future applicants.

Sura KT, Ye H, C CV, **Robertson JM** and **Kabolizadeh P** (2017). "How many lymph nodes are enough? Defining the optimal lymph node dissection in stage I-III gastric cancer using the National Cancer Database." Journal of Clinical Oncology 35(15): Abstract No. 4034.

[Request Form](#)

*Department of Radiation Oncology*

Background: Gastric cancer is one of the most causes of cancer-related death worldwide. Surgical resection with lymph node dissection is the primary therapeutic modality. However, the appropriate extent of lymph node dissection remains controversial. Herein, the National Cancer Database (NCDB) was used to determine the optimal number of lymph nodes (LNs) to be dissected for resectable gastric cancer. Methods: The NCDB was queried from 2004-2013 for patients with invasive gastric cancer who underwent surgical resection with negative margins. The optimal number of LNs dissected was determined using a univariate  $\chi^2$  cut-point analysis. Actuarial survival was determined using the Kaplan Meier method, and comparisons of survival estimates were completed with log-rank tests. Multiple sensitivity analyses were utilized to decrease bias. Results: 17,851 patients were included. The mean ( $\pm$ SD) number of LNs examined was  $16 \pm 11$ . For all patients, the optimal number of LNs needed to be examined was 20+ nodes. When correcting for stage migration ( $< 7$  LNs removed), the optimal cut-off value was 20+ LNs. When stratifying by pathologic nodal stage, the cutpoint was 10+ LNs for pN1 and pN2. The 5-year survival was  $30.6 \pm 1.6\%$  for 0-9 removed LNs compared to  $48.2 \pm 1.2\%$  for 10+ removed LNs ( $p < 0.001$ ) in pN1 disease and  $18.3 \pm 1.7\%$  for 0-9 removed LNs compared to  $32.6 \pm 1.2\%$  for 10+ removed LNs ( $p < 0.001$ ) in pN2 disease. For pN3 disease, the optimal cut-off point was 20+ LNs; the 5-year survival was  $17.2 \pm 1.3\%$  for 0-19 removed LNs compared to  $28.5 \pm 1.7\%$  for 20+ removed LNs ( $p < 0.001$ ). Moreover, the outcome was inferior among patients who had  $> 10\%$  positive dissected LNs ( $p < 0.05$ ). Conclusions: The optimal number of dissected LNs of 20+ LNs was associated with superior survival. Extended LN dissection is to be considered especially in patients with  $> 10\%$  positive dissected LNs.



Thompson A, Thapa R, Galoforo S, Hang X, Buelow K and **Wilson GD** (2017). "Targeting stem cells in head and neck cancer using superparamagnetic iron oxide nanoparticles." International Journal of Radiation Oncology Biology Physics 99(2): E621.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Head and neck squamous cell carcinoma (HNSCC) is a major cause of morbidity and mortality. In HNSCC, as with other malignancies, cancer stem cells (CSCs) have been increasingly shown to have an integral role in tumor initiation, disease progression, and metastasis and treatment resistance. CD44 is one of the well-recognized CSC markers and serves as a receptor for hyaluronic acid (HA). We explored new avenues to target the CD44 population for both treatment and imaging by using dextran coated superparamagnetic iron oxide nanoparticles functionalized with HA (HA-DESPIONS). Two different aspects of the research are presented. The first reports the ability of an alternating magnetic (AMF) to selectively generate hyperthermia in the CD44 population and the second investigates the utility of MRI to monitor CSCs during and after radiation treatment. Purpose/Objective(s): An AMF generator was developed and UT-SCC-14 cells were exposed to HA-DESPIONS or non HA-coated DESPIONS at a concentration of 200 µg/ml, allowed to attach for 24 hours before being exposed to an AMF for 30 minutes. Twenty-four hours after exposure, cells were processed to assess apoptosis by flow cytometry. In the second study, UT-SCC-14 xenografts were established and exposed to a single dose of 15 Gy and exposed to HADESPIONS at a concentration of 0.25mg Fe/ml. Animals were injected on Days 0, 4, 10 and 20 following radiation. At each exposure, mice were imaged 30 minutes after injection using a 3.0 T benchtop MRI, immediately sacrificed and the tumors processed for immunohistochemical (IHC) analysis of CD44 expression. Results: Dual staining of CD44 and apoptosis revealed that cell death was only increased in the CD44 positive population that was exposed to HA-DESPIONS and not the uncoated DESPIONS only when the magnetic field was activated. The baseline apoptotic rate increased from 1.4% to 27.5% in the CD44 positive cells. In the in vivo experiments, HADESPIONS quenched the T2w scans with a mean intensity of -0.32 at Day 0, quenching was steadily reduced after treatment such that the signal was increased to -0.14 at day 20 representing a 57% change. This change was consistent with a reduction in CD44 positive cells observed in the IHC-stained tissue sections throughout the time period after irradiation. Conclusion: Flow cytometry results demonstrated that HA-DESPIONS were targeted to UT-SCC-14 cells through binding to the over expressed surface receptor CD44 and were activated in the presence of an AMF to generate a significant amount of localized heat that ultimately led to tumor cell death. This may be a promising strategy to specifically target CSCs in HNSCC for treatment. MRI scans demonstrated quenching changes which were consistent with a decreased binding of HADESPIONS which correlated with a decreased expression of CD44 following radiation. This may be a promising strategy to image CSCs in vivo and assess their response to treatment.

Tonlaar N, Galoforo S, Thibodeau BJ, **Ahmed S**, Wilson TG, Yumpo Cardenas P, Marples B and **Wilson GD** (2017). "Antitumor activity of the dual PI3K/MTOR inhibitor, PF-04691502, in combination with radiation in head and neck cancer." Radiotherapy and Oncology 124(3): 504-512.

[Full-Text](#)

*Department of Family Medicine*

*Department of Radiation Oncology*

Traylor S, **Bastani A**, Butris-Daut N, **Christensen M**, Marsack P, Rodgers L and **Todd B** (2017). "Are three ports better than one? An evaluation of flow rates using all ports of a triple lumen central venous catheter in volume resuscitation." American Journal of Emergency Medicine. ePub Ahead of Print.

[Full-Text](#)

*Department of Emergency Medicine*

**Vakharia PP**, Chopra R, Sacotte R, Patel N, Immaneni S, White T, Kantor R, Hsu DY and Silverberg JI (2017). "Validation of patient-reported global severity of atopic dermatitis in adults." Allergy. ePub Ahead of Print.

