

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

PUBLICATION LIST

April - June 2019

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Abbas AE and Pibarot P (2019). "Hemodynamic characterization of aortic stenosis states." *Catheterization and Cardiovascular Interventions* 93(5): 1002-1023.

[Full Text](#)

Department of Internal Medicine

Aortic stenosis (AS) has become an increasingly prevalent clinical condition, as a result of the "greying of the population", the widespread application of sophisticated diagnostic tools including non-invasive imaging and invasive techniques, and the advent of minimally invasive surgical and percutaneous valve therapies. The diagnosis of severe AS traditionally has relied on the assessment of the mean transvalvular gradient (ΔP mean) and aortic valve area (AVA) by either echocardiography or catheterization. However, other hemodynamic variables as flow, pressure recovery, and jet eccentricity also play a major role in determining the final hemodynamic state of AS. Moreover, mismatch between ΔP mean and AVA as in low flow low gradient AS and discordance between catheterization and echocardiographic studies in grading severity of AS have increased the complexity of AS diagnosis. The present case-based treatise emphasizes a multi-modality approach to delineation of the hemodynamic pathophysiology of different AS states. Key points: Reduction in the aortic valve area, flow across the aortic valve, and direction of the aortic stenosis jet determine the pressure gradient generated across the aortic valve in patients with aortic stenosis. Discordance between echo and catheterization maximum gradients is related to the inherent temporal differences between the times of their acquisition. Discordance between echo and catheterization mean gradients is related to pressure recovery and assumptions in the application of Bernoulli equation to estimate the aortic valve gradient. Pressure recovery relates to the ratio of the aortic valve area and ascending aortic diameter as well as the jet direction. Mismatch between area and gradient criteria for aortic stenosis severity may occur with or without concordance between echocardiographic and catheterization data. Errors of measurement should be excluded prior to assuming any mismatch or discordance between the data. Area gradient mismatch occurs when the aortic valve area is in the severe range, while the gradient is in the non-severe range as in low flow low gradient aortic stenosis. Reverse area gradient mismatch occurs when the gradient is in the severe range, while the aortic valve area is in the non-severe range as in congenital aortic stenosis with an eccentric jet.

Abukhalaf SA, Alqarajeh F, Alzughayyar TZ, Abukarsh R, Ghazzawi I and **Novotny NM** (2019). "H-type anorectal malformation associated with H-type tracheoesophageal fistula." Journal of Pediatric Surgery Case Reports 44: May 2019.

[Full Text](#)

Department of Surgery

An extremely rare association of H-type anorectal malformation (ARM) and H-type tracheoesophageal fistula case is presented with literature review of the previously reported cases. Characteristics of the most commonly reported male H-type ARM patients are discussed. The proposed embryology and options for repair are discussed as well. Most surgical approaches have satisfactory results leaving approach selection to the surgeon experience and comfortability.

Abukhalaf SA, Alzughayyar TZ, Baniowda MA, Abukarsh R, Ghazzawi I, **Novotny NM** and Al Hammouri A (2019). "Postoperative intestinal intussusception in children, an easily missed culprit of postoperative intestinal obstruction: Case series and literature review." International Journal of Surgery Case Reports 60: 336-339.

[Full Text](#)

Department of Surgery

Background: Postoperative intestinal intussusception (POI) is a rare cause of intestinal obstruction with POI after surgical reduction of ileocolic intussusception being an extremely rare variant. POI was reported to follow many abdominal and non-abdominal operations. A late diagnosis can risk ischemia and necrosis. POI also increases the morbidity and mortality, rendering an early diagnosis and prompt management as lifesaving. Methods: We reviewed the medical charts retrospectively for the last ten years for patients with POI at Palestine Red Crescent Society Hospital, Hebron, Palestine. We reviewed the literature and presented the characteristics of the most reported cases of POI following surgical reduction of ileocolic intussusception. Results: We presented three cases of ileoileal POI and one case of ileocolic POI followed different primary operations. All but one patient presented in the first two weeks. The delayed presentation came two months after revision of a prolapsed colostomy. All patients managed successfully with operative manual reduction with no postoperative complications. Initially, we had struggles in the diagnosis of POI largely due to a low suspicion for this rare entity, but thereafter we kept POI in mind and managed the after-coming cases in an expeditious manner. Conclusion: Frequently, POI is misdiagnosed as postoperative adhesive obstruction. POI is challenging in diagnosis and needs a very high index of suspicion, mainly due to its rarity and atypical presentation. By keeping the possibility of POI in mind, one can easily diagnose it and prevent its consequences.

Ali-Ahmed F, Goyal V, Patel M, **Orelaru F, Haines DE** and Wong WS (2019). "High-power, low-flow, short-ablation duration-the key to avoid collateral injury?" Journal of Interventional Cardiac Electrophysiology 55(1): 9-16.

[Full Text](#)

OUWB Medical Student Author

Department of Internal Medicine

Background: A common approach to ablating along the posterior wall of the left atrium in atrial fibrillation ablation is to use low power with longer duration for durable lesions and reducing thermal injury. We hypothesize that similar lesions can be safely obtained at high power with low open-irrigation flow and low duration. Methods: Twenty-two porcine ventricles were placed in a tissue bath with circulating 0.45% NaCl at a maintained temperature of 37 degrees C. Bipolar radiofrequency ablation (RFA) with a 4-mm-tip irrigated, force-sensing catheter was performed with various combinations of irrigation, power, and duration at 20g of contact force. Fiber optic temperature probes were placed at depths of 3 mm and 5 mm. Temperature was measured during and 30 s after each ablation. Results: Two hundred sixty-eight lesions were made. At a fixed power and flow rate, lesion surface diameter, maximum lesion width, and lesion depth all increased with longer ablation duration. At fixed duration and irrigation flow rate, increased power led to increased lesion dimensions. At a lower flow rate (2 ml/min), surface lesion diameter and maximum width were significantly larger compared to a higher flow rate (17 ml/min), but lesion depth was not significantly different. The maximum temperature and the rate of temperature rise at a depth of 5 mm with different power settings and ablation durations were lower as compared to a depth of 3 mm at both flow rates (2 ml/min and 17 ml/min). Conclusions: Effective lesions can be performed with high-power and short-ablation durations,

thereby reducing RFA procedure time. Higher power, shorter duration lesions result in adequate temperature for myocardial lesion formation at 3 mm, but do not result in excessive temperature at 5 mm depth, potentially reducing the risk of collateral injury. Compared to higher irrigation flow rate, larger surface lesions and comparable maximum lesion width are achieved with lower irrigation flow rate, thus resulting in better lesion contiguity.

Bahado-Singh R, Vishweswaraiah S, Mishra NK, Guda C and **Radhakrishna U** (2019). "Placental DNA methylation changes for the detection of tetralogy of Fallot." [Ultrasound in Obstetrics and Gynecology](#). ePub Ahead of Print.

[Full Text](#)

Department of Obstetrics and Gynecology

Objectives: To determine whether the methylation level of cytosine nucleotides in placental DNA can be used to predict Tetralogy of Fallot (TOF) and provide insights into its mechanism of development. Methods: The Illumina HumanMethylation450 BeadChips assay was used to measure cytosine ('CpG' or 'cg') methylation (i.e. the addition 'methyl group') levels at loci throughout the placental genome. Area under the ROC curve (AUC) and 95% CI was calculated for TOF detection for CpG loci with significant methylation changes in TOF. False Discovery Rate (FDR) p-value <0.05 was considered significant. Ingenuity Pathway Analysis (IPA) (QIAGEN) was used to identify gene pathways that were significantly overexpressed and thus altered in TOF compared to controls. Results: We used 8 cases of isolated TOF and 10 unaffected newborn placentas. We found a total of 166 significantly differentially methylated CpG loci: TOF versus controls, in 166 separate genes. These biomarkers demonstrated from fair up to excellent individual predictive accuracy for TOF detection, with AUC ROC ≥ 0.75 (FDR p-value <0.001). The following CpG loci [gene] had high predictive accuracy: cg05273049 [ARHGAP22]: AUC (95% CI) = 1.0 (1.0, 1.0), cg02540011 [CDK5]: AUC (95% CI) = 0.96 (0.87, 1.0), cg08404201 [TRIM27] AUC (95% CI) = 0.95 (0.84, 1.0), cg00687252 [IER3]: AUC (95% CI) = 0.95 (0.84, 1.0). Pathway Analysis revealed over-representation (dysregulation) of gene pathways involved in normal cardiac development. Examples include: Cardiomyocyte Differentiation via BMP Receptors, Cardiac Hypertrophy Signaling, Role of NFAT in Cardiac Hypertrophy. Cardiac hypertrophy is an important feature of TOF. Conclusion: Placental cytosine methylation yielded accurate markers for TOF detection and provided mechanistic information on TOF development. Our work appears to confirm a central role of epigenetic changes and of the placenta in the development of TOF.

Bahado-Singh RO, Vishweswaraiah S, Aydas B, Mishra NK, Guda C and **Radhakrishna U** (2019). "Deep learning/artificial intelligence and blood-based DNA epigenomic prediction of cerebral palsy." [International Journal of Molecular Sciences](#) 20(9): 2075

[Full Text](#)

Department of Obstetrics and Gynecology

The etiology of cerebral palsy (CP) is complex and remains inadequately understood. Early detection of CP is an important clinical objective as this improves long term outcomes. We performed genome-wide DNA methylation analysis to identify epigenomic predictors of CP in newborns and to investigate disease pathogenesis. Methylation analysis of newborn blood DNA using an Illumina HumanMethylation450K array was performed in 23 CP cases and 21 unaffected controls. There were 230 significantly differentially-methylated CpG loci in 258 genes. Each locus had at least 2.0-fold change in methylation in CP versus controls with a FDR p-value ≤ 0.05 . Methylation level for each CpG locus had an area under the receiver operating curve (AUC) ≥ 0.75 for CP detection. Using Artificial Intelligence (AI) platforms/Machine Learning (ML) analysis, CpG methylation levels in a combination of 230 significantly differentially-methylated CpG loci in 258 genes had a 95% sensitivity and 94.4% specificity for newborn prediction of CP. Using pathway analysis, multiple canonical pathways plausibly linked to neuronal function were over-represented. Altered biological processes and functions included: neuromotor damage, malformation of major brain structures, brain growth, neuroprotection, neuronal development and de-differentiation, and cranial sensory neuron development. In conclusion, blood leucocyte epigenetic changes analyzed using AI/ML techniques appeared to accurately predict CP and provided plausible mechanistic information on CP pathogenesis.

Bahado-Singh RO, Yilmaz A, Bisgin H, Turkoglu O, Kumar P, Sherman E, Mrazik A, Odibo A and **Graham SF** (2019). "Artificial intelligence and the analysis of multi-platform metabolomics data for the detection of intrauterine growth restriction." [PLoS One](#) 14(4): e0214121.

[Full Text](#)

Department of Obstetrics and Gynecology

Objective: To interrogate the pathogenesis of intrauterine growth restriction (IUGR) and apply Artificial Intelligence (AI) techniques to multi-platform i.e. nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS) based metabolomic analysis for the prediction of IUGR. Materials and Methods: MS and NMR based metabolomic analysis were performed on cord blood serum from 40 IUGR (birth weight < 10th percentile) cases and 40 controls. Three variable selection algorithms namely: Correlation-based feature selection (CFS), Partial least squares regression (PLS) and Learning Vector Quantization (LVQ) were tested for their diagnostic performance. For each selected set of metabolites and the panel consists of metabolites common in three selection algorithms so-called overlapping set (OL), support vector machine (SVM) models were developed for which parameter selection was performed using 10-fold cross validations. Area under the receiver operating characteristics curve (AUC), sensitivity and specificity values were calculated for IUGR diagnosis. Metabolite set enrichment analysis (MSEA) was performed to identify which metabolic pathways were perturbed as a direct result of IUGR in cord blood serum. Results: All selected metabolites and their overlapping set achieved statistically significant accuracies in the range of 0.78-0.82 for their optimized SVM models. The model utilizing all metabolites in the dataset had an AUC = 0.91 with a sensitivity of 0.83 and specificity equal to 0.80. CFS and OL (Creatinine, C2, C4, lysoPC.a.C16.1, lysoPC.a.C20.3, lysoPC.a.C28.1, PC.aa.C24.0) showed the highest performance with sensitivity (0.87) and specificity (0.87), respectively. MSEA revealed significantly altered metabolic pathways in IUGR cases. Dysregulated pathways include: beta oxidation of very long fatty acids, oxidation of branched chain fatty acids, phospholipid biosynthesis, lysine degradation, urea cycle and fatty acid metabolism. Conclusion: A systematically selected panel of metabolites was shown to accurately detect IUGR in newborn cord blood serum. Significant disturbance of hepatic function and energy generating pathways were found in IUGR cases.

Bahl A, Hang B, Brackney A, Joseph S, Karabon P, Mohammad A, Nnanabu I and Shotkin P (2019). "Standard long IV catheters versus extended dwell catheters: A randomized comparison of ultrasound-guided catheter survival."

[American Journal of Emergency Medicine](#) 37(4): 715-721.

[Full Text](#)

Department of Emergency Medicine

Introduction: Establishing peripheral intravenous (IV) access is a vital step in providing emergency care. Ten to 30% of Emergency Department (ED) patients have difficult vascular access (DVA). Even after cannulation, early failure of US-guided IV catheters is a common complication. The primary goal of this study was to compare survival of a standard long IV catheter to a longer extended dwell catheter. Methods: This study was a prospective, randomized comparative evaluation of catheter longevity. Two catheters were used in the comparison: [1] a standard long IV catheter, the 4.78cm 20 gauge Becton Dickinson (BD); and [2] a 6cm 3 French (19.5 gauge) Access Scientific POWERWAND extended dwell catheter (EDC). Adult DVA patients in the ED with vein depths of 1.20cm-1.60cm and expected hospital admissions of at least 24h were recruited. Results: 120 patients were enrolled. Ultimately, 70 patients were included in the survival analysis, with 33 patients in the EDC group and 37 patients in the standard long IV group. EDC catheters had lower rates of failure (p=0.0016). Time to median catheter survival was 4.04days for EDC catheters versus 1.25days for the standard long IV catheter. Multivariate survival analysis also showed a significant survival benefit for the EDC catheter (p=0.0360). Conclusion: A longer extended dwell catheter represents a viable and favorable alternative to the standard longer IVs used for US-guided cannulation of veins >1.20cm in depth. These catheters have significantly improved survival rates with similar insertion success characteristics.

Basir MB, Kapur NK, Patel K, Salam MA, Schreiber T, Kaki A, **Hanson I, Almany S, Timmis S, Dixon S**, Kolski B, Todd J, Senter S, Marso S, Lasorda D, Wilkins C, Lalonde T, Attallah A, Larkin T, Dupont A, Marshall J, Patel N, Overly T, Green M, Tehrani B, Truesdell AG, Sharma R, Akhtar Y, McRae T, O'Neill B, Finley J, Rahman A, Foster M, Askari R, Goldsweig A, Martin S, Bharadwaj A, Khuddus M, Caputo C, Korpas D, Cawich I, McAllister D, Blank N, Alraies MC, Fisher R, Khandelwal A, Alaswad K, Lemor A, Johnson T, Hacala M, O'Neill WW and Natl Cardiogenic Shock I (2019). "Improved outcomes associated with the use of shock protocols: updates from the National Cardiogenic Shock Initiative." [Catheterization and Cardiovascular Interventions](#) 93(7): 1173-1183.

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Department of Internal Medicine

Background: The National Cardiogenic Shock Initiative is a single-arm, prospective, multicenter study to assess outcomes associated with early mechanical circulatory support (MCS) in patients presenting with acute myocardial infarction and cardiogenic shock (AMICS) treated with percutaneous coronary intervention (PCI). Methods: Between July 2016 and February 2019, 35 sites participated and enrolled into the study. All centers agreed to treat patients with AMICS using a standard protocol emphasizing invasive hemodynamic monitoring and rapid initiation of MCS. Inclusion and exclusion criteria mimicked those of the "SHOCK" trial with an additional exclusion criteria of intra-aortic balloon pump counter-pulsation prior to MCS. Results: A total of 171 consecutive patients were enrolled. Patients had an average age of 63 years, 77% were male, and 68% were admitted with AMICS. About 83% of patients were on vasopressors or inotropes, 20% had a witnessed out of hospital cardiac arrest, 29% had in-hospital cardiac arrest, and 10% were under active cardiopulmonary resuscitation during MCS implantation. In accordance with the protocol, 74% of patients had MCS implanted prior to PCI. Right heart catheterization was performed in 92%. About 78% of patients presented with ST-elevation myocardial infarction with average door to support times of 85 +/- 63 min and door to balloon times of 87 +/- 58 min. Survival to discharge was 72%. Creatinine ≥ 2 , lactate >4 , cardiac power output (CPO) <0.6 W, and age ≥ 70 years were predictors of mortality. Lactate and CPO measurements at 12-24 hr reliably predicted overall mortality postindex procedure. Conclusion: In contemporary practice, use of a shock protocol emphasizing best practices is associated with improved outcomes.

Baugh CW, Sun BC, Su E, Nicks BA, Shah MN, Adler DH, **Bastani A**, Caterino JM, **Clark CL**, Diercks DB, **Hollander JE**, Malveau SE, Nishijima DK, Stiffler KA, Storrow AB, Wilber ST, Yagapen AN, Weiss RE, Gibson TA and the Syncope Risk Stratification Study G (2019). "Variation in diagnostic testing for older patients with syncope in the emergency department." *American Journal of Emergency Medicine* 37(5): 810-816.

[Full Text](#)

Department of Urology

Department of Emergency Medicine

Background: Older adults presenting with syncope often undergo intensive diagnostic testing with unclear benefit. We determined the variation, frequency, yield, and costs of tests obtained to evaluate older persons with syncope. Methods: We conducted a prospective, multicenter observational cohort study in 11 academic emergency departments in the United States of 3686 patients aged ≥ 60 years presenting with syncope or presyncope. We measured the frequency, variation, yield, and costs (based on Medicare payment tables) of diagnostic tests performed at the index visit. Results: While most study rates were similar across sites, some were notably discordant (e.g., carotid ultrasound: mean 9.5%, range 1.1% to 49.3%). The most frequently-obtained diagnostic tests were initial troponin (88.6%), chest x-ray (75.1%), head CT (42.5%) and echocardiogram (35.5%). The yield or proportion of abnormal findings by diagnostic test ranged from 1.9% (electrocardiogram) to 42.0% (coronary angiography). Among the most common tests, echocardiogram had the highest proportion of abnormal results at 22.1%. Echocardiogram was an outlier in total cost at \$672,648, and had a cost per abnormal test of \$3129. Conclusion: Variation in diagnostic testing in older patients presenting with syncope exists. The yield and cost per abnormal result for common tests obtained to evaluate syncope are also highly variable. Selecting tests based on history and examination while also prioritizing less resource intensive and higher yield tests may ensure a more informed and cost-effective approach to evaluating older patients with syncope.

Bezjak A, Paulus R, Gaspar LE, Timmerman RD, Straube WL, Ryan WF, Garces YI, Pu AT, Singh AK, Videtic GM, McGarry RC, Iyengar P, Pantarotto JR, Urbanic JJ, Sun AY, Daly ME, **Grills IS**, Sperduto P, Normolle DP, Bradley JD and Choy H (2019). "Safety and efficacy of a five-fraction stereotactic body radiotherapy schedule for centrally located non-small-cell lung cancer: NRG Oncology/RTOG 0813 Trial." *Journal of Clinical Oncology* 37(15): 1316-1325.

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Department of Radiation Oncology

Purpose: Patients with centrally located early-stage non-small-cell lung cancer (NSCLC) are at a higher risk of toxicity from high-dose ablative radiotherapy. NRG Oncology/RTOG 0813 was a phase I/II study designed to determine the maximum tolerated dose (MTD), efficacy, and toxicity of stereotactic body radiotherapy (SBRT) for centrally located NSCLC. Materials and Methods: Medically inoperable patients with biopsy-proven, positron emission tomography-staged T1 to 2 (≤ 5 cm) N0M0 centrally located NSCLC were accrued into

a dose-escalating, five-fraction SBRT schedule that ranged from 10 to 12 Gy/fraction (fx) delivered over 1.5 to 2 weeks. Dose-limiting toxicity (DLT) was defined as any treatment-related grade 3 or worse predefined toxicity that occurred within the first year. MTD was defined as the SBRT dose at which the probability of DLT was closest to 20% without exceeding it. Results: One hundred twenty patients were accrued between February 2009 and September 2013. Patients were elderly, there were slightly more females, and the majority had a performance status of 0 to 1. Most cancers were T1 (65%) and squamous cell (45%). Organs closest to planning target volume/most at risk were the main bronchus and large vessels. Median follow-up was 37.9 months. Five patients experienced DLTs; MTD was 12.0 Gy/fx, which had a probability of a DLT of 7.2% (95% CI, 2.8% to 14.5%). Two-year rates for the 71 evaluable patients in the 11.5 and 12.0 Gy/fx cohorts were local control, 89.4% (90% CI, 81.6% to 97.4%) and 87.9% (90% CI, 78.8% to 97.0%); overall survival, 67.9% (95% CI, 50.4% to 80.3%) and 72.7% (95% CI, 54.1% to 84.8%); and progression-free survival, 52.2% (95% CI, 35.3% to 66.6%) and 54.5% (95% CI, 36.3% to 69.6%), respectively. Conclusion: The MTD for this study was 12.0 Gy/fx; it was associated with 7.2% DLTs and high rates of tumor control. Outcomes in this medically inoperable group of mostly elderly patients with comorbidities were comparable with that of patients with peripheral early-stage tumors.

Buehring GC, DeLaney A, Shen H, **Chu DL**, Razavian N, Schwartz DA, Demkovich ZR and Bates MN (2019). "Bovine leukemia virus discovered in human blood." [BMC Infectious Diseases](#) 19(1): 297.

[Full Text](#)

Department of Internal Medicine

Bovine leukemia virus (BLV) infection is widespread in cattle globally and is present in marketed beef and dairy products. Human infection with BLV has been reported in breast and lung cancer tissues and was significantly associated with breast cancer in 3 case-control studies. The purpose of this current research was to determine if BLV is present in human blood cells and if antibodies to BLV are related to blood cell infection.

Cappell MS and Gjeorgjievski M (2019). "Case report of a gastroenterologist successfully extracting at EGD a blunt, semi-rigid foreign body tightly impacted at the UES." [Minerva Gastroenterologica e Dietologica](#). ePub Ahead of Print.

[Request Form](#)

Department of Internal Medicine

Cappell MS, Gjeorgjievski M and Orosey M (2019). "Case report of novel endoscopic findings in SMA syndrome demonstrated by video endoscopy: Visibly pulsating, band-like, compression in third portion of duodenum, with the pulsations corresponding one-for-one with the radial pulse and EKG cycle." [Digestive Diseases and Sciences](#) 64(6): 1715-1718.

[Full Text](#)

Department of Internal Medicine

Cascino TM, McLaughlin VV, Richardson CR, **Behbahani-Nejad N**, Moles VM, Visovatti SH and Jackson EA (2019). "Barriers to physical activity in patients with pulmonary hypertension." [Pulmonary Circulation](#) 9(2).

[Full Text](#)

OUWB Medical Student Author

Patients with pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension (CTEPH) have low levels of physical activity (PA). Increased PA has health benefits including improved quality of life. This study aimed to identify patient-perceived barriers to PA that correlate with objectively measured PA in this population. We performed a cross-sectional survey of 40 patients with PAH and CTEPH. Participants rated how often 15 barriers interfere with being physically active on a 5-point Likert Scale. The primary outcome measure was PA quantified using the Fitbit Zip activity tracker for two weeks. The primary independent variables were the 15 barriers and a summary score (total average barriers). Separate multivariable linear regressions were performed to assess the association between the 15 barriers and the summary score and PA adjusting for age, sex, and PAH etiology. Of the participants, 85% (34/40) had valid step counts and were included. Of these 34, 85% (n = 29) were female and 91% (n = 31) had PAH. The median (interquartile range [IQR]) number of daily steps was 3913 (2309–6313). The barriers endorsed most strongly were lack of self-discipline, lack of energy, and lack of interest. In the multivariable analysis, a 1-unit

increase in perceived lack of interest, lack of enjoyment, and lack of skills was associated with a significant decrease in step counts of -1414 steps (95% confidence interval [CI] = (-2580 – -248), -1458 steps (-2404 – -511), and -1533 steps (-2910 – -156), respectively. Counseling and interventions aimed at increasing PA in patients with PAH should address interest, enjoyment, and skill development.

Cascino TM, McLaughlin VV, Richardson CR, **Behbahani-Nejad N**, Moles VM, Visovatti SH and Jackson EA (2019). "Physical activity and quality of life in patients with pulmonary hypertension." *The European Respiratory Journal* 53(6).
[Full Text](#)

OUWB Medical Student Author

Castillo E, Castillo R, Vinogradskiy Y, Dougherty M, Solis D, Myziuk N, Thompson A, Guerra R, **Nair G** and **Guerrero T** (2019). "Robust CT ventilation from the integral formulation of the Jacobian." *Medical Physics* 46(5): 2115-2125.
[Full Text](#)

Department of Internal Medicine

Department of Radiation Oncology

Computed tomography (CT) derived ventilation algorithms estimate the apparent voxel volume changes within an inhale/exhale CT image pair. Transformation-based methods compute these estimates solely from the spatial transformation acquired by applying a deformable image registration (DIR) algorithm to the image pair. However, approaches based on finite difference approximations of the transformation's Jacobian have been shown to be numerically unstable. As a result, transformation-based CT ventilation is poorly reproducible with respect to both DIR algorithm and CT acquisition method. Purpose: We introduce a novel Integrated Jacobian Formulation (IJF) method for estimating voxel volume changes under a DIR-recovered spatial transformation. The method is based on computing volume estimates of DIR mapped subregions using the hit-or-miss sampling algorithm for integral approximation. The novel approach allows for regional volume change estimates that (a) respect the resolution of the digital grid and (b) are based on approximations with quantitatively characterized and controllable levels of uncertainty. As such, the IJF method is designed to be robust to variations in DIR solutions and thus overall more reproducible. Methods: Numerically, Jacobian estimates are recovered by solving a simple constrained linear least squares problem that guarantees the recovered global volume change is equal to the global volume change obtained from the inhale and exhale lung segmentation masks. Reproducibility of the IJF method with respect to DIR solution was assessed using the expert-determined landmark point pairs and inhale/exhale phases from 10 four-dimensional computed tomographies (4DCTs) available on www.dir-lab.com. Reproducibility with respect to CT acquisition was assessed on the 4DCT and 4D cone beam CT (4DCBCT) images acquired for five lung cancer patients prior to radiotherapy. RESULTS: The ten Dir-Lab 4DCT cases were registered twice with the same DIR algorithm, but with different smoothing parameter. Finite difference Jacobian (FDJ) and IJF images were computed for both solutions. The average spatial errors (300 landmarks per case) for the two DIR solution methods were 0.98 (1.10) and 1.02 (1.11). The average Pearson correlation between the FDJ images computed from the two DIR solutions was 0.83 (0.03), while for the IJF images it was 1.00 (0.00). For intermodality assessment, the IJF and FDJ images were computed from the 4DCT and 4DCBCT of five patients. The average Pearson correlation of the spatially aligned FDJ images was 0.27 (0.11), while it was 0.77 (0.13) for the IJF method. Conclusion: The mathematical theory underpinning the IJF method allows for the generation of ventilation images that are (a) computed with respect to DIR spatial accuracy on the digital voxel grid and (b) based on DIR-measured subregional volume change estimates acquired with quantifiable and controllable levels of uncertainty. Analyses of the experiments are consistent with the mathematical theory and indicate that IJF ventilation imaging has a higher reproducibility with respect to both DIR algorithm and CT acquisition method, in comparison to the standard finite difference approach.

Catherwood MA, Gonzalez D, **Donaldson D**, Clifford R, Mills K and Thornton P (2019). "Relevance of TP53 for CLL diagnostics." *Journal of Clinical Pathology* 72(5): 343-346.

[Full Text](#)

Department of Emergency Medicine

TP53 disruption in chronic lymphocytic leukaemia (CLL) is a well-established prognostic marker and informs on the appropriate course of treatment for patients. TP53 status is commonly assessed by fluorescence in situ hybridisation for del(17 p) and Sanger sequencing for TP53 mutations. At present, current screening

methods for TP53 mutations fail to detect diagnostically relevant mutations potentially leading to inappropriate treatment decisions. In addition, low levels of mutations that are proving to be clinically relevant may not be discovered with current less sensitive techniques. This review describes the structure, function and regulation of the TP53 protein, the mutations found in cancer and CLL, the relevance of TP53 disruption in CLL and the current screening methods for TP53 mutations including next-generation sequencing.

Chagpar AB, Tsangaris T, Garcia-Cantu C, Howard-McNatt M, Chiba A, Berger AC, Levine E, Gass JS, Gallagher K, Lum SS, Martinez RD, Willis AI, Pandya SV, **Brown EA**, Fenton A, Mendiola A, Murray M, Haddad V, Solomon NL, Senthil M, Bansil H, Ollila D, Snyder SK, Edmonson D, Lazar M, Namm JP, Li F, Butler M, McGowan NE, Herrera ME, Avitan YP, Yoder B and Dupont E (2019). "Does resection of cavity shave margins result in lower positive margin and re-excision rates in patients with stage 0-III breast cancer? Results from a prospective multicenter randomized controlled trial." Cancer Research 79(4). S1.

[Full Text](#)

Department of Surgery

Introduction: Routine resection of cavity shave margins has been shown in single center studies to result in a significant reduction in positive margin and re-excision rates. In this prospective multicenter randomized controlled trial, we sought to validate these findings across practice settings. Methods: Nine centers across the United States, varying in practice setting and patient population, participated in this clinical trial of 398 stage 0-III breast cancer patients undergoing partial mastectomy (with or without resection of selective cavity margins). Participants were stratified by clinical stage and randomized 1:1 to either have routine cavity shave margins resected ("shave") or not ("no shave"). Randomization group was revealed to the surgeon intraoperatively, after they had completed their standard partial mastectomy and were ready to close. Positive margins were defined as "tumor at ink" for invasive cancer or within 2 mm for ductal carcinoma in situ (DCIS). Adverse events were defined as seromas requiring percutaneous drainage, and/or hematomas or abscesses requiring operative intervention. Results: Median patient age was 65 (range? 29-94). 116 patients had invasive disease, 74 had DCIS, 179 had both, and 29 had no residual cancer at the time of partial mastectomy. The median invasive cancer size was 1.2 cm (range? 0.05-8.00 cm)? the median extent of DCIS was 0.9 cm (range? 0.05-6.40 cm). The "shave" and "no shave" groups were well matched at baseline for clinicopathologic and demographic factors. View inline Prior to randomization, positive margin rates were similar in the "shave" and "no shave" groups (38.1% vs. 37.3%, respectively, $p=0.918$). After randomization, however, those in the "shave" group were significantly less likely than those in the "no shave" group to have positive margins (8.6% vs. 37.3%, respectively, $p<0.001$). They were also less likely to require re-excision or mastectomy for margin clearance (8.6% vs. 23.9%, $p<0.001$). There were no significant differences between the two groups in terms of adverse events ($p=0.280$). Rates of seroma (1.5% vs. 0.5%, $p=0.368$), hematoma (0.5% vs. 0.5%, $p=1.000$) and abscess (0.3% vs. 0%, $p=0.495$) were similar between the "shave" and "no shave" groups, respectively. Conclusion: Resection of cavity shave margins significantly reduces positive margin and re-excision rates in patients with stage 0-III breast cancer undergoing partial mastectomy.

Chang AM, Hollander JE, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2019).

"Recurrent syncope is not an independent risk predictor for future syncopal events or adverse outcomes." American Journal of Emergency Medicine 37(5): 869-872.

[Full Text](#)

OUWB Medical Student Author

Department of Urology

Department of Emergency Medicine

Almost 20% of patients with syncope will experience another event. It is unknown whether recurrent syncope is a marker for a higher or lower risk etiology of syncope. The goal of this study is to determine whether older adults with recurrent syncope have a higher likelihood of 30-day serious clinical events than patients experiencing their first episode. Methods: This study is a pre-specified secondary analysis of a multicenter prospective, observational study conducted at 11 emergency departments in the US. Adults 60 years or older who presented with syncope or near syncope were enrolled. The primary outcome was occurrence of 30-day serious outcome. The secondary outcome was 30-day serious cardiac arrhythmia. In multivariate analysis, we

assessed whether prior syncope was an independent predictor of 30-day serious events. Results: The study cohort included 3580 patients: 1281 (35.8%) had prior syncope and 2299 (64.2%) were presenting with first episode of syncope. 498 (13.9%) patients had 1 prior episode while 771 (21.5%) had >1 prior episode. Those with recurrent syncope were more likely to have congestive heart failure, coronary artery disease, previous diagnosis of arrhythmia, and an abnormal ECG. Overall, 657 (18.4%) of the cohort had a serious outcome by 30 days after index ED visit. In multivariate analysis, we found no significant difference in risk of events (adjusted odds ratio 1.09; 95% confidence interval 0.90-1.31; p=0.387). Conclusion: In older adults with syncope, a prior history of syncope within the year does not increase the risk for serious 30-day events.

Chen CJ, Shabo LM, Ding D, Ironside N, Kano H, Mathieu D, Kondziolka D, Feliciano C, Rodriguez-Mercado R, **Grills IS**, Barnett G, Lunsford LD, Sheehan JP and Int Radiosurg Res F (2019). "Seizure presentation in patients with brain arteriovenous malformations treated with stereotactic radiosurgery: A multicenter study." World Neurosurgery 126: E634-E640.

[Full Text](#)

Department of Radiation Oncology

Background: Seizures are the second most common clinical presentation in patients with brain arteriovenous malformations (AVMs) and the most common presentation of unruptured AVMs. The aim of the present multicenter, retrospective cohort study was to identify the predictors of seizure presentation in patients with AVM who had undergone stereotactic radiosurgery (SRS). Methods: We performed a retrospective review of patients with AVM who had been treated with SRS at 8 participating International Radiosurgery Research Foundation sites. The patient and AVM characteristics were compared between those with and without seizure presentation in univariable and multivariable models. A subgroup analysis of patients with cortical AVMs was performed. Results: The study cohort included 2333 patients with AVM, including 419 (18%) with and 1914 (82%) without a seizure presentation. Previous AVM resection (odds ratio [OR], 7.65; P = 0.001), a lack of previous AVM hemorrhage (OR, 0.004; P < 0.001), a cortical AVM location (OR, 1559.42; P < 0.001), a lower Spetzler-Martin grade (OR, 0.51; P = 0.007), and a higher Virginia radiosurgery AVM score (OR, 1.46; P = 0.008) were independent predictors of seizure presentation. The rate of seizure presentation in patients with cortical AVMs was 27%. Previous AVM resection (OR, 8.36; P < 0.001), a lack of previous AVM hemorrhage (OR, 0.004; P < 0.001), and temporal AVM location (OR, 4.15; P < 0.001) were independent predictors of seizure presentation for cortical AVMs. Conclusion: We identified multiple factors associated with seizure presentation in patients with AVM to undergo SRS. Previous AVM resection, a cortical AVM location, and a lack of previous AVM hemorrhage were the strongest predictors of pre-SRS seizures. The Spetzler-Martin grade and Virginia radiosurgery AVM score might have a role in seizure risk stratification. For cortical AVMs, a temporal lobe location was predictive of seizure presentation.

Chuang YC, Tyagi P, Luo HL, Lee WC, Wang HJ, Huang CC and **Chancellor MB** (2019). "Long-term functional change of cryoinjury-induced detrusor underactivity and effects of extracorporeal shock wave therapy in a rat model." International Urology and Nephrology 51(4): 617-626.

[Full Text](#)

Department of Urology

Purpose: To investigate the long-term functional change of cryoinjury-induced detrusor underactivity (DU) and the therapeutic potential of repeated low-energy shock wave therapy (LESW). Methods: Fifty-six female Sprague-Dawley rats were assigned into sham and cryoinjury of bladder with or without LESW (0.05 or 0.12 mJ/mm²; 200 pulses; twice a week for 2 weeks after cryoinjury). Under halothane anesthesia, an incision was made in lower abdomen, and cryoinjury was provoked by bilateral placement of a chilled aluminum rod on the bladder filled with 1 ml saline. Measurement of contractile responses to KCl and carbachol in vitro, conscious voiding, and histological and protein changes were performed on week 1, 2, and 4 after cryoinjury. Results: Cryoinjury of bladder induced a significant decrease in the detrusor contraction amplitude at week 1 (55.0%) and week 2 (57.2%), but the decrease in the contractile response to KCl and carbachol was only noted at week 1. At week 1, significantly increased COX-2 and TGF- β 1 expression accompanied a decrease of VEGF and CGRP expression. At week 4, there was a partial recovery of voiding function and a significant increase in the Ki-67 staining. LESW treatment at higher energy level further amplified the Ki-67 staining and improved the recovery of contraction amplitude and the expression of TGF- β 1 and VEGF. Conclusions: Cryoinjury of detrusor induces DU/UAB with functional impairment lasting for up

to 4 weeks, but the associated molecular changes are restored by 2 weeks. LESW improved bladder wall composition, and hastened functional recovery from cryoinjury.

Clark CL, Gibson TA, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, Diercks DB, **Hollander JE**, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2019). "Do high-sensitivity troponin and natriuretic peptide predict death or serious cardiac outcomes after syncope?" Academic Emergency Medicine 26(5): 528-538.

[Full Text](#)

Department of Emergency Medicine

Department of Urology

Objectives: An estimated 1.2 million annual emergency department (ED) visits for syncope/near syncope occur in the United States. Cardiac biomarkers are frequently obtained during the ED evaluation, but the prognostic value of index high-sensitivity troponin (hscTnT) and natriuretic peptide (NT-proBNP) are unclear. The objective of this study was to determine if hscTnT and NT-proBNP drawn in the ED are independently associated with 30-day death/serious cardiac outcomes in adult patients presenting with syncope. Methods: A prespecified secondary analysis of a prospective, observational trial enrolling participants \geq age 60 presenting with syncope, at 11 United States hospitals, was conducted between April 2013 and September 2016. Exclusions included seizure, stroke, transient ischemic attack, trauma, intoxication, hypoglycemia, persistent confusion, mechanical/electrical invention, prior enrollment, or predicted poor follow-up. Within 3 hours of consent, hscTnT and NT-proBNP were collected and later analyzed centrally using Roche Elecsys Gen 5 STAT and 2010 Cobas, respectively. Primary outcome was combined 30-day all-cause mortality and serious cardiac events. Adjusting for illness severity, using multivariate logistic regression analysis, variations between primary outcome and biomarkers were estimated, adjusting absolute risk associated with ranges of biomarkers using Bayesian Markov Chain Monte Carlo methods. Results: The cohort included 3,392 patients; 367 (10.8%) experienced the primary outcome. Adjusted absolute risk for the primary outcome increased with hscTnT and NT-proBNP levels. HscTnT levels \leq 5 ng/L were associated with a 4% (95% confidence interval [CI] = 3%-5%) outcome risk, and hscTnT $>$ 50 ng/L, a 29% (95% CI = 26%-33%) risk. NT-proBNP levels \leq 125 ng/L were associated with a 4% (95% CI = 4%-5%) risk, and NT-proBNP $>$ 2,000 ng/L a 29% (95% CI = 25%-32%) risk. Likelihood ratios and predictive values demonstrated similar results. Sensitivity analyses excluding ED index serious outcomes demonstrated similar findings. Conclusions: hscTnT and NT-proBNP are independent predictors of 30-day death and serious outcomes in older ED patients presenting with syncope.

Cohen L, Lohani S, Butler R and Coffey M (2019). "Factors associated with hemodialysis withdrawal: Analysis of a single institution's experience." American Journal of Kidney Diseases 73(5): 665-666.

[Request Form](#)

Department of Internal Medicine

Cole DW, Svider PF, **Shenouda KG**, **Lee PB**, Yoo NG, McLeod TM, Mutchnick SA, Yoo GH, Kaufman RJ, Callaghan MU and Fribley AM (2019). "Targeting the unfolded protein response in head and neck and oral cavity cancers." Experimental Cell Research. 382(1): 111386.

[Full Text](#)

OUIWB Medical Student Author

Many FDA-approved anti-cancer therapies, targeted toward a wide array of molecular targets and signaling networks, have been demonstrated to activate the unfolded protein response (UPR). Despite a critical role for UPR signaling in the apoptotic execution of cancer cells by many of these compounds, the authors are currently unaware of any instance whereby a cancer drug was developed with the UPR as the intended target. With the essential role of the UPR as a driving force in the genesis and maintenance of the malignant phenotype, a great number of pre-clinical studies have surged into the medical literature describing the ability of dozens of compounds to induce UPR signaling in a myriad of cancer models. The focus of the current work is to review the literature and explore the role of the UPR as a mediator of chemotherapy-induced cell death in squamous cell carcinomas of the head and neck (HNSCC) and oral cavity (OCSCC), with an emphasis on preclinical studies.

Crist K, Murphy D, Wright MO, **Wallace E** and Manning ML (2019). "The role of the infection preventionist in a transformed healthcare system: Meeting healthcare needs in the 21(st) century." [American Journal of Infection Control](#) 47(4): 352-357.

[Full Text](#)

Department of Family Medicine and Community Health

Culcasi R, Hanna A, Dabjan M, Buelow K, **Wilson G** and Snyder M (2019). "Eulerian amplification to predict skin toxicity in radiotherapy." [Medical Physics](#) 46(6): E665-E665.

[Request Form](#)

Department of Radiation Oncology

Da Silva GR, **Graham S**, Ugur Z, Yilmaz A, Kee F, Young I, Woodside J and Green B (2019). "Application of LC-MS-based metabolomics to identify and validate nutritional biomarkers in a cohort of Northern Irish older adults." [European Journal of Clinical Investigation](#) 49: 77-78.

[Request Form](#)

Department of Obstetrics and Gynecology

Daley E, Nahm N, Koueiter D and **Zaltz I** (2019). "Does compensatory anterior pelvic tilt decrease after bilateral periacetabular osteotomy?" [Clinical Orthopaedics and Related Research](#) 477(5): 1168-1175.

[Full Text](#)

Department of Orthopedic Surgery

Background: The kinetic link among the lumbar spine, pelvic tilt, and the hip has been hypothesized, but this relationship requires further study in acetabular dysplasia. Anecdotal reports suggest that patients may compensate for acetabular dysplasia with an involuntary increase in anterior pelvic tilt; it is not known if this relationship is affected by acetabular reorientation. Questions/purposes (1) Does compensatory pelvic tilt decrease on preoperatively obtained standing AP pelvis radiographs compared with those obtained at a minimum of 6 months after bilateral periacetabular osteotomy (PAO)? (2) Does a modified surrogate measurement of pelvic tilt, the pubic symphysis to sacroiliac (PS-SI) index, correlate with a physical synthetic bones model in which pelvic tilt can be directly measured? (3) Can the PS-SI index demonstrate high interrater reliability? Methods: We assessed the surgical records of one surgeon, who participates in the longitudinally maintained Academic Network of Conservational Hip Outcomes Research (ANCHOR) registry, for patients who had undergone the second side of a staged bilateral PAO between 2007 and 2016; there were 113 such patients. Of those, 70 (62%) were lost to followup within 6 months of the second PAO or did not have adequate imaging studies, and another three (3%) were excluded for prespecified reasons, leaving 40 (35%) for evaluation in this retrospective study. Standing preoperative and most recent postoperative AP pelvis radiographs were used to measure the Tönnis angle, anterior wall index, posterior wall index, lateral center-edge angle, pubis symphysis-to-sacrococcygeal junction distance, and the PS-SI index. The most recent radiographs were obtained at a mean of 16 ± 6 months after the second PAO. We chose 6 months as the minimum because at this time point, the majority of patients have reached their maximum clinical improvement and are no longer limited by postoperative muscle dysfunction. Statistical analysis was performed using the intraclass correlation coefficient (ICC) for interrater reliability and paired t-tests for assessing change in measurements from pre- to postoperative. Additionally, a model was created using a physical synthetic bones model in which pelvic tilt could be directly measured. This model was secured through bilateral acetabuli on a mount and rotated through 5° increases in pelvic tilt. AP pelvis radiographs were obtained at each point, the PS-SI index was measured, and a regression analysis performed to evaluate for trend. Results: Overall, 37 of 40 patients (93%) had a decrease in pelvic tilt, as measured by the PS-SI index. The mean amount of pelvic tilt as measured by the PS-SI index decreased after surgery when comparing the preoperative with latest radiographs on this parameter (97 ± 14 mm versus 89 ± 13 mm, mean difference 8 ± 9 mm; 95% confidence interval, -11 to -5; range 17 increase to 24 decrease, $p < 0.001$). A linear relationship between pelvic tilt and PS-SI index ($\text{PS-SI index} = 5.0^\circ + 3.6^\circ \cdot \text{tilt}$, $R^2 = 0.99$) was identified in the synthetic bones validation model. Finally, the interrater reliability was found to be excellent for the PS-SI index preoperatively (ICC = 0.986) and postoperatively (ICC = 0.988). Conclusions: We found a modest reduction in anterior pelvic tilt after bilateral PAO. This finding suggests that acetabular reorientation affects pelvic position. In clinical practice, patients with acetabular dysplasia may compensate with dynamic

and reversible changes in pelvic tilt. The PS-SI index is a reproducible tool to measure the height of the pelvic inlet as an assessment of pelvic tilt. In the future, clinical studies should evaluate the clinical implications of these radiographic findings, including the assessment of back pain, which although multifactorial may be influenced by pelvic tilt. Level of Evidence Level III, therapeutic study.

Daley E and **Zaltz I** (2019). "Strategies to avoid osteonecrosis in unstable slipped capital femoral epiphysis: A critical analysis review." *JBJS reviews* 7(4): e7.

[Full Text](#)

Department of Orthopedic Surgery

Osteonecrosis of the femoral epiphysis following slipped capital femoral epiphysis (SCFE) causes substantial patient morbidity. The etiology of osteonecrosis following SCFE is multifactorial, and multiple treatment strategies, including techniques of epiphyseal reduction, capsulotomy, and timing of surgical intervention, that are intended to reduce this risk have been utilized. At the present time, because of conflicting data and the lack of high-level evidence, there are a paucity of data to determine the role that these techniques play in reducing the risk of osteonecrosis. Further scientific research is needed to understand the etiology of osteonecrosis following SCFE.

Dallo FJ, Ruterbusch JJ, McCullough JR, Sreedhar S, Schwartz K and **Mulhem E** (2019). "Diabetes management among Arab Americans who sought care at a large metropolitan hospital system in Michigan." *Journal of Immigrant and Minority Health* 21(3): 490-496.

[Full Text](#)

Department of Family Medicine and Community Health

To estimate and compare the management of diabetes among Arab, Asian, non-Hispanic Black, and non-Hispanic Whites attending a large health system in metropolitan Detroit. Data were electronically abstracted for 6622 adult patients with diabetes. Dependent variables were uptake of A1c testing and results, LDL-C testing and results, and eye examination frequency. The independent variable was race/ethnicity. Logistic regression models were used to examine the association between Arab Americans and non-Hispanic Whites for each of the dependent variables while controlling for confounders. Arab Americans were 38% more likely than non-Hispanic Whites to report an A1c > 7% (OR 1.38; 95% CI 1.03, 1.87). Arab Americans were 62% less likely to receive an eye exam compared to non-Hispanic Whites (OR 1.62; 95% CI 1.21, 2.17). Population based studies about diabetes management among Arab Americans will facilitate tailored interventions aimed at preventing/delaying diabetes complications and reducing premature mortality due to diabetes.

Danko M, Karabon P, Pople B and **Dekhne N** (2019). "Evaluating patient satisfaction in autologous breast reconstruction vs. implant reconstruction." *Annals of Surgical Oncology* 26: 151-152.

[Request Form](#)

Department of Surgery

OUIWB Medical Student Author

David SW, Khan ZA, Patel NC, Metzger DC, Wood FO, Wasserman HS, Lotfi AS, **Hanson ID**, **Dixon SR**, LaLonde TA, Genereux P, Ozan MO, Maehara A and Stone GW (2019). "Evaluation of intracoronary hyperoxemic oxygen therapy in acute anterior myocardial infarction: The IC-HOT study." *Catheterization and Cardiovascular Interventions* 93(5): 882-890.

[Full Text](#)

Department of Internal Medicine

Background: In the randomized AMIHOT-II trial, supersaturated oxygen [SSO₂] delivered into the left anterior descending (LAD) artery via an indwelling intracoronary infusion catheter following primary percutaneous coronary intervention (PCI) significantly reduced infarct size in patients with anterior ST-segment elevation myocardial infarction (STEMI) but resulted in a numerically higher incidence of safety events. Objectives: The IC-HOT study evaluated the safety of SSO₂ therapy selectively delivered to the left main coronary artery (LMCA) for 60minutes after PCI in patients with anterior STEMI. Methods: SSO₂ therapy was administered to the LMCA after stent implantation in 100 patients with anterior STEMI and proximal or mid-LAD occlusion presenting within 6hours of symptom onset. The primary endpoint was the 30-day composite rate of net adverse clinical events (NACE) (death, reinfarction, clinically driven target vessel

revascularization, stent thrombosis, severe heart failure, or TIMI major/minor bleeding) compared against an objective performance goal of 10.7%. Cardiac magnetic resonance imaging was performed at 4 and 30 days to assess infarct size. Results: SSO(2) delivery was successful in 98% of patients. NACE at 30 days occurred 7.1% of patients (meeting the primary safety endpoint of the study); there were no deaths, only one stent thrombosis and one case of severe heart failure. Median [interquartile range] infarct size was 24.1% [14.4%, 31.6%] at 4 days and 19.4% [8.8%, 28.9%] at 30 days. Conclusion: Following primary PCI in acute anterior STEMI, infusion of SSO2 via the LMCA was feasible and was associated with a favorable early safety profile.

Ding DL, Chen CJ, Starke RM, Kano H, Lee JYK, Mathieu D, Feliciano C, Rodriguez-Mercado R, Almodovar L, **Grills IS**, Kondziolka D, Barnett GH, Lunsford LD and Sheehan JP (2019). "Risk of brain arteriovenous malformation hemorrhage before and after stereotactic radiosurgery: A multicenter study." *Stroke* 50(6): 1384-1391.

[Request Form](#)

Department of Radiation Oncology

Background and Purpose: Understanding the hemorrhage risks associated with brain arteriovenous malformations (AVMs) before and after stereotactic radiosurgery (SRS) is important. The aims of this multicenter, retrospective cohort study are to evaluate and compare the rates of pre- and post-SRS AVM hemorrhage and identify risk factors. Methods: We pooled AVM SRS data from 8 institutions participating in the International Radiosurgery Research Foundation. Predictors of post-SRS hemorrhage were determined using a multivariate logistic regression model. Pre- and post-SRS hemorrhage rates were compared using Fisher exact test. Ruptured and unruptured AVMs were matched in a 1:1 ratio using propensity scores, and their outcomes were compared. Results: The study cohort comprised 2320 AVM patients who underwent SRS. Deep AVM location (odds ratio, 1.86; 95% CI, 1.19-2.92; P=0.007), the presence of an AVM-associated arterial aneurysm (odds ratio, 2.44; 95% CI, 1.63-3.66; P<0.001), and lower SRS margin dose (odds ratio, 0.93; 95% CI, 0.88-0.98; P=0.005) were independent predictors of post-SRS hemorrhage. The post-SRS hemorrhage rate was lower for obliterated versus patent AVMs (6.0 versus 22.3 hemorrhages/1000 person-years; P<0.001). The AVM hemorrhage rate decreased from 15.4 hemorrhages/1000 person-years before SRS to 11.9 after SRS (P=0.001). The outcomes of the matched ruptured versus unruptured AVM cohorts were similar. Conclusions: SRS appears to reduce the risk of AVM hemorrhage, although this effect is predominantly driven by obliteration. Deep-seated AVMs are more likely to rupture during the latency period after SRS. AVM-associated aneurysms should be considered for selective occlusion before SRS of the nidus to ameliorate the post-SRS hemorrhage rate of these lesions.

Ding X, Li X, Liu G, Stevens C, Yan D and Kabolizadeh P (2019). "Energy layer switching sequence optimization algorithm for an efficiency proton arc therapy delivery." *Radiotherapy and Oncology* 133: S489-S489.

[Request Form](#)

Department of Radiation Oncology

Ding XF, Zhou J, Li XQ, Blas K, Liu G, Wang YA, Qin A, Chinnaiyan P, Yan D, Stevens C, Grills I and Kabolizadeh P (2019). "Improving dosimetric outcome for hippocampus and cochlea sparing whole brain radiotherapy using spot-scanning proton arc therapy." *Acta Oncologica* 58(4): 483-490.

[Request Form](#)

Department of Radiation Oncology

Purpose: Recently, there have been significant interests towards whole-brain radiotherapy (WBRT) with hippocampal and cochlea sparing. Herein, we present a novel robust, continuous and delivery-efficient spot-scanning proton arc therapy technique (SPArc) to improve such dosimetric outcome. Material and Methods: Eight patients were selected for whole brain radiotherapy to evaluate the feasibility of using SPArc for hippocampal and cochlea sparing. Both SPArc and robust optimized Intensity Modulated Proton Therapy (ro-IMPT) plans were generated using the robust optimization of +/- 3.5% range and 3 mm setup uncertainties and were compared to the Volumetric Modulated Arc Therapy (VMAT). Root-mean-square deviation doses (RMSDs) Volume Histogram, or RVH, was used for proton plan robustness evaluation. Proton plan delivery time was calculated based on a using full gantry rotation with 1 RPM, 2 ms spot switching time, minimum monitor unit per spot = 0.01, and simulate different proton system with energy-layer-switching-time (ELST) from 0.2 to 5 s. Results: SPArc plans showed significant dosimetric improvements in multiple dosimetric parameters. The mean dose to the hippocampus was reduced to 6.20 Gy [RBE] compared to

VMAT 10.89 Gy [RBE] ($p < .001$) and ro-IMPT 9.38 Gy [RBE] ($p < .001$); D100% to the hippocampus was reduced to 4.50 Gy [RBE] compared to VMAT 9.16 Gy [RBE] ($p = .001$) and ro-IMPT 7.02 Gy [RBE] ($p = .002$); cochlear mean dose was reduced to 7.75 Gy [RBE] compared to VMAT 11.52 Gy [RBE] ($p = .018$) and ro-IMPT 10.15 Gy [RBE] ($p = .037$); and maximum dose was reduced to 33.84 Gy [RBE] compared to ro-IMPT 36.37 Gy [RBE]. RVH analysis shows SPArc is more robust in Organs-at-risk(OARs) sparing such as hippocampus, cochlea, lens, and eyes. The average total estimated treatment delivery time were 412 s, 627 s, and 1694 s using ELST of 0.2 s, 1 s, and 5 s for SPArc plans, respectively, compared with values of 547 s ($p < .001$), 626 s ($p = .484$), and 1025 s ($p = .002$) for ro-IMPT plans. Conclusion: SPArc could significantly reduce the dose delivered to the hippocampus and cochlea in patients being treated with WBRT. In addition, SPArc plans could potentially achieve similar or faster delivery time in modern proton machine with ELST of less than 1 s.

Eden CL, **Long G**, Major M, Studzinski D and **Brown OW** (2019). "Does type II endoleak with an enlarging aortic sac predispose to development of a type IA endoleak?" *Journal of Vascular Surgery* 69(6): E206-E206.

[Request Form](#)

Department of Surgery

Engel TW, Thomas C, Medado P, **Bastani A**, Reed B, Millis S and O'Neil BJ (2019). "End tidal CO₂ and cerebral oximetry for the prediction of return of spontaneous circulation during cardiopulmonary resuscitation." *Resuscitation* 139: 174-181.

[Full Text](#)

Department of Emergency Medicine

Background: End Tidal CO₂ (ETCO₂) is a reasonable predictor of Return of Spontaneous Circulation (ROSC) in cardiac arrest (CA), though with many limitations. Cerebral Oximetry (CerOx) non-invasively measures brain O₂ saturation and correlates with flow. Objectives This study compares ETCO₂ and CerOx for ROSC prediction during both out of hospital (OHCA) and emergency department cardiac arrests (EDCA). Methods: We conducted a prospective study on CA patients resuscitated in the ED. ETCO₂ and CerOx simultaneously measured during ED CPR. Data was analyzed with logistic regression modeling and area under the curve (AUC). Results: 176 patients were analyzed, 66.7% were witnessed, 52.8% had bystander CPR. EMS alert to ED arrival was 27.0 ± 10.6 min. Initial rhythm was 31.8% asystole, 27.8% PEA, 25.6% VF/VT with 26.1% achieving ROSC. AUC predictors of ROSC were: last 5 min trend [CerOx = 0.82 ; ETCO₂ = 0.74], delta first to last [CerOx = 0.86 ; ETCO₂ = 0.73], the penultimate minute [CerOx = 0.81 ; ETCO₂ = 0.76], and final minute [CerOx = 0.89 ; ETCO₂ = 0.77]. AUC comparison of simultaneous measurements ($n = 125$) revealed: last 5 min trend [CerOx = 0.80 ; ETCO₂ = 0.79], delta first to last [CerOx = 0.83 ; ETCO₂ = 0.75], penultimate minute [CerOx = 0.83 ETCO₂ = 0.74], and final minute [CerOx = 0.89 ; ETCO₂ = 0.75]. Conclusions: Our data shows, both ETCO₂ and rSO₂ are good predictors of ROSC. We found CerOx superior to ETCO₂ in predicting ROSC.

Esfandiari H, Taubenslag K, Shah P, Goyal S, **Weiner AJ**, Severson ML, Weiner A, Grover DS, Bussel, II and Loewen NA (2019). "Two-year data comparison of ab interno trabeculectomy and trabecular bypass stenting using exact matching." *Journal of Cataract and Refractive Surgery* 45(5): 608-614.

[Request Form](#)

OUWB Medical Student Author

Purpose: To create a balanced comparison of ab interno trabeculectomy (AIT) (Trabectome) and trabecular bypass stenting (TBS) (iStent). Setting: Eye and Ear Institute, Pittsburgh, Pennsylvania, Ross Eye Institute, Buffalo, New York, and Glaucoma Associates of Texas, Dallas, USA. Design: Retrospective case series. Methods: The primary outcome measure was an unmedicated intraocular pressure (IOP) of 21 mm Hg or less and the secondary measure was an unmedicated IOP reduction of 20% or more at 2 years. Patients were matched by baseline IOP, number of glaucoma medications, and glaucoma type using exact matching and by age using nearest neighbor matching. Individuals without a close match were excluded. All surgeries were combined with phacoemulsification. Results: One hundred fifty-four AIT eyes and 110 TBS eyes were analyzed. Forty-eight AIT patients were exactly matched with 48 TBS patients. Both groups had a mean baseline IOP of 15.3 mm Hg \pm 3.1 (SD). At 24 months, the mean IOP was 13.9 \pm 3.3 mm Hg in AIT patients and 16.8 \pm 2.8 mm Hg in TBS patients and the mean number of medications was 0.7 \pm 1.0 and 1.7 \pm 1.2, respectively (both $P = .04$). At 24 months, the IOP was 21 mm Hg or less without medications in 53% of AIT patients and 16.6% of TBS patients ($P < .05$). At that time, 17.6% of patients in the AIT group but

no patient in the TBS group had an IOP reduction of 20% or more without medication. Conclusion: An exact matching comparison of AIT and TBS showed greater IOP reduction with fewer medications after AIT.

Fay K, Almendares O, **Robinson-Dunn B** and Schrag S (2019). "Antenatal and intrapartum nucleic acid amplification test use for group B Streptococcus screening-United States, 2016." Diagnostic Microbiology and Infectious Disease 94(2): 157-159.

[Full Text](#)

Department of Pathology

Perinatal group B Streptococcus (GBS) disease prevention guidelines in 2010 allowed for processing of screening specimens by nucleic acid amplification tests (NAATs); however, the extent of NAAT use is unknown. A 2016 laboratory survey sent to 10 surveillance sites found that 18.7% of responding laboratories offered NAAT for GBS screening (antenatal only: 7.3%; intrapartum only: 4.1%; both: 3.4%).

Figuroa Rodriguez F, Faieta Lasarcina A and **Davila Grijalva F** (2019). "Mitral valve endocarditis with perforation from a urinary source: An unusual case and literature review." Case Reports in Cardiology 2019: 5496851.

[Full Text](#)

Department of Internal Medicine

Aerococcus urinae (AU) is a rare pathogen, identified as gram-positive, catalase-negative coccus that grows in pairs and clusters which has been reported to mainly cause urinary tract infections (UTI), especially in elderly males. Treatment for this microorganism is usually with beta-lactams although cultures with antibiotic susceptibility testing are imperative. We present a case of AU endocarditis initially treated with IV antibiotics; nevertheless, the patient required emergent mitral valve replacement due to severe mitral insufficiency and perforation. We also present an analysis with high-yield points summarizing epidemiology, risk factors, microbiology, clinical features, diagnostic workup, and management of AU in general and AU endocarditis. Finally, we post a literature review of relevant cases and the impact of different variables associated with it.

Figuroa Rodriguez F, Uddin A and **Nasr J** (2019). "Primary pulmonary malignant melanoma found while evaluating new onset cough: A case presentation and literature review." Case Reports in Pulmonology 2019: 3867831.

[Full Text](#)

Department of Internal Medicine

Malignant melanoma is a nonepithelial neoplasm of melanocytes. It is tremendously rare for this condition to primarily involve the respiratory tract, accounting only for 0.01% of the lung malignancies. It often presents as a solitary nodule provoking mass effect and/or obstructive symptom. It most commonly affects patients 50 years old and older, with no gender predilection. Complete surgical excision is the treatment of choice; nevertheless, chemotherapy or radiation might be necessary depending on tumor location and/or metastasis status. Recently, biochemotherapy and immunotherapy have emerged as promising treatment modalities. We present a case of Primary Pulmonary Malignant Melanoma (PPMM) in a 76-year-old male with no previous personal or family history of cancer who presented with new onset nonproductive cough. We also present an analysis with high yield points summarizing clinical features, diagnostic workup, and management of PPMM. Finally, we post a table summarizing all the cases ever reported in English literature.

Fischgrund JS, Rhyne A, Frank J, Sasso R, Kitchel S, Bae H, Yeung C, Truumees E, Schaufele M, Yuan P, Vajkoczy P, Depalma M, Anderson DG, Thibodeau L and Meyer B (2019). "Intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 2-Year results from a prospective randomized double-blind sham-controlled multicenter study." International Journal of Spine Surgery 13(2): 110-119.

[Full Text](#)

Department of Orthopedic Surgery

Background: The purpose of the present study is to report the 2-year clinical outcomes for chronic low back pain (CLBP) patients treated with radiofrequency (RF) ablation of the basivertebral nerve (BVN) in a randomized controlled trial that previously reported 1-year follow up. Methods: A total of 147 patients were treated with RF ablation of the BVN in a randomized controlled trial designed to demonstrate safety and efficacy as part of a Food and Drug Administration-Investigational Device Exemption trial. Evaluations, including patient self-assessments, physical and neurological examinations, and safety assessments, were performed at 2 and 6 weeks, and 3, 6, 12, 18, and 24 months postoperatively. Participants randomized to the

sham control arm were allowed to cross to RF ablation at 12 months. Due to a high rate of crossover, RF ablation treated participants acted as their own control in a comparison to baseline for the 24-month outcomes. Results: Clinical improvements in the Oswestry Disability Index (ODI), Visual Analog Scale (VAS), and the Medical Outcomes Trust Short-Form Health Survey Physical Component Summary were statistically significant compared to baseline at all follow-up time points through 2 years. The mean percent improvements in ODI and VAS compared to baseline at 2 years were 53.7 and 52.9%, respectively. Responder rates for ODI and VAS were also maintained through 2 years with patients showing clinically meaningful improvements in both: ODI \geq 10-point improvement in 76.4% of patients and ODI \geq 20-point improvement in 57.5%; VAS \geq 1.5 cm improvement in 70.2% of patients. Conclusions: Patients treated with RF ablation of the BVN for CLBP exhibited sustained clinical benefits in ODI and VAS and maintained high responder rates at 2 years following treatment. Basivertebral nerve ablation appears to be a durable, minimally invasive treatment for the relief of CLBP.

Flierl MA, Sobh AN, Culp BM, **Baker EA** and Sporer SM (2019). "Evaluation of the painful total knee arthroplasty." *Journal of the American Academy of Orthopaedic Surgeons*. ePub Ahead of Print.

[Full Text](#)

Department of Orthopedic Surgery

Total knee arthroplasty (TKA) has been associated with notable improvements in health-related quality of life of patients with end-stage knee arthritis. Although most patients experience substantial symptomatic relief after TKA, up to 19% of patients are unsatisfied with their outcome. With the dramatic, projected increase in the number of TKAs performed annually, it is crucial to appreciate the various modes of failure associated with this procedure. A comprehensive understanding of the symptomatology and thorough clinical examination aid in identifying the etiology of ongoing knee pain. Ancillary testing including conventional laboratory analyses, imaging studies, and diagnostic injections supplement a thorough history and physical examination. In addition, novel laboratory markers, RNA/DNA-based tests, and novel imaging modalities are emerging as beneficial tools in evaluating patients with a painful TKA. A well-structured, algorithmic approach in the management of these patients is essential in correctly diagnosing the patient and optimizing clinical outcomes.

Foster B, Jackson W, Foster C, Dess R, Abu-Isa E, McLaughlin PW, Merrick G, Hearn J, Spratt D, Liauw S and **Hamstra D** (2019). "Application of a prognostic stratification system for high-risk prostate cancer to patients treated with radiotherapy: Implications for treatment optimization." *American Journal of Clinical Oncology* 42(4): 382-390.

[Full Text](#)

Department of Radiation Oncology

Objectives: We applied an established prognostic model to high-risk prostate cancer (HRPC) patients treated with radiotherapy (RT) and evaluated the influence of clinical and treatment variables on treatment outcomes. Methods: In total, 1075 HRPC patients undergoing definitive radiotherapy (RT) between 1995 and 2010 were retrospectively reviewed. Median follow-up was 62.3 months. Patients received either dose-escalated external beam radiotherapy (n=628, EBRT) or combined-modality radiotherapy (n=447, pelvic RT and low-dose rate brachytherapy boost, CMRT). 82.9% received androgen-deprivation therapy (ADT). A prognostic model stratified patients into predefined groups (good, intermediate, and poor). Kaplan-Meier methods and Cox proportional hazards regressions assessed biochemical failure (BF), distant metastasis (DM), prostate cancer-specific mortality (PCSM) and overall mortality (OM). C-indices analyzed predictive value. Results: The model was prognostic; C-indices for BF, DM, PCSM and OM were: 0.62, 0.64, 0.61, and 0.57. On multivariate analysis, CMRT and longer ADT (\geq 24 mo) were associated with improved BF, DM, and PCSM. Gleason score (GS) 9-10 was the strongest predictor of PCSM. C-indices for BF, DM, PCSM, and OM using a 4-compartment model incorporating GS 9-10 were: 0.62, 0.65, 0.68, and 0.56. In poor-prognosis patients (GS 8-10+additional risk factors), CMRT+LTADT ($>$ 12 mo) had 10-year PCSM (3.7% \pm 3.6%), comparing favorably to 25.8% \pm 9.2% with EBRT+LTADT. Conclusions: The model applies to high-risk RT patients; GS 9-10 remains a powerful predictor of PCSM. Comparing similar prognosis patients, CMRT is associated with improved disease-specific outcomes relative to EBRT. In poor-prognosis patients, CMRT+LTADT yields superior 10-year PCSM, potentially improving RT treatment personalization for those with HRPC.

Francis JH, Milman T, Grossniklaus H, Albert D, **Folberg R**, Levitin G, Coupland S, Catalanotti F, Rabady D, Kandoth C, Busam K and Abramson D (2019). "GNAQ mutations in diffuse and solitary choroidal hemangiomas." [Ophthalmology](#) 126(5): 759-763.

[Full Text](#)

Department of Ophthalmology

Department of Pathology

Purpose: GNAQ mutations have been identified in port wine stains (both syndromic and nonsyndromic) and melanocytic ocular neoplasms. This study investigates the presence of GNAQ mutations in diffuse (those associated with Sturge–Weber syndrome [SWS]) and solitary choroidal hemangiomas. Participants: Tissue from 11 patients with the following diagnoses: port wine stain (n = 3), diffuse choroidal hemangioma (n = 1), solitary choroidal hemangioma (n = 6), and choroidal nevus (n = 1). Methods: Ten specimens were interrogated with Memorial Sloan Kettering–Integrated Mutation Profiling of Actionable Cancer Targets, a hybridization capture-based next-generation sequencing assay for targeted deep sequencing of all exons and selected introns of 468 key cancer genes in formalin-fixed, paraffin-embedded tumors. Digital polymerase chain reaction was used to detect GNAQ Q209 mutation in 1 specimen. Main Outcome Measures: Detection of GNAQ codon-specific mutation. Results: Activating somatic GNAQ mutations (c.547C > T; p.Arg183Cys) were found in 100% (3 of 3) of the port wine stain and in the diffuse choroidal hemangioma. Somatic GNAQ mutations (c.626A > T; p.Gln209Leu) were found in 100% (6 of 6) of the solitary choroidal hemangiomas and (c.626A > C; p.Gln209Pro) in the choroidal nevus. Conclusions: GNAQ mutations occur in both diffuse and solitary hemangiomas, although at distinct codons. An R183 codon is mutant in diffuse choroidal hemangiomas, consistent with other Sturge–Weber vascular malformations. By contrast, solitary choroidal hemangiomas have mutations in the Q209 codon, similar to other intraocular melanocytic neoplasms.

Ghiam BK, Xu LY and Berry JL (2019). "Aqueous humor markers in retinoblastoma." [Translational Vision Science & Technology](#) 8(2):110-119.

[Full Text](#)

OUWB Medical Student Author

Purpose: Retinoblastoma (Rb) is the most common primary intraocular cancer in children. Unlike with most solid tumors, direct biopsy is contraindicated due to risk of tumor dissemination. However, recent therapeutic techniques have allowed for the safe extraction of aqueous humor (AH) from eyes undergoing therapy, providing the unique opportunity to use AH as a liquid biopsy for Rb. Although the extraction of AH in Rb eyes undergoing therapy is new, the consideration of whether there are tumor biomarkers in the AH is not. The current manuscript is a systematic review of all studies that have examined biomarkers in the AH of Rb eyes. The authors hypothesized that AH sampling and analysis of tumor biomarkers may have new clinical relevance for the diagnosis, prognosis, and/or management of Rb. Methods: A comprehensive database search (PubMed, Web of Science, Embase, and Cochrane Databases) was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement to identify articles on AH markers in Rb eyes. Inclusion criteria included English language articles with original reports on AH markers in the eyes of patients with confirmed Rb. Data on marker type, number of eyes, marker means and ranges, and when available, control values and clinicopathological correlations were collected. Articles were stratified based on marker type, and assessed quantitatively and qualitatively. Results: An initial database search produced 325 articles, and an additional 11 articles were identified through searching citations. After removing duplicates and applying the eligibility criteria, we selected 27 articles to be included in the current review. A total of 463 eyes with histologically confirmed Rb were included in this review. The various markers and their values, with comparison to controls and clinicopathological correlations, are discussed. Conclusions: AH sampling and tumor biomarker analysis in eyes without undergoing enucleation have the potential to revolutionize the management of Rb.

Gnanenthiran SR, Naoum C, Leipsic JA, Achenbach S, Al-Mallah MH, Andrieni D, Bax JJ, Berman DS, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Cury RC, DeLago A, Feuchtner G, Hadamitzky M, Hausleiter J, Kaufman PA, Kim YJ, Maffei E, Marques H, de Araujo Goncalves P, Pontone G, **Raff GL**, Rubinshtein R, Shaw LJ, Villines TC, Gransar H, Lu Y, Jones EC, Pena JM, Lin FY, Kritharides L and Min JK (2019). "Long-term prognostic utility of computed tomography coronary angiography in older populations." [European Heart Journal Cardiovascular](#)

[Imaging](#) April 2019: jez067.

[Full Text](#)

Department of Internal Medicine

Aims: The long-term prognostic value of coronary computed tomography angiography (CCTA)-identified coronary artery disease (CAD) has not been evaluated in elderly patients (≥ 70 years). We compared the ability of coronary CCTA to predict 5-year mortality in older vs. younger populations. **Methods and Results:** From the prospective CONFIRM (COronary CT Angiography EvaluatioN For Clinical Outcomes: An InteRnational Multicenter) registry, we analysed CCTA results according to age < 70 years ($n = 7198$) vs. ≥ 70 years ($n = 1786$). The severity of CAD was classified according to: (i) maximal stenosis degree per vessel: none, non-obstructive (1-49%), or obstructive ($> 50\%$); (ii) segment involvement score (SIS): number of segments with plaque. Cox-proportional hazard models assessed the relationship between CCTA findings and time to mortality. At a mean 5.6 \pm 1.1 year follow-up, CCTA-identified CAD predicted increased mortality compared with patients with a normal CCTA in both < 70 years [non-obstructive hazard ratio (HR) confidence interval (CI): 1.70 (1.19-2.41); one-vessel: 1.65 (1.03-2.67); two-vessel: 2.24 (1.21-4.15); three-vessel/left main: 4.12 (2.27-7.46), $P < 0.001$] and ≥ 70 years [non-obstructive: 1.84 (1.15-2.95); one-vessel: HR (CI): 2.28 (1.37-3.81); two-vessel: 2.36 (1.33-4.19); three-vessel/left main: 2.41 (1.33-4.36), $P = 0.014$]. Similarly, SIS was predictive of mortality in both < 70 years [SIS 1-3: 1.57 (1.10-2.24); SIS ≥ 4 : 2.42 (1.65-3.57), $P < 0.001$] and ≥ 70 years [SIS 1-3: 1.73 (1.07-2.79); SIS ≥ 4 : 2.45 (1.52-3.93), $P < 0.001$]. CCTA findings similarly predicted long-term major adverse cardiovascular outcomes (MACE) (all-cause mortality, myocardial infarction, and late revascularization) in both groups compared with patients with no CAD. **Conclusion:** The presence and extent of CAD is a meaningful stratifier of long-term mortality and MACE in patients aged < 70 years and ≥ 70 years old. The presence of obstructive and non-obstructive disease and the burden of atherosclerosis determined by SIS remain important predictors of prognosis in older populations.

Gupta A, Gabbard A, **Smith MD, Micale M, Boyanton BL and Huang J** (2019). "Biclonal splenic marginal zone lymphoma with T cell-rich background and aggressive transformation to large cell lymphoma." [Journal of Hematopathology](#) 12(2): 91-98.

[Full Text](#)

Department of Pathology

Marginal zone B cell lymphomas (MZL) are biologically heterogeneous, rarely demonstrating biclonality, complex cytogenetic abnormalities, or T cell predominance. We report a case of biclonal splenic MZL, T cell-rich variant with an abnormal karyotype that progressed to large B cell lymphoma. A 74-year-old female presented with pancytopenia, weight loss, fever, and splenomegaly. Microscopically, the spleen revealed an extensive, vaguely nodular lymphoid proliferation, composed of small lymphocytes, majority of which were reactive T cells. B cells were mostly small and $< 5\%$ of total lymphocytes. Focal follicular dendritic cell networks were present, but germinal centers were absent. Flow cytometric analysis revealed two distinct CD5 and CD10 negative B cell clones, one kappa positive and one lambda positive. Conventional cytogenetic analysis revealed the following abnormal karyotype: 47,XX,add(7)(q36),del(7)(q22),add(21)(p11.2),+mar[10]/46,XX[10]. Immunoglobulin heavy chain gene rearrangement showed two monoclonal peaks of different magnitude, consistent with biclonality. Overall, these features favored a low-grade splenic MZL. The staging bone marrow biopsy was normocellular with few interstitial lymphoid aggregates, composed of small lymphocytes, consistent with minimal involvement by low-grade B cell lymphoma. The patient improved without adjuvant chemotherapy; however, 12 months later, she developed anemia and lymphocytosis. Subsequent bone marrow biopsy showed extensive involvement by a large B cell lymphoma and complex karyotype with the previously identified abnormalities, as well as additional numerical and structural aberrations, consistent with cytogenetic evolution and biclonal gene rearrangement. These findings were consistent with transformation. This case demonstrates a unique pathological presentation of splenic MZL with disease progression, highlighting the importance of an integrated approach for lymphoma classification and the difficulties in diagnosing such cases.

Gupta MP, Yonekawa Y, Campbell JP, Rusu I, Zahid S, Patel SN, Chau F, Jonas KE, Oltra E, Orlin A, Chang J, Horowitz J, Abramson DH, Marr B, **Capone A** and Paul Chan RV (2019). "Early diagnosis and management of aggressive posterior vitreoretinopathy presenting in premature neonates." [Ophthalmic Surgery, Lasers & Imaging Retina](#) 50(4): 201-207.

[Full Text](#)

Department of Ophthalmology

Background and Objective: Aggressive posterior vitreoretinopathy (APVR) manifests with a broad area of retinal avascularity, progressive neovascularization, and/or tractional retinal detachment during the neonatal period. Patients and Methods: A multicenter, retrospective, observational, consecutive case series study was performed to evaluate the retinal findings and structural retinal outcomes in patients treated for APVR within the first 3 months of life. Results: Three premature neonates with a non-retinopathy of prematurity (ROP) APVR identified during routine ROP screening exams exhibited relatively severe, rapidly progressive retinal vascular abnormalities. Immediate laser photocoagulation of the avascular retina and vitrectomy for traction retinal detachment within several days to weeks improved or stabilized the retinal anatomy in all cases. Conclusions: This series describes clinical features in APVR in premature infants and suggests that early diagnosis and intervention may mitigate the typical aggressive course and poor prognosis of this condition.

Gurm HS, Mavromatis K, Bertolet B, Kereiakes DJ, Amin AP, Shah AP, **Hanzel GS**, Rao S, Thomas JL and Kumar G (2019). "Minimizing radiographic contrast administration during coronary angiography using a novel contrast reduction system: A multicenter observational study of the DyeVert™ plus contrast reduction system." *Catheterization and Cardiovascular Interventions* 93(7): 1228-1235.

[Full Text](#)

Department of Internal Medicine

Objective: To evaluate contrast media (CM) volume (CMV) saved using the DyeVert™ Plus Contrast Reduction System (DyeVert Plus System, Osprey Medical) in patients undergoing diagnostic coronary angiogram (CAG) and/or percutaneous coronary interventional (PCI) procedures performed with manual injections. Background: Current guidelines advocate for monitoring and minimization of the total volume of CM in chronic kidney disease (CKD) patients undergoing invasive cardiac procedures. The DyeVert Plus System is an FDA cleared device designed to reduce CMV delivered during angiography and permit real-time CMV monitoring. Methods: We performed a multicenter, single-arm, observational study. Eligible subjects were ≥ 18 years old with baseline estimated glomerular filtration rate (eGFR) 20–60 mL/min/1.73 m². The primary endpoint was % CMV saved over the total procedure. A secondary objective was to evaluate adverse events (AEs) related to DyeVert Plus System or to CM use. Results: A total of 114 subjects were enrolled at eight centers. Mean age was 72 ± 9 years, 72% were male, and mean body mass index was 29 ± 5 . Baseline eGFR was 43 ± 11 mL/min/1.73 m². CAG-only was performed in 65% of cases. One hundred and five subjects were evaluable for the primary endpoint. Mean CMV attempted was 112 ± 85 mL (range 22–681) and mean CMV delivered was 67 ± 51 mL (range 12–403), resulting in an overall CMV savings of $40.1 \pm 8.8\%$ (95% CI 38.4, 41.8; P < 0.0001) per procedure. Image quality was maintained in all but one case where the system was turned off for one injection. No DyeVert Plus System-related AEs were reported. Acute kidney injury (AKI; defined as serum creatinine rise of > 0.3 mg/dL from baseline) was reported in 11 cases with seven occurring in subjects with baseline eGFR ≤ 30 and three AKI events were attributed to CM. AKI rates increased as CMV/eGFR ratios increased. Conclusions: These data suggest DyeVert Plus System use in CKD patients undergoing CAG and/or PCI results in clinically meaningful CMV savings while maintaining image quality.

Haines DE (2019). "Can an expanding lattice electrode catheter expand our success in catheter ablation?" *Circulation. Arrhythmia and Electrophysiology* 12(4): e007306.

[Request Form](#)

Department of Internal Medicine

Hakim S, Orosey M, Edhi A, **Amin M** and **Cappell MS** (2019). "Complete response for 36 months after BRAF & MEK inhibitor therapy for locally advanced gallbladder melanoma." *Minerva Gastroenterologica e Dietologica*. ePub Ahead of Print.

[Request Form](#)

Department of Pathology

Department of Internal Medicine

Halford R, **Yan D** and Snyder M (2019). "Driven damped harmonic oscillator for MR motion quality assurance."

[Medical Physics](#) 46(6): E117-E117.

[Request Form](#)

Department of Radiation Oncology

Halka JT, **Yee D, Angus A**, Mohammed A, Sevak S and **Robbins J** (2019). "Alexis St. Martin Gastropexy: A novel technique for gastropexy during percutaneous endoscopic gastrostomy tube placement." [Surgical Laparoscopy Endoscopy Percutaneous Techniques](#) 29(2): e20-e23.

[Full Text](#)

Department of Surgery

OUWB Medical Student Author

Background: Percutaneous endoscopic gastrostomy (PEG) is a preferred method of long-term enteral nutritional support. Despite its ease of placement, it has a 4% major complication rate, requiring surgical intervention or hospitalization. Early PEG tube dislodgment can cause peritonitis, requiring emergent laparotomy at significant morbidity and cost. T-fasteners have been used as an adjunct gastropexy, but nearly one third migrate into the abdominal wall within the first 2 weeks. We describe a low-cost, minimally invasive technique using widely available surgical instruments to appose the gastric and abdominal walls. Methods: All PEG procedures were performed in our 60-bed surgical intensive care unit. Institutional IRB approval was obtained along with procedure specific consent for all patients. The adjunctive gastropexy procedure was performed on four patients at high risk for early PEG tube dislodgment. Following routine PEG tube placement, both ends of four 2-0 polyglactin ties were brought through the gastric and abdominal walls through separate stab incisions adjacent to the PEG tube exit site in the 3, 6, 9, and 12 o'clock positions. These were tied in the subcutaneous tissue, securing the gastric wall to the abdominal wall. Results: No PEG tube complications occurred. All patients were discharged to long-term care facilities with PEG tubes intact or electively removed. Conclusions: We describe the results of a pilot study for a cost-effective, easily implementable, adjunct technique, named after the namesake of our institution, to decrease the incidence and severity of complications associated with PEG tube dislodgment. It was used in 4 patients at high risk for PEG tube dislodgment with satisfactory early results in all 4. Further recruitment of larger numbers of patients using this technique is ongoing to determine if this technique is truly effective at reducing PEG tube complications.

Huang J, Chaudhary R, Cohen AL, Fink K, Goldlust S, Boockvar J, **Chinnaiyan P**, Wan L, **Marcus S** and Campian JL (2019). "A multicenter phase II study of temozolomide plus disulfiram and copper for recurrent temozolomide-resistant glioblastoma." [Journal of Neurooncology](#) 142(3): 537-544.

[Full Text](#)

Department of Pediatrics

Department of Radiation Oncology

Purpose: Preclinical studies have suggested promising activity for the combination of disulfiram and copper (DSF/Cu) against glioblastoma (GBM) including re-sensitization to temozolomide (TMZ). A previous phase I study demonstrated the safety of combining DSF/Cu with adjuvant TMZ for newly diagnosed GBM. This phase II study aimed to estimate the potential effectiveness of DSF/Cu to re-sensitize recurrent GBM to TMZ. Methods: This open-label, single-arm phase II study treated recurrent TMZ-resistant GBM patients with standard monthly TMZ plus concurrent daily DSF 80 mg PO TID and Cu 1.5 mg PO TID. Eligible patients must have progressed after standard chemoradiotherapy and within 3 months of the last dose of TMZ. Known isocitrate dehydrogenase (IDH) mutant or secondary GBMs were excluded. The primary endpoint was objective response rate (ORR), and the secondary endpoints included progression-free survival (PFS), overall survival (OS), clinical benefit (response or stable disease for at least 6 months), and safety. Results: From March 2017 to January 2018, 23 recurrent TMZ-resistant GBM patients were enrolled across seven centers, and 21 patients were evaluable for response. The median duration of DSF/Cu was 1.6 cycles (range: 0.1-12.0). The ORR was 0%, but 14% had clinical benefit. Median PFS was 1.7 months, and median OS was 7.1 months. Only one patient (4%) had dose-limiting toxicity (grade three elevated alanine transaminase). Conclusions: Addition of DSF/Cu to TMZ for TMZ-resistant IDH-wild type GBM appears well tolerated but has limited activity for unselected population.

Hutchinson PJ, Koliass AG, Tajsic T, Adeleye A, Aklilu AT, Apriawan T, Bajamal AH, Barthelemy EJ, Devi BI, Bhat D, Bulters

D, Chesnut R, Citerio G, Cooper DJ, Czosnyka M, Edem I, El-Ghandour NMF, Figaji A, Fountas KN, Gallagher C, Hawryluk GWJ, Iaccarino C, Joseph M, Khan T, Laeke T, Levchenko O, Liu B, Liu W, Maas A, Manley GT, Manson P, Mazzeo AT, Menon DK, **Michael DB**, Muehlschlegel S, Okonkwo DO, Park KB, Rosenfeld JV, Rosseau G, Rubiano AM, Shabani HK, Stocchetti N, Timmons SD, Timofeev I, Uff C, Ullman JS, Valadka A, Waran V, Wells A, Wilson MH and Servadei F (2019). "Consensus statement from the International Consensus Meeting on the Role of Decompressive Craniectomy in the Management of Traumatic Brain Injury : Consensus statement." Acta Neurochirurgica (Wien) 161(7): 1261-1274.

[Full Text](#)

Department of Neurosurgery

Background: Two randomised trials assessing the effectiveness of decompressive craniectomy (DC) following traumatic brain injury (TBI) were published in recent years: DECRA in 2011 and RESCUEicp in 2016. As the results have generated debate amongst clinicians and researchers working in the field of TBI worldwide, it was felt necessary to provide general guidance on the use of DC following TBI and identify areas of ongoing uncertainty via a consensus-based approach. Methods: The International Consensus Meeting on the Role of Decompressive Craniectomy in the Management of Traumatic Brain Injury took place in Cambridge, UK, on the 28th and 29th September 2017. The meeting was jointly organised by the World Federation of Neurosurgical Societies (WFNS), AO/Global Neuro and the NIHR Global Health Research Group on Neurotrauma. Discussions and voting were organised around six pre-specified themes: (1) primary DC for mass lesions, (2) secondary DC for intracranial hypertension, (3) peri-operative care, (4) surgical technique, (5) cranial reconstruction and (6) DC in low- and middle-income countries. Results: The invited participants discussed existing published evidence and proposed consensus statements. Statements required an agreement threshold of more than 70% by blinded voting for approval. Conclusions: In this manuscript, we present the final consensus-based recommendations. We have also identified areas of uncertainty, where further research is required, including the role of primary DC, the role of hinge craniotomy and the optimal timing and material for skull reconstruction.

Ionescu F, Anusim N, **Douglas-Nikitin V** and **Stender M** (2019). "When leucocytosis is not leukaemia." BMJ Case Reports 12(5): e228219.

[Full Text](#)

Department of Pathology

Department of Internal Medicine

A female aged 84 years with a history of Clostridium difficile-associated diarrhoea presented from an extended care facility with altered mental status and respiratory distress. She was haemodynamically unstable and initial laboratory results revealed hyperleucocytosis ($110.3 \times 10^9 /L$). The presence of immature myeloid precursors, thrombocytopenia and respiratory distress, raised concern for an acute leukaemic process requiring emergent leucapheresis. However, on evaluation of the peripheral smear, prominent left shift and toxic granulation were noted, along with absence of blast cells. Considering her history of C. difficile infection, a CT scan of the abdomen and pelvis was obtained, which was suggestive of toxic megacolon. She was taken to the operating room for emergent colectomy. The pathology specimen showed pseudomembrane formation consistent with fulminant C. difficile infection. She was treated with oral vancomycin and intravenous metronidazole, followed by clinical improvement and resolution of leucocytosis and thrombocytopenia.

Jarrett NL, **Yamane DE**, Gildner DJ and Pickett SM (2019). "The indirect effect of sleep quality on emotional exhaustion through emotion regulation difficulties and perceived stress in a sample of US medical students." Sleep 42(S1): A87.

[Request Form](#)

OUIB Medical Student Author

John J, Garg L, Orosey M, **Desai T**, **Haines DE** and Wong WS (2019). "The effect of esophageal cooling on esophageal injury during radiofrequency catheter ablation of atrial fibrillation." Journal of Interventional Cardiac Electrophysiology. ePub Ahead of Print.

[Full Text](#)

Department of Internal Medicine

Introduction: Catheter ablation of atrial fibrillation (AF) may lead to collateral damage to the esophagus. We

tested the hypothesis that luminal esophageal temperature (LET)-guided esophageal cooling might reduce the incidence of esophageal thermal lesions (ETL). Methods: Seventy-six patients from August 2015 to March 2017 with paroxysmal or persistent AF underwent a first-time catheter ablation procedure with or without LET-guided active esophageal cooling through an orogastric tube placed in the esophagus. Esophageal cooling occurred if and only if LET exceeded 0.5 degrees C from baseline while ablating the LA posterior wall. All patients underwent esophagogastroduodenoscopy the next day. Results: Of the 76 patients studied, 38 (50%) patients underwent esophageal cooling. Baseline characteristics of the non-cooled and cooled groups were comparable. Of these, 59% of patients had ETL. There was a non-significant trend for more severe lesions (grades 3, 4) in the non-cooled group (29% vs. 13.5%, $p = 0.10$). Average power delivered on the left atrial posterior wall (27 ± 1.8 W vs. 27 ± 3.8 W, $p = 0.34$) and average force of contact (10.1 g vs. 9.8 g, $p = 0.38$) were similar in both groups while more time was spent ablating on the posterior wall in the non-cooled group (24.6 ± 7.3 min vs. 20.4 ± 5.9 min, $p = 0.014$). In a multivariate analysis, esophageal cooling had no significant effect on the esophageal lesion grade post-ablation. Conclusion: The incidence of ETL in patients undergoing left atrial posterior wall isolation is substantial. Our method of esophageal cooling did not decrease the incidence of ETL. There was a non-significant trend toward fewer severe lesions with cooling, but one cannot conclude the value of cooling from this pilot study.

Kaplan LM, Siljander MP, **Verner JJ**, **Baker KC**, Gehrke CK, Salisbury MR and **Baker EA** (2019). "Analysis of retrieved unicompartmental knee implants and tissue: Third-body wear as a potential contributor to progression of arthritis to adjacent compartments." *Orthopedics* 42(3): 149-157.

[Full Text](#)

Department of Orthopedic Surgery

Unicompartmental knee arthroplasty (UKA) for the treatment of single-compartment osteoarthritis has been associated with polyethylene wear and progression of osteoarthritis into adjacent compartments, leading to revision. In this study, damage and clinical failure modes of retrieved UKA implants were investigated and protein expression profiles between articular cartilage adjacent to UKA and primary osteoarthritic cartilage were compared. Fifty retrieved UKA implants were analyzed for various damage. Records review and radiographic analysis were performed to collect clinical data and implant characteristics. Cartilage harvested from revision UKA and primary total knee arthroplasty surgeries was characterized with a proteome profiling array detecting levels of 36 different cytokines, chemokines, and acute phase inflammatory proteins. Progression of osteoarthritis ($n=18$, 36%) and component loosening ($n=17$, 34%) were the most common reasons for revision. Liners exhibited the highest frequency of damage modes. Progression of arthritis positively correlated with radiographic presence of extruded bone cement and burnishing of liner components. A protein-level profile between revision UKA and primary total knee arthroplasty cartilage showed 12 differentially expressed cytokines. Failure of UKA may be secondary to the effects of wear debris particulate migration into the adjacent compartment, suggesting an additional pathway of cartilage damage manifesting as traditional clinical symptoms.

Kara S, Hanna A, Pirela-Morillo GA, Gilliam CT and **Wilson GD** (2019). "Molecular Interaction Network Approach (MINA) identifies association of novel candidate disease genes." *MethodsX* 6: 1286-1291.

[Full Text](#)

Department of Radiation Oncology

Molecular Interaction Network Approach (MINA) was used to elucidate candidate disease genes. The approach was implemented to identify novel gene association with commonly known autoimmune diseases [1]. In MINA, we evaluated the hypothesis that "network proximity" within a whole genome molecular interaction network can be used to inform the search for multigene inheritance. There are now numerous examples of gene discoveries based upon network proximity between novel and previously identified disease genes (Yin et al., 2017 [2], Wang et al., 2011 [3], and Barrenas et al., 2009 [4]). This study extends the application of interaction networks to the interrogation of Genome Wide Association studies: first, by showing that a group of nine autoimmune diseases (AuD) genes "seed genes", are connected in a highly non-random manner within a whole genome network; and second, by showing that the minimal number of connecting genes required to connect a maximal number of AuD candidate genes are highly enriched as candidate genes for AuD predisposing mutations. The findings imply that a threshold number of candidate genes for any heritable disorder can be used to "seed" a molecular interaction network that *Serves to

validate the disease status of closely associated seed genes*Identifies genes that are highly enriched as novel candidate disease genes*Provides a strategy for elucidation of epistatic gene x gene interactions The method could provide a critical toll for understanding the genetic architecture of common traits and disorders.

Keihani S, Putbrese BE, Rogers DM, Zhang C, Nirula R, Luo-Owen X, Mukherjee K, Morris BJ, Majercik S, Piotrowski J, Dodgion CM, Schwartz I, Elliott SP, Desoucy ES, Zakaluzny S, Sherwood BG, Erickson BA, Baradaran N, Breyer BN, Fick CN, Smith BP, Okafor BU, Askari R, Miller B, Santucci RA, Carrick MM, Kocik JF, **Hewitt T, Burks FN**, Heilbrun ME and Myers JB (2019). "The associations between initial radiographic findings and interventions for renal hemorrhage after high-grade renal trauma: Results from the Multi-Institutional Genitourinary Trauma Study." Journal of Trauma and Acute Care Surgery 86(6): 974-982.

[Full Text](#)

OUWB Medical Student Author

Department of Urology

Background: Indications for intervention after high-grade renal trauma (HGRT) remain poorly defined. Certain radiographic findings can be used to guide the management of HGRT. We aimed to assess the associations between initial radiographic findings and interventions for hemorrhage after HGRT and to determine hematoma and laceration sizes predicting interventions. Methods: The Genitourinary Trauma Study is a multicenter study including HGRT patients from 14 Level I trauma centers from 2014 to 2017. Admission computed tomography scans were categorized based on multiple variables, including vascular contrast extravasation (VCE), hematoma rim distance (HRD), and size of the deepest laceration. Renal bleeding interventions included angioembolization, surgical packing, renorrhaphy, partial nephrectomy, and nephrectomy. Mixed-effect Poisson regression was used to assess the associations. Receiver operating characteristic analysis was used to define optimal cutoffs for HRD and laceration size. Results: In the 326 patients, injury mechanism was blunt in 81%. Forty-seven (14%) patients underwent 51 bleeding interventions, including 19 renal angioembolizations, 16 nephrectomies, and 16 other procedures. In univariable analysis, presence of VCE was associated with a 5.9-fold increase in risk of interventions, and each centimeter increase in HRD was associated with 30% increase in risk of bleeding interventions. An HRD of 3.5 cm or greater and renal laceration depth of 2.5 cm or greater were most predictive of interventions. In multivariable models, VCE and HRD were significantly associated with bleeding interventions. Conclusion: Our findings support the importance of certain radiographic findings in prediction of bleeding interventions after HGRT. These factors can be used as adjuncts to renal injury grading to guide clinical decision making. Level of Evidence: Prognostic and Epidemiological Study, Level III and Therapeutic/Care Management, Level IV.

Keihani S, Rogers DM, Putbrese BE, Moses RA, Zhang C, Presson AP, Hotaling JM, Nirula R, Luo-Owen X, Mukherjee K, Morris BJ, Majercik S, Piotrowski J, Dodgion CM, Schwartz I, Elliott SP, Desoucy ES, Zakaluzny S, Sherwood BG, Erickson BA, Baradaran N, Breyer BN, Smith BP, Okafor BU, Askari R, Miller B, Santucci RA, Carrick MM, Kocik JF, **Hewitt T, Burks FN**, Heilbrun ME, Myers JB, in conjunction with the T and Urologic Reconstruction Network of S (2019). "A nomogram predicting the need for bleeding interventions after high-grade renal trauma: Results from the American Association for the Surgery of Trauma Multi-institutional Genito-Urinary Trauma Study (MiGUTS)." Journal of Trauma and Acute Care Surgery 86(5): 774-782.

[Full Text](#)

OUWB Medical Student Author

Department of Urology

Background: The management of high-grade renal trauma (HGRT) and the indications for intervention are not well defined. The American Association for the Surgery of Trauma (AAST) renal grading does not incorporate some important clinical and radiologic variables associated with increased risk of interventions. We aimed to use data from a multi-institutional contemporary cohort to develop a nomogram predicting risk of interventions for bleeding after HGRT. Methods: From 2014 to 2017, data on adult HGRT (AAST grades III-V) were collected from 14 level 1 trauma centers. Patients with both clinical and radiologic data were included. Data were gathered on demographics, injury characteristics, management, and outcomes. Clinical and radiologic parameters, obtained after trauma evaluation, were used to predict renal bleeding interventions. We developed a prediction model by applying backward model selection to a logistic

regression model and built a nomogram using the selected model. Results: A total of 326 patients met the inclusion criteria. Mechanism of injury was blunt in 81%. Median age and injury severity score were 28 years and 22, respectively. Injuries were reported as AAST grades III (60%), IV (33%), and V (7%). Overall, 47 (14%) underwent interventions for bleeding control including 19 renal angioembolizations, 16 nephrectomies, and 12 other procedures. Of the variables included in the nomogram, a hematoma size of 12 cm contributed the most points, followed by penetrating trauma mechanism, vascular contrast extravasation, pararenal hematoma extension, concomitant injuries, and shock. The area under the receiver operating characteristic curve was 0.83 (95% confidence interval, 0.81-0.85). Conclusion: We developed a nomogram that integrates multiple clinical and radiologic factors readily available upon assessment of patients with HGRT and can provide predicted probability for bleeding interventions. This nomogram may help in guiding appropriate management of HGRT and decreasing unnecessary interventions.

Kemp K and Poe C (2019). "Stressed: The unfolded protein response in T cell development, activation, and function." *International Journal of Molecular Sciences* 20(7): 1792.

[Full Text](#)

Department of Foundational Medical Studies

The unfolded protein response (UPR) is a highly conserved pathway that allows cells to respond to stress in the endoplasmic reticulum caused by an accumulation of misfolded and unfolded protein. This is of great importance to secretory cells because, in order for proteins to traffic from the endoplasmic reticulum (ER), they need to be folded appropriately. While a wealth of literature has implicated UPR in immune responses, less attention has been given to the role of UPR in T cell development and function. This review discusses the importance of UPR in T cell development, homeostasis, activation, and effector functions. We also speculate about how UPR may be manipulated in T cells to ameliorate pathologies.

Khalil J, Smuck M, Koreckij T, Keel J, Beall D, Goodman B, Kalapos P, **Nguyen D** and Garfin S (2019). "A prospective, randomized, multi-center study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain." *Spine Journal*. ePub Ahead of Print.

[Full Text](#)

Department of Emergency Medicine

Department of Orthopedic Surgery

Background Context: Current literature suggests that degenerated or damaged vertebral endplates are a significant cause of chronic low back pain (LBP) that is not adequately addressed by standard care. Prior 2-year data from the treatment arm of a sham-controlled randomized controlled trial (RCT) showed maintenance of clinical improvements at 2 years following radiofrequency (RF) ablation of the basivertebral nerve (BVN). Purpose: The purpose of this RCT was to compare the effectiveness of intraosseous RF ablation of the BVN to standard care for the treatment of chronic LBP in a specific subgroup of patients suspected to have vertebrogenic related symptomatology. Study Design/Setting: A prospective, parallel, open label RCT was conducted at 20 U.S. sites. Patient Sample: A total of 140 patients with chronic LBP of at least 6 months duration, with Modic Type 1 or 2 vertebral endplate changes between L3 to S1, were randomized 1:1 to undergo either RF ablation of the BVN or continue standard care. Outcome Measures: Oswestry Disability Index (ODI) was collected at baseline, 3, 6, 9, and 12-months post-procedure. Secondary outcome measures included a 10-point Visual Analog Scale (VAS) for LBP, ODI and VAS responder rates, SF-36, and EQ-5D-5L. The primary endpoint was a between-arm comparison of the mean change in ODI from baseline to 3 months post-treatment. Methods: Patients were randomized 1:1 to receive RF ablation or to continue standard care. Self-reported patient outcomes were collected using validated questionnaires at each study visit. An interim analysis to assess for superiority was pre-specified and overseen by an independent data management committee (DMC) when a minimum of 60% of patients had completed their 3-month primary endpoint visit. Results: The interim analysis showed clear statistical superiority ($p < 0.001$) for all primary and secondary patient-reported outcome measures in the RF ablation arm compared to the standard care arm. This resulted in a DMC recommendation to halt enrollment in the study and offer early cross-over to the control arm. These results are comprised of the outcomes of the 104 patients included in the intent-to-treat (ITT) analysis of the 3-month primary endpoint, which included 51 patients in the RF ablation arm and 53 patients in the standard care arm. Baseline ODI was 46.1, VAS was 6.67, and mean age was 50 years. The percentage of patients with LBP symptoms ≥ 5 years was 67.3%. Comparing the RF ablation arm to the standard care

arm, the mean changes in ODI at three months were -25.3 points versus -4.4 points, respectively, resulting in an adjusted difference of 20.9 points ($p < 0.001$). Mean changes in VAS were -3.46 versus -1.02, respectively, an adjusted difference of 2.44 cm ($p < 0.001$). In the RF ablation arm, 74.5% of patients achieved a ≥ 10 -point improvement in ODI, compared with 32.7% in the standard care arm ($p < 0.001$). Conclusions: Minimally invasive RF ablation of the BVN led to significant improvement of pain and function at 3-months in patients with chronic vertebrogenic related LBP.

Khan AJ, **Chen PY**, Yashar C, Poppe MM, Li L, Abou Yehia Z, Vicini FA, Moore D, Dale R, Arthur D, Shah C, Haffty BG and Kuske R (2019). "Three-fraction accelerated partial breast irradiation (APBI) delivered with brachytherapy applicators is feasible and safe: First results from the TRIUMPH-T trial." International Journal of Radiation Oncology Biology Physics 104(1): 67-74.

[Full Text](#)

Department of Radiation Oncology

Purpose: Shorter courses of accelerated partial-breast irradiation delivered as single-fraction intraoperative therapy are now offered as an alternative to 4 to 6 weeks of whole-breast irradiation after lumpectomy. However, this approach has potential shortcomings in patient selection and target volume definition and in dosimetric, radiobiological, and logistical issues. We designed a prospective, phase 2, multi-institution clinical trial to study 2- or 3-day accelerated partial breast irradiation delivered with brachytherapy applicators. Methods and Materials: This trial treats select breast cancers after breast-conserving surgery with brachytherapy applicators that deliver 22.5 Gy in 3 fractions of 7.5 Gy. The planning treatment volume was 1 to 1.5 cm beyond the surgical cavity. Eligible women were aged ≥ 45 years with unicentric invasive or in situ tumors ≤ 3.0 cm with positive estrogen or progesterone receptors and no metastasis to axillary nodes that have been excised with negative margins. Strict dosimetric parameters were required to be met before acceptance into the trial. Results: A group of 200 patients was prospectively enrolled and followed for a minimum of 6 months. Two- or 3-day brachytherapy was associated with low acute or subacute toxicity, 97.25% excellent or good cosmetic outcomes, and excellent local control in select breast cancers. Conclusions: Ultrashort breast brachytherapy is dosimetrically feasible and can be delivered with excellent short-term tolerance and low toxicity.

Khoury J, Chacko R, Macari D, Gbadamosi B, Ezekwudo D, Blankenship L, **Anderson JM** and **Jaiyesimi IA** (2019). "Metastatic patterns and prognostic significance of signet ring cell carcinoma of the colon: Retrospective analysis of SEER database." Journal of Clinical Oncology 37(S4).

[Full Text](#)

Department of Internal Medicine

Background: Signet ring cell carcinoma of the colon (SRCC) represents less than 1% of all colon carcinomas. We retrospectively examined the metastatic patterns and prognosis of SRCC in comparison to adenocarcinoma (AC) of the colon. Methods: A total of 763 patients diagnosed with SRCC and 42,875 patients with AC of the colon from 2010 to 2012 were identified from the Surveillance, Epidemiology and End Results (SEER) database. Age, race, gender, primary site, grade, stage, metastatic site and survival data were collected. Results: Out of 43,638 patients, 78.7% were white, 12.5% black and 8.8% other races. Median age of diagnosis was 67.5 years for SRCC as compared to 69.1 years for AC. SRCC was more likely to be grade III or IV (92% vs 21.6%; $p < 0.001$), to be found in the right colon (63.7% vs 49.4%; $p < 0.001$) and to present as advanced stage (40.2% vs 29.4% for stage III and 37.1% vs 22.3% for stage IV; $p < 0.001$). SRCC was more likely to present with metastases to the brain (11.0% vs 1.3%; $p < 0.001$) and bone (6.4% vs 4.1%; $p < 0.001$), while AC subjects were more likely to present with metastases to the liver (77.0% vs 22.1%; $p < 0.001$) and lung (21.2% vs 5.8%; $p < 0.001$). The 5 year overall survival rate (5-YSR) was 28.2% (CI, 24.5% to 32.4%) for SRCC compared to 50.8% (CI, 50.1% to 51.6%) for AC (Hazard ratio for death, 1.38; CI, 1.26 to 1.52; $P < 0.001$). The differences in stage specific 5-year survival rates for SRCC and AC were not statistically significant for stage I and stage II. However, SRCC had a lower 5-YSR for stage III (34.5% vs 55.4%) and stage IV (3.3% vs 10.8%). Conclusions: SRCC of the colon has worse survival rates for advanced stages when compared to AC. SRCC presents at earlier age, with advanced tumor grade and stage at diagnosis. The metastatic behavior of SRCC is different than AC with a higher incidence of brain and bone metastases at diagnosis.

Knill C, Sandhu R, Halford R and **Seymour Z** (2019). "Validating the Brainlab Cranial SRS Element for the Versa HD." Medical Physics 46(6): E659-E659.

[Request Form](#)

Department of Radiation Oncology

Kobeissi SS, Majdalany BS, Majdalany CI, **Kanaan CN**, Gilbert LN and Khaja MS (2019). "Pelvic congestion syndrome." Journal of Radiology Nursing 38(2): 82-85.

[Full Text](#)

OUIWB Medical Student Author

Kocher KE, Arora R, Bassin BS, Benjamin LS, Bolton M, **Dennis BJ**, Ham JJ, Krupp SS, **Levasseur KA**, Macy ML, O'Neil BJ, Pribble JM, Sherwin RL, Sroufe NS, Uren BJ and Nypaver MM (2019). "Baseline performance of real-world clinical practice within a statewide emergency medicine quality network: The Michigan Emergency Department Improvement Collaborative (MEDIC)." Annals of Emergency Medicine. ePub Ahead of Print.

[Full Text](#)

Department of Emergency Medicine

Study Objective: Large-scale quality and performance measurement across unaffiliated hospitals is an important strategy to drive practice change. The Michigan Emergency Department Improvement Collaborative (MEDIC), established in 2015, has baseline performance data to identify practice variation across 15 diverse emergency departments (EDs) on key emergency care quality indicators. Methods: MEDIC is a unique physician-led partnership supported by a major third-party payer. Member sites contribute electronic health record data and trained abstractors add supplementary data for eligible cases. Quality measures include computed tomography (CT) appropriateness for minor head injury, using the Canadian CT Head Rule for adults and Pediatric Emergency Care Applied Network rules for children; chest radiograph use for children with asthma, bronchiolitis, and croup; and diagnostic yield of CTs for suspected pulmonary embolism. Baseline performance was established with statistical process control charts. Results: From June 1, 2016, to October 31, 2017, the MEDIC registry contained 1,124,227 ED visits, 23.2% for children (<18 years). Overall baseline performance included the following: 40.9% of adult patients with minor head injury (N=11,857) had appropriate CTs (site range 24.3% to 58.6%), 10.3% of pediatric minor head injury cases (N=11,183) exhibited CT overuse (range 5.8% to 16.8%), 38.1% of pediatric patients with a respiratory condition (N=18,190) received a chest radiograph (range 9.0% to 62.1%), and 8.7% of pulmonary embolism CT results (N=16,205) were positive (range 7.5% to 14.3%). Conclusion: Performance varied greatly, with demonstrated opportunity for improvement. MEDIC provides a robust platform for emergency physician engagement across ED practice settings to improve care and is a model for other states.

Kohli M, **Yadav S**, Tan W, Riaz IB, Zheng T, **Wang A**, Montesinos C, Wong C, Du P and Yu SJJ (2019). "Plasma cell-free DNA-based prognosis in metastatic hormone sensitive prostate cancer." Journal of Clinical Oncology 37(S7).

[Full Text](#)

Department of Diagnostic Radiology and Molecular Imaging

OUIWB Medical Student Author

Background: We evaluated plasma cell free based genomic aberrations for prognosticating survival of newly diagnosed metastatic hormone sensitive prostate cancer (mHSPC) patients (pts). Methods: Plasma was collected from mHSPC pts enrolled between 2009-2014. Platelet poor plasma (PPP) fractions were processed uniformly and cell free DNA (cfDNA) extracted using Qiagen kits. Pts were followed after initiating hormonal therapy until death. Next Gen Sequencing (NGS) of cfDNA was performed using Illumina HiSeq X for a preselected panel of 128 genes (PredicineDDR-77 cancer driver genes; 29 genes in BRCA-FA homologous recombination deficiency (HRD) pathway; 22 DNA damage repair pathway genes). Statistical analyses of plasma genome based aberrations with overall survival (OS) were performed in R 3.5.1. Cox proportional-hazard models were used for survival analysis. Results: An average of 2.5 ml PPP from 99 pts yielded a median of 10.5 ng (range: 2.8-702) cfDNA per sample. 15/99 pt samples with a yield < 5 ng were excluded from sequencing; 9/99 samples failed NGS. Median follow-up time was 80.2 months (mths) (Range: 74.7, 87]); median OS was 69.1 mths (range: 54,NR). 29 pts with full NGS data had high volume metastatic disease. cfDNA yield correlated with metastatic volume (P = 0.01). Univariate analysis revealed both variables prognostic for OS (Metastatic volume: log-rank P=0.01, HR=2.1, 95% CI: 1.1-3.8; cfDNA yield: P =0.04, HR =

1.3, 95% CI: 1.03-1.7). Multivariate regression showed prognostic value of cfDNA yield remained independent of metastatic volume (P = 0.03, HR = 1.34, 95% CI: 1.02-1.76). 54/67 samples with NGS data had at least one mutation/copy number variation detected. Top mutated genes included TP53 (N=18), ATM (N=9), CHEK2 (N=7), FANCM (N=6), RB1 (N=6), BRCA2 (N=5), PIK3CA (N=4) and 37/67 pts harbored 1> variant in HDR pathways. These pts had a shorter survival (median: 58.6 mths) (P=0.04, HR= 2.28, 95% CI: 1.01-5.18) and pts with ATM mutations did significantly worse (median survival: 47.4 mths) (HR=4.03, P=0.0005, 95% CI: 1.73-9.37). Conclusions: Plasma cfDNA yield is prognostic for survival in newly diagnosed mHSPC state and presence of HRD pathway genomic aberrations in plasma cfDNA are associated with poor survival.

Kokkinos P, Faselis C, **Franklin B**, Lavie CJ, Sidossis L, Moore H, Karasik P and Myers J (2019). "Cardiorespiratory fitness, body mass index and heart failure incidence." European Journal of Heart Failure 21(4): 436-444.

[Full Text](#)

Department of Internal Medicine

Aims: Obesity is associated with increased risk of heart failure (HF). This risk may be modulated by improved cardiorespiratory fitness (CRF) as CRF is associated with favourable health outcomes. Thus, we assessed the interaction between body mass index (BMI), CRF and HF. Methods and Results: Cardiorespiratory fitness and BMI were assessed in 20 254 US male veterans (mean age 58.0 ± 11.3 years), who completed a maximal exercise treadmill test between 1987 and 2017. All had no evidence of ischaemia or HF prior to the exercise test. They were classified based on age-stratified quartiles of peak metabolic equivalents (METs) achieved as: least-fit (4.5 ± 1.3), low-fit (6.7 ± 1.3), moderate-fit (8.1 ± 1.1), and high-fit (11.2 ± 2.4); and according to BMI as normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), and obese (≥ 30.0 kg/m²). During a median follow-up of 13.4 years, there were 2979 HF events (10.8 events/1000 person-years). HF risk was significantly higher in the obese category [hazard ratio (HR) 1.22, 95% confidence interval (CI) 1.10–1.36; P < 0.001], but was no longer significant after further adjustment for METs. When compared to the least-fit, HF risk declined progressively with increased CRF within all BMI categories. The risk was 63% (HR 0.37, 95% CI 0.30–0.47; P < 0.001), 66% (HR 0.37, 95% CI 0.28–0.40; P < 0.001), and 73% (HR 0.27, 95% CI 0.22–0.34; P < 0.001) lower for high-fit individuals within normal weight, overweight and obese categories, respectively. Conclusions: Increased CRF was associated with progressively lower HF risk regardless of BMI, suggesting that the elevated HF risk associated with obesity may be modulated by improved CRF.

Koreckij TD, Gandhi SD and **Park DK** (2019). "Cervical disk arthroplasty." The Journal of the American Academy of Orthopaedic Surgeons 27(3): e96-e104.

[Full Text](#)

Department of Orthopedic Surgery

Anterior cervical discectomy and fusion has been and remains the benchmark surgical management of cervical degenerative disk disease. However, an increased use of cervical disk arthroplasty (CDA) has been found in the past few years. The purported benefits of CDA included preserved motion, less adjacent-level degeneration, and less morbidity. Short-term results from randomized control trials clearly showed noninferiority of CDA compared with fusion. With long-term comparison data becoming available, results are equivalent and superior in many metrics compared, favoring CDA. Concerns remain regarding the best way to manage CDA failures. Nonetheless, appropriate patient selection and adherence to strict surgical technique make CDA a viable treatment.

Korot E, Wood E, **Weiner A**, **Sim DA** and **Trese M** (2019). "A renaissance of teleophthalmology through artificial intelligence." Eye (Lond) 33(6): 861-863.

[Full Text](#)

OUWB Medical Student Author

Department of Family Medicine and Community Health

Department of Ophthalmology

Kurdziel MD, Davidson A, Ross D, Seta J, **Doshi S**, **Baker KC** and Maerz T (2019). "Biomechanical properties of the repaired and non-repaired rat supraspinatus tendon in the acute postoperative period." Connective Tissue Research 60(3): 254-264.

[Request Form](#)

Department of Diagnostic Radiology and Molecular Imaging

Department of Orthopedic Surgery

Purpose: The rat rotator cuff (RC) model is used to study RC pathology and potential treatment; however, native scar-mediated healing allows the rat RC to recover at 4-6 weeks but little is known about acute healing. This study characterized the properties of the repaired and non-repaired rat RC following surgical detachment. Materials and Methods: Forty-eight rats underwent surgical RC detachment and received surgical repair (Repair) or left unrepaired (Defect) to either 12 or 19 days. Healthy controls were obtained from contralateral limbs. Biomechanical properties were assessed using stress relaxation and failure testing and mechanical modeling performed using quasilinear viscoelastic (QLV) and structurally based elastic models. Histology and micro-magnetic resonance imaging were used to qualitatively grade tendon-to-bone healing. Results: Repair and Defect exhibited significantly inferior mechanical properties compared to Healthy at both time points. Repair had significant increases in peak, equilibrium, and ultimate stress, modulus, and stiffness and significant decreases in cross-sectional area, % relaxation, and QLV constant "C" between 12 and 19 days, whereas Defect showed no change. Conclusions: This study demonstrates acute differences in mechanical properties of the rat supraspinatus tendon in the presence and absence of surgical repair. Understanding the longitudinal recovery of mechanical properties can facilitate more accurate characterization of RC pathology or future treatments.

LaBan MM (2019). "Letter to the editor regarding Bilgilişoy Felix M, Kilic Z, Uckum A, et al: Mechanical traction for lumbar radicular pain: Supine or prone? A randomized control trial.: Am J Phys Med Rehabil: 2018;97:433–439." *American Journal of Physical Medicine & Rehabilitation* 98(6): e60.

[Full Text](#)

Department of Physical Medicine & Rehabilitation

LaBan MM, Braddom RL and Melvin JL (2019). "Ernest W. Johnson, M.D. - Apodictically speaking, A Phys-ee-at'-Trist for all seasons." *PM & R*. ePub Ahead of Print.

[Full Text](#)

Department of Physical Medicine and Rehabilitation

Lee JH, Rizvi A, Hartaigh BÓ, Han D, Park MW, Roudsari HM, Stuijzand WJ, Gransar H, Lu Y, Callister TQ, Berman DS, DeLago A, Hadamitzky M, Hausleiter J, Al-Mallah MH, Budoff MJ, Kaufmann PA, **Raff GL, Chinnaiyan K**, Cademartiri F, Maffei E, Villines TC, Kim YJ, Leipsic J, Feuchtner G, Pontone G, Andreini D, Marques H, de Araújo Gonçalves P, Rubinshtein R, Achenbach S, Shaw LJ, Chow BJW, Cury RC, Bax JJ, Chang HJ, Jones EC, Lin FY, Min JK and Peña JM (2019). "The predictive value of coronary artery calcium scoring for major adverse cardiac events according to renal function (from the Coronary Computed Tomography Angiography Evaluation for Clinical Outcomes: An International Multicenter [CONFIRM] Registry)." *American Journal of Cardiology* 123(9): 1435-1442.

[Full Text](#)

Department of Internal Medicine

The prognostic performance of coronary artery calcium score (CACS) for predicting adverse outcomes in patients with decreased renal function remains unclear. We aimed to examine whether CACS improves risk stratification by demonstrating incremental value beyond a traditional risk score according to renal function status. 9,563 individuals without known coronary artery disease were enrolled. Estimated glomerular filtration rate (eGFR, ml/min/1.73 m²) was ascertained using the modified Modification of Diet in Renal Disease formula, and was categorized as: ≥90, 60 to 89, and <60. CACS was categorized as 0, 1 to 100, 101 to 400, and >400. Multivariable Cox regression was used to estimate hazard ratios (HR) with 95% confidence intervals (95% CI) for major adverse cardiac events (MACE), comprising all-cause mortality, myocardial infarction, and late revascularization (>90 days). Mean age was 55.8 ± 11.5 years (52.8% male). In total, 261 (2.7%) patients experienced MACE over a median follow-up of 24.5 months (interquartile range: 16.9 to 41.1). Incident MACE increased with higher CACS across each eGFR category, with the highest rate observed among patients with CACS >400 and eGFR <60 (95.1 per 1,000 person-years). A CACS >400 increased MACE risk with HR 4.46 (95% CI 1.68 to 11.85), 6.63 (95% CI 4.03 to 10.92), and 6.14 (95% CI 2.85 to 13.21) for eGFR ≥90, 60 to 89, and <60, respectively, as compared with CACS 0. Further, CACS improved discrimination and reclassification beyond Framingham 10-year risk score (FRS) (AUC: 0.70 vs 0.64; category

free-NRI: 0.51, all $p < 0.001$) for predicting MACE in patients with impaired renal function (eGFR < 90). In conclusion, CACS improved risk stratification and provided incremental value beyond FRS for predicting MACE, irrespective of eGFR status.

Lertjirachai I, Wood EH, **Moinuddin O** and **Drenser KA** (2019). "Late re-activation of Coats disease." [American Journal of Ophthalmology Case Reports](#) 15: 100458.

[Full Text](#)

OUWB Medical Student Author

Department of Ophthalmology

Purpose: To report case of Coats disease with the longest known interval of disease quiescence prior to first reactivation (17 years). Observation: A 25-year-old male was regularly followed for Coats disease since age 4. After initial treatment with cryoablation, disease quiescence was achieved at age 8. The disease activity was well controlled for 17 years after which he developed decreased vision in the right eye at age 25. Late reactivation of Coats disease was diagnosed and multiple treatments ensued. Despite aggressive therapy, the patient experienced progressive exudation warranting surgical management and eventually developed neovascular glaucoma. Conclusion: Once diagnosed with Coats disease, lifelong monitoring is essential to early detection and treatment of potential disease reactivation. The interval between disease quiescence and reactivation is variable, with this case representing the longest known interval of disease quiescence prior to first reactivation (17 years).

Li C, Zhang Y, Levin AM, Fan BY, Teng H, **Ghannam MM**, Chopp M and Zhang ZG (2019). "Distal axonal proteins and their related miRNAs in cultured cortical neurons." [Molecular Neurobiology](#) 56(4): 2703-2713.

[Full Text](#)

OUWB Medical Student Author

Proteins and microRNAs (miRNAs) within the axon locally regulate axonal development. However, protein profiles of distal axons of cortical neurons have not been fully investigated. In particular, networks of genes encoding axonal proteins and their related miRNAs in sub compartments of neurons such as axons remain unknown. Using embryonic cortical neurons cultured in a microfluidic device and proteomic approaches, we found that distal axons contain 883 proteins. Bioinformatics analysis revealed that 94 out of these 883 proteins are related to regulating axonal growth. Of the 94 genes encoding these proteins, there were 56 candidate genes that can be putatively targeted by axon-enriched 62 miRNAs with 8mer sites that exactly match these target genes. Among them, we validated 11 proteins and 11 miRNAs, by means of western blot and RT-PCR, respectively. Treatment of distal axons with chondroitin sulfate proteoglycans (CSPGs) that inhibit axonal growth elevated miR-133b, -203a, -29a, and -92a, which were associated with reduced protein level of AKT, MTOR, PI3K, DPYSL2, MAP1B, and PPP2CA. In contrast, reduction of miR-128, -15b, -195, -26b, -34b, -376b, and -381 by CSPGs was accompanied by increased EZR, KIF5A, DCX, GSK3B, and ROCK2 proteins. In silico pathway analysis revealed an interconnected network of these miRNAs and protein coding genes that is highly related to regulating axonal growth. Our data provide new insights into networks of miRNAs and their related proteins in distal axons in mediating axonal growth.

Li X, Ding X, Liu G, Janssens G, Souris K, Montero AB, **Yan D, Stevens C** and **Kabolizadeh P** (2019). "Linear energy transfer incorporated spot scanning proton arc therapy (SPArc) optimization." [Medical Physics](#) 46(6): E292-E292.

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Department of Radiation Oncology

Li X, Liu G, Janssens G, De Wilde O, Bossier V, Lerot X, Pouppez A, **Yan D, Stevens C, Kabolizadeh P** and **Ding X** (2019). "From concept to first delivery of the spot-scanning proton arc therapy." [Medical Physics](#) 46(6): E290-E290.

[Request Form](#)

Department of Radiation Oncology

Lodise TP, Rosenkranz SL, Finnemeyer M, Evans S, **Sims M**, Zervos MJ, Creech CB, Patel PC, Keefer M, Riska P, Silveira FP, Scheetz M, Wunderink RG, Rodriguez M, Schrank J, Bleasdale SC, Schultz S, Barron M, Stapleton A, Wray D, Chambers H, Fowler V and Holland TL (2019). "The Emperor's New Clothes: Prospective observational evaluation of the association between initial vancomycin exposure and failure rates among adult hospitalized patients with MRSA

bloodstream infections (PROVIDE)." [Clinical Infectious Diseases](#). ePub Ahead of Print.

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Department of Internal Medicine

Background: Vancomycin is the most commonly administered antibiotic in hospitalized patients, but optimal exposure targets remain controversial. To clarify the therapeutic exposure range, this study evaluated the association between vancomycin exposure and outcomes in MRSA bacteremic patients. Methods: Prospective, multicenter (n=14), observational study of 265 hospitalized adults with MRSA bacteremia treated with vancomycin. The primary outcome was treatment failure (TF), defined as 30-day mortality or persistent bacteremia ≥ 7 days. Secondary outcomes included acute kidney injury (AKI). The study was powered to compare TF between patients who achieved or did not achieve day-2 area under the curve to minimum inhibitory concentration (AUC/MIC) thresholds previously found to be associated with lower incidences of TF. The thresholds, analyzed separately as co-primary endpoints, were AUC/MIC by broth microdilution ≥ 650 and AUC/MIC by Etest ≥ 320 . Results: Treatment failure and AKI occurred in 18% and 26% of patients, respectively. Achievement of the pre-specified day-2 AUC/MIC thresholds was not associated with less TF. Alternative day-2 AUC/MIC thresholds associated with lower TF risks were not identified. A relationship between the day-2 AUC and AKI was observed. Patients with day-2 AUC ≤ 515 experienced the best global outcomes (no TF and no AKI). Conclusions: Higher vancomycin exposures did not confer a lower TF risk but were associated with more AKI. The findings suggest that vancomycin dosing should be guided by the AUC and day-2 AUCs should be ≤ 515 . As few patients had day-2 AUCs < 400 , further study is needed to define the lower bound of the therapeutic range. TRIAL REGISTRATION: Registration was not required for this study.

Lombardo DJ, Siljander MP, Gehrke CK, **Moore DD**, **Karadsheh MS** and **Baker EA** (2019). "Fretting and corrosion damage of retrieved dual-mobility total hip arthroplasty systems." [The Journal of Arthroplasty](#) 34(6): 1273-1278.

[Full Text](#)

Department of Orthopedic Surgery

Background: Dual-mobility (DM) total hip arthroplasty (THA) systems are designed to increase stability while potentially avoiding problems associated with large femoral heads. Complications of these systems are not yet fully understood. This study aims at characterizing in vivo performance of DM hip systems and assessing modes of clinical failure. Methods: Under an institutional review board–approved implant retrieval protocol, 18 DM THA systems from 17 patients were included. Implants were graded at the head-neck junction for fretting and corrosion based on the system of Goldberg et al. Components were also macroscopically examined for different damage modes. Demographics and surgical data were collected from medical records, and radiographs were assessed for component positioning. Data were analyzed through Spearman rank-order correlation and Mann-Whitney U-tests, with $\alpha = 0.05$. Results: The average length of implantation was 13.4 months with mild to moderate fretting corrosion damage. Polyethylene (PE) liners exhibited edge deformation, scratching, and pitting damage. Metallic components exhibited burnishing and scratching damage. Summed fretting and corrosion scores were strongly correlated ($\rho = 0.967$, $P < .0001$). Summed corrosion score was moderately correlated with presence of embedding on the PE liner ($\rho = 0.690$, $P = .017$). PE liner abrasion and edge deformation of the femoral stem taper were moderately positively correlated ($\rho = 0.690$, $P = .017$). Fretting and corrosion damage were not significantly correlated with patient demographics or radiographic positioning of implants. There were no differences in scores between modular and monoblock designs. Conclusion: These findings demonstrate that dual-mobility THA systems may be susceptible to the same fretting and corrosion damage observed in traditional modular THA systems. Future studies are needed to confirm these results and clinical significance.

Macari D, Kawak S, Hanna L, Ezekwudo D, Khoury J, **Wasvary H** and **Jaiyesimi IA** (2019). "Recurrence pattern and outcomes in T4 colon cancer: A single institution analysis." [Journal of Clinical Oncology](#) 37(S4).

[Full Text](#)

Department of Surgery

Department of Internal Medicine

Background: Patients with T4 colon adenocarcinoma have an increased risk of peritoneal recurrence due to direct seeding malignant cells. It has been theorized that adjuvant chemotherapy may not sterilize the peritoneal surface due to inadequate intraperitoneal concentration. We seek to further define the metastatic

pattern, predictors of recurrence, and efficacy of adjuvant treatment in T4 colon cancer. Methods: We reviewed records of 181 adults [median age 71 (22-97)] with T4 N0-3 colon adenocarcinoma at Beaumont Hospital, Michigan from May 2005 -Nov 2015. Baseline factors and data on follow up, metastasis, and survival were collected and analyzed. Results: Overall recurrence rates for N0, N1, and N2 were 27/85 (32%), 17/50 (34%), and 29/46 (63%) ($p = 0.001$). Locoregional recurrence (LR) rates for N0, N1, and N2 were 21/85 (24.7%), 14/50 (28%), and 21/46 (45.7%) ($p = 0.014$). Multivariate analysis for distant recurrence was significant only for positive nodes with hazard ratio (HR) 3.3, 95% confidence interval (CI) 1.1-9.9. Multivariate analysis for increased risk of LR was significant for the following variables: perforation (HR 2.7, 95% CI 1.2 - 6.2), lymphovascular invasion (HR 2.7, 95% CI 1.1 - 6.7), positive nodes (HR 2.8, 95% CI 1.2 - 6.9), and positive margins (HR 5.0, 95% CI 2.1 - 12.1). Adjuvant chemotherapy did not decrease risk of LR (HR 0.6, 95% CI 0.3-1.2) or distant recurrence (HR 0.9, 95% CI 0.3-2.8). Multivariate analysis for overall survival revealed the following to be associated with increased risk of mortality: signet ring (HR 2.5, 95% CI 1.2-5.8), positive nodes (HR 2.3, 95% CI 1.2-4.4), positive margin (HR 2.8, 95% CI 1.4-5.8). Adjuvant chemotherapy was not associated with improved survival (HR 0.8, 95% CI 0.4-1.7). Recurrence was strongly associated with colon cancer-specific death with a $p < 0.001$. Conclusions: Adjuvant chemotherapy is standard of care for most T4 colon cancer patients, however, this data suggests there is no improvement in survival or other significant outcomes. We have identified several risk factors which predict increased risk of LR. This data suggests LR is frequent and not affected by systemic chemotherapy. Prospective trials are needed to reduce the substantial risk of LR in T4 colon cancer.

Macias S, Green B, Woodside J, **Graham S** and Yilmaz A (2019). "Application of 1H-NMR Metabolomics for the discovery of blood plasma biomarkers associated with adherence to a Mediterranean dietary pattern in a Northern European population." European Journal of Clinical Investigation 49: 78-78.

[Request Form](#)

Department of Obstetrics and Gynecology

Major M, **Long G**, Eden CL, Studzinski D, **Devaraj V** and **Brown OW** (2019). "Long-term outcomes and interventions of postoperative type IA endoleaks after elective endovascular aneurysm repair." Journal of Vascular Surgery 69(6): E212-E213.

[Request Form](#)

Department of Surgery

OUIB Medical Student Author

McConachie SM, Caputo RA, **Wilhelm SM** and Kale-Pradhan PB (2019). "Efficacy of capsaicin for the treatment of cannabinoid hyperemesis syndrome: A systematic review." Annals of Pharmacotherapy: 1060028019852601.

[Full Text](#)

OUIB Medical Student Author

Objective: Cannabinoid hyperemesis syndrome (CHS) is characterized by cyclic vomiting, abdominal pain, and alleviation of symptoms via hot showers in chronic cannabinoid users. Capsaicin is recommended as a reasonable first-line treatment approach for CHS despite limited clinical evidence regarding its use. The objective of this study is to systematically review the efficacy data for capsaicin in CHS. Data Sources: A literature search using keywords related to cannabinoids, emesis, and capsaicin was performed in MEDLINE, CINAHL, and EMBASE from inception through March 31, 2019. Study Selection and Data Extraction: Studies and published abstracts in which capsaicin was used for CHS and clinical outcomes were reported were eligible for inclusion. Data Synthesis: A total of 241 articles were screened, of which 5 full-text articles and 6 conference abstracts were included. Full-text case reports ($n = 3$) and case series ($n = 2$) found capsaicin to be effective in a total of 18 patients. Published abstracts were in the form of case reports ($n = 1$), case series ($n = 3$), and retrospective cohort studies ($n = 2$). Relevance to Patient Care and Clinical Practice: Capsaicin use was described as beneficial in all case series and case reports; however, both retrospective cohort studies were unable to find a significant benefit for capsaicin on primary outcomes (emergency department length of stay). Conclusion: Current data for capsaicin efficacy in CHS is of low methodological quality. However, the limited data on alternative antiemetic therapies and capsaicin's favorable risk-benefit profile make it a reasonable adjunctive treatment option.

Meurer WJ, Dome M, Brown D, Delemos D, **Oska S**, Gorom V and Skolarus L (2019). "Feasibility of emergency department-initiated, mobile health blood pressure intervention: An exploratory, randomized clinical trial." Academic Emergency Medicine 26(5): 517-527.

[Full Text](#)

OUWB Medical Student Author

Objectives: We aimed to assess the feasibility of a text messaging intervention by determining the proportion of emergency department (ED) patients who responded to prompted home blood pressure (BP) self-monitoring and had persistent hypertension. We also explored the effect of the intervention on systolic blood pressure (sBP) over time. **Methods:** We conducted a randomized, controlled trial of ED patients with expected discharge to home with elevated BP. Participants were identified by automated alerts from the electronic health record. Those who consented received a BP cuff to take home and enrolled in the 3-week screening phase. Text responders with persistent hypertension were randomized to control or weekly prompted BP self-monitoring and healthy behavior text messages. **Results:** Among the 104 patients enrolled in the ED, 73 reported at least one home BP over the 3-week run-in (screening) period. A total of 55 of 73 reported a home BP of $\geq 140/90$ and were randomized to SMS intervention (n = 28) or control (n = 27). The intervention group had significant sBP reduction over time with a mean drop of 9.1 mm Hg (95% confidence interval = 1.1 to 17.6). **Conclusions:** The identification of ED patients with persistent hypertension using home BP self-monitoring and text messaging was feasible. The intervention was associated with a decrease in sBP likely to be clinically meaningful. Future studies are needed to further refine this approach and determine its efficacy.

Mohammed N, Hung YC, Xu Z, Starke RM, Kano H, Lee J, Mathieu D, Kaufmann AM, **Grills IS**, Cifarelli CP, Vargo JA, Chytka T, Janouskova L, Feliciano CE, Mercado RR, Lunsford LD and Sheehan JP (2019). "A propensity score-matched cohort analysis of outcomes after stereotactic radiosurgery in older versus younger patients with dural arteriovenous fistula: An international multicenter study." World Neurosurgery 125: e1114-e1124.

[Full Text](#)

Department of Radiation Oncology

Objective: This study aims to evaluate the outcomes of Gamma Knife stereotactic radiosurgery (SRS) for dural arteriovenous fistulas (dAVFs) in older patients (≥ 65 years) compared with younger patients (age < 65 years). **Methods:** Two groups with a total of 96 patients were selected from a database of 133 patients with dAVF from 9 international medical centers with a minimum 6 months follow-up. A 1:2 propensity matching was performed by nearest-neighbor matching criteria based on sex, Borden grade, maximum radiation dose given, and location. The older cohort consisted of 32 patients and the younger cohort consisted of 64 patients. The mean overall follow-up in the combined cohort was 42.4 months (range, 6–210 months). **Results:** In the older cohort, a transverse sinus location was found to significantly predict dAVF obliteration (P = 0.01). The post-SRS actuarial 3-year and 5-year obliteration rates were 47.7% and 78%, respectively. There were no cases of post-SRS hemorrhage. In the younger cohort, the cavernous sinus location was found to significantly predict obliteration (P = 0.005). The 3-year and 5-year actuarial obliteration rates were 56% and 70%, respectively. Five patients (7.8%) hemorrhaged after SRS. Margin dose ≥ 25 Gy was predictive of unfavorable outcome. The obliteration rate (P = 0.3), post-SRS hemorrhage rate (P = 0.16), and persistent symptoms after SRS (P = 0.83) were not statistically different between the 2 groups. **Conclusions:** SRS achieves obliteration in most older patients with dAVF, with an acceptable rate of complication. There was no increased risk of postradiosurgery complications in the older cohort compared with the younger patients.

Muir R, Hemmelgarn J, **Li W**, **Kanaan H**, Misuraca M and **Zhang P** (2019). "IGG4 staining can serve as a screening biomarker for primary membranous glomerulopathy (MGN)." American Journal of Kidney Diseases 73(5): 708-709.

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Department of Pathology

Musa A, Acosta FL, Tuchrnan A, Movahedi R, Pendi K, Nassif L, Farhan SA, **Muallem E** and Gucev G (2019). "Addition of intrathecal morphine for postoperative pain management in pediatric spine surgery: A meta-analysis." Clinical Spine Surgery 32(3): 104-110.

[Full Text](#)

OUWB Medical Student Author

Study Design: Meta-analysis. Objective: The objective of this study was to determine whether adjunctive intrathecal morphine (ITM) reduces postoperative analgesic consumption following pediatric spine surgery. Summary of Background Data: Previous studies that have tested supplemental ITM to manage pain after pediatric spine surgery have been limited by small sample sizes. Methods: A comprehensive search of PubMed, Web of Science, Clinicaltrials.gov, and the Cochrane Central Register of Controlled Trials was performed for clinical trials and observational studies. Time to first analgesic demand, postoperative analgesic use, pain scores, and complication data were abstracted from each study. Mean difference (MD) and 95% confidence interval (CI) were used to compare continuous outcomes and odds ratios (OR) and 95% CI were used for dichotomous outcomes. Results: A total of 5 studies, including 3 randomized controlled trials and 2 retrospective chart reviews, containing 636 subjects, were incorporated into meta-analysis. Subjects that were administered ITM in addition to postoperative analgesics (ITM group) were compared with those receiving postoperative analgesics only (control group). In the ITM group, time to first analgesic demand was longer (MD, 8.79; 95% CI, 4.20-13.37; $P < 0.001$), cumulative analgesic consumption was reduced at 24 hours (MD, -0.40; 95% CI, -0.56 to -0.24; $P < 0.001$), and cumulative analgesic consumption was reduced at 48 hours (MD, -0.43; 95% CI, -0.59 to -0.27; $P < 0.001$). Neither postoperative pain scores at 24 hours ($P = 0.16$) nor 48 hours ($P = 0.18$) were significantly different between ITM and control groups. Rates of respiratory depression, nausea, vomiting, and pruritus were not different between groups (all $P > 0.05$). Conclusions: Addition of ITM in pediatric spine surgery produced a potent analgesic effect in the immediate postoperative period. Patients administered ITM did not request opiates as early as control and consumed fewer opiates by the second postoperative day. Furthermore, use of ITM did not increase complications such as respiratory depression, nausea, vomiting, or pruritus.

Myziuk N, **Sakthivel G**, **Foster L**, Solis D, Sala I, Castillo E and **Guerrero T** (2019). "Predicting post-SBRT pulmonary function using 4DCT-derived ventilation idadamaging." Medical Physics 46(6): E644-E644.

[Request Form](#)

OUWB Medical Student Author

Department of Radiation Oncology

Neumann M, Evans M and **Sargent E** (2019). "Internal auditory canal exostosis: A case report and review of literature." Otolaryngology Case Reports 11(June): 100119.

[Full Text](#)

Department of Surgery

Objective: Exostosis of the internal auditory canal (IAC) is a rarely reported entity. We present a case of unilateral IAC exostosis with longitudinal radiographic imaging and its associated abnormal neurodiagnostic and audiologic studies. To our knowledge, this is the first documented report of a patient with hyperostosis of the IAC who was radiologically followed for over a decade. Methods: One patient with unilateral IAC exostosis from the Michigan Ear Institute, a private tertiary referral center, is presented. Radiologic, neurodiagnostic, and audiologic modalities are reviewed with a discussion of the pertinent literature and current treatment options. Results: No change in radiologic findings or clinical symptoms in over a decade of follow-up. Abnormal audiograms, facial nerve electroneuronography, audio brainstem reflex, and videonystagmography were documented. Conclusions: Bony exostosis of the IAC is a rare condition and the natural history is still largely unknown. In this case, there was no progression of bony narrowing of the porus acousticus over a 12-year time period. This, in conjunction with stable symptomatology, has led us to recommend a trial of watchful waiting with conservative management. Future studies should be performed to monitor patients over time with serial imaging, audiograms, and neurodiagnostic testing to elucidate the natural history of this condition.

Neves S and **Soto RG** (2019). "Distraction in the OR: Bells and whistles on silent mode." International Anesthesiology Clinics 57(3): 62-67.

[Full Text](#)

Department of Anesthesiology

Nguyen B, Blasco M, Svider PF, Lin HS, **Liu JK**, Eloy JA and **Folbe AJ** (2019). "Recurrence of ventral skull base lesions attributed to tumor seeding: A systematic review." World Neurosurgery 124: e395-e403.

[Full Text](#)

Department of Pathology

Department of Surgery

OUWB Medical Student Author

Objective: To evaluate ventral skull base lesion recurrences along surgical access pathways attributed to iatrogenic seeding. Methods: A systematic review of the literature was performed searching for recurrence of ventral skull base lesions attributed to iatrogenic implantation. Studies were assessed for level of evidence. Primary intervention, pathology, and other clinical factors were reported following Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. Results: Among 69 patients with recurrent skull base lesions attributed to seeding, the most common pathologies were craniopharyngioma (52.2%), chordoma (33.3%), adenocarcinoma (4.3%), adenoid cystic carcinoma (2.9%), and squamous cell carcinoma (2.9%). Median time to recurrence was 36 months. Time to recurrence was significantly longer for craniopharyngiomas than for chordomas (42 months vs. 24 months, $P \leq 0.05$). Surgical approaches included craniotomy (62.0%), transseptal (11.3%), transfacial (12.7%), and transpalatal (4.2%). Mean time to recurrence after craniotomy was 69 months. Endoscopic/endoscopic-assisted approaches were used in 5 cases (7.0%). Commonly reported recurrence sites included subarachnoid (29.6%), dura (21.1%), incision (12.7%), septum (7.0%), and ethmoid sinuses (4.2%). Conclusions: The potential for iatrogenic tumor seeding exists for numerous skull base lesions, most notably craniopharyngioma and chordomas. Routine surveillance may be necessary owing to significant latency intervals to ectopic recurrence. Although transnasal endoscopic techniques have been extensively employed in recent decades, only a handful of reported cases involve lesions originally treated with this approach. Further direct comparison of traditional approaches with endoscopic approaches may be invaluable in further elucidating the role of surgical technique in tumor implantation and recurrence.

Nguyen BK, Yuhan BT, Folbe E, Eloy JA, Zuliani GF, Hsueh WD, Paskhover B, Folbe AJ and Svider PF (2019).

"Perioperative analgesia for patients undergoing septoplasty and rhinoplasty: An evidence-based review."

Laryngoscope 129(6): E200-E212.

[Full Text](#)

OUWB Medical Student Author

Department of Surgery

Objectives/Hypothesis: Opioid misuse and diversion is a pressing topic in today's healthcare environment. The objective of this study was to conduct a review of non-opioid perioperative analgesic regimens following septoplasty, rhinoplasty, and septorhinoplasty. Study Design: Evidence-based systematic review. Methods: PubMed, MEDLINE, Cochrane Library, and Embase databases were reviewed for articles related to perioperative analgesic use in septoplasty, rhinoplasty, and septorhinoplasty. Quality of studies were assessed via the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) criteria, Jadad scores, and the Cochrane bias tool. Patient demographic data and clinical outcomes, including medication type, dose, administration time, pain scores, and adverse events, were obtained from included studies. Summary tables detailing the benefits and harms of each investigated regimen are included. Results: Thirty-seven studies met inclusion criteria for this evidence-based review. The quality of the studies was determined to be of moderate quality based off of GRADE standardized criteria with a mean Jadad score of 3.1. A preponderance of evidence showed reduced perioperative pain scores and rescue analgesic requirements, supporting the use of local anesthetics for analgesic control. Nonsteroidal anti-inflammatory drugs (NSAIDs) demonstrated similar decreased visual analog scores and postoperative analgesic demand; however, increased adverse events in this class warrant caution. Conclusions: Contemporary literature supports the use of NSAIDs, gabapentin, local anesthetics, and α -agonists as effective perioperative analgesic opioid alternatives for septoplasty and septorhinoplasty. Local anesthetic use is a cost-effective option resulting in decreased postoperative pain scores and rescue analgesic requirements. Further large-scale, multi-institutional, controlled studies are needed to provide definitive recommendations. Level of Evidence: NA. *Laryngoscope*, 129:E200–E212, 2019.

Niedermaier MS, **Nair GB**, Matt U, Herold S, Pennington K, Crothers K, Cummings M and Schluger NW (2019). "Update in lung infections and tuberculosis 2018." *American Journal of Respiratory and Critical Care Medicine*. ePub Ahead of Print.

[Full Text](#)

Department of Internal Medicine

Nyalakonda R and **Berman B** (2019). "A teenage female with transient dysarthria, pallor, and petechiae." [Clinical Pediatrics \(Phila\)](#): 9922819850487.

[Full Text](#)

OUWB Medical Student Author

Department of Pediatrics

Nyalakonda R and **Zarouk S** (2019). "Acute kidney injury in neurofibromatosis type 1." [American Journal of Kidney Diseases](#) 73(5): 711-712.

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OUWB Medical Student Author

Department of Internal Medicine

O'Connell RL, Rattay T, Dave RV, Trickey A, Skillman J, Barnes NLP, Gardiner M, Harnett A, Potter S, Holcombe C, Blazeby J, Conroy E, Dave RV, Gardiner M, Harnett A, Holcombe C, O'Brien C, Potter S, Williamson P, Curnier A, Tadros A, Depasquale I, Masannat YA, Smyth E, Fuller M, Bourne R, Heys S, Hamo I, Aloraifi F, Fopp L, Bali R, Bache S, Benyon SL, Irwin MS, Agrawal A, Malata CM, Murphy C, Misky A, Chicken DW, Abdullah N, Hill ADK, Cullinane C, Irwin G, McIntosh SA, Refsum S, Sloan S, Mallon P, Sirianni C, Khattak I, Sirianni C, Nagachandra G, Kiruparan P, Debanth D, Davey S, Curran TA, Svenning M, Govindarajulu S, Rayter Z, Ainsworth R, Cawthorn S, Sahu A, Wilson S, Prouskaia E, Accurso A, Rocco N, Di Micco R, Accurso A, Limite G, Ceccarino R, Liccardo R, Coco G, Nizamoglu M, Morgan M, Ramakrishnan V, Catanuto G, Wilkins A, McManus P, Kneeshaw P, Grover K, Mahapatra T, Wooler B, Elahi B, Ihsan N, Bucknor A, Reissis D, Hunter J, Wood S, Jallali N, Henry FP, Verjee LS, Lee J, Khan SM, Azmy I, Massey J, Hollywood C, Oluwajana M, Bathla S, Seward J, Harding-MacKean C, Lane R, Murali K, Biswas B, Trapszo P, Seetharam S, Kennedy K, Alder L, Graja T, Amin K, Kokan J, Roshanlall C, Gill E, Kulkarni D, Dixon JM, Young O, Saleem T, Biddle M, Kearns M, Weiler-Mithoff E, Chew B, Malyon A, Scott J, McGill D, Mackay I, Bains S, Barrows S, Rattay T, Pilgrim S, Shokuhi S, Lambert K, Kenny F, Valassiadou K, Kaushik M, Krupa J, Dragoumis D, Ain Q, Lampropoulos P, Moss S, Khalil H, Haq A, Balasubramanian B, Charalampou-Dis P, Hamed H, Kothari A, Kovacs T, Douek M, Mehmood I, Ray B, Adelekan M, Humphreys L, Tayeh S, Choy C, Parvanta L, Michieletto S, Saibene T, O'Brien J, Down S, Downey S, Pereira J, Sami AS, Gvaramadze A, Jibril JA, Thekkinkattil D, Udayasankar S, Khawaja S, Shariha Y, Holt S, James R, Rizki H, Kirkpatrick K, Ravichandran D, Shrestha D, Barua E, Akolekar D, Hamad A, Kleidi E, Hignett S, Pope V, Naseem S, Isherwood J, Soulsby R, Taylor A, Chin K, Nguyen D, Guest F, Thorne A, Kirchoff C, Murphy DC, Lo M, Harcourt R, Pain SJ, Hussien MI, Zechmeister K, Sassoon EM, Figus A, Haywood RM, Ali R, Alexander S, Harnett A, Geropantas K, Epurescu D, Lewis R, Fafemi O, Gahir J, Gandamihardja T, Kelsall J, Muhibullah N, Otieno C, Mazari F, Dauria M, Whisker L, Macmillan D, Gutteridge E, Rasheed T, Khout H, Asgeirsson K, McCulley S, Mariniello MD, Roncella M, Ghilli M, Colizzi L, Rossetti E, Marzia LR, Fustaino L, Li AQ, Harvey KL, Windle R, Remoundos DD, Roy P, MacLean G, Adwani A, Popa E, Goh S, Shetty G, Clark S, Bernaudo L, Agrawal A, Mansfield L, Tebbal S, Patel A, Grassi V, Pujji O, Hamnett K, Basu N, Granger E, Durbar M, Pikoulas P, Garnsey C, Walker P, Vollmer AJ, Michalakis I, Jones R, Youssef M, Ives C, Masood M, Dunn J, Olsen S, Ferguson D, Tillett R, Allan A, Woollard A, Canny R, Woollard A, Mosahebi A, Hamilton S, Ghali S, Marsh D, Chana J, Sojitra N, Younis I, Rainsbury D, Chand N, Kalles V, Stebbing A, Harris K, Laws S, Holcombe C, Tansley A, Mitchell G, de Sousa E, Henderson J, Chandrashekar M, Pereira B, Constantinou C, Elfadl D, Irakleidis F, Hernan I, Byrne M, To N, O'Connell R, Rusby J, Barry P, Krupa K, Allum W, MacNeill F, Roche N, Gui G, Ramsey K, **Harris P**, James S, Power K, Potter S, Sutton R, McIntosh J, Laurence N, MacLennan L, Milligan R, Cain H, Critchley A, O'Donoghue J, Kalra L, Collis N, Weston-Petrides G, Fiddes R, Brown V, Aertssen A, Slade-Sharman D, Khan M, McGuinness C, Amorosi V, Fabio SD, Exarchos G, Jiwa N, Hu J, Ledwidge S, Johnson L, Peel A, Dhooma N, Farrell E, Devane L, Tevlin R, McDermott E, Prichard R, Evoy D, Rothwell J, Geraghty J, Morrison C, Lawlor C, Langlands F, Taylor L, Turton P, Achuthan R, Horgan K, McKenzie S, Hogan B, Lansdown M, Navin C, Sherwin L, Mortimer C, Garg N, Adam R, Arif T, Kryjak Z, Ali D, Sowdi R, Fage E, Mylvaganam S, Matey P, Vidya R, Sircar T, Asaad O, Bhaskar P, Dordea M, Chrysafi A, McCartan D, Dave R, Foster R, Wilson R, Okwemba S, Majeed Y, O'Brien C, Mathen V, Murphy J, Barnes N, Gandhi A, Harvey J, Kirwan CC, Johnson R, Patel K, Ribas MD, Vigneswaran N, Challoner T, Skillman J, Park A, Rizkalla M, Tomlins A, McEvoy K, Jafferbhoy S, Soumian S, Narayanan S, Kirby R, Bajrusevic S, Maalo J, Charalambous M, Lai LM, Chong K, Thomson S, Monib S, Chagla L, Audisio R, Taghizadeh R, Iqbal A, James K, Callaghan M, Poonawala S, Lund J, Vinayagam R, Jafferbhoy S, Thrush S, Thomas RB, Mullan M, Taylor J, Yoshimura R, Mathew T, Jones B, Munot K, Nasr

R, Piper J, El-Sharief D, Mustafa M, Dumitru D, Christopoulos P, O'Leary P, Athanasiou I, Johns N, Mehta D, Bibi S, Syed F, Koris J, Healy S, Shanks L, Oliver J, Bucata C, Clarke N, Bignell K, Akerlund M, Brock L, Hallam K, Howes R, Armstrong A, Sethu C, Zeidan B, Sjkovist O, Tasoulis M, Sundaramoorthy S, Harris C, Wintrip D, Lymperopoulos N, Jain Y, Balata SA, i BRASG and Breast Reconstruction Res C (2019). "The impact of immediate breast reconstruction on the time to delivery of adjuvant therapy: the iBRA-2 study." [British Journal of Cancer](#) 120(9): 883-895.

[Request Form](#)

Department of Diagnostic Radiology and Molecular Imaging

Background: Immediate breast reconstruction (IBR) is routinely offered to improve quality-of-life for women requiring mastectomy, but there are concerns that more complex surgery may delay adjuvant oncological treatments and compromise long-term outcomes. High-quality evidence is lacking. The iBRA-2 study aimed to investigate the impact of IBR on time to adjuvant therapy. Methods: Consecutive women undergoing mastectomy +/- IBR for breast cancer July-December, 2016 were included. Patient demographics, operative, oncological and complication data were collected. Time from last definitive cancer surgery to first adjuvant treatment for patients undergoing mastectomy +/- IBR were compared and risk factors associated with delays explored. Results: A total of 2540 patients were recruited from 76 centres; 1008 (39.7%) underwent IBR (implant-only [n = 675, 26.6%]; pedicled flaps [n = 105, 4.1%] and free-flaps [n = 228, 8.9%]). Complications requiring re-admission or re-operation were significantly more common in patients undergoing IBR than those receiving mastectomy. Adjuvant chemotherapy or radiotherapy was required by 1235 (48.6%) patients. No clinically significant differences were seen in time to adjuvant therapy between patient groups but major complications irrespective of surgery received were significantly associated with treatment delays. Conclusions: IBR does not result in clinically significant delays to adjuvant therapy, but post-operative complications are associated with treatment delays. Strategies to minimise complications, including careful patient selection, are required to improve outcomes for patients.

O'Neill BP, Cohen MG, Basir MB, Schreiber T, Kapur NK, **Dixon S**, Khandelwal AK, Grines C, Ohman EM and O'Neill WW (2019). "Outcomes among patients transferred for revascularization with impella for acute myocardial infarction with cardiogenic shock from the cVAD registry." [American Journal of Cardiology](#) 123(8): 1214-1219.

[Full Text](#)

Department of Internal Medicine

The outcomes for patients transferred with cardiogenic shock and later treated with revascularization and Impella support have not previously been studied. To evaluate these outcomes, patients in cardiogenic shock were recruited from the catheter-based ventricular assist device registry, a prospective registry enrolling patients who underwent percutaneous coronary intervention with hemodynamic support using Impella 2.5 or CP. Analysis was performed on subgroups of patients who were characterized as those directly admitted to a tertiary care hospital (direct), or those transferred from an outside hospital (transfer). Patients who were transferred with acute myocardial infarction with cardiogenic shock (AMICS) more often presented in shock were in shock longer than 24 hours, and were more likely to be on intra-aortic balloon pump but were less likely to sustain cardiac arrest. The number of pressors, EF, diseased, and treated vessels were similar between the 2 groups. Despite baseline differences, the mortality was similar in the transfer versus direct patients (47.0% vs 53.5% p = 0.19). In a multivariate model, the factors independently associated with 30-day mortality in AMICS treated with revascularization and Impella support were cardiopulmonary resuscitation (CPR) (p <0.01), age (p <0.01), and ST-segment elevation myocardial infarction (STEMI) (p = 0.02). Whether the patient was transferred or directly admitted with AMICS was not an independent predictor of death. In conclusion, these findings suggest that considerations should be given to transfer patients with AMICS to allow them to be treated in a contemporary manner.

Parzen JS, Ye H, **Gustafson GS**, Martinez A, Sebastian E, Limbacher A and **Krauss DJ** (2019). "Rectal toxicity results for patients treated with HDR brachytherapy as monotherapy versus dose-escalated external beam radiotherapy for localized prostate cancer." [Journal of Clinical Oncology](#) 37(S7).

[Full Text](#)

Department of Radiation Oncology

Background: We present a large retrospective analysis comparing rectal toxicity following high dose rate (HDR) brachytherapy as monotherapy relative to dose-escalated external beam radiotherapy (EBRT) for patients with localized prostate cancer. Methods: 2683 patients treated with HDR or EBRT between 1994 and

2017 were included. 545 (20.3%) received HDR and 2138 (79.7%) EBRT. HDR fractionation was 38 Gy/4 fractions (n=321), 24 Gy/2 (n=96), or 27 Gy/2 (n=128). EBRT patients received a median dose of 75.6 Gy in 1.8 Gy fractions [range 70.2-82.8 Gy], using either 3D conformal or intensity modulated radiotherapy (IMRT). All EBRT patients underwent 3D image guidance via an off-line adaptive process. Treatment was directed to prostate only (n=780) or prostate and seminal vesicles (n=1351). No nodal therapy was given. Target volume for HDR patients included the prostate with no expansion. Acute and chronic gastrointestinal (GI) toxicity was defined as occurring ≤ 6 and > 6 months, respectively, after radiotherapy and was graded per CTCAE version 3.0. Toxicity variables were analyzed with χ^2 test. Results: Median follow-up was 7.5 years (7.4 years for EBRT and 7.9 years for HDR). 69.1% of EBRT patients received IMRT with the remainder treated using 3D conformal technique. Compared to EBRT, HDR was associated with decreased rates of acute grade ≥ 2 diarrhea (0.7% vs. 4.5%, $p < 0.001$), rectal pain/tenesmus (0.6% vs. 7.9%, $p < 0.001$), and rectal bleeding (0% vs. 1.6%, $p=0.001$). Rates of chronic grade ≥ 2 rectal bleeding (1.3% vs. 8.7%, $p < 0.001$) and radiation proctitis (0.9% vs. 3.3%, $p=0.001$) favored HDR over EBRT. Rates of any chronic rectal toxicity grade ≥ 2 were 2.4% vs. 10.5% ($p < 0.001$) for HDR vs. EBRT, respectively. For the 1478 EBRT patients treated with IMRT, acute and chronic rates of any grade ≥ 2 GI toxicity were 4.2% and 5.6%, respectively, compared to 1.5% ($p=0.002$) and 2.4% ($p=0.002$), respectively, for HDR patients. Conclusions: In appropriately selected patients with localized prostate cancer undergoing definitive radiation therapy, HDR brachytherapy as monotherapy is an effective strategy for reducing acute and chronic rectal toxicity.

Paulauskis JD, Blanc VM, Carey T, Chesla DW, Frey RC, Geddes T, Keats J, Loup A, Pruetz B, Rohrer DC, Valley DR, Tomlinson T, Akervall J, **Wilson GD** and Jewell SD (2019). "Great Lakes Biorepository Research Network's Annual Biobanking Symposium: A focus on precision medicine." Biopreservation and Biobanking. ePub Ahead of Print.
[Request Form](#)

Department of Radiation Oncology

Popa T, Morris LS, **Hunt R**, Deng ZD, Horovitz S, Mente K, Shitara H, Baek K, Hallett M and Voon V (2019). "Modulation of resting connectivity between the mesial frontal cortex and basal ganglia." Frontiers in Neurology 10: 587.

[Full Text](#)

OUWB Medical Student Author

Background: The mesial prefrontal cortex, cingulate cortex, and the ventral striatum are key nodes of the human mesial fronto-striatal circuit involved in decision-making and executive function and pathological disorders. Here we ask whether deep wide-field repetitive transcranial magnetic stimulation (rTMS) targeting the mesial prefrontal cortex (MPFC) influences resting state functional connectivity. Methods: In Study 1, we examined functional connectivity using resting state multi-echo and independent components analysis in 154 healthy subjects to characterize default connectivity in the MPFC and mid-cingulate cortex (MCC). In Study 2, we used inhibitory, 1 Hz deep rTMS with the H7-coil targeting MPFC and dorsal anterior cingulate (dACC) in a separate group of 20 healthy volunteers and examined pre- and post-TMS functional connectivity using seed-based and independent components analysis. Results: In Study 1, we show that MPFC and MCC have distinct patterns of functional connectivity with MPFC-ventral striatum showing negative, whereas MCC-ventral striatum showing positive functional connectivity. Low-frequency rTMS decreased functional connectivity of MPFC and dACC with the ventral striatum. We further showed enhanced connectivity between MCC and ventral striatum. Conclusions: These findings emphasize how deep inhibitory rTMS using the H7-coil can influence underlying network functional connectivity by decreasing connectivity of the targeted MPFC regions, thus potentially enhancing response inhibition and decreasing drug-cue reactivity processes relevant to addictions. The unexpected finding of enhanced default connectivity between MCC and ventral striatum may be related to the decreased influence and connectivity between the MPFC and MCC. These findings are highly relevant to the treatment of disorders relying on the mesio-prefrontal-cingulo-striatal circuit.

Pople B, Kiran S, Kopicky L, **Chen P** and **Dekhne N** (2019). "A single-institution review of APBI using brachytherapy versus IORT: A patterns-of-care analysis." Annals of Surgical Oncology 26: 146-147.

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OUWB Medical Student Author

Department of Surgery

Porter E, **Fuentes P**, Siddiqui Z, Thompson A and **Guerrero T** (2019). "Hippocampal segmentation from CT scans with a convolutional neural network." Medical Physics 46(6): E431-E431.

[Request Form](#)

Department of Radiation Oncology

OUIB Medical Student Author

Quindry JC, **Franklin BA**, Chapman M, Humphrey R and Mathis S (2019). "Benefits and risks of high-intensity interval training in patients with coronary artery disease." American Journal of Cardiology 123(8): 1370-1377.

[Full Text](#)

Department of Internal Medicine

Exercise-based cardiac rehabilitation is integral to secondary prevention in patients with coronary artery disease. Recently, the effectiveness and "superiority" of high-intensity interval training (HIIT) is a purported time-saving alternative to "traditional" moderate-intensity continuous training (MICT) in cardiac rehabilitation. The rationale for HIIT adoption is, however, not fully substantiated in the scientific literature. Established guidelines for exercise testing and training, when carefully adhered to, reduce the likelihood of triggering a cardiac event or inducing musculoskeletal injury. Clinicians should likewise consider patient risk stratification and introduce HIIT as an alternative to MICT only after patients exhibit stable and asymptomatic responses to vigorous exercise training. Although HIIT adherence appears comparable with MICT during outpatient rehabilitation, compliance drops dramatically for unsupervised exercise. Despite the enthusiasm surrounding HIIT, its main advantage over MICT appears to be short-term exercise performance outcomes and indices of vascular function. Regarding benefits to cardiovascular disease risk factor modification, management of vital signs, and measures of cardiac performance, current evidence indicates that HIIT does not outperform MICT. Long-term outcomes to HIIT are currently uncertain and logistical constraints to HIIT incorporation need additional clarification. Based on these limited findings, derived from facilities and clinicians at the forefront of cardiac rehabilitation, the routine adoption of HIIT should be viewed cautiously. In conclusion, the current review highlights numerous specific research directives that are needed before the safety and effectiveness of HIIT can be confirmed and widely adopted in patients with known or suspected coronary artery disease, especially in unsupervised, nonmedical settings.

Rapp CM, Shields EJ, **Wiater BP** and **Wiater JM** (2019). "Venous thromboembolism after shoulder arthroplasty and arthroscopy." Journal of the American Academy of Orthopaedic Surgeons 27(8): 265-274.

[Full Text](#)

Department of Orthopedic Surgery

Venous thromboembolism (VTE) in the orthopaedic literature largely focuses on lower extremity trauma and arthroplasty, with relatively few investigations of VTE after shoulder surgery. Because the rate of shoulder surgery, especially arthroplasty, continues to expand, it is important for practicing surgeons to understand the magnitude of risk, potential consequences, and prevention methods with regard to VTE. VTE after shoulder surgery has been a topic of increasing interest over the past decade, and the purpose of this review is to examine the recent literature on pathophysiology, risk factors, incidence, diagnosis, sequelae, prevention, treatment, and current recommendations regarding VTE after shoulder surgery.

Reitsma M, Fox J, Borre PV, Cavanaugh M, Chudnovsky Y, Erlich RL, Gribbin TE and Anhorn R (2019). "Effect of a collaboration between a health plan, oncology practice, and comprehensive genomic profiling company from the payer perspective." Journal of Managed Care and Specialty Pharmacy 25(5): 601-611.

[Full Text](#)

OUIB Medical Student Author

Background: Comprehensive genomic profiling (CGP) is a next-generation sequencing-based methodology that detects 4 classes of genomic alterations, as well as gene signature biomarkers such as microsatellite instability and tumor mutational burden. In the context of precision oncology, CGP can help to direct treatment to genomically matched therapies. Objective: To describe the results of a 3-year observational analysis of patients undergoing testing with CGP assays (either FoundationOne or FoundationOne Heme) at a community oncology practice after a regional health plan implemented a medical policy that enabled

coverage of CGP. Methods: A retrospective analysis of medical records was completed at the oncology practice from November 2013 to January 2017; this date range was chosen to coincide with the regional health plan's medical policy implementation of CGP. The medical policy provided coverage of CGP for patients with advanced solid and hematologic cancers. A medical record review assessed all previous and current molecular test results, matched therapy or clinical trial enrollment, and clinical outcomes (clinical benefit or disease progression). The potential cost diversion, from payer to study sponsor, for patients who enrolled in clinical trials was explored. Results: There were 96 patients in the community oncology practice who received CGP over the 3-year period, 86 of whom had clinically relevant genomic alterations. Of the 86, 15 patients were treated with genomically matched therapy, and 6 patients enrolled in clinical trials based on CGP results. In a subset of 32 patients who previously underwent conventional testing, most (84%) had clinically relevant genomic alterations detected by CGP that conventional testing did not identify, and a portion of these patients subsequently received treatment based on the CGP results. In the separate cost diversion analysis of 20 patients who enrolled in phase 1 clinical trials, an estimated \$25,000 per-patient cost-benefit may have been accrued to the payer. Conclusions: This observational analysis characterized the use of CGP in a large community oncology practice among a group of patients insured by a regional health plan. Clinical trial enrollment was facilitated by CGP use in the community setting and may have contributed to cost diversion from the payer to study sponsors.

Richardson CR, **Franklin B**, Moy ML and Jackson EA (2019). "Advances in rehabilitation for chronic diseases: Improving health outcomes and function." *BMJ* 365: l2191.

[Full Text](#)

Department of Internal Medicine

Much of the burden on healthcare systems is related to the management of chronic conditions such as cardiovascular disease and chronic obstructive pulmonary disease. Although conventional outpatient cardiopulmonary rehabilitation programs significantly decrease morbidity and mortality and improve function and health related quality of life for people with chronic diseases, rehabilitation programs are underused. Barriers to enrollment are multifactorial and include failure to recommend and refer patients to these services; poor communication with patients about potential benefits; and patient factors including logistical and financial barriers, comorbidities, and competing demands that make participation in facility based programs difficult. Recent advances in rehabilitation programs that involve remotely delivered technology could help deliver services to more people who might benefit. Problems with intensity, adherence, and safety of home based programs have been investigated in recent clinical trials, and larger dissemination and implementation trials are under way. This review summarizes the evidence for benefit of in-person cardiac and pulmonary rehabilitation programs. It also reviews the literature on newer developments, such as home based remotely mediated exercise programs developed to decrease cost and improve accessibility, high intensity interval training in cardiac rehabilitation, and alternative therapies such as tai chi and yoga for people with chronic obstructive pulmonary disease.

Rooney DM, Shadid HR, **Siegel LI**, Watnick RL, **Lesser GR**, **Obertynski T**, **Siegel MJ**, **Citron ME**, Hasbrook M and **Siegel MJ** (2019). "Postoperative complications of ab interno gelatin microstent." *Journal of Glaucoma* 28(5): e77-e81.

[Full Text](#)

Department of Ophthalmology

Purpose: To report 4 previously undescribed postoperative complications in 4 cases of ab interno XEN45 Gel Stent (XEN) implantation following uncomplicated surgeries. Patients and Methods: A total of 51 consecutive XEN implantations performed between July 1, 2017 and April 30, 2018 were reviewed. All cases were performed by 7 experienced glaucoma surgeons affiliated with the William Beaumont Hospital, Department of Ophthalmology. Cases with postoperative complications were identified, and a literature review was performed on PubMed.gov between April 5, 2018 and June 2, 2018 to identify previously unreported XEN complications. Results: Case 1 consisted of an 86-year-old woman who suffered a suprachoroidal hemorrhage and associated rhegmatogenous retinal detachment following XEN implantation. One month after sclerotomy drainage and pars plana vitrectomy repair, an amputated XEN was found to have eroded through the conjunctiva. Case 2 consisted of a 68-year-old man with persistent elevated intraocular pressure due to recurrent Tenon's capsule fibrosis who developed complete XEN retraction into the subconjunctival space. Cases 3 and 4 consisted of a 68-year-old man and a 78-year-old woman who developed occlusion of

the microstent's internal ostium by a partially detached Descemet's membrane. Case 3 maintained normal intraocular pressure on timolol, whereas case 4 resulted in bleb failure, despite Nd:YAG laser lysis of the occluded XEN internal ostium. Conclusions: Although the XEN is a promising new surgical option for the management of primary open-angle glaucoma, it can present unique postoperative challenges that are still being elucidated. Timely intervention or prevention of these complications can be improved by early surgeon recognition and effective communication with comanaging ophthalmologists.

Rothschild DP, **Goldstein JA**, **Ciacchi J** and **Bowers TR** (2019). "Ultrasound-accelerated thrombolysis (USAT) versus standard catheter-directed thrombolysis (CDT) for treatment of pulmonary embolism: A retrospective analysis." Vascular Medicine 24(3): 234-240.

[Full Text](#)

Department of Internal Medicine

Department of Diagnostic Radiology and Molecular Imaging

Ultrasound-accelerated thrombolysis (USAT) is advocated in pulmonary embolism (PE) based on the hypothesis that adjunctive ultrasound provides superior clinical efficacy compared to standard catheter-directed thrombolysis (CDT). This retrospective study was designed to compare outcomes between the two modalities. We analyzed patients with computed tomography-diagnosed PE at our institution treated with either USAT or standard CDT. Efficacy parameters assessed included invasive pulmonary artery systolic pressure (PASP; pre- and 24 hours post-treatment), non-invasive right-to-left ventricle (RV/LV) ratio (pre- and post-treatment), and general clinical outcomes (length-of-stay, significant bleeding, and mortality). We analyzed 98 cases (62 USAT and 36 CDT), in whom massive PE was diagnosed in 7%, intermediate/high risk in 81%, and intermediate/low risk in 12%. Overall, 92% had bilateral clot and 40% saddle embolus. At 24 hours, PASP decreased similarly in both groups (CDT Delta 14.7 mmHg, USAT Delta 10.8 mmHg; $p = 0.14$). Post-treatment, CDT showed similar improvement in the RV/LV ratio (CDT Delta 0.58 vs USAT Delta 0.45; $p = 0.07$), despite the baseline ratio being greater in the CDT group, indicating more severe RV strain (1.56 +/- 0.36 vs 1.40 +/- 0.29; $p = 0.01$). Intensive care unit and hospital length-of-stays were similar in both groups. A trend toward lesser significant bleeding rates in the CDT group (8.3% vs 12.9%, $p = 0.74$) as well as improved survival-to-discharge (97.2% vs 91.9%, $p = 0.66$) was observed. Compared to USAT, standard CDT achieves similar beneficial effects on hemodynamics, RV/LV ratios, and clinical outcomes. These observations suggest that salutary clinical results may be achieved without the need for very expensive devices.

Sala I, Solis D, Ramirez H, Myziuk N, Pankuch M and **Guerrero T** (2019). "Retrospective phantom study for evaluating the dosimetric effects of high frequency percussive ventilation motion for photon radiotherapy." Medical Physics 46(6): E235-E236.

[Request Form](#)

Department of Radiation Oncology

Sanders DS, **Fennell T** and **Chisti M** (2019). "MDS with 5q deletion and rare cKIT positive mastocytosis: A diagnostic and therapeutic challenge." BMJ Case Reports 12(4): e227768.

[Full Text](#)

OUWB Medical Student Author

Department of Internal Medicine

A patient with a diagnosis of myelodysplastic syndrome (MDS) with isolated 5q deletion underwent repeat bone marrow biopsy to assess haematological response after 6 months of initial lenalidomide therapy. Subsequent bone marrow biopsies revealed persistent MDS with del(5q) in addition to a small atypical mast cell population with >25% of mast cells with spindle-shaped morphology and immunohistochemistry characteristics consistent with mastocytosis. Molecular testing on the bone marrow was positive for cKIT D816V and the patient was diagnosed with systemic mastocytosis (SM) with an associated haematological neoplasm. MDS with SM is well known to be associated; however, to the best of our knowledge, only one prior case report identifies MDS with del(5q) and associated cKIT D816V positive mastocytosis. While the exact clonal origin of both chromosomal aberrations is unclear, this case illustrates the therapeutic efficacy of lenalidomide in a patient with MDS with del(5q) and rarely associated cKIT positive SM.

Sandhu R, Knill C, Halford R, **Seymour Z**, **Lee K** and Hyde C (2019). "Commissioning and clinical experience of

Brainlab's Multimet Element Planning System for Cranial SRS Treatments on Elekta's VersaHD." [Medical Physics](#) 46(6): E421-E421.

[Request Form](#)

Department of Radiation Oncology

Sandler KA, Cook RR, Ciezki JP, Ross AE, Pomerantz MM, Nguyen PL, Shaikh T, Tran PT, Stock RG, Merrick GS, Demanes DJ, Spratt DE, Abu-Isa EI, Wedde TB, Lilleby W, **Krauss DJ**, Shaw GK, Alam R, Reddy CA, Song DY, Klein EA, Stephenson AJ, Tosoian JJ, Hegde JV, Yoo SM, Fiano R, D'Amico AV, Nickols NG, Aronson WJ, Sadeghi A, Greco SC, Deville C, Jr., McNutt T, DeWeese TL, Reiter RE, Said JW, Steinberg ML, Horwitz EM, Kupelian PA, King CR and Kishan AU (2019). "Prostate-only versus whole-pelvis radiation with or without a brachytherapy boost for Gleason Grade Group 5 Prostate Cancer: A retrospective analysis." [European Urology](#). ePub Ahead of Print.

[Full Text](#)

Department of Radiation Oncology

Background: The role of elective whole-pelvis radiotherapy (WPRT) remains controversial. Few studies have investigated it in Gleason grade group (GG) 5 prostate cancer (PCa), known to have a high risk of nodal metastases. Objective: To assess the impact of WPRT on patients with GG 5 PCa treated with external-beam radiotherapy (EBRT) or EBRT with a brachytherapy boost (EBRT+BT). Design, Setting, and Participants: We identified 1170 patients with biopsy-proven GG 5 PCa from 11 centers in the United States and one in Norway treated between 2000 and 2013 (734 with EBRT and 436 with EBRT+BT). Outcome Measurements and Statistical Analysis: Biochemical recurrence-free survival (bRFS), distant metastasis-free survival (DMFS), and prostate cancer-specific survival (PCSS) were compared using Cox proportional hazards models with propensity score adjustment. Results and Limitations: A total of 299 EBRT patients (41%) and 320 EBRT+BT patients (73%) received WPRT. The adjusted 5-yr bRFS rates with WPRT in the EBRT and EBRT+BT groups were 66% and 88%, respectively. Without WPRT, these rates for the EBRT and EBRT+BT groups were 58% and 78%, respectively. The median follow-up was 5.6yr. WPRT was associated with improved bRFS among patients treated with EBRT+BT (hazard ratio [HR] 0.5, 95% confidence interval [CI] 0.2-0.9, p=0.02), but no evidence for improvement was found in those treated with EBRT (HR 0.8, 95% CI 0.6-1.2, p=0.4). WPRT was not significantly associated with improved DMFS or PCSS in the EBRT group (HR 1.1, 95% CI 0.7-1.7, p=0.8 for DMFS and HR 0.7, 95% CI 0.4-1.1, p=0.1 for PCSS), or in the EBRT+BT group (HR 0.6, 95% CI 0.3-1.4, p=0.2 for DMFS and HR 0.5 95% CI 0.2-1.2, p=0.1 for PCSS). Conclusions: WPRT was not associated with improved PCSS or DMFS in patients with GG 5 PCa who received either EBRT or EBRT+BT. However, WPRT was associated with a significant improvement in bRFS among patients receiving EBRT+BT. Strategies to optimize WPRT, potentially with the use of advanced imaging techniques to identify occult nodal disease, are warranted. Patient Summary: When men with a high Gleason grade prostate cancer receive radiation with external radiation and brachytherapy, the addition of radiation to the pelvis results in a longer duration of prostate-specific antigen control. However, we did not find a difference in their survival from prostate cancer or in their survival without metastatic disease. We also did not find a benefit for radiation to the pelvis in men who received radiation without brachytherapy.

Savoie C, Rajanna V and **Khandhar P** (2019). "Propofol-associated priapism in a prepubescent pediatric patient." [Global Pediatric Health](#) 6: 2333794x19859731.

[Full Text](#)

Department of Pediatrics

Introduction. Propofol is a commonly used sedative medication for procedural sedation with a limited side effect profile. Although well tolerated with minimal adverse reactions, uncommon side effects have been reported. Methods. Case report of priapism in a 9-year-old male following the use of propofol for sedation in the pediatric intensive care unit (PICU) setting. The patient was admitted to the PICU for postoperative management following laryngotracheal reconstruction. On postoperative day 2, our patient was initiated on continuous infusion of propofol and he developed priapism. Propofol was then immediately discontinued, and the priapism quickly resolved without any medical or surgical interventions. Results. Priapism is a low-flow state and is considered a urological emergency requiring prompt recognition, withdrawal of suspected offending agents, and possible need for urologic consultation to alleviate complications. Although rare, priapism with propofol has been reported but never in a prepubescent male. The mechanism of propofol-associated priapism is not well understood, but it is thought that it may result from an autonomic system

imbalance, leading to an increase in parasympathetic activity. In addition, propofol has been shown to affect nitric oxide-mediated smooth muscle relaxation. In our patient, we suspected propofol to be contributing factor to his priapism based on the temporal relationship between the initiation of the medication and symptoms and resolution of symptoms after propofol discontinuation. Discussion. Given the expansive use of propofol in pediatrics for sedation and anesthesia, pediatric clinicians should be cognizant of this rare adverse effect in pediatric patients with potentially disastrous complications.

Schaefer JK, Li Y, Gu X, Souphis NM, Haymart B, Kline-Rogers E, **Almany SL**, Kaatz S, Kozlowski JH, Krol GD, Sood SL, Froehlich JB and Barnes GD (2019). "Association of adding aspirin to warfarin therapy without an apparent indication with bleeding and other adverse events." JAMA Internal Medicine 179(4): 533-541.

[Full Text](#)

Department of Internal Medicine

Importance: It is not clear how often patients receive aspirin (acetylsalicylic acid) while receiving oral anticoagulation with warfarin sodium without a clear therapeutic indication for aspirin, such as a mechanical heart valve replacement, recent percutaneous coronary intervention, or acute coronary syndrome. The clinical outcomes of such patients treated with warfarin and aspirin therapy compared with warfarin monotherapy are not well defined to date. Objective: To evaluate the frequency and outcomes of adding aspirin to warfarin for patients without a clear therapeutic indication for combination therapy. Design, Setting, and Participants: A registry-based cohort study of adults enrolled at 6 anticoagulation clinics in Michigan (January 1, 2010, to December 31, 2017) who were receiving warfarin therapy for atrial fibrillation or venous thromboembolism without documentation of a recent myocardial infarction or history of valve replacement. Exposure: Aspirin use without therapeutic indication. Main Outcomes and Measures: Rates of any bleeding, major bleeding events, emergency department visits, hospitalizations, and thrombotic events at 1, 2, and 3 years. Results: Of the study cohort of 6539 patients (3326 men [50.9%]; mean [SD] age, 66.1 [15.5] years), 2453 patients (37.5%) without a clear therapeutic indication for aspirin were receiving combination warfarin and aspirin therapy. Data from 2 propensity score-matched cohorts of 1844 patients were analyzed (warfarin and aspirin vs warfarin only). At 1 year, patients receiving combination warfarin and aspirin compared with those receiving warfarin only had higher rates of overall bleeding (cumulative incidence, 26.0%; 95% CI, 23.8%-28.3% vs 20.3%; 95% CI, 18.3%-22.3%; $P < .001$), major bleeding (5.7%; 95% CI, 4.6%-7.1% vs 3.3%; 95% CI, 2.4%-4.3%; $P < .001$), emergency department visits for bleeding (13.3%; 95% CI, 11.6%-15.1% vs 9.8%; 95% CI, 8.4%-11.4%; $P = .001$), and hospitalizations for bleeding (8.1%; 6.8%-9.6% vs 5.2%; 4.1%-6.4%; $P = .001$). Rates of thrombosis were similar, with a 1-year cumulative incidence of 2.3% (95% CI, 1.6%-3.1%) for those receiving combination warfarin and aspirin therapy compared with 2.7% (95% CI, 2.0%-3.6%) for those receiving warfarin alone ($P = .40$). Similar findings persisted during 3 years of follow-up as well as in sensitivity analyses. Conclusions and Relevance: Compared with warfarin monotherapy, receipt of combination warfarin and aspirin therapy was associated with increased bleeding and similar observed rates of thrombosis. Further research is needed to better stratify which patients may benefit from aspirin while anticoagulated with warfarin for atrial fibrillation or venous thromboembolism; clinicians should be judicious in selecting patients for combination therapy.

Scherzer ZA, Alvarez C, Renner JB, Schwartz TA, Jordan JM, Golightly YM and **Nelson AE** (2019). "Effects of comorbid cardiovascular disease and diabetes mellitus on hand osteoarthritis state transitions." Journal of the American Geriatrics Society 67: S307-S307.

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OUWB Medical Student Author

Seymour ZA, Daignault S, Bosch W, Gay HA, Michalski JM, **Hamstra DA** and Pinkawa M (2019). "Long-term follow-up after radiotherapy for prostate cancer with and without rectal hydrogel spacer: A pooled prospective evaluation of quality of life." Journal of Clinical Oncology 37(S7).

[Full Text](#)

Department of Radiation Oncology

Background: Hydrogel spacers are a tool to improve dosimetry and overall quality of life with limited follow-up in men receiving radiotherapy for prostate cancer. This present study is a pooled analysis of a prospective cohorts with Long-term follow-up quality of life (QOL) data with or without hydrogel spacers to minimize

dose adjacent organs at risk. Methods: QOL was examined using the Expanded Prostate Cancer Index Composite (EPIC) to compare mean changes from baseline. A total of 215 patients from a randomized multiinstitutional trial of radiation with or without hydrogel spacer with a QOL endpoint were pooled with 165 nonrandomized patients from a single institution with prospective QOL collection in both patients with or without hydrogel spacer. The proportions of men with minimally important differences (MIDs) relative to pretreatment baseline in each domain were tested using repeated measures logistic models with pre-specified thresholds for clinically significant decline. Results: A total of 380 men were evaluated (64% with spacer and 36% without) with QOL data being available for 199 men beyond 24 months of follow-up (median: 39.5 months, range: 3171.4 mo). Treatment with spacer was associated with less decline in average Long-term bowel QOL (89.4 for control and 94.7 for experimental) with differences at > 2 years meeting the threshold of MID difference between cohorts (Bowel Score Difference from baseline: control = 5.1 spacer2= 0.3 Diff = 5.4 p = 0.0003). When evaluated over time men without spacer were more likely to have 1xMID (5 points) declines in bowel QOL (p = 0.01). At Long-term follow-up 1xMID was 36% without spacer vs 14% with spacer (p = 0.0006 OR2= 3.5) while 2x MID was seen in 19% vs 6% (p = 0.008 OR2= 3.6). The use of spacer was associated with improved bowel frequency (p = 0.002), reduced bleeding (p = 0.005) and less overall bowel problems (p = 0.007). Conclusions: In this pooled analysis of QOL after prostate radiotherapy with up to 5-years of follow-up utilization of a hydrogel spacer was associated with preservation of bowel QOL. This QOL benefit was preserved with Long-term follow-up.

Shaffer K, **Danko M**, DeLaere A, Chant E, Pople B, Grisby S and **Dekhne N** (2019). "Patient satisfaction following nipple-sparing mastectomy and assessment of nipple-areolar sensation." Breast Journal 25(3): 542-544.

[Request Form](#)

Department of Surgery

OUWB Medical Student Author

Smith BC, George LC, Svider PF, Nebor I, **Folbe AJ**, Sheyn A, Johnson AP and Eloy JA (2019). "Rhinogenic headache in pediatric and adolescent patients: an evidence-based review." International Forum of Allergy & Rhinology 9(5): 443-451.

[Full Text](#)

Department of Surgery

Background: Although some causes of rhinogenic headache, such as acute sinusitis, have clear diagnostic criteria, others, such as "sinus headache" and mucosal contact points, are more nebulous. Misdiagnosis of these entities and primary headaches may result in unnecessary medical or surgical treatment. The purpose of this systematic review is to delineate current understanding of diagnosis and treatment of rhinogenic headaches, including sinus and mucosal contact point headaches, in children. Methods: PubMed, SCOPUS, and the Cochrane databases were searched for studies on sinus headache and mucosal contact point headaches in children. Studies were assessed for level of evidence, and risk of bias was assessed by Methodological Index for Non-Randomized Studies (MINORS) scoring. Diagnostic criteria, management strategies, and other clinical data were analyzed. Results: Eight studies met the inclusion criteria. Level of evidence was predominantly 4. Forty percent of pediatric patients with migraine had been previously misdiagnosed with sinus headache. Of 327 pediatric patients in two studies, between 55% and 73% had at least 1 cranial autonomic symptom associated with their migraine. For children with mucosal contact point headaches, surgical management in select patients improved headache intensity or severity in 17 (89%) cases. Conclusion: The majority of pediatric patients with sinus headache harbor a primary headache disorder, with migraine being most common. Physicians should suspect primary headache disorders in pediatric patients with chronic headaches and a normal exam. Although some case series are supportive of surgical management for mucosal contact point headaches in children, the level of evidence supporting these recommendations is insufficient. High-quality clinical trials are necessary for continuing to improve outcomes in patients with these clinical entities.

Smith RK and **Gerrits PM** (2019). "A rare case of autoimmune polyglandular syndrome type 2 in a child with persistent fatigue." Global Pediatric Health 6: 2333794x19845074.

[Full Text](#)

Department of Pediatrics

Adrenal insufficiency is a rare, potentially life-threatening condition whose diagnosis requires a high index of suspicion. Adrenal insufficiency may be primary, secondary, or tertiary with varied etiologies. Primary insufficiency may be part of a cluster of autoimmune diseases, referred to as autoimmune polyglandular syndrome(s) (APS). We describe a case of a 15-year-old male who presents to a local emergency department complaining of fatigue, fever, abdominal pain, nausea, and vomiting for a few days with a preceding viral illness. The patient was hyponatremic and hyperkalemic with skin hyperpigmentation, raising concern for adrenal insufficiency. Laboratory workup confirmed autoimmune primary adrenal insufficiency, with subsequent laboratory studies revealing autoimmune thyroiditis and celiac disease. Concomitant Addison's and Hashimoto's diseases led to a diagnosis of APS type 2. The patient was started on steroid replacement with rapid clinical improvement.

Snyder M, Halford R and **Yan D** (2019). "Hydraulic phantom for MR motion quality assurance." Medical Physics 46(6): E184-E185.

[Request Link](#)

Department of Radiation Oncology

Sosa LE, Njie GJ, Lobato MN, Morris SB, Buchta W, Casey ML, **Goswami ND**, Gruden M, Hurst BJ, Khan AR, Kuhar DT, Lewinsohn DM, **Mathew TA**, Mazurek GH, Reves R, Paulos L, Thanassi W, Will L and Belknap R (2019). "Tuberculosis screening, testing, and treatment of US health care personnel: Recommendations from the National Tuberculosis Controllers Association and CDC, 2019." MMWR-Morbidity and Mortality Weekly Report 68(19): 439-443.

[Full Text](#)

Department of Surgery

Department of Internal Medicine

Stewart MT, **Haines DE**, Verma A, Kirchhof N, Barka N, Grassl E and Howard B (2019). "Intracardiac pulsed field ablation: Proof of feasibility in a chronic porcine model." Heart Rhythm 16(5): 754-764.

[Full Text](#)

Department of Internal Medicine

Background: Radiofrequency (RF) has become an accepted energy source for myocardial ablation but may result in discontinuous lesions and nontargeted tissue injury. We examined the feasibility and safety of lesion formation using high-amplitude, bipolar pulsed electric fields delivered from a multielectrode array catheter. Objective: The purpose of this study was to compare duty-cycled radiofrequency ablation (RFA) to pulsed field ablation (PFA) in terms of acute electrical effects, 2-week lesion formation, and injury to nontargeted tissues. Methods: Intracardiac ablations were performed in 6 pigs using a circular pulmonary vein ablation catheter. The energy source for ablation delivery was randomized to deliver either PFA or RFA to 3 atrial endocardial sites. Bipolar pace capture and electrogram amplitude measurements were recorded at each site. Histopathology and necropsies were performed after 2 weeks. Results: The circular pulmonary vein ablation catheter was used to deliver pulsed electric fields to produce cardiac lesions without skeletal muscle stimulation. Evaluating all ablations in each site, electrogram amplitudes were reduced to <0.5 mV in 67.5% of PFA vs 27.0% of RFA deliveries (P <.001). Bipolar cardiac capture was lost after 100% vs 92.0% of PFA vs RFA (P = .005). At 2 weeks, PFA resulted in consistent transmural and homogeneous replacement fibrosis devoid of lingering myocyte "sequesters." RFA lesions showed a stronger inflammatory response extending to the epicardial fat, arterial injury, and thrombosis. Neither PFA nor RFA lesions showed endocardial thrombus. Conclusion: Intracardiac PFA can be feasibly delivered from a circular catheter to create fibrotic lesions that have acute electrical effects, without injury to nontargeted tissue.

Sukul D, Seth M, Barnes GD, Dupree JM, Syrjamaki JD, **Dixon SR**, Madder RD, Lee D and Gurm HS (2019). "Cardiac rehabilitation use after percutaneous coronary intervention." Journal of the American College of Cardiology 73(24): 3148-3152.

[Full Text](#)

Department of Internal Medicine

Tapper A, **Leale D**, Megahan G, Nacker K, Killinger K and **Hafron J** (2019). "Robotic instrument failure-a critical analysis of cause and quality improvement strategies." Urology. ePub Ahead of Print.

[Full Text](#)

OUWB Medical Student Author

Department of Urology

Objective: To introduce a quality improvement initiative tracking robotic instrument failures on a per case basis. It is imperative to understand rates of failure, financial implications of failures, and identify factors suggesting common mechanisms of failure. Materials and Methods: Starting in January 1, 2014 a quality reporting system for failed robotic equipment began. Staff was instructed to submit an incident report when a robotic instrument failed and the instrument returned to central processing. Instruments were then returned to the manufacturer (Intuitive Surgical Inc, Sunnyvale, CA) for analysis and reimbursement. Results of failure analysis by the manufacturer, including reimbursement rates, were recorded and correlated with the procedure and surgical specialty. Results: A total of 3935 robotic cases were performed during the study period with a reported instrument failure incidence of 6.2% (247 total instruments). Etiology of instrument failure was as follows: tip or wrist (46.9%), cable (30.0%), unknown (12.6%), control housing (5.3%), and shaft (3.2%). Highest instrument failure incidence was seen in colorectal surgery cases at 4.0%, Urology had the lowest at 2.7%. Manufacturer reimbursement rate was 57.9%; the most common reason for denial being mishandling/misuse of equipment, determined by manufacturer analysis. Conclusion: Herein, we have demonstrated that improved process flow of reporting is necessary to better track incidence and etiology of instrument failures. Cost savings comes from improved training of not only surgeons but operating room and central processing staff in handling equipment to prevent high rates of reimbursement denial.

Thanos A, Ozturk T, **Faia LJ** and **Capone A, Jr.** (2019). "Spontaneous hyaloidal contraction and complex retinal detachment in a patient with Von Hippel-Lindau Syndrome." *Ophthalmic Surgery, Lasers & Imaging Retina* 50(4): 238-241.

[Full Text](#)

Department of Ophthalmology

The authors present an interventional case report of a patient with von Hippel-Lindau (VHL) syndrome who developed simultaneous exudative and combined tractional, rhegmatogenous, and exudative retinal detachment (RD) in the right and left eyes, respectively, following uneventful cryotherapy application of retinal capillary hemangioblastoma (RCH). After pars plana vitrectomy combined with encircling scleral buckling with radial element placement and silicone oil injection, complete retinal reattachment was achieved. The exudative RD of the fellow eye was managed initially with intense topical corticosteroid treatment and subsequent placement of a radial scleral buckle due to the presence of clinically apparent traction. Both eyes remained stable after successful surgical interventions, and long-term follow-up revealed no evidence of recurrent disease. The authors conclude that rapid worsening of vitreoretinal traction and exudation are complications that can occur after treatment of RCH in patients with VHL syndrome leading to complex retinal detachments.

Thomas AM and **Fahim DK** (2019). "Stand-alone balloon kyphoplasty for treatment of traumatic burst fracture in pediatric patient." *World Neurosurgery* 125: 475-480.

[Full Text](#)

Department of Neurosurgery

OUWB Medical Student Author

Background: Kyphoplasty is commonly employed in the treatment of compression fractures in the elderly and is increasingly used in the treatment of adult trauma along with concomitant instrumentation. Although kyphoplasty with instrumentation has been reported in pediatric patients, concerns regarding retardation of spinal growth and iatrogenic spinal deformity have been raised. The utilization of kyphoplasty without instrumentation has yet to be reported in the case of pediatric patients. Case Description: A 13-year-old male presented to the emergency department with a traumatic L2 burst fracture with 50% loss of height, which continued to cause severe pain after a trial of bracing. He was subsequently treated with a kyphoplasty without instrumentation. He experienced a rapid and excellent recovery and resumed all previous activity. Conclusions: Kyphoplasty alone without instrumentation is a less invasive means to treat these patients and also prevents iatrogenic deformity or retardation of growth in the pediatric spine.

To D, Xhaferllari I, Liu M, Liang J, Knill C, **Yan D**, **Nandalur S**, **Gustafson G** and Lack D (2019). "Evaluation of VMAT

planning strategies for prostate patients with bilateral hip prostheses." Medical Physics 46(6): E430-E430.

[Request Form](#)

Department of Radiation Oncology

Topf JM and Hiremath S (2019). "Got CKD? There's an app for that!" Clinical Journal of the American Society of Nephrology 14(4): 491-492.

[Full Text](#)

Department of Surgery

Vemulapalli S, Carroll JD, Mack MJ, Li Z, Dai D, Kosinski AS, Kumbhani DJ, Ruiz CE, Thourani VH, **Hanzel G**, Gleason TG, Herrmann HC, Brindis RG and Bavaria JE (2019). "Procedural volume and outcomes for transcatheter aortic-valve replacement." New England Journal of Medicine 380(26): 2541-2550.

[Full Text](#)

Department of Internal Medicine

Background: During the introduction of transcatheter aortic-valve replacement (TAVR) in the United States, requirements regarding procedural volume were mandated by the Centers for Medicare and Medicaid Services as a condition of reimbursement. A better understanding of the relationship between hospital volume of TAVR procedures and patient outcomes could inform policy decisions. Methods: We analyzed data from the Transcatheter Valve Therapy Registry regarding procedural volumes and outcomes from 2015 through 2017. The primary analyses examined the association between hospital procedural volume as a continuous variable and risk-adjusted mortality at 30 days after transfemoral TAVR. Secondary analysis included risk-adjusted mortality according to quartile of hospital procedural volume. A sensitivity analysis was performed after exclusion of the first 12 months of transfemoral TAVR procedures at each hospital. Results: Of 113,662 TAVR procedures performed at 555 hospitals by 2960 operators, 96,256 (84.7%) involved a transfemoral approach. There was a significant inverse association between annualized volume of transfemoral TAVR procedures and mortality. Adjusted 30-day mortality was higher and more variable at hospitals in the lowest-volume quartile (3.19%; 95% confidence interval [CI], 2.78 to 3.67) than at hospitals in the highest-volume quartile (2.66%; 95% CI, 2.48 to 2.85) (odds ratio, 1.21; P=0.02). The difference in adjusted mortality between a mean annualized volume of 27 procedures in the lowest-volume quartile and 143 procedures in the highest-volume quartile was a relative reduction of 19.45% (95% CI, 8.63 to 30.26). After the exclusion of the first 12 months of TAVR procedures at each hospital, 30-day mortality remained higher in the lowest-volume quartile than in the highest-volume quartile (3.10% vs. 2.61%; odds ratio, 1.19; 95% CI, 1.01 to 1.40). Conclusions: An inverse volume–mortality association was observed for transfemoral TAVR procedures from 2015 through 2017. Mortality at 30 days was higher and more variable at hospitals with a low procedural volume than at hospitals with a high procedural volume.

Vinekar A, Dogra M, Azad R, Gilbert C, Gopal L and **Trese M** (2019). "The changing scenario of retinopathy of prematurity in middle and low income countries: Unique solutions for unique problems." Indian Journal of Ophthalmology 67(6): 717-719.

[Full Text](#)

Department of Ophthalmology

Wang WG, **Qin A**, **Kabolizadeh P**, **Li X**, **Yan D**, Liu G, **Deraniyagala R**, **Grills I**, **Stevens C**, **Krauss D** and **Ding X** (2019). "Which planning strategy is better for head and neck cancer: PTV based or CTV based robust IMPT ?" Radiotherapy and Oncology 133: S352-S352.

[Request Form](#)

Department of Radiation Oncology

Werede A, Gerhardt S, **Marijanovich N** and **Zarouk S** (2019). "Saved by the clot: A rare case of ileo-ureteric fistula." American Journal of Kidney Diseases 73(5): 746-746.

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OUIWB Medical Student Author

Department of Internal Medicine

White JL, Chang AM, Hollander JE, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2019). "QTc prolongation as a marker of 30-day serious outcomes in older patients with syncope presenting to the Emergency Department." *American Journal of Emergency Medicine* 37(4): 685-689.

[Full Text](#)

Department of Emergency Medicine

Background: Syncope is a common chief complaint in the ED, and the electrocardiogram (ECG) is a routine diagnostic tool in the evaluation of syncope. We assessed whether increasingly prolonged QTc intervals are associated with composite 30-day serious outcomes in older adults presenting to the ED with syncope.

Methods: This is a secondary analysis of a prospective, observational study at 11 EDs in adults 60years or older who presented with syncope or near syncope. We excluded patients presenting without an ECG, measurement of QTc, non-sinus rhythm, bundle branch block or those without 30-day follow-up. We categorized QTc cutoffs into values of <451; 451-470; 471-500, and >500ms. We determined the rate of composite 30-day serious outcomes including ED serious outcomes and 30-day arrhythmias not identified in ED. Results: The study cohort included 2609 patients. There were 1678 patients (64.3%) that had QTc intervals <451ms; 544 (20.8%) were 451-470ms; 302 (11.6%) were 471-500ms, and 85 (3.3%) had intervals >500ms. Composite 30-day serious outcomes was associated with increasingly prolonged QTc intervals (13.0%, 15.3%, 18.2%, 22.4%, p=0.01), but this association did not persist in multivariate analysis.

Conclusions: In a cohort of older patients presenting with syncope, increased QTc interval was a marker of but was not independently predictive of composite 30-day serious outcomes.

Williams CM, Alweis RL, O'Connor AB, **Dalal B**, Rai D, Abdullah A, Kopelman R, Cornett P, Frank MO, Luther VP and Muchmore EA (2019). "Inappropriate communication during internal medicine fellowship recruitment: A mixed-methods analysis." *American Journal of Medicine* 132(6): 770-775.

[Full Text](#)

Department of Internal Medicine

Wood EH, Tang PH, De la Huerta I, Korot E, Muscat S, Palanker DA and **Williams GA** (2019). "Stem cell therapies, gene-based therapies, optogenetics, and retinal prosthetics: Current state and implications for the future." *Retina (Philadelphia, Pa.)* 39(5): 820-835.

[Full Text](#)

Department of Ophthalmology

Purpose: To review and discuss current innovations and future implications of promising biotechnology and biomedical offerings in the field of retina. We focus on therapies that have already emerged as clinical offerings or are poised to do so. Methods: Literature review and commentary focusing on stem cell therapies, gene-based therapies, optogenetic therapies, and retinal prosthetic devices. Results: The technologies discussed herein are some of the more recent promising biotechnology and biomedical developments within the field of retina. Retinal prosthetic devices and gene-based therapies both have an FDA-approved product for ophthalmology, and many other offerings (including optogenetics) are in the pipeline. Stem cell therapies offer personalized medicine through novel regenerative mechanisms but entail complex ethical and reimbursement challenges. Conclusion: Stem cell therapies, gene-based therapies, optogenetics, and retinal prosthetic devices represent a new era of biotechnological and biomedical progress. These bring new ethical, regulatory, care delivery, and reimbursement challenges. By addressing these issues proactively, we may accelerate delivery of care to patients in a safe, efficient, and value-based manner.

Wu JC, Mills A, **Grant KD** and **Wiater PJ** (2019). "Fracture fixation using shape-memory (Nitinol) staples." *Orthopedics Clinics of North America* 50(3): 367-374.

[Full Text](#)

Department of Orthopedic Surgery

Shape-memory alloy (SMA) staples are a recent innovation in fracture fixation. These staples have inherent compressive properties that create a stable fracture environment that promotes primary bone healing. They have been used successfully for osteotomies, arthrodesis, and fracture fixation. Understanding where SMA staple compression can be optimized and using proper indications are important for obtaining consistent

success and minimizing failures. SMA staples are not a substitute for lag screw fixation or traditional plate and screw constructs.

Yan D, Chen S, Krauss DJ, Chen PY, Chinnaiyan P and Wilson GD (2019). "Tumor voxel dose-response matrix and dose prescription function derived using 18 F-FDG PET/CT images for adaptive dose painting by number." International Journal of Radiation Oncology Biology Physics 104(1): 207-218.

[Full Text](#)

Department of Radiation Oncology

Purpose: To construct a tumor voxel dose response matrix (DRM) and dose prescription function (DPF) for adaptive dose painting by number (DPbN) based on treatment feedback of fluoro-2-deoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) imaging. Methods and Materials: FDG-PET/CT images obtained before and after chemoradiation therapy and at weekly chemoradiation therapy sessions for each of 18 patients with head and neck cancer, as well as the treatment outcomes, were used in the modeling. All weekly and posttreatment PET/CT images were registered voxel-to-voxel to the corresponding pretreatment baseline PET/CT image. Tumor voxel DRM was created using serial FDG-PET imaging of each patient with respect to the baseline standardized uptake value (SUV₀). A tumor voxel control probability (TVCP) lookup table was created using the maximum likelihood estimation on the tumor voxel (SUV₀, DRM) domain of all tumors. Tumor voxel DPF was created from the TVCP lookup table and used as the objective function for DPbN-based inverse planning optimization. Results: Large intertumoral and intratumoral variations on both tumor voxels (SUV₀, DRM) were identified. Tumor voxel dose resistance did not show correlation with its baseline SUV₀ value and was the major cause of the tumor local failures. Tumor voxel DPF as the function of tumor voxel (SUV₀, DRM) values also showed a very large intertumoral and intratumoral heterogeneity. Most human papillomavirus–negative tumors require a treatment dose >100 Gy to certain local tumor regions. These treatment doses, which are most unlikely to be implementable in conventional radiation therapy, can be achieved using adaptive DPbN treatment. Clinical feasibility was evaluated by comparing the adaptive DPbN treatment plan with the conventional intensity modulated radiation therapy plan. Conclusions: Tumor voxel (SUV₀, DRM) provides an intratumoral prognostic map to target tumor locoregional-resistant regions. The corresponding TVCP or DPF provides a quantitative objective to optimize the intratumoral dose distribution for the individuals. The adaptive DPbN with FDG-PET/CT imaging feedback is feasible to implement in clinics.

Yilmaz A, Ugur Z, Ustun I, Aasly JO, **Bahado-Singh R, Maddens M and Graham S** (2019). "Metabolic profiling of CSF from people suffering from Parkinson's disease." Journal of the American Geriatrics Society 67: S254-S255.

[Request Form](#)

Department of Obstetrics and Gynecology

Department of Internal Medicine

Yorke A, Sala I, Solis D and **Guerrero T** (2019). "A statistically characterized reference data set for image registration of pelvis using combinatorial affine registration optimization." Medical Physics 46(6): E340-E340.

[Request Form](#)

Department of Radiation Oncology

Ysunza PA, Chaiyasate K, Rontal M, Shaheen K and Bartholomew B (2019). "Comparison of three different surgical techniques for designing pharyngeal flaps according to findings of videonasopharyngoscopy and multiplanar videofluoroscopy." International Journal of Pediatric Otorhinolaryngology 120: 123-129.

[Full Text](#)

Department of Physical Medicine and Rehabilitation

Department of Surgery

Background: Velopharyngeal insufficiency (VPI) occurs when the velopharyngeal sphincter (VPS) is unable to completely seal anatomical closure between the nasal and oral cavities during speech. Palatal repair can restore VPS function but the prevalence of VPI after repair has been reported ranging from 20% to 40%. The combination of flexible videonasopharyngoscopy (FVNP) and multiplanar videofluoroscopy (MPVF) has been reported as the best approach for assessing the VPS mechanism and planning effective surgical procedures aimed to correct VPI. Objective: To study the outcome of three different techniques for performing

pharyngeal flaps with the common denominator of individually designing the flap according to findings of VFNP and MPVF. Material and Methods: A total of 140 cases of pharyngeal flap surgery were reviewed. Three surgeons performed 3 different surgical techniques. All cases underwent nasometry, VNP and MPVF preoperatively. All surgical procedures were carefully planned and designed according to findings of VNP and MPVF. Results: Nasal emission was completely eliminated in all cases. One-hundred-thirty-four patients (95%) demonstrated mean nasalance within normal limits after the surgical procedure whereas 6 patients persisted with mean nasalance scores above reference values postoperatively. There were no intraoperative or postoperative complications in any of the cases. No clinical data of sleep disordered breathing was detected in any of the cases after 2 months of postoperative follow-up. However, one case presented with clinical data of sleep disordered breathing 8 months postoperatively. Conclusions: The results of this study suggest that as long as pharyngeal flaps are being designed according to the findings of imaging procedures, different surgical techniques can provide similar successful outcomes with minimal complications.

Zakaria HM, Mansour T, Telemi E, Xiao S, Bazydlo M, Schultz L, Nerenz D, **Perez-Cruet M**, Seyfried D, Aleem IS, **Easton R**, Schwalb JM, Abdulhak M and Chang V (2019). "Patient demographic and surgical factors which affect completion of patient-reported outcomes (PROs) 90 days and 1 year after spine surgery: Analysis from the Michigan Spine Surgery Improvement Collaborative (MSSIC)." [World Neurosurgery](#). ePub Ahead of Print.

[Full Text](#)

Department of Neurosurgery

Department of Orthopedic Surgery

Background: The Michigan Spine Surgery Improvement Collaborative (MSSIC) is a statewide multicenter quality improvement registry. Since missing data can affect registry results, we used MSSIC to find demographic and surgical characteristics that affect the completion of patient-reported outcomes (PROs) at 90d and 1yr. Methods: 24404 patients who had lumbar (17813 patients) or cervical (6591 patients) surgery were included. Multivariate logistic regression models of patient pathology were constructed to identify risk factors for failure to complete scheduled PRO surveys. Results: Patients ≥ 65 yo and female patients were both more likely to respond at 90d and 1yr. Increasing education was associated with greater response rate at 90d and 1yr. Caucasians and African Americans had no differences in response rates. Calling provided the highest response rate at 90d and 1yr. For cervical spine patients, only discharge to rehab increased completion rates, at 90d but not 1yr. For lumbar spine patients, spondylolisthesis or stenosis (vs herniated disc) had a greater response rate at 1yr. Patients with leg (vs back) pain had a greater response only at 1yr. Patients with multi-level surgery had an increased response at 1yr. Patients who underwent fusion were more likely to respond at 90d, but not 1yr. Discharge to rehab increased response at 90d and 1yr. Conclusions: A multivariate analysis from a multicenter prospective database identified surgical factors that affect PRO follow-up, up to 1yr. This information can be helpful for imputing missing PRO data, and could potentially be used to strengthen data derived from large prospective databases.

Zhong YC, Vinogradskiy Y, Chen LY, Myziuk N, Castillo R, Castillo E, **Guerrero T**, Jiang S and Wang J (2019). "Technical Note: Deriving ventilation imaging from 4DCT by deep convolutional neural network." [Medical Physics](#) 46(5): 2323-2329.

[Full Text](#)

Department of Radiation Oncology

Purpose: Ventilation images can be derived from four-dimensional computed tomography (4DCT) by analyzing the change in HU values and deformable vector fields between different respiration phases of computed tomography (CT). As deformable image registration (DIR) is involved, accuracy of 4DCT-derived ventilation image is sensitive to the choice of DIR algorithms. To overcome the uncertainty associated with DIR, we develop a method based on deep convolutional neural network (CNN) to derive ventilation images directly from the 4DCT without explicit image registration. Methods: A total of 82 sets of 4DCT and ventilation images from patients with lung cancer were used in this study. In the proposed CNN architecture, the CT two-channel input data consist of CT at the end of exhale and the end of inhale phases. The first convolutional layer has 32 different kernels of size $5 \times 5 \times 5$, followed by another eight convolutional layers each of which is equipped with an activation layer (ReLU). The loss function is the mean-squared-error (MSE) to measure the intensity difference between the predicted and reference ventilation images. Results: The

predicted images were comparable to the label images of the test data. The similarity index, correlation coefficient, and Gamma index passing rate averaged over the tenfold cross validation were 0.880 ± 0.035 , 0.874 ± 0.024 , and 0.806 ± 0.014 , respectively. Conclusions: The results demonstrate that deep CNN can generate ventilation imaging from 4DCT without explicit deformable image registration, reducing the associated uncertainty.