

## OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

### PUBLICATION LIST

July - September 2018

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**Alapati A** and **Trese M** (2018). "A retrospective analysis of the timing of initial treatment of bedside-screened versus photographically screened eyes with retinopathy of prematurity." *Ophthalmic Surgery, Lasers & Imaging Retina* 49(9): e32-e35.

[Full Text](#)

*Department of Ophthalmology*

*OUWB Medical Student Author*

Background and Objective: A retrospective clinical study was performed to assess whether photographically screened and remotely read images for retinopathy of prematurity (ROP) allowed for timely and accurate diagnosis of treatment-warranted ROP compared to bedside examination. Patients and Methods: The study included 130 eyes of 65 premature neonates in born at William Beaumont Hospital, Royal Oak NICU. Bedside examined (2006 to 2010) and telemedicine screened (2010 to 2014) neonates were compared to identify whether there is a statistical difference in postmenstrual age (PMA) at the time of treatment. Results: One hundred thirty eyes of 65 infants met the inclusion and exclusion criteria. Thirty-five infants who needed laser treatment were screened bedside with an average PMA at treatment of 36.5 weeks. Thirty infants who needed treatment were photographically screened, with an average PMA at treatment of 36.4 weeks. Neither group had statistically different PMAs ( $P = .58$ ). Conclusion: This study confirms that telemedicine also allows for appropriately timed treatment for early ROP.

**Al-Katib S**, Gupta G, **Brudvik A**, Ries S, Krauss J and **Farah M** (2018). "A practical guide to managing CT findings in the breast." *Clinical Imaging*. ePub Ahead of Print.

[Full Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

While it is well accepted that CT is not an optimal imaging study to evaluate the breasts, findings on chest CT may be the first indication of an occult malignancy. The nonspecific appearance of breast findings and the lack of consensus guidelines for managing incidental breast findings may dissuade radiologists from thoroughly evaluating the breasts on CT. We review commonly encountered breast findings on CT and present an algorithm for managing incidentally detected breast findings.

Allen O, Edhi A, Hafeez A and **Halalau A** (2018). "A very rare complication of hepatitis A infection: Acute myocarditis—A case report with literature review." Case Reports in Medicine: 3625139, 1-6.

[Full Text](#)

*Department of Internal Medicine*

Hepatitis A is a common viral infection with a benign course but in rare cases can progress to acute liver failure. It usually presents with abdominal pain, nausea, vomiting, diarrhea, jaundice, anorexia, or asymptotically, but it can also present atypically with relapsing hepatitis and prolonged cholestasis. In addition, extrahepatic manifestations have been reported, including urticarial and maculopapular rash, acute kidney injury, autoimmune hemolytic anemia, aplastic anemia, acute pancreatitis, mononeuritis, reactive arthritis, glomerulonephritis, cryoglobulinemia, Guillain–Barre syndrome, and pleural or pericardial effusion. A rare manifestation of hepatitis A is acute myocarditis. We report a case of a young woman who presented with “flu-like symptoms” and was found to have severe elevation of liver enzymes due to acute hepatitis A infection. On her 3rd day of admission, the patient developed chest pain and nonspecific electrocardiographic changes. Her troponins rose to 16.4 ng/mL, and a transthoracic echocardiogram revealed global hypokinesis and a depressed ejection fraction at 30%. A CT angiography showed no evidence of significant coronary artery disease. The patient was managed supportively, and symptoms and laboratory findings slowly improved over the next 7 days. Her chest pain resolved and a follow-up echocardiogram showed improved ejection fraction to 45%.

Andrade P, **Kaura AS**, Bryant JR and Burke E (2018). "Thermal burn injury from a wedding ring: An unusual case." The Journal of the American College of Clinical Wound Specialists 9(1-3): 32-34.

[Full Text](#)

*OUWB Medical Student Author*

Thermal ring injuries are rarely reported in the literature. For this reason, treatment is varied without a standard approach. We describe a case of a thermal wedding ring injury sustained during a welding accident. It is critical to understand the 3 zones of burn injuries when managing these infrequent cases. Furthermore, the dynamic progression that ensues a thermal burn will directly affect outcome. A case is presented along with a graduated approach to the management of such injuries.

**Arianpour K, Nguyen B, Yuhan B**, Svider PF, Eloy JA and Folbe AJ (2018). "Opioid prescription among sinus surgeons." American Journal of Rhinology and Allergy 32(4): 323-329.

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*OUWB Medical Student Author*

Background: Misuse and diversion of opioids have contributed to the U.S. opioid crisis, making an understanding of specialty-specific and procedure-specific trends essential. Objective: The objective of this analysis was to evaluate nationwide trends in opioid prescribing patterns among sinus surgeons performing functional endoscopic sinus surgery and maxillary sinus balloon dilation, specifically examining factors associated with variations. Methods: High-volume sinus surgeons were identified through the Centers for Medicare and Medicaid Services database and cross-referenced against prescriptions to Medicare Part D beneficiaries during 2013 through 2015. Number of opioid prescriptions, prescription lengths, and demographic information were obtained. Results: This cohort of 570 surgeons wrote 21,042 opioid prescriptions (5.4 days per prescription) in 2015, with 80.3% and 54.7% writing >10 and >25 prescriptions, respectively. Surgeons writing a greater amount of prescriptions wrote lengthier courses throughout all 3 years (P = .01, P = .002, P = .003). Female otolaryngologists wrote lengthier prescriptions (6.2 vs 5.3 days, P = .01). Early career otolaryngologists (≤10 years) offered fewer prescriptions compared to those who had greater experience (31.1 vs 39.3, P = .02). Moreover, 73.6% of fellowship-trained otolaryngologists offered >10 prescriptions versus 82.7% of nonfellowship-trained otolaryngologists (P = .02). Practitioners in the South on average prescribed the greatest amount of opioids (P < .05). Conclusion: A majority of sinus surgeons prescribe ≥25 opioid prescriptions annually, with otolaryngologists who write a greater amount of prescriptions writing lengthier courses. As the mean opioid prescription length is 5.4 days, recent legislation limiting opioid prescriptions to 5 days may only have a modest impact for preventing the diversion of perioperative opioid prescriptions. These data suggest further standardized guidelines may be beneficial in elucidating the appropriate indications for the prescription of opioids among sinus surgeons.

**Arianpour K, Svider PF, Guys N, Shenouda K, Folbe E, Hsueh WD, Eloy JA and Folbe AJ** (2018). "Incorporation of antibiotics and systemic steroids by sinus surgeons: is there widespread consensus?" International Forum of Allergy and Rhinology 8(9): 1034-1040.

[Full Text](#)

*OUWB Medical Student Author*

Background: The objective of this work was to evaluate factors associated with antibiotic and oral corticosteroid (OCS) prescription among otolaryngologists regularly performing sinus surgery. Methods: Fellowship-trained rhinologists, including fellowship directors, were identified via the American Rhinologic Society (ARS) website. Non-fellowship-trained otolaryngologists performing  $\geq 25$  balloons (frontal/maxillary) or  $\geq 25$  functional endoscopic sinus surgeries (FESSs) (frontal/maxillary/ethmoids) were also included in "balloon surgeons" and "sinus surgeon" cohorts, respectively. Prescribing data for Medicare Part D beneficiaries was obtained for 2015. Results: Otolaryngologists included in this analysis wrote a median of 54 scripts for antibiotics, with a 15.1% antibiotic prescription rate. The overall script length per antibiotic was 11.1 days. Of fellowship-trained rhinologists, 90.2% wrote fewer than 100 scripts, compared to 25.6% and 32.5% of sinus surgeons and balloon surgeons, respectively. Fellowship-trained rhinologists wrote lengthier antibiotic scripts (14.1 vs 10.3 days,  $p < 0.05$ ). Clinicians who have been in practice longer prescribed antibiotics significantly more frequently. Fellowship-trained rhinologists had a greater OCS rate (8.9%) than balloon and sinus surgeons (7.1%), also writing lengthier courses (15.0 vs 8.1 days). Early-career otolaryngologists wrote lengthier steroid prescriptions than those with 11 to 20 years and  $> 20$  years in practice. Conclusion: Antibiotic and OCS utilization varies by type of training, as non-fellowship-trained sinus surgeons and balloon surgeons tend to utilize antibiotics more aggressively, and fellowship-trained rhinologists utilize OCS more frequently. Otolaryngologists with more years in practice are more likely to incorporate antibiotics in the management of sinus disorders, although these conclusions must be considered in the context of this resource's limitations. Further clarification of guidelines may be helpful for minimizing divergent practices and maintaining a consensus.

**Arianpour K, Svider PF, Yuhan B, Hooda Z, Eloy JA and Folbe AJ** (2018). "Evolving patterns in the diagnosis and management of allergy-mediated disorders." International Forum of Allergy and Rhinology 8(8): 928-933.

[Full Text](#)

*OUWB Medical Student Author*

Background: This analysis explores the increasing heterogeneity of trends in allergy management under the premise that the practice of allergy has undergone significant changes in national economics, healthcare delivery, and treatment options from 2007 to 2016. Methods: Centers for Medicare and Medicaid Services (CMS) data were obtained for: (1) temporal trends in allergy immunotherapy injection (Current Procedural Terminology [CPT] codes 95115, 95117) and testing (CPT 95004, 95024) from 2007 to 2016; (2) geographic trends; and (3) practitioners administering immunotherapy. Although there are no sublingual immunotherapy (SLIT) CPT codes, billing for unlisted allergy/immunologic services (CPT 95199) were obtained. Results: Since 2007, there were 99.5 million allergy tests and 33.5 million immunotherapy injections billed to Medicare beneficiaries. Increases in testing have outpaced rising immunotherapy administration (49.7% vs 19.6% increase). Significant regional variation in testing rates was noted, with the greatest ratio of testing to immunotherapy in the South (0.35) and smallest ratio in the Northeast (0.18). The maximum unlisted allergy services billed was 594 (of which includes SLIT), compared to annual subcutaneous immunotherapy (SCIT) totals in the millions. The majority of immunotherapy in 2016 was administered by allergists/immunologists (51.6%) followed by otolaryngologists (31.2%), trends that have remained consistent since 2012. Conclusion: Physicians have been more aggressive in the workup of allergy-mediated disorders in recent years. Although differences in allergen load exist, there is tremendous geographic variation in the ratio of testing to immunotherapy. While the role otolaryngologists play in immunotherapy remains stable, allergists manage the majority of patients, reinforcing the importance of interdisciplinary cooperation and outreach. SLIT does not appear to play a significant role in this population.

**Armstrong K, Lanni T, Anderson MM and Patricolo GE** (2018). "Integrative medicine and the oncology patient: options and benefits." Supportive Care in Cancer 26(7): 2267-2273.

[Full Text](#)

*Department of Family Medicine and Community Health  
Department of Radiation Oncology*

Cancer is a major public health problem, and cancer patients and survivors face many physical and emotional challenges after the initial diagnosis, through treatment, and in the post-treatment period. Different integrative medicine (IM) modalities can be used to mitigate some of the physical issues that originate from the cancer itself or the treatment and to promote well-being and emotional health. Here, we discuss how an IM Department can function in a hospital system, particularly with regard to oncology patients, the modalities appropriate for oncology patients, how these modalities can benefit this patient population, and the role of IM in cancer survivorship. A dedicated IM Department that works with oncologists provides support and care for the whole person. These different modalities work together to reduce pain, anxiety, and chemotherapy-induced nausea and peripheral neuropathy, while promoting immune function and improving sleep, range of motion, and an overall sense of well-being. However, each modality has different contraindications for the oncology patient, and proper training is required for safe and effective care. We illustrate how IM can be a valuable component of the care of the oncology patient.

**Bahl A, Hang B, Brackney A, Joseph S, Karabon P, Mohammad A, Nnanabu I and Shotkin P (2018).** "Standard long IV catheters versus extended dwell catheters: A randomized comparison of ultrasound-guided catheter survival." [The American Journal of Emergency Medicine](#). ePub Ahead of Print.

[Full Text](#)

*Department of Emergency Medicine*

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

Baker D, **Long G**, Callahan P, Studzinski D, **Altshuler J** and **Brown OW** (2018). "Intramural hematomas of the thoracic aorta: Current management and outcomes: A single institution's experience during a decade." [Journal of Vascular Surgery](#) 68(3): E53-E54.

[Full Text](#)

*Department of Surgery*

Barnes GD, Kong X, Cole D, Haymart B, Kline-Rogers E, **Almany S**, Dahu M, Ekola M, Kaatz S, Kozlowski J and Froehlich JB (2018). "Extended international normalized ratio testing intervals for warfarin-treated patients." [Journal of Thrombosis and Haemostasis](#) 16(7): 1307-1312.

[Full Text](#)

*Department of Internal Medicine*

Essentials: Warfarin typically requires International Normalized Ratio (INR) testing at least every 4 weeks. We implemented extended INR testing for stable warfarin patients in six anticoagulation clinics. Use of extended INR testing increased from 41.8% to 69.3% over the 3 year study. Use of extended INR testing appeared safe and effective. Summary: Background A previous single-center randomized trial suggested that patients with stable International Normalized Ratio (INR) values could safely receive INR testing as infrequently as every 12 weeks. Objective To test the success of implementation of an extended INR testing interval for stable warfarin patients in a practice-based, multicenter collaborative of anticoagulation clinics. Methods: At six

anticoagulation clinics, patients were identified as being eligible for extended INR testing on the basis of prior INR value stability and minimal warfarin dose changes between 2014 and 2016. We assessed the frequency with which anticoagulation clinic providers recommended an extended INR testing interval (> 5 weeks) to eligible patients. We also explored safety outcomes for eligible patients, including next INR values, bleeding events, and emergency department visits. Results: At least one eligible period for extended INR testing was identified in 890 of 3362 (26.5%) warfarin-treated patients. Overall, the use of extended INR testing in eligible patients increased from 41.8% in the first quarter of 2014 to 69.3% in the fourth quarter of 2016. The number of subsequent out-of-range next INR values were similar between eligible patients who did and did not have an extended INR testing interval (27.3% versus 28.4%, respectively). The numbers of major bleeding events were not different between the two groups, but rates of clinically relevant non-major bleeding (0.02 per 100 patient-years versus 0.09 per 100 patient-years) and emergency department visits (0.07 per 100 patient-years versus 0.19 per 100 patient-years) were lower for eligible patients with extended INR testing intervals than for those with non-extended INR testing intervals. Conclusions: Extended INR testing for stable warfarin patients can be successfully and safely implemented in diverse, practice-based anticoagulation clinic settings.

Bartolone SN, Tree MO, Conway MJ, **Chancellor MB** and **Lamb LE** (2018). "Reverse transcription-loop-mediated isothermal amplification (RT-LAMP) assay for zika virus and housekeeping genes in urine, serum, and mosquito samples." *Journal of Visualized Experiments* 2018(139), e58436.

[Full Text](#)

*Department of Urology*

Infection with Zika virus (ZIKV) can be asymptomatic in adults, however, infection during pregnancy can lead to miscarriage and severe neurological birth defects. The goal of this protocol is to quickly detect ZIKV in both human and mosquito samples. The current gold standard for ZIKV detection is quantitative reverse transcription PCR (qRT-PCR); reverse transcription loop-mediated isothermal amplification (RT-LAMP) may allow for a more efficient and low-cost testing without the need for expensive equipment. In this study, RT-LAMP is used for ZIKV detection in various biological samples within 30 min, without first isolating the RNA from the sample. This technique is demonstrated using ZIKV infected patient urine and serum, and infected mosquito samples. 18S ribosomal ribonucleic acid and actin are used as controls in human and mosquito samples, respectively.

Baugh CW, **Clark CL**, Wilson JW, Stiell IG, Kocheril AG, Luck KK, Myers TD, Pollack CV, Jr., Roumpf SK, Tomassoni GF, Williams JM, Patel BB, Wu F and Pines JM (2018). "Creation and implementation of an outpatient pathway for atrial fibrillation in the emergency department setting: Results of an expert panel." *Academic Emergency Medicine* 25(9): 1065-1075.

[Full Text](#)

*Department of Emergency Medicine*

Atrial fibrillation and flutter (AF) is a common condition among emergency department (ED) patients in the United States. Traditionally, ED care for primary complaints related to AF focus on rate control, and patients are often admitted to an inpatient setting for further care. Inpatient care may include further telemetry monitoring and diagnostic testing, rhythm control, a search for identification of AF etiology, and stroke prophylaxis. However, many patients are eligible for safe and effective outpatient management pathways. They are widely used in Canada and other countries but less widely adopted in the United States. In this project, we convened an expert panel to create a practical framework for the process of creating, implementing, and maintaining an outpatient AF pathway for emergency physicians to assess and treat AF patients, safely reduce hospitalization rates, ensure appropriate stroke prophylaxis, and effectively transition patients to longitudinal outpatient treatment settings from the ED and/or observation unit. To support local pathway creation, the panel also reached agreement on a protocol development plan, a sample pathway, consensus recommendations for pathway components, sample pathway metrics, and a structured literature review framework using a modified Delphi technique by a technical expert panel of emergency medicine, cardiology, and other stakeholder groups.

Bayci A and **Akay B** (2018). "Advanced techniques in the use of negative pressure wound therapy for closure of complex neonatal abdominal wounds." *Journal of Wound Ostomy and Continence Nursing* 45(5): 468-471.

[Full Text](#)

*Department of Surgery*

Background: Negative pressure wound therapy (NPWT) has been described for closure of complex neonatal abdominal wounds, but advanced techniques for stoma or fistula control, skin protection, and the use of high pressure therapy not as well established. Cases: We identified neonatal patients at our institution who received NPWT for a complex abdominal wound, defined as a wound associated with a stoma or fistula with partial or complete dehiscence of the abdominal fascia or skin. We then reviewed techniques for decreasing wound contamination and protecting the newborn's skin. One patient had an especially complex wound; she was born at ~23 weeks' gestational age (birth weight 580 g). She developed necrotizing enterocolitis and strictures, requiring multiple surgeries to relieve obstruction, ultimately resulting in an end ileostomy with mucous fistula. She suffered from wound dehiscence and retraction of her surgically created stoma, resulting in a complex abdominal wound with significant damage to the surrounding skin. We used advanced NPWT techniques to heal her wound, including topical skin protectants, placement of an adhesive dressing over the skin prior to placement of negative pressure dressing, placement of a negative pressure sponge directly on the wound bed and stoma, diversion of enteric contents away from the wound using a Malecot catheter, and an increase in the negative pressure applied. Conclusion: Complex neonatal abdominal wounds can be treated effectively using NPWT. The techniques we describe divert enteric contents away from the wound bed while maintaining negative pressure and protecting the surrounding skin. In addition, we used negative pressure up to -125 mm Hg and found it was well tolerated by our patients.

Bhutani VK, **Maisels MJ**, Schutzman DL, Castillo Cuadrado ME, Aby JL, Bogen DL, Christensen RD, Watchko JF, Wong RJ and Stevenson DK (2018). "Identification of risk for neonatal haemolysis." *Acta Paediatrica* 107(8): 1350-1356.

[Full Text](#)

*Department of Pediatrics*

Aim: To identify neonates at risk of haemolytic hyperbilirubinaemia through near-concurrent measurements of total serum/plasma bilirubin (TB) or transcutaneous bilirubin (TcB) and end-tidal breath carbon monoxide (CO), corrected for ambient CO (ETCOc), an index of bilirubin production and haemolysis. Methods: Paired TB/TcB (mg/dL) and ETCOc (ppm) measurements were obtained in newborns (n = 283) at 20 to <60 hours of age in five nurseries. TB/TcB values were assigned TB/TcB percentile risk values using the Bhutani hour-specific nomogram. In infants having two serial TB/TcB measurements (n = 76), TB rate of rise (ROR, mg/dL/h) was calculated. Results: For the entire cohort (n = 283), 67.1% and 32.9% had TB/TcB <75th and ≥75th percentile, respectively. TB/TcB ( $5.79 \pm 1.84$  vs  $9.14 \pm 2.25$  mg/dL) and ETCOc ( $1.61 \pm 0.45$  vs  $2.02 \pm 1.35$  ppm, p = 0.0002) were different between the groups. About 36.6% of infants with TB/TcB ≥75th percentile had ETCOc ≥ 2.0 ppm. In the subcohort of infants with serial TB/TcB measurements (n = 76), 44.7% and 55.3% had TB/TcB <75th and ≥75th percentile, respectively. TB/TcB ( $5.28 \pm 1.97$  vs  $9.53 \pm 2.78$  mg/dL), ETCOc ( $1.72 \pm 0.48$  vs  $2.38 \pm 1.89$  ppm, p = 0.05) and TB ROR ( $0.011 \pm 0.440$  vs  $0.172 \pm 0.471$  mg/dL/h) were different between the groups. Conclusion: The combined use of TB/TcB percentile risk assessments and ETCOc measurements can identify infants with haemolytic hyperbilirubinaemia. The addition of TB ROR can identify those infants with elimination disorders.

Bowdon M, **Franklin BA**, **Marcovitz P**, **Jain SK**, Boura J and **Liroff KG** (2018). "Exercise training in "at-risk" black and white women: A comparative cohort analyses." *Medicine & Science in Sports & Exercise* 50(7): 1350-1356.

[Full Text](#)

*Department of Internal Medicine*

*OUIWB Medical Student Author*

Purpose: Few data on the effect of exercise interventions in black women at risk for cardiovascular disease are available. Methods: Women ≥18 yr of age without known cardiovascular disease with ≥1 coronary risk factor were enrolled in a community-based exercise program ≥3 d-wk<sup>-1</sup> for ≥30 min per session for 6 months. Exercise training intensity ~50% to 80% of functional capacity, using heart rate (HR) and/or rating of perceived exertion (RPE) as the primary intensity modulators. Preconditioning versus postconditioning quality of life assessments (depression and level of daytime sleepiness), dietary fat intake, Duke Activity Status Index score, changes in cardiovascular efficiency (systolic/diastolic blood pressure (SBP/DBP), HR, RPE during a standardized submaximal workload), and anthropometric measures, including body weight, body mass index, and waist circumference, were evaluated. Results: Of 556 volunteers, 143 were excluded, leaving

413 women (222 white, 191 black; mean  $\pm$  SD age, 61  $\pm$  9 yr) who met compliance criteria. Both groups demonstrated significant ( $P < 0.05$ ) postconditioning decreases in body mass index, waist circumference, resting SBP/DBP, and total and LDL cholesterol, and reductions in HR, SBP/DBP, and RPE at a fixed submaximal workload, and in fat screener, depression, and sleep scores. Duke Activity Status Index scores increased significantly ( $P < 0.0001$ ) for both groups, signifying increases in self-reported functional capacity. Although 87 women (21%) experienced a musculoskeletal injury/discomfort during the program, there were no exercise-related cardiovascular events. Conclusions: A progressive moderate-to-vigorous exercise intervention without preliminary exercise testing elicited comparable improvements in coronary risk factors, anthropometric and quality of life measures, and cardiovascular efficiency in "at-risk" black and white women. These adaptations were achieved at exercise levels below those recommended in contemporary physical activity guidelines.

Braley TJ, Huber AK, Segal BM, Kaplish N, **Saban R**, Washnock-Schmid JM and Chervin RD (2018). "A randomized, subject and rater-blinded, placebo-controlled trial of dimethyl fumarate for obstructive sleep apnea." *Sleep* 41(8), zsy109.

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*OUWB Medical Student Author*

Study Objectives: To investigate the therapeutic effect of dimethyl fumarate (DMF, an immunomodulatory agent) on obstructive sleep apnea (OSA), and potential influence of any such effect by selected proinflammatory molecules. Methods: Patients with OSA who deferred positive airway pressure therapy were randomized (2:1) to receive DMF or placebo for 4 months. Participants underwent polysomnography before randomization and at 4 months. Blood was collected monthly. The primary outcome was the mean group change in respiratory disturbance index (delta-RDI). Secondary analyses focused on the association between treatment effect of DMF (on RDI) and expression of plasma cytokines and chemokines, or nuclear factor kappa-B (NFkappaB) signaling molecules in peripheral blood mononuclear cells. Results: N = 65 participants were randomized. N = 50 participants (DMF = 35, placebo = 15) had complete data for final analyses. The mean difference in delta-RDI between groups was 13.3 respiratory events/hour of sleep: -3.1+/-12.9 vs. 10.2+/-13.1 in DMF and placebo groups, respectively (mixed-effects model treatment effect: beta = -0.14, SE = 0.062, p = 0.033). Plasma levels of TNF-alpha showed only nonsignificant decreases, and IL-10 and IL-13 only nonsignificant increases, in DMF-treated participants compared with placebo. No significant interaction or main effect on RDI for selected cytokines and chemokines was found. Participants with a therapeutic response to DMF did experience significant reductions in intracellular NFkappaB signaling molecules at 4 months. Overall, DMF was well-tolerated. Conclusions: The immunomodulatory drug DMF partially ameliorates OSA severity. Suppression of systemic inflammation through reduction of NFkappaB signaling may mediate this effect.

**Brown OW** (2018). "Invited Commentary." *Annals of Vascular Surgery* 51: 29-30.

*Department of Surgery*

I read with interest the preceding article in this issue of *Annals of Vascular Surgery* by Phair et al. regarding medical malpractice and vascular surgeons. The authors make an excellent attempt at giving us a better understanding of the factors that lead to the filing of medical malpractice claims against members of our specialty by reviewing cases from a national databank. However, as noted in their manuscript, the Westlaw database is extremely limited and contains only a small fraction of the cases that are filed each year.

Cami E, **Safian R**, **Raff G**, Tagami T, Renard B, **Gallagher M**, **Chinnaiyan K**, Bilolikar AN, **Fan A** and Hafeez A (2018). "TCT-578 assessment of lesion-specific ischemia using fractional flow reserve (FFR) profiles derived from coronary computed tomography angiography (FFRCT) and invasive measurements (FFRINV): Importance of the site of measurement and implications for patient referral for invasive coronary angiography." *Journal of the American College of Cardiology (JACC)* 72(13): B231-B232.

[Full Text](#)

*Department of Internal Medicine*

*OUWB Medical Student Author*

**Cappell MS**, **Hader I** and **Amin M** (2018). "Acute liver failure secondary to severe systemic disease from fatal

hemophagocytic lymphohistiocytosis: Case report and systematic literature review." World Journal of Hepatology 10(9): 629-636.

[Full Text](#)

*Department of Internal Medicine*

*Department of Pathology*

Aim: To systematically review liver disease associated with hemophagocytic lymphohistiocytosis (HLH), propose reasonable contraindications for liver transplantation for liver failure in HLH, and report an illustrative case. Methods: Systematic review according to PRISMA guidelines of hepatic manifestations of HLH using computerized literature search via PubMed of articles published since 1980 with keywords ("hemophagocytic lymphohistiocytosis" or "HLH") AND ("liver" or "hepatic"). Two authors independently performed literature search and incorporated articles into this review by consensus. Illustrative case report presented based on review of medical chart, and expert re-review of endoscopic photographs, radiologic images, and pathologic slides. Results: A 47-year-old Caucasian male, was hospitalized with high-grade pyrexia, rash, total bilirubin = 45 g/dL, moderately elevated hepatic transaminases, ferritin of 3300 ng/dL, leukopenia, and profound neutropenia (absolute neutrophil count < 100 cells/mm<sup>3</sup>). Viral serologies for hepatitis A, B, and C were negative. Abdominal computed tomography scan and magnetic resonance imaging revealed no hepatic or biliary abnormalities. Pathologic analysis of liver biopsy revealed relatively well-preserved hepatic parenchyma without lymphocytic infiltrates or macrophage invasion, except for sparse, focal hepatocyte necrosis. Bone marrow biopsy and aspirate revealed foamy macrophages engulfing mature and precursor erythrocytes, consistent with HLH. Interleukin-2 receptor (CD25) was highly elevated, confirming diagnosis of HLH according to Histiocytic Society criteria. Patient initially improved after high-dose prednisone therapy. Patient was judged not to be a liver transplant candidate despite model for end stage liver disease (MELD) score = 33 because liver failure was secondary to severe systemic disease from HLH, including septic shock, focal centrilobular hepatocyte necrosis from hypotension, bone marrow failure, and explosive immune activation from HLH. The patient eventually succumbed to overwhelming sepsis, progressive liver failure, and disseminated intravascular coagulopathy. Systematic review reveals liver injury is very common in HLH, and liver failure can sometimes occur. Data on liver transplantation for patients with HLH are very limited, and so far the results have shown a generally much worse prognosis than for other liver transplant indications. Liver transplantation should not be guided solely by MELD score, but should include liver biopsy results and determination whether liver failure is from intrinsic liver injury vs multisystem (extrahepatic) organ failure from HLH. Conclusion: This case report illustrates that liver transplantation may not be warranted when liver failure associated with HLH is primarily from multisystem failure from HLH. Liver biopsy may be very helpful in determining the severity and pathophysiology of the liver disease.

Chae J, Siljander M and **Wiater JM** (2018). "Instability in reverse total shoulder arthroplasty." Journal of the American Academy of Orthopaedic Surgeons 26(15). 587-596.

[Full Text](#)

*Department of Orthopedic Surgery*

Recently, indications for reverse total shoulder arthroplasty have expanded to include glenohumeral arthritis, rotator cuff arthropathy, irreparable rotator cuff tears, complex proximal humerus fractures, sequelae of trauma, and failed shoulder prostheses. Dislocation is a common complication, with rates ranging from 1.5% to 31%. The literature pertaining to management of instability in reverse total shoulder arthroplasty is scanty. Assessment of the patient and biomechanical and surgical factors is critical in determining the best course of treatment. Future studies involving patient selection, prosthetic design, surgical technique, and biomechanics may help reduce the rate of instability.

Chang AJ, McBride S, Keyes M, Chung HT, Davis BJ, Cox BW, Crook J, Demanes DJ, Hsu IC, Kamrava M, **Krauss DJ**, Morton G, III PFO, III MR, Venkat PS, Vigneault E and Zelefsky MJ (2018). "The American Brachytherapy Society and the American Radium Society Appropriate Use Criteria Genitourinary Committee endorse the American Society of Clinical Oncology/Cancer Care Ontario Guidelines." Journal of Clinical Oncology 36(33): 3342-3344.

[Full Text](#)

*Department of Radiation Oncology*

Chang AM, Hollander JE, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM,

**Clark CL**, Diercks DB, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2018). "Recurrent syncope is not an independent risk predictor for future syncopal events or adverse outcomes." The American Journal of Emergency Medicine. ePub Ahead of Print.

[Full Text](#)

*Department of Emergency Medicine*

Almost 20% of patients with syncope will experience another event. It is unknown whether recurrent syncope is a marker for a higher or lower risk etiology of syncope. The goal of this study is to determine whether older adults with recurrent syncope have a higher likelihood of 30-day serious clinical events than patients experiencing their first episode. **Methods** This study is a pre-specified secondary analysis of a multicenter prospective, observational study conducted at 11 emergency departments in the US. Adults 60 years or older who presented with syncope or near syncope were enrolled. The primary outcome was occurrence of 30-day serious outcome. The secondary outcome was 30-day serious cardiac arrhythmia. In multivariate analysis, we assessed whether prior syncope was an independent predictor of 30-day serious events. **Results** The study cohort included 3580 patients: 1281 (35.8%) had prior syncope and 2299 (64.2%) were presenting with first episode of syncope. 498 (13.9%) patients had 1 prior episode while 771 (21.5%) had >1 prior episode. Those with recurrent syncope were more likely to have congestive heart failure, coronary artery disease, previous diagnosis of arrhythmia, and an abnormal ECG. Overall, 657 (18.4%) of the cohort had a serious outcome by 30 days after index ED visit. In multivariate analysis, we found no significant difference in risk of events (adjusted odds ratio 1.09; 95% confidence interval 0.90–1.31;  $p = 0.387$ ). **Conclusion** In older adults with syncope, a prior history of syncope within the year does not increase the risk for serious 30-day events.

**Chapman J, Bartholomew B and Al-Katib S** (2018). "Extrauterine endometrial stromal sarcoma arising in a background of endometriosis following prior total abdominal hysterectomy." Journal of Endometriosis and Pelvic Pain Disorders 10(3): 133-135.

[Request Form](#)

*Department of Diagnostic Radiology and Molecular Imaging*

*OUIWB Medical Student Author*

This article describes a case of endometrial stromal sarcoma arising in a background of endometriosis presenting several years after total abdominal hysterectomy. Discussion of endometrial stromal sarcoma ensues as well as review of pertinent imaging findings.

Chatterjee NA, Moorthy MV, Pester J, Schaecter A, Panicker GK, Narula D, Lee DC, Goldberger JJ, Kadish A, Cook NR, Albert CM, Elbert CM, Mahal S, Sobolski J, Danciu S, Dyke C, Phang R, Wolinsky D, Biederman R, McLaurin B, Trichon B, Serfas D, Aslam A, Bugni W, Hany A, Jiang L, Marais H, Durr S, Reinoehl J, Graham S, Sadler D, Erenrich N, Spencer R, Griffin JEA, Geohas C, Treasure CB, Baki T, Huneycutt D, Jr., Saliba W, Svinarich JT, Whang W, Jetty P, Shanes J, McGarvey J, Hankins S, White LL, DeLurgio D, Karunaratne H, Flores E, Gillespie E, McKenzie J, Staniloae C, Altschuller A, Schuger C, Radin M, Pohost G, Myers M, Bunch TJ, Wickemeyer W, Mendelson R, Berger R, Ross T, Sumner A, Arcement L, Malik B, Claxton N, Rohr K, Weiss R, Garcia-Rinaldi R, Kazmierski J, Rosenbaum D, Blonder R, Ramanathan K, O'Neill G, Cochran K, Kaufman E, Costantini O, Husted S, Sahul Z, Bengston J, Lader E, Nora M, Gornick C, Adabag S, Tishler S, Klein S, Lamas G, Baig M, Ratliff M, Iwai S, Johnson G, Oliver T, Langer M, Ahn J, Silver KH, Mattson SE, Schmidt J, Ramanathan PK, Heitner J, Riba A, Thadani U, Shah S, Sandler D, Bello D, Mostel E, Patel R, Simpson P, Hack T, Shoultz C, Figueredo R, Atieh M, Herre J, Bhasin M, Gauri A, Gottlieb C, Hotvedt P, Chaudhry M, Greenberg S, Tsai WK, Averbach M, Cheong B, Mittal S, Baker J, McGrew F, III, Kraus D, Skopicki H, Lee S, Gredler F, Islam J, Mohiuddin S, Valderrabano M, Nasir N, Anderson D, Niebauer M, Colon-Hernandez P, Mackall J, Sandhu R, Ott P, Nayak H, Dunlap S, Aranda J, Hsu S, Owens S, See V, Menees D, Flaker G, Saba S, Fong M, Aktas M, O'Brien T, Bernstein V, Saavedra P, Koshy M, Whalen S, Eldadah Z, **Haines D** and Marzo K (2018). "Sudden death in patients with coronary heart disease without severe systolic dysfunction." JAMA Cardiology 3(7): 591-600.

[Full Text](#)

*Department of Internal Medicine*

**Importance:** The majority of sudden and/or arrhythmic deaths (SAD) in patients with coronary heart disease occur in those without severe systolic dysfunction, for whom strategies for sudden death prevention are lacking. **Objective:** To provide contemporary estimates of SAD vs other competing causes of death in patients with coronary heart disease without severe systolic dysfunction to search for high-risk subgroups that might be targeted in future trials of SAD prevention. **Design, Setting, and Participants:** This prospective

observational cohort study included 135 clinical sites in the United States and Canada. A total of 5761 participants with coronary heart disease who did not qualify for primary prevention implantable cardioverter defibrillator therapy based on left ventricular ejection fraction (LVEF) of more than 35% or New York Heart Association (NYHA) heart failure class (LVEF >30%, NYHA I). EXPOSURES Clinical risk factors measured at baseline including age, LVEF, and NYHA heart failure class. Main Outcomes and Measures: Primary outcome of SAD, which is a composite of SAD and resuscitated ventricular fibrillation arrest. RESULTS The mean (SD) age of the cohort was 64 (11) years. During a median of 3.9 years, the cumulative incidence of SAD and non-SAD was 2.1% and 7.7%, respectively. Sudden and/or arrhythmic death was the most common mode of cardiovascular death accounting for 114 of 202 cardiac deaths (56%), although noncardiac death was the primary mode of death in this population. The 4-year cumulative incidence of SAD was lowest in those with an LVEF of more than 60% (1.0%) and highest among those with LVEF of 30% to 40% (4.9%) and class III/IV heart failure (5.1%); however, the cumulative incidence of non-SAD was similarly elevated in these latter high-risk subgroups. Patients with a moderately reduced LVEF (40%-49%) were more likely to die of SAD, whereas those with class II heart failure and advancing age were more likely to die of non-SAD. The proportion of deaths due to SAD varied widely, from 14% (18 of 131 deaths) in patients with NYHA II to 49% (37 of 76 deaths) in those younger than 60 years. Conclusions and Relevance: In a contemporary population of patients with coronary heart disease without severe systolic dysfunction, SAD accounts for a significant proportion of overall mortality. Moderately reduced LVEF, age, and NYHA class distinguished SAD and non-SAD, whereas other markers were equally associated with both modes of death. Absolute and proportional risk of SAD varied significantly across clinical subgroups, and both will need to be maximized in future risk stratification efforts.

Chaudhury A, Dendi VSR, Chaudhury M, Jain A, Kasarla MR, Panuganti K, Jain G, Ramanujam A, Rena B, Koyagura SR, **Fogla S**, Kumar S, Shekhawat NS and Maddur S (2018). "HSV1/2 genital infection in mice cause reversible delayed gastrointestinal transit: A model for enteric myopathy." *Frontiers in Medicine* 5: 176-176.

[Full Text](#)

*Department of Family Medicine and Community Health*

In an interesting investigation by Khoury-Hanold et al. (1), genital infection of mice with herpes simplex virus 1 (HSV1) were reported to cause multiple pelvic organ involvement and obstruction. A small subset of mice succumbed after the first week of HSV1 infection. The authors inferred that the mice died due to toxic megacolon. In a severe form of mechanical and/or functional obstruction involving gross dilation of the colon and profound toxemia, the presentation is called "toxic megacolon." The representative observations by Khoury-Hanold likely do not resemble toxic megacolon. The colon was only slightly dilated and benign appearing. Importantly, HSV1 infection affected the postjunctional mechanisms of smooth muscle relaxation like the sildenafil-response proteins, which may have been responsible for defective nitric neurotransmission and the delayed transit. Orally administered polyethylene glycol reversed the gastrointestinal "obstruction," suggesting a mild functional type of slowed luminal transit, resembling constipation, rather than toxic megacolon, which cannot be reversed by an osmotic laxative without perforating the gut. The authors suggest that the mice did not develop HSV1 encephalitis, the commonly known cause of mortality. The premature death of some of the mice could be related to the bladder outlet obstruction, whose backflow effects may alter renal function, electrolyte abnormalities and death. Muscle strip recordings of mechanical relaxation after electrical field stimulation of gastrointestinal, urinary bladder or cavernosal tissues shall help obtain objective quantitative evidence of whether HSV infection indeed cause pelvic multi-organ dysfunction and impairment of autonomic neurotransmission and postjunctional electromechanical relaxation mechanisms of these organs.

Chen C-J, Ding D, Kano H, Mathieu D, Kondziolka D, Feliciano C, Rodriguez-Mercado R, **Grills IS**, Barnett G, Lunsford LD and Sheehan JP (2018). "Stereotactic radiosurgery for pediatric versus adult brain arteriovenous malformations." *Stroke* 49(8): 1939-1945.

[Full Text](#)

*Department of Radiation Oncology*

Background and Purpose: The aim of this international, multicenter, retrospective matched cohort study is to directly compare the outcomes after stereotactic radiosurgery (SRS) for brain arteriovenous malformations (AVM) in pediatric versus adult patients. Methods: We performed a retrospective review of patients with

AVM who underwent SRS at 8 institutions participating in the International Gamma Knife Research Foundation from 1987 to 2014. Patients were categorized into pediatric (<18 years of age) and adult (≥18 years of age) cohorts and matched in a 1:1 ratio using propensity scores. Favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-induced changes. Results: From a total of 2191 patients who were eligible for inclusion in the overall study cohort, 315 were selected for each of the matched cohorts. There were no significant differences between matched pediatric versus adult cohorts with respect to the rates of favorable outcome (59% versus 58%; P=0.936), AVM obliteration (62% versus 63%; P=0.934), post-SRS hemorrhage (9% versus 7%; P=0.298), radiological radiation-induced changes (26% versus 26%; P=0.837), symptomatic radiation-induced changes (7% versus 9%; P=0.383), or permanent radiation-induced changes (2% versus 3%; P=0.589). The all-cause mortality rate was significantly lower in the matched pediatric cohort (3% versus 10%; P=0.003). Conclusions: The outcomes after SRS for comparable AVMs in pediatric versus adult patients were not found to be appreciably different. SRS remains a reasonable treatment option for appropriately selected pediatric patients with AVM, who harbor a high cumulative lifetime hemorrhage risk. Age seems to be a poor predictor of AVM outcomes after SRS.

**Chu D, Xiao J, Shah P and Todd B** (2018). "How common are cognitive errors in cases presented at emergency medicine resident morbidity and mortality conferences?" Diagnosis (Berl) 5(3): 143-150.

[Request Form](#)

*OUWB Medical Student Author*

*Department of Emergency Medicine*

Daley E, Kurdziel MD, Koueiter D and **Moore DD** (2018). "Characterization of doxycycline-loaded calcium phosphate cement: implications for treatment of aneurysmal bone cysts." Journal of Materials Science: Materials in Medicine 29(7): 109.

[Full Text](#)

*Department of Orthopedic Surgery*

Percutaneous doxycycline for treatment for aneurysmal bone cysts (ABCs) has been shown to decrease recurrence rates, however, this requires multiple procedures, includes the risks soft tissue necrosis, and does not provide structural support. We propose utilizing curettage with doxycycline-loaded calcium phosphate cement. This study aimed to evaluate the elution profile of doxycycline from calcium phosphate cement. Calcium phosphate cement underwent an in vitro elution protocol evaluating doxycycline concentrations of 0, 5, 10, and 15 mg/mL. Eluted concentrations were quantified utilizing high performance liquid chromatography at predetermined time points over 96 h. Compressive strength was evaluated both pre- and post-elution and micro-computed tomography was utilized to assess changes in cement porosity. Cement with 15 mg/mL of doxycycline maintained a higher average concentration (mean, 95% confidence intervals) (14.5 µg/mL [9.2–19.9 µg/mL]) compared to both 5 mg/mL (5.8 µg/mL [3.1–8.6 µg/mL]; P < 0.001) and 10 mg/mL (8.4 ± µg/mL [6.0–10.9 µg/mL]; P < 0.001). Ultimate stress significantly decreased between pre- and post-elution samples for 10 mg/mL (P = 0.001) and 15 mg/mL (P = 0.004) groups. This study demonstrated a dose-dependent response in ultimate strength and compressive modulus with addition of doxycycline to calcium phosphate cement.

David JM, Gresham G, Jabbour SK, Deek M, Thomassian S, Robertson JM, Newman NB, Herman JM, Osipov A, **Kabolizadeh P** and Tuli R (2018). "Neoadjuvant PET and MRI-based intensity modulated radiotherapy leads to less toxicity and improved pathologic response rates in locally advanced rectal cancer." Journal of Gastrointestinal Oncology 9(4): 641-649.

[Full Text](#)

*Department of Radiation Oncology*

Background: Neoadjuvant chemoradiation (NeoCRT) is standard of care for the treatment of locally advanced rectal cancer (LARC). Contemporary radiation techniques and pre-treatment imaging may impact toxicities and pathologic response (PR). Herein we compare intensity modulated radiotherapy (IMRT) and advanced pre-treatment imaging in the neoadjuvant treatment of LARC and resulting impact on toxicities and pathologic outcomes relative to 3 dimensional conformal radiotherapy (3DCRT). Methods: LARC patients treated at 4 large academic centers in the US from 2007-2016 were reviewed. Patients received 5-FU-based

NeoCRT concurrently with IMRT or 3DCRT. PR was recorded as none, partial, or complete. Common terminology for adverse events version 4 was used to grade toxicities. Toxicity rates were compared using Chi-square analysis. Multivariable models were fit adjusting for age, gender, pre-tx CT to identify independent predictors of PR and toxicity. RESULTS: A total of 128 patients were analyzed: 60.1% male and 39.8% female, median age 57.7 years (range, 31-85 years). Clinical characteristics were similar across RT groups. The outcome of partial and complete PR was similar for IMRT and 3DCRT (48.1%, 23.1% vs. 31.7%, 23.3%), respectively. After adjusting for gender, age, and pre-RT chemotherapy type, IMRT and pretreatment PET and/or MRI imaging was significantly associated with increased odds for complete and partial response (OR =2.95, 95% CI: 1.21-7.25, P=0.018; OR =14.70, 95% CI: 3.69-58.78, P<0.0001). Additionally, IMRT was associated with reduced rates of dehydration, dermatitis, rectal pain, rectal bleeding, and diverting ostomy (P<0.05). Overall rates of grade 2 and higher toxicities were significantly reduced in IMRT vs. 3DCRT after adjusting for confounders (OR =0.27, 95% CI: 0.08-0.87). Conclusions: NeoCRT IMRT with pretreatment PET and/or MRI for LARC leads to reduced acute toxicities and improved PR compared to 3DCRT. Given the challenges associated with prospective validation of these data, IMRT with pretreatment PET and/or MRI should be considered standard treatment for LARC.

Davis FM, Albright J, Kazmers A, Monsour A, **Bove P** and Henke PK (2018). "Evaluating patterns and appropriateness of aortic aneurysm repair within a statewide vascular surgery registry." Journal of Vascular Surgery 68(3): E48-E48.

[Full Text](#)

*Department of Surgery*

Ding XF, **Li XQ, Qin A, Zhou J, Yan D, Chen P**, Prakash C, **Stevens C, Deraniyagala R** and **Kabolizadeh P** (2018). "Redefine the role of range shifter in treating bilateral head and neck cancer in the era of Intensity Modulated Proton Therapy." Journal of Applied Clinical Medical Physics 19(5): 749-755.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Radiation Oncology*

Disbrow D, Seelbach CL, Albright J, Ferraro J, Wu J, **Hain JM**, Shanker BA and Cleary RK (2018). "Statin medications are associated with decreased risk of sepsis and anastomotic leaks after rectal resections." American Journal of Surgery 216(1): 31-36.

[Full Text](#)

*Department of Surgery*

Background: This study was designed to determine the effect of statins on colorectal postoperative complications related to sepsis. Previous studies have reported conflicting results. Methods: This is a retrospective propensity score analysis of postoperative outcomes from a large regional database of patients who underwent elective colorectal resection from June 2012–July 2015. Results: 7285 patients met inclusion criteria: 34.5% received statins. Propensity score matching revealed that patients taking statins had reduced risk of sepsis (3.75% vs 5.32%, p =.03). Subgroup analysis revealed that this difference was driven by patients undergoing rectal resections. Among the rectal resection group, anastomotic leaks were more common in the non-statin group (4.1% vs. 1.3%, p =.01). There was no significant difference between those taking statins and those not on statin medications with respect to composite SSI or 30-day mortality. Conclusions: Statin medications are associated with decreased risk of sepsis after colorectal surgery and anastomotic leaks after rectal resection. Future studies should focus on medication type, dosage, and duration to confirm these results and identify patient populations that would benefit most from statin therapy.

Eijsvogels TMH, Thompson PD and **Franklin BA** (2018). "The "Extreme Exercise Hypothesis": Recent findings and cardiovascular health implications." Current Treatment Options in Cardiovascular Medicine 20(10): 84-84.

[Full Text](#)

*Department of Internal Medicine*

Purpose of Review: The "Extreme Exercise Hypothesis" is characterized by a U-shaped or reverse J-shaped, dose-response curve between physical activity volumes and cardiovascular health outcomes. In this review, we summarize recent findings that may support or refute the "Extreme Exercise Hypothesis." Furthermore, we discuss potential cardiovascular health implications of the cardiac anatomical, structural, contractility, and

biomarker abnormalities that have been reported in some veteran endurance athletes. Recent Findings: Emerging evidence from epidemiological studies and observations in cohorts of endurance athletes suggest that potentially adverse cardiovascular manifestations may occur following high-volume and/or high-intensity long-term exercise training, which may attenuate the health benefits of a physically active lifestyle. Accelerated coronary artery calcification, exercise-induced cardiac biomarker release, myocardial fibrosis, atrial fibrillation, and even higher risk of sudden cardiac death have been reported in athletes. There is primarily circumstantial evidence that supports the "Extreme Exercise Hypothesis." Subclinical and atherosclerotic coronary artery disease (CAD) as well as structural cardiovascular abnormalities and arrhythmias are present in some of the most active veteran endurance athletes and need appropriate clinical follow-up to reduce the risk for adverse cardiovascular outcomes. Future studies are warranted to establish the long-term cardiovascular health effects of these findings in veteran endurance athletes.

Engel T, Thomas C, Medado P, **Bastani A**, Reed B, Millis S and O'Neil B (2018). "End tidal CO<sub>2</sub> vs cerebral oximetry during cardiopulmonary resuscitation." *Resuscitation* 130: e5-e5.

[Full Text](#)

*Department of Emergency Medicine*

Fahs AM, Koueiter DM, Kurdziel MD, **Huynh KA**, Perry CR and **Verner JJ** (2018). "Psoas compartment block vs periarticular local anesthetic infiltration for pain management after anterior total hip arthroplasty: A prospective, randomized study." *Journal of Arthroplasty* 33(7): 2192-2196.

[Full Text](#)

*Department of Orthopedic Surgery*

*OUWB Medical Student Author*

Background: The psoas compartment block (PCB) or periarticular soft-tissue local anesthetic injection are forms of regional anesthesia often used as one of the components in multimodal anesthesia applied during total hip arthroplasty (THA). The most efficacious form of regional anesthesia for THA has yet to be determined. Methods: In a single-surgeon, prospective, clinical trial, patients undergoing THA via direct anterior approach were randomized to receive an intraoperative periarticular local anesthetic infiltration (periarticular injection) or a PCB. Postoperative pain scores, narcotic consumption, and complications were recorded. Results: Forty-nine patients were randomized to the PCB and 50 were randomized to the periarticular injection. The resting pain score 3 hours postoperatively was statistically significantly lower in the periarticular injection group by 1.1 point ( $2.9 \pm 2.2$  vs  $4.0 \pm 2.2$ ,  $P = .036$ ). No difference was found in resting pain scores or ambulatory pain scores in the morning or evening of postoperative day 1, 2, or at the 3-week follow-up visit. There was no difference in in-hospital narcotic consumption between groups ( $P = 1.0$ ). There were no major complications directly related to the block in either group. A total of 6 patients reported complaints of transient numbness, 5 in the PCB group (5/49, 10.2%), and one in the periarticular injection group (1/50, 2%,  $P = .087$ ). Conclusion: These results demonstrate similarity between the 2 methods. We prefer periarticular anesthetic infiltration over PCB due to improved immediate postoperative pain scores and avoidance of potential symptoms associated with nerve blockade.

**Faraj K**, Dave CN, Patel K, **Seifman B**, **Vartanian S**, Frontera R, Nelson R, **Hafron J** and Schervish EW (2018). "A retrospective comparative outcomes and cost analysis of office based, ultrasound guided renal mass biopsy performed by urologists and standard hospital biopsies for small renal masses." *Urology Practice* 5(4): 260-265.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Urology*

*Department of Diagnostic Radiology and Molecular Imaging*

Introduction: Renal mass biopsy is useful in the evaluation of small renal masses. We have previously reported that office based, ultrasound guided renal mass biopsy is safe, effective and feasible when performed by urologists. This study compares office based, ultrasound guided renal mass biopsy performed by urologists and hospital based renal mass biopsy. Methods: We retrospectively studied 70 patients who underwent office based, ultrasound guided renal mass biopsy and 155 who underwent hospital based, ultrasound or computerized tomography guided renal mass biopsy for evaluation of a small renal mass (4.0 cm or less) between January 2010 and February 2016. Results: A total of 70 patients underwent office based,

ultrasound guided renal mass biopsy. Median age in this group was 69.5 years, median body mass index was 29.5 kg/m<sup>2</sup> and 61.4% of the patients (43) were male. A total of 103 patients underwent hospital based, ultrasound guided biopsy. Median age in this group was 68.0 years, median body mass index was 29.3 kg/m<sup>2</sup> and 53.4% of the patients (55) were male. Finally, 52 patients underwent hospital based, computerized tomography guided biopsy. Median age in this group was 69 years, median body mass index was 30.1 kg/m<sup>2</sup> and 51.9% of the patients (27) were male. Median tumor size was 2.7 cm in patients undergoing office based, ultrasound guided renal mass biopsy, 2.2 cm in those undergoing hospital based, ultrasound guided biopsy and 2.1 cm in those undergoing hospital based, computerized tomography guided biopsy (p = 0.001). Renal cell carcinoma was found in 43 of 70 (61.4%), 74 of 103 (71.8%) and 33 of 52 (63.5%) respective biopsies. Respective diagnostic rates were 81.4% (57 of 70 cases), 88.3% (91 of 103) and 86.5% (45 of 52, p = 0.434). Concordance with surgical pathology was 97.7% (42 of 43 cases), 100% (35 of 35) and 100% (15 of 15), respectively. Complication rates were 4.3% (3 of 70 patients), 13.6% (14 of 103) and 13.5% (7 of 52), respectively (p = 0.096). Cost analysis revealed that when available, office based, ultrasound guided renal mass biopsy provides the health care system a total savings of approximately \$46,011 yearly. Conclusions: Office based, ultrasound guided renal mass biopsy for small renal masses is a safe and efficacious option for select patients, and potentially offers greater convenience and availability as well as decreased health care costs.

Fisher A and **Halalau A** (2018). "A case report and literature review of clostridium difficile negative antibiotic associated hemorrhagic colitis caused by klebsiella oxytoca." Case Reports in Gastrointestinal Medicine 2018: 7264613-7264613.

[Full Text](#)

*Department of Internal Medicine*

Klebsiella oxytoca hemorrhagic colitis is a rare form of antibiotic associated hemorrhagic colitis that is Clostridium difficile negative. Klebsiella oxytoca colitis has been shown to be triggered by penicillin administration, yet other antibiotics have been implicated as well. It can mimic the appearance of ischemic colitis on endoscopy; however it will generally be found in young, otherwise healthy patients without risk factors. We present a case of a 33-year-old Caucasian female who presented to the emergency room with profuse, bloody diarrhea for 5 days, after a one-week course of ampicillin. Colonoscopy was notable for ulcerated mucosa with erythema and easy friability and the biopsy was suggestive of ischemic colitis. Stool culture was positive for many Klebsiella oxytoca. The patient was discharged home with resolution of symptoms after three days in the hospital. She was instructed to avoid penicillin antibiotics and minimize nonsteroidal anti-inflammatory drug use.

**Fortunato JT, Wasserman JA and Menkes DL** (2018). "Placebo analgesia as nocebo reduction." AJOB Neuroscience 9(3): 198-199.

[Full Text](#)

*Department of Neurology*

*OUWB Medical Student Author*

*Department of Foundational Medical Studies*

**Franklin BA, Kaminsky LA and Kokkinos P** (2018). "Quantitating the dose of physical activity in secondary prevention: Relation of exercise intensity to survival." Mayo Clinic Proceedings 93(9): 1158-1163.

[Full Text](#)

*Department of Internal Medicine*

Gaines N, Gupta P, Khourdaji AS, Ehlert M, **Parikh K**, Kohli H and Sirls LT (2018). "Radiographic misdiagnoses after periurethral bulking agents." Female Pelvic Medicine and Reconstructive Surgery 24(4): 312-314.

[Full Text](#)

*OUWB Medical Student Author*

Objectives: Injectable urethral bulking agents are commonly used to manage stress urinary incontinence. Urologic or other symptoms may prompt pelvic imaging at a later date, when bulking agents may be visualized and incorrectly interpreted. Our goal was to evaluate the incidence of misdiagnosis and which pathologies were the most common misinterpretations and their frequency. Methods: All records were

reviewed for patients who underwent periurethral injection for stress urinary incontinence for pelvic imaging after treatment from 2005 to 2015. Radiological reports were reviewed for any description potentially related to injection therapy, and descriptive statistics performed. Results: A total of 528 patients underwent injection of a urethral bulking agent. Of these, 79 patients (15%) had a total of 111 additional abdominal or pelvic imaging studies performed with abnormal periurethral findings mentioned. Thirty-nine (35%) of 111 studies were correctly interpreted as urethral bulking agents, and in 72 (65%) of 111 studies, the urethral bulking agents were not correctly identified. The most common misdiagnoses were bladder calcification (26; 23%), urethral diverticulum with stone (12; 11%), periurethral calcification (9; 8%), unknown pelvic density (8; 7%), and mass suspicious for malignancy (6; 5%). Conclusions: Urethral bulking agents commonly were not mentioned on subsequent imaging but, when commented on, were misinterpreted 65% of the time including worrisome pathologies (diverticulum with stone, unknown mass, and malignancy), requiring subsequent evaluation and potentially procedural/surgical management. It is critical for the ordering clinician to inform the radiologist of this history and for radiologists to consider bulking agents in the differential diagnosis of radiographic findings in this location.

Gaines N, **Odom BD**, Killinger KA and **Peters KM** (2018). "Pudendal neuromodulation as a treatment for persistent genital arousal disorder - A case series." [Female Pelvic Medicine and Reconstructive Surgery](#) 24(4): e1-e5.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Urology*

Background: Persistent genital arousal disorder (PGAD) is a rare life-altering condition characterized by unwanted, uncomfortable genital sensations or spontaneous orgasms without physical or emotional stimulation. Its etiology remains unclear, and a variety of treatments have been attempted with incomplete resolution. We propose that chronic pudendal neuromodulation (CPN) may be a useful treatment for PGAD symptoms. Methods: A retrospective chart review was performed for women older than 18 years with a diagnosis of PGAD that had staged neuromodulation with placement of a tined lead at the pudendal nerve. Demographic, operative, and postoperative data were collected. A survey was then sent to these women to assess additional demographic data, preoperative and postoperative symptoms, and patient satisfaction. Descriptive statistics were performed. Results: Six women underwent CPN for PGAD. Mean age was 52 (SD, 9) years. Five (83%) of 6 were still implanted at time of survey, at a mean of 38 months after implantation; 1 device was removed for nonuse. Four of 6 completed surveys and were still using their device. Three of 4 had met their treatment goals and were satisfied with CPN; 3 of 4 felt CPN was the most useful treatment modality they had used overall. Chronic pudendal neuromodulation also improved chronic pelvic pain (4/4), bowel function (3/4), and bladder function (3/4). Conclusions: Chronic pudendal neuromodulation can be an effective treatment for decreasing frequency of PGAD symptoms and providing symptom relief.

Gbadamosi B, Ezekwudo D, Bastola S and **Jaiyesimi I** (2018). "Predictive and prognostic markers in adults with acute myeloid leukemia: A single-institution experience." [Clinical Lymphoma, Myeloma and Leukemia](#) 18(7): e287-e294.

[Full Text](#)

*Department of Internal Medicine*

Outcomes in acute myeloid leukemia (AML) have been correlated with predictive and prognostic factors including age, performance status, comorbidities, cytogenetics, and molecular mutations. Retrospective review of 137 adult AML patients identified 3+7 (3 days of anthracycline and 7 days of cytarabine) induction and absence of monosomal karyotype to positively predict complete remission whereas positive predictors of overall survival were younger age and the absence of monosomal karyotype. Background: Acute myeloid leukemia (AML) is a heterogeneous malignancy with diverse genetic abnormalities, clinical presentations, and outcomes. Known predictive and prognostic factors in AML include age, performance status, comorbidities, cytogenetics, and molecular mutations. Identifying prognostic and predictive factors can inform the choice of induction therapy and outcomes prediction. Patients and Methods: A retrospective review was performed of 137 adult AML patients from 2010 to 2015. Predictors of complete remission (CR) and overall survival (OS) were determined for patients treated with 3+7 (3 days of anthracycline and 7 days of cytarabine) or hypomethylating agent. Variables associated with CR or OS were assessed using univariate Cox regression and a multivariate Cox model. Results: The average age was 65 years and 91 patients (66%), sample size is 137 patients had primary AML. Patients in the 3+7 induction group were younger, had a higher bone

marrow blast percentage, and more de novo AML compared with those in the hypomethylating agent group (P <.001, P <.001, P =.005, respectively). Univariate logistic regression for CR showed a significant association between age (P <.001), choice of induction (P <.001), and monosomy (P =.015), although only induction with 3+7 (P <.001) and absence of monosomy (P =.042) remained significant in multivariate analysis. Univariate Cox regression indicated that age (P =.003), AML status (de novo or secondary; P =.0277), choice of induction (P =.030), and monosomy (P =.010) had a significant association with OS. Only younger age (P =.018) and absence of monosomy (P =.022) were predictive of OS in multivariate Cox analysis. Conclusion: Positive predictors of CR in adult AML include absence of monosomy and induction treatment with 3+7; whereas positive predictors of OS are younger age and absence of monosomy.

**Genova R**, Meyerson J and Miller MJ (2018). "Miller-Meyerson maneuver for left-handed surgeons." Plastic and Reconstructive Surgery 142(1): 104E-105E.

[Full Text](#)

*OUWB Medical Student Author*

Gjeorgjievski M, Orosey M and **Cappell MS** (2018). "Hepatitis C virus–related cryoglobulinemic vasculitis." Clinical Gastroenterology and Hepatology 16(8): e81.

[Full Text](#)

*Department of Internal Medicine*

**Graham SF**, Pan X, Yilmaz A, Macias S, Robinson A, Mann D and Green BD (2018). "Targeted biochemical profiling of brain from Huntington's disease patients reveals novel metabolic pathways of interest." Biochimica et Biophysica Acta - Molecular Basis of Disease 1864(7): 2430-2437.

[Full Text](#)

*Department of Obstetrics and Gynecology*

Huntington's disease (HD) is a devastating, progressive neurodegenerative disease with a distinct phenotype characterized by chorea and dystonia, incoordination, cognitive decline and behavioral difficulties. The precise mechanisms of HD progression are poorly understood; however, it is known that there is an expansion of the trinucleotide cytosine-adenine-guanine (CAG) repeat in the Huntingtin gene. Herein DI/LC-MS/MS was used to accurately identify and quantify 185 metabolites in post mortem frontal lobe and striatum from HD patients and healthy control cases. The findings link changes in energy metabolism and phospholipid metabolism to HD pathology and also demonstrate significant reductions in neurotransmitters. Further investigation into the oxidation of fatty acids and phospholipid metabolism in pre-clinical models of HD are clearly warranted for the identification of potential therapies. Additionally, panels of 5 metabolite biomarkers were identified in both the frontal lobe (AUC = 0.962 (95% CI: 0.85–1.00) and striatum (AUC = 0.988 (95% CI: 0.899–1.00). This could have clinical utility in more accessible biomatrices such as blood serum for the early detection of those entering the prodromal phase of the disease, when treatment is believed to be most effective. Further evaluation of these biomarker panels in human cohorts is justified to determine their clinical efficacy.

**Graham SF**, Rey NL, Yilmaz A, Kumar P, Madaj Z, **Maddens M**, **Bahado-Singh RO**, Becker K, Schulz E, Meyerdirk LK, Steiner JA, Ma JY and Brundin P (2018). "Biochemical profiling of the brain and blood metabolome in a mouse model of prodromal Parkinson's disease reveals distinct metabolic profiles." Journal of Proteome Research 17(7): 2460-2469.

[Full Text](#)

*Department of Obstetrics and Gynecology*

*Department of Internal Medicine*

Parkinson's disease is the second most common neurodegenerative disease. In the vast majority of cases the origin is not genetic and the cause is not well understood, although progressive accumulation of alpha-synuclein aggregates appears central to the pathogenesis. Currently, treatments that slow disease progression are lacking, and there are no robust biomarkers that can facilitate the development of such treatments or act as aids in early diagnosis. Therefore, we have defined metabolomic changes in the brain and serum in an animal model of prodromal Parkinson's disease. We biochemically profiled the brain tissue and serum in a mouse model with progressive synucleinopathy propagation in the brain triggered by unilateral injection of preformed alpha-synuclein fibrils in the olfactory bulb. In total, we accurately identified

and quantified 71 metabolites in the brain and 182 in serum using NMR and targeted mass spectrometry, respectively. Using multivariate analysis, we accurately identified which metabolites explain the most variation between cases and controls. Using pathway enrichment analysis, we highlight significantly perturbed biochemical pathways in the brain and correlate these with the progression of the disease. Furthermore, we identified the top six discriminatory metabolites and were able to develop a model capable of identifying animals with the pathology from healthy controls with high accuracy (AUC (95% CI) = 0.861 (0.755-0.968)). Our study highlights the utility of metabolomics in identifying elements of Parkinson's disease pathogenesis and for the development of early diagnostic biomarkers of the disease.

Gray CP, **Yakir M** and Hung DY (2018). "Physician engagement with metrics in lean primary care transformation." *Quality Management in Health Care* 27(3): 117-122.

[Full Text](#)

*OUIWB Medical Student Author*

**Gupta A, Micale M** and **Bernacki KD** (2018). "Fluorescence in situ hybridization analysis on cytologic smears: An accurate and efficient method in the diagnosis of melanotic Xp11 translocation renal cancer." *Diagnostic Cytopathology* 46(9): 786-789.

[Full Text](#)

*Department of Pathology*

**Halalau A**, Shelden D, Keeney S and Hehar J (2018). "Pharm-MD; an open-label, randomized controlled, phase II study to evaluate the efficacy of a pharmacist-managed diabetes clinic in high-risk diabetes patients - study protocol for a randomized controlled trial." *Trials* 19(1): 458.

[Full Text](#)

*Department of Internal Medicine*

Background: Millions of Americans are currently living with diabetes and approximately 1.5 million cases are being diagnosed each year. Diabetes is now the seventh leading cause of death in the United States. In addition, the economic burden of the disease has resulted in billions of dollars in health care costs. In spite of these investments, the United States lags behind other developed countries on diabetes life expectancy and disease-related deaths. The purpose of this study is to assess the impact of a pharmacist-managed diabetes clinic (PMDC) model on diabetes core measures. Our hypothesis is that a PMDC would have a significant positive impact on the diabetes measures and will result in higher-quality care at a lower price. Methods: This study is a randomized, open-label, controlled, parallel-group trial which will be conducted in the outpatient clinic at Beaumont Hospital, Royal Oak, Michigan. Patients will be randomly assigned to one of two groups: standard of care (SOC) or standard of care plus PMDC (SOC + PMDC). Included in the study will be patients older than 18 years of age with a diagnosis of type 2 diabetes mellitus and a hemoglobin A1c  $\geq 9\%$ , who are established with a primary care resident and who have not been seen in the PMDC within the last 3 months. The primary outcome is the change in hemoglobin A1c, measured at 6 and 12 months. Secondary outcomes include the impact on all diabetes core measures, patient quality of life, harms, and cost impact related to the intervention. Discussion: If the results of this trial are consistent with the previous retrospective analysis that a pharmacy clinic has a significant impact in controlling hemoglobin A1c levels as well as other diabetes core measures to improve clinical outcomes, it will constitute a scaffold for a future multicenter, randomized controlled trial. In addition, these results may influence future diabetes guidelines, leading to the inclusion of a PMDC as the standard of care. The impact of these results on the economic burden, life expectancy, and diabetes-related deaths are needed and have yet to be studied.

Hamouri S, Hammouri H, Daradkeh H, Al Manasra AR, Al-Zoubi N and **Novotny NM** (2018). "Finding the optimal level and method for thoracoscopic treatment of primary palmar hyperhidrosis." *Jordan Medical Journal* 52(3): 117-125.

[Request Form](#)

*Department of Surgery*

Background: The standard treatment of primary palmar hyperhidrosis had been thoracoscopic R2 sympathectomy, yet this sympathectomy level has been associated with serious unwanted side effects. Therefore, some recent experiences have recommended R2-sparing R3 or R4 thoracoscopic sympathectomy with less side effects, particularly compensatory hyperhidrosis (CH). The aim of this study is to compare the

effect of R2-sparing thoracoscopic sympathectomy at R3 vs R4 levels in the treatment of palmar hyperhidrosis. Materials and Methods: Medical records of all patients were retrospectively reviewed between January 2010 and January 2017. Patients were assessed at 1 week, 1 month, and 6 months or more for success of the procedure, side effects, such as compensatory hyperhidrosis (CH), pneumothorax, Horner's syndrome, and brachial plexus injuries were recorded. Patient satisfaction was assessed. Results: Seventy-nine patients were operated on for palmar hyperhidrosis. At 6 months follow up, all patients reported complete disappearance of the symptoms with dry hands after surgery except three patients in R4 group who have a mild sweating. No failure or worsening of the symptoms developed. Any immediate post-operative complications disappeared within 4 weeks. Ten patients in the R3 group developed some degree of CH (48%) compared to 11 patients in the R4 group (19%) ( $p = 0.014$ ). At a follow up period of R3 (78?7.6) and R4 (37?15), a telephone interview was conducted using a questionnaire and revealed that the rate of CH and palmar over dryness was significantly lower in the R4 group than in the R3 group ( $pP = 0.001, 0.004$ , respectively). No patient developed recurrence. Conclusion: Both R3 and R4 thoracoscopic sympathectomies are effective with a high success rate and minimally invasive methods for the treatment of palmar hyperhidrosis. R4 appeared to be a better technique with significantly less compensatory hyperhidrosis and over dryness of the palms. With the removal of a segment of the sympathetic chain, there were no recurrences in either group.

Han E, Nguyen L, **Sirls L** and **Peters K** (2018). "Current best practice management of interstitial cystitis/bladder pain syndrome." *Therapeutic Advances in Urology* 10(7): 197-211.

[Full Text](#)

*Department of Urology*

Introduction: Over the last 100 years, the terminology and diagnosis criteria for interstitial cystitis have evolved. Many therapeutic options have changed, but others have endured. This article will review the idea of separating 'classic' Hunner lesion interstitial cystitis (HL IC) from non-Hunner lesion interstitial cystitis and bladder pain syndrome (N-HL IC/BPS) and their respective treatment algorithms. Methods/Results: A literature search was performed to identify articles and research on HL IC and N-HL IC/BPS including definitions, etiological theories, and treatments. This article is an overview of the existing literature. We also offer insight into how HL IC and N-HL IC/BPS are approached at our tertiary referral center. Additionally, American Urological Association guidelines have been integrated and newer treatment modalities and research will be introduced at the conclusion. Conclusion: The AUA guidelines have mapped out a stepwise fashion to treat IC/BPS; at our institution we separate patients with HL IC from those with N-HL IC/BPS prior to them entering a treatment pathway. We identify the rarer patient with HL as having classic 'IC'; this cystoscopic finding is critical in guiding treatment. We believe HL IC is a distinct disease from N-HL IC/BPS and therapy should focus on the bladder. The vast majority of patients with N-HL IC/BPS need management of their pelvic floor muscles as the primary therapy, complemented by bladder-directed therapies as needed as well as a multidisciplinary team to manage a variety of other regional/systemic symptoms. Ongoing research into IC/BPS will help us better understand the pathophysiology and phenotypes of this complex disease while exciting and novel research studies are developing promising treatments.

Holden TR, Shah MN, Gibson TA, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Hollander JE, Nicks BA, Nishijima DK, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2018). "Outcomes of patients with syncope and suspected dementia." *Academic Emergency Medicine* 25(8): 880-890.

[Full Text](#)

*Department of Anesthesiology*

*Department of Emergency Medicine*

Objectives: Syncope and near-syncope are common in patients with dementia and a leading cause of emergency department (ED) evaluation and subsequent hospitalization. The objective of this study was to describe the clinical trajectory and short-term outcomes of patients who presented to the ED with syncope or near-syncope and were assessed by their ED provider to have dementia. Methods: This multisite prospective cohort study included patients 60 years of age or older who presented to the ED with syncope or near-syncope between 2013 and 2016. We analyzed a subcohort of 279 patients who were identified by the treating ED provider to have baseline dementia. We collected comprehensive patient-level, utilization, and outcomes data through interviews, provider surveys, and chart abstraction. Outcome measures included

serious conditions related to syncope and death. Results: Overall, 221 patients (79%) were hospitalized with a median length of stay of 2.1 days. A total of 46 patients (16%) were diagnosed with a serious condition in the ED. Of the 179 hospitalized patients who did not have a serious condition identified in the ED, 14 (7.8%) were subsequently diagnosed with a serious condition during the hospitalization, and an additional 12 patients (6.7%) were diagnosed postdischarge within 30 days of the index ED visit. There were seven deaths (2.5%) overall, none of which were cardiac-related. No patients who were discharged from the ED died or had a serious condition in the subsequent 30 days. Conclusions: Patients with perceived dementia who presented to the ED with syncope or near-syncope were frequently hospitalized. The diagnosis of a serious condition was uncommon if not identified during the initial ED assessment. Given the known iatrogenic risks of hospitalization for patients with dementia, future investigation of the impact of goals of care discussions on reducing potentially preventable, futile, or unwanted hospitalizations while improving goal-concordant care is warranted.

Holland TL, Raad I, Boucher HW, Anderson DJ, Cosgrove SE, Ayccock PS, Baddley JW, Chaftari AM, Chow SC, Chu VH, Carugati M, Cook P, Corey GR, Crowley AL, Daly J, Gu JZ, Hachem R, Horton J, Jenkins TC, Levine D, Miro JM, Pericas JM, Riska P, Rubin Z, Rupp ME, Schrank J, **Sims M**, Wray D, Zervos M, Fowler VG and Staphylococcal Bacteremia I (2018). "Effect of algorithm-based therapy vs usual care on clinical success and serious adverse events in patients with staphylococcal bacteremia: A randomized clinical trial." [Jama-Journal of the American Medical Association](#) 320(12): 1249-1258.

[Full Text](#)

*Department of Internal Medicine*

**Importance** The appropriate duration of antibiotics for staphylococcal bacteremia is unknown. **Objective:** To test whether an algorithm that defines treatment duration for staphylococcal bacteremia vs standard of care provides noninferior efficacy without increasing severe adverse events. **Design, Setting, and Participants:** A randomized trial involving adults with staphylococcal bacteremia was conducted at 16 academic medical centers in the United States (n = 15) and Spain (n = 1) from April 2011 to March 2017. Patients were followed up for 42 days beyond end of therapy for those with *Staphylococcus aureus* and 28 days for those with coagulase-negative staphylococcal bacteremia. Eligible patients were 18 years or older and had 1 or more blood cultures positive for *S aureus* or coagulase-negative staphylococci. Patients were excluded if they had known or suspected complicated infection at the time of randomization. **Interventions:** Patients were randomized to algorithm-based therapy (n = 255) or usual practice (n = 254). Diagnostic evaluation, antibiotic selection, and duration of therapy were predefined for the algorithm group, whereas clinicians caring for patients in the usual practice group had unrestricted choice of antibiotics, duration, and other aspects of clinical care. **Main Outcomes and Measures:** Coprimary outcomes were (1) clinical success, as determined by a blinded adjudication committee and tested for noninferiority within a 15% margin; and (2) serious adverse event rates in the intention-to-treat population, tested for superiority. The prespecified secondary outcome measure, tested for superiority, was antibiotic days among per-protocol patients with simple or uncomplicated bacteremia. **Results:** Among the 509 patients randomized (mean age, 56.6 [SD, 16.8] years; 226 [44.4%] women), 480 (94.3%) completed the trial. Clinical success was documented in 209 of 255 patients assigned to algorithm-based therapy and 207 of 254 randomized to usual practice (82.0% vs 81.5%; difference, 0.5% [1-sided 97.5% CI, -6.2% to ∞]). Serious adverse events were reported in 32.5% of algorithm-based therapy patients and 28.3% of usual practice patients (difference, 4.2% [95% CI, -3.8% to 12.2%]). Among per-protocol patients with simple or uncomplicated bacteremia, mean duration of therapy was 4.4 days for algorithm-based therapy vs 6.2 days for usual practice (difference, -1.8 days [95% CI, -3.1 to -0.6]). **Conclusions and Relevance:** Among patients with staphylococcal bacteremia, the use of an algorithm to guide testing and treatment compared with usual care resulted in a noninferior rate of clinical success. Rates of serious adverse events were not significantly different, but interpretation is limited by wide confidence intervals. Further research is needed to assess the utility of the algorithm.

Hollingsworth J, Lau A, Tone A, Kollara A, Allen L, Colgan TJ, Dube V, **Rosen B**, Murphy KJ, Greenblatt EM, Feigenberg T, Virtanen C and Brown TJ (2018). "BRCA1 mutation status and follicular fluid exposure alters NFκB signaling and

ISGylation in human fallopian tube epithelial cells." Neoplasia (United States) 20(7): 697-709.

[Full Text](#)

*Department of Obstetrics and Gynecology*

Germline BRCA1 or BRCA2 mutations (mtBRCA1 and mtBRCA2) increase risk for high-grade serous ovarian cancer (HGSOC), the most commonly diagnosed epithelial ovarian cancer histotype. Other identified risk factors for this cancer, which originates primarily in the distal fallopian tube epithelium (FTE), implicate ovulation, during which the FTE cells become transiently exposed to follicular fluid (FF). To test whether mtBRCA1 or mtBRCA2 nonmalignant FTE cells respond differently to periovulatory FF exposure than control patient FTE cells, gene expression profiles from primary FTE cultures derived from BRCA1 or BRCA2 mutation carriers or control patients were compared at baseline, 24 hours after FF exposure, and 24 hours after FF replacement with culture medium. Hierarchical clustering revealed both FF exposure and BRCA mutation status affect gene expression, with BRCA1 mutation having the greatest impact. Gene set enrichment analysis revealed increased NFκB and EGFR signaling at baseline in mtBRCA1 samples, with increased interferon target gene expression, including members of the ISGylation pathway, observed after recovery from FF exposure. Gene set enrichment analysis did not identify altered pathway signaling in mtBRCA2 samples. An inverse relationship between EGFR signaling and ISGylation with BRCA1 protein levels was verified in an immortalized FTE cell line, OE-E6/E7, stably transfected with BRCA1 cDNA. Suppression of ISG15 and ISGylated protein levels by increased BRCA1 expression was found to be mediated by decreased NFκB signaling. These studies indicate that increased NFκB signaling associated with decreased BRCA1 expression results in increased ISG15 and protein ISGylation following FF exposure, which may be involved in predisposition to HGSOC.

**Huang D, Bastani A, Anderson W, Crabtree J, Kleiman S and Jones S** (2018). "Communication and bed reservation: Decreasing the length of stay for emergency department trauma patients." The American Journal of Emergency Medicine 36(10): 1874-1879.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Emergency Medicine*

Background: Prolonged emergency department (ED) length of stay (LOS) is associated with poorer clinical outcomes and patient experience. At our community hospital, trauma patients were experiencing extended ED LOS incommensurate with their clinical status. Our objective was to determine if operational modifications to patient flow would reduce the LOS for trauma patients. Method: We conducted a retrospective chart review of admitted trauma patients from January 1, 2015 to June 30, 2016 to study two interventions. First, a communication intervention [INT1], which required the ED provider to directly notify the trauma service, was studied. Second, a bed intervention [INT2], which reserved two temporary beds for trauma patients, was added. The primary outcome was the average ED LOS change across three time periods: (1) Baseline data [BASE] collected from January 1, 2015 to June 30, 2015, (2) INT1 data collected from July 1, 2015 to October 18, 2015, and (3) INT2 data collected from October 19, 2015 to June 30, 2016. Data was analyzed using descriptive statistics, two-sample t-tests, and multivariate linear regression. Results: A total of 777 trauma patients were reviewed, with 151, 150 and 476 reviewed during BASE, INT1, and INT2 time periods, respectively. BASE LOS for trauma patients was 389 min. After INT1, LOS decreased by 74.35 min ( $\pm 31.92$ ;  $p < 0.0001$ ). After INT2 was also implemented, LOS decreased by 164.56 min ( $\pm 22.97$ ;  $p < 0.0001$ ) from BASE LOS. Conclusion: Direct communication with the trauma service by the ED provider and reservation of two temporary beds significantly decreased the LOS for trauma patients.

Jae SY, **Franklin BA**, Kurl S, Fernhall B, Kunutsor SK, Kauhanen J and Laukkanen JA (2018). "Effect of cardiorespiratory fitness on risk of sudden cardiac death in overweight/obese men aged 42 to 60 years." American Journal of Cardiology 122(5): 775-779.

[Full Text](#)

*Department of Internal Medicine*

The purpose of this study was to examine the subject and combined associations of cardiorespiratory fitness (fitness) and body mass index (BMI) with the risk of sudden cardiac death (SCD) in middle-aged men. This prospective study was based on a population sample of 2,357 men aged 42 to 60 years, who were followed up in the Kuopio Ischemic Heart Disease cohort study. Fitness was directly measured by peak oxygen uptake

(VO<sub>2</sub>peak) during progressive exercise testing to volitional fatigue. Participants were divided into 4 groups (fit-normal weight, unfit-normal weight, fit-overweight/obese, and unfit-overweight/obese) based on the median values of fitness and BMI. A total of 253 (10.7 %) SCDs occurred during an average follow-up of 22 years. After adjusting for potential confounders, the hazard ratio (HR) and 95% confidence interval (CI) for SCD was 1.80 (95% CI 1.21 to 2.68) for BMI  $\geq$  30.0 kg/m<sup>2</sup> versus normal weight cohort, that is, BMI corresponding to 18.5 to 24.9 kg/m<sup>2</sup>). However, these associations were no longer statistically significant after adjusting for VO<sub>2</sub>peak (1.49, 95% CI 0.98 to 2.24). Compared with the lower levels of fitness, upper levels of fitness had a 39% lower risk of SCD (HR 0.61, 95% CI 0.40 to 0.92) after adjusting for potential confounders, including BMI. In the combined associations of fitness and BMI with the risk of SCD, unfit-overweight/obese men had 1.80 times (95% CI 1.06 to 3.06) increased risk of SCD, but fit-overweight/obese men were not at increased risk of SCD (HR 1.22, 95% CI 0.66 to 2.25) as compared with their fit-normal weight counterparts. In conclusion, both overweight/obesity and fitness were independently associated with the risk of SCD; however, fitness appears to attenuate the risk of SCD in overweight/obese men, suggesting that improving fitness may reduce the risk of SCD in this population.

Jae SY, Kurl S, Fernhall B, Kunutsor SK, **Franklin BA** and Laukkanen JA (2018). "Are metabolically healthy overweight/obese men at increased risk of sudden cardiac death?" Mayo Clinic Proceedings 93(9): 1266-1270.

[Full Text](#)

*Department of Internal Medicine*

**Objective:** To the association between metabolically healthy overweight/obesity and the risk of sudden cardiac death in middle-aged men. **Participants and Methods:** This prospective study was based on a population sample of 2185 men aged 42 to 60 years from the Kuopio Ischaemic Heart Disease Risk Factor Study. Participants were divided into 4 groups on the basis of body mass index and metabolic health status. Metabolically healthy overweight/obesity was defined as body mass index  $\geq$  25 kg/m<sup>2</sup> or greater without metabolic abnormalities, and metabolically unhealthy normal weight was defined as body mass index less than 25 kg/m<sup>2</sup> with 1 or more metabolic abnormalities. **Results:** During a median follow-up of 26 years (interquartile range, 18.7-28.1 years), 240 sudden cardiac deaths (11%) occurred. Compared with metabolically healthy normal weight men, metabolically unhealthy overweight/obese men had a higher risk of sudden cardiac death (hazard ratio, 1.99; 95% CI, 1.03-3.85) after adjusting for potential confounders. However, metabolically healthy overweight/obese men were not at increased risk of sudden cardiac death (hazard ratio, 0.95; 95% CI, 0.40-2.24) as compared with their metabolically healthy normal weight counterparts after adjusting for age, smoking, low-density lipoprotein cholesterol level, high-sensitivity C-reactive protein level, insulin level, history of myocardial infarction, and directly measured peak oxygen uptake. **Conclusion:** Our findings indicate that metabolically healthy normal weight men and metabolically healthy overweight/obese men were at comparable risk of sudden cardiac death over a 26-year follow-up period, suggesting that a baseline body mass index of  $\geq$  25 kg/m<sup>2</sup> or greater per se does not adversely affect the risk of sudden cardiac death.

**Kaura AS**, Srinivasa DR and Kasten SJ (2018). "Optimal timing of alveolar cleft bone grafting for maxillary clefts in the cleft palate population." Journal of Craniofacial Surgery 29(6): 1551-1557.

[Full Text](#)

*OUWB Medical Student Author*

**Purpose:** Timing of bone grafting for maxillary alveolar clefts is not standardized. Secondary bone grafting is often performed; however, consensus does not exist regarding use of chronologic versus dental age to guide treatment. Several authors suggest an early chronologic age is associated with greater success. Available literature was systematically reviewed for evidence for optimal timing for grafting maxillary alveolar clefts. **Methods:** PubMed, MEDLINE, and Cochrane Central Registrar of Controlled Trials databases were queried for manuscripts pertaining to maxillary alveolar cleft bone grafting. Inclusion criteria included manuscripts with level of evidence 4 or greater. Studies not using bone graft, lacking postoperative follow up, and clinical reports were excluded. Seventeen articles met criteria. **Results:** Nine manuscripts recommended grafting based on dental age prior to eruption of the permanent canines, while 8 recommended grafting between ages 7 to 12. The most commonly reported complication was wound dehiscence, followed by graft-site infection. Ten studies used perioperative treatment protocols, 8 of which included preoperative and/or postoperative orthodontia for maxillary expansion. Correlation between chronologic age and success was

not significant, but trended towards greater success with increasing age. Conclusion: Success of secondary grafting is high, but significant variability exists in the timing of grafting. Evidence is lacking to support specific chronologic age; rather, perioperative protocols, systematic surgical technique, and a multidisciplinary discussion are likely more substantial in achieving success, and may be confounders in studies where an early age at grafting appears associated with success. The timing of bone grafting for maxillary alveolar clefts would benefit from a prospective randomized study.

Kesarwani P, **Prabhu A**, Kant S, Kumar P, **Graham SF**, Buelow KL, **Wilson GD**, Miller CR and **Chinnaiyan P** (2018). "Tryptophan metabolism contributes to radiation-induced immune checkpoint reactivation in glioblastoma." Clinical Cancer Research 24(15): 3632-3643.

[Full Text](#)

*Department of Obstetrics and Gynecology*

*Department of Radiation Oncology*

*Department of Pediatrics*

Purpose: Immune checkpoint inhibitors designed to revert tumor-induced immunosuppression have emerged as potent anticancer therapies. Tryptophan metabolism represents an immune checkpoint, and targeting this pathway's rate-limiting enzyme IDO1 is actively being investigated clinically. Here, we studied the intermediary metabolism of tryptophan metabolism in glioblastoma and evaluated the activity of the IDO1 inhibitor GDC-0919, both alone and in combination with radiation (RT). Experimental Design: LC/GC-MS and expression profiling was performed for metabolomic and genomic analyses of patient-derived glioma. Immunocompetent mice were injected orthotopically with genetically engineered murine glioma cells and treated with GDC-0919 alone or combined with RT. Flow cytometry was performed on isolated tumors to determine immune consequences of individual treatments. Results: Integrated cross-platform analyses coupling global metabolomic and gene expression profiling identified aberrant tryptophan metabolism as a metabolic node specific to the mesenchymal and classical subtypes of glioblastoma. GDC-0919 demonstrated potent inhibition of this node and effectively crossed the blood-brain barrier. Although GDC-0919 as a single agent did not demonstrate antitumor activity, it had a strong potential for enhancing RT response in glioblastoma, which was further augmented with a hypofractionated regimen. RT response in glioblastoma involves immune stimulation, reflected by increases in activated and cytotoxic T cells, which was balanced by immune checkpoint reactivation, reflected by an increase in IDO1 expression and regulatory T cells (Treg). GDC-0919 mitigated RT-induced Tregs and enhanced T-cell activation. Conclusions: Tryptophan metabolism represents a metabolic node in glioblastoma, and combining RT with IDO1 inhibition enhances therapeutic response by mitigating RT-induced immunosuppression.

Khalili H, Mansi IA, **Hanzel GS** and Banerjee S (2018). "Transcatheter closure of the left atrial appendage: A focused update on the Watchman closure device." Catheterization and Cardiovascular Interventions 92(1): E28-E34.

[Full Text](#)

*Department of Internal Medicine*

Kogachi K, Lin TC, Palejwala NV, Itty S, **Wolfe JD**, **Drenser KA**, **Capone A**, Dugel PU, Jiang XJ, Shahidzadeh A, Chu ZD, Wang RKK and Kashani AH (2018). "Quantitative assessment of changes in retinal vascular density and morphology among patients with diabetic retinopathy using spectral domain optical coherence tomography angiography (SD-OCTA)." Investigative Ophthalmology & Visual Science 59(9).

[Full Text](#)

*Department of Ophthalmology*

Purpose: To describe and quantify SD-OCTA metrics among subjects with varying severities of diabetic retinopathy (DR) and determine correlation with disease severity. Methods: Retrospective, observational, multicenter, Institutional Review Board-approved study of patients with and without DR at 3 tertiary-care centers using ZEISS AngioPlex™ SD-OCTA (Cirrus, Carl Zeiss Meditec, Dublin, CA). A total of 110 subjects and 201 eyes were included (38 normal, 61 mild non-proliferative DR (NPDR), 27 moderate NPDR, 24 severe NPDR, and 51 proliferative DR (PDR) eyes). A semi-automated segmentation algorithm was used to assess retinal microvasculature in superficial (SRL), deep (DRL), and full-thickness (RET) retinal layers with 3x3-mm scans centered on the fovea. Quantified capillary metrics included vessel skeletal density (VSD), flow impairment region (FIR), and flux. Associations between SD-OCTA metrics and DR status were analyzed with

generalized estimating equations accounting for correlations between two eyes from one subject. Results: When comparing normal to mild NPDR eyes, mean VSD was decreased in SRL ( $0.153 \pm 0.007$  vs  $0.147 \pm 0.010$ ) and DRL ( $0.151 \pm 0.008$  vs  $0.143 \pm 0.013$ ) ( $p < 0.05$  for both). Mean FIR were greater in RET ( $1.27 \pm 0.35$  mm<sup>2</sup> vs  $1.60 \pm 0.61$  mm<sup>2</sup>), SRL ( $1.57 \pm 0.37$  mm<sup>2</sup> vs  $1.92 \pm 0.58$  mm<sup>2</sup>), and DRL ( $2.03 \pm 0.48$  mm<sup>2</sup> vs  $2.56 \pm 0.88$  mm<sup>2</sup>) ( $p < 0.05$  for all). Mean FIR in all 3 layers were significantly greater for progressively worse DR stages ( $p < 0.05$  for all). No differences in flux were observed in normal versus mild NPDR eyes. Significant interactions between age and mild NPDR were seen in FIR of SRL and DRL ( $p < 0.05$  for both). Significant trends were also noted in other OCTA morphology parameters. Conclusions: There are significant differences in capillary density (SRL and DRL) and morphology among normal eyes compared to mild NPDR eyes. Progressively greater changes in density and morphology are seen with worsening DR status. The OCTA-based metrics may objectively assess DR severity.

Kurdziel MD, Davidson A, Ross D, Seta J, **Doshi S, Baker KC** and Maerz T (2018). "Biomechanical properties of the repaired and non-repaired rat supraspinatus tendon in the acute postoperative period." Connective Tissue Research: 1-11.

[Full Text](#)

*Department of Diagnostic Radiology and Molecular Imaging  
Department of Orthopedic Surgery*

Kurdziel MD, Newton MD, Hartner S, **Baker KC** and **Wiater JM** (2018). "Quantitative evaluation of retrieved reverse total shoulder arthroplasty liner surface deviation and volumetric wear." Journal of Orthopaedic Research 36(7): 2007-2014.

[Full Text](#)

*Department of Orthopedic Surgery*

Polyethylene wear is a known complication in total joint arthroplasty, however, in vivo wear rates in reverse total shoulder arthroplasty (RTSA) remain largely unknown. This study aimed to quantify volumetric and surface deviation changes in retrieved RTSA humeral liners using a novel micro-computed tomography ( $\mu$ CT)-based technique. After IRB-approval, 32 humeral liners (single manufacturer and model) with term-of-service greater than 90 days were analyzed. Clinical demographics and surgical data were collected via chart review. Unworn liners were used as geometric controls. Retrieved and unworn liners underwent  $\mu$ CT scanning. Retrieved liner volumes were isolated, co-registered to controls of matching geometry, and surface deviations of the articulation surface and rim were computed. Differences in total volume loss (TVL), volumetric wear rate (VWR), and surface deviation were reported. Semi-quantitative grading evaluated rim damage presence and severity. Mean term-of-service for all liners was  $2.07 \pm 1.33$  years (range: 0.30–4.73). Mean TVL and VWR were  $181.3 \pm 208.2$  mm<sup>3</sup> and  $114.5 \pm 160.3$  mm<sup>3</sup>/year, respectively. Mean articulation and rim surface deviations were  $0.084 \pm 0.065$  and  $0.177 \pm 0.159$  mm, respectively. Articulation surface deviation was positively correlated to term-of-service. Rim damage was present on 63% of liners and correlated significantly to rim surface deviation. This study reports in vivo wear rates of retrieved RTSA implants. Our results demonstrate volumetric and articulation surface wear in select RTSA liners that is correlated to term-of-service. Calculation of in vivo wear rates can help bridge the gap between clinical outcomes and experimental models such as wear simulations and computational models.

Lack D, Liang J, Benedetti L, Knill C and **Yan D** (2018). "Early detection of potential errors during patient treatment planning." Journal of Applied Clinical Medical Physics 19(5): 724-732.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: Data errors caught late in treatment planning require time to correct, resulting in delays up to 1 week. In this work, we identify causes of data errors in treatment planning and develop a software tool that detects them early in the planning workflow. Methods: Two categories of errors were studied: data transfer errors and TPS errors. Using root cause analysis, the causes of these errors were determined. This information was incorporated into a software tool which uses ODBC-SQL service to access TPS's Postgres and Mosaiq MSSQL databases for our clinic. The tool then uses a read-only FTP service to scan the TPS unix file system for errors. Detected errors are reviewed by a physicist. Once confirmed, clinicians are notified to correct the error and educated to prevent errors in the future. Time-cost analysis was performed to estimate

the time savings of implementing this software clinically. Results: The main errors identified were incorrect patient entry, missing image slice, and incorrect DICOM tag for data transfer errors and incorrect CT-density table application, incorrect image as reference CT, and secondary image imported to incorrect patient for TPS errors. The software has been running automatically since 2015. In 2016, 84 errors were detected with the most frequent errors being incorrect patient entry (35), incorrect CT-density table (17), and missing image slice (16). After clinical interventions to our planning workflow, the number of errors in 2017 decreased to 44. Time savings in 2016 with the software is estimated to be 795 h. This is attributed to catching errors early and eliminating the need to replan cases. Conclusions: New QA software detects errors during planning, improving the accuracy and efficiency of the planning process. This important QA tool focused our efforts on the data communication processes in our planning workflow that need the most improvement.

Lee S-E, Sung JM, Rizvi A, Lin FY, Kumar A, Hadamitzky M, Kim Y-J, Conte E, Andreini D, Pontone G, Budoff MJ, Gottlieb I, Lee BK, Chun EJ, Cademartiri F, Maffei E, Marques H, Leipsic JA, Shin S, Choi JH, **Chinnaiyan K, Raff G**, Virmani R, Samady H, Stone PH, Berman DS, Narula J, Shaw LJ, Bax JJ, Min JK and Chang H-J (2018). "Quantification of coronary atherosclerosis in the assessment of coronary artery disease." *Circulation: Cardiovascular Imaging* 11(7): e007562.

[Full Text](#)

*Department of Internal Medicine*

Background: Diagnosis of coronary artery disease and management strategies have relied solely on the presence of diameter stenosis  $\geq 50\%$ . We assessed whether direct quantification of plaque burden (PB) and plaque characteristics assessed by coronary computed tomography angiography could provide additional value in terms of predicting rapid plaque progression. Methods and Results: From a 13-center, 7-country prospective observational registry, 1345 patients ( $60.4 \pm 9.4$  years old; 57.1% male) who underwent repeated coronary computed tomography angiography  $> 2$  years apart were enrolled. For conventional angiographic analysis, the presence of stenosis  $\geq 50\%$ , number of vessel involved, segment involvement score, and the presence of high-risk plaque feature were determined. For quantitative analyses, PB and annual change in PB ( $\Delta PB/y$ ) in the entire coronary tree were assessed. Clinical outcomes (cardiac death, nonfatal myocardial infarction, and coronary revascularization) were recorded. Rapid progressors, defined as a patient with  $\geq$  median value of  $\Delta PB/y$  ( $0.33\%/y$ ), were older, more frequently male, and had more clinical risk factors than nonrapid progressors (all  $P < 0.05$ ). After risk adjustment, addition of baseline PB improved prediction of rapid progression to each angiographic assessment of coronary artery disease, and the presence of high-risk plaque further improved the predictive performance (all  $P < 0.001$ ). For prediction of adverse outcomes, adding both baseline PB and  $\Delta PB/y$  showed best predictive performance (C statistics, 0.763;  $P < 0.001$ ). Conclusions: Direct quantification of atherosclerotic PB in addition to conventional angiographic assessment of coronary artery disease might be beneficial for improving risk stratification of coronary artery disease.

Li C, Zhang Y, Levin AM, Fan BY, Teng H, **Ghannam MM**, Chopp M and Zhang ZG (2018). "Distal axonal proteins and their related miRNAs in cultured cortical neurons." *Molecular Neurobiology*. ePub Ahead of Print.

[Full Text](#)

*OUIB Medical Student Author*

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

that is highly related to regulating axonal growth. Our data provide new insights into networks of miRNAs and their related proteins in distal axons in mediating axonal growth.

**Liu J**, Murray AM, Mankus EB, Ireland KE, Acosta OM and Ramsey PS (2018). "Adjuvant use of rifampin for refractory intrahepatic cholestasis of pregnancy." *Obstetrics and Gynecology* 132(3): 678-681.

[Full Text](#)

*Department of Pathology*

Background: Intrahepatic cholestasis of pregnancy is an incompletely understood disease that poses significant fetal risks, including stillbirth. Treatment of intrahepatic cholestasis of pregnancy is aimed at relieving maternal symptoms and improving fetal outcomes. Case: A 21-year-old gravid woman, 3 para 0111, presented at 27 2/7 weeks of gestation with severe intrahepatic cholestasis of pregnancy. Her clinical course was refractory to first-line therapy with ursodiol, and she was started on rifampin with rapid improvement of symptoms and transaminitis. Despite maternal improvement, she was delivered at 31 weeks of gestation for persistent nonreassuring fetal status. Conclusion: Rifampin may be an effective adjunctive therapy for intrahepatic cholestasis of pregnancy refractory to ursodiol alone. Additional research is needed to assess short-term and long-term maternal and newborn outcomes, because fetal deterioration still occurred in spite of maternal improvement.

Liu Q, Liang J, Zhou DY, **Krauss DJ**, **Chen PY** and **Yan D** (2018). "Dosimetric evaluation of incorporating patient geometric variations into adaptive plan optimization through probabilistic treatment planning in head and neck cancers." *International Journal of Radiation Oncology Biology Physics* 101(4): 985-997.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: Four-dimensional (4D) adaptive radiation therapy (ART) treatment planning is an alternative to the conventional margin-based treatment planning approach. In 4D ART, interfraction patient geometric variations, gathered from computed tomography (CT) or cone beam CT (CBCT) images acquired during the patient treatment course, are directly incorporated into the adaptive plan optimization using a probabilistic treatment planning method. The goal of the present planning study was to evaluate the dosimetric differences between 4D ART and conventional margin-based adaptive planning strategies for head and neck cancers. In addition, we examined whether the dose differences achieved with 4D ART would translate into clinically relevant toxicity reductions using the existing normal tissue complication probability (NTCP) models. Methods and Materials: For 18 head and neck cancer patients, the treatment plans were retrospectively generated for 4 different treatment strategies, including a solely image guided radiation therapy (IGRT) strategy (IGRT-only), 2 conventional adaptive treatment planning strategies using 3- and 0-mm planning target volume (PTV) margins, and the 4D ART strategy. In the IGRT-only strategy, a conventional 3-mm PTV margin treatment plan was applied for the entire treatment course. In the 2 conventional adaptive strategies, 2 new treatment plans were generated during the treatment course using diagnostic planning CT scans acquired after the 10th and 22nd fractions. The 4D ART followed the same adaptive schedule, except that the 4D adaptive plan was generated using 5 CBCT images acquired during the 5 most recent treatment fractions. For each strategy, the actual delivered dose for the entire treatment course was constructed by calculating the daily doses on 35 CBCT scans, deforming back to the pretreatment planning CT scan, and accumulating over all 35 fractions. The target coverage was evaluated using the percentage of target volume receiving  $\geq 100\%$  of the prescription dose (V-100%) and the minimum dose to 99% of the target volume (D-99). It was considered adequate if the V-100% was  $\geq 95\%$  and the dose deficit in D-99 was  $\leq 2$  Gy (with respect to the prescription dose). For each strategy, the dose received by the organs at risk (OARs) was also evaluated, and the corresponding NTCP values were subsequently calculated using 3 NTCP models. Results: Adequate target coverage was achieved for the primary clinical target volume (CTV1) and elective nodal CTV (CTV2) with a 3-mm PTV margin, regardless of adaptation. The 3-mm ART plan reduced the OAR mean dose by 1 to 2 Gy compared with the IGRT-only plan. The 0-mm ART plan further reduced the OAR dose by another 2 to 3 Gy at the expense of target coverage: 3 and 1 patient had V-100%  $< 95\%$ , and 6 and 5 patients had a  $> 2$  Gy dose deficit in D(99) for the CTV1 and CTV2, respectively. Use of 4D ART improved target coverage and attained OAR sparing similar to that with 0-mm ART. The number of patients with V 100%  $< 95\%$  and  $> 2$  Gy D-99 deficit decreased to 0 and 0 for CTV1 and 0 and 2 for CTV2, respectively. The NTCP calculations suggested that 4D ART could benefit a substantial

portion of patients compared with IGRT-only because 17 and 12 patients had  $\geq 5\%$  and  $\geq 10\%$  NTCP reductions for parotid toxicity and 18 and 3 patients had  $\geq 5\%$  and  $\geq 10\%$  NTCP reductions for swallowing toxicity, respectively. Conclusions: Compared with margin-based adaptive planning strategies, 4D ART provides a better balance between target coverage and OAR sparing. NTCP estimation predicted for theoretical clinical benefits that warrant further clinical validation.

Lohasammakul S, Turbpaiboon C, **Chaiyasate K**, Tatsanavivat P, Chompoopong S, Roham A, Ratanalekha R and Aojanepong C (2018). "Anatomy of medial plantar superficial branch artery perforators: Facilitation of medial plantar superficial branch artery perforator (MPAP) flap harvesting and design for finger pulp reconstruction." Microsurgery 38(5): 536-543.

[Full Text](#)

*Department of Surgery*

Background: Medial plantar artery perforator (MPAP) flap was proposed as proper option for finger pulp reconstruction. To provide the previously unavailable vessel information required for this small flap design, this study aimed to gather all necessary anatomy of MPA, MPAP, and their territories of blood supply to apply in clinical MPAP flap reconstruction minimizing perforator injury. Methods: Dissection of 30 Thai cadaveric feet for visualizing superficial branch of MPA and its perforators (MPAP) using acrylic dye cannulation were performed. Diameter, length, number of branches, course, distributing areas of these vessels, and also their areas of blood supply were recorded in relation to specified landmarks, eg, C-MTH line; medial calcaneal tuberosity to plantar side of the first metatarsal head and S point; emerging point of superficial branch of MPA from deep fasciae into subcutaneous layer. Results: Average diameter of MPA at its origin and total length are  $1.63 \pm 0.3$  and  $52.8 \pm 16.1$  mm, respectively. It provides 1–3 perforators, with an average size and length of  $0.36 \pm 0.11$  and  $23.2 \pm 5.47$  mm, respectively. Its distribution is mostly in the posteromedial quadrant within 50 and 30 mm from the midpoint of C-MTH line and the S point, respectively. The estimated perforator flap area is  $2.5 \text{ cm} \times 1.5 \text{ cm}$  and  $4.5 \text{ cm} \times 2.5 \text{ cm}$  for single and double perforators, respectively. Conclusions: MPAP flap was proved as another ideal option for finger pulp reconstruction. Its limitation is small size of perforators but this can be overcome by using MPA for microsurgical anastomosis instead.

Loy BN, Zimel M, Gowda AL, **Tooley TR**, Maerz T, **Bicos J** and **Guettler J** (2018). "A biomechanical and structural comparison of articular cartilage and subchondral bone of the glenoid and humeral head." Orthopaedic Journal of Sports Medicine 6(7): 1-7.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Orthopedic Surgery*

Background: The underlying cause of glenohumeral arthritis is poorly understood. Glenohumeral arthrosis patterns have been classified and described, and differential contact stresses within the joint have been implicated as a cause of joint degeneration, but the intrinsic cause of degeneration patterns in the glenohumeral joint (GHJ) remains largely unknown. Purpose/Hypothesis: The purpose of this study was to assess morphological and mechanical differences in articular cartilage (AC) and subchondral bone (SCB) of the glenoid and humeral head in matched cadaveric specimens. We hypothesized that there would be significant zone-dependent differences between the intrinsic characteristics (AC thickness, SCB thickness, compressive forces) of the glenoid and humeral head. Study Design: Descriptive laboratory study. Methods: Ten human cadaveric GHJs (mean age, 60.2 years) were dissected to expose articular surfaces to facilitate biomechanical testing. A 2-mm and 6-mm osteochondral plug was harvested at 5 zones (central, anterior, posterior, inferior, superior) on the glenoid and humeral head (N = 200 plugs). Each 2-mm core was histologically sectioned and stained with hematoxylin and eosin. AC thickness measurements were taken using light microscopy. The 6-mm plugs were imaged using micro-computed tomography to measure SCB thickness. After imaging, AC specimens were removed from the SCB and tested in confined compression. The compressive aggregate modulus (HA0), compressive stiffening coefficient ( $\beta$ ), and compressive modulus at 16% strain (HA0.16) and at 50% strain (HA0.50) were calculated. Results: The overall AC thickness was significantly greater on the glenoid. The glenoid also had significantly thicker AC at the inferior, posterior, and superior zones as well as significantly higher SCB thickness overall and significantly greater SCB thickness at the anterior and central zones. The glenoid had significantly greater overall HA0.50 and HA0.50

values at the superior zone and had a significantly greater overall compressive stiffening coefficient ( $\beta$ ). Conclusion: The glenoid had thicker AC, thicker SCB, and greater compressive stiffness at high strain. Clinical Relevance: These intrinsic differences may help better elucidate the cause of differential degeneration patterns between the glenoid and humeral head.

Lynch AI, McGowan E and **Zalesin KC** (2018). "Take Me through the History of Your Weight": Using qualitative interviews to create personalized weight trajectories to understand the development of obesity in patients preparing for bariatric surgery." Journal of the Academy of Nutrition and Dietetics 118(9): 1644-1654.

[Full Text](#)

*Department of Internal Medicine*

Background: Obesity can develop during any life stage. Understanding the contexts within which obesity develops can inform our understanding of the disease and help tailor interventions specific to life stages. Objective: Using life-course theory as a guiding framework, this study aimed to explain the development of obesity in bariatric surgery patients by creating personalized weight trajectories. Design: Qualitative methods using semistructured interviews were used to uncover participants' experiences with and explanations for the development of obesity. A grounded theory approach using the constant comparative method was used to analyze transcripts for categories and themes. Participants/Setting: Thirty pre-bariatric surgery patients (24 women, 6 men) were recruited from a bariatric surgery center; 25 participants were available for follow-up. Participants were interviewed before surgery and at 6 and 12 months postsurgery. Results: Four weight history groups were created based on patterns of weight changes from adolescence through adulthood: Always Heavy, Late Peak, Steady Progression, and Weight Cycling. Participants' explanations for weight changes centered around themes of transitions and life-course events or stressors. Differences in the weight history groups could be explained by the timing of transitions, life events, and responses to stress. Conclusions: The development of obesity does not follow the same pattern for all individuals. Weight gain patterns can be explained by the timing of life-course events, stressors, and the type and effects of environmental transitions. Weight management counseling should include strategies tailored to an individual's current life-stage and circumstance, but also acknowledge previous responses to transitions and stressors.

Mando R, **Barbat JJ** and Vivacqua A (2018). "The mysterious mitral mass: A case of valvular myxoma." Case Reports in Cardiology 2018: 3927948-3927948.

[Full Text](#)

*OUWB Medical Student Author*

Myxomas are the most common benign cardiac neoplasms in adults. The vast majority of cardiac myxomas arise from the left atrium near the fossa ovalis of the intra-atrial septum. There have been reports of myxomas arising from the ventricles accounting for about 5% of cases. In our literature review, we have found 55 reported cases of myxomas originating from the mitral valve reported in the adult population dating back to 1871. The majority of these cases presented with embolic complications or syncope. We present an incidental mitral valve myxoma which we excised in efforts to prevent debilitating complications.

Matuszak MM, Paximadis P, Yudelev M, Grubb M, Wilson ML, Fraser C, Dalmia P, Alkhatib A, Sieffert DE, Haywood JR, Tatro D, Parker J, Ettaher O, **Grills I**, Kestin L, Walker EM, Friedle C, Kim H, Radawski JD, Boike T, Moran JM, Pierce LJ and Hayman JA (2018). "Managing motion in conventionally fractionated lung cancer radiation therapy: Collaborative quality improvement from a statewide consortium of academic and community practices." Practical Radiation Oncology 8(4): e208-e211.

[Full Text](#)

*Department of Radiation Oncology*

Mehta GU, Zenonos G, Patibandla MR, Lin CJ, Wolf A, **Grills I**, Mathieu D, McShane B, Lee JY, Blas K, Kondziolka D, Lee CC, Lunsford LD and Sheehan JP (2018). "Outcomes of stereotactic radiosurgery for foramen magnum meningiomas: An international multicenter study." Journal of Neurosurgery 129(2): 383-389.

[Full Text](#)

*Department of Radiation Oncology*

Objective: Meningiomas are the most common benign extramedullary lesions of the foramen magnum;

however, their optimal management remains undefined. Given their location, foramen magnum meningiomas (FMMs) can cause significant morbidity, and complete microsurgical removal can be challenging. Anterior and anterolateral FMMs carry greater risks with surgery, but they comprise the majority of these lesions. As an alternative to resection, stereotactic radiosurgery (SRS) has been used to treat FMMs in small case series. To more clearly define the outcomes of SRS and to delineate a rational management paradigm for these lesions, the authors analyzed the safety and efficacy of SRS for FMM in an international multicenter trial. Methods: Seven medical centers participating in the International Gamma Knife Research Foundation (IGKRF) provided data for this retrospective cohort study. Patients who were treated with Gamma Knife radiosurgery and whose clinical and radiological follow-up was longer than 6 months were eligible for study inclusion. Data from pre- and post-SRS radiological and clinical evaluations were analyzed. Stereotactic radiosurgery treatment variables were recorded. Results: Fifty-seven patients (39 females and 18 males, with a median age of 64 years) met the study inclusion criteria. Thirty-two percent had undergone prior microsurgical resection. Patients most frequently presented with cranial neuropathy (39%), headache (35%), numbness (32%), and ataxia (30%). Median pre-SRS tumor volume was 2.9 cm<sup>3</sup>. Median SRS margin dose was 12.5 Gy (range 10–16 Gy). At the last follow-up after SRS, 49% of tumors were stable, 44% had regressed, and 7% had progressed. Progression-free survival rates at 5 and 10 years were each 92%. A greater margin dose was associated with a significantly increased likelihood of tumor regression, with 53% of tumors treated with > 12 Gy regressing. Fifty-two percent of symptomatic patients noted some clinical improvement. Adverse radiation effects were limited to hearing loss and numbness in 1 patient (2%). Conclusions: Stereotactic radiosurgery for FMM frequently results in tumor control or tumor regression, as well as symptom improvement. Margin doses > 12 Gy were associated with increased rates of tumor regression. Stereotactic radiosurgery was generally safe and well tolerated. Given its risk-benefit profile, SRS may be particularly useful in the management of small- to moderate-volume anterior and anterolateral FMMs.

Mertens A, Dalal P, Ashbrook M and **Hanson I** (2018). "Coil embolization of coronary-cameral fistula complicating revascularization of chronic total occlusion." *Case Reports in Cardiology* 2018: 6857318-6857318.

[Full Text](#)

*Department of Internal Medicine*

Traumatic vessel perforation is a potential complication of chronic total occlusion (CTO) percutaneous coronary artery intervention (PCI). A rare consequence of this complication is a coronary-cameral fistula. The management of this condition is not well elucidated. Herein, we present such a case of symptomatic left anterior descending to the right ventricle (LAD-RV) fistula which was treated with coil embolization.

Mettler J and **Al-Katib S** (2018). "Aggressive renal angiomyolipoma in a patient with tuberous sclerosis resulting in pulmonary tumor embolus and pulmonary infarction." *Urology* 119: e1-e2.

[Full Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Renal angiomyolipoma (AML) is the most commonly encountered mesenchymal tumor of the kidney which can present spontaneously or in association with tuberous sclerosis complex. Rarely, renal AMLs may demonstrate aggressive features such as renal vein invasion. This common entity and its uncommon complications are diagnosed based on physical examination and computed tomography results. Here we report imaging findings of a renal AML with renal vein and inferior vena cava invasion resulting in pulmonary tumor embolus and pulmonary infarction.

Mikhail M, Bakhsh S, Thanos A, **Moinuddin O**, Stem M, **Williams GA**, **Drenser KA**, **Capone A** and Trese MT (2018). "Rhegmatogenous retinal detachments and retinal tears in adult retinopathy of prematurity." *Investigative Ophthalmology & Visual Science* 59(9): 3771.

[Full Text](#)

*OUIWB Medical Student Author*

*Department of Ophthalmology*

Miller JM, Binnicker MJ, Campbell S, Carroll KC, Chapin KC, Gilligan PH, Gonzalez MD, Jerris RC, Kehl SC, Patel R, Pritt BS, Richter SS, **Robinson-Dunn B**, Schwartzman JD, Snyder JW, Telford S, Theel ES, Thomson RB, Weinstein MP and

Yao JD (2018). "A guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2018 update by the Infectious Diseases Society of America and the American Society for Microbiology." Clinical Infectious Diseases 67(6): 813-816.

[Full Text](#)

*Department of Pathology*

The critical nature of the microbiology laboratory in infectious disease diagnosis calls for a close, positive working relationship between the physician/advanced practice provider and the microbiologists who provide enormous value to the healthcare team. This document, developed by experts in laboratory and adult and pediatric clinical medicine, provides information on which tests are valuable and in which contexts, and on tests that add little or no value for diagnostic decisions. This document presents a system-based approach rather than specimen-based approach, and includes bloodstream and cardiovascular system infections, central nervous system infections, ocular infections, soft tissue infections of the head and neck, upper and lower respiratory infections, infections of the gastrointestinal tract, intra-abdominal infections, bone and joint infections, urinary tract infections, genital infections, and other skin and soft tissue infections; or into etiologic agent groups, including arthropod-borne infections, viral syndromes, and blood and tissue parasite infections. Each section contains introductory concepts, a summary of key points, and detailed tables that list suspected agents; the most reliable tests to order; the samples (and volumes) to collect in order of preference; specimen transport devices, procedures, times, and temperatures; and detailed notes on specific issues regarding the test methods, such as when tests are likely to require a specialized laboratory or have prolonged turnaround times. In addition, the pediatric needs of specimen management are also emphasized. There is intentional redundancy among the tables and sections, as many agents and assay choices overlap. The document is intended to serve as a guidance for physicians in choosing tests that will aid them to quickly and accurately diagnose infectious diseases in their patients.

Mitton KP, Dailey WA, **Knapp A, Chen P**, Moore M, Felisky J, Thomas A, Guzman E and Deshpande M (2018). "The neuropilin-1 interacting region of VEGFA-165 shifts the activation of MAPK and AKT to a pseudo-binary dose response within primary human retinal endothelial cells." Investigative Ophthalmology & Visual Science 59(9).

[Full Text](#)

*OUIWB Medical Student Author*

Moses RA, Selph JP, Voelzke BB, Piotrowski J, Eswara JR, Erickson BA, Gupta S, Dmochowski RR, Johnsen NV, Shridharani A, Blaschko SD, Elliott SP, Schwartz I, Harris CR, Borawski K, Figler BD, Osterberg EC, 3rd, **Burks FN**, Bihle W, 3rd, Miller B, Santucci RA, Breyer BN, Flynn B, Higuchi T, Kim FJ, Broghammer JA, Presson AP, Myers JB, from the T and Urologic Reconstruction Network of S (2018). "An American Association for the Surgery of Trauma (AAST) prospective multi-center research protocol: Outcomes of urethral realignment versus suprapubic cystostomy after pelvic fracture urethral injury." Translational Andrology and Urology 7(4): 512-520.

[Full Text](#)

*Department of Urology*

Background: Pelvic fracture urethral injuries (PFUI) occur in up to 10% of pelvic fractures. It remains controversial whether initial primary urethral realignment (PR) after PFUI decreases the incidence of urethral obstruction and the need for subsequent urethral procedures. We present methodology for a prospective cohort study analyzing the outcomes of PR versus suprapubic cystostomy tube (SPT) after PFUI. Methods: A prospective cohort trial was designed to compare outcomes between PR (group 1) and SPT placement (group 2). Centers are assigned to a group upon entry into the study. All patients will undergo retrograde attempted catheter placement; if this fails a cystoscopy exam is done to confirm a complete urethral disruption and attempt at gentle retrograde catheter placement. If catheter placement fails, group 1 will undergo urethral realignment and group 2 will undergo SPT. The primary outcome measure will be the rate of urethral obstruction preventing atraumatic passage of a flexible cystoscope. Secondary outcome measures include: subsequent urethral interventions, post-injury complications, urethroplasty complexity, erectile dysfunction (ED) and urinary incontinence rates. Results: Prior studies demonstrate PR is associated with a 15% to 50% reduction in urethral obstruction. Ninety-six men (48 per treatment group) are required to detect a 15% treatment effect (80% power, 0.05 significance level, 20% loss to follow up/death rate). Busy trauma centers treat complete PFUI approximately 1-6 times per year, thus our goal is to recruit 25 trauma centers and enroll patients for 3 years with a goal of 100 or more total patients with complete urethral

disruption. Conclusions: The proposed prospective multi-institutional cohort study should determine the utility of acute urethral realignment after PFUI.

Moysidis SN, Koulisis N, Rodger DC, Burkemper B, **Williams GA**, Humayun MS and Elliott D (2018). "Ocular TASER trauma." *Investigative Ophthalmology & Visual Science* 59(9): 6177.

[Full Text](#)

*Department of Ophthalmology*

Mukherjee D, Coffey M and **Maisels MJ** (2018). "Frequency and duration of phototherapy in preterm infants <35 weeks gestation." *Journal of Perinatology* 38(9): 1246-1251.

*Department of Pediatrics*

Objective: To evaluate the frequency, age at phototherapy (PT) initiation, and duration of PT use in infants 23(0/7) to 34(6/7) weeks of gestation in two neonatal intensive care units (NICUs) over 4 time periods. Study Design: We reviewed the charts of all infants born at 23(0/7)-34(6/7) weeks of gestational age (GA) and admitted to the NICUs of two hospitals between January 2009 and September 2015. We calculated the proportion of infants who received PT and the total duration of PT exposure. Results: Overall 2023 (81.8%) received PT, and PT use was inversely related to GA and birthweight. More infants received PT when GA was added as a criterion for initiating PT. The median duration (interquartile range (IQR)) of PT for all infants was 50 (27-85) h and in the lowest GA group was 74 (42-111) h. Conclusions: Recent US consensus guidelines appear to have led to an increased use of PT in our NICUs and studies from Norway indicate that we use PT considerably more frequently and for longer durations than do our Norwegian colleagues.

Newton MD, Hartner SE, Gawronski K, Davenport EJ, Timmons SC, **Baker KC** and Maerz T (2018). "Nondestructive, indirect assessment of the biomechanical properties of the rat intervertebral disc using contrast-enhanced  $\mu$ CT." *Journal of Orthopaedic Research* 36(7): 2030-2038.

[Full Text](#)

*Department of Orthopedic Surgery*

Mechanical characterization of the intervertebral disc involves labor-intensive and destructive experimental methodology. Contrast-enhanced micro-computed tomography is a nondestructive imaging modality for high-resolution visualization and glycosaminoglycan quantification of cartilaginous tissues. The purpose of this study was to determine whether anionic and cationic contrast-enhanced micro-computed tomography of the intervertebral disc can be used to indirectly assess disc mechanical properties in an ex vivo model of disc degeneration. L3/L4 motion segments were dissected from female Lewis rats. To deplete glycosaminoglycan, samples were treated with 0 U/ml (Control) or 5 U/ml papain. Contrast-enhanced micro-computed tomography was performed following incubation in 40% Hexabrix (anionic) or 30 mg I/ml CA4+ (cationic) for 24 h (n = 10/contrast agent/digestion group). Motion segments underwent cyclic mechanical testing to determine compressive and tensile modulus, stiffness, and hysteresis. Glycosaminoglycan content was determined using the dimethylmethylene blue assay. Correlations between glycosaminoglycan content, contrast-enhanced micro-computed tomography attenuation, and mechanical properties were assessed via the Pearson correlation. The predictive accuracy of attenuation on compressive properties was assessed via repeated random sub-sampling cross validation. Papain digestion produced significant decreases in glycosaminoglycan content and corresponding differences in attenuation and mechanical properties. Attenuation correlated significantly to glycosaminoglycan content and to all compressive mechanical properties using both Hexabrix and CA4+. Predictive linear regression models demonstrated a predictive accuracy of attenuation on compressive modulus and stiffness of 79.8–86.0%. Contrast-enhanced micro-computed tomography was highly predictive of compressive mechanical properties in an ex vivo simulation of disc degeneration and may represent an effective modality for indirectly assessing disc compressive properties.

O'Shea TM, Joseph RM, Allred EN, Taylor HG, Leviton A, Heeren T, Douglass LM, Frazier JA, Jara H, Kuban KCK, Shah B, Singh R, Van Marter L, Martin C, Ware J, Cole C, Perrin E, Bednarek F, Ehrenkranz R, Benjamin J, Bose C, Warner D, Engelke S, Poortenga M, Pastyrnak S, Karna P, Paneth N, Lenski M, Schreiber M, Hunter S, Msall M, Batton D, **Klarr J**, Christianson K, Klein D, Pimental M, Hallisey C, Coster T, Nylan E, Neger E, Mattern K, Venuti L, Powers B, Foley A, Williams J, Romano E, Hiatt D, Peters N, Brown P, Anusinha E, Bose G, Wereszczak J, Bernhardt J, Adams J, Wilson D,

Darden-Saad N, Sutton D, Rathbun J, Miras K, Weiland D, Yoon G, Ramoskaite R, Wiggins S, Washington K, Martin R, Prendergast B, Kring B, Smith A, McQuiston S, Butler S, Wilson R, McGhee K, Lee P, Asgarian A, Sadhwani A, Henson B, Keller C, Walkowiak J, Barron S, Miller A, Dessureau B, Wood M, Damon-Minow J, Mayes L, Tsatsanis K, Chawarska K, Kim S, Dieterich S, Bearrs K, Waldrep E, Friedman J, Hounshell G, Allred D, Helms R, Whitley L, Stainback G, Bostic L, Jacobson A, McKeeman J, Meyer E, Price J, Lloyd M, Plesha-Troyke S, Scott M, Solomon KM, Brooklier K, Vogt K and for the ESI (2018). "Accuracy of the Bayley-II mental development index at 2 years as a predictor of cognitive impairment at school age among children born extremely preterm." Journal of Perinatology 38(7): 908-916.

[Request Form](#)

*Department of Pediatrics*

Objective: To describe the accuracy of the Bayley Scales of Infant Development-Second Edition (BSID-II) Mental Development Index (MDI) at 2 years of age for prediction of cognitive function at school age of children born extremely preterm. Design: Study participants were enrolled in the Extremely Low Gestational Age Newborn Study between 2002 and 2004. Two-thirds of surviving children (n = 795) were assessed at 2 years with the BSID-II and at 10 years with an intelligence quotient (IQ) test. We computed test characteristics for a low MDI (<70), including predictive value positive. Results: Almost two-thirds of children with a low MDI had a normal IQ ( $\geq 70$ ) at 10 years. Concordance between MDI and IQ was highest among children with major motor and/or sensory impairment, and when MDI was adjusted for gestational age. Conclusion: Most children born extremely preterm with low BSID-II MDI at 2 years have normal intelligence at school age.

O'Connor AB, Williams CM, **Dalal B**, Sulistio MS, Roth TK, Milne CK, Collichio FA, Muchmore EA and Alweis R (2018). "Internal medicine fellowship directors' perspectives on the quality and utility of letters conforming to residency program director letter of recommendation guidelines." Journal of Community Hospital Internal Medicine Perspectives 8(4): 173-176.

[Full Text](#)

*Department of Internal Medicine*

Background: In May 2017, the Alliance for Academic Internal Medicine (AAIM) published guidelines intending to standardize and improve internal medicine residency program director (PD) letters of recommendation (LORs) for fellowship applicants. Objectives: This study aimed to examine fellowship PDs impressions of the new guidelines, letter writers' adherence to the guidelines, and the impact of LORs that conformed to guidelines compared to non-standardized letters. Methods: The authors anonymously surveyed fellowship PDs from January to March 2018 to gather input about LORs submitted to their programs during the 2017 fellowship application cycle. Results: A total of 78% of survey respondents were satisfied with letters that followed the AAIM guidelines, whereas 48% of respondents were satisfied with letters that did not. Fellowship PDs felt that letters that followed the AAIM guidelines were more helpful than letters that did not, especially for differentiating between applicants from the same institution and for understanding residents' performance across the six core competency domains. Fellowship PDs provided several suggestions for residency PDs to make the LORs even more helpful. Conclusion: Fellowship PD respondents indicated that LORs that followed the new AAIM guidelines were more helpful than letters that did not.

**Ogunyemi D**, Jovanovski A, **Liu J**, Friedman P, Sugiyama N, **Creps J** and **Madan I** (2018). "The contribution of untreated and treated anxiety and depression to prenatal, intrapartum, and neonatal outcomes." American Journal of Perinatology Reports 8(3): e146-e157.

[Full Text](#)

*Department of Pathology*

*Department of Obstetrics and Gynecology*

*OUIB Medical Student Author*

Objective: To determine independent perinatal associations of anxiety and depression in women who were and were not treated with psychotropic drugs in comparison to unaffected pregnancies. Study Design: From 2013 to 2014, 978 (6.3%) cases of anxiety/depression, of which 35% used psychotropic drugs, were compared with 14,514 (93.7%) unaffected pregnancies using logistic regression. Results: Subjects were more likely to be Non-Hispanic Whites, use tobacco and illegal substances, be unmarried, use public insurance, and have medical complications of pregnancy. For independent maternal outcomes, untreated

anxiety/depression was associated with labor induction (adjusted odds ratio [aOR] = 2.02), cesarean deliveries (aOR = 1.69), longer length of stay (aOR = 1.96), readmission (aOR = 2.40), fever (aOR = 2.03), magnesium exposure (aOR = 1.82), and postpartum hemorrhage (aOR = 2.57), whereas treated cases were associated with increased blood transfusion (aOR = 4.81), severe perineal lacerations (aOR = 2.93), and postpartum hemorrhage (aOR = 3.85), but decreased risk of cesarean deliveries (aOR = 0.59). Independent neonatal outcomes included small for gestational age (aOR = 3.04), meconium-stained fluid (aOR = 1.85; 2.61), respiratory failure (aOR = 5.84), neonatal adaptation syndrome (aOR = 11; 10.2), and neonatal seizures (aOR = 12.3) in treated cases, whereas untreated cases were associated with hypoxia (aOR = 2.83), low Apgar score (aOR = 3.82), and encephalopathy (aOR = 18.3). Exposure to multiple psychotropic medications independently increased the risk of neonatal adaptation syndrome, neonatal length of stay, and hypoglycemia. Conclusion: Untreated cases were associated with increased maternal adverse outcomes, whereas treated cases were associated with more adverse neonatal outcomes when compared with unaffected pregnancies.

**Ogunyemi D**, McGlynn S, Ronk A, Knudsen P, Andrews-Johnson T, Raczkiewicz A, Jovanovski A, **Kaur S**, **Dykowski M**, **Redman M** and **Bahado-Singh R** (2018). "Using a multifaceted quality improvement initiative to reverse the rising trend of cesarean births." *Obstetrical and Gynecological Survey* 73(7): 383-385.

[Full Text](#)

*Department of Obstetrics and Gynecology*  
*Department of Internal Medicine*

O'Neill WW, Grines C, Schreiber T, Moses J, Maini B, **Dixon SR** and Ohman EM (2018). "Analysis of outcomes for 15,259 US patients with acute myocardial infarction cardiogenic shock (AMICS) supported with the Impella device." *American Heart Journal* 202: 33-38.

[Full Text](#)

*Department of Internal Medicine*

Background: The Impella percutaneous ventricular assist device (PVAD) rapidly deploys mechanical circulatory support (MCS) in patients with acute myocardial infarction complicated by cardiogenic shock (AMICS). We present findings from a quality improvement (IQ) registry for US patients with AMICS who received Impella devices. Methods and Results: From January 2009 to December 2016, 46,949 patients from 1010 US hospitals were entered into the IQ registry; of these, 15,259 had AMICS. Limited de-identified patient information, product performance, and survival to explantation were recorded. Of those with AMICS, 51% survived to explantation of PVAD. There was a significant difference between survival at explantation with quintile volume at hospitals (range: 0–100%; 30% survival rate in lowest quintile vs. 76% in top quintile;  $P < .0001$ ). Use of the Impella device as first-line treatment pre-PCI was associated with a 59% survival rate, compared with 52% when used as a salvage strategy ( $P < .001$ ). The survival rate among those who received hemodynamic monitoring with pulmonary artery catheters was 63% as compared with 49% in those who did not ( $P < .0001$ ). Overall institutional Impella volume was related to survival (56% survival at sites with  $>7$ /year vs. 51% at sites with  $\leq 1$ ;  $P < .001$ ). Conclusions: In this early clinical experience with Impella support for AMICS, wide variation in outcomes existed across centers. Survival was higher when Impella was used as first support strategy, when invasive hemodynamic monitoring was used, and at centers with higher Impella implantation volume.

Pamplona MdC and **Ysunza PA** (2018). "Deliberate practice: Preliminary results of a useful strategy for correcting articulation in children with cleft palate." *Journal of Craniofacial Surgery* 29(6): 1490-1494.

[Full Text](#)

*Department of Physical Medicine & Rehabilitation*

Children with cleft palate frequently show speech and language disorders. In the related scientific literature, several reports have described the use of different strategies for treating speech disorders in children with cleft palate. However, only a few studies have addressed the use of these strategies within a meaningful linguistic context. Deliberate practice is a procedure or strategy, which proposes that the key for achieving high levels of expert performance is dedicating long time for practice. Deliberate practice has been studied mainly in the areas of sports and intellectual games. The purpose of this article is to study whether the use of a strategy originally designed for achieving expert performance in sports and intellectual games, can be

useful for the speech intervention of children with cleft palate. For this project, 32 children with cleft palate were studied. The children were randomly assigned to 2 independent groups. Both groups received speech therapy based on the principles of the Whole Language Model. In addition, deliberate practice was used in the children included in the active group. After a speech intervention, although both groups of children demonstrated significant improvement in articulation placement, the active group demonstrated a significantly higher improvement as compared with the control group. In conclusion, these preliminary results seem to suggest that the use of deliberate practice can be effective for enhancing articulation in children with cleft palate.

**Pandurangadu AV**, Tucker J, **Brackney AR** and Bahl A (2018). "Ultrasound-guided intravenous catheter survival impacted by amount of catheter residing in the vein." *Emergency Medicine Journal* 35(9): 550.

[Request Form](#)

*Department of Emergency Medicine*

Objective: Ultrasound (US)-guided peripheral IVs have a high failure rate. We explore the relationship between the quantity of catheter residing within the vein and the functionality of the catheter over time. Methods: This was a prospective, observational single-site study. Adult ED patients with US-guided IVs had the catheter visualised under ultrasound post-placement. IV placement time and catheter length residing in the vein was obtained. Exclusions included catheter not visualised, patient discharged from ED unless IV failed, 24 hour hospitalisation unless IV failed or patient self-removed IV. Inpatient follow-up occurred within 24, 48 and 72 hours from the IV placement time. Catheter functionality was noted. If the catheter failed, the time and reason for failure was documented. Results: 113 patients were enrolled; 27 were excluded. Of the 86 study subjects, 29 (33.7%) patients' IVs failed and 57 (66.3%) remained functional. Median time to IV failure was 15.6 hours. 100% of IVs failed when 30% of the catheter was in the vein; 32.4% of IVs failed when 30%–64% of the catheter was in the vein; no IVs failed when  $\geq 65\%$  of the catheter was in the vein ( $p < 0.0002$ ). The HR was 0.71 (95% CI 0.60 to 0.83), and for every 5% increase of catheter in vein, the hazard of the IV failing decreases by 29% (0.0001). Conclusion: The quantity of catheter residing in the vein is a key predictor of long-term functionality of US-guided IVs and is strongly associated with the hazard of failure within 72 hours. Catheter failure is high when 30% of the catheter resided in the vein. Optimum catheter survival occurs when  $\geq 65\%$  of the catheter is placed in the vein.

Papalekas E and **Fisher J** (2018). "Trends in route of hysterectomy after the implementation of a comprehensive robotic training program." *Minimally Invasive Surgery* 2018: 7362489-7362489.

[Full Text](#)

*Department of Obstetrics and Gynecology*

Objective: To evaluate trends in surgical approach for hysterectomy following the introduction and implementation of a comprehensive robotic surgery program. Methods: A retrospective review of all hysterectomies done at two institutions, a community hospital and a suburban, tertiary-care teaching hospital, in the same health system over a five-year period, January 2010 through December 2014. A robotic surgery training program was implemented during the first year of the study and trends in route of hysterectomy were evaluated in the subsequent years. Results: A total of 5175 patients undergoing hysterectomy, for both benign and malignant indications, were included in the study. There was a significant decrease in the percent of cases performed through an abdominal approach at both the community and teaching hospitals (19.3% decline at each institution). There was an inversely related significant increase in the percent of robotic procedures at both the community and teaching hospitals (44.5% and 17%, respectively). A decrease in number of cases performed vaginally over this period was only noted in the community hospital site (25.2% decrease), and there was a slightly higher rate of vaginal hysterectomies at the teaching hospital over this study period (21.9% in 2010, 24.1% in 2014). Conclusion: The decrease in number of abdominal and laparoscopic hysterectomies and increase in number of robotic hysterectomies that was seen are consistent with national trends. The initiation of a robotic training program did not prevent the proliferation of use of the robot but did aim to ensure proficiency on the robot prior to gaining privileges for patient use. This type of comprehensive training and monitoring program could be applied to future technologic advances to ensure a standard level of surgical proficiency. Trends in route of hysterectomy are clearly multifactorial and involve patient, provider, and location-specific factors that are likely to continue to change.

Patel SN, Gupta MP, Rusu I, Yonekawa Y, Jonas K, Oltra E, Orlin A, Chang JS, Horowitz J, **Capone A** and Chan RVP (2018). "Early diagnosis and management of aggressive posterior neonatal vitreoretinopathy presenting in premature neonates." *Investigative Ophthalmology & Visual Science* 59(9): 3758.

[Full Text](#)

*Department of Ophthalmology*

Purpose: We report a case series of advanced ischemic vitreoretinopathies in premature infants that were more consistent with familial exudative vitreoretinopathy (FEVR) than with retinopathy of prematurity (ROP). Methods: The charts of three consecutive patients who met ROP screening criteria and were diagnosed with FEVR-like, non-ROP aggressive posterior neonatal vitreoretinopathy were retrospectively reviewed. Results: Table 1 shows clinical characteristics of each case. Severe, rapidly progressive retinal vascular abnormalities were noted in all cases (Figure 1). Average time to intervention (laser or surgery) was 39 weeks gestational age (range 35-46), and prompt treatment resulted in anatomic stabilization or improvement in the retinal detachment and maintenance of at least light perception vision in all cases. Conclusions: This series supports the existence of a clinical entity more consistent with a FEVR-like ischemic vitreoretinopathy than ROP in premature infants and suggests that early diagnosis and intervention may mitigate the typical aggressive course and poor prognosis of this condition.

Pathak R, Singh P, Ananthakrishnan S, Adamczyk S, **Schimmel O** and Govind CK (2018). "Acetylation-dependent recruitment of the FACT complex and its role in regulating Pol II occupancy genome-wide in *Saccharomyces cerevisiae*." *Genetics* 209(3): 743-756.

[Full Text](#)

*OUWB Medical Student Author*

Histone chaperones, chromatin remodelers, and histone modifying complexes play a critical role in alleviating the nucleosomal barrier for DNA-dependent processes. Here, we have examined the role of two highly conserved yeast (*Saccharomyces cerevisiae*) histone chaperones, facilitates chromatin transcription (FACT) and Spt6, in regulating transcription. We show that the H3 tail contributes to the recruitment of FACT to coding sequences in a manner dependent on acetylation. We found that deleting a H3 histone acetyltransferase Gcn5 or mutating lysines on the H3 tail impairs FACT recruitment at ADH1 and ARG1 genes. However, deleting the H4 tail or mutating the H4 lysines failed to dampen FACT occupancy in coding regions. Additionally, we show that FACT depletion reduces RNA polymerase II (Pol II) occupancy genome-wide. Spt6 depletion leads to a reduction in Pol II occupancy toward the 3'-end, in a manner dependent on the gene length. Severe transcription and histone-eviction defects were also observed in a strain that was impaired for Spt6 recruitment (spt6 $\Delta$ 202) and depleted of FACT. Importantly, the severity of the defect strongly correlated with wild-type Pol II occupancies at these genes, indicating critical roles for Spt6 and Spt16 in promoting high-level transcription. Collectively, our results show that both FACT and Spt6 are important for transcription globally and may participate during different stages of transcription.

Patibandla MR, Ding D, Kano H, Xu Z, Lee JYK, Mathieu D, Whitesell J, Pierce JT, Huang PP, Kondziolka D, Feliciano C, Rodriguez-Mercado R, Almodovar L, **Grills IS**, Silva D, Abbassy M, Missios S, Barnett GH, Lunsford LD and Sheehan JP (2018). "Stereotactic radiosurgery for Spetzler-Martin Grade IV and V arteriovenous malformations: an international multicenter study." *Journal of Neurosurgery* 129(2): 498-507.

[Request Form](#)

*Department of Radiation Oncology*

Objective: Due to the complexity of Spetzler-Martin (SM) Grade IV-V arteriovenous malformations (AVMs), the management of these lesions remains controversial. The aims of this multicenter, retrospective cohort study were to evaluate the outcomes after single-session stereotactic radiosurgery (SRS) for SM Grade IV-V AVMs and determine predictive factors. Methods: The authors retrospectively pooled data from 233 patients (mean age 33 years) with SM Grade IV (94.4%) or V AVMs (5.6%) treated with single-session SRS at 8 participating centers in the International Gamma Knife Research Foundation. Pre-SRS embolization was performed in 71 AVMs (30.5%). The mean nidus volume, SRS margin dose, and follow-up duration were 9.7 cm<sup>3</sup>, 17.3 Gy, and 84.5 months, respectively. Statistical analyses were performed to identify factors associated with post-SRS outcomes. Results: At a mean follow-up interval of 84.5 months, favorable outcome was defined as AVM obliteration, no post-SRS hemorrhage, and no permanently symptomatic radiation-

induced changes (RIC) and was achieved in 26.2% of patients. The actuarial obliteration rates at 3, 7, 10, and 12 years were 15%, 34%, 37%, and 42%, respectively. The annual post-SRS hemorrhage rate was 3.0%. Symptomatic and permanent RIC occurred in 10.7% and 4% of the patients, respectively. Only larger AVM diameter ( $p = 0.04$ ) was found to be an independent predictor of unfavorable outcome in the multivariate logistic regression analysis. The rate of favorable outcome was significantly lower for unruptured SM Grade IV–V AVMs compared with ruptured ones ( $p = 0.042$ ). Prior embolization was a negative independent predictor of AVM obliteration ( $p = 0.024$ ) and radiologically evident RIC ( $p = 0.05$ ) in the respective multivariate analyses. Conclusions: In this multi-institutional study, single-session SRS had limited efficacy in the management of SM Grade IV–V AVMs. Favorable outcome was only achieved in a minority of unruptured SM Grade IV–V AVMs, which supports less frequent utilization of SRS for the management of these lesions. A volume-staged SRS approach for large AVMs represents an alternative approach for high-grade AVMs, but it requires further investigation.

Phasukkijwatana N, Freund KB, Dolz-Marco R, Al-Sheikh M, Keane PA, Egan CA, **Randhawa S**, Stewart JM, Liu QY, Hunyor AP, Kreiger A, Nagiel A, Lalane R, Rahimi M, Lee WK, Jampol LM and Sarraf D (2018). "Peripapillary pachychoroid syndrome." Retina-the Journal of Retinal and Vitreous Diseases 38(9): 1652-1667.

[Full Text](#)

*Department of Ophthalmology*

Pomeraniec IJ, Kano H, Xu Z, **Nguyen B**, Siddiqui ZA, Silva D, Sharma M, Radwan H, Cohen JA, Dallapiazza RF, Iorio-Morin C, Wolf A, Jane JA, Grills IS, Mathieu D, Kondziolka D, Lee CC, Wu CC, Cifarelli CP, Chytka T, Barnett GH, Lunsford LD and Sheehan JP (2018). "Early versus late Gamma Knife radiosurgery following transsphenoidal surgery for nonfunctioning pituitary macroadenomas: A multicenter matched-cohort study." Journal of Neurosurgery 129(3): 648-657.

[Request Form](#)

*OUWB Medical Student Author*

Objective: Gamma Knife radiosurgery (GKRS) is frequently used to treat residual or recurrent nonfunctioning pituitary macroadenomas. There is no consensus as to whether GKRS should be used early after surgery or if radiosurgery should be withheld until there is evidence of imaging-defined progression of tumor. Given the high incidence of adenoma progression after subtotal resection over time, the present study intended to evaluate the effect of timing of radiosurgery on outcome. Methods: This is a multicenter retrospective review of patients with nonfunctioning pituitary macroadenomas who underwent transsphenoidal surgery followed by GKRS from 1987 to 2015 at 9 institutions affiliated with the International Gamma Knife Research Foundation. Patients were matched by adenoma and radiosurgical parameters and stratified based on the interval between last resection and radiosurgery. Operative results, imaging data, and clinical outcomes were compared across groups following early ( $= 6$  months after resection) or late ( $> 6$  months after resection) radiosurgery. Results: After matching, 222 patients met the authors' study criteria (from an initial collection of 496 patients) and were grouped based on early ( $n = 111$ ) or late ( $n = 111$ ) GKRS following transsphenoidal surgery. There was a greater risk of tumor progression after GKRS ( $p = 0.013$ ) and residual tumor ( $p = 0.038$ ) in the late radiosurgical group over a median imaging follow-up period of 68.5 months. No significant difference in the occurrence of post-GKRS endocrinopathy was observed ( $p = 0.68$ ). Thirty percent of patients without endocrinopathy in the early cohort developed new endocrinopathies during the follow-up period versus 27% in the late cohort ( $p = 0.84$ ). Fourteen percent of the patients in the early group and 25% of the patients in the late group experienced the resolution of endocrine dysfunction after original presentation ( $p = 0.32$ ). Conclusions: In this study, early GKRS was associated with a lower risk of radiological progression of subtotally resected nonfunctioning pituitary macroadenomas compared with expectant management followed by late radiosurgery. Delaying radiosurgery may increase patient risk for long-term adenoma progression. The timing of radiosurgery does not appear to significantly affect the rate of delayed endocrinopathy.

**Radhakrishna U**, Vishweswaraiah S, Veerappa AM, Zafra R, Albayrak S, Sitharam PH, Saiyed NM, Mishra NK, Guda C and **Bahado-Singh R** (2018). "Newborn blood DNA epigenetic variations and signaling pathway genes associated with Tetralogy of Fallot (TOF)." PLoS ONE 13(9).

[Full Text](#)

#### *Department of Obstetrics and Gynecology*

Tetralogy of Fallot (TOF) is the most common Critical Congenital Heart Defect (CCHD). The etiology of TOF is unknown in most cases. Preliminary data from our group and others suggest that epigenetic changes may play an important role in CHD. Epidemiologically, a significant percentage of CHD including TOF fail to be diagnosed in the prenatal and early newborn period which can negatively affect health outcomes. We performed genome-wide methylation assay in newborn blood in 24 non-syndromic TOF cases and 24 unaffected matched controls using Illumina Infinium HumanMethylation450 BeadChips. We identified 64 significantly differentially methylated CpG sites in TOF cases, of which 25 CpG sites had high predictive accuracy for TOF, based on the area under the receiver operating characteristics curve (AUC ROC) 0.90). The CpG methylation difference between TOF and controls was 10% in 51 CpG targets suggesting biological significance. Gene ontology analysis identified significant biological processes and functions related to these differentially methylated genes, including: CHD development, cardiomyopathy, diabetes, immunological, inflammation and other plausible pathways in CHD development. Multiple genes known or plausibly linked to heart development and post-natal heart disease were found to be differentially methylated in the blood DNA of newborns with TOF including: ABCB1, PPP2R5C, TLR1, SELL, SCN3A, CREM, RUNX and LHX9. We generated novel and highly accurate putative molecular markers for TOF detection using leucocyte DNA and thus provided information on pathogenesis of TOF.

Renz P, Hasan S, Gresswell S, Hajjar RT, Trombetta M and **Fontanesi J** (2018). "Dose effect in adjuvant radiation therapy for the treatment of resected keloids." International Journal of Radiation Oncology, Biology, Physics 102(1): 149-154.

[Full Text](#)

#### *Department of Neurosurgery*

Purpose: Surgical excision of keloids can result in an insidious cycle of tissue injury and repeat keloid formation unless combined with adjuvant therapy to halt this cycle. We present our results of postoperative radiation therapy for keloids with various dose regimens. Methods and Materials: A retrospective review of 124 patients with 250 keloid lesions treated with postoperative radiation therapy was analyzed. In this institutional review board-approved study, 125 keloids were treated to 20 Gy in 5 fractions and 125 keloids were treated to 12 to 16 Gy in 3 to 4 fractions. Local failure was defined as redevelopment of any clinically apparent keloid at the treated site. The median age was 34 years (14-84 years). Keloids were located on the ear (34%), neck/shoulder (19%), abdomen (13%), chest (10%), face (9%), breast (7%), extremities (4%), and back (3%). Median keloid size was 4 cm (0.5-20 cm). Results: At a median follow-up of 40 months, the recurrence rate for all lesions was 5.6%. Lesions treated to 20 Gy had a recurrence rate of 1.6% compared with 9.6% with <20 Gy and an odds ratio of 0.16 (P = .02). Upon univariate and multivariate analysis there were no differences in recurrence rate with respect to location, race, gender, age, previously treated lesions, and presence of multiple keloids. The lone predictor for improved control rate was the dose of 20 Gy in 5 fractions compared with less than that. Control rate for lesions treated to a biologically equivalent dose of 35 to 36 Gy<sub>2</sub>, 48 to 52.5 Gy<sub>2</sub>, and 60 to 72 Gy<sub>2</sub> were 10% (P = .007), 8.9% (P = .16), and 1.6% (P = .02), respectively. Conclusions: Surgical excision followed by immediate adjuvant radiation therapy for keloids provides excellent local control and cosmesis. Treatment with a biologically equivalent dose > 60 (20 Gy in 5 fractions) yielded superior local control over lower dose regimens.

**Reygaert WC** (2018). "Green tea catechins: Their use in treating and preventing infectious diseases." BioMed Research International 9105261: 1-9.

[Full Text](#)

#### *Department of Foundational Medical Studies*

Green tea is one of the most popular drinks consumed worldwide. Produced mainly in Asian countries from the leaves of the *Camellia sinensis* plant, the potential health benefits have been widely studied. Recently, researchers have studied the ability of green tea to eradicate infectious agents and the ability to actually prevent infections. The important components in green tea that show antimicrobial properties are the catechins. The four main catechins that occur in green tea are (-)-epicatechin (EC), (-)-epicatechin-3-gallate (ECG), (-)-epigallocatechin (EGC), and (-)-epigallocatechin-3-gallate (EGCG). Of these catechins, EGCG and EGC are found in the highest amounts in green tea and have been the subject of most of the studies. These catechins have been shown to demonstrate a variety of antimicrobial properties, both to organisms affected

and in mechanisms used. Consumption of green tea has been shown to distribute these compounds and/or their metabolites throughout the body, which allows for not only the possibility of treatment of infections but also the prevention of infections.

Ricart PH, Gandhi SD, Geisinger J, **Baker K** and **Park DK** (2018). "Clinical and CT analysis of lumbar spine arthrodesis:  $\beta$ -tricalcium phosphate versus demineralized bone matrix." Journal of the American Academy of Orthopaedic Surgeons. Global Research & Reviews 2(9): e024-e024.

[Full Text](#)

*Department of Orthopedic Surgery*

Background: Bone graft substitutes have been developed to circumvent donor site morbidity associated with iliac crest bone graft, but sparse literature compares the efficacy of various substitutes. Two commonly used bone graft substitutes used in lumbar fusion are  $\beta$ -tricalcium phosphate (BTP) and demineralized bone matrix (DBM). Methods: A retrospective review of patients who underwent instrumented posterolateral lumbar fusion was conducted by a single surgeon from January 2013 to December 2016. Patients were divided into two groups based on whether DBM or BTP as graft in conjunction with local autograft. Clinical outcomes scores were collected at a minimum of 1-year follow-up. Postoperative CT scans were evaluated to assess fusion. Results: Forty-one patients (DBM, 21 and BTP, 20) were reviewed. No significant differences were found in terms of age, sex, body mass index, smoking, diabetes, steroids, osteoporosis, American Society of Anesthesiologists classification, number of levels fused, estimated blood loss, length of stay, or surgical time between the DBM and BTP groups. A trend was found toward lower revision surgery (zero versus 15%), improved visual analog scale scores (postoperative change of 1.81 versus 3.25;  $P = 0.09$ ), and higher rates of fusion (90% versus 70%;  $P = 0.09$ ) in the DBM group compared with the BTP group. Conclusions: No significant difference was found in clinical outcomes at 1 year, with a trend toward a higher fusion rate and lower revision surgery with DBM.

Richardson-Hatcher A, MacPherson B, **Gould D** and Brueckner-Collins J (2018). "Assessing the impact of the Graduate Certificate in Anatomical Sciences Instruction: A post-degree survey." Anatomical Sciences Education 11(5): 516-524.

[Full Text](#)

*Department of Foundational Medical Studies*

There are few graduate programs available for pursuing a doctorate in anatomy where students gain specific training in gross anatomy dissection and the responsibilities of a medical educator. In light of this fact, the University of Kentucky created a Graduate Certificate in Anatomical Sciences Instruction in 2006. This 12-credit hour curriculum includes detailed training in gross anatomy and/or neuroscience courses, practicum experiences, a seminar class in pedagogical literature, and a course in educational strategies for the anatomical sciences. The award of certificate completion affirms that the candidate has demonstrated faculty-supervised proficiency in anatomy dissection, instruction in anatomy topics, and teaching strategies for anatomy. Seventeen graduate students have earned the certificate since its inception; nine students accepted teaching positions in anatomy following their graduate training and currently nine certificate graduates have assistant (six) or associate (three) professor positions in academia. In 2016, an anonymous survey including Likert-style and open-ended questions was emailed to all certificate graduates. Graduates favorably responded (each question averaged 4.4 or greater out of 5) that the certificate increased their awareness of teaching-faculty responsibilities, adequately prepared them for teaching-related duties, and positively contributed toward their first employment. Graduates indicated that the lecturing and dissection experience, awareness of faculty responsibilities, and job preparation (e.g., teaching philosophy development) were the most helpful aspects of the certificate. These results indicate that the Graduate Certificate in Anatomical Sciences Instruction is viewed by its graduates and their employers as a valuable teaching credential that can be attained alongside a basic science degree. *Anat Sci Educ* 11: 516–524. © 2018 American Association of Anatomists.

Robinson LA, Tanvetyanon T, Grubbs D, Antonia S, Creelan B, Fontaine J, Toloza E, Keenan R, Dilling T, **Stevens CW**, Sommers KE and Vronis F (2018). "Induction chemoradiotherapy versus chemotherapy alone for superior sulcus lung cancer." Lung Cancer 122: 206-213.

[Full Text](#)

*Department of Radiation Oncology*

Objectives: Although treatment of superior sulcus tumors with induction chemoradiotherapy (CRT) followed by surgery employed in the Intergroup INT-0160 trial is widely adopted as a standard of care, there may be significant associated morbidity and mortality. We describe our experience using standard and alternative induction regimens to assess survival rates and treatment toxicity in these patients. Materials and Methods: Electronic medical records of all patients who underwent multimodality treatment including resection of lung cancer invading the superior pulmonary sulcus between 1994 and 2016 were retrospectively reviewed. Multivariable Cox Proportional Hazards model was constructed. Results: Of 102 consecutive patients, 53 (52%) underwent induction CRT, 34 (33%) underwent induction chemotherapy only (Ch) followed by adjuvant radiotherapy, and 15 (15%) underwent no induction therapy followed by adjuvant therapy. There were 2 postoperative deaths (1.9%). To date, 42 patients are alive with a median follow-up 72.5 months. Overall 5-year survival rate was 45.4%. Survival was significantly influenced by age, FEV1, positive resection margins, surgical complications, but not the induction regimen. CRT resulted in higher complete pathological response rate than Ch: 38% vs. 3% ( $p < 0.001$ ). CRT was associated with higher post-operative re-intubation rate: 13% vs. 0% ( $p = 0.03$ ). Conclusions: Our single-institutional experience indicated that while induction CRT produced greater complete pathological response than Ch, it also increased the risk of post-operative complications. With careful patient selection, induction Ch followed by adjuvant radiotherapy may provide comparable survival outcomes to induction CRT. Since induction Ch is associated with lower risk of complications, it may be a particularly desirable choice for patients with impaired performance status.

Rodriguez M, Ryan E, Ryan C, Kakulavarapu S, Mardis P, Stefater JA, Forbes N, Gupta O, **Capone A**, Joseph D, Elliott D and Yonekawa Y (2018). "Impact of viewing system choice during primary retinal detachment repair." Investigative Ophthalmology & Visual Science 59(9): 1162.

[Full Text](#)

*Department of Ophthalmology*

Purpose: Vitrectomy can be performed either with non-contact wide-angle viewing systems or wide-angle contact lenses. It is unknown whether there are differences in surgical outcomes based on choice of viewing system. The purpose of this study is to assess whether there are differences in anatomic vitrectomy outcomes of primary non-complex retinal detachment (RD) repair, based on viewing system used. Methods: This is a multicenter, interventional, retrospective, comparative study. Eyes that underwent non-complex primary RD repair by either pars plana vitrectomy (PPV) alone or in combination with scleral buckle (SB/PPV) were identified. Eyes that underwent repair by primary SB, pneumatic retinopexy, or retinopexy alone were excluded from the analysis. The viewing system used at the time of RD repair was identified. The primary outcome of our study was single surgery anatomic success (SSAS), which was defined as no re-operations for RD during the post-operative 90-day window. Significance was determined using Pearson's  $\chi^2$  test. Results: A total of 1811 eyes were included in our analysis. Of those, 1529 (84.4%) had RD repaired using non-contact viewing systems, while 282 (15.6%) were repaired using a contact lens system. SSAS for non-contact viewing systems was 86.5% and 86.9% for contact lenses, which was not statistically different ( $p=0.87$ ). A total of 1073 eyes had PPV alone for RD repair, of which 916 (85.4%) were performed using non-contact viewing systems. Of those eyes repaired by PPV alone, non-contact systems had an 84.3% SSAS compared to 84.1% for contact lenses. This difference was not significant ( $p=0.94$ ). Similarly, a total of 738 eyes were repaired using a combined SB/PPV approach, 613 (83.1%) of which were repaired using non-contact viewing systems. Of those eyes repaired by a combined SB/PPV approach there was no statistically significant difference between the two viewing systems, with an 89.9% SSAS for non-contact systems vs. 90.4% for contact lenses ( $p=0.86$ ). Conclusions: There was no significant difference in SSAS for primary RD repair when comparing non-contact viewing systems to contact lens systems.

Rothschild DP and **Goldstein JA** (2018). "Submassive pulmonary embolus: The challenge of thrombolytic decision-making in a heterogenous cohort." Catheterization and Cardiovascular Interventions 92(2): 372-373.

[Full Text](#)

*Department of Internal Medicine*

Sandler KA, Cook RR, Ciezki JP, Ross AE, Pomerantz MM, Nguyen PL, Shaikh T, Tran PT, Stock RG, Merrick GS, Demanes DJ, Spratt DE, Abu-Isa EI, Wedde TB, Lilleby W, **Krauss DJ**, Shaw GK, Alam R, Reddy CA and Song DY (2018).

"Clinical cutcomes for patients with Gleason score 10 prostate adenocarcinoma: Results from a multi-institutional consortium study." [International Journal of Radiation Oncology, Biology, Physics](#) 101(4): 883-888.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: Gleason score (GS) 10 disease is the most aggressive form of clinically localized prostate adenocarcinoma (PCa). The long-term clinical outcomes and overall prognosis of patients presenting with GS 10 PCa are largely unknown because of its rarity. Methods and Materials: The study included 112 patients with biopsy-determined GS 10 PCa who received treatment with radical prostatectomy (RP, n = 26), external beam radiation therapy (EBRT, n = 48), or EBRT with a brachytherapy boost (EBRT-BT, n = 38) between 2000 and 2013. Propensity scores were included as covariates for comparative analysis. Overall survival, prostate cancer-specific survival, and distant metastasis-free survival (DMFS) were estimated by the Kaplan-Meier method with inverse probability of treatment weighting to control for confounding. Results: The median follow-up period was 4.9 years overall (3.9 years for RP, 4.8 years for EBRT, and 5.7 years for EBRT-BT). Significantly more EBRT patients than EBRT-BT patients received upfront androgen deprivation therapy (98% vs 79%,  $P < .01$  by  $\chi^2$  test), though the durations were similar (median, 24 months vs 22.5 months). Of the RP patients, 34% received postoperative EBRT, and 35% received neoadjuvant systemic therapy. The propensity score-adjusted 5-year overall survival rate was 80% for the RP group, 73% for the EBRT group, and 83% for the EBRT-BT group. The corresponding adjusted 5-year prostate cancer-specific survival rates were 87%, 75%, and 94%, respectively. The EBRT-BT group trended toward superior DMFS when compared with the RP group (hazard ratio, 0.3; 95% confidence interval 0.1-1.06;  $P = .06$ ) and had superior DMFS when compared with the EBRT group (hazard ratio, 0.4; 95% confidence interval 0.1-0.99;  $P = .048$ ). Conclusions: To our knowledge, this is the largest series ever reported on the clinical outcomes of patients with biopsy-determined GS 10 PCa. These data provide useful prognostic benchmark information for physicians and patients. Aggressive therapy with curative intent is warranted, as >50% of patients remain free of systemic disease 5 years after treatment.

**Sangal RB** (2018). "Baseline sleep efficiency and arousal index do not predict who will benefit from sedatives in improving positive airway pressure adherence in sleep apnea to 90%." [Clinical EEG and Neuroscience](#) 49(4): 285-289.

[Full Text](#)

*Department of Family Medicine and Community Health*

Positive airway pressure (PAP) is the preferred treatment for obstructive sleep apnea (OSA), but adherence is low. Educational or ongoing supportive intervention improves the number of PAP adherent patients from the 50% to the 70% range. A common side effect of PAP is increased awakenings. This prospective trial examined baseline polysomnographically derived sleep efficiency and arousal index in PAP adherent and nonadherent patients, and in patients needing sedating medicines to attain PAP adherence versus those who did not need such medicines. Patients with OSA were titrated on PAP during a polysomnography or treated with autotitrating PAP, followed by educational and supportive interventions. Patients with PAP related awakenings (patients describing waking up and taking PAP off in the middle of the night) or difficulty tolerating PAP were additionally treated with medicines that suppress arousals/awakenings (trazodone, mirtazapine, doxepin). A total of 120 of 151 (79%) new patients were 70% PAP adherent over a continuous 30-day period, typically within the first 90 days of starting PAP, without sedating medicines. Nineteen of the remaining patients were treated with medicines that suppress arousals and awakenings, and 16 became adherent, resulting in 136 (90%) of 151 new patients achieving adherence. There were no differences in baseline sleep efficiency or arousal index, between adherent and nonadherent patients, as well as between patients who needed sedating medicines for PAP adherence and those who did not. Adding medicines that suppress arousals and awakenings for patients having trouble tolerating PAP, increases the number of patients who are PAP adherent. The need for such medicines seems to be related to the PAP side effect of increased awakenings rather than baseline impaired sleep.

Sankar WN, Novais E, Koueiter D, Refakis C, Sink E, Millis MB, Young-jo K, Clohisy J, Wells J, Nepple J, **Zaltz I** and Kim Y-J (2018). "Analysis of femoral version in patients undergoing periacetabular osteotomy for symptomatic acetabular dysplasia." [Journal of the American Academy of Orthopaedic Surgeons](#) 26(15): 545-551.

[Full Text](#)

*Department of Orthopedic Surgery*

Introduction: A paucity of information exists on the range of femoral version, its effect on hip stability, clinical examination, and presentation in patients with symptomatic acetabular dysplasia. The purpose of this study was to describe the range of version in symptomatic acetabular dysplasia, the association between femoral version and proximal femoral morphology and degree of dysplasia, and the effect of version on clinically measured hip range of motion and on preoperatively measured hip outcome scores. Methods: We reviewed 314 patients prospectively enrolled in a longitudinal clinical study on periacetabular osteotomy between January 2014 and August 2015 and measured femoral version, morphologic characteristics of the upper femur and acetabulum, and preoperative clinical outcome scores. Results: The average femoral version was  $19.7^\circ \pm 11.2^\circ$  (range,  $-20^\circ$  to  $50^\circ$ ). Femoral version correlated strongly with clinically measured hip range of motion but did not correlate linearly with either radiographic severity of acetabular dysplasia or preoperative symptomatology. Discussion: Despite concerns that transverse plane femoral anatomy influences the stability of the hip joint after skeletal maturity, we did not find a statistical association between femoral version and severity of dysplasia or presenting symptomatology. This finding suggests that femoral version is not a major influence on the clinical presentation of acetabular dysplasia. Level Of Evidence: Level IIIb.

Sczepanski M and **Bozyk P** (2018). "Institutional incidence of severe tPA-induced angioedema in ischemic cerebral vascular accidents." Critical Care Research and Practice 2018: 9360918-9360918.

[Full Text](#)

*Department of Internal Medicine*

Introduction: Tissue plasminogen activator (tPA) is commonly used in ischemic cerebral vascular accidents (CVAs). tPA is generally well tolerated; however, orolingual angioedema is a well-documented adverse effect. Angioedema is generally mild, transient, and unilateral but can manifest as severe, life-threatening upper airway obstruction requiring intubation. Reported incidence for all severities ranges from one to five percent, whereas reported incidence of severe cases ranges from 0.18 to 1 percent of patients receiving tPA for ischemic CVA. Angiotensin-converting enzyme (ACE) inhibitors and middle cerebral artery distribution have been associated with a higher risk of developing angioedema. The aim of this study is to evaluate the incidence of severe tPA-induced angioedema and its effects on length of stay (LOS) and death. Methods: A retrospective chart review of patients receiving tPA for ischemic CVA from January 2014 through December 2016 was conducted at a large tertiary center with Comprehensive Stroke Center designation. Subjects were eighteen or older. Baseline demographics and clinical data were collected. Results: 147 patients were included with four developing severe angioedema due to tPA resulting in an incidence of 2.72%. All four were female. The median LOS was thirty days for patients with angioedema and twelve days for those without. The survival probability was higher in the angioedema group and mean time to death was twenty-two days in the angioedema group and twenty-one days in the nonangioedema group. Twenty-five patients died, one from the angioedema group. ACE inhibitor use was found to have an OR of 7.72. Conclusion: This study found a higher incidence of severe angioedema than that reported. Development of severe angioedema increased length of stay but was not shown to worsen outcomes in regards to death. Consistent with previous studies, ACE inhibitor use was associated with a higher risk of developing angioedema.

Sevak S, **Lurvey B**, **Woodfin AA**, Hothem Z, Callahan RE, **Robbins J** and **Ziegler K** (2018). "Solid, cystic, and tubular: Novice ultrasound skills training using a versatile, affordable practice model." Journal of Surgical Education 75(5): 1403-1409.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Surgery*

Objective: In spite of the recognized benefits of ultrasound, many physicians have little experience with using ultrasound to perform procedures. Many medical schools and residency programs lack a formal ultrasound training curriculum. We describe an affordable ultrasound training curriculum and versatile, inexpensive practice model. Design: Participants underwent a didactic session to teach the theory required to perform ultrasound-guided procedures. Motor skills were taught using a practice model incorporating analogs of common anatomic and pathologic structures into an opacified gelatin substrate. Setting: The Marcia and Eugene Applebaum Simulation Learning Institute, Beaumont Hospital, Royal Oak, MI; a private nonprofit tertiary care hospital associated with the OUWB School of Medicine, Rochester, MI. Participants: The model

was tested in a cohort of 50 medical students and general surgery residents. Results: The gelatin model can be constructed for \$1.03 per learner. The solid, cystic, and vascular structural analogs were readily identifiable on ultrasound and easily differentiated based on their echotextures. Eighty-four percent of participants successfully aspirated the cystic structure, 88% successfully biopsied a portion of the solid structure, and 76% successfully cannulated the tubular structure. Overall, 82% of participants achieved a passing score for the exercise based on a validated Objective Structured Assessment of Technical Skill instrument. There were no significant differences between the medical students and residents. Conclusion: This model can be used to teach basic ultrasound skills such as aspiration, biopsy, and vessel cannulation, providing a foundation for the use of ultrasound in a broad range of clinical procedures, as well as providing practice opportunities for medical students and residents to gain increased ultrasound competency and confidence.

Sevak S, **Woodfin A**, Hothem Z, Callahan R, **Robbins J** and **Ziegler K** (2018). "Gelatin thoracic paravertebral teaching model for placement of a continuous infusion catheter in the extrathoracic paravertebral space." Journal of Surgical Education 75(5): 1389-1394.

[Full Text](#)

*OUWB Medical Student Author  
Department of Surgery*

**Shams C, Cannon M**, Bortman J and Hakim S (2018). "Stone-induced purulent choledocoduodenal fistula presenting with ascending cholangitis." ACG Case Reports Journal 5: e60-e60.

[Full Text](#)

*OUWB Medical Student Author  
Department of Internal Medicine*

A biliary enteric fistula (BEF) is a rare, abnormal communication between any segment of the biliary tree with any portion of the small or large intestine. BEF is more frequently diagnosed with the increasingly widespread use of endoscopic retrograde cholangiopancreatography. Different theories have been postulated regarding the etiology of this fistula formation, with the most likely cause being gallstones. Treatment modalities, ranging from conservative management to surgical reconstruction, show varying levels of success. We present a case of BEF secondary to large common bile duct stones, successfully treated with endoscopic sphincterotomy (EST) followed by papillary balloon dilatation, and we briefly discuss large stone retrieval in the setting of atypical anatomy.

**Shams C**, Hakim S, **Amin M** and Cappell MS (2018). "Case report and literature review illustrating the clinical, endoscopic, radiologic, and histopathologic findings with prepouch ileitis after IPAA and restorative proctocolectomy for refractory ulcerative colitis." Case Reports in Gastrointestinal Medicine 2018: 7506069-7506069.

[Full Text](#)

*OUWB Medical Student Author  
Department of Pathology  
Department of Internal Medicine*

Prepouch ileitis (PI) is an uncommon complication of ileal pouch anal anastomosis (IPAA) and restorative proctocolectomy (RPC) for treatment of refractory ulcerative colitis (UC). A case is reported of PI in a 16-year-old girl who presented with severe UC that was initially stabilized with infliximab therapy but re-presented 1 year later with severe UC, refractory to infliximab and corticosteroid therapy, which required IPAA and RPC. Her symptoms resolved postoperatively, but she re-presented 1 year later with 10 loose, bloody, bowel movements/day and involuntary 6-Kg weight-loss. Computerized tomographic enterography showed focal narrowing and mucosal enhancement of the pouch and focal narrowing, abnormal mucosal enhancement, and mural thickening of the prepouch ileum. Pouchoscopy revealed exudates and ulcerations in both the pouch and prepouch ileum up to 50 cm proximal to pouch, as confirmed by histopathology of pouch and ileal biopsies. Capsule endoscopy revealed no small intestinal lesions beyond 50 cm from the pouch. She required antibiotics, hydrocortisone enemas, and eventually azathioprine to control her symptoms. She remains asymptomatic 4 years later while chronically administered azathioprine therapy. Comprehensive literature review demonstrates that this case illustrates the classical clinical, radiologic, endoscopic, and histopathologic findings in PI, a relatively rare syndrome.

Shepard MJ, Mehta GU, Xu Z, Kano H, Sisterson N, Su YH, Krsek M, Nabeel AM, El-Shehaby A, Kareem KA, Martinez-Moreno N, Mathieu D, McShane BJ, Blas K, Kondziolka D, **Grills I**, Lee JY, Martinez-Alvarez R, Reda WA, Liscak R, Lee CC, Lunsford LD, Lee Vance M and Sheehan JP (2018). "Technique of whole-sellar stereotactic radiosurgery for cushing disease: Results from a multicenter, international cohort study." World Neurosurgery 116: e670-e679.

[Full Text](#)

*Department of Radiation Oncology*

Background: Stereotactic radiosurgery (SRS) is used to manage patients with Cushing disease (CD) who have failed surgical/medical management. Because many patients with recurrent/persistent CD lack an identifiable adenoma on neuroimaging, whole-sellar SRS has been increasingly used. Thus, we sought to define the outcomes of patients undergoing whole-sellar SRS. Methods: An international, multicenter, retrospective cohort design was used to define clinical/endocrine outcomes for patients undergoing whole-sellar SRS for CD. Propensity-score matching was used to compare patients undergoing whole-sellar SRS and patients who underwent discreet adenoma-targeted SRS. Results: A total of 68 patients underwent whole-sellar SRS, with a mean endocrine follow-up of 5.3 years. The mean treatment volume was 2.6 cm<sup>3</sup>, and the mean margin dose was 22.4 Gy. The 5-year actuarial remission rate was 75.9%, and the median time to remission was 12-months. Treatment volumes  $\geq 1.6$  cm<sup>3</sup> were associated with shorter times to remission ( $P < 0.05$ ). The 5-year recurrence-free survival rate was 86.0%. Decreased margin and maximum treatment doses were associated with recurrence ( $P < 0.05$ ). New pituitary hormone deficiency occurred in 15 patients (22.7%). An additional 210 patients were identified who underwent adenoma-targeted SRS. There was no difference in remission rate, time to remission, recurrence-free survival or new endocrinopathy development between patients who underwent whole-sellar SRS and those who underwent discreet adenoma-targeted SRS. Conclusions: Whole-sellar GKRS is effective in controlling CD when an adenoma is not clearly defined on imaging or when an invasive adenoma is suspected at the time of initial surgery. Patients who undergo whole-sellar SRS have outcomes and rates of new pituitary hormone deficiency similar to those of patients who undergo discrete adenoma-targeted GKRS.

Shields E and **Wiater JM** (2018). "Patient outcomes after revision of anatomic total shoulder arthroplasty to reverse shoulder arthroplasty for rotator cuff failure or component loosening: A matched cohort study." JAAOS - Journal of the American Academy of Orthopaedic Surgeons. ePub Ahead of Print.

[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 ( $2.4 \pm 2.8$  versus  $1.7 \pm 2.8$ ;  $P = 0.24$ ) and American Shoulder and Elbow Surgeons ( $68 \pm 26$  versus  $76 \pm 24$ ;  $P = 0.14$ ) scores were similar. The revision group had worse subjective shoulder value scores ( $63 \pm 30$  versus  $79 \pm 21$ ;  $P = 0.002$ ), 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.

**Simha S**, Shields EJW and **Wiater JM** (2018). "Periprosthetic infections of the shoulder." JBJS Reviews 6(9): e6-e6.

[Full Text](#)

*OUIWB Medical Student Author*

*Department of Orthopedic Surgery*

Periprosthetic joint infection is a major complication after both anatomical and reverse total shoulder arthroplasty. Factors such as diabetes mellitus and high body mass index play a role in increasing the risk of infection after shoulder arthroplasty. Infection after shoulder surgery is caused by a variety of organisms, most of which, such as *Staphylococcus aureus* and *Propionibacterium acnes*, are normal skin flora. Treatment options include single-stage revision, 2-stage revision, component retention with irrigation and

debridement, and treatment with antibiotics alone. The efficacy of these treatment modalities is discussed. With the increasing prevalence of shoulder arthroplasty, preventive measures such as antibiotic prophylaxis and adequate surgical skin preparation are of the utmost importance.

Stanhope CW, Drake DG, Liang J, Alber M, Söhn M, Habib C, Willcut V and **Yan D** (2018). "Evaluation of machine log files/MC-based treatment planning and delivery QA as compared to ArcCHECK QA." *Medical Physics* 45(7): 2864-2874.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: A treatment planning/delivery QA tool using linac log files (LF) and Monte Carlo (MC) dose calculation is investigated as a standalone alternative to phantom-based patient-specific QA (ArcCHECK (AC)). Methods: Delivering a variety of fields onto MapCHECK2 and ArcCHECK, diode sensitivity dependence on dose rate (in-field) and energy (primarily out-of-field) was quantified. AC and LF QAs were analyzed with respect to delivery complexity by delivering 12 × 12 cm static fields/arcs comprised of varying numbers of abutting sub-fields onto ArcCHECK. About 11 clinical dual-arc VMAT patients planned using Pinnacle's convolution-superposition (CS) were delivered on ArcCHECK and log file dose (LF-CS and LF-MC) calculated. To minimize calculation time, reduced LF-CS sampling (1/2/3/4° control point spacing) was investigated. Planned ("Plan") and LF-reconstructed CS and MC doses were compared with each other and AC measurement via statistical [mean ± StdDev( $\sigma$ )] and gamma analyses to isolate dosimetric uncertainties and quantify the relative accuracies of AC QA and MC-based LF QA. Results: Calculation and ArcCHECK measurement differed by up to 1.5% in-field due to variation in dose rate and up to 5% out-of-field. For the experimental segment-varying plans, despite CS calculation deviating by as much as 13% from measurement, Plan-MC and LF-MC doses generally matched AC measurement within 3%. Utilizing 1° control point spacing, 2%/2 mm LF-CS vs AC pass rates (97%) were slightly lower than Plan-CS vs AC pass rates (97.5%). Utilizing all log file samples, 2%/2 mm LF-MC vs AC pass rates (97.3%) were higher than Plan-MC vs AC (96.5%). Phantom-dependent, calculation algorithm-dependent (MC vs CS), and delivery error-dependent dose uncertainties were 0.8 ± 1.2%, 0.2 ± 1.1%, and 0.1 ± 0.9% respectively. Conclusion: Reconstructing every log file sample with no increase in computational cost, MC-based LF QA is faster and more accurate than CS-based LF QA. Offering similar dosimetric accuracy compared to AC measurement, MC-based log files can be used for treatment planning QA.

Stem MS, **Moinuddin O**, **Kline N**, Thanos A, Rao P, **Williams GA** and **Hassan TS** (2018). "Outcomes of anti-vascular endothelial growth factor treatment for choroidal neovascularization in fellow eyes of previously treated patients with neovascular age-related macular degeneration." *JAMA Ophthalmology* 136(7): 820-823.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Ophthalmology*