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*OUIB Medical Student Author*

**BACKGROUND:** Atopic dermatitis (AD) is associated with a heterogeneous presentation and clinical course. There is a lack of simple and validated severity assessments that are feasible for clinical practice and epidemiological research. **OBJECTIVES:** We sought to validate patient-reported global AD severity in adults. **METHODS:** We performed a prospective dermatology practice-based study using questionnaires and evaluation by a dermatologist (n = 265). **RESULTS:** At baseline and follow-up, patient-reported global AD severity significantly correlated with oSCORAD (Spearman rho = 0.56 and 0.49), SCORAD (0.64 and 0.56), EASI (0.56 and 0.50), BSA (0.52 and 0.45), NRS-itch (0.60 and 0.53), POEM (0.50 and 0.48), and DLQI (0.50 and 0.49) (P < .0001 for all). Patient-reported moderate and severe AD vs mild AD were associated with significantly higher oSCORAD, SCORAD, EASI, BSA, NRS-itch, POEM, and DLQI (P < .0001 for all). There was moderate concordance between patient-reported AD severity (mild, moderate, and severe) and previously developed severity strata for oSCORAD (kappa = 0.39), SCORAD (kappa = 0.47), EASI (kappa = 0.37), NRS-itch (kappa = 0.49), POEM (kappa = 0.37), and DLQI (kappa = 0.40). Among patients with severe disease at baseline, those who reported mild or moderate disease on follow-up had significantly greater absolute reductions of oSCORAD (-23.4/-9.7/-1.8), SCORAD (-33.0/-13.2/-2.3), EASI (-17.1/-9.8/-3.2), BSA (-46%/-15%/-4%), NRS-itch (-5/-2/0), POEM (-5/-2/0), and DLQI (-8/-6/-1) than those who continued to report severe disease (Kruskal-Wallis, P <= .0003 for all). **CONCLUSIONS:** Patient-reported AD severity appears to be sufficiently valid for assessing AD severity in the clinical and epidemiological setting.

**Vakharia PP**, Chopra R, Sacotte R, Patel N, Immaneni S, White T, Kantor R, Hsu DY, Simpson EL and Silverberg JI (2017). "Severity strata for five patient-reported outcomes in adults with atopic dermatitis." British Journal of Dermatology. ePub Ahead of Print.

[Full-Text](#)

*OUIB Medical Student Author*

**BACKGROUND:** Multiple patient-reported outcomes have been used to assess the burden of atopic dermatitis (AD). Some are disease specific, e.g. the Patient Oriented Eczema Measure (POEM). While others pertain to itch, e.g. Numerical Rating Scale (NRS)-itch, ItchyQoL and 5-D itch, or dermatologic disease in general, e.g. Dermatology Life Quality Index (DLQI). Development of severity strata is essential for proper interpretability of these assessments. We sought to confirm previously developed strata for POEM, DLQI and raw ItchyQoL, and develop strata for the NRS-itch, mean ItchyQoL and 5-D itch scale for use in adults with AD. **METHODS:** Self-administered questionnaires were completed by 210 adults with AD in a dermatology practice setting. Strata were selected using an anchoring approach based on patient-reported disease severity. **RESULTS:** We confirmed the existing strata for POEM (mild=0-7, moderate=8-16, severe=17-28) (kappa=0.440), DLQI (mild=0-5, moderate=6-10, severe=11-30) (kappa=0.398) and NRS-itch (mild=0-3, moderate=4-6, severe=7-10) (kappa=0.499). However, the preferred band for raw ItchyQoL was mild=22-58, moderate=59-74 and severe=75-110 (kappa=0.379) and mean ItchyQoL was mild=1-2.9, moderate=3.0-3.9, severe=4.0-5.0 (kappa=0.374). The preferred band for 5-D itch scale was mild=0-11, moderate=12-17 and severe=18-25 (kappa=0.331). **CONCLUSIONS:** Existing strata for POEM and DLQI perform well in adult AD. Previously reported strata for VAS-itch performed best for NRS-itch. We identified banding for the raw ItchyQoL for our AD population that varies slightly from the banding published for a more heterogeneous population. Finally, we proposed strata for mean ItchyQoL and 5-D itch scale in adult AD. This article is protected by copyright. All rights reserved.

**Vakharia PP** and Silverberg JI (2017). "Monoclonal antibodies for atopic dermatitis: Progress and potential." Biodrugs 31(5): 409-422.

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*OUIB Medical Student Author*

Atopic dermatitis (AD) is a complex and heterogeneous inflammatory skin disorder with a profound symptom and lesional burden. Moderate-to-severe AD is particularly challenging to manage, as topical

treatments are often inadequate and the systemic immunosuppressants are limited by concerns of toxicity and tolerability. Recent AD research has elucidated the mechanisms and immunologic factors involved in AD pathogenesis. These breakthroughs have led to the development of multiple therapeutic monoclonal antibodies that are directed against specific immunologic targets. This review provides an overview on the pathogenesis of AD as well as the rationale for the targets of various monoclonal antibodies. Additionally, this review explores the efficacy and safety of use for various monoclonal antibodies in the management of AD, as well as the potential role of these agents in the treatment of AD.

Vu CC, Blas KG, **Lanni T**, **Gustafson GS** and **Krauss DJ** (2017). "Cost effectiveness of prostate boost with high-dose rate brachytherapy versus intensity modulated radiation therapy in the treatment of intermediate-high risk prostate cancer." *International Journal of Radiation Oncology Biology Physics* 99(2): S37-S38.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): The recently published ASCENDE-RT randomized clinical trial demonstrated improved biochemical control, albeit with increased toxicity, for a prostate boost with brachytherapy versus external beam radiation therapy alone. Our single-institution retrospective review demonstrated similar findings. It is unknown whether the increased biochemical control of a prostate brachytherapy boost outweighs its increased cost and toxicity. In this study, we investigated the cost-effectiveness of these two modalities in the treatment of intermediate-high risk prostate cancer. Purpose/Objective(s): A multi-state Markov decision tree was created to model a patient with intermediate-high risk prostate cancer. The two treatment options modeled were: (1) 23 fractions of IMRT and 2 fractions of HDR prostate brachytherapy (brachytherapy boost), and (2) 44 fractions of IMRT (IMRT alone). Each patient received 1 year of hormone therapy, per the ASCENDE-RT protocol. Model assumptions, including clinical outcomes, toxicity, and utilities were obtained from the medical literature. Costs were estimated using Medicare reimbursement data. The expected lifetime costs and quality-adjusted life years (QALY) were then estimated. If applicable, an Incremental Cost-Effectiveness Ratio (ICER) was computed. One-way sensitivity analyses were performed over a range of cancer progression rates, utilities, and cost assumptions. We assumed a maximum willingness to pay of \$50,000/QALY. Results: The estimated expected lifetime costs of brachytherapy boost were \$71,978, compared to \$81,543 for IMRT alone. While having a higher upfront cost, brachytherapy boost reduced expected lifetime costs because it decreased the incidence of metastatic castration-resistant prostate cancer (mCRPC), cutting the use of expensive targeted therapy for mCRPC. Brachytherapy boost had an expected QALY of 11.20 years, compared to 9.1 years for IMRT alone. Therefore, brachytherapy boost is a dominant treatment strategy over IMRT alone. One-way sensitivity analyses found brachytherapy boost to be cost-effective over a range of cost, utility, and cancer progression rate assumptions. Conclusion: IMRT with HDR brachytherapy boost is a cost-effective treatment for intermediate-high risk prostate cancer compared to IMRT alone.

Vu CC, **Lanni T** and **Nandalur SR** (2017). "Trends in medicare Work Relative Value Unit (WRVU) production in radiation oncology." *International Journal of Radiation Oncology Biology Physics* 99(2): E419.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Prior analyses of the Medicare payments database analyzed the dollar amounts paid to individual radiation oncologists. A limitation of this analysis was that only a fraction of radiation oncologists were directly reimbursed for technical services. This study aims to overcome this limitation by analyzing the work Relative Value Units (wRVUs) produced by each radiation oncologist. Trends in Medicare reimbursement from 2012-2014 were also analyzed. Purpose/Objective(s): The Medicare Physician Supplier and Other Provider Public Use File (POSPUF) and the CMS Physician Fee Schedule Relative Value Files (to calculate wRVUs) for the calendar years 2012, 2013, and 2014 were used in this analysis. The data were filtered and analyzed by physician and by billing code. Statistical analysis was performed to identify differences in reimbursements based on sex, billing of technical services, and location in a certificate of need (CON) state. Results: In 2014, 4,260 radiation oncologists produced 11,354,563 wRVUs, compared to 11,352,286 wRVUs produced in 2012 and 11,355,846 wRVUs produced in 2013. These datasets include only

Medicare reimbursements and do not include wRVUs produced from private insurances or other payers. In 2014, radiation oncologists produced a median of 2,253 wRVUs from Medicare (range 2-19,844). In 2014, 499 radiation oncologists produced at least 5,000 wRVUs, and 45 radiation oncologists produced at least 10,000 wRVUs. Billing to HCPCS Code 77427 (radiation tx management x 5), a proxy for total radiation treatments, fell from 1,111,670 in 2012 to 1,051,436, a decline of 5.4%. The number of new consults (HCPCS Codes 99201-99205) have been stable over this period (225,329 new visits in 2014 compared to 225,424 new visits in 2013 and 224,698 new visits in 2012). On univariate analysis, male gender, billing of technical services, and location in a Certificate of Need (CON) state were associated with higher wRVU production. Conclusion: The total number of wRVUs produced by radiation oncologists has been stable from 2012-2014. The number of fractions delivered during this period has declined, likely due to a trend towards hypofractionated courses of treatment. Male gender, billing of technical services, and location in a Certificate of Need (CON) state were associated with higher wRVU production.

Vu CC, Sura K, **Lanni T, Gustafson GS and Krauss DJ** (2017). "Cost-effectiveness of single-fraction high-dose rate brachytherapy versus intensity modulated radiation therapy for the treatment of low-intermediate risk prostate cancer." International Journal of Radiation Oncology Biology Physics 99(2): S37.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): There are many excellent treatment options for the treatment of low-intermediate risk prostate cancer. We recently published the preliminary outcomes of a prospective clinical trial investigating the safety and efficacy of single-fraction high-dose rate (HDR) brachytherapy (19Gy) as monotherapy for low-intermediate risk prostate cancer. In this study, we investigated the cost-effectiveness of these two modalities in the treatment of low-intermediate risk prostate cancer. Purpose/Objective(s): A multi-state Markov decision tree was created to model a patient with low-intermediate risk prostate cancer. The two treatment options modeled were: (1) single-fraction HDR brachytherapy, and (2) 44 fractions of intensity modulated radiation therapy (IMRT). Model assumptions, including clinical outcomes, toxicity, and utilities, were obtained from the medical literature. Costs, including initial treatment and possible subsequent treatments for recurrence, were estimated using Medicare reimbursement data. The expected lifetime costs and quality-adjusted life years (QALY) were then estimated. One-way sensitivity analyses were used to test our baseline assumptions, with a maximum willingness to pay of \$50,000/QALY. Results: The estimated expected lifetime costs of HDR was \$35,768, compared to \$56,398 for IMRT. HDR had an expected QALY of 12.04 years, compared to 11.70 years for IMRT. Therefore, in the base case scenario, HDR is a dominant treatment strategy over IMRT. However, sensitivity analyses showed that the cost-effectiveness of HDR compared to IMRT is highly dependent on the biochemical control rates of the two treatments. Conclusion: Single-fraction HDR brachytherapy is a potentially cost-effective treatment for low-intermediate risk prostate cancer. Long-term outcomes in patients receiving single-fraction HDR brachytherapy are needed to confirm these findings.

**Wang AC, Darlin S, Lai W, Svider PF, Jacob JT, Liu JK, Eloy JA and Folbe AJ** (2017). "Pituitary and skull-base lesions and the litigious patient." International Forum of Allergy and Rhinology 7(10): 1022-1028.

[Full-Text](#)

*OUWB Medical Student Author*

*Department of Neurosurgery*

*Department of Pathology*

Wang WGA, Ye H and **Chinnaiyan P** (2017). "Practice patterns and survival outcomes of intracranial germinoma: An analysis of the National Cancer Database." International Journal of Radiation Oncology Biology Physics 99(2): S208-S209.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): To examine the practice pattern and survival outcome of patient with intracranial germinoma by analyzing the National Cancer Database (NCDB). Purpose/Objective(s): Patients from the

NCDB brain tumor registry between the years 2004-2014 with intracranial germinoma were extracted for analysis. The patient demographics and treatments received were examined and survival data was analyzed. Patients who had distant metastasis, received no treatments, or only surgery/chemotherapy alone were excluded from the survival analysis. An age cutoff of >21 years old was used to define the pediatric population. Patients were separated into the treatment groups of radiation therapy alone (RT) and chemotherapy followed by radiation therapy (C+RT) and survival outcome was analyzed. Results: 551 patients with intracranial germinoma meeting our inclusion criteria were identified in the NCDB. The median age was 18.4 years old and 67.2% of the patients were male. 382 patients were pediatric patients and 169 were adults. Of the adult patients, 65.7% received RT and 34.3% received C+RT, compared to the pediatric patients, where 31.8% received RT and 68.2% received C+RT. The median adult radiation dose was 4500 cGy and 3600 cGy for the pediatric patients ( $p < 0.001$ ). Those patients who received C+RT had a lower radiation dose compared to the RT group ( $p < 0.001$ ). African American patients and those with private insurance were more likely to receive RT alone. Cut point analysis showed no significant trends in the use of RT vs C+RT over the years. The 5 and 10 year overall survival (OS) for the entire cohort was 92.6% and 87.9%, respectively. Univariate analysis demonstrated improved OS with younger age, private insurance, C+RT treatment, and pediatric patients. Only age and insurance type remained significant on multivariate analysis. The 5 year OS was 92.6% (RT) vs 97.2% (C+RT) ( $p = 0.307$ ) and 83.4% (RT) vs 95.4% (C+RT) ( $p = 0.122$ ) in the pediatric and adult patients, respectively. Conclusion: There is a higher use of C+RT with an accompanied reduction in RT dose in the treatment of intracranial germinoma in the pediatric population. There is no difference in survival between the treatment approaches of RT or C+RT in the NCDB patient cohort.

Ward N, Baqai J, Zehnpfennig A, Fine N, **Huang J** and **Smith MD** (2017). "Bcl-2 maturation pattern in T-cells distinguishes thymic neoplasm/hyperplasia, T-lymphoblastic lymphoma, and reactive lymph nodes." Cytometry Part B - Clinical Cytometry. ePub Ahead of Print.

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*Department of Pathology*

Anterior mediastinal biopsies consisting predominantly of small lymphocytes can be a diagnostic challenge, especially in small core biopsies. In these cases, immunophenotyping is often employed using flow cytometry, and/or immunohistochemistry. However, due the overlap in T-cell phenotype between thymic neoplasm/hyperplasia (THY), T-lymphoblastic lymphoma (T-LBL), and reactive lymph nodes (RLN), biopsies consisting predominantly of T-cells may still be difficult to differentiate. Previous studies have shown a specific CD3/bcl-2 staining pattern in thymic T cells of humans and mice using flow cytometry. However, the utility of this finding in distinguishing T-cells of THY, T-LBL, and RLN has not been carefully evaluated. Our findings show that the pattern of CD3/bcl-2 expression in thymic T-cells can be used to help diagnose anterior mediastinal biopsies, even when limited specimen is provided.

Wenzler DL, Gulli F, Cooney M, **Chancellor MB**, **Gilleran J** and **Peters KM** (2017). "Treatment of ulcerative compared to non-ulcerative interstitial cystitis with hyperbaric oxygen: A pilot study." Therapeutic Advances in Urology 9(12): 263-270.

[Full-Text](#)

*Department of Urology*

Wilkinson JB, **Chen PY**, Wallace MF, Shah CS, **Benitez PR**, Martinez AA and Vicini FA (2017). "Six-year results from a phase I/II trial for hypofractionated accelerated partial breast irradiation using a 2-day dose schedule." American Journal of Clinical Oncology. ePub Ahead of Print.

[Full-Text](#)

*Department of Radiation Oncology*

*Department of Surgery*

BACKGROUND: To report 6-year outcomes from a phase I/II trial using balloon-based brachytherapy to deliver APBI in 2 days. METHODS: A total of 45 patients with early-stage breast cancer received adjuvant APBI in 2 days with high-dose rate (HDR) brachytherapy totaling 2800 cGy in 4 fractions (700 cGy BID) using a balloon-based applicator as part of a prospective phase I/II clinical trial. All patients had negative margins

and skin spacing  $\geq 8$  mm. We evaluated toxicities (CTCAE v3) as well as ipsilateral breast tumor recurrence (IBTR), regional nodal failure (RNF), distant metastasis, disease-free survival, cause-specific survival, and overall survival. RESULTS: Median age and tumor size were 66 years old (48 to 83) and 0.8 cm (0.2 to 2.3 cm), respectively. Four percent of patients were N1 (n=2) and 73% were estrogen receptor (ER) positive (n=32). Median follow-up was 6.2 years (2.4 to 8.0 y). Nearly all toxicities at 6 years were grade 1 to 2 except 1 instance of grade 3 telangiectasia (2%). Eleven percent (n=5) of patients had chronic asymptomatic fat necrosis whereas asymptomatic seromas were noted on mammogram in 13% of cases (n=6). Cosmesis at last follow-up was good or excellent in 91% of cases (n=40) and fair in 9% (n=4). Two of the previously reported rib fractures healed with conservative measures. There were no IBTR or RNF (6 y IBTR/RNF rate 0%); however, 2 patients experienced distant metastasis (4% at 6 y). The 6-year actuarial disease-free survival, cause-specific survival, and overall survival were 96%, 100%, and 93%, respectively. CONCLUSIONS: Hypofractionated 2-day APBI using brachytherapy resulted in excellent clinical outcomes with acceptable chronic toxicities.

**Williams GA** (2017). "How the AAO helped stop a Washington disaster: Two seemingly contradictory proposals shelved as a result of AAO action." Retina Today 2017(Jun): 23-24.

[Request Form](#)

*Department of Ophthalmology*

**Williams GA** (2017). "Surgical viewing; Do you see what i see?" Retina 37(7): 1219.

[Full-Text](#)

*Department of Ophthalmology*

**Williamson BD**, Gohn DC, Ramza BM, Singh B, Zhong Y, Li S and Shanahan L (2017). "Real-world evaluation of magnetic resonance imaging in patients with a magnetic resonance imaging conditional pacemaker system. Results of 4-year prospective follow-up in 2,629 patients." JACC: Clinical Electrophysiology. ePub Ahead of Print.

[Full-Text](#)

*Department of Internal Medicine*

Xiang XM and **Phillips DJ** (2017). "Nonepileptic myoclonus following bupropion overdose." Clinical Pediatrics: 9922817737082. ePub Ahead of Print.

[Full-Text](#)

*Department of Pediatrics*

Xie JX, Eshtehardi P, Varghese T, Goyal A, Mehta PK, Kang W, Leipsic J, Ó Hartaigh B, Bairey Merz CN, Berman DS, Gransar H, Budoff MJ, Achenbach S, Callister TQ, Marques H, Rubinshtein R, Al-Mallah MH, Andreini D, Pontone G, Cademartiri F, Maffei E, **Chinnaiyan K, Raff G**, Hadamitzky M, Hausleiter J, Feuchtner G, Kaufmann PA, Villines TC, Chow BJW, Min JK and Shaw LJ (2017). "Prognostic significance of nonobstructive left main coronary artery disease in women versus men: Long-term outcomes from the CONFIRM (Coronary CT Angiography Evaluation For Clinical Outcomes: An International Multicenter) registry." Circulation. Cardiovascular imaging 10(8): e006246.

[Full-Text](#)

*Department of Internal Medicine*

Xu Z, Mathieu D, Heroux F, Abbassy M, Barnett GH, Mohammadi AM, Kano H, Caruso J, **Grills IS**, Lee KC, Krishnan S, Kaufmann AM, Lee JYK, Pierce J, Maloney E, Kondziolka D, Hess JA, Chiang VL, Lunsford LD and Sheehan JP (2017). "Stereotactic radiosurgery for trigeminal neuralgia in patients with multiple sclerosis: A multicenter study."

International Journal of Radiation Oncology Biology Physics 99(2): E512-E513.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Facial pain response to various surgical interventions in patients with multiple sclerosis (MS)-related trigeminal neuralgia (TN) is considered much less favorable than for typical TN. No large patient series has been published regarding stereotactic radiosurgery (SRS), the least invasive treatment modality for



MS patients with medically refractory TN. This is a multicenter retrospective study investigating the clinical outcomes following SRS for patients with MS-related TN. Purpose/Objective(s): A total of 263 patients contributed by nine member institutions of the International Gamma Knife Research Consortium (IGKRF) constituted this study. The median age at the time of SRS was 57 years (range, 31 to 90 years). Eighty-seven patients (33%) had undergone various surgical procedures prior to SRS. Results: The median latency period of pain response after SRS was one month (range, 1 day to 14.1 months). Reasonable pain control (BNI Pain Scores I-IIIb) was achieved in 232 patients (88.2%). The median maintenance period from SRS was 14.1 months (range, 10 days to 10 years). The actuarial reasonable pain control maintenance rate at 1 year, 2 years, and 4 years was 54%, 35%, and 24%, respectively. There was a statistically significant correlation between the status of achieving BNI-I and the maintenance of facial pain recurrence-free rate. The median recurrence-free rate was 36 months and 12.2 months in patients achieving BNI-I and those of BNI greater than I, respectively (log rank test,  $P = 0.046$ ). A negative correlation between the time interval from the last initiation of MS exacerbation to the first SRS and possibility of reaching BNI-I was identified ( $P = 0.002$ , OR = 1.99, 95% CI, 1.30 to 3.12). Among 210 patients with known status of post-SRS complications, the new-onset of facial numbness (BNI-I or II) after SRS occurred in 21 patients (10%). Conclusion: In the largest series investigating the efficacy and safety of MS-related TN treated SRS, this approach offers a reasonable benefit to risk profile for patients who have exhausted medical management. More favorable initial response to SRS may predict a long-lasting pain control. Earlier treatment with SRS in the presence of MS relapse may lead to an increasing rate of achieving BNI-I facial pain relief.

Yadav S, Reeves A, Campian S, Sufka A and **Zakalik D** (2017). "Preoperative genetic testing impacts surgical decision making in BRCA mutation carriers with breast cancer: A retrospective cohort analysis." [Hereditary Cancer in Clinical Practice](#) 15(11): 1-8.

[Full-Text](#)

*Department of Internal Medicine*

Background: The impact of timing of genetic testing on surgical decision making in women with breast cancer and BRCA mutation is not well known. Methods: Women who were found to carry a deleterious BRCA mutation and had been diagnosed with breast cancer were identified from a database at Beaumont Health. Women who had received BRCA positive results at least a day prior to their index surgery were considered to be aware of their mutation status prior to surgery. Baseline characteristics and surgical choices were compared between women who were aware of their mutation status prior to surgery and those who were not. Fischer's exact test was used for categorical variables and Mann-Whitney U-Test was used for continuous variables. Results: A total of 220 patients were included in the final analysis, 208 (94.5%) with unilateral breast cancer and 12 (5.5%) with bilateral breast cancer. Out of the 208 patients with unilateral breast cancer, 106 (51.0%) patients were aware of their mutation status prior to index surgery while 102 (49%) were not. A significantly ( $p < 0.05$ ) higher proportion of women underwent contralateral prophylactic mastectomy in the group that was aware of their mutation status prior to index surgery compared to the group that was not (76.4% vs 14.7%). Conclusions: Our study demonstrates that knowledge of BRCA mutation status impacts surgical decision making in favor of bilateral mastectomy in patients who are aware of their results prior to index surgery. This finding supports the practice of preoperative genetic testing in patients with newly diagnosed breast cancer.

**Yan D**, Chen S, **Krauss DJ**, **Chen PY** and **Wilson GD** (2017). "FDG-PET imaging and assessment of tumor dose response (SF2) distribution." [International Journal of Radiation Oncology Biology Physics](#) 99(2): S197-S198.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): To derive tumor cell survival fraction after 2 Gy (SF2) distribution from multiple FDG-PET images obtained during the early weeks of radiotherapy, and evaluate the predictability of SF2 distribution on tumor local failure and recurrent location. Purpose/Objective(s): FDG-PET/CT images with PET image voxel size of  $4 \times 4 \times 4$  mm<sup>3</sup> obtained at the pre, weekly and 3/6 months post chemo-radiation treatment for each of 18 HN cancer patients were used for the study. Four of the 18 patients had biopsy proven local failure (22.2%) with the median follow-up time 22.2 (7.5 ~ 43.3) months. All weekly and post-

treatment PET/CT images of each patient were registered voxel by voxel to the pre-treatment planning PET/CT image. Tumor dose response marker, SF2(v), for each tumor voxel v was derived using the linear regression on the logarithm of the first 4 weekly tumor metabolic ratios defined as  $\ln TMR_i(v) = \ln(SUV_i(v)/SUV_0(v))$ ,  $i = 1$  to 4. Sensitivity and specificity of SF2-Volume parameters on the prediction of local tumor control and failure were calculated. The relationship between a locally recurrent tumor volume and radio-resistant tumor volume was evaluated. The locally recurrent tumor volume was defined as the iso-SUV volume formed using the %SUVmax on the post-treatment PET image, while the radio-resistant tumor volume was created using the tumor voxels with SF2 > 0.9. Results: The inter-and intra-tumor heterogeneities of SF2 distribution were large with the individual mean from 0.56 to 0.89, and the individual STD from 0.08 to 0.16. All failures had either large mean SF2 or large STD. Sensitivity and specificity, as well as the accuracy, of using  $V(SF2 > x)$  to predict treatment local failure were listed in Table 1. Tumor sub-volume with SF2 > 0.9 shows highly predictability on tumor local recurrence after the standard chemo-radiotherapy. In addition, Tumor local recurrent volume (defined using the 70, 80, or 90% of the Post-SUVmax) always contains the radio-resistant tumor voxels (Table 1). Conclusion: Tumor voxel dose response SF2 can be derived using multiple FDG-PET imaging obtained during the early weeks of radiation treatment. Distribution of SF2 has significant predictability power on tumor local failure, and the recurrent location. It can be used as the objective function to target radio-resistant tumor cells.

Ye H, **Krauss DJ**, **Dilworth JT** and **Stevens CW** (2017). "Using discrete-time survival analysis to examine hazard estimates of biochemical failure among prostate cancer patients." International Journal of Radiation Oncology Biology Physics 99(2): E420-E421.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): To research and explicate under what conditions the discrete-time survival method is comparable with Cox regression model respect to hazard estimation. Purpose/Objective(s): A medical research prostate cancer data in Michigan largest health care system was used. The survival and hazard functions of biochemical failure were tested under both Cox regression and discrete-time survival models. Data were restructured from "Person-Level" to "Person-Period" before testing in the discrete-time survival model. This study was undertaken to examine the effect of four different sample sizes and two different time periods to investigate their corresponding impact survival and hazard estimation and goodness of fit statistics between Cox regression and discrete-time survival models. Results: The univariate analysis was tested for each individual factor for different sample size  $n=1577$ ,  $n=1213$ ,  $n=809$ , and  $n=422$  under both Cox regression and discrete-time survival models. All single covariates were strong predictors of biochemical failure in the univariate analysis. In the Cox regression under sample size  $n=1577$ , the patient in high-risk group, with nadir time less than 2 years, or with no hormone treatment before RT had 2.541, 3.947, or 4.974 times more likely to have biochemical failure than the patient in the intermediate-risk group, nadir time greater than 2 year, or with hormone treatment before RT. In the discrete-time survival model with 10 time periods, the hazard estimates were 2.717 times for high-risk patient group, 5.457 times for no hormone receiver before RT, and 4.161 times higher for patients with less than 2 year nadir time. Similarly, in the discrete-time model with 5 time periods, the hazard estimates were 3.242, 5.150 and 3.303 times higher correspondingly. Conclusion: Both discrete-time survival model and Cox regression model provided similar hazard estimations. Sample size had an impact on survival analysis and hazard estimates. Small sample size had larger hazard estimation in general.

Yorke A, Zhang J, Vinogradskiy Y, Castillo E, **Grills I**, **Stevens C** and **Guerrero T** (2017). "Evaluation of automated treatment planning system for lung functional avoidance." Medical Physics 44(6): 2763.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: IMRT and VMAT treatment planning is a tedious and time-consuming process for the planner. Treatment plan quality can vary widely with the dosimetrist's experience and available time. We perform a retrospective study to evaluate automated treatment planning (AP) v. manual planning for functional avoidance in non-small cell lung cancer cases. The methods are compared on their dosimetric performance

in achieving planning criteria and required planning time. Methods: The treatment planning 4DCT images for 8 cases from an active functional avoidance clinical trial (NCT02528942) were re-planned using the AP techniques created in Pinnacle3 9.14. Two AP techniques were created one each for IMRT and VMAT, using organ at risk (OAR) and planning target volume (PTV) treatment criteria from our institution. AP plans were created using the technique that matched the patient prescription. The OAR objectives analyzed for, Lung-GTV and total vent were V20%, V5%, and mean dose. Other OAR include maximum dose to the great vessels, cord, esophagus, trachea and heart. A Wilcoxon ranked sum test was performed to evaluate the statistical significance between the two plans. Results: The average planning time for AP was about an hour, which was lower compared to the four hours for manual plans. In each case dose volume histogram analysis revealed that both the clinical plan and the AP plan satisfied the dose constraints criteria. A Wilcoxon ranked sum shows  $p = 0.742$  for D95% PTV,  $p = 0.383$  for mean dose for total ventilation, and  $p = 0.641$ ,  $p = 0.078$  and  $p = 0.547$  for max dose of heart, esophagus and trachea respectively. Conclusion: There was no significant difference in dosimetric values between the clinical plans and the AP plans except for the maximum dose to the cord ( $p = 0.039$ ), proximal bronchial tree ( $P = 0.039$ ) and V60% ( $p = 0.039$ ) of the esophagus. AP plans were faster to generate and easy to adapt in busy clinical workflow.

Yue Y, David J, Li Q, Blas K, Fraass B, **Kabolizadeh P** and Tuli R (2017). "18F-FDG PET-defined therapy response predicts acute hematologic toxicity for anal cancer patients treated with chemoradiation." *Medical Physics* 44(6): 3279. [Full-Text](#)

*Department of Radiation Oncology*

Purpose: Irradiation-induced hematologic toxicities (HT) during radiotherapy( RT) for anal cancer can lead to increased infection rates, bleeding, asthenia, and decreased treatment intensity via unplanned breaks. We hypothesize that HT in anal cancer patients treated with chemoradiation(CRT) correlates with change in active bone marrow (ABM) characterized by pre- and post- CRT PET/CT. Methods: Twenty-one locally advanced anal cancer patients treated with CRT from 2011-2016 were identified. 18F-FDG PET/CT scans were obtained 2 weeks pre- and 6 weeks post-CRT. HT was evaluated by weekly white blood cell count, absolute neutrophil count(ANC), hemoglobin and platelet nadirs. Total bone marrow (TBM) was defined on CT images, and segmented into three subregions: lumbosacral(LS), left and right iliac pelvis. PET images were normalized by liver uptakes. ABM was characterized in all PET images as the volume having standard uptake value (SUV) larger than mean uptakes in the TBM. Image variables (global, subregional SUVmean, SUVmax, ABMs) of pre- and post-CRT and their differential changes were evaluated as potential predictors of HT. Locoregional radiomics features were calculated using a 3D kernel-based approach. HT prediction was modeled by logistic regression with the Lasso algorithm with 10- fold cross-validation. HT endpoints were defined as change between baseline blood nadir and the lowest nadir values during and up to 2 weeks after treatment. Results: The lasso regression identified 5 predictors (pre-SUVmax, post-LS-ABM, LS-ABM change, homogeneity texture change, and variance). Ratios of LS-ABMs to TBM were reduced from 18.9% (pre-CRT) to 16.3% (post-CRT). This reduction of LS-ABM is significantly correlated to acute HT measured by ANC ( $p = 0.023$ ) and hemoglobin ( $p = 0.012$ ) nadirs. Conclusion: 18F-FDG-PET-derived active BM changes between pre- and post- CRT is significantly associated with HT in anal cancer patients undergoing CRT. LS-ABM is a robust surrogate for evaluation of HT and can be used to develop BM-sparing radiotherapy for reduction of potential HT.

Zamdborg L, Castillo E and **Guerrero TM** (2017). "A deep neural network for automated normal structure segmentation derived from normal clinical operations." *International Journal of Radiation Oncology Biology Physics* 99(2): S108.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Recent developments in the field of deep learning demonstrated its power for image classification and segmentation. If applied to radiotherapy planning, it promises greatly reduced contouring times, thus substantially improving clinical throughput. One major limitation of the technique, however, is its reliance on expert-generated ground truth for training. We present a proof of concept system for normal structure segmentation that is trained strictly on contours derived from normal clinical operations, without

any additional manual segmentation. Purpose/Objective(s): A data preprocessing system was engineered to automatically import all valid treatment plans from a clinically deployed treatment planning system (TPS). It converted the proprietary TPS contour format to industry-standard DICOM RTSTRUCT and selected a set of structure classes for training the neural network, dividing them into training and validation sets. No registration was performed on input images. All contours were assumed to represent the ground truth. The resulting dataset consisted of pairs of axial CT slices and voxel label maps. A fully-convolutional, deep residual neural network was constructed and trained on a single GPU core using the training set. Training was performed with the Adam algorithm and a categorical cross entropy loss. The output of the network was a probability map for the image, representing the probability that each voxel belonged to any of the available structure classes. The top probability was interpreted as the selected label for a voxel. No post-processing was performed. Dice scores were calculated on the validation set for each structure class. Results: All patients with radiotherapy plans from 2015 to 2016 at a single institution were included in this pilot analysis. Two thousand eight hundred sixty-seven plans from 1536 patients were imported. Forty structure classes, including background, were used for training. The network was trained with a batch size of 25 over 35 epochs on an NVIDIA M5000M GPU with 8 GB of RAM. The network as trained resulted in an average Dice score of 0.58 across all 40 structure classes; however, a wide range of labeling accuracies was evident, depending on the consistency and quantity of training data for a particular class. The system performed well on bone-bounded, well-demarcated soft tissue, and poorly-demarcated soft tissue structures. Excellent Dice scores of >0.95 were demonstrated for bilateral cochleas, 0.87 for the heart, and 0.88 for breast tissue. However, rarely and/or inconsistently contoured structures such as the brachial plexus exhibited a far lower Dice score of 0.11, and were often entirely extinguished in validation images. Conclusion: This preliminary work demonstrates good initial results for a fully-automated normal structure contouring system based on deep neural networks, trained on contours generated during normal clinic operations. Further work is needed to improve performance on rarely and/or inconsistently contoured structures.

Zazove P, Plegue MA, Kileny PR, McKee MM, Schleicher LS, Green LA, Sen A, Rapai ME, Guetterman TC and **Mulhem E** (2017). "Initial results of the Early Auditory Referral-Primary Care (EAR-PC) Study." [American Journal of Preventive Medicine](#) 53(4): e139-e146.

[Full-Text](#)

*Department of Family Medicine*

Zhang J, Chen S, Ding X, **Krauss D** and **Yan D** (2017). "Dosimetric accuracy for MRI based intensity modulated proton therapy for prostate cancer." [Medical Physics](#) 44(6): 3214.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: Magnetic Resonance Imaging (MRI) based radiotherapy treatment planning workflow for prostate and brain cancer has gained increasing popularity and rapid clinical adaptation. This study aims to investigate the dosimetric accuracy of intensity modulated proton therapy (IMPT) plans based on synthetic computed tomography (sCT) for prostate cancer. Methods: The sCT data of two patients were reconstructed using a previously published algorithm, which consists of atlas-based auto-segmentation and deformable image registration of MR-CT image pairs. T2-weighted turbo spin-echo (TE/ TR = 110/5000 ms, 90 flip angle, 0.45 × 0.45 × 3 mm<sup>3</sup> pixel resolution) images were acquired right after CT simulation on a 3T Philips Ingenia system. Laterally opposed two-field IMPT plans with robustness optimization (3.5% and 5 mm) were created for both standard simulation CT and sCT in a commercial treatment planning system. Dose agreement was evaluated using 3D gamma criteria (1%, 1 mm) for CTV coverage and normal tissue structures. Both pencil beam (PB) and Monte Carlo (MC) dose calculations were performed independently for comparison. Results: The maximum absolute dose difference between sCT and standard CT in CTV, femoral heads, rectum, and bladder were 4.2%, 0.33%, 0.37%, and 2.2% respectively for the PB dose engine; 3.67%, 2.99%, 1.96%, and 3.14% of dose difference was observed for the MC dose calculation. There was no significant change in gamma passing rate between the two dose calculation methods. The overall global gamma passing rate for the sCT IMPT plans were 97.9% (PB) and 95.8% (MC). The maximum dose difference of 31.5% occurs near the external surface. Conclusion: The current study found that IMPT with both pencil beam and MC dose

calculations on sCT showed favorable dose agreement with the simulation CT. Future studies will include more patient data and investigate sCT generation algorithms that can further improve the HU value accuracy near patient surface.

Zhang J, Vinogradskiy Y, Castillo E, Faught A, **Stevens C, Grills I** and **Guerrero T** (2017). "Considerations for further pulmonary toxicity reduction with 4DCT derived functional avoidance intensity modulated proton therapy." Medical Physics 44(6): 2751.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: With the advent of 4DCT based functional image-guided radiotherapy for lung cancer, CTventilation images have been translated into clinical usage for functional avoidance radiotherapy. The purpose of this study is to evaluate the potential dosimetric gains for functional avoidance with Intensity Modulated Proton Therapy (IMPT). Methods: Functional ventilation images were created using a prior published algorithm based on deformable registration and underlying CT density characteristics. 4DCT data from patients enrolled in a prospective functional avoidance clinical trial are replanned with robustness optimized IMPT (3.5% and 5 mm) and compared with VMAT. Dose degradation due to proton spot arrangement and breathing motion was studied by evaluating dynamic dose accumulation based on 4DCT with an in-house built interplay Python script. Patient tumor excursion was estimated by both weekly 4DCBCT and simulation 4DCT. Dosimetric parameters were compared between IMPT and VMAT. Both pencil beam and MC dose algorithms were evaluated. Dose re-painting (layer) method was applied to increase target coverage on the IMPT plans and decrease the motion interplay effect. Results: The CTV target coverage was adequate for all IMPT plans (D95 > 60 Gy). Compared with VMAT, IMPT plans have a relative dose reduction to most of the OARs (P < 0.05), including functional mean lung dose (-4.4 Gy), fV20 (-5.1%), and fV5 (-39.7%). Compared with pencil beam method, MC engine has a significant regional dose difference of 28% of the total prescription. Conclusion: We perform one of the first studies to investigate IMPT for functional avoidance thoracic RT. We found that IMPT was able to further spare healthy functional lung tissue with layer repainting technique to avoid excess dose to normal structures while maintaining satisfying target coverage. Studies have shown that the risk of pulmonary complications can be reduced with functional radiotherapy; our data demonstrate that even further toxicity reductions are possible with IMPT.

Zhou D, Liang J, Chen S and **Yan D** (2017). "Intra-treatment tumor position estimation: Feasibility and achievable accuracy." Medical Physics 44(6): 3184.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose: To investigate the feasibility and accuracy of using intra-treatment diaphragm motion to estimate lung tumor motion. Methods: Eighty-one paired 4D-CBCT images obtained at daily pre- and post-treatment from 19 lung cancer SBRT patients were used in the study. For each treatment fraction, the geometric relationship between diaphragm and tumor in S-I direction manifested on the pre-treatment images were obtained. Rigid registration was performed between the end-exhalation phase and each of the other 9 phases; diaphragm was registered based on its apex and tumor was registered based on a 3D-shaped ROI. Two estimation models for intra-treatment tumor position tracking were constructed using the linear and quadratic regression between diaphragm and tumor positions manifested on the pretreatment images. Applying the estimation model on the diaphragm motion obtained from the post-treatment 4D-CBCT image, the tumor motion positions were estimated, and compared with the actual tumor positions measured from post-treatment 4D-CBCT. Geometric relationships between diaphragm and tumor were used to test the estimation accuracy. Receiver-operating-characteristic (ROC) analysis was used to perform the statistic test. Results: Both the linear and quadratic models provide similar estimation accuracy. 95% of daily intra-treatment tumor motion positions can be estimated within 3 mm; 83% within 2 mm and 54% within 1 mm. Linear regression residual determined from pre-treatment image shows the largest prediction power for the intra-treatment tumor position estimation discrepancy < 3 mm with the AUC = 0.92 (p < 0.05). Conclusion: Utilizing the relationship between diaphragm and tumor positions manifested on the pre-treatment 4D CBCT image, intra-treatment tumor motion position can be estimated using the intra-treatment diaphragm motion

positions with the accuracy < 3 mm for 95% of confidence. The estimation accuracy can be predicted using the regression residual determined from the pre-treatment 4D CBCT image.

**Zhou J, Kabolizadeh P, Grills IS, Li X, Wang Y, Yan D and Ding X (2017).** "First feasibility study: Spot-scanning proton arc Stereotactic Radiosurgery (SRS) for localized spine metastasis." International Journal of Radiation Oncology Biology Physics 99(2): E747.

[Full-Text](#)

*Department of Radiation Oncology*

Purpose/Objective(s): Due to range uncertainties and large lateral penumbra in spot-scanning proton beam therapy, it could be challenging to treat spine metastasis with SRS. This is the first feasibility study to explore the potential dosimetric and clinical benefits of using SParc, a robust and delivery-efficient proton arc therapy technique, for spine metastasis SRS. Purpose/Objective(s): Five previously treated T-spine metastases were re-planned with SParc, IMPT (3 posterior beams), and VMAT (2 full arcs), per RTOG 0631, using Elekta Agility photon model and IBA's Proteus One PBS model (3.2mm spot size @230MeV). The prescription (RX) was 18 Gy in single fraction to 90% of the target volume. Two partial arcs (120 to 240) w and w/o 25 couch kick were used with a total of 104 control point sampling. A 3.5% range uncertainties were applied for robust optimization. All plans were normalized to the RX. Dmax and D0.35cc to the cord, as well as D10% and Dmean to the partial cord were analyzed. The doses to the lung (D1000cc), esophagus (D5cc and Dmax), and heart (D15cc, Dmax, and Dmean) were also evaluated. Conformity index (IDLX/target volume covered by RX) and R50 (IDL50/target volume) were calculated for all plans. Total delivery time for SParc and 3-field IMPT were calculated, assuming a 0.5s and 0.2s energy layer switching time. Results: The mean dose to the partial cord in SParc plans is significantly less than those of IMPT plans, 547±72 cGy vs. 607±78 cGy (p<0.03), but not for Dmax, D0.35cc and D10%. Lung D1000cc are 5±6 and 2±3 cGy for SParc and IMPT plans, respectively, vs. 101±89 cGy for the VMAT plans (p=0.02). The Dmax to the esophagus are significantly less with SParc, 1444±114 vs. 1528±90 cGy for the IMPT (p<0.05). D5cc to esophagus are significantly less in both SParc and IMPT plans, 522±239 and 625±243 cGy, vs. 791±179 cGy in the VMAT plans (p<0.01). The D15cc, Dmax and Dmean to the heart are significantly less in SParc/IMPT plans, 73±52/90±62, 415±312/614±454, 8±4/9±3 cGy, vs. 460±289, 759±494, 181±27 cGy in VMAT plans (p<0.01). Despite the range uncertainties associated with the proton beam therapy, the conformity index from SParc plans is comparable to the VMAT plans, 1.1±0.1 vs. 1.1±0.0, significantly higher than the IMPT of 1.3±0.1 (p<0.01). The R50 of SParc plans is significantly superior, 3.3 vs. 3.7 (p<0.01) for IMPT plans. Both are significantly better than VMAT plans of 4.1 (p<0.05). Conclusion: SParc therapy provide dosimetric advantage over IMPT in offering similar target volume coverage along with superior sparing of spinal cord and other adjacent critical structures, while offering better conformity index and delivery efficiency.VMATIMPTSParcTarget Vol. (cc)42 ± 20Cord Dmax (cGy)853 ± 87886 ± 94840 ± 56Cord D0.35cc683 ± 85754 ± 79699 ± 44Partial Cord D10%(cGy)738 ± 121792 ± 95744 ± 83Partial Cord Dmean532 ± 74607 ± 78547 ± 72Esophagus Dmax (cGy)1426 ± 1421529 ± 911444 ± 114Delivery time assuming 0.5s energy layer switching time309 ± 57316 ± 47Delivery time assuming 0.2s energy layer switching time330 ± 56274 ± 55.

**Zhou J, Liang J, Zhou D and Yan D (2017).** "Extraction of diaphragm motion curve from sinogram of KV cone beam projection images using Connected Threshold Image Filter (CTIF), a validation study." Medical Physics 44(6): 3143.

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*Department of Radiation Oncology*

Purpose: Diaphragm motion has been reported to be a reliable surrogate for lung tumor motion. We investigate extraction of diaphragm motion curve from sinogram of kV cone-beam projections using CTIF. Methods: Eight on-board cone beam (CB) projection image sets of lung tumor were used in this study. Acquisition sampling frequency was 5.6 Hz. A Gaussian gradient operator in the cranial-caudal (CC) direction was applied to each projection and the projection was projected to one line in the CC direction. All lines from all projections within one scan were aligned to form a 2D sinogram image ('Amsterdam Shroud' image). One or several seed points were manually selected within the diaphragm motion curve on the sinogram and a CTIF was used to extract the breathing curve. To evaluate the accuracy, reference curves were created with semi-automatically determined and manually verified diaphragm position on each projection. The mean and



the Pearson correlation coefficient between the extracted and the reference motion curve were analyzed. Results: Mean diaphragm motions (RMS value) were  $0.477 \pm 0.084$  cm and  $0.492 \pm 0.074$  cm for the extracted and reference curves, respectively. Mean differences between them and the Pearson correlation coefficient were  $0.015 \pm 0.231$  cm and 0.863 ( $p < 0.001$ ), respectively. 75% of the differences were  $<0.250$  cm. The majority of higher discrepancies occurred at the max in-hale positions. Conclusion: Diaphragm motion can be reliably and efficiently extracted from sinogram of the CB projection images. The effect of less accuracy at the max inhale positions could be insignificant due to the short period of tumor staying at those positions and the limited phase resolution of 4D-CT image sets. The extraction algorithm can be improved in the future with the help of pre-knowledge and advanced imaging process.

Zhou Y, **Krishnan A**, **Hafron J** and **Peters K** (2017). "Brain functional magnetic resonance imaging in children with spina bifida after nerve rerouting." *Medical Physics* 44(6): 3028-3029.

[Full-Text](#)

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Purpose: The mechanisms responsible for improved voiding after nerve rerouting surgery were not entirely clear and have not been thoroughly studied in patients with spina bifida. The purpose of this study is to assess functional activity in the areas of the brain that have been associated with bladder sensation and voiding with fMRI. Methods: Patients from our previous nerve rerouting pilot study were included in this study. The fMRI studies were performed on a 3.0T Philips MRI scanner using a single shot gradient echo EPI (GRE-EPI) pulse sequence with a twenty-channel head coil. The typical paradigms for a patient with maximum bladder capacity of 500 cc are shown in Figure 1. The filling and emptying bladder was automatically controlled by a modified in-house power injector. The MRI protocol is summarized in Table 1. Preprocessing and analysis of the fMRI data was conducted using the nordicBrainEx software (Nordic neurolab, Norway). Results: Four subjects were evaluated using the fMRI protocol described previously. All of them exhibited greater brain activations during different bladder activities. The regions that were activated shown in figure 2 using the p value of  $<0.001$  included the frontal cortex, supplemental motor area (SMA), opercula, hypothalamus, thalamus, cerebellum, periaqueductal gray (PAG) and pons after nerve rerouting surgery. Random-effects analysis showed that brain activity at large bladder volume or strong desire to void was generally stronger and more extensive than those at the condition of smaller bladder volume. Conclusion: Brain activation was seen in all 4 patients following the nerve rerouting surgery. The study suggests that the nerve rerouting in patients with spina bifida may result in brain functional reorganization and improve the neurological mechanisms of normal voiding. In conclusion, fMRI can be used to identify areas of brain activation with bladder filling/emptying in patients that have had nerve rerouting.