

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE
PUBLICATION LIST
January - March 2019

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Adhikari A, **Chisti MM**, Bastola S and KC O (2019). "Rare case of catastrophic antiphospholipid syndrome with spontaneous intracranial haemorrhage." *BMJ Case Reports* 12(3): e227171.

[Full Text](#)

Department of Internal Medicine

Catastrophic antiphospholipid syndrome (CAPS) is a rare but severe form of antiphospholipid syndrome (APS). The syndrome manifests itself as a rapidly progressive multiorgan failure that is believed to be caused by widespread micro-thrombosis. Seldom does bleeding comanifest with thrombosis. We present a patient with APS who presented with nausea, vomiting and fatigue, and rapidly progressed into multiorgan failure before being diagnosed with CAPS. The clinical course was complicated by an atraumatic intracranial haemorrhage which demanded discontinuation of anticoagulation. The patient was treated with high dose steroid, intravenous immunoglobulin, followed by weekly rituximab infusion. Although the trigger for CAPS was not obvious during her hospital stay, she was diagnosed with acute cytomegalovirus (CMV) infection soon after discharge. In this case report, we explore the differential diagnoses of CAPS, investigate the possibility of CMV infection as a potential trigger, present the therapeutic challenges of anticoagulation and discuss the emerging use of rituximab.

Akella SS, Schlachter DM, **Black EH** and Barmettler A (2019). "Ophthalmic eosinophilic granulomatosis with polyangiitis (Churg-Strauss Syndrome): A systematic review of the literature." *Ophthalmic Plastic and Reconstructive Surgery* 35(1): 7-16.

[Full Text](#)

Department of Ophthalmology

Purpose: To review and summarize the clinical features, presentations, diagnostic modalities, and management of ophthalmic manifestations of eosinophilic granulomatosis with polyangiitis (EGPA, formerly Churg-Strauss Syndrome). Methods: A systematic PubMed search of all English articles on EGPA with ophthalmic involvement was performed. Emphasis was placed on English-language articles, but any article with an abstract translated into English was also included. Only those cases that satisfied the American Rheumatology criteria (1990) for diagnosis were included. Data examined included epidemiology, pathogenesis, presentations, diagnostic modalities, and management. Results: There was a wide range in

ophthalmic manifestations of EGPA. In order of most frequent presentation to least frequent, these include central retinal artery or vein occlusion, ischemic optic neuropathy, conjunctival nodules, orbital myositis, proptosis, dacryoadenitis, retinal vasculitis/infarcts/edema, cranial nerve palsy, and amaurosis. The 46 qualifying cases were divided into the categories of ischemic vasculitis versus idiopathic orbital inflammation due to prognostic significance. Ischemic vasculitis cases tended to be older patients ($p = 0.03$), unilateral ($p = 0.006$), require immunosuppressive therapy beyond steroids ($p = 0.015$), and were less likely to show improvement on therapy ($p = 0.0003$). Conclusions: Prompt diagnosis of EGPA by the ophthalmologist can decrease patient morbidity and mortality. This requires knowledge of likely ophthalmic EGPA presentations, as well as recommended workups and treatment.

Al'Aref SJ, Su A, Gransar H, van Rosendael AR, Rizvi A, Berman DS, Callister TQ, DeLago A, Hadamitzky M, Hausleiter J, Al-Mallah MH, Budoff MJ, Kaufmann PA, Raff GL, **Chinnaiyan K**, Cademartiri F, Maffei E, Villines TC, Kim Y-J, Leipsic J, Feuchtner G, Pontone G, Andreini D, Marques H, de Araújo Gonçalves P, Rubinshtein R, Achenbach S, Chang H-J, Chow BJW, Cury R, Lu Y, Bax JJ, Jones EC, Peña JM, Shaw LJ, Min JK and Lin FY (2019). "A cross-sectional survey of coronary plaque composition in individuals on non-statin lipid lowering drug therapies and undergoing coronary computed tomography angiography." Journal of Cardiovascular Computed Tomography. ePub Ahead of Print.

[Full Text](#)

Department of Internal Medicine

Introduction: Non-statin therapy (NST) is used as second-line treatment when statin monotherapy is inadequate or poorly tolerated. Objective: To determine the association of NST with plaque composition, alone or in combination with statins, in patients undergoing coronary computed tomography angiography (coronary CTA). Methods: From the multicenter CONFIRM registry, we analyzed individuals who underwent coronary CTA with known lipid-lowering therapy status and without prior coronary artery disease at baseline. We created a propensity score for being on NST, followed by stepwise multivariate linear regression, adjusting for the propensity score as well as risk factors, to determine the association between NST and the number of coronary artery segments with each plaque type (non-calcified (NCP), partially calcified (PCP) or calcified (CP)) and segment stenosis score (SSS). Results: Of the 27,125 subjects in CONFIRM, 4,945 met the inclusion criteria; 371 (7.5%) took NST. At baseline, patients on NST had more prevalent risk factors and were more likely to be on concomitant cardiac medications. After multivariate and propensity score adjustment, NST was not associated with plaque composition: NCP (0.07 increase, 95% CI: $-0.05, 0.20$; $p = 0.26$), PCP (0.10 increase, 95% CI: $-0.10, 0.31$; $p = 0.33$), CP (0.18 increase, 95% CI: $-0.10, 0.46$; $p = 0.21$) or SSS (0.45 increase, 95% CI: $-0.02, 0.93$; $p = 0.06$). The absence of an effect of NST on plaque type was not modified by statin use (p for interaction > 0.05 for all). Conclusion: In this cross-sectional study, non-statin therapy was not associated with differences in plaque composition as assessed by coronary CTA.

Alhousseini A, Zeineddine S, Hussein A, Baddah H, Saker H, Mody S, Ibrahim SA, Thakur M, Hernandez-Andrade E and **Bahado-Singh R** (2019). "Familial hydrocephalus and dysgenesis of the corpus callosum associated with Xp22.33 duplication and stenosis of the aqueduct of Sylvius with x-linked recessive inheritance pattern." Gynecologic and Obstetric Investigation. ePub Ahead of Print.

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Department of Obstetrics and Gynecology

X-linked recessive mutations predominantly affect male fetuses with milder or no abnormalities in female siblings. Most reports show only one affected member in the family. We are reporting a family affected with hydrocephalus, stenosis of the aqueduct of Sylvius, dysgenesis of the corpus callosum, and Xp22.33 microduplication. Case Presentation: Eighteen-year-old patient was evaluated for her 2 pregnancies; the first was a male fetus with severe hydrocephalus and the second a female fetus with mild hydrocephalus. Postnatal MRI evaluation of the male neonate revealed stenosis of the aqueduct of Sylvius, dysgenesis of the corpus callosum, and severe hydrocephalus requiring ventriculoperitoneal shunt. Postnatal MRI evaluation of the female neonate revealed mild hydrocephalus, stenosis of the aqueduct of Sylvius, and mild dysgenesis of the corpus callosum. The female baby did not require surgical intervention. Genetic testing of the mother and the 2 children revealed a 439 Kb duplication of Xp22.33. Discussion: This family demonstrates typical X-linked recessive heritability. X-inactivation is a compensatory mechanism that explains the mild symptoms of the female child and the severe symptoms of the male child. This familial case shows the importance of prenatal testing and genetic counseling and testing, including karyotype and chromosomal microarray.

Alpay Savasan Z, Yilmaz A, Ugur Z, Aydas B, **Bahado-Singh RO** and **Graham SF** (2019). "Metabolomic profiling of cerebral palsy brain tissue reveals novel central biomarkers and biochemical pathways associated with the disease: A pilot study." *Metabolites* 9(2): 27.

[Full Text](#)

Department of Obstetrics and Gynecology

Cerebral palsy (CP) is one of the most common causes of motor disability in childhood, with complex and heterogeneous etiopathophysiology and clinical presentation. Understanding the metabolic processes associated with the disease may aid in the discovery of preventive measures and therapy. Tissue samples (caudate nucleus) were obtained from post-mortem CP cases (n = 9) and age- and gender-matched control subjects (n = 11). We employed a targeted metabolomics approach using both ¹H NMR and direct injection liquid chromatography-tandem mass spectrometry (DI/LC-MS/MS). We accurately identified and quantified 55 metabolites using ¹H NMR and 186 using DI/LC-MS/MS. Among the 222 detected metabolites, 27 showed significant concentration changes between CP cases and controls. Glycerophospholipids and urea were the most commonly selected metabolites used to develop predictive models capable of discriminating between CP and controls. Metabolomics enrichment analysis identified folate, propanoate, and androgen/estrogen metabolism as the top three significantly perturbed pathways. We report for the first time the metabolomic profiling of post-mortem brain tissue from patients who died from cerebral palsy. These findings could help to further investigate the complex etiopathophysiology of CP while identifying predictive, central biomarkers of CP.

Alser O, Hamouri S and **Novotny NM** (2019). "Esophageal caustic injuries in pediatrics: a sobering global health issue." *Asian Cardiovascular and Thoracic Annals*: 0218492319842441.

[Full Text](#)

Department of Surgery

Caustic material ingestion by children is considered a global healthcare issue, especially in low-to-middle income countries. The aim of this article was to review the epidemiology, prevention, and management of caustic material ingestion in pediatric patients, comparing low-to-middle income countries with high-income countries. We conducted an English literature review using PubMed with the following keywords: (caustic OR corrosive) AND ingestion AND (pediatric OR pediatric). Our search retrieved 253 citations; all abstracts were screened by the authors, and 52 articles were finally included in our review. Prevention is key in tackling this issue, but legislation is scarce in low-to-middle income countries. Diagnosis of caustic ingestion is mostly achieved using flexible endoscopy, computed tomography, and endoscopic ultrasound, but access is limited in low-to middle income countries and diagnosis is often delayed. After stabilizing patients, the mainstay of treatment is graded endoscopic dilatation, and rarely, esophageal replacement. We concluded that caustic ingestion represents a serious condition where prevention is the key. Once a child suffers an injury, rapid and careful evaluation of the injury with endoscopy, and a course of close observation and dilations if needed, will often avoid esophageal replacement. When necessary, the stomach is the best first option if it is viable, followed by the colon, and finally, the jejunum.

Arianpour K, Forman SN, Karabon P and **Thottam PJ** (2019). "Pediatric acquired subglottic stenosis: Associated costs and comorbidities of 7,981 hospitalizations." *International Journal of Pediatric Otorhinolaryngology* 117: 51-56.

[Full Text](#)

OUWB Medical Student Author

Department of Surgery

Objectives: Numerous risk factors have been characterized for acquired subglottic stenosis (ASGS) in the pediatric population. This analysis explores the comorbidities of hospitalized ASGS patients in the United States and associated costs and length of stay (LOS). Methods: A retrospective analysis of the Kids' Inpatient Database (KID) from 2009 to 2012 for inpatients ≤ 20 years of age who were diagnosed with ASGS. International Classification of Diseases, Clinical Modification, Version 9 diagnosis codes were used to extract diagnoses of interest from 14, 045, 425 weighted discharges across 4179 hospitals in the United States. An algorithm was created to identify the most common co-diagnoses and subsequently evaluated for total charges and LOS. Results: ASGS was found in 7981 (0.06%) of total discharges. The mean LOS in discharges with ASGS is 13.11 days while the mean total charge in discharges with ASGS is \$114,625; these values are

significantly greater in discharges with ASGS than discharges without ASGS. Patients with ASGS have greater odds of being co-diagnosed with gastroesophageal reflux, Trisomy 21, other upper airway anomalies and asthma, while they have lower odds of being diagnosed with prematurity and dehydration. Aside from Trisomy 21 and asthma, hospitalizations of ASGS patients with the aforementioned comorbidities incurred a greater LOS and mean total charge. Conclusion: Our analysis identifies numerous comorbidities in children with ASGS that are associated with increased resource utilization amongst US hospitalizations. The practicing otolaryngologist should continue to advocate interdisciplinary care and be aware of the need for future controlled studies that investigate the management of such comorbidities.

Ashbrook M, **Bilollikar AN**, Vargas Y and Podolsky R (2019). "Gender differences in plaque characteristics by coronary computerized tomographic angiography." Journal of the American College of Cardiology 73(9): 1647-1647.

[Full Text](#)

Department of Internal Medicine

Bahado-Singh R, Vishweswaraiah S, Sayed NM, Aydas B, Veerappa AM, Mishra NK, Guda C and **Radhakrishna U** (2019). "Deep learning/artificial intelligence and the epigenomic prediction of coarctation of the aorta." American Journal of Obstetrics and Gynecology 220(1): S50-S50.

[Full Text](#)

Department of Obstetrics and Gynecology

Bahl A and Hixson CC (2019). "July phenomenon impacts efficiency of emergency care." Western Journal of Emergency Medicine 20(1): 157-162.

[Full Text](#)

Department of Emergency Medicine

Introduction: The "July effect" describes the period in which new interns begin learning patient care while senior residents take on additional responsibility in an academic hospital setting. The annual change in staffing creates inefficiencies in patient care, which may negatively impact quality of care. Our objective was to evaluate the impact of the annual resident turnover on emergency department (ED) efficiency in a teaching hospital. Methods: This was an institutional review board-approved retrospective chart review spanning two academic years analyzing 79,921 records. We grouped July and August into the period of least experience (PLE) and May and June into the period of most experience (PME). Outcomes included faculty and resident productivity, ED door-to-doctor time, and time to disposition. Results: Patients were evaluated by 117 emergency residents and 73 emergency faculty. We excluded patient records for 35 off-service residents. Residents saw 15.8% more patients in the PME compared to the PLE ($p < 0.0001$). The residents' average door-to-doctor time during the PLE was 45.63 minutes (standard deviation [SD] 33.01, median 36) compared to 34.69 minutes (SD 25.22, median 28) during the PME, with a decrease in time by 21.3% ($p = 0.0203$). The residents' average time to disposition during the PLE was 304.6 minutes (SD 308, median 217) compared to 269.0 minutes (SD 282, median 194) during the PME, decreasing by 12.4% ($p = 0.0001$). Residents had an average ED length of stay for discharged patients of 358.5 minutes (SD 374.6, median 238) during the PLE compared to 309.9 minutes (SD 346.4, median 209) during the PME, decreasing 13.7% for discharged patients ($p = 0.0017$). Conclusion: Annual turnover of resident staffing has a significant impact on common ED efficiency metrics. EDs should consider interventions to mitigate the impact of these expected inefficiencies.

Bahl A, Karabon P and **Chu D** (2019). "Comparison of venous thrombosis complications in midlines versus peripherally inserted central catheters: Are midlines the safer option?" Clinical and Applied Thrombosis/Hemostasis 25: 1076029619839150.

[Full Text](#)

Department of Emergency Medicine

OUIB Medical Student Author

Catheter-related (CR) thrombosis is a significant complication of midline catheters (MCs) and peripherally inserted central catheters (PICCs). Limited existing data for MCs suggest a favorable complication profile for MCs. To compare incidence of CR thrombosis between MCs and PICCs and to evaluate the impact of quantity of lumens and catheter diameter on CR thrombosis. This was a retrospective comparison spanning

13 months of MCs and PICCs for symptomatic CR thrombosis at an 1100 bed tertiary care academic medical center. Adult patients who had an MC or a PICC placed by the were included. Data were collected using the electronic medical record. Statistical analysis was performed using SAS software. A total of 2577 catheters were included in the analysis with 1094 MCs and 1483 PICCs. One hundred thirty (11.88%) MCs developed CR thrombosis (deep vein thrombosis [DVT] or superficial venous thrombophlebitis [SVT]) as compared to 112 (6.88%) PICCs (odds ratio [OR]: 1.82; P < .0001). Midline catheters had a 53% greater odds of developing CR DVT than PICCs (7.04% MCs and 4.72% PICCs; OR: 1.53; P = .0126). For CR SVT, MCs have a 2.29-fold greater odds of developing CR SVT than PICCs (4.84% MCs and 2.16% PICCs; OR: 2.29; P = .0002). For MCs and PICCs, the incidence of CR thrombosis was 13.50% for double lumen/5F lines and was 6.92% for single lumen/4F lines (OR: 2.10; P = <.0001). Symptomatic CR thrombosis is a serious, life-threatening complication that occurs more frequently in MCs compared to PICCs. Inserters should consider placement of single lumen catheters with the smallest diameter to reduce this risk when a midline is used.

Baker D, Sevak S, Callahan RE, **Czako PF**, Lloyd LR and **Nagar S** (2019). "Outcomes in patients with renal hyperparathyroidism requiring cinacalcet pre-operatively followed by parathyroidectomy." *American Journal of Surgery* 217(1): 146-151.

[Full Text](#)

Department of Surgery

Background: Cinacalcet is an effective treatment for renal hyperthyroidism when traditional medical therapy has failed. We studied the impact of pre-operative cinacalcet administration on post-surgical outcomes. Methods: A retrospective analysis was performed of patients from 2002 to 2017 diagnosed with renal hyperparathyroidism requiring parathyroidectomy to evaluate the need for post-operative supplementation and outcomes. Results: 102 patients were identified; 34 patients were treated with cinacalcet prior to undergoing parathyroidectomy. The cinacalcet treatment cohort (CT) demonstrated a greater duration of renal replacement therapy (p = 0.03) relative to the untreated cohort (NC). NC had greater proportion receiving peritoneal dialysis (p = <0.0001) compared to other forms of renal replacement, greater pre-operative PTH levels (p = 0.001) and greater decrease in PTH after resection (p = 0.0086). Post-operative vitamin D supplementation was more frequent in the CT group (p = 0.02). After propensity matching for pre-operative PTH and duration of renal replacement therapy, there were no differences in post-operative supplementation or outcomes. Conclusions: Cinacalcet patients may have advanced disease. These patients have longer duration of renal failure and higher PTH levels. After propensity matching, no significant differences were noted in terms of need for supplementation or outcomes.

Barinsky GL, Buziashvili D, Svider PF, Carron MA, **Folbe AJ**, Hsueh WD, Eloy JA and Johnson AP (2019). "Perioperative desmopressin for patients undergoing otolaryngologic procedures: A systematic review." *Otolaryngology-Head and Neck Surgery*: 0194599819831288.

[Full Text](#)

Department of Surgery

Objective: Desmopressin (DDAVP) is a hemostatic agent used to manage bleeding in patients with hemostatic disorders, and there is a lack of published data to guide its use during otolaryngology procedures. The objective of this study was to conduct an evidence-based systematic review of the reported uses, efficacy, and adverse effects of DDAVP in the otolaryngology surgical setting. Data Sources: PubMed, MEDLINE, and EmBase were searched for articles on the use of DDAVP in otolaryngology. Review Methods: The Methodological Index for Non-Randomized Studies criteria and Cochrane bias tool were used to assess study quality. Patient demographics, DDAVP dosing and route, and outcomes such as bleeding and adverse events were collected. A summary of evidence table was created specifying levels of evidence, benefits, and harm. Results: Nineteen studies encompassing 440 patients were included. Sixteen studies discussed DDAVP for prophylaxis, and 3 discussed postoperative use. DDAVP effectively prevented bleeding in high-risk patients and successfully facilitated a dry surgical field when necessary. DDAVP had a 100% success rate when used symptomatically. Five studies described adverse effects, including hyponatremia (12.3%), nausea (2.0%), emesis (0.9%), and seizure (0.2%). The aggregate level of evidence for its use was Level B for adenotonsillectomy, septoplasty, and turbinate procedures and Level C for rhinoplasty. Conclusion: Current literature supports the use of DDAVP in otolaryngology surgical procedures as both a perioperative prophylactic agent and a postoperative symptomatic intervention for bleeding. Both modalities are effective

with minimal adverse events. Further well-designed randomized trials are necessary to conclusively formulate guidelines for DDAVP use in otolaryngology.

Barnes GD, Li Y, Gu X, Haymart B, Kline-Rogers E, **Almany S**, Kozlowski J, Krol G, McNamara M, Froehlich JB and Kaatz S (2019). "Periprocedural bridging anticoagulation: Measuring the impact of a clinical trial on care delivery." [American Journal of Medicine](#) 132(1): 109.e101-109.e107.

[Full Text](#)

Department of Internal Medicine

Use of bridging anticoagulation has been shown to be harmful and without benefit in warfarin-treated patients with atrial fibrillation. We performed a quasi-experimental interrupted time series analysis between 2010 and 2017 in the Michigan Anticoagulation Quality Improvement Initiative (MAQI 2) collaborative before and after the BRIDGE trial publication (July 2015). Predicted use of bridging at the end of the study period was calculated with and without the effect of the BRIDGE trial after adjustment for patient-level clustering. Predictors of bridging anticoagulation use in the post-BRIDGE trial period were analyzed. In adjusted analyses, the use of bridging anticoagulation declined from a predicted 27.8% (95% confidence interval, 20.5%-35.1%) to 13.6% (95% confidence interval, 9.0%-18.2%) at the end of 2017 (P =.001) in response to the BRIDGE trial. Use of bridging anticoagulation declined similarly among atrial fibrillation patients at low risk for stroke (29.0% to 14.4%) and intermediate or high risk for stroke (38.0%-20.3%). Younger age and a prior history of stroke were independent predictors of bridging anticoagulation use following the BRIDGE trial publication. The BRIDGE trial publication is associated with a rapid and significant decline in the use of periprocedural bridging anticoagulation.

Bastani A, Su E, Adler DH, Baugh C, Caterino JM, **Clark CL**, Diercks DB, Hollander JE, Malveau SE, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST, Yagapen AN, Weiss RE and Sun BC (2019). "Comparison of 30-day serious adverse clinical events for elderly patients presenting to the emergency department with near-syncope versus syncope." [Annals of Emergency Medicine](#) 73(3): 274-280.

[Full Text](#)

Department of Emergency Medicine

Study Objective: Controversy remains in regard to the risk of adverse events for patients presenting with syncope compared with near-syncope. The purpose of our study is to describe the difference in outcomes between these groups in a large multicenter cohort of older emergency department (ED) patients. Methods: From April 28, 2013, to September 21, 2016, we conducted a prospective, observational study across 11 EDs in adults (≥ 60 years) with syncope or near-syncope. A standardized data extraction tool was used to collect information during their index visit and at 30-day follow-up. Our primary outcome was the incidence of 30-day death or serious clinical events. Data were analyzed with descriptive statistics and multivariate logistic regression analysis adjusting for relevant demographic or historical variables. Results: A total of 3,581 patients (mean age 72.8 years; 51.6% men) were enrolled in the study. There were 1,380 patients (39%) presenting with near-syncope and 2,201 (61%) presenting with syncope. Baseline characteristics revealed a greater incidence of congestive heart failure, coronary artery disease, previous arrhythmia, nonwhite race, and presenting dyspnea in the near-syncope compared with syncope cohort. There were no differences in the primary outcome between the groups (near-syncope 18.7% versus syncope 18.2%). A multivariate logistic regression analysis identified no difference in 30-day serious outcomes for patients with near-syncope (odds ratio 0.94; 95% confidence interval 0.78 to 1.14) compared with syncope. Conclusion: Near-syncope confers risk to patients similar to that of syncope for the composite outcome of 30-day death or serious clinical event.

Beall DP, Chambers MR, Thomas S, Amburgy J, Webb JR, Jr, Goodman BS, Datta DK, **Easton RW**, Linville D, II, Talati S and Tillman JB (2019). "Prospective and multicenter evaluation of outcomes for quality of life and activities of daily living for balloon kyphoplasty in the treatment of vertebral compression fractures: The EVOLVE trial." [Neurosurgery](#) 84(1): 169-178.

[Full Text](#)

Department of Orthopedic Surgery

Osteoporotic and neoplastic vertebral compression fractures (VCF) are common and painful, threatening quality of life and increasing risk of morbidity and mortality. Balloon kyphoplasty is a percutaneous option

for treating painful cancer- and osteoporosis-related VCFs, supported by 2 randomized trials demonstrating efficacy benefits of BKP over nonsurgical care. To investigate 12-mo disability, quality of life, and safety outcomes specifically in a Medicare-eligible population, representing characteristic patients seen in routine clinical practice. A total of 354 patients with painful VCFs were enrolled at 24 US sites with 350 undergoing kyphoplasty. Four coprimary endpoints—Numerical Rating Scale (NRS) back pain, Oswestry Disability Index (ODI), Short Form-36 Questionnaire Physical Component Summary (SF-36v2 PCS), EuroQol-5-Domain (EQ-5D)—were evaluated for statistically significant improvement 3 mo after kyphoplasty. Data were collected at baseline, 7 d, and 1, 3, 6, and 12 mo (www.clinicaltrials.gov registration NCT01871519). At the 3-mo primary endpoint, NRS improved from 8.7 to 2.7 and ODI improved from 63.4 to 27.1; SF-36 PCS was 24.2 at baseline improving to 36.6, and EQ-5D improved from 0.383 to 0.746 ($P < .001$ for each). These outcomes were statistically significant at every follow-up time point. Five device-/procedure-related adverse events, intraoperative asymptomatic balloon rupture, rib pain, and aspiration pneumonia, and a new VCF 25 d postprocedure, and myocardial infarction 105 d postprocedure were reported and each resolved with proper treatment. This large, prospective, clinical study demonstrates that kyphoplasty is a safe, effective, and durable procedure for treating patients with painful VCF due to osteoporosis or cancer.

Bonekamp D, Wolf MB, Roethke MC, Pahernik S, Hadaschik BA, Hatiboglu G, Kuru TH, Popeneciu IV, Chin JL, Billia M, **Relle J, Hafron J, Nandalur KR**, Staruch RM, Burtnyk M, Hohenfellner M and Schlemmer H-P (2019). "Twelve-month prostate volume reduction after MRI-guided transurethral ultrasound ablation of the prostate." European Radiology 29(1): 299-308.

[Full Text](#)

Department of Urology

Department of Diagnostic Radiology and Molecular Imaging

To quantitatively assess 12-month prostate volume (PV) reduction based on T2-weighted MRI and immediate post-treatment contrast-enhanced MRI non-perfused volume (NPV), and to compare measurements with predictions of acute and delayed ablation volumes based on MR-thermometry (MR-t), in a central radiology review of the Phase I clinical trial of MRI-guided transurethral ultrasound ablation (TULSA) in patients with localized prostate cancer.

Brahmamdham P, Carveth SL, Smyth M, Gendelman BS and Maisels MJ (2019). "Factors influencing choice of medical vs. surgical treatment of pediatric appendicitis." Journal of Pediatric Surgery. ePub Ahead of Print.

[Full Text](#)

Department of Surgery

OUWB Medical Student Author

Department of Pediatrics

Purpose: To examine what proportion of caregivers, if given a choice, would choose medical versus surgical treatment of appendicitis and what factors would be important in their decision. Methods: A survey was devised and given to the caregivers of children presenting to the pediatrician for a routine visit in community and academic pediatric clinics. The survey presented a summary of outcomes after medical (non-operative) and surgical treatment of uncomplicated appendicitis. Participants were then asked to choose medical versus surgical treatment if their child were to develop appendicitis. They were also asked to rate the importance of certain factors in their decision –1 being "not important" and 5 being "very important". Results: Four hundred surveys were distributed with an 86.2% (345/400) response rate. Six percent (21/342) of respondents reported a history of appendicitis and 49.4% (168/340) reported having known someone who had appendicitis. The majority of respondents, 85.3% (284/333), were mothers. A minority of respondents, 41.7% (95% CI: 36.7, 47.0), chose medical treatment over surgery for appendicitis. There was no statistical difference in the proportion of mothers (41.6%) versus fathers who chose medical treatment (41.3%). Caregivers who chose medical treatment were more likely to rate time in hospital ($p = .008$) and time out of school ($p = .05$) as important in decision making when compared with those who chose surgery. Those who chose surgical treatment were more likely to rate risk of recurrent appendicitis ($p < .001$) as important to decision making. In the multivariate analysis, those who rated time in hospital as very important had more than twice the odds of choosing medical therapy (OR 2.20, $p = 0.02$) when compared with those who rated it as less important. Not knowing someone who has had appendicitis was significantly associated with choosing medical therapy when compared with those who do know someone who has had appendicitis, OR

2.3, $p = .002$. Rating pain as very important was also significantly associated with choosing medical therapy, when compared to those rating pain 1–3, OR 3.38, $p = .03$. Conclusions: In this survey of caregivers of children presenting for routine care, 41.7% would choose medical, or non-operative, therapy for their children with acute appendicitis. The risk of recurrence, time in hospital, and time out of school, pain, and knowing someone who has had appendicitis were all important factors that families may consider when making a decision. These data may be useful for surgeons counseling patients on which treatment to pursue.

Cami E, Tagami T, **Raff G, Gallagher M, Chinnaiyan K, Bilolikor AN**, Hafeez A, Willner S and **Safian R** (2019). "Fractional flow reserve by coronary computed tomography angiography (FFRCT): Impact of measurement site on assessment of lesion-specific ischemia and statistical performance." Journal of the American College of Cardiology 73(9): 1449-1449.

[Full Text](#)

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: 1-4.

[Full Text](#)

Department of Internal Medicine

Casiano RR, **Folbe AJ**, Golfinos JG, Snyderman CH and Billin NBPC (2019). "An editorial on NASBS white paper: Coding and reimbursement for endoscopic endonasal surgery of the skull base." Journal of Neurological Surgery Part B-Skull Base 80: S245-S245.

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Department of Surgery

Technological advances are a major driver of surgical advances. The introduction of endoscopic technology ushered in a paradigm shift in the management of skull base pathology. Coding practices often lag far behind changes in surgical practice, resulting in confusion and a myriad of coding solutions until there is sufficient impetus for the development of new surgical codes. Endoscopic endonasal surgery of the skull base (EESSB) is now well established as an alternate surgical technique/approach for the treatment of skull base pathology but is not universally practiced at all institutions that perform skull base surgery. As a result, CPT codes do not exist for most EESSB procedures. Typically, EESSB is performed jointly by the otolaryngologist-head and neck surgeon (ENT) and neurosurgeon (NS). Therefore, coding can be complicated, third-party payers are often not familiar with the services provided, and reimbursement issues such as delayed or reduced payments result. As the number of trained surgeons continues to expand, there is diversity of opinion and practice regarding optimal CPT coding. There is a recognized knowledge gap regarding current coding options for EESSB. The purpose of this white paper is to provide surgeons, coders, billers, and third-party payers a comprehensive understanding of current coding and reimbursement implications for EESSB procedures. Payer medical directors and associated professionals will find this paper a valuable source of information about EESSB to facilitate medical policy development and appropriate adjudication and payment of claims. This white paper is a collaboration of KarenZupko & Associates, Inc. (KZA) and the North American Skull Base Society, with representation from NS and ENT. As such, it provides *guidelines* for coding but is not intended to represent the official recommendations of physician specialty societies, governmental regulatory agencies, insurance providers, or healthcare consultants. Areas of controversy are noted with acknowledgement of divergent opinions.

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.

Caterino JM, Adler D, Durham DD, Yeung SCJ, Hudson MF, **Bastani A**, Bernstein SL, Baugh CW, Coyne CJ, Grudzen CR, Henning DJ, Klotz A, Madsen TE, Pallin DJ, Reyes-Gibby CC, Rico JF, Ryan RJ, Shapiro NI, **Swor R**, Venkat A, Wilson J, Thomas CR, Bischof JJ and Lyman GH (2019). "Analysis of diagnoses, symptoms, medications, and admissions among patients with cancer presenting to emergency departments." *JAMA Network Open* 2(3): e190979.

[Full Text](#)

Department of Emergency Medicine

Importance: Better understanding of the emergency care needs of patients with cancer will inform outpatient and emergency department (ED) management. Objective: To provide a benchmark description of patients who present to the ED with active cancer. Design, Setting, and Participants: This multicenter prospective cohort study included 18 EDs affiliated with the Comprehensive Oncologic Emergencies Research Network (CONCERN). Of 1564 eligible patients, 1075 adults with active cancer were included from February 1, 2016, through January 30, 2017. Data were analyzed from February 1 through August 1, 2018. Main Outcomes and Measures: The proportion of patients reporting symptoms (eg, pain, nausea) before and during the ED visit, ED and outpatient medications, most common diagnoses, and suspected infection as indicated by ED antibiotic administration. The proportions observed, admitted, and with a hospital length of stay (LOS) of no more than 2 days were identified. Results: Of 1075 participants, mean (SD) age was 62 (14) years, and 51.8% were female. Seven hundred ninety-four participants (73.9%; 95% CI, 71.1%-76.5%) had undergone cancer treatment in the preceding 30 days; 674 (62.7%; 95% CI, 59.7%-65.6%) had advanced or metastatic cancer; and 505 (47.0%; 95% CI, 43.9%-50.0%) were 65 years or older. The 5 most common ED diagnoses were symptom related. Of all participants, 82 (7.6%; 95% CI, 6.1%-9.4%) were placed in observation and 615 (57.2%; 95% CI, 54.2%-60.2%) were admitted; 154 of 615 admissions (25.0%; 95% CI, 21.7%-28.7%) had an LOS of 2 days or less (median, 3 days; interquartile range, 2-6 days). Pain during the ED visit was present in 668 patients (62.1%; 95% CI, 59.2%-65.0%; mean [SD] pain score, 6.4 [2.6] of 10.0) and in 776 (72.2%) during the prior week. Opioids were administered in the ED to 228 of 386 patients (59.1%; 95% CI, 18.8%-23.8%)

with moderate to severe ED pain. Outpatient opioids were prescribed to 368 patients (47.4%; 95% CI, 3.14%-37.2%) of those with pre-ED pain, including 244 of 428 (57.0%; 95% CI, 52.2%-61.8%) who reported quite a bit or very much pain. Nausea in the ED was present in 336 (31.3%; 95% CI, 28.5%-34.1%); of these, 160 (47.6%; 95% CI, 12.8%-17.1%) received antiemetics in the ED. Antibiotics were administered in the ED to 285 patients (26.5%; 95% CI, 23.9%-29.2%). Of these, 209 patients (73.3%; 95% CI, 17.1%-21.9%) were admitted compared with 427 of 790 (54.1%; 95% CI, 50.5%-57.6%) not receiving antibiotics. Conclusions and Relevance: This initial prospective, multicenter study profiling patients with cancer who were treated in the ED identifies common characteristics in this patient population and suggests opportunities to optimize care before, during, and after the ED visit. Improvement requires collaboration between specialists and emergency physicians optimizing ED use, improving symptom control, avoiding unnecessary hospitalizations, and appropriately stratifying risk to ensure safe ED treatment and disposition of patients with cancer.

Chapman J, Sutherland E and Palka J (2019). "Hepatobiliary iminodiacetic acid scanning detects previously unknown hepatic metastases from colorectal adenocarcinoma." Journal of Nuclear Medicine Technology 47(1): 83-84.

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OUWB Medical Student Author

Department of Diagnostic Radiology and Molecular Imaging

A case of previously unknown metastatic colorectal adenocarcinoma presented as focal photopenia on hepatobiliary iminodiacetic acid scintigraphy. Differential diagnosis of focal photopenia and heterogenous hepatic radiotracer uptake on hepatobiliary scintigraphy is reviewed.

Chen C-J, Shabo LM, Ding D, Ironside N, Kano H, Mathieu D, Kondziolka D, Feliciano C, Rodriguez-Mercado R, **Grills IS**, Barnett G, Lunsford LD and Sheehan JP (2019). "Seizure presentation in patients with brain arteriovenous malformations treated with stereotactic radiosurgery: A multicenter study." World Neurosurgery. ePub Ahead of Print.

[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.

Cheung AY, Anderson BJ, **Heidemann DG** and **Gupta C** (2019). "Late-onset diffuse lamellar keratitis following laser in situ keratomileusis." Canadian Journal of Ophthalmology 54(1): 125-129.

[Full Text](#)

Department of Ophthalmology

Objective: To analyze 12 cases of late-onset diffuse lamellar keratitis (DLK) following uncomplicated LASIK and propose a method of management. Design Retrospective observational case series, literature review. Participants Patients who developed late-onset DLK following LASIK. Methods: Retrospective chart review of

all patients with late-onset DLK from January 2014 to August 2015. Data collected included demographic information, probable cause of DLK, stage of DLK, baseline examination, treatment, clinical course, outcomes, complications, and last follow-up examination. Review of relevant literature included searching for all prior cases and case series relating to "diffuse lamellar keratitis," "late-onset DLK," "Secondary Sands," and "delayed-onset DLK" by searching PubMed with these search terms. Results: Twelve eyes of 11 patients presented with late-onset DLK following LASIK. Onset ranged from 8 months to 17 years following LASIK. Stage of DLK ranged from stage I to III, and all patients responded well to aggressive corticosteroids without lifting of the LASIK flap. Final visual acuity for stage I/II and III eyes did not demonstrate a significant difference ($p = 0.218$). DLK resolved by a mean of 4.86 weeks for all eyes. Conclusion: Late-onset DLK can present at any time following LASIK with a wide range of inciting factors causing a nonspecific (and likely immune-related) inflammatory reaction. Based on our findings, aggressive oral and topical corticosteroids should be tried before lifting the LASIK flap as long as infection is not suspected or inciting debris is not seen in the flap because the vast majority resolve with such therapy.

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 25(5): 528-538.

[Full Text](#)

Department of Emergency Medicine

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.

Dalal PK, Mertens A, Shah D and **Hanson I** (2019). "Hemodynamic support using percutaneous transfemoral impella 5.0 and impella RP for refractory cardiogenic shock." Case Reports in Cardiology 2019: 4591250-4591250.

[Full Text](#)

Department of Internal Medicine

Acute myocardial infarction (AMI) resulting in cardiogenic shock continues to be a substantial source of morbidity and mortality despite advances in recognition and treatment. Prior to the advent of percutaneous and more durable left ventricular support devices, prompt revascularization with the addition of vasopressors and inotropes were the standard of care in the management of this critical population. Recent published studies have shown that in addition to prompt revascularization, unloading of the left ventricle with the placement of the Impella percutaneous axillary flow pump can lead to improvement in mortality. Parameters such as the cardiac power output (CPO) and pulmonary artery pulsatility index (PAPi), obtained

through pulmonary artery catheterization, can help ascertain the productivity of right and left ventricular function. Utilization of these parameters can provide the information necessary to escalate support to the right ventricle with the insertion of an Impella RP or the left ventricle with the insertion of larger devices, which provide more forward flow. Herein, we present a case of AMI complicated by cardiogenic shock resulting in biventricular failure treated with the percutaneous insertion of an Impella RP and Impella 5.0 utilizing invasive markers of left and right ventricular function to guide the management and escalation of care.

Davis FM, Jerzal E, Albright J, Kazmers A, Monsour A, **Bove P** and Henke PK (2019). "Variation in the elective management of small abdominal aortic aneurysms and physician practice patterns." Journal of Vascular Surgery. ePub Ahead of Print.

[Full Text](#)

Department of Surgery

Objective: Recent vascular societal guidelines have recommended an abdominal aortic aneurysm (AAA) size threshold for elective intervention; however, limited data have documented how well these AAA diameter benchmarks are being met. The objective of this study was to analyze variation in management of AAAs based on diameter and to determine the physician's rationale for intervention on small AAAs in relation to recommended treatment guidelines. Methods: A retrospective review of a statewide vascular surgery registry of all elective endovascular or open surgical AAA repairs from January 2012 to January 2016 was performed. Patients were dichotomized on the basis of aortic diameter at time of intervention into either guideline size AAAs or small AAAs, which were defined as <5.5 cm in men, <5.0 cm in women, or with growth <1.0 cm/y. An internal review was conducted of all small AAAs to determine the physician's rationale for intervention. The primary outcomes were variation in adherence to recommended treatment guidelines and the physician's rationale for treatment of small AAAs. Risk-adjusted major complication and mortality rates were calculated at 30 days and 1 year using a propensity score matching analysis. Results: Among the 3932 patients who underwent an elective AAA repair, 485 (12.3%) were repaired at diameters smaller than recommended by guidelines. The median AAA size in the small AAA cohort was 5.1 cm (interquartile range, 4.7-5.3 cm) vs 5.6 cm (interquartile range, 5.2-6.1 cm) in the guideline-based group. Percentage of small AAA repairs varied widely between hospitals from 1.4% to 44.4%. The physician's rationale for the majority of early interventions included the patient's anxiety (12.0%), combined aortoiliac occlusive disease (14.8%), aneurysm anatomy (28.2%), and does not adhere to guidelines (30%). The small AAA cohort had no significant difference in the 30-day or 1-year risk-adjusted mortality in comparison to guideline size AAAs. Conclusions: Despite well-established aortic diameter threshold guidelines, marked variation exists both at the hospital level and in terms of the physician's rationale for the management of elective AAA repairs. These findings demonstrate the challenge of providing uniform care for patients with AAAs despite established guidelines.

Deraniyagala R (2019). "Is it necessary to test oropharyngeal cancer for both p16 and human papillomavirus?" Practical Radiation Oncology 9(2): 61-62.

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Department of Radiation Oncology

Dilan TL, Moyer AR, Salido EM, Saravanan T, Kolandaivelu S, **Goldberg AFX** and Ramamurthy V (2019). "ARL13B, a Joubert Syndrome-associated protein, is critical for retinogenesis and elaboration of mouse photoreceptor outer segments." Journal of Neuroscience 39(8): 1347-1364.

[Full Text](#)

OUIB Medical Student Author

Mutations in the Joubert syndrome-associated small GTPase ARL13B are linked to photoreceptor impairment and vision loss. To determine the role of ARL13B in the development, function, and maintenance of ciliated photoreceptors, we generated a pan-retina knock-out (Six3-Cre) and a rod photoreceptor-specific inducible conditional knock-out (Pde6g-CreERT2) of ARL13B using murine models. Embryonic deletion of ARL13B led to defects in retinal development with reduced cell proliferation. In the absence of ARL13B, photoreceptors failed to develop outer segment (OS) membranous discs and axonemes, resulting in loss of function and rapid degeneration. Additionally, the majority of photoreceptor basal bodies did not dock properly at the

apical edge of the inner segments. The removal of ARL13B in adult rod photoreceptor cells after maturation of OS resulted in loss of photoresponse and vesiculation in the OS. Before changes in photoresponse, removal of ARL13B led to mislocalization of rhodopsin, prenylated phosphodiesterase-6 (PDE6), and intraflagellar transport protein-88 (IFT88). Our findings show that ARL13B is required at multiple stages of retinogenesis, including early postnatal proliferation of retinal progenitor cells, development of photoreceptor cilia, and morphogenesis of photoreceptor OS discs regardless of sex. Last, our results establish a need for ARL13B in photoreceptor maintenance and protein trafficking. SIGNIFICANCE STATEMENT The normal development of photoreceptor cilia is essential to create functional, organized outer segments with stacked membrane discs that house the phototransduction proteins necessary for sight. Our study identifies a complex role for ARL13B, a small GTPase linked to Joubert syndrome and visual impairment, at various stages of photoreceptor development. Loss of ARL13B led to defects in retinal proliferation, altered placement of basal bodies crucial for components of the cilium (transition zone) to emanate, and absence of photoreceptor-stacked discs. These defects led to extinguished visual response and dysregulated protein trafficking. Our findings show the complex role ARL13B plays in photoreceptor development, viability, and function. Our study accounts for the severe retinal impairment observed in ARL13B-linked Joubert syndrome patients.

Ding D, Mehta GU, Patibandla MR, Lee CC, Liscak R, Kano H, Pai FY, Kosak M, Sisterson ND, Martinez-Alvarez R, Martinez-Moreno N, Mathieu D, **Grills IS**, Blas K, **Lee K**, Cifarelli CP, Katsevman GA, Lee JYK, McShane B, Kondziolka D, Lunsford LD, Vance ML and Sheehan JP (2019). "Stereotactic radiosurgery for acromegaly: An international multicenter retrospective cohort study." Neurosurgery 84(3): 717-724.

[Request Form](#)

Department of Radiation Oncology

Background: Stereotactic radiosurgery (SRS) is a treatment option for persistent or recurrent acromegaly secondary to a growth hormone secreting pituitary adenoma, but its efficacy is inadequately defined. Objective: To assess, in a multicenter, retrospective cohort study, the outcomes of SRS for acromegaly and determine predictors. Methods: We pooled and analyzed data from 10 participating institutions of the International Gamma Knife Research Foundation for patients with acromegaly who underwent SRS with endocrine follow-up of 6 mo. Results: The study cohort comprised 371 patients with a mean endocrine follow-up of 79 mo. IGF-1 lowering medications were held in 56% of patients who were on pre-SRS medical therapy. The mean SRS treatment volume and margin dose were 3.0 cm(3) and 24.2 Gy, respectively. The actuarial rates of initial and durable endocrine remission at 10 yr were 69% and 59%, respectively. The mean time to durable remission after SRS was 38 mo. Biochemical relapse after initial remission occurred in 9%, with a mean time to recurrence of 17 mo. Cessation of IGF-1 lowering medication prior to SRS was the only independent predictor of durable remission (P = .01). Adverse radiation effects included the development of 1 new endocrinopathy in 26% and 1 cranial neuropathy in 4%. Conclusion: SRS is a definitive treatment option for patients with persistent or recurrent acromegaly after surgical resection. There appears to be a statistical association between the cessation of IGF-1 lowering medications prior to SRS and durable remission.

Dokter J, Nguyen L, Tennyson L, Han E and **Sirls LT** (2019). "The clinical rate of antibiotic change following empiric treatment for suspected urinary tract infections." Neurourology and Urodynamics 38: S190-S190.

[Full Text](#)

OUWB Medical Student

Department of Urology

Elhalawani H, Elgohari B, Lin TA, Mohamed ASR, Fitzgerald TJ, Laurie F, Ulin K, Kalpathy-Cramer J, **Guerrero T**, Holliday EB, Russo G, Patel A, Jones W, Walker GV, Awan M, Choi M, Dagan R, Mahmoud O, Shapiro A, Kong FMS, Gomez D, Zeng J, Decker R, Spoelstra FOB, Gaspar LE, Kachnic LA, Thomas CR, Okunieff P and Fuller CD (2019). "An in-silico quality assurance study of contouring target volumes in thoracic tumors within a cooperative group setting." Clinical and Translational Radiation Oncology 15: 83-92.

[Full Text](#)

Department of Radiation Oncology

Introduction: Target delineation variability is a significant technical impediment in multi-institutional trials

which employ intensity modulated radiotherapy (IMRT), as there is a real potential for clinically meaningful variances that can impact the outcomes in clinical trials. The goal of this study is to determine the variability of target delineation among participants from different institutions as part of Southwest Oncology Group (SWOG) Radiotherapy Committee's multi-institutional in-silico quality assurance study in patients with Pancoast tumors as a "dry run" for trial implementation. Methods: CT simulation scans were acquired from four patients with Pancoast tumor. Two patients had simulation 4D-CT and FDG-FDG PET-CT while two patients had 3D-CT and FDG-FDG PET-CT. Seventeen SWOG-affiliated physicians independently delineated target volumes defined as gross primary and nodal tumor volumes (GTV_P & GTV_N), clinical target volume (CTV), and planning target volume (PTV). Six board-certified thoracic radiation oncologists were designated as the 'Experts' for this study. Their delineations were used to create a simultaneous truth and performance level estimation (STAPLE) contours using ADMIRE software (Elekta AB, Sweden 2017). Individual participants' contours were then compared with Experts' STAPLE contours. Results: When compared to the Experts' STAPLE, GTV_P had the best agreement among all participants, while GTV_N showed the lowest agreement among all participants. There were no statistically significant differences in all studied parameters for all TVs for cases with 4D-CT versus cases with 3D-CT simulation scans. Conclusions: High degree of inter-observer variation was noted for all target volume except for GTV_P, unveiling potentials for protocol modification for subsequent clinically meaningful improvement in target definition. Various similarity indices exist that can be used to guide multi-institutional radiotherapy delineation QA credentialing.

Elterman D, Hatiboglu G, Hetou K, **Relle J**, Staruch R, Burtnyk M and Chin J (2019). "Relief of lower urinary tract symptoms after MRI-guided transurethral ultrasound ablation (TULSA): subgroup analyses in patients with symptoms of benign prostatic hyperplasia." Neurourology and Urodynamics 38: S204-S205.

[Full Text](#)

Department of Urology

Emery CL, Belich RF, Davis TH, Young SA, **Sims MD** and **Boyanton BL** (2019). "Multicenter evaluation of NeuMoDx group B streptococcus assay on the NeuMoDx 288 molecular system." Journal of Clinical Microbiology 57(2): e01324-18.

[Full Text](#)

Department of Internal Medicine

Department of Pathology

Group B Streptococcus (GBS) is the leading cause of neonatal sepsis and meningitis in developed countries. Recommendations for antepartum GBS detection include enriched culture with several options for identifying GBS, some of which are time-consuming. To reduce the time for identification and determination of the maternal GBS colonization status, rapid nucleic acid amplification technologies have been developed and commercialized. For rapid detection of GBS, a three-site clinical study was conducted to evaluate the NeuMoDx GBS assay, a real-time PCR test performed for vaginal/rectal swab specimens in Lim broth enrichment culture on the NeuMoDx 288 molecular system (NeuMoDx system); these data were used to support 510(k) submission. A total of 1,250 eligible remnant samples were prospectively enrolled and tested during the study. The results of the PCR assay were compared to the results of the Centers for Disease Control and Prevention (CDC)-recommended enriched-culture method, which served as the gold standard reference method for the study. The NeuMoDx GBS assay results yielded a sensitivity of 96.9% (95% confidence interval [CI] = 94.1 to 98.4), specificity of 96.0% (95% CI = 94.6 to 97.1), and a total agreement with the reference method of 96.2% (95% CI = 93.8 to 98.3). NeuMoDx GBS assay results were also compared to results obtained using the BD MAX GBS assay on the BD MAX system. The two systems demonstrated a total percent agreement of 98.0% (95% CI = 95.5 to 100.0). The performance of the NeuMoDx GBS assay implemented on the NeuMoDx system compared favorably to the CDC enriched-culture method and to the BD MAX GBS assay.

Feldmann K, Cami E and **Safian RD** (2019). "Planning percutaneous coronary interventions using computed tomography angiography and fractional flow reserve-derived from computed tomography: A state-of-the-art review." Catheterization and Cardiovascular Interventions 93(2): 298-304.

[Full Text](#)

Department of Internal Medicine

Fractional flow reserve derived by coronary computed tomography angiography (CTA; FFRCT) is an accurate noninvasive method for identifying coronary artery disease (CAD) and detecting hemodynamically significant stenosis. Although initially proposed as noninvasive tools to "rule out" significant CAD in low-risk patients, CTA and FFRCT are now utilized in higher-risk patients. Furthermore, new applications of CTA and FFRCT include a planning tool for percutaneous coronary intervention (PCI), which allows the cardiologist to assess lesion-specific ischemia, plan stent locations and sizes, and use virtual remodeling of the lumen (virtual stenting) to assess the functional impact of PCI. The purpose of this review is to discuss the principles of CTA and FFRCT acquisition, and their application for PCI planning, even before invasive angiography is performed.

Foerster R, Cho BCJ, Fahim DK, Gerszten PC, Flickinger JC, **Grills IS, Jawad MS**, Kersh CR, Letourneau D, Mantel F, Sahgal A, Shin JH, Winey BA and Guckenberger M (2019). "Histopathological findings after reirradiation compared to first irradiation of spinal bone metastases with stereotactic body radiotherapy: A cohort study." Neurosurgery 84(2): 435-441.

[Request Form](#)

Department of Radiation Oncology

Background: Stereotactic body radiotherapy (SBRT) of the spine provides superior tumor control, but vertebral compression fractures are increased and the pathophysiological process underneath is not well understood. Data on histopathological changes, particularly after salvage SBRT (sSBRT) following conventional irradiation, are scarce. Objective: To investigate surgical specimens after sSBRT and primary SBRT (pSBRT) regarding histopathological changes. Methods: We assessed 704 patients treated with spine SBRT 2006 to 2012. Thirty patients underwent salvage surgery; 23 histopathological reports were available. Clinical and histopathological findings were analyzed for sSBRT (69.6%) and pSBRT (30.4%). Results: Mean time to surgery after sSBRT/pSBRT was 8.3/10.3 mo (P = .64). Reason for surgery included pain (sSBRT/pSBRT: 12.5%/71.4%, P = .25), fractures (sSBRT/pSBRT: 37.5%/28.6%, P = .68), and neurological symptoms (sSBRT/pSBRT: 68.8%/42.9%, P = .24). Radiological tumor progression after sSBRT/pSBRT was seen in 71.4%/42.9% (P = .2). Most specimens displayed viable/proliferative tumor (sSBRT/pSBRT: 62.5%/71.4%, P = .68 and 56.3%/57.1%, P = .97). Few specimens showed soft tissue necrosis (sSBRT/pSBRT: 20%/28.6%, P = .66), osteonecrosis (sSBRT/pSBRT: 14.3%/16.7%, P = .89), or bone marrow fibrosis (sSBRT/pSBRT: 42.9%/33.3%, P = .69). Tumor bed necrosis was more common after sSBRT (81.3%/42.9%, P = .066). Radiological tumor progression correlated with viable/proliferative tumor (P = .03/P = .006) and tumor bed necrosis (P = .03). Fractures were increased with bone marrow fibrosis (P = .07), but not with osteonecrosis (P = .53) or soft tissue necrosis (P = .19). Neurological symptoms were common with radiological tumor progression (P = .07), but not with fractures (P = .18). Conclusion: For both, sSBRT and pSBRT, histopathological changes were similar. Neurological symptoms were attributable to tumor progression and pathological fractures were not associated with osteonecrosis or tumor progression.

Fortunato JT and Menkes DL (2019). "The aging physician: A practical approach to protect our patients." Clinical Ethics 14(1): 46-49.

[Full Text](#)

OUWB Medical Student Author

Department of Neurology

As the median age of practicing physicians increases, ethical dilemmas due to age-related cognitive decline among clinicians will become ever more pressing. Compelling data show that despite acknowledgement of their duty to protect the public, physicians often fail to report themselves, their colleagues, or their physician-patients when cognitive decline appears to impact medical practice adversely. As such, efforts to educate physicians about ethical obligations and various tactful methodologies to report themselves or others seem ineffective. Illustrated by a case report of age-related cognitive decline in a practicing physician, practical recommendations are made both to develop and validate cognitive screening in middle-aged physicians, presumably before the onset of age-related cognitive decline.

Franklin BA and Kokkinos P (2019). "Exertion-related acute cardiovascular events: Pathophysiologic considerations, risk modulators, and prophylactic interventions," In Kokkinos P and Narayan P (ed). Cardiorespiratory Fitness in Cardiometabolic Diseases: Prevention and Management in Clinical Practice. Cham: Springer International Publishing.

pp: 123-136.

[Full Text](#)

Although considerable evidence strongly supports that regular aerobic exercise, increased lifestyle physical activity (PA), improved cardiorespiratory fitness, or combinations thereof, may protect against the development of cardiovascular disease (CVD), exertion-related cardiovascular events have been reported in the medical literature and the lay press, suggesting that vigorous PA (≥ 6 metabolic equivalents) may trigger sudden cardiac death (SCD) or acute myocardial infarction (AMI) in persons with known or occult CVD. Structural cardiovascular abnormalities, most commonly hypertrophic cardiomyopathy, are the major causes of SCD in younger individuals, whereas atherosclerotic CVD is the most common autopsy finding in individuals >40 years of age. The estimated relative risk of exercise-related cardiac events is inversely related to the individual's habitual frequency of PA (bouts/week), generally ranges from 2 to 56, and in some cases may increase >100 -fold. In the general population, the absolute risk that a cardiovascular event will occur during or soon after vigorous PA has been estimated to be between 1 in 500,000 and 1 in 2.6 million hours. Although higher event rates are reported in exercise-based cardiac rehabilitation, the associated fatality rate remains low in medically supervised programs that are equipped to handle cardiovascular emergencies. Racquet sports, water or cross-country skiing, marathon and triathlon events, highly competitive sports (e.g., basketball), deer hunting, and snow removal are associated with a greater incidence of AMI and SCD than other activities. In conclusion, if the current mantra "exercise is medicine" is embraced, underdosing and overdosing are possible. Thus, exercise may have a typical dose-response curve with a plateau in benefit or even adverse effects, in some individuals, at more extreme levels (i.e., reverse J-shaped curve).

Friedman P, Yilmaz A, Zeb A, Buket A, **Whitten A**, **Alhousseini A**, Ogunyemi D, Han B, Mandal R, Wishart D, **Graham S** and **Bahado-Singh R** (2019). "Metabolomic prediction of prematurity in asymptomatic short cervix." [American Journal of Obstetrics and Gynecology](#) 220(1): S315-S316.

[Full Text](#)

Department of Obstetrics and Gynecology

Garber AJ, Abrahamson MJ, Barzilay JL, Blonde L, Bloomgarden ZT, Bush MA, Dagogo-Jack S, DeFronzo RA, Einhorn D, Fonseca VA, Garber JR, Garvey WT, **Grunberger G**, Handelsman Y, Hirsch IB, Jellinger PS, McGill JB, Mechanick JL, Rosenblit PD and Umpierrez GE (2019). "Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm-2019 executive summary." [Endocrine Practice](#) 25(1): 69-100.

[Full Text](#)

Department of Internal Medicine

This document represents the official position of the American Association of Clinical Endocrinologists and American College of Endocrinology. Where there were no randomized controlled trials or specific U.S. FDA labeling for issues in clinical practice, the participating clinical experts utilized their judgment and experience. Every effort was made to achieve consensus among the committee members. Position statements are meant to provide guidance, but they are not to be considered prescriptive for any individual patient and cannot replace the judgment of a clinician.

Grenell A, Wang Y, Yam M, Swarup A, Dilan TL, Hauer A, Linton JD, Philp NJ, Gregor E, Zhu S, Shi Q, Murphy J, Guan T, Lohner D, Kolandaivelu S, Ramamurthy V, **Goldberg AFX**, Hurley JB and Du J (2019). "Loss of MPC1 reprograms retinal metabolism to impair visual function." [Proceedings of the National Academy of Sciences](#) 116(9): 3530-3535.

[Full Text](#)

OUWB Medical Student Author

Mitochondrial pyruvate carrier (MPC) is responsible for transporting pyruvate from glycolysis into mitochondria for oxidative phosphorylation. In the vertebrate retinas, the majority of glucose is metabolized into lactate by glycolysis rather than being oxidized in the mitochondria. Here, we show that although a small percentage of glucose is transported through MPC, deletion of MPC impairs visual function, decreases the viability of photoreceptors, disrupts photoreceptor ultrastructure, and causes glial activation. We find that MPC is required for maintaining the retinal metabolism in amino acids, neurotransmitters, and ketone bodies. Glucose metabolism in vertebrate retinas is dominated by aerobic glycolysis (the "Warburg Effect"),

which allows only a small fraction of glucose-derived pyruvate to enter mitochondria. Here, we report evidence that the small fraction of pyruvate in photoreceptors that does get oxidized by their mitochondria is required for visual function, photoreceptor structure and viability, normal neuron–glial interaction, and homeostasis of retinal metabolism. The mitochondrial pyruvate carrier (MPC) links glycolysis and mitochondrial metabolism. Retina-specific deletion of MPC1 results in progressive retinal degeneration and decline of visual function in both rod and cone photoreceptors. Using targeted-metabolomics and ¹³C tracers, we found that MPC1 is required for cytosolic reducing power maintenance, glutamine/glutamate metabolism, and flexibility in fuel utilization.

Grewal DS, Charles S, Parolini B, Kadonosono K and **Mahmoud TH** (2019). "Autologous retinal transplant for refractory macular holes: Multicenter international collaborative study group." *Ophthalmology*. ePub Ahead of Print.

[Full Text](#)

Department of Ophthalmology

Purpose: To report the structural and functional outcomes of autologous neurosensory retinal transplant for closure of refractory large macular holes (MHs). **Design:** Multicenter, retrospective, consecutive case series. **Participants** A total of 41 eyes of 41 patients with a full-thickness MH refractory to prior vitrectomy with internal limiting membrane (ILM) peel and tamponade. **Methods:** All patients underwent pars plana vitrectomy, autologous neurosensory retinal transplant with gas, silicone oil tamponade, or short-term perfluoro-n-octane heavy-liquid tamponade. All patients had at least 6 months' follow-up. **Main Outcome Measures:** Anatomic closure of MH, change in ellipsoid zone (EZ) and external limiting membrane (ELM) defect on OCT, visual acuity (VA) recovery, and surgical complications were analyzed. **Results:** Mean number of prior surgeries was 1.5 ± 0.94 (range, 1–3), and patients were followed for a mean of 11.1 ± 7.7 months (range, 6–36 months). Complete anatomic closure of MH by OCT was achieved in 36 of 41 eyes (87.8%). Mean corrected VA (logarithm of the minimum angle of resolution [logMAR]) improved ($P = 0.03$) from 1.11 ± 0.66 (range, 0.48–3) to 1.03 ± 0.51 (range, 0.1–2) at the last postoperative visit. The VA improved (≥ 0.3 logMAR units) in 15 eyes (36.6%), was stable in 17 eyes (41.5%), and worsened in 9 eyes (21.9%). Among eyes with anatomic closure, VA improved in 52.3% and worsened in 13.8%, whereas in those without closure, VA worsened in 20% and improved in none. Mean preoperative largest basal diameter was 1468.1 ± 656.4 μm (range, 621–2600 μm), and mean inner-opening diameter was 825 ± 422.5 μm (range, 336–1649 μm). Mean preoperative EZ defect was 1777.3 ± 513.8 μm (range, 963–2808 μm), which decreased to 1370 ± 556.9 μm (range, 288–2000 μm) at final follow-up ($P = 0.007$). Mean preoperative ELM was 1681.5 ± 429 μm (range, 1172–2606 μm), which decreased to 1408.5 ± 571.2 μm (range, 200–2000 μm) at final follow-up ($P = 0.017$). Major postoperative complications were retinal detachment ($n = 1$) and vitreous hemorrhage ($n = 1$). There were no cases of proliferative vitreoretinopathy, endophthalmitis, suprachoroidal hemorrhage, or choroidal neovascularization. **Conclusions:** The autologous retinal transplant technique offers a high degree of anatomic success and proved safe in this initial experience for closure of refractory MHs.

Gupta A and Bonadio W (2019). "Lack of utility in performing blood glucose measurement and electrocardiogram in the outpatient evaluation of benign pediatric syncope." *Clinical Pediatrics* 58(2): 146-150.

[Full Text](#)

OUWB Medical Student Author

We aimed to determine the frequency of blood glucose and electrocardiogram (EKG) abnormalities in previously healthy children who present to an emergency department (ED) with a diagnosis of benign syncope. Chart review of consecutive children aged 5 to 18 years presenting to the pediatric ED from 2004 to 2014 with a discharge diagnosis of benign syncope was done. Of 969 patients, hypoglycemia (serum glucose < 60 mg/dL) was present in only 3 cases (0.3%). Of 754 patients with EKG performed, only 4 cases (0.6%) was an abnormality requiring further cardiac evaluation identified; cardiac echocardiogram was performed in 3 of these 4 patients, which revealed no cardiac pathology. Financial analysis for performing blood glucose measurement and EKG on these patients amounted to total health care cost of \$222,526. We concluded that previously healthy children with syncope rarely have hypoglycemia or underlying cardiac abnormality. The routine performance of tests can incur significant health care expenditure.

Halka JT, Vasylyuk A, **Demare A**, **Iacco A** and **Janczyk R** (2019). "Hybrid robotic-assisted transversus abdominis release versus open transversus abdominis release: A comparison of short-term outcomes." *Hernia* 23(1): 37-42.

[Full Text](#)

OUWB Medical Student Author

Department of Surgery

Although the open transversus abdominis release (oTAR) is an effective operation for large ventral hernias, it is historically associated with a relatively long length of stay. Robotic retromuscular transversus abdominis release (rTAR) allows minimally invasive repair of complex ventral hernias with shorter length of stay (LOS) compared to open repairs (TAR), but hybrid robotic TAR (hrTAR), partial open intervention via incision through the overlying hernia sac for fascial closure, may be required to accomplish effective repair of large defects. We compare LOS and short-term outcomes of a cohort of our hrTAR patients to our historical oTAR patients.

Hall E, Finch A, Jacobson M, **Rosen B**, Metcalfe K, Sun P, Narod SA and Kotsopoulos J (2019). "Effects of bilateral salpingo-oophorectomy on menopausal symptoms and sexual functioning among women with a BRCA1 or BRCA2 mutation." *Gynecologic Oncology* 152(1): 145-150.

[Full Text](#)

Department of Obstetrics and Gynecology

Introduction: Prophylactic bilateral salpingo-oophorectomy (BSO) is recommended at an early age to BRCA mutation carriers to prevent ovarian cancer. It is critical to evaluate the impact of BSO on non-cancer outcomes, including quality of life (QOL), menopausal symptoms and sexual functioning. Methods: BRCA mutation carriers who elected to undergo a BSO completed three questionnaires prior to surgery and then again approximately one and three years following surgery which included: 1) medical history questionnaire, 2) Menopause-Specific Quality of Life Intervention questionnaire and 3) Sexual Activity Questionnaire. The change in quality of life, menopausal symptoms and sexual functioning before and after oophorectomy was determined using a paired t-test and stratified by menopausal status at surgery. Results: We included 140 BRCA mutation carriers with an average follow-up of 3.5 years following BSO. Among 93 women who were premenopausal, oophorectomy was associated with an increase in menopausal symptoms (vasomotor, physical) ($P < 0.001$) and a decline in sexual functioning (discomfort, pleasure) ($P \leq 0.0001$), but had no impact on overall QOL ($P = 0.31$). HRT mitigated, but did not eliminate the adverse effects. Women who were postmenopausal at surgery ($n = 47$) experienced an increase in physical symptoms ($P = 0.03$) and a decline in sexual functioning (discomfort) ($P = 0.004$) and in overall QOL ($P = 0.04$). Conclusions: This study demonstrates that 3.5 years after oophorectomy, BRCA mutation carriers experience a significant worsening of menopausal symptoms and a decline in sexual functioning, particularly among those who underwent surgery prior to natural menopause. The use of HRT mitigated some but not all the effects. Overall, women who were premenopausal at surgery did not experience a decline in their QOL.

Han E, Nguyen L, **Gilleran J, Bartley J**, Odabachian L, Killinger K, **Peters K, Dai YL**, Boura J and **Sirls L** (2019). "OES [sic] pelvic surgery impact the efficacy of pelvic floor physical therapy for pelvic pain?" *Neurourology and Urodynamics* 38: S235-S236.

[Full Text](#)

Department of Urology

OUWB Medical Student Author

Han E, Nguyen LN, **Gilleran J, Bartley J**, Killinger KA, Boura JA and **Sirls LT** (2019). "Pelvic floor distress inventory scores improve after prolapse surgery regardless of surgical approach but not after observation alone." *Urology* 124: 62-71.

[Full Text](#)

Department of Urology

Objective: To evaluate the effect of different surgical procedures on Pelvic Floor Distress Inventory (PFDI) scores in women with pelvic organ prolapse. Materials and Methods: Women with prolapse were enrolled from 2008 to 2014. Baseline data and outcomes at 1 year were collected including subscales of the PFDI. Patients who had surgery (SGY) within the first year were compared to those who did not (N-SGY). Subanalyses of SGY included vaginal vs abdominal, with or without concurrent hysterectomy (HYST, N-HYST), placement of mesh (MESH, N-MESH), and concurrent posterior repair/perineorrhaphy (POST, N-POST). Results: A total of 233/239 patients underwent surgery in the first year. For SGY vs N-SGY, SGY had

significant improvements in PFDI and all subscale scores at 1 year while N-SGY did not. When comparing vaginal to abdominal approach, MESH to N-MESH and HYST to N-HYST, there were no differences between any scores at baseline or 1 year between the groups. However, all within group symptom scores improved from baseline to 1 year ($P < .0001$ for all). In comparing POST to N-POST, there were no differences between groups at 1 year in PFDI and Urogenital Distress Inventory and Pelvic Organ Prolapse Distress Inventory subscale scores. Colorectal-Anal Distress Inventory scores were significantly higher at baseline for POST ($P < .0001$) but not at 1 year ($P = 0.37$). All within group scores statistically significant improved at 1 year. Conclusion: Women who underwent surgical repair for prolapse had significantly improved overall PFDI and subscale scores regardless of surgical approach and concurrent procedures.

Han E, Tennyson L, **Gilleran J, Bartley J and Peters K** (2019). "Small fiber polyneuropathy in hunner lesion and non-hunner lesion bladder pain syndrome." *Neurourology and Urodynamics* 38: S192-S192.

[Full Text](#)

Department of Urology

Hojjat H, Svider PF, **Hong R, Folbe AJ**, Eloy JA and **Shkoukani MA** (2019). "In response to To image or not to image? A cost-effectiveness analysis of MRI for patients with asymmetric sensorineural hearing loss." *Laryngoscope* 129(2): E50-E50.

[Full Text](#)

Department of Surgery

Jae SY, Bunsawat K, Kunutsor SK, Yoon ES, Kim HJ, Kang M, Choi YH and **Franklin BA** (2019). "Relation of exercise heart rate recovery to predict cardiometabolic syndrome in men." *American Journal of Cardiology* 123(4): 582-587.

[Full Text](#)

Department of Internal Medicine

We examined the hypothesis that delayed heart rate recovery (HRR) after exercise testing, an estimate of decreased autonomic function, predicts the risk of cardiometabolic syndrome (MetS) and is associated with continuous MetS risk scores in healthy men. Participants were 2,740 men who underwent general health examinations and had no evidence of MetS, cardiovascular diseases, diabetes, and hypertension at baseline. Baseline HRR was calculated as the difference between peak heart rate attained during exercise testing and the heart rate at 1 (HRR 1) and 2 minutes (HRR 2) after test termination. Incident MetS was defined as participants having ≥ 3 MetS components, and continuous MetS risk score was computed as the sum of z-score of 5 risk factors at follow-up. The incidence of MetS was 61/1,000 person-years during an average follow-up of 5 years. The relative risks and 95% confidence interval (CI) of incident MetS in the lowest quartiles of HRR 1 and HRR 2 versus the highest quartile were 1.24 (95% CI 1.02 to 1.51) and 2.02 (95% CI 1.58 to 2.60), respectively, after adjusting for potential confounders, including peak oxygen uptake and resting heart rate. HRR 1 ($= -0.052$, $p = 0.005$) and HRR 2 ($= -0.058$, $p = 0.009$) were independently associated with clustered MetS risk scores after adjusting for covariates. In conclusion, the independent association between delayed HRR after exercise testing and incident MetS and continuous MetS risk scores suggests that decreased autonomic function may be considered as a parameter to predict the future likelihood of MetS.

Jae SY, Kurl S, Kim HJ, **Franklin BA**, Kunutsor SK, Kang M and Laukkanen JA (2019). "Is there an "asymptote of gain" beyond which further increases in cardiorespiratory fitness convey no additional benefits on mortality and atrial fibrillation?" *Mayo Clinic Proceedings* 94(3): 545-547.

[Full Text](#)

Department of Internal Medicine

Jaward LR, O'Neil TA, Marks A and **Smith MA** (2019). "Differences in adverse effect profiles of corticosteroids in palliative care patients." *American Journal of Hospice and Palliative Medicine* 36(2): 158-168.

[Full Text](#)

Department of Pathology

Background: Corticosteroids are frequently utilized in the palliative care setting to combat symptoms such as fatigue, dyspnea, pain, weakness, anorexia, cachexia, nausea, and vomiting. Often times, adverse effects arise

with corticosteroid use, and it is unclear whether switching to another corticosteroid would reduce the risk of specific adverse effects or what measures can be taken to alleviate the adverse effects. Objective: This article aims to review the differentiating pharmacokinetics, potency, and adverse effect profiles of corticosteroids and summarize their clinical applicability. Methods: A literature review of "corticosteroids" and "palliative care" was performed using the PubMed database through July 2018. Original studies relevant to the purpose of this study were identified and those that met inclusion criteria were included. Results: Although corticosteroids share many common factors, including similar pharmacokinetic, pharmacodynamic, and adverse effect profiles, they have significant differences when the details of these variables are reviewed. Providers that prescribe corticosteroids for symptom management should be aware of these differences and the recommended management strategies. Conclusions: Recognition of corticosteroid induced adverse effect profiles and possible management strategies is crucial to optimal symptom management in palliative care patients.

Johnson SB, Hung J, Kapadia N, Oh KS, Kim M and **Hamstra DA** (2019). "Spinal growth patterns after craniospinal irradiation in children with medulloblastoma." *Practical Radiation Oncology* 9(1): E22-E28.

[Full Text](#)

Department of Radiation Oncology

Purpose: This study aimed to evaluate the impact on spine growth in children with medulloblastoma using either photon or electron craniospinal irradiation (CSI). Methods and Materials: This was a single institution retrospective review of children who were treated with CSI for medulloblastoma. Spine growth was measured on magnetic resonance imaging scans at defined locations on the basis of a published predictive model of spine growth after CSI. Differences between spine growth in the anterior, middle, and posterior aspect of the designated vertebral segments were also assessed. Differences between the groups treated with photons or electrons were assessed with student's t test. Results: A total of 19 patients (10 patients treated with electrons and 9 with photons) with a median follow-up time of 45.5 months (confidence interval, 34.9-55.1 months) were evaluated. Patients treated with electrons were younger than those who received photons (5.1 years [range, 3.8-9.0 years] vs 9.6 years [range, 3.5-12.9 years]); however, there were no differences in other clinical characteristics, treatment, or follow-up between the groups. Spine growth rate for patients treated with electrons fit the predictive model (104% +/- 5.2%), but patients treated with photons had growth that was faster than predicted by the model (150% +/- 47%) and different from that observed with electrons. The differences between treatment modalities were statistically significant ($P = .03$). For patients treated with photons, there were no statistical differences between the growth rate of the anterior vertebral body compared with the posterior aspect, but for patients treated with electrons, a faster spine growth in the anterior L1-L5 lumbar spine was observed compared with the posterior lumbar spine (3.90 vs 2.52 mm/year; $P = .006$) without differences in the cervical or thoracic spine. Conclusions: The use of electrons to treat the craniospinal axis in children with medulloblastoma resulted in no significant difference in spine growth compared with the predicted spine growth on the basis of previously published models using photons, but with a clinically insignificant faster spine growth rate in the anterior lumbar spine.

Kara S, Pirela-Morillo GA, Gilliam CT and **Wilson GD** (2019). "Identification of novel susceptibility genes associated with seven autoimmune disorders using whole genome molecular interaction networks." *Journal of Autoimmunity* 97: 48-58.

[Full Text](#)

Department of Radiation Oncology

Convergent evidence from multiple and independent genetics studies implicate a small number of genes that predispose individuals to multiple autoimmune disorders (AuD). These intersecting loci reinforced the hypothesis that disorders with overlapping etiology group into a cluster of closely related genes within a whole genome molecular interaction network. We tested the hypothesis that "biological network proximity" within a whole genome molecular interaction network can be used to inform the search for multigene inheritance. Using a set of nine previously published genome wide association studies (GWAS) of AuD genes, we generated AuD-specific molecular interaction networks to identify networks of associated genes. We show that all nine "seed genes" can be connected within a 35-member network via interactions with 26 connecting genes. We show that this network is more connected than expected by chance, and 13 of the connecting genes showed association with multiple AuD upon GWAS reanalysis. Furthermore, we report

association of SNPs in five new genes (IL10RA, DGKA, GRB2, STAT5A, and NFATC2) which were not previously considered as AuD candidates, and show significant association in novel disease samples of Crohn's disease and systemic lupus erythematosus. Furthermore, we show that the connecting genes show no association in four non-AuD GWAS. Finally, we test the connecting genes in psoriasis GWAS, and show association to previously identified loci and report new loci. These findings support the hypothesis that molecular interaction networks can be used to inform the search for multigene disease etiology, especially for disorders with overlapping etiology.

Keihani S, Putbrese BE, Rogers DM, Patel DP, Stoddard GJ, 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, 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). "Optimal timing of delayed excretory phase computed tomography scan for diagnosis of urinary extravasation after high-grade renal trauma." Journal of Trauma and Acute Care Surgery 86(2): 274-281.

[Full Text](#)

Department of Urology

Background: Excretory phase computed tomography (CT) scan is used for diagnosis of renal collecting system injuries and accurate grading of high-grade renal trauma. However, optimal timing of the excretory phase is not well established. We hypothesized that there is an association between excretory phase timing and diagnosis of urinary extravasation and aimed to identify the optimal excretory phase timing for diagnosis of urinary extravasation. Methods: The Genito-Urinary Trauma Study collected data on high-grade renal trauma (grades III-V) from 14 Level I trauma centers between 2014 and 2017. The time between portal venous and excretory phases at initial CT scans was recorded. Poisson regression was used to measure the association between excretory phase timing and diagnosis of urinary extravasation. Predictive receiver operating characteristic analysis was used to identify a cutoff point optimizing detection of urinary extravasation. Results: Overall, 326 patients were included; 245 (75%) had excretory phase CT scans for review either initially (n = 212) or only at their follow-up (n = 33). At initial CT with excretory phase, 46 (22%) of 212 patients were diagnosed with urinary extravasation. Median time between portal venous and excretory phases was 4 minutes (interquartile range, 4-7 minutes). Time of initial excretory phase was significantly greater in those diagnosed with urinary extravasation. Increased time to excretory phase was positively associated with finding urinary extravasation at the initial CT scan after controlling for multiple factors (risk ratio per minute, 1.15; 95% confidence interval, 1.09-1.22; p < 0.001). The optimal delay for detection of urinary extravasation was 9 minutes. Conclusion: Timing of the excretory phase is a significant factor in accurate diagnosis of renal collecting system injury. A 9-minute delay between the early and excretory phases optimized detection of urinary extravasation.

Khandhar P, Chan J, Rajanna V and Novotny N (2019). "Intraleural administration of TPA and dornase alfa in pediatric patients with empyema." Critical Care Medicine 47(1): 320.

[Full Text](#)

Department of Pediatrics

Kim DP, **Kus KJB** and Ruiz E (2019). "Basal cell carcinoma review." Hematology/Oncology Clinics of North America 33(1): 13-24.

[Full Text](#)

OUWB Medical Student Author

Basal cell carcinoma (BCC) is the most common malignancy and the incidence is rising. BCCs have low mortality but can cause significant morbidity primarily through local destruction. The pathogenesis is linked to the interplay between environmental and patient-derived characteristics. There are multiple therapeutic modalities, and appropriate selection requires knowledge of complications, cosmetic outcomes, and recurrence rates. This article reviews the epidemiology, staging, treatment, and prevention of BCC.

Kim SK, Vishweswaraiah S, **Macknis J**, Lalwani A, Mishra NK, Guda C, Ogunyemi D, **Radhakrishna U** and **Bahado-Singh R** (2019). "New-onset postpartum preeclampsia: Mechanisms and prediction." American Journal of Obstetrics and Gynecology 220(1): S343-S343.

[Full Text](#)

Department of Pathology

Department of Obstetrics and Gynecology

Kmiecik MJ, **Brisson RJ** and Morrison RG (2019). "The time course of semantic and relational processing during verbal analogical reasoning." *Brain and Cognition* 129: 25-34.

[Full Text](#)

OUWB Medical Student Author

Analogy is an important ability that allows humans to discover relationships between information domains that often vary in surface and relational characteristics. Cognitive neuroscience studies of analogy have demonstrated the importance of the prefrontal cortex during relational comparisons, but little is known about how semantic and relational similarity interact throughout its time course. We used scalp electroencephalography (EEG) analyzed with event-related potentials (ERPs) to examine the neural time course of analogical reasoning while 16 participants solved four-term verbal analogies. Semantic similarity was manipulated by increasing the semantic distance between source and target analogs creating semantically near and far analogies. Relational similarity was manipulated by creating relationally valid and invalid analogies. Only valid analogies were impacted by semantic distance such that far analogies were solved slower and less accurately than near analogies. Correctly solving near analogies elicited more positive waveforms at the N400 and during later relational processing. However, valid analogies elicited more positive signals during only later relational processing and not during the N400. These results suggest that semantic information impacts both early semantic and late relational comparison stages, while relational properties exert more influence in later stages of analogical reasoning. The degree of semantic similarity shared between knowledge domains demonstrated a potent effect throughout the time course of analogy that affected not only semantic access, but also the mapping of relational structures.

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.

Kopicky L, Pople B and **Dekhne N** (2019). "Feasibility of breast conserving therapy (BCT) in early stage breast cancer patients (ESBC) with cosmetic augmentation." *Annals of Surgical Oncology* 26: S94-S94.

[Full Text](#)

Department of Surgery

Kopicky L, Pople B, Karabon P, **Danko M** and **Dekhne N** (2019). "Trends in axillary management of breast cancer patients with 1 to 3-positive nodes undergoing mastectomy: A NCDB analysis." *Annals of Surgical Oncology* 26: S76-S76.

[Full Text](#)

Department of Surgery

OUWB Medical Student Author

Koreckij TD, Gandhi SD and **Park DK** (2019). "Cervical disk arthroplasty." JAAOS - 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: 1-3.

[Full Text](#)

OUWB Medical Student Author

Department of Ophthalmology

Kuang SY (2019). "A broader outlook to reduce pre-exam stress." Medical Teacher: 1-2.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Stress, depression, and job burnout are plaguing the medical field. These issues have many causes, one of which is a stigma or the fear of being stigmatized that leads the sufferer to deny the problem or delay seeking help. In this article, I will share a recent story of how a mind adjustment from a negative view of the past failure to a broader outlook quickly and effectively reduced the pre-exam stress of a student in a class I am teaching.

LaBan MM (2019). "Predatory open-access medical publishers "Caveat Emptor"." American Journal of Physical Medicine & Rehabilitation 98(2): e13-e14.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Lauter CB, Aneese AM, Rodriguez FF and Eilender L (2019). "Severe CD4 lymphocytopenia in patients with multiple sclerosis treated with fingolimod." Journal of Allergy and Clinical Immunology 143(2): AB111-AB111.

[Full Text](#)

Department of Internal Medicine

OUWB Medical Student Author

Le A, **Amin M** and **Cappell MS** (2019). "Case report of a proposed, novel, endoscopic "Whitehead Pimple" sign of ectopic esophageal sebaceous glands based on their mimicking the dermatologic and histopathologic characteristics of cutaneous whitehead pimples/closed comedones." Digestive Diseases and Sciences: 1-5.

[Full Text](#)

Department of Internal Medicine

Department of Pathology

Lee S-E, Sung JM, Andreini D, Budoff MJ, Cademartiri F, **Chinnaiyan K**, Choi JH, Chun EJ, Conte E, Gottlieb I, Hadamitzky M, Kim YJ, Kumar A, Lee BK, Leipsic JA, Maffei E, Marques H, Pontone G, Raff G, Shin S, Stone PH, Samady H, Virmani R, Narula J, Berman DS, Shaw LJ, Bax JJ, Lin FY, Min JK and Chang H-J (2019). "Differential association between the progression of coronary artery calcium score and coronary plaque volume progression according to

statins: the Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging (PARADIGM) study." [European Heart Journal - Cardiovascular Imaging](#): 1-8.

[Full Text](#)

Department of Internal Medicine

Coronary artery calcium score (CACs) is a strong predictor of major adverse cardiac events (MACE). Conversely, statins, which markedly reduce MACE risk, increase CACS. We explored whether CACS progression represents compositional plaque volume (PV) progression differently according to statin use. From a prospective multinational registry of consecutive patients (n = 2252) who underwent serial coronary computed tomography angiography (CCTA) at a ≥ 2 -year interval, 654 patients (61 \pm 10 years, 56% men, inter-scan interval 3.9 \pm 1.5 years) with information regarding the use of statins and having a serial CACS were included. Patients were divided into non-statin (n = 246) and statin-taking (n = 408) groups. Coronary PVs (total, calcified, and non-calcified; sum of fibrous, fibro-fatty, and lipid-rich) were quantitatively analysed, and CACS was measured from both CCTAs. Multivariate linear regression models were constructed for both statin-taking and non-statin group to assess the association between compositional PV change and change in CACS. In multivariate linear regression analysis, in the non-statin group, CACS increase was positively associated with both non-calcified ($\beta = 0.369$, $P = 0.004$) and calcified PV increase ($\beta = 1.579$, $P < 0.001$). However, in the statin-taking group, CACS increase was positively associated with calcified PV change ($\beta = 0.756$, $P < 0.001$) but was negatively associated with non-calcified PV change ($\beta = -0.194$, $P = 0.026$). In the non-statin group, CACS progression indicates the progression of both non-calcified and calcified PV progression. However, under the effect of statins, CACS progression indicates only calcified PV progression, but not non-calcified PV progression. Thus, the result of serial CACS should be differently interpreted according to the use of statins.

Liu J, Murray AM, Mankus EB, Ireland KE, Acosta OM and Ramsey PS (2019). "Adjuvant use of rifampin for refractory intrahepatic cholestasis of pregnancy reply." [Obstetrics and Gynecology](#) 133(2): 385-385.

[Full Text](#)

Department of Obstetrics and Gynecology

Logan JW, Allred EN, Msall ME, Joseph RM, Michael O'Shea TT, Heeren T, Leviton A, Kuban KCK, Ware J, Coster T, Henson B, Wilson R, McGhee K, Lee P, Asgarian A, Sadhwani A, Perrin E, Neger E, Mattern K, Walkowiak J, Barron S, Frazier J, Venuti L, Powers B, Foley A, Dessureau B, Wood M, Damon-Minow J, Ehrenkranz R, Benjamin J, Romano E, Tsatsanis K, Chawarska K, Kim S, Dieterich S, Bearrs K, O'Shea TM, Peters N, Brown P, Anusinha E, Waldrep E, Friedman J, Hounshell G, Allred D, Engelke SC, Darden-Saad N, Stainback G, Warner D, Wereszczak J, Bernhardt J, McKeeman J, Meyer E, Pastyrnak S, Burdo-Hartman W, Rathbun J, Nota S, Crumb T, Lenski M, Weiland D, Lloyd M, Hunter S, Msall M, Ramoskaite R, Wiggins S, Washington K, Martin R, Prendergast B, Scott M, **Klarr J**, Kring B, DeRidder J, Vogt K and for the ESI (2019). "Neurocognitive function of 10-year-old multiples born less than 28 weeks of gestational age." [Journal of Perinatology](#) 39(2): 237-247.

[Request Form](#)

Department of Pediatrics

Few studies have examined the relationship between birth plurality and neurocognitive function among children born extremely preterm.

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." [Journal of Arthroplasty](#). ePub Ahead of Print.

[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.

Luehmann NC, Staubach ME, **Akay B, Collier PJ, Han RE**, Riggs TW and **Novotny NM** (2019). "Benefits of a family-centered approach to pediatric induction of anesthesia." Journal of Pediatric Surgery 54(1): 189-193.

[Full Text](#)

Department of Surgery

Department of Anesthesiology

Background/Purpose: We initiated a pediatric surgical program including a caregiver for the induction of anesthesia. We measured preoperative midazolam administration, preoperative time, induction time, and program satisfaction. Methods: Families with children undergoing surgery during the study period were included. Preoperative midazolam administration, preoperative time, and induction time were compared between participants and controls. Satisfaction surveys were given to participating caregivers and staff. Results: The rate of preoperative midazolam use decreased from 41% (392/964) to 13% (16/118) among participants vs controls ($p < 0.0001$). After linear regression analysis, this difference persisted as an adjusted odds ratio of 0.29 (95% CI = 0.16–0.52). Preoperative and induction times (minutes) were similar between groups (76.2 vs 82.2, 13.8 vs 16.2, $p =$ nonsignificant). Based on 5-point Likert surveys, the program was rated as "beneficial" or "very beneficial" to the patient by caregivers (99.2%) and staff (77.5%). Caregivers stated it "reduced" or "greatly reduced" anxiety for them (87.1%) and their child (93.2%). Conclusions: Opponents of similar programs suggest familial presence slows care and is disruptive. Our program decreased utilization of preoperative anxiolytics with no effect on operating room efficiency. Both hospital staff and participants felt the program was beneficial to the patient. Perceived caregiver and child anxiety was reduced. Type of study Treatment study. Level of evidence Level III.

Majdalany BS, Kobeissi SS, Goodson CI, **Kanaan CN**, Gilbert LN and Khaja MS (2019). "Transradial interventions." Journal of Radiology Nursing 38(1): 17-20.

[Full Text](#)

OUWB Medical Student Author

Mando R, **Abbas AE, Gallagher M, Hanzel GS, Shannon F** and Abdulla RK (2019). "Aortic valve calcium score and aortic valve gradient." Journal of the American College of Cardiology 73(9): 1991-1991.

[Full Text](#)

Department of Internal Medicine

Department of Surgery

Mando R, **Abbas AE, Gallagher M, Safian RD, Hanzel GS**, Pibarot P and **Shannon F** (2019). "ECHO overestimates trans-aortic gradients immediately post TAVR: A pressure recovery phenomenon in a simultaneous CATH and ECHO study." Journal of the American College of Cardiology 73(9): 1251-1251.

[Full Text](#)

Department of Internal Medicine

Department of Surgery

Mando R, Sigua-Arce P, **Spencer L** and **Halalau A** (2019). "Slippery stents: A case report and review of the literature describing patients with May-Thurner Syndrome that experienced stent migration." Case Reports in Vascular Medicine 2019: 7606727-7606727.

[Full Text](#)

OUWB Medical Student Author

Department of Internal Medicine

Endovascular stent placement is an effective treatment for relieving chronic venous obstruction in patients with May-Thurner Syndrome (MTS) with or without the presence of thrombotic lesions. Stent migration is a rare but potentially life-threatening complication of endovascular stenting. Herein, we describe a case of stent migration from the left common iliac vein into the right heart, requiring open-heart surgery. We also completed a literature review of MTS patients with stent migration in hopes of raising awareness of this rare and life-threatening complication.

Mauck MC, Hu J, Sefton C, **Swor RA**, Peak DA, Jones JS, Rathlev NK, Lee DC, Domeier RM, Hendry PL and McLean SA (2019). "Obesity increases the risk of chronic pain development after motor vehicle collision." *Pain* 160(3): 670-675.

[Full Text](#)

Department of Emergency Medicine

Obesity has been found to increase the risk of musculoskeletal pain (MSP) in other settings, but to our knowledge, the influence of increased body mass index on pain outcomes after common trauma exposures such as motor vehicle collision (MVC) has not been assessed. In addition, obesity results in biomechanical changes, as well as physiologic changes including reduced hypothalamic pituitary adrenal axis negative feedback inhibition, but mechanisms by which obesity may result in worse post-traumatic outcomes remain poorly understood. In this study, we evaluated the influence of body mass index on axial and overall MSP severity (0-10 numeric rating scale) 6 weeks, 6 months, and 1 year after MVC among 917 European Americans who presented to the emergency department for initial evaluation. After adjusting for an array of sociodemographic factors, obesity (particularly morbid obesity) was an independent risk factor for worse MSP after MVC (eg, RR 1.41 [95% CI 1.11, 1.80] for moderate or severe MSP 6 months after MVC among morbidly obese vs normal weight MVC survivors). Interestingly, substantial effect modification was observed between obesity risk and a genetic variant known to reduce hypothalamic pituitary adrenal axis negative feedback inhibition (FKBP5 rs9380526). (eg, 41% vs 16% increased risk of moderate or severe MSP at 6 months among obese individuals with and without the risk allele.) Further studies are needed to elucidate mechanisms underlying chronic pain development in obese trauma survivors and to develop interventions that will reduce chronic pain severity among this common, at-risk group.

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*. ePub Ahead of Print.

[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.

Mir A, Guys N, **Arianpour K**, Svider PF, Rayess H, Zuliani G, Raza SN and Lin H (2019). "Negative pressure wound therapy in the head and neck: An evidence-based approach." *Laryngoscope* 129(3): 671-683.

[Full Text](#)

OUWB Medical Student Author

Objective: To perform an evidence-based review with recommendations that evaluates the indications and utility of negative pressure wound therapy (NPWT) in the head and neck. **Methods:** The authors searched the PubMed, Medline, Embase, Web of Science, and Cochrane Library databases for relevant literature. The primary outcome was successful intended use of NPWT, be it for granulation tissue formation, infection control, or complete wound closure. Patient demographics, etiology, and other clinical characteristics were explored. Meta-analysis of observational studies was used to examine response rates and wound sizes. **Results:** Fifty-seven articles encompassing 522 patients were included. The most common etiologies reported included: neoplasm (343 patients [65.7%]), oro-/pharyngocutaneous fistula (9.8%), infection (10.5%), and trauma (9.6%). The majority of wounds treated were in the neck (61.6%). Potential risk factors that may compromise wound healing were noted in 217 of 522 patients (41.6%). Of these 217 patients, 135 had properly documented risk factors, with the most common being prior irradiation (63%). The overall mean response across studies was 85.7% (95% confidence interval: 0.806–0.896, $P < 0.001$, $I^2 = 0\%$). **Conclusion:** Negative pressure wound therapy is useful for the management of head and neck wounds and should be considered for patients in whom wound healing is progressing insufficiently, including those with a history of head and neck cancer, oro-/pharyngocutaneous fistula, and trauma. Randomized controlled trials further comparing NPWT versus other modalities may be invaluable in further delineating its appropriate role.

Patibandla M, Ding D, Kano H, Starke R, Lee J, Mathieu, D, Whitehall J, Pierce J, Huang P, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Almodovar L, **Grills, I**, Silva D, Abbassy M, Missios S, Barnett G, Lunsford LD and Sheehan J (2019). "Effect of treatment period on outcomes after stereotactic radiosurgery for brain arteriovenous malformations: an international multicenter study." *Journal of Neurosurgery JNS* 130(2): 579-588.

[Request Form](#)

Department of Radiation Oncology

Objective: The role of and technique for stereotactic radiosurgery (SRS) in the management of arteriovenous malformations (AVMs) have evolved over the past four decades. The aim of this multicenter, retrospective cohort study was to compare the SRS outcomes of AVMs treated during different time periods. **Methods:** The authors selected patients with AVMs who underwent single-session SRS at 8 different centers from 1988 to 2014 with follow-up ≥ 6 months. The SRS eras were categorized as early (1988–2000) or modern (2001–2014). Statistical analyses were performed to compare the baseline characteristics and outcomes of the early versus modern SRS eras. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes (RICs). **Results:** The study cohort comprised 2248 patients with AVMs, including 1584 in the early and 664 in the modern SRS eras. AVMs in the early SRS era were significantly smaller ($p < 0.001$ for maximum diameter and volume), and they were treated with a significantly higher radiosurgical margin dose ($p < 0.001$). The obliteration rate was significantly higher in the early SRS era (65% vs 51%, $p < 0.001$), and earlier SRS treatment period was an independent predictor of obliteration in the multivariate analysis ($p < 0.001$). The rates of post-SRS hemorrhage and radiological, symptomatic, and permanent RICs were not significantly different between the two groups. Favorable outcome was achieved in a significantly higher proportion of patients in the early SRS era (61% vs 45%, $p < 0.001$), but the earlier SRS era was not statistically significant in the multivariate analysis ($p = 0.470$) with favorable outcome. **Conclusions:** Despite considerable advances in SRS technology, refinement of AVM selection, and contemporary multimodality AVM treatment, the study failed to observe substantial improvements in SRS favorable outcomes or obliteration for patients with AVMs over time. Differences in baseline AVM characteristics and SRS treatment parameters may partially account for the significantly lower obliteration rates in the modern SRS era. However, improvements in patient selection and dose planning are necessary to optimize the utility of SRS in the contemporary management of AVMs.

Murray S, Kishbaugh JC, Hayek LAC, Kutinsky I, Dennis PM, **Devlin W**, Hope KL, Danforth MD and Murphy HW (2019). "Diagnosing cardiovascular disease in western lowland gorillas (*Gorilla gorilla gorilla*) with brain natriuretic peptide." *PLOS ONE* 14(3).

[Full Text](#)

Department of Internal Medicine

Cardiovascular disease is a leading cause of death in zoo-housed great apes, accounting for 41% of adult gorilla death in North American zoological institutions. Obtaining a timely and accurate diagnosis of cardiovascular disease in gorillas is challenging, relying on echocardiography which generally requires anesthetic medications that may confound findings and can cause severe side effects in cardiovascularly compromised animals. The measurement of brain natriuretic peptide (BNP) has emerged as a modality of interest in the diagnosis, prognosis and treatment of human patients with heart failure. This study evaluated records for 116 zoo-housed gorillas to determine relationships of BNP with cardiovascular disease. Elevations of BNP levels correlated with the presence of visible echocardiographic abnormalities, as well as reported clinical signs in affected gorillas. Levels of BNP greater 150 pb/mL should alert the clinician to the presence of myocardial strain and volume overload, warranting medical evaluation and intervention.

Myziuk N, **Guerrero T**, **Sakthivel G**, Solis D, **Nair G**, Guerra R and Castillo E (2019). "Pulmonary blood mass dynamics on 4DCT during tidal breathing." *Physics in Medicine & Biology* 64(4): 045014.

[Full Text](#)

OUWB Medical Student Author

Department of Internal Medicine

Department of Radiation Oncology

We previously reported that apparent lung mass varies across the phases of 4D computed tomography (4DCT) images. We hypothesize that these variations correspond to the physiologic changes in pulmonary perfusion induced during normal tidal breathing, and should therefore be present in every breathing patient. In this study, we characterize and quantify the respiratory induced variation in pulmonary blood mass (triangle upPBM) on 89 patients treated with stereotactic body radiotherapy. triangle upPBM was computed from the treatment planning helical 4DCT images of each patient. Conversion from Hounsfield Units (HU) to density and mass per voxel was made using the density calibration curve, applied to the lung parenchyma volume within each phase. A difference in the lung mass with breathing was found for all cases, as was a substantial individual variation in lung volume. We found that the triangle upPBM increased during inhalation, and decreased during exhalation. A significant correlation between the individual triangle upPBM and tidal volume was observed; triangle upPBM increased with tidal volume. We further evaluated the anatomic distribution of triangle upPBM variation comparing the central versus peripheral lung, cranial versus caudal, dependent versus non-dependent lung. Our observations regarding spatial distribution of the triangle upPBM agree with previously reported differences among similar regions for the supine patient. These results show that a variation in pulmonary mass during respiration is apparent on 4DCT and suggest that these variations reflect respiratory induced changes in the pulmonary perfusion. Therefore, the 4DCT derived respiratory induced triangle upPBM signal can provide further insight into the pulmonary circulation and advance the overall understanding and diagnosis of human health and disease.

Nakahama H, Jankowski M, **Dixon SR** and **Abbas AE** (2019). "Long-term outcome of brachytherapy treatment for coronary in-stent restenosis: Ten-year follow-up." *Catheterization and Cardiovascular Interventions* 93(4): E211-E216.

[Full Text](#)

OUWB Medical Student Author

Department of Internal Medicine

Objectives: The objective of this study was to determine the long-term major adverse cardiac events (MACE) in patients treated with intracoronary brachytherapy (ICBT) for coronary in-stent restenosis (ISR). **Background:** ICBT was commonly used to treat coronary ISR prior to the availability of drug-eluting stents (DES). The long-term outcomes of ICBT for ISR remain unknown. **Methods:** Six hundred and eighty consecutive patients who underwent ICBT treated for ISR between September 1998 and April 2005 were included in the study. Clinical and angiographic data were collected and the long-term MACE were measured for all-cause death, myocardial infarction (MI), and target vessel revascularization (TVR) at 10-year follow-up. **Results:** Patients were 63 ± 11 years old (66% male). The majority of patients were treated with a bare metal stent 670/680 (99%) prior to ICBT. Significant baseline clinical findings include high incidence of smokers 479/680 (70%), hyperlipidemia 638/680 (94%), and multivessel disease 526/680 (77%). The majority of target lesions were diffuse 407/680 (60%), and either in the left anterior descending 258/680 (38%) or

right coronary artery 215/680 (32%). At 10-year follow-up, the rate of death was 25%, MI was 22.4%, and TVR was 48%. Conclusion: MACE at 10-year follow-up following ICBT for ISR indicates steady rate of death and MI and declining rate of TVR after 5 years.

Navin MC* and **Wasserman JA** (2019). "Capacity for preferences and pediatric assent implications for pediatric practice." Hastings Center Report 49(1): 43-51.

[Full Text](#)

Department of Foundational Medical Studies (OU)

**Oakland University College of Arts and Sciences - Department of Philosophy*

In the past thirty to forty years, clinicians and bioethicists have expanded the scope for children's participation in decision-making about their medical care, often under the banner of "pediatric assent." The success of this movement was signaled perhaps most strongly by the creation of American Academy of Pediatrics guidance on pediatric assent in 1995. We agree with the AAP that both the best interests of the child patient and the need to respect the child patient are reasons to take seriously children's treatment preferences. However, we argue that the AAP could provide a stronger and more stable ethical foundation for pediatric assent. Current policy documents invoke a conception of respect that is grounded in autonomy and cannot apply in most cases of pediatric assent. We argue that the mere fact that children have treatment preferences is a reason to support pediatric assent. We defend this claim by focusing on the importance of what we have called "capacity for preferences." The notion of capacity for preferences underscores that the moral value of a patient's preferences is not reducible to considerations of either autonomy or best interests.

Navin MC*, **Wasserman JA**, **Ahmad M** and Bies S (2019). "Vaccine education, reasons for refusal, and vaccination behavior." American Journal of Preventive Medicine 56(3): 359-367.

[Full Text](#)

Department of Foundational Medical Studies (OU)

OUWB Medical Student Author

**Oakland University College of Arts and Sciences - Department of Philosophy*

Introduction: Little is known about associations between the reasons parents refuse or delay vaccines for their children, their responsiveness to vaccine counseling, and their children's vaccination status at various ages. Since 2015, Michigan has required parents to attend education sessions at local health departments to receive nonmedical exemptions. This requirement provides an opportunity to study otherwise opaque aspects of vaccine refusal. Methods: In 2017 and 2018, researchers analyzed a combined data set that included electronic medical records (n=4,098) generated by one Michigan health department during 2015 immunization education sessions, and immunization records from an August 2016 report of the Michigan Care Improvement Registry immunization registry. Analyses employed difference of proportions and ANOVAs to explore group differences in vaccination behaviors after education sessions and on-time vaccination status at various ages. Results: Children whose parents stated a commitment to an alternative schedule at the education session subsequently received a vaccine their parents had refused at a much higher rate (39.2%) than did children whose parents refused for reasons of religion (4.4%), concerns about the risks of vaccines (8.1%), or beliefs that vaccines provide little benefit (10.5%). Conclusions: Different reasons for refusal are associated with different patterns of vaccination behavior. Furthermore, results suggest that education sessions may overcome vaccine refusal in some cases, and that distinct refusal reasons mark real differences in parental motivations regarding vaccination choices. These differences in parental motivations may indicate the existence of different sites for potential pro-vaccination interventions.

Nolan DA, **Chen B**, Michon AM, Salatka E and **Arndt D** (2019). "A Rasmussen encephalitis, autoimmune encephalitis, and mitochondrial disease mimicker: Expanding the DNM1L-associated intractable epilepsy and encephalopathy phenotype." Epileptic Disorders 21(1): 112-116.

[Full Text](#)

Department of Pediatrics

OUWB Medical Student Author

Dynammin-1-like protein (DNM1L) gene variants have been linked to childhood refractory epilepsy, developmental delay, encephalopathy, microcephaly, and progressive diffuse cerebral atrophy. However, only a few cases have been reported in the literature and there is still a limited amount of information about

the symptomatology and pathophysiology associated with pathogenic variants of DNM1L. We report a 10-year-old girl with a one-year history of mild learning disorder and absence seizures who presented with new-onset focal status epilepticus which progressed to severe encephalopathy and asymmetric hemispheric cerebral atrophy. Differential diagnosis included mitochondrial disease, Rasmussen's encephalitis, and autoimmune encephalitis. Disease progressed from one hemisphere to the other despite anti-seizure medications, hemispherectomy, vagus nerve stimulator, ketogenic diet, and immunomodulators. Continued cerebral atrophy and refractory seizures evolved until death four years after initial presentation. Post-mortem whole-exome sequencing revealed a pathogenic DNM1L variant. This paper presents a novel case of adolescent-onset DNM1L-related intractable epilepsy and encephalopathy.

Nudleman E, Muftuoglu IK, Gaber R, Robinson J, **Drenser K**, Capone A and **Trese M** (2019). "Reply." *Ophthalmology* 126(1): e4-e5.

[Full Text](#)

Department of Ophthalmology

Opolski MP, Gransar H, Lu Y, Achenbach S, Al-Mallah MH, Andreini D, Bax JJ, Berman DS, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Cury RC, DeLago A, Feuchtner GM, Hadamitzky M, Hausleiter J, Kaufmann PA, Kim YJ, Leipsic JA, Maffei EC, Marques H, Pontone G, Raff G, Rubinshtein R, Shaw LJ, Villines TC, Gomez M, Jones EC, Pena JM, Min JK and Lin FY (2019). "Prognostic value of chronic total occlusions detected on coronary computed tomographic angiography." *Heart* 105(3): 196-203.

[Request Form](#)

Department of Internal Medicine

Objective: Data describing clinical relevance of chronic total occlusion (CTO) identified by coronary CT angiography (CCTA) have not been reported to date. We investigated the prognosis of CTO on CCTA. Methods: We identified 22 828 patients without prior known coronary artery disease (CAD), who were followed for a median of 26 months. Based on CCTA, coronary lesions were graded as normal (no atherosclerosis), non-obstructive (1%-49%), moderate-to-severe (50%-99%) or totally occluded (100%). All-cause mortality, and major adverse cardiac events defined as mortality, non-fatal myocardial infarction and late coronary revascularisation (≥ 90 days after CCTA) were assessed. Results: The distribution of patients with normal coronaries, non-obstructive CAD, moderate-to-severe CAD and CTO was 10 034 (44%), 7965 (34.9%), 4598 (20.1%) and 231 (1%), respectively. The mortality rate per 1000 person-years of CTO patients was non-significantly different from patients with moderate-to-severe CAD (22.95; 95% CI 12.71 to 41.45 vs 14.46; 95% CI 12.34 to 16.94; $p=0.163$), and significantly higher than of those with normal coronaries and non-obstructive CAD ($p<0.001$ for both). Among 14 382 individuals with follow-up for the composite end point, patients with CTO had a higher rate of events than those with moderate-to-severe CAD (106.56; 95% CI 76.51 to 148.42 vs 65.45; 95% CI 58.01 to 73.84, $p=0.009$). This difference was primarily driven by an increase in late revascularisations in CTO patients (27 of 35 events). After multivariable adjustment, compared with individuals with normal coronaries, the presence of CTO conferred the highest risk for adverse cardiac events (14.54; 95% CI 9.11 to 23.20, $p<0.001$). Conclusions: The detection of CTO on non-invasive CCTA is associated with increased rate of late revascularisation but similar 2-year mortality as compared with moderate-to-severe CA

Osborne JD, **Luczak SB**, Acker WB and **Bicos J** (2019). "Patellofemoral joint contact pressures: Current concepts and use in patellar instability studies." *Orthopedics* 42(2): E172-E179.

[Request Form](#)

OUWB Medical Student Author

Department of Orthopedic Surgery

The patellofemoral joint is thought to be a common source for knee pain. Improper alignment and function of the patellofemoral joint can lead to abnormal contact pressures, which may explain patients' symptoms. In this review, the authors examine techniques for measuring patellofemoral joint contact pressures and summarize the relevant patellofemoral joint anatomy and contact pressures in normal knee kinematics. Finally, they discuss the results of studies investigating contact pressure changes in cases of patellar instability. This includes both reconstruction of the medial patellofemoral ligament and tibial tubercle osteotomy.

Ozcan A, **Kahale K** and **Nguyen D** (2019). "An 8-month-old girl with vesicular rash." Global Pediatric Health 6: 2333794X19838526-12333794X19838526.

[Full Text](#)

Department of Emergency Medicine

OUWB Medical Student Author

This is a case report of an 8-month-old girl who presented to the pediatric emergency department with vesicular rash and fever. She was diagnosed with eczema herpeticum (EH). EH is an acute, rapidly progressive rare dermatologic disease, and if it is not treated promptly, it can cause life-threatening complications. It often occurs in a patient with an underlying skin disorder, such as atopic dermatitis or other erosive dermatoses. Diagnosis is mainly made by clinical examination usually presented as many very similar shaped and sized eroded vesicles. It is important for clinicians to recognize the sign and symptoms of EH and have a high suspicion for patients with atopic dermatitis who present with rapidly disseminating blisters. Treatment is with oral or intravenous acyclovir. If the patient has widespread eruptions or systemic symptoms such as fever, malaise, and poor oral intake, the patient should be admitted for intravenous acyclovir.

Padmanabhan S, Waly MI, **Taranikanti V**, Guizani N, Ali A, Rahman MS, Al-Attabi Z, Al-Malky RN, Al-Maskari SNM, Al-Ruqaishi BRS, Dong JA and Deth RC (2019). "Folate/vitamin B12 supplementation combats oxidative stress-associated carcinogenesis in a rat model of colon cancer." Nutrition and Cancer-an International Journal 71(1): 100-110.

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Department of Foundational Medical Studies (OU)

Folate and vitamin B12 deficiency is associated with depletion of the major intracellular antioxidant glutathione, and oxidative stress is emerging as an etiological mechanism for colon cancer. Azoxymethane (AOM), a potent carcinogen, induces colon cancer in rats by causing pathophysiological changes and oxidative stress. We investigated the synergistic effect of folate and vitamin B12 supplementation against AOM-induced carcinogenesis and oxidative stress in rat colon. Adult male rats were distributed into four groups: 1) Basal diet only; 2) AOM injection (15 mg/kg once per week in weeks 5 and 6); 3) Folate and vitamin B12 supplemented diet; 4) Folate and B12 diet with AOM injection. After 16 weeks, rats were sacrificed, colon tissue dissected, indicators of oxidative stress were measured, and immunohistochemical and ultrastructural changes were evaluated. AOM-injected rats showed oxidative stress, evident by glutathione depletion, oxidation of cellular proteins, and DNA oxidative damage. AOM increased mucosal levels of antiapoptotic and proapoptotic proteins Bcl2 and Bax and caused ultrastructure changes in colonic cell organelles. Folate and vitamin B12 supplementation decreased the level of oxidative stress and ameliorated the cytotoxic effects of AOM. In this in vivo experimental model of colon cancer, folate and vitamin B12 supplementation combats carcinogen-induced oxidative stress.

Pe'er J and **Folberg R** (2019). "Conjunctival and corneal tumors: Melanoma," In Pe'er J, Singh AD and Damato BE (ed). Clinical Ophthalmic Oncology: Eyelid and Conjunctival Tumors. Cham: Springer International Publishing. pp: 197-207.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Conjunctival melanoma is a rare tumor. It is similar in its biological features and clinical behavior to cutaneous melanoma. It can arise from primary acquired melanosis (PAM) with atypia, conjunctival nevus, nevus accompanied by PAM with atypia, or de novo. Its incidence is higher in some parts of the world than others. This tumor is more common in middle-aged and older persons and in Caucasians. Recent evidence indicates that ultraviolet radiation may be an important etiological factor in the development of conjunctival melanoma. The tumor is usually bulbar but may involve any part of the conjunctiva. The cornea can also be involved. The definitive diagnosis of conjunctival melanoma is made by histological examination, often with the assistance of immunohistochemistry and molecular pathology. The primary treatment for conjunctival melanoma is complete surgical excision. Because of the high rate of local recurrence, surgical excision should always be combined with adjuvant therapy, such as cryotherapy, brachytherapy, topical chemotherapy, and/or immunotherapy. The 10-year, disease-related mortality is as high as 30%. The most important prognostic factors are tumor location, with non-bulbar tumors having a higher risk of metastasis; tumor thickness; treatment by tumor excision alone, without adjuvant therapy; pagetoid spread; presence of

epithelioid cells; lymphatic invasion; and high mitotic activity. Conjunctival melanomas can spread within the conjunctiva and may invade the eyelid, orbit, and sinuses. They can also metastasize to the regional lymph nodes and other parts of the body. Spread to regional lymph nodes is often detected before systemic metastasis, and therefore, some authorities advocate sentinel lymph node biopsy in patients with high-risk conjunctival melanoma.

Pe'er J and **Folberg R** (2019). "Conjunctival and corneal tumors: Primary acquired melanosis," In Pe'er J, Singh AD and Damato BE (ed). Clinical Ophthalmic Oncology: Eyelid and Conjunctival Tumors. Cham: Springer International Publishing. pp: 185-195.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Conjunctival primary acquired melanosis (PAM) appears clinically as a flat and variegated brown usually monocular lesion, ranging from golden brown to dark chocolate, which may involve any area of the conjunctiva. PAM occurs typically in adults and elderly. PAM may remain stable for long periods of time or may grow in size. A "waxing and waning" phenomenon is well known; thus, the borders of the lesion often cannot be identified. The lesion designed as PAM clinically may feature no atypia histologically (PAM without atypia), or one detects melanocytic atypia histologically (PAM with atypia). PAM without atypia does not progress to melanoma, whereas PAM with atypia should be considered a melanoma precursor. Recently, the term "conjunctival melanocytic intraepithelial (C-MIN) with or without atypia" was suggested for histological use. There are no clinical criteria by which ophthalmologists can anticipate the histological diagnosis. Therefore, when PAM is suspected, the lesion should be biopsied. A small lesion should be completely excised, while in widespread lesions, incisional biopsies should be performed in various sites of the affected conjunctiva. In addition to surgical excision, cryotherapy may be performed, and in PAM with atypia, topical mitomycin C chemotherapy and in small series also topical interferon α -2b were found to be effective.

Pe'er J and **Folberg R** (2019). "Eyelid tumors: Cutaneous melanoma," In Pe'er J, Singh AD and Damato BE (ed). Clinical Ophthalmic Oncology: Eyelid and Conjunctival Tumors. Cham: Springer International Publishing. pp: 63-69.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Cutaneous melanoma of the eyelid is a rare tumor, which occurs mostly in adults and the elderly. It may occur in the eyelid margin, involving the palpebral conjunctiva. In such cases, conjunctival melanoma as the primary site should be ruled out. Cutaneous melanoma in the eyelid is histologically similar to skin melanoma in other locations. Complete surgical excision of the melanoma with free surgical margins is the treatment of choice. However, the ideal width of the surgical margins in the eyelid melanoma is a matter of controversy and is limited because of difficulties in the eyelid reconstruction as compared to cutaneous melanoma in other sites. Adjuvant treatment such as immunotherapy is advocated in advanced and metastatic cases. Sentinel lymph node biopsy has been used in some centers.

Perez D, **Fullmer JM** and Naous R (2019). "A rare case of TLE1-positive sclerosing epithelioid fibrosarcoma expanding the differential diagnosis of TLE1-positive tumors: a case report." AME Case Reports 3: 6-6.

[Full Text](#)

Department of Pathology

Transducin-like enhancer of split 1 (TLE1) is a transcription factor known for its strong overexpression and immunopositivity in synovial sarcoma. Several studies have revealed that its immunopositivity is not always specific to synovial sarcoma, with several cases showing positivity in peripheral nerve sheath tumors and solitary fibrous tumors. Occasional weak staining for TLE1 has also been described in clear cell sarcoma, high-grade chondrosarcoma, Ewing sarcoma, rhabdomyosarcoma, GIST, myxofibrosarcoma, and leiomyosarcoma. Here we present the first unique case of sclerosing epithelioid fibrosarcoma with strong, diffuse TLE1 positivity, resulting in a new consideration for the differential diagnosis of TLE1 positivity.

Perez-Cruet M, Beeravolu N, McKee C, **Brougham J**, Khan I, Bakshi S and Chaudhry GR (2019). "Potential of human nucleus pulposus-like cells derived from umbilical cord to treat degenerative disc disease." Neurosurgery 84(1): 272-283.

[Full Text](#)

Department of Neurosurgery
OUWB Medical Student Author

Background: Degenerative disc disease (DDD) is a common spinal disorder that manifests with neck and lower back pain caused by the degeneration of intervertebral discs (IVDs). Currently, there is no treatment to cure this debilitating ailment. Objective: To investigate the potential of nucleus pulposus (NP)-like cells (NPCs) derived from human umbilical cord mesenchymal stem cells (MSCs) to restore degenerated IVDs using a rabbit DDD model. Methods: NPCs differentiated from MSCs were characterized using quantitative real-time reverse transcription polymerase chain reaction and immunocytochemical analysis. MSCs and NPCs were labeled with fluorescent dye, PKH26, and transplanted into degenerated IVDs of a rabbit model of DDD (n = 9 each). Magnetic resonance imaging of the IVDs was performed before and after IVD degeneration, and following cell transplantation. IVDs were extracted 8 wk post-transplantation and analyzed by various biochemical, immunohistological, and molecular techniques. Results: NPC derivatives of MSCs expressed known NP-specific genes, SOX9, ACAN, COL2, FOXF1, and KRT19. Transplanted cells survived, dispersed, and integrated into the degenerated IVDs. IVDs augmented with NPCs showed significant improvement in the histology, cellularity, sulfated glycosaminoglycan and water contents of the NP. In addition, expression of human genes, SOX9, ACAN, COL2, FOXF1, KRT19, PAX6, CA12, and COMP, as well as proteins, SOX9, ACAN, COL2, and FOXF1, suggest NP biosynthesis due to transplantation of NPCs. Based on these results, a molecular mechanism for NP regeneration was proposed. Conclusion: The findings of this study demonstrating feasibility and efficacy of NPCs to regenerate NP should spur interest for clinical studies to treat DDD using cell therapy.

Pinder-Arabbpour A, Jones B, Castillo R, Castillo E, **Guerrero T**, Goodman K, Schefter T, Kwak J, Miften M and Vinogradskiy Y (2019). "Characterizing spatial lung function for esophageal cancer patients undergoing radiation therapy." *International Journal of Radiation Oncology*Biophysics* 103(3): 738-746.

[Full Text](#)

Department of Radiation Oncology

Purpose: Patients with esophageal cancer treated with chemoradiation and surgery can develop pulmonary complications. Four-dimensional computed tomography–ventilation (4DCT-ventilation) is a developing imaging modality that uses 4DCT data to calculate lung ventilation. 4DCT-ventilation has been studied in the lung-cancer population but has yet to be extended to patients with esophageal cancer. The purpose of this study was to characterize 4DCT-ventilation–based spatial lung function for patients with esophageal cancer. Methods and Materials: Thirty-five patients with esophageal cancer who underwent 4DCT scans participated in the study. A 4DCT-ventilation map was calculated using the patient's 4DCT imaging and a density change–based algorithm. To assess each patient's ventilation profile, radiologist interpretations and quantitative metrics were used. A radiologist interpreted the 4DCT-ventilation images for lobar-based defects and gravity-dependent atelectasis. The 4DCT-ventilation maps were reduced to single metrics intended to reflect the degree of ventilation heterogeneity. The quantitative metrics included the coefficient of variation and metrics based on the ventilation in each lung and each lung third (superior-inferior ventilation [Vent-SI] and anteroposterior ventilation). The functional profile of patients with esophageal cancer was characterized and compared (using the Mann-Whitney test) for cohorts based on thoracic comorbidities and radiologist-identified defects. Results: Radiologist observations revealed that 26% of patients with esophageal cancer had lobar-based defects and 46% had gravity-dependent atelectasis. The baseline values were 0.52 ± 0.20 (mean \pm SD), 11.2 ± 12.5 , and 72.5 ± 14.6 for the coefficient of variation, the ventilation ratio of right to left lung, and Vent-SI metrics, respectively. The Vent-SI values were significantly different between patients with and without thoracic comorbidities ($P = .05$), and the anteroposterior ventilation metric was able to delineate patients with and without gravity-dependent atelectasis ($P < .01$). Conclusions: Our data demonstrate that approximately 30% of patients with esophageal cancer have significant ventilation heterogeneities. The current work uses radiologist observations and quantitative metrics to characterize 4DCT ventilation–based lung function for patients with esophageal cancer and presents data that can be used for future applications of 4DCT-ventilation to reduce thoracic toxicity for patients with esophageal cancer.

Poe C, Youngblood C, Hodge K and **Kemp K** (2019). "Treatment of established TH2 cells with 4 μ 8c, an inhibitor of IRE1 α , blocks IL-5 but not IL-4 secretion." *BMC Immunology* 20(1): 3-3.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Background: T cell activation induces ER stress and upregulates Inositol Requiring Enzyme 1 alpha (IRE1 α), an activator of the unfolded protein response (UPR) pathway. Inhibition of IRE1 α RNase activity in activated CD4(+) splenocytes from naïve mice, via treatment of the cells with the commercially available drug 4 μ 8c upon activation, results in the reduction of the secretion of proteins IL-5, IL-4, and IL-13. Prior to this work, it was unknown if 4 μ 8c could inhibit TH2 cytokines in established TH2 cells, cells that are crucial in promoting disease in severe asthma. Results: Treatment of a mouse T helper (TH)2 cell line and differentiated human TH2 cells with 4 μ 8c resulted in inhibition of IL-5, but not IL-4, as measured by ELISA. The reduced cytokine expression was not due to differences in mRNA stability or mRNA levels; it appears to be due to a defect in secretion, as the cells produce cytokines IL-5 as measured by flow cytometry and western blot. Conclusion: These data suggest that the inhibition of IL-5 was due to post-translational processes. IL-5 promotes chronic, inflammatory asthma, and 4 μ 8c blocks its expression in T cells in vitro. Future studies will determine if 4 μ 8c treatment can ameliorate the effects of the cytokine IL-5 in a disease model.

Pollock KJ, Casiano RR, **Folbe AJ**, Golfinos JG and Snyderman CH (2019). "Coding and reimbursement for endoscopic endonasal surgery of the skull base." *Journal of Neurological Surgery Part B-Skull Base* 80: S247-S254.

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Department of Surgery

The American Medical Association's (AMA) Current Procedural Terminology (CPT) codes provide the national standard for reporting medical services and procedures performed by physicians. As such, these codes must be used to report services to third party payers and are the basis for reimbursement. Unfortunately, the codes do not always sufficiently describe the procedure, or may not even exist for the procedure, performed. Endoscopic endonasal surgery of the skull base (EESSB) is now well established as an alternate surgical technique/approach for the treatment of skull base pathology but is not universally practiced at all institutions that perform skull base surgery. As a result, CPT codes do not exist for most EESSB procedures. Typically, EESSB is performed jointly by the otolaryngologist-head and neck surgeon (ENT) and neurosurgeon (NS). Therefore, coding can be complicated and third-party payers are often not familiar with the services provided, and reimbursement issues such as delayed or reduced payments result. As the number of trained surgeons continues to expand, there is diversity of opinion and practice regarding optimal CPT coding. There is a recognized knowledge gap regarding current coding options for EESSB. The purpose of this white paper is to provide surgeons, coders, billers, and third party payers a comprehensive understanding of current coding and reimbursement implications for EESSB procedures. Payer medical directors and associated professionals will find this paper a valuable source of information about EESSB to facilitate medical policy development and appropriate adjudication and payment of claims. This white paper is a collaboration of KarenZupko & Associates, Inc. (KZA) and the North American Skull Base Society, with representation from NS and ENT. As such, it provides *guidelines* for coding but is not intended to represent the official recommendations of physician specialty societies, governmental regulatory agencies, insurance providers, or healthcare consultants. Areas of controversy are noted with acknowledgement of divergent opinions. The NASBS and KZA assume no liability for any fraudulent claims or penalties resulting from coding practices as represented here.

Prabhu AH, Kant S, Kesarwani P, Ahmed K, Forsyth P, Nakano I and **Chinnaiyan P** (2019). "Integrative cross-platform analyses identify enhanced heterotrophy as a metabolic hallmark in glioblastoma." *Neuro-Oncology* 21(3): 337-347.

[Full Text](#)

Department of Pediatrics

Department of Radiation Oncology

Although considerable progress has been made in understanding molecular alterations driving gliomagenesis, the diverse metabolic programs contributing to the aggressive phenotype of glioblastoma remain unclear. The aim of this study was to define and provide molecular context to metabolic reprogramming driving gliomagenesis. Integrative cross-platform analyses coupling global metabolomic profiling with genomics in patient-derived glioma (low-grade astrocytoma [LGA; n = 28] and glioblastoma [n = 80]) were performed. Identified programs were then metabolically, genomically, and functionally

evaluated in preclinical models. Clear metabolic programs were identified differentiating LGA from glioblastoma, with aberrant lipid, peptide, and amino acid metabolism representing dominant metabolic nodes associated with malignant transformation. Although the metabolomic profiles of glioblastoma and LGA appeared mutually exclusive, considerable metabolic heterogeneity was observed in glioblastoma. Surprisingly, integrative analyses demonstrated that O-6-methylguanine-DNA methyltransferase methylation and isocitrate dehydrogenase mutation status were equally distributed among glioblastoma metabolic profiles. Transcriptional subtypes, on the other hand, tightly clustered by their metabolomic signature, with proneural and mesenchymal tumor profiles being mutually exclusive. Integrating these metabolic phenotypes with gene expression analyses uncovered tightly orchestrated and highly redundant transcriptional programs designed to support the observed metabolic programs by actively importing these biochemical substrates from the microenvironment, contributing to a state of enhanced metabolic heterotrophy. These findings were metabolomically, genomically, and functionally recapitulated in preclinical models. Despite disparate molecular pathways driving the progression of glioblastoma, metabolic programs designed to maintain its aggressive phenotype remain conserved. This contributes to a state of enhanced metabolic heterotrophy supporting survival in diverse microenvironments implicit in this malignancy.

Prabhu RS, Turner BE, Asher AL, Marcrom SR, Fiveash JB, Foreman PM, Press RH, Patel KR, Curran WJ, Jr, Breen WG, Brown PD, Jethwa KR, **Grills IS**, Arden JD, **Foster LM**, Manning MA, Stern JD, Soltys SG and Burri SH (2019). "A multi-institutional analysis of presentation and outcomes for leptomeningeal disease recurrence after surgical resection and radiosurgery for brain metastases." *Neuro-Oncology*. ePub Ahead of Print.

[Full Text](#)

Department of Radiation Oncology

OUWB Medical Student Author

Radiographic leptomeningeal disease (LMD) develops in up to 30% of patients following postoperative stereotactic radiosurgery (SRS) for brain metastases. However, the clinical relevancy of this finding and outcomes after various salvage treatments are not known. Patients with brain metastases, of which 1 was resected and treated with adjunctive SRS, and who subsequently developed LMD were combined from 7 tertiary care centers. LMD pattern was categorized as nodular (nLMD) or classical ("sugarcoating," cLMD). The study cohort was 147 patients. Most patients (60%) were symptomatic at LMD presentation, with cLMD more likely to be symptomatic than nLMD (71% vs. 51%, $P = 0.01$). Salvage therapy was whole brain radiotherapy (WBRT) alone (47%), SRS (27%), craniospinal radiotherapy (RT) (10%), and other (16%), with 58% receiving a WBRT-containing regimen. WBRT was associated with lower second LMD recurrence compared with focal RT (40% vs 68%, $P = 0.02$). Patients with nLMD had longer median overall survival (OS) than those with cLMD (8.2 vs 3.3 mo, $P < 0.001$). On multivariable analysis for OS, pattern of initial LMD (nodular vs classical) was significant, but type of salvage RT (WBRT vs focal) was not. Nodular LMD is a distinct pattern of LMD associated with postoperative SRS that is less likely to be symptomatic and has better OS outcomes than classical "sugarcoating" LMD. Although focal RT demonstrated increased second LMD recurrence compared with WBRT, there was no associated OS detriment. Focal cranial RT for nLMD recurrence after surgery and SRS for brain metastases may be a reasonable alternative to WBRT.

Radhakrishna U, Albayrak S, Zafra R, Baraa A, Vishweswaraiah S, Veerappa AM, Mahishi D, Saiyed N, Mishra NK, Guda C, Ali-Fehmi R and **Bahado-Singh RO** (2019). "Placental epigenetics for evaluation of fetal congenital heart defects: Ventricular Septal Defect (VSD)." *PLOS ONE* 14(3): e0200229.

[Full Text](#)

Department of Obstetrics and Gynecology

Ventricular Septal Defect (VSD), the most common congenital heart defect, is characterized by a hole in the septum between the right and left ventricles. The pathogenesis of VSD is unknown in most clinical cases. There is a paucity of data relevant to epigenetic changes in VSD. The placenta is a fetal tissue crucial in cardiac development and a potentially useful surrogate for evaluating the development of heart tissue. To understand epigenetic mechanisms that may play a role in the development of VSD, genome-wide DNA methylation assay on placentas of 8 term subjects with isolated VSD and no known or suspected genetic syndromes and 10 unaffected controls was performed using the Illumina HumanMethylation450 BeadChip assay. We identified a total of 80 highly accurate potential CpGs in 80 genes for detection of VSD; area under the receiver operating characteristic curve (AUC ROC) 1.0 with significant 95% CI (FDR) p -values < 0.05 for

each individual locus. The biological processes and functions for many of these differentially methylated genes are previously known to be associated with heart development or disease, including cardiac ventricle development (HEY2, ISL1), heart looping (SRF), cardiac muscle cell differentiation (ACTC1, HEY2), cardiac septum development (ISL1), heart morphogenesis (SRF, HEY2, ISL1, HEYL), Notch signaling pathway (HEY2, HEYL), cardiac chamber development (ISL1), and cardiac muscle tissue development (ACTC1, ISL1). In addition, we identified 8 microRNAs that have the potential to be biomarkers for the detection of VSD including: miR-191, miR-548F1, miR-148A, miR-423, miR-92B, miR-611, miR-2110, and miR-548H4. To our knowledge this is the first report in which placental analysis has been used for determining the pathogenesis of and predicting VSD.

Radhakrishna U, Vishweswaraiah S, Ratnamala U, **Bahado-Singh R** and Saiyed N (2019). "DNA methylation and microRNA biomarkers for noninvasive detection of hidradenitis suppurativa." *Experimental Dermatology* 28: 6-7.

Department of Obstetrics and Gynecology

[Full Text](#)

Ramsey T, Hojjat H, **Yuhan B**, Svider PF, Eloy JA, **Folbe AJ**, Raza SN and Fribley AM (2019). "Disparities in impact of nasopharyngeal cancer: An analysis of global health burden." *Laryngoscope*. ePub Ahead of Print.

[Full Text](#)

OUWB Medical Student Author

Department of Surgery

Objectives: Nasopharyngeal carcinoma has a unique worldwide racial and geographic distribution. Our objective was to evaluate socioeconomic disparities in the burden of nasopharyngeal cancer (NPC) between endemic and nonendemic regions. Methods: To demonstrate trends regarding societal burden of NPC and socioeconomic development, national disability-adjusted life year (DALY) rates and human development indices (HDI) between 1990 and 2015 were evaluated. Countries were divided based on the endemic versus nonendemic presence of NPC and further analyzed by HDI status as specified by the United Nations Development Program. Gini coefficients and concentration index were used to evaluate global equality in NPC burden over this period. Results: Age-standardized DALYs dropped from 36.1 in 1990 to 26.5 in 2015 (26.6% decline) ($r = -0.991$, $P < 0.001$). Lower socioeconomic countries harbored greater NPC burden upon controlling by endemic and nonendemic regions, as demonstrated by progressively negative concentration indexes. Health inequality was greater in nonendemic countries than in endemic countries ($P < 0.01$). Conclusion: To our knowledge, this is the first study to investigate socioeconomic-related changes in NPC burden using statistical tools such as the Gini coefficient and concentration index. Although the burden of NPC has steadily decreased, there remain persistent inequalities associated with socioeconomic disparities. Nasopharyngeal cancer burden is more pronounced in countries with lower HDI. Our results reinforce the importance of increasing resources for developing countries and continuing inquiry into the screening, diagnosis, and management of NPC. Level of Evidence NA. *Laryngoscope*, 2019

Rezvani S, Tominna M, **Al-Katib S**, **Smith MD**, Cousineau C and Al-Katib A (2019). "Lymphomatoid granulomatosis in a patient with chronic lymphocytic leukemia and rapidly progressing peribronchovascular pulmonary infiltrates." *Case Reports in Pulmonology* 2019: 9870494-9870494.

[Full Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Department of Pathology

Lymphomatoid granulomatosis (LG) is an EBV-associated angiodestructive lymphoproliferative disease with multiorgan involvement that predominantly affects the lungs. We present a case of a 72-year-old man with a history of chronic lymphocytic leukemia who presented with upper respiratory symptoms and multiple erythematous skin papules. Chest CT showed ill-defined, irregular solid pulmonary nodules with peripheral ground-glass opacities in a peribronchovascular distribution. The differential for this pattern of lung disease is vast which includes but is not limited to infection, vasculitis, sarcoidosis, lymphoma, and Kaposi sarcoma. Subsequent PET/CT showed rapid progression of lung opacities and marked FDG uptake of pulmonary opacities and skin nodules, which raised the question of Richter syndrome. Wedge biopsy under video-assisted thoracoscopic surgery was performed. Pathology showed an extensive lymphoid infiltrate involving lymphatic and bronchovascular bundles and consisting of a mixture of large lymphocytes and

inflammatory cells. Special stains showed that the large lymphocytes expressed B-cell markers and EBV virus. Overall, the findings were consistent with LG.

Roach VA, Fraser GM, Kryklywy JH, Mitchell DGV and Wilson TD (2019). "Guiding low spatial ability individuals through visual cueing: The dual importance of where and when to look." [Anatomical Sciences Education](#) 12(1): 32-42.
[Full Text](#)

Department of Foundational Medical Studies (OU)

Research suggests that spatial ability may predict success in complex disciplines including anatomy, where mastery requires a firm understanding of the intricate relationships occurring along the course of veins, arteries, and nerves, as they traverse through and around bones, muscles, and organs. Debate exists on the malleability of spatial ability, and some suggest that spatial ability can be enhanced through training. It is hypothesized that spatial ability can be trained in low-performing individuals through visual guidance. To address this, training was completed through a visual guidance protocol. This protocol was based on eye-movement patterns of high-performing individuals, collected via eye-tracking as they completed an Electronic Mental Rotations Test (EMRT). The effects of guidance were evaluated using 33 individuals with low mental rotation ability, in a counterbalanced crossover design. Individuals were placed in one of two treatment groups (late or early guidance) and completed both a guided, and an unguided EMRT. A third group (no guidance/control) completed two unguided EMRTs. All groups demonstrated an increase in EMRT scores on their second test ($P < 0.001$); however, an interaction was observed between treatment and test iteration ($P = 0.024$). The effect of guidance on scores was contingent on when the guidance was applied. When guidance was applied early, scores were significantly greater than expected ($P = 0.028$). These findings suggest that by guiding individuals with low mental rotation ability "where" to look early in training, better search approaches may be adopted, yielding improvements in spatial reasoning scores. It is proposed that visual guidance may be applied in spatial fields, such as STEMM (science, technology, engineering, mathematics and medicine), surgery, and anatomy to improve student's interpretation of visual content. Anat Sci Educ.

Rothschild DP, **Goldstein JA** and **Bowers TR** (2019). "Low-dose systemic thrombolytic therapy for treatment of submassive pulmonary embolism: Clinical efficacy but attendant hemorrhagic risks." [Catheterization and Cardiovascular Interventions](#) 93(3): 506-510.

[Full Text](#)

Department of Internal Medicine

Objectives: The purpose of the present study is to evaluate the safety and efficacy of "low-dose" systemic thrombolytic therapy (TT) for treatment of patients with intermediate-high risk submassive pulmonary embolism (PE). Background: TT is increasingly utilized in acute submassive PE. Strategies for TT include catheter-directed administration as well as traditional IV systemic therapy. Regardless of the route, most studies document the attendant significant bleeding complication rates expected from induction of a systemic lytic state. To mitigate bleeding, "low-dose" systemic TT (Alteplase 50 mg) has been advocated, based on recent studies which demonstrated clinical efficacy with elimination of any significant bleeding complications. Methods: Over a 24-month period, our institutional PE Response Team treated 45 acute submassive PE patients with "Low Dose" IV Alteplase 50 mg. Clinical outcomes and bleeding complications were assessed. Results: Overall clinical outcome was excellent, with 97.8% of patients surviving to discharge and a 30-day, all-cause mortality of 4.4%. Despite no patients having a HAS-BLED score > 2 (average score = 0.8 ± 0.1), ISTH major and GUSTO moderate bleeding was observed in 11% ($n = 5$) of cases. Conclusions: The present observations document that low-dose systemic TT is associated with excellent clinical outcome for intermediate-high risk submassive PE, but with attendant risk for bleeding. These findings are consistent with the concept that induction of a therapeutic lytic state carries inextricable bleeding risk.

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](#): 1358863X19838350.

[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 \pm 14.7 mmHg, USAT \pm 10.8 mmHg; $p = 0.14$). Post-treatment, CDT showed similar improvement in the RV/LV ratio (CDT \pm 0.58 vs USAT \pm 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.

Said A, Keeney S and **Halalau A** (2019). "Concomitant use of direct oral anticoagulants and aspirin for cardiovascular disease prevention in atrial fibrillation and flutter." Journal of the American College of Cardiology 73(9): 321-321.

[Full Text](#)

Department of Internal Medicine

Sandrone S, Berthaud JV, Chuquilin M, Cios J, Ghosh P, Gottlieb-Smith RJ, Kushlaf H, Mantri S, Masangkay N, **Menkes DL**, Nevel KS, Sarva H and Schneider LD (2019). "Neurologic and neuroscience education: Mitigating neurophobia to mentor health care providers." Neurology 92(4): 174-179.

[Request Form](#)

Department of Neurology

Neurologic disorders are among the most frequent causes of morbidity and mortality in the United States. Moreover, the current shortfall of neurologists is expected to worsen over the coming decade. As a consequence, many patients with neurologic disorders will be treated by physicians and primary care providers without formal neurologic training. Furthermore, a pervasive and well-described fear of neurology, termed neurophobia, has been identified in medical student cohorts, residents, and among general practitioners. In this article, members of the American Academy of Neurology A.B. Baker Section on Neurological Education review current guidelines regarding neurologic and neuroscience education, contextualize the genesis and the negative consequences of neurophobia, and provide strategies to mitigate it for purposes of mentoring future generations of health care providers.

Saon M, Walker D, **Nair GB** and **Al-Katib S** (2019). "Pulmonary fat embolism syndrome after liposuction surgery." Clinical Pulmonary Medicine 26(1): 32-35.

[Full Text](#)

OUWB Medical Student Author

Department of Internal Medicine

Department of Diagnostic Radiology and Molecular Imaging

Fat embolism syndrome (FES) after liposuction is very rare. Up until now, only 18 cases, including this case, of liposuction-induced FES have been reported. FES is underdiagnosed due to the lack of sensitive and specific laboratory tests and clinical findings. We present the case of a 52-year-old woman who developed FES as a complication of liposuction of the axilla, pectoris, and back. This case presents the typical radiologic findings in a patient with liposuction-induced FES. With the growing number of liposuction procedures, it is important for physicians to become aware of the fact that liposuction is not a risk-free procedure. © 2019 Wolters Kluwer Health, Inc. All rights reserved.

Sawarynski KE, **Baxa DM** and **Folberg R** (2019). "Embarking on a journey of discovery: Developing transitional skill

sets through a scholarly concentration program." [Teaching and Learning in Medicine](#) 31(2): 195-206.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Problem: Medical student participation in research enhances appreciation of the scientific literature and the conduct of investigation, and may lead to an interest in academic medicine. Independent medical student research offers frequently overlooked opportunities to develop and assess professional practice abilities, including project design and implementation, interprofessional team communication, and time management. These skills, useful to physicians, are often challenging for medical students to master as they transition into clinical careers. To address this challenge, we designed and embedded interventional modalities into a highly mentored and longitudinal scholarly concentration component of the curriculum. **Intervention:** The Embark scholarly concentration program incorporates traditional research training with the development of professional practice skills essential for transitioning to clinical practice. The program includes individualized and just-in-time components enabling student access to information and feedback specific to their projects and development of professional practice skills. **Context:** The Embark program is a required longitudinal component of the Oakland University William Beaumont School of Medicine undergraduate medical curriculum. The Embark program consists of courses that inform and facilitate a required longitudinal independent research project. **Outcome:** A retrospective evaluation of the Embark program's success with development of professional practice skills through the lens of both faculty and student perceptions included analysis of project records and course evaluation feedback. Evaluation of individual student development of transitional skill ability is possible through both quantitative and qualitative analysis of data collected from student project records. More than 80% of course evaluation commentary on strengths of the program addressed activities related to professional practice skills. To systematize the evaluation of these data sources, we have piloted a framework, iSAIL, designed to assess student development in these skills during the planning and conduct of a research project. **Lessons Learned:** By developing professional practice skills in the context of a scholarly concentration program, medical students can build a foundation for future engagement in research while they develop skills to overcome challenges that they are likely to encounter in their clinical careers. Modalities designed to evaluate individualized student development of professional practice skills through research participation define program successes and may lead to the identification of additional resources needed by students. By offering medical students opportunities to develop professional practice skills within the protected environment of an independent research project, this scholarly concentration program provides a valuable opportunity to influence the early development of skills necessary throughout their clinical careers.

Schaufele M, Rhyne A and **Fischgrund J** (2019). "Two-year outcomes of patients treated with BVN ablation for the relief of chronic low back pain: results of the SMART trial." [Journal of Vascular & Interventional Radiology](#) 30(3): S90-S90.

[Full Text](#)

Department of Orthopedic Surgery

Schott J, Hafeez A, **Chinnaiyan K, Raff G, Gallagher M, Bilolikar AN and Safian R** (2019). "Patients with acute chest pain in the emergency room: Early and late outcomes after negative coronary computed tomography angiography-derived fractional flow reserve." [Journal of the American College of Cardiology](#) 73(9): 1429-1429.

[Full Text](#)

Department of Internal Medicine

Seiwert TY, Foster CC, Blair EA, Karrison TG, Agrawal N, Melotek JM, Portugal L, **Brisson RJ**, Dekker A, Kochanny S, Gooi Z, Lingen MW, Villafior VM, Ginat DT, Haraf DJ and Vokes EE (2019). "OPTIMA: a phase II dose and volume de-escalation trial for human papillomavirus-positive oropharyngeal cancer." [Annals of Oncology](#) 30(2): 297-302.

[Full Text](#)

OUWB Medical Student Author

Patients with HPV+ oropharyngeal squamous cell carcinoma were assigned to dose and volume de-escalated radiotherapy (RT) or chemoradiotherapy (CRT) based on response to induction chemotherapy in an effort to limit treatment-related toxicity while preserving efficacy. Patients were classified as low-risk ($\leq T3$, $\leq N2B$, ≤ 10 pack-year history) or high-risk ($T4$ or $\geq N2C$ or ≥ 10 PYH). After three cycles of

carboplatin/nab-paclitaxel, response was assessed using Response Evaluation Criteria in Solid Tumors 1.1. Low-risk patients with $\geq 50\%$ response received 50 Gray (Gy) RT (RT50) while low-risk patients with 30%–50% response or high-risk patients with $\geq 50\%$ response received 45 Gy CRT (CRT45). Patients with lesser response received standard-of-care 75 Gy CRT (CRT75). RT/CRT was limited to the first echelon of uninvolved nodes. The primary end point was 2-year progression-free survival compared with a historic control of 85%. Secondary end points included overall survival and toxicity. Sixty-two patients (28 low risk/34 high risk) were enrolled. Of low-risk patients, 71% received RT50 while 21% received CRT45. Of high-risk patients, 71% received CRT45. With a median follow-up of 29 months, 2-year PFS and OS were 95% and 100% for low-risk patients and 94% and 97% for high-risk patients, respectively. The overall 2-year PFS was 94.5% and within the 11% noninferiority margin for the historic control. Grade 3+ mucositis occurred in 30%, 63%, and 91% of the RT50, CRT45, and CRT75 groups, respectively ($P = 0.004$). Rates of any PEG-tube use were 0%, 31%, and 82% for RT50, CRT45, and CRT75 groups, respectively ($P < 0.0001$). Induction chemotherapy with response and risk-stratified dose and volume de-escalated RT/CRT for HPV+ OPSCC is associated with favorable oncologic outcomes and reduced acute and chronic toxicity. Further evaluation of induction-based de-escalation in large multicenter studies is justified.

Sellers T, Ghannam M, Asantey K, Klei J, Olive E and Roach V (2019). "Low-cost laparoscopic skill training for medical students using homemade equipment." [MedEdPortal](#) 15(10810).

[Full Text](#)

OUWB Medical Student Author

Department of Foundational Medical Studies (OU)

Introduction: Despite the increasing prevalence of minimally invasive surgery (MIS), medical students receive little training in MIS techniques like laparoscopy. Cost is perhaps the biggest obstacle, as expensive laparoscopic skill simulators (box trainers) are needed to mimic the laparoscopic environment. Low-cost, homemade box trainers have been built and described in the literature but are generally relegated to self-directed practice for surgical residents. These do-it-yourself (DIY) box trainers are uniquely capable of addressing cost as a major barrier to laparoscopic skills training for medical students but have not previously been used specifically for this purpose. Methods: Students from the Oakland University William Beaumont School of Medicine ($n = 17$) participated in a laparoscopic skills training course using DIY box trainers. Four basic laparoscopic tasks were taught using live demonstrations followed by directed practice. Learners were instructed to record their first and last attempts in order to enable self-assessment of their progress. Results: All learners were able to successfully complete each of the four laparoscopic tasks by the end of their respective sessions. Feedback from the learners in the form of a postsession survey indicated that the course provided an enjoyable and high-quality experience. Discussion: This resource is effective at providing medical students with a low-cost opportunity to experience laparoscopy and develop basic laparoscopic skills.

Selvaraj J, Lebesque J, Hope A, Guckenberger M, Werner-Wasik M, Peulen H, Giuliani M, Mantel F, Belderbos J, **Grills I** and Sonke JJ (2019). "Modeling radiation pneumonitis of pulmonary stereotactic body radiotherapy: The impact of a local dose-effect relationship for lung perfusion loss." [Radiotherapy and Oncology](#) 132: 142-147.

[Full Text](#)

Department of Radiation Oncology

Purpose: To investigate if a local dose-effect (LDE) relationship for perfusion loss improves the NTCP model fit for SBRT induced radiation pneumonitis (RP) compared to conventional LDEs. Methods and Materials: Multi-institutional data of 1015 patients treated with SBRT were analyzed. Dose distributions were converted to NTD with $\alpha/\beta = 3$ Gy. The Lyman-Kutcher-Burman NTCP model was fitted to the incidence grade ≥ 2 RP by maximum likelihood estimation with mean lung dose (MLD), equivalent uniform doses (EUD) using three LDE functions (power-law (EUDpower), logistic with 2 free parameters (EUDlog-free) and logistic with fixed parameters describing local perfusion loss (EUDPerfusion)) and volume above a threshold dose ($V-x$). Models were compared with the Akaike weights (A_w) derived from the Akaike information criteria (AIC). Results: The median time to grade ≥ 2 RP was 4.2 months and plateaued after 17 months at 5.4%. A strong dose-effect relationship for RP incidence was observed. The EUDPerfusion based NTCP model had the lowest AIC. The A_w were 0.53, 0.19, 0.11, 0.11, 0.05 for the EUDPerfusion, $V-x$, MLD, EUDlog-free and EUDpower LDEs respectively. Conclusion: A LDE for perfusion loss provided modest improvement in NTCP

model fit for SBRT induced radiation pneumonitis.

Shah S and **Topf J** (2019). "Mentorship in the digital age nephrology social media collective internship." Clinical Journal of the American Society of Nephrology 14(2): 294-296.

[Full Text](#)

Department of Internal Medicine

Sharkia R, Wierenga KJ, Kessel A, Azem A, Bertini E, Carrozzo R, Torracco A, Goffrini P, Berti CC, **McCormick ME**, Plecko B, Klein A, Abela L, Hengel H, Schols L, Shalev S, Khayat M, Mahajnah M and Spiegel R (2019). "Clinical, radiological, and genetic characteristics of 16 patients with ACO2 gene defects: Delineation of an emerging neurometabolic syndrome." Journal of Inherited Metabolic Disease 42(2): 264-275.

[Full Text](#)

Department of Pediatrics

Mitochondrial aconitase is the second enzyme in the tricarboxylic acid (TCA) cycle catalyzing the interconversion of citrate into isocitrate and encoded by the nuclear gene ACO2. A homozygous pathogenic variant in the ACO2 gene was initially described in 2012 resulting in a novel disorder termed infantile cerebellar retinal degeneration (ICRD, OMIM#614559). Subsequently, additional studies reported patients with pathogenic ACO2 variants, further expanding the genetic and clinical spectrum of this disorder to include milder and later onset manifestations. Here, we report an international multicenter cohort of 16 patients (of whom 7 are newly diagnosed) with biallelic pathogenic variants in ACO2 gene. Most patients present in early infancy with severe truncal hypotonia, truncal ataxia, variable seizures, evolving microcephaly, and ophthalmological abnormalities of which the most dominant are esotropia and optic atrophy with later development of retinal dystrophy. Most patients remain nonambulatory and do not acquire any language, but a subgroup of patients share a more favorable course. Brain magnetic resonance imaging (MRI) is typically normal within the first months but global atrophy gradually develops affecting predominantly the cerebellum. Ten of our patients were homozygous to the previously reported c.336C>G founder mutation while the other six patients were all compound heterozygotes displaying 10 novel mutations of whom 2 were nonsense predicting a deleterious effect on enzyme function. Structural protein modeling predicted significant impairment in aconitase substrate binding in the additional missense mutations. This study provides the most extensive cohort of patients and further delineates the clinical, radiological, biochemical, and molecular features of ACO2 deficiency.

Shields E and **Wiater JM** (2019). "Patient outcomes after revision of anatomic total shoulder arthroplasty to reverse shoulder arthroplasty for rotator cuff failure or component loosening: A matched cohort study." Journal of the American Academy of Orthopaedic Surgeons 27(4): e193-e198.

[Full Text](#)

Department of Orthopedic Surgery

Purpose: To compare outcomes after conversion of anatomic total shoulder arthroplasty (aTSA) to reverse total shoulder arthroplasty (RTSA) and a matched cohort. Methods: Patients converted from aTSA to RTSA for rotator cuff failure or component loosening and a primary RTSA matched cohort were retrospectively identified from a prospective database. Demographics and preoperative and postoperative outcomes were obtained and compared. Results: Age, sex, body mass index, follow-up length, and preoperative function were similar between revision (n = 35) and primary (n = 70) groups. At final follow-up, visual analog scale pain (2.4 +/- 2.8 versus 1.7 +/- 2.8; P = 0.24) and American Shoulder and Elbow Surgeons (68 +/- 26 versus 76 +/- 24; P = 0.14) scores were similar. The revision group had worse subjective shoulder value scores (63 +/- 30 versus 79 +/- 21; P = 0.002), satisfaction (74% versus 90%; P = 0.03), and more complications (31% versus 13%; P = 0.02). Conclusion: Revision of aTSA to RTSA for component loosening or rotator cuff failure results in function comparable to primary RTSA; however, more complications, worse subjective shoulder value scores, and lower patient satisfaction should be expected. LEVEL OF EVIDENCE: Level III, retrospective comparative.

Shore BJ, Miller PE, **Zaltz I**, Schoenecker PL and Sankar WN (2019). "Determining hinge abduction in Legg-Calvé-Perthes disease: Can we reliably make the diagnosis?" Journal of Pediatric Orthopaedics 39(2): e95-e101.

[Full Text](#)

Department of Orthopedic Surgery

Background: Although hinge abduction is recognized as an important finding in children with Legg-Calvé-Perthes disease, variable diagnostic criteria exist. The purpose of this study was (1) to test the interobserver and intraobserver agreement of the current definition of hinge abduction and (2) to develop consensus regarding key diagnostic features that could be used to improve our diagnostic criteria. Methods: Four orthopaedic surgeons with subspecialty pediatric hip interest independently assessed 30 randomly ordered cases of Legg-Calvé-Perthes disease. Each case included 2 fluoroscopic images of hip arthrograms (anteroposterior and abduction views). Surgeons graded the cases in a binary manner (hinge/no-hinge) on 2 separate occasions separated by a 4-week interval. Following reliability testing and comprehensive review of the literature, consensus-building sessions were conducted to identify key diagnostic features. Surgeons then regraded a new series of cases. Interobserver and intraobserver agreement between first/second and third/fourth readings were assessed using the Fleiss κ . Results: Interobserver κ for hinge abduction between the first and second surveys was 0.52 (with 0.41 to 0.60 considered moderate agreement), compared with 0.56 for the third and fourth surveys. First and second reading intraobserver agreement ranged from 0.59 to 0.83 compared with 0.75 to 1.00 for third and fourth reading. Consensus sessions identified several key diagnostic factors including: adequate visualization of the labral contour and ability of the lateral epiphysis to slip below the chondrolabral complex in abduction. Medial dye pooling, often due to asphericity of the femoral head, was not found to be a useful diagnostic criterion. Conclusions: Despite a combined experience of over 70 years among the reviewers, we found just slightly better than 50:50 agreement in what constitutes hinge abduction. Consensus discussions did improve our agreement but these modest changes emphasize how difficult it is to develop reliable diagnostic criteria for hinge abduction. As a result, we caution against using hinge abduction as an inclusion criteria or outcome measure for research purposes, as the diagnostic agreement can be inconsistent.

Siddiqui ZA, **Gustafson GS**, Ye H, Martinez AA, Mitchell B, Sebastian E, Limbacher A and **Krauss DJ** (2019). "Five-year outcomes of a single-institution prospective trial of 19-Gy single-fraction high-dose-rate brachytherapy for low- and intermediate-risk prostate cancer." *International Journal of Radiation Oncology*Biography*Physics*. ePub Ahead of Print. [Full Text](#)

Department of Radiation Oncology

Purpose: To update outcome and toxicity results of a prospective trial of 19-Gy single-fraction high-dose-rate (HDR) brachytherapy for men with low- and intermediate-risk prostate cancer. Methods and Materials: Patients were treated on a prospective study of single-fraction HDR brachytherapy. All patients had low- or intermediate-risk prostate cancer. Patients with prostate volumes >50 cm³, taking alpha-blockers for urinary symptoms, or with baseline American Urologic Association symptom scores >12 were ineligible. Patients underwent transrectal ultrasound-guided interstitial implant of the prostate followed by single-fraction HDR brachytherapy to a prescription dose of 19 Gy. Results: Sixty-eight patients were enrolled with a median follow-up of 3.9 years. Median age was 62 years. Median gland volume at the time of treatment was 35 cm³, 92.6% of patients had T1 disease, 63.2% had a Gleason score of 6, and median pretreatment prostate-specific antigen was 5.0 ng/mL. Chronic grade 2 genitourinary toxicity was 14.7%. No grade 3 urinary toxicity occurred. A single patient experienced grade 2+ rectal toxicity (grade 3 diarrhea) that was transient and resolved with medical management. The 5-year estimated disease-free survival was 77.2% with no significant difference between low- and intermediate-risk patients. A single patient developed distant metastases during the follow-up period. Biopsy-proven local failure at 5 years was 18.8%, occurring at a median interval of 4.0 years posttreatment. No deaths occurred during follow-up. Conclusions: With extended follow-up, toxicity rates after single-fraction 19-Gy HDR brachytherapy remain low. Higher-than-expected rates of biochemical and local failure, however, raise concerns regarding the adequacy of this dose. Additional investigation to define the optimal single-fraction HDR brachytherapy dose is warranted, and single-fraction treatment currently should not be offered outside the context of a clinical trial.

Siljander MP, Gehrke CK, Wheeler SD, Sobh AH, **Moore DD**, **Flierl MA** and **Baker EA** (2019). "Does taper design affect taper fretting corrosion in ceramic-on-polyethylene total hip arthroplasty? A retrieval analysis." *Journal of Arthroplasty*. ePub Ahead of Print. [Full Text](#)

Department of Orthopedic Surgery

Background: Ceramic-on-polyethylene (CoP) implants have exhibited lower fretting and corrosion scores than metal-on-polyethylene implants. This study aims at investigating the effect of taper design on taper corrosion and fretting in modular CoP total hip arthroplasty (THA) systems. Methods: Under an institutional review board--approved protocol, a query of an implant retrieval library from 2002 to 2017 identified 120 retrieved CoP THA systems with zirconia toughened alumina femoral heads. Femoral stem trunnions were visually evaluated and graded for fretting, corrosion, and damage at the taper interface. Medical records were reviewed for patient demographics and implant characteristics. Data were statistically analyzed using Spearman correlation and rank-sum tests with a Dunn's post hoc test, with a significance level of $\alpha = 0.05$. Results: Four different taper designs were evaluated: 11/13 (n = 18), 12/14 (n = 53), 16/18 (n = 21), and V40 (n = 28). There were no statistically significant demographic differences between taper groups for duration of implantation, laterality, patient age, and patient sex, but patients with 16/18 tapers had a higher body mass index than V40 tapers (P = .012). Duration of implantation had a weak positive correlation with both trunnion fretting ($\rho = 0.224$, P = .016) and corrosion ($\rho = 0.253$, P = .006). Summed fretting and corrosion scores were significantly greater on the V40 and 16/18 tapers compared with the 12/14 tapers (all P \leq .001). Conclusion: Taper fretting and corrosion were observed in CoP THA implants and were greatest with V40 and 16/18 tapers and lowest with 12/14 tapers. Differences in taper design characteristics may lead to greater micromotion at the taper-head interface, leading to increased fretting and corrosion.

Simon MR, Chiari EF, Co NP and Brown SC (2019). "Polymeric plasma IgA recovered from Cohn Fraction III precipitate binds recombinant human secretory component." *Journal of Allergy and Clinical Immunology* 143(2): AB233-AB233.

[Full Text](#)

Department of Internal Medicine

Sirls E, Pfannes R and **Sirls LT** (2019). "Intradetrusor onabotulinumtoxin injection for refractory bladder spasms before vesicovaginal fistula repair." *Neurourology and Urodynamics* 38: S183-S183.

[Full Text](#)

Department of Urology

Sirls LT, **Jafri M**, **Burks F**, **Korman H**, Banouch D, Avaniss-Aghajani E, Opel M, Luke N, Kelly C and Wojno KJ (2019). "PCR based urinary tract infection (UTI) analysis compared to traditional urine culture in identifying significant uropathogens in symptomatic patients." *Neurourology and Urodynamics* 38: S108-S109.

[Full Text](#)

Department of Urology

Sirls LT, Schonhoff A, Waldvogel A, Hasenau D and **Peters KM** (2019). "Early evaluation of an implanted chronic tibial nerve stimulation device versus percutaneous nerve stimulation for the treatment of urinary urge incontinence." *Neurourology and Urodynamics* 38: S180-S180.

[Full Text](#)

Department of Urology

Storey PP, Tauqeer Z, Yonekawa Y, Todorich B, **Wolfe JD**, Shah SP, Shah AR, Koto T, Abbey AM, Morizane Y, Sharma P, Wood EH, Morizane-Hosokawa M, Pendri P, Pancholy M, Harkey S, Jeng-Miller KW, Obeid A, Borkar DS, Chen E, Williams P, Okada AA, Inoue M, Shiraga F, Hirakata A, Shah CP, Prenner J and Garg S (2019). "The impact of prefilled syringes on endophthalmitis following intravitreal injection of ranibizumab." *American Journal of Ophthalmology* 199: 200-208.

[Full Text](#)

Department of Ophthalmology

Purpose: To compare the rates of infectious endophthalmitis following intravitreal injection of ranibizumab using prefilled syringes vs conventional preparation. Design: Multicenter retrospective cohort study. Methods: All eyes receiving intravitreal injection of 0.5 mg ranibizumab for retinal vascular diseases at 10 retina practices across the United States (2016 to 2017) and Japan (2009 to 2017) were included. The total numbers of eyes and injections were determined from billing codes. Endophthalmitis cases were determined from billing records and evaluated with chart review. Primary outcome was the rate of postinjection acute

endophthalmitis. Secondary outcomes were visual acuity and microbial spectrum. Results: A total of 243 754 intravitreal 0.5 mg ranibizumab injections (165 347 conventional and 78 407 prefilled) were administered to 43 132 unique patients during the study period. In the conventional ranibizumab group, a total of 43 cases of suspected endophthalmitis occurred (0.026%; 1 in 3845 injections) and 22 cases of culture-positive endophthalmitis occurred (0.013%; 1 in 7516 injections). In the prefilled ranibizumab group, 12 cases of suspected endophthalmitis occurred (0.015%; 1 in 6534 injections) and 2 cases of culture-positive endophthalmitis occurred (0.0026%; 1 in 39 204 injections). Prefilled syringes were associated with a trend toward decreased risk of suspected endophthalmitis (odds ratio 0.59; 95% confidence interval 0.31-1.12; P = .10) and a statistically significant decreased risk of culture-positive endophthalmitis (odds ratio 0.19; 95% confidence interval 0.045-0.82; P = .025). Average logMAR vision loss at final follow-up was significantly worse for eyes that developed endophthalmitis from the conventional ranibizumab preparation compared to the prefilled syringe group (4.45 lines lost from baseline acuity vs 0.38 lines lost; P = .0062). Oral-associated flora was found in 27.3% (6/22) of conventional ranibizumab culture-positive endophthalmitis cases (3 cases of *Streptococcus viridans*, 3 cases of *Enterococcus faecalis*) compared to 0 cases in the prefilled ranibizumab group. Conclusion: In a large, multicenter, retrospective study the use of prefilled syringes during intravitreal injection of ranibizumab was associated with a reduced rate of culture-positive endophthalmitis, including from oral flora, as well as with improved visual acuity outcomes.

Sun E, Mello MM, Rishel CA, Vaughn MT, Kheterpal S, Saager L, Fleisher LA, Damrose EJ, Kadry B, Jena AB, Kooij F, Wilczak J, **Soto R**, Berris J, **Price Z**, Urman RD, Lins S, Harris JM, Cummings KC, Berman MF, Nanamori M, Adelman BT, Wedeven C, Bittner EA, LaGorio J, McCormick PJ, Tom S, Aziz MF, Coffman T, Ellis TA, Molina S, Peterson W, Mackey SC, van Klei WA, Mahajan A, Geffen D, Jameson LC, Biggs DA, Craft R, Pace NL, Paganelli WC, Durieux ME, Nair BJ, Wanderer JP, Miller SA, Helsten DL, Turnbull ZA, Schonberger RB and Mpog (2019). "Association of overlapping surgery with perioperative outcomes." *JAMA-Journal of the American Medical Association* 321(8): 762-772.

[Full Text](#)

Department of Anesthesiology

Importance: Overlapping surgery, in which more than 1 procedure performed by the same primary surgeon is scheduled so the start time of one procedure overlaps with the end time of another, is of concern because of potential adverse outcomes. Objective: To determine the association between overlapping surgery and mortality, complications, and length of surgery. Design, Setting, and Participants: Retrospective cohort study of 66 430 operations in patients aged 18 to 90 years undergoing total knee or hip arthroplasty; spine surgery; coronary artery bypass graft (CABG) surgery; and craniotomy at 8 centers between January 1, 2010, and May 31, 2018. Patients were followed up until discharge. Exposures: Overlapping surgery (≥ 2 operations performed by the same surgeon in which ≥ 1 hour of 1 case, or the entire case for those < 1 hour, occurs when another procedure is being performed). Main Outcomes and Measures: Primary outcomes were in-hospital mortality or complications (major: thromboembolic event, pneumonia, sepsis, stroke, or myocardial infarction; minor: urinary tract or surgical site infection) and surgery duration. Results: The final sample consisted of 66 430 operations (mean patient age, 59 [SD, 15] years; 31 915 women [48%]), of which 8224 (12%) were overlapping. After adjusting for confounders, overlapping surgery was not associated with a significant difference in in-hospital mortality (1.9% overlapping vs 1.6% nonoverlapping; difference, 0.3%[95% CI, -0.2% to 0.7%]; P = .21) or risk of complications (12.8% overlapping vs 11.8% nonoverlapping; difference, 0.9%[95% CI, -0.1% to 1.9%]; P = .08). Overlapping surgery was associated with increased surgery length (204 vs 173 minutes; difference, 30 minutes [95% CI, 24 to 37 minutes]; P < .001). Overlapping surgery was significantly associated with increased mortality and increased complications among patients having a high preoperative predicted risk for mortality and complications, compared with low-risk patients (mortality: 5.8% vs 4.7%; difference, 1.2%[95% CI, 0.1% to 2.2%]; P = .03; complications: 29.2% vs 27.0%; difference, 2.3%[95% CI, 0.3% to 4.3%]; P = .03). Conclusions and Relevance: Among adults undergoing common operations, overlapping surgery was not significantly associated with differences in in-hospital mortality or postoperative complication rates but was significantly associated with increased surgery length. Further research is needed to understand the association of overlapping surgery with these outcomes among specific patient subgroups.

Sundram U (2019). "Cutaneous lymphoproliferative disorders: What's new in the revised 4th Edition of the World Health Organization (WHO) Classification of Lymphoid Neoplasms." *Advances in Anatomic Pathology* 26(2): 93-113.

[Full Text](#)

Department of Pathology

Cutaneous lymphoproliferative disorders remain a challenging aspect of dermatopathology, in part due to the rarity of the entities and extreme variability in clinical outcomes. Although many of the entities remain unchanged, the approach to some of them has changed in the new 2016 classification scheme of the World Health Organization. Chief among these are Epstein-Barr virus-associated lymphoproliferative disorders such as Epstein-Barr virus-associated mucocutaneous ulcer and hydroa vacciniforme-like lymphoproliferative disorder, primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma, primary cutaneous acral CD8+ T-cell lymphoma, primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder, and breast implant-associated anaplastic large cell lymphoma. In addition, translocations and gene rearrangements such as those involving the 6p25.3 locus have started to inform diagnosis and classification of anaplastic large cell lymphoma and lymphomatoid papulosis. In this review, we will examine what is new in the diagnostic toolbox of cutaneous lymphoproliferative disorders.

Sutherland EL, Dabajeh MM, Zintsmaster S, Feraco DK, Bassett MJ, Tran KV, Kolderman N, Mir S, Rezvani S, **Davila FR** and Coffey M (2019). "A retrospective evaluation of time to obtain an MRI for English- versus non-English-speaking patients." Journal of the American College of Radiology 16(2): 178-184.

[Full Text](#)

OUWB Medical Student Author

Department of Internal Medicine

Purpose: Americans with limited English proficiency (LEP) face significant barriers to health care that result in health disparities in the LEP population. LEP could delay an MRI, potentially increasing morbidity and mortality in the LEP population. This study compares the time to obtain a neurological MRI in English versus non-English language preference patients. Methods: 24,219 unique patients at a single health system who underwent inpatient neurological MRI were included in the study. Bivariate and multivariate analyses were used to identify characteristics predictive of time to examination (TTE) from the set: patient preferred language, gender, race, age, performing hospital, and order priority (routine versus stat). Results: Bivariate analysis showed a longer TTE is associated with increasing age category, non-English language preference, and routine priority. A multivariate analysis showed non-English language preference effect on TTE is reduced in magnitude and is no longer significant in a model that includes age group, priority, and hospital ($P = .23$, effect estimate = 4%, 95% CI: -2.5%, 11.0%). Routine order priority ($P < .0001$) and increasing age ($P < .0001$) were associated with increased TTE. In a model that included interactions, the effect of language preference did not depend on order priority ($P = .59$) or age group ($P = .11$). Conclusion: There is no significant difference in the time to obtain a neurological MRI in English versus non-English language preference patients when age, order priority, and performing hospital are accounted for. This finding supports the effectiveness of the protocols and resources in place to support patients with LEP at the sponsoring health system.

Tennyson L, Han E, **Peters KM** and **Sirls LT** (2019). "Is less more? A cadaver model to assess diffusion patterns of intradetrusor injections." Neurourology and Urodynamics 38: S149-S150.

[Full Text](#)

Department of Urology

Tennyson LE, Nguyen L, Sirls E, Han E, **Vecellio P**, Killinger K, **Bartley J**, **Gilleran J**, **Peters KM** and **Sirls LT** (2019). "Urinary tract infections in geriatric ambulatory patients with indwelling catheters." Neurourology and Urodynamics 38: S211-S212.

[Full Text](#)

OUWB Medical Student Author

Department of Urology

Thottam PJ, Gilliland T, Ettinger N, Bajjal R and Mehta D (2019). "Outcomes using a postoperative protocol in pediatric single-stage laryngotracheal reconstruction." Annals of Otology, Rhinology & Laryngology: 0003489419830107.

[Full Text](#)

Department of Surgery

Objectives: The aim of this study was to evaluate single-stage laryngotracheal reconstruction (ssLTR) outcomes before and after the implementation of a postoperative care protocol in pediatric patients. **Methods:** A case-control study with chart review was conducted at 2 tertiary academic centers from 2010 to 2016. Pediatric patients who underwent ssLTR with a postoperative care protocol were compared with those who did not receive care under this protocol. Data regarding perioperative management were collected and compared using χ^2 and Wilcoxon rank tests. Planned extubation, length of intubation in the intensive care unit, and complications were examined. **Results:** Nineteen patients completed ssLTR after the protocol was initiated, and 26 prior patients were used as control subjects. Planned extubation failed in 9 patients (35%) in the control group compared with 1 patient (5%) in the protocol group ($P < .05$). Using a structured protocol demonstrated a decrease in delayed extubation and intensive care unit stay ($P < .05$). Despite more postprotocol patients requiring posterior graft placement, preprotocol patients were less likely to be extubated within 7 days ($P < .05$). **Conclusions:** The authors propose an intensive care unit protocol that uses a combination of pharmacologic agents to optimally reduce the risk for adverse events that delay time to extubation and thus decannulation. Timely extubation was more likely with the use of this postoperative care protocol using a multidisciplinary approach involving otolaryngologists, pharmacists, intensivists, and anesthesiologists.

Todorich B, Thanos A, Yonekawa Y, Korot E, **Trese MT, Drenser KA** and Capone A, Jr. (2019). "Surgical management of tractional retinoschisis associated with vitreous hemorrhage in retinopathy of prematurity." Retinal Cases & Brief Reports 13(1): 72-74.

[Full Text](#)

Department of Ophthalmology

Purpose: The tractional retinoschisis is a poorly understood, rare, and likely underappreciated entity in retinopathy of prematurity. The purpose of this article is to describe clinical findings and surgical management of tractional retinoschisis in retinopathy of prematurity, masquerading as Stage 4 retinopathy of prematurity retinal detachment. **Methods:** A retrospective review of a single case with literature review and case discussion. **Results:** In this report, we describe a child with retinopathy of prematurity and tractional schisis, who initially presented with vitreous hemorrhage and was effectively managed by vitrectomy and inner wall retinectomy. At 5 months after vitrectomy, the child demonstrated complete collapse of the retinoschisis with intact posterior pole and brisk light perception. **Conclusion:** Vitrectomy with or without inner wall retinectomy is effective in the management of tractional retinoschisis.

Tooley TR, Siljander MP and Hubers M (2019). "Development of a periprosthetic joint infection by abiotrophia defectiva years after total knee arthroplasty." Arthroplasty Today 5(1): 49-51.

[Full Text](#)

OUWB Medical Student Author

Department of Orthopedic Surgery

A 74-year-old male presented with acute right knee pain and inability to ambulate. The patient had a total knee arthroplasty, previously complicated by a periprosthetic femur fracture requiring surgical fixation and subsequent methicillin-resistant Staphylococcus epidermidis periprosthetic joint infection treated via two-stage revision. Cultures from knee fluid aspiration were positive for Abiotrophia defectiva. Identification was confirmed using matrix-assisted laser desorption ionization-time of flight mass spectrometry. The patient underwent a two-stage revision. Between stages, the patient received intravenous ceftriaxone for six weeks with subsequent normalization of inflammatory markers. Diagnosis of periprosthetic joint infection with identification of the organism is important to guide appropriate treatment.

VanDam I, **Dai J** and Rosenman K (2019). "Role of diabetes management in occupational health: Perceptions and practices of occupational and environmental medicine providers." Journal of Occupational and Environmental Medicine 61(2): 115-119.

[Full Text](#)

OUWB Medical Student Author

Objective: Diabetes mellitus is a common and costly disease, affecting millions of working age adults in the United States. Although many risk factors for diabetes are well described and manageable, the management

of diabetes in the occupational setting is not well defined. Methods: This study used a 17-item survey to explore the practices and perceptions of occupational medicine providers in Michigan on the management and prevention of diabetes in the workplace. Results: Most providers utilize many strategies to manage diabetes. Nonetheless, results from the survey demonstrate variability in practices. Most providers indicate that specific guidelines for caring for workers with diabetes would be useful. Conclusion: A specific guideline would help delineate the role of an occupational health provider in managing diabetes and support better outcomes for the many patients with diabetes who work.

Varrey A, Mehrmohammadi M, Garg A, Qureshi F, Yan Y, Basij M, Siddiqui A, **Alhousseini A**, Gomez-Lopez N, Romero R and Hassan S (2019). "Photoacoustic imaging of the uterine cervix: A novel method to characterize tissue composition." *American Journal of Obstetrics and Gynecology* 220(1): S14-S15.

[Full Text](#)

Department of Obstetrics and Gynecology

Vaupel Z (2019). "Transarticular screw technique for stabilization of lisfranc injuries." *Techniques in Foot and Ankle Surgery* 18(1): 16-22.

[Full Text](#)

Department of Orthopedic Surgery

Injuries to the tarsometatarsal joint complex are known as Lisfranc injuries. Although relatively rare when considered with all other injuries about the foot and ankle, they are frequently seen in the orthopedic clinic. These injuries are often missed and can lead to long-standing pain and disability. Therefore, a high index of suspicion must be maintained by the evaluating orthopedic surgeon. Studies have shown that anatomic reduction is critical to obtain a good result. Transarticular screw fixation has the ability to obtain and maintain an anatomic reduction. This technique has historically been the most common method of treatment. But, follow-up studies have shown a high rate of posttraumatic arthritis and reoperation. This has led to the consideration of other means of treatment such as primary arthrodesis, extra-articular plating, and suture button fixation. Regardless of the chosen method, the goal of treatment is a stable, pain-free, plantigrade foot.

Vidal CI, Armbrect EA, Andea AA, Bohlke AK, Comfere NI, Hughes SR, Kim J, Kozel JA, Lee JB, Linos K, Litzner BR, Missall TA, Novoa RA, **Sundram U**, Swick BL, Hurley MY, Alam M, Argenyi Z, Duncan LM, Elston DM, Emanuel PO, Ferringer T, Fung MA, Hosler GA, Lazar AJ, Lowe L, Plaza JA, Prieto VG, Robinson JK, Schaffer A, Subtil A and Wang W-L (2019). "Appropriate use criteria in dermatopathology: Initial recommendations from the American Society of Dermatopathology." *Journal of the American Academy of Dermatology* 80(1): 189-207.e111.

[Full Text](#)

Department of Pathology

Background: Appropriate use criteria (AUC) provide physicians guidance in test selection, and can affect health care delivery, reimbursement policy, and physician decision-making. Objectives: The American Society of Dermatopathology, with input from the American Academy of Dermatology and the College of American Pathologists, sought to develop AUC in dermatopathology. Methods: The RAND/UCLA appropriateness methodology, which combines evidence-based medicine, clinical experience, and expert judgment, was used to develop AUC in dermatopathology. Results: With the number of ratings predetermined at 3, AUC were developed for 211 clinical scenarios involving 12 ancillary studies. Consensus was reached for 188 (89%) clinical scenarios, with 93 (44%) considered "usually appropriate" and 52 (25%) "rarely appropriate" and 43 (20%) having "uncertain appropriateness." Limitations The methodology requires a focus on appropriateness without comparison between tests and irrespective of cost. Conclusions: The ultimate decision to order specific tests rests with the physician and is one where the expected benefit exceeds the negative consequences. This publication outlines the recommendations of appropriateness—the AUC for 12 tests used in dermatopathology. Importantly, these recommendations may change considering new evidence. Results deemed "uncertain appropriateness" and where consensus was not reached may benefit from further research.

Villarreal CM, Yedavally S and **Mulhem E** (2019). "Vegetable fibre in an infected ovarian dermoid cyst." *BMJ Case Reports* 12(3): e224867.

[Full Text](#)

OUWB Medical Student Author

Department of Family Medicine and Community Health

Tubo-ovarian abscesses (TOAs) are inflammatory masses involving the fallopian tube, ovary and occasionally other adjacent pelvic organs. A 32-year-old woman with no significant medical history presented with a chief complaint of lower abdominal pain. Initial CT of the abdomen was suggestive of a colon abscess; however, a repeat CT suggested a TOA. The left ovary was densely adherent to the left pelvic sidewall and the rectosigmoid colon. The content of the ovary was consistent with a dermoid and suspected of superinfection. Pathological examination of the tissue revealed normal ovarian cortical tissue, hair cells, melanin, and epidermal and neural tissue, as well as evidence of a foreign object resembling vegetable matter. The vegetable fibre found in this patient's biopsy was of an unclear aetiology, but probably indicates a perforation of the bowel. Any cause of bowel perforation adjacent to the adnexa can lead to TOA, therefore providing a rational speculation for this case.

Vishweswaraiah S, Swierkowska J, Ratnamala U, Mishra NK, Guda C, Chettiar SS, Johar KR, Mrugacz M, Karolak JA, Gajicka M and **Radhakrishna U** (2019). "Epigenetically dysregulated genes and pathways implicated in the pathogenesis of non-syndromic high myopia." *Scientific Reports* 9(1): 4145-4145.

[Full Text](#)

Department of Obstetrics and Gynecology

Myopia, commonly referred to as nearsightedness, is one of the most common causes of visual disability throughout the world. It affects more people worldwide than any other chronic visual impairment condition. Although the prevalence varies among various ethnic groups, the incidence of myopia is increasing in all populations across globe. Thus, it is considered a pressing public health problem. Both genetics and environment play a role in development of myopia. To elucidate the epigenetic mechanism(s) underlying the pathophysiology of high-myopia, we conducted methylation profiling in 18 cases and 18 matched controls (aged 4-12 years), using Illumina MethylationEPIC BeadChips array. The degree of myopia was variable among subjects, ranging from -6 to -15D. We identified 1541 hypermethylated CpGs, representing 1745 genes (2.0-fold or higher) (false discovery rate (FDR) $p \leq 0.05$), multiple CpGs were $p < 5 \times 10^{-8}$ with a receiver operating characteristic area under the curve (ROC-AUC) ≥ 0.75 in high-myopia subjects compared to controls. Among these, 48 CpGs had excellent correlation (AUC ≥ 0.90). Herein, we present the first genome-wide DNA methylation analysis in a unique high-myopia cohort, showing extensive and discrete methylation changes relative to controls. The genes we identified hold significant potential as targets for novel therapeutic intervention either alone, or in combination.

Weiner AJ, Weiner Y, Severson ML and Weiner A (2019). "Clinical experience with urgent tube shunt implantation through the ciliary sulcus in phakic eyes." *International Ophthalmology* 39(3): 639-649.

[Full Text](#)

OUWB Medical Student Author

To review the clinical course and outcomes of 3 phakic, ischemic, and inflamed eyes in which we performed urgent tube shunt implantation through the ciliary sulcus without lensectomy.

White JL, Hollander JE, Chang AM, Nishijima DK, Lin AL, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Nicks BA, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2019). "Orthostatic vital signs do not predict 30 day serious outcomes in older emergency department patients with syncope: A multicenter observational study." *American Journal of Emergency Medicine*. ePub Ahead of Print.

[Full Text](#)

Department of Emergency Medicine

Background: Syncope is a common chief complaint among older adults in the Emergency Department (ED), and orthostatic vital signs are often a part of their evaluation. We assessed whether abnormal orthostatic vital signs in the ED are associated with composite 30-day serious outcomes in older adults presenting with syncope. Methods: We performed a secondary analysis of a prospective, observational study at 11 EDs in adults ≥ 60 years who presented with syncope or near syncope. We excluded patients lost to follow up. We used the standard definition of abnormal orthostatic vital signs or subjective symptoms of lightheadedness upon standing to define orthostasis. We determined the rate of composite 30-day serious outcomes,

including those during the index ED visit, such as cardiac arrhythmias, myocardial infarction, cardiac intervention, new diagnosis of structural heart disease, stroke, pulmonary embolism, aortic dissection, subarachnoid hemorrhage, cardiopulmonary resuscitation, hemorrhage/anemia requiring transfusion, with major traumatic injury from fall, recurrent syncope, and death) between the groups with normal and abnormal orthostatic vital signs. Results: The study cohort included 1974 patients, of whom 51.2% were male and 725 patients (37.7%) had abnormal orthostatic vital signs. Comparing those with abnormal to those with normal orthostatic vital signs, we did not find a difference in composite 30-serious outcomes (111/725 (15.3%) vs 184/1249 (14.7%); unadjusted odds ratio, 1.05 [95%CI, 0.81–1.35], $p = 0.73$). After adjustment for gender, coronary artery disease, congestive heart failure (CHF), history of arrhythmia, dyspnea, hypotension, any abnormal ECG, physician risk assessment, medication classes and disposition, there was no association with composite 30-serious outcomes (adjusted odds ratio, 0.82 [95%CI, 0.62–1.09], $p = 0.18$). Conclusions: In a cohort of older adult patients presenting with syncope who were able to have orthostatic vital signs evaluated, abnormal orthostatic vital signs did not independently predict 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](#). ePub Ahead of Print.

[Full Text](#)

Department of Internal Medicine

Willner S, Imam Z and **Hader I** (2019). "Rothia dentocariosa endocarditis in an unsuspecting Host: A case report and literature review." [Case Reports in Cardiology](#) 2019: 7464251-7464251.

[Full Text](#)

Department of Internal Medicine

Rothia dentocariosa, a gram-positive coccobacillus, is a commensal bacterium that is part of the oropharynx and respiratory tract. In the past, it was known to be a cause for periodontal disease, but in recent years, Rothia dentocariosa has been found to be the cause of several other infectious entities, of which endocarditis is the most predominant. We present the case of a healthy 62-year-old female who, after undergoing routine dental cleaning two months prior, developed subacute bacterial endocarditis of the mitral valve, with subsequent cerebral septic emboli causing an occipital hemorrhagic cerebrovascular accident, all secondary to Rothia dentocariosa.

Wren JD, Doerkson RJ, Toby IT, Nanduri B, **Homayouni R**, Manda P and Thakkar S (2019). "Proceedings of the 2018 MidSouth Computational Biology and Bioinformatics Society (MCBIOS) conference." [BMC Bioinformatics](#) 20(Suppl 2): 95-95.

[Full Text](#)

Department of Foundational Medical Studies (OU)

Wright JO, Ho A, Kalma J, Koueiter D, Esterle J, **Marcantonio D**, **Wiater JM** and **Wiater B** (2019). "Uncemented reverse total shoulder arthroplasty as initial treatment for comminuted proximal humerus fractures." [Journal of Orthopaedic Trauma](#).

Department of Diagnostic Radiology and Molecular Imaging

Department of Orthopedic Surgery

[Full Text](#)

Objectives: To determine if uncemented implants would provide similar outcomes while avoiding the complications associated with cement in the treatment of elderly patients with proximal humerus fractures (PHFs) with primary reverse total shoulder arthroplasty (RTSA). Design: Case series Setting: A single Level I trauma center Patients/Participants: A prospectively-obtained cohort of 30 patients who underwent uncemented RTSA as initial treatment for a comminuted PHF: 4 male, 26 female; average age 71 +/- 11 years. Intervention: Uncemented reverse total shoulder arthroplasty. Main Outcome Measures: 1) Radiographic analysis, 2) Postoperative clinical range of motion (ROM), and 3) Functional Outcome Scores: the American Shoulder and Elbow Surgeons Shoulder (ASES) score and the Simple Shoulder Test (SST) score. Results: Radiographic analysis showed 97% achieved stable humeral stem fixation and 70% had healing of

the tuberosities in anatomic position. Average ROM was 130 +/- 31 degrees of forward flexion, 32 +/- 18 degrees of external rotation, and internal rotation to the mid-lumbar spine. Average ASES score was 82.0 +/- 13.5 (with an average pain rating of 0.8 +/- 1.3), and average SST score was 69.4 +/- 19.1%. Conclusions: Our data show that treatment of comminuted PHFs in elderly patients with uncemented RTSA can consistently produce good clinical outcomes with a low rate of complications and suggest that cement may not be necessary for RTSA in the trauma setting.

Wu J, Rapp CM, Shields EJ and **Wiater JM** (2019). "Management of the failed anatomic total shoulder arthroplasty," In Tashjian RZ (ed). Complex and Revision Shoulder Arthroplasty : An Evidence-Based Approach to Evaluation and Management. Cham: Springer International Publishing. pp: 135-155.

[Full Text](#)

Department of Orthopedic Surgery

The increasing use of shoulder arthroplasty over the past two decades brings with it a steady need for qualified surgeons to manage the complications and failures. The most common modes of failure after anatomic total shoulder arthroplasty include glenoid component failure (loosening, wear, fracture), glenohumeral joint instability, and rotator cuff tear or dysfunction. Less common but no less significant complications that can lead to failure include periprosthetic fracture, infection, nerve injury, deltoid injury or dysfunction, and heterotopic ossification. These modes of failure can occur in isolation or in combination. A thorough understanding of the complications is necessary in order to offer patients the most appropriate treatment strategy. Strategies for each mode of failure and reported outcomes will be reviewed in addition to a decision-making treatment algorithm.

Xu ZY, Mathieu D, Heroux F, Abbassy M, Barnett G, Mohammadi AM, Kano H, Caruso J, Shih HH, **Grills IS, Lee K, Krishnan S, Kaufmann AM, Lee JYK, Alonso-Basanta M, Kerr M, Pierce J, Kondziolka D, Hess JA, Gerrard J, Chiang V, Lunsford LD and Sheehan JP** (2019). "Stereotactic radiosurgery for trigeminal neuralgia in patients with multiple sclerosis: A multicenter study." Neurosurgery 84(2): 499-505.

[Full Text](#)

Department of Radiation Oncology

Background: Facial pain response (PR) to various surgical interventions in patients with multiple sclerosis (MS)-related trigeminal neuralgia (TN) is much less optimal. No large patient series regarding stereotactic radiosurgery (SRS) has been published. Objective: To evaluate the clinical outcomes of MS-related TN treated with SRS. Methods: This is a retrospective cohort study. A total of 263 patients contributed by 9 member tertiary referral Gamma Knife centers (2 in Canada and 7 in USA) of the International Gamma Knife Research Consortium (IGKRF) constituted this study. Results: The median latency period of PR after SRS was 1 mo. Reasonable pain control (Barrow Neurological Institute [BNI] Pain Scores I-IIIb) was achieved in 232 patients (88.2%). The median maintenance period from SRS was 14.1 months (range, 10 days to 10 years). The actuarial reasonable pain control maintenance rates at 1 yr, 2 yr, and 4 yr were 54%, 35%, and 24%, respectively. There was a correlation between the status of achieving BNI-I and the maintenance of facial pain recurrence-free rate. The median recurrence-free rate was 36 mo and 12.2 mo in patients achieving BNI-I and BNI > I, respectively (P = .046). Among 210 patients with known status of post-SRS complications, the new-onset of facial numbness (BNI-I or II) after SRS occurred in 21 patients (10%). Conclusion: In this largest series SRS offers a reasonable benefit to risk profile for patients who have exhausted medical management. More favorable initial response to SRS may predict a long-lasting pain control.

Yadav S, Hartkop S, Cardenas PY, Ladkany R, **Halalau A, Shoichet S, Maddens M and Zakalik D** (2019). "Utilization of a breast cancer risk assessment tool by internal medicine residents in a primary care clinic: Impact of an educational program." BMC Cancer 19(1): 228-228.

[Full Text](#)

Department of Internal Medicine

Background: Despite strong evidence of benefit, breast cancer risk assessment and chemoprevention are underutilized by primary care physicians. This study evaluates the impact of an educational program on knowledge and utilization of the NCI Breast Cancer Risk Assessment Tool (BCRAT) by internal medicine residents. Methods: Internal medicine residents at the primary care clinic at William Beaumont Hospital participated in an educational program on breast cancer risk assessment and chemoprevention. A

questionnaire was used to assess knowledge and practice before and after participation. Electronic health records of women between the ages of 35 and 65 who were seen by participating residents for annual health exams between Dec 15, 2015 and Dec 14, 2016 were reviewed. Utilization of BCRAT by the residents was compared pre- and post-educational program. Results: A total of 43 residents participated in the study. 31 (72.1%) residents reported no prior knowledge about BCRAT. The remaining 12 (27.9%) reported limited knowledge of BCRAT, but the majority of these (n = 10, 83.3%) had not used it in the last six months. For each question on the pre-educational knowledge assessment, fewer than 10% of the residents responded correctly. After implementation of the educational program, there was a significant increase in the proportion of residents who answered correctly (Range: 67 to 100%, p < 0.001). Electronic health records of 301 clinic patients were reviewed, 118 (39.2%) in the pre-educational program group and 183 (60.8%) in the post-educational program group. There was a higher use of BCRAT in the post-educational program group compared to the pre-intervention group (3.8% vs. 0%, p < 0.05). However, a majority (n = 294, 98.7%) of eligible patients from both groups did not undergo breast cancer risk assessment. Conclusions: Our study demonstrates that an educational intervention improved residents' knowledge of BCRAT. Despite this improvement, a significant proportion of patients did not undergo breast cancer risk assessment. Expanding the scope and duration of this intervention and combining it with innovative use of technology to improve utilization should be the subject of future investigation.

Yedavally-Yellayi S, Ho AM and **Patalinghug EM** (2019). "Update on osteoporosis." *Primary Care* 46(1): 175-190.
[Full Text](#)

Department of Family Medicine and Community Health

Osteoporosis is often a silent disease that reveals itself at the time of a fracture. Assessing risk factors and applying appropriate screening guidelines in the population at risk can potentially decrease the looming high disease burden in the United States. FRAX is a validated tool that can be used to determine 10-year fracture risk to assist in medical decision making. Bone mineral density testing of the hip or spine using DEXA can be used alone or in combination with FRAX to determine patients' risk for fracture and determine if patients are candidates for treatment of osteoporosis.

Zhong Y, Vinogradskiy Y, Chen L, 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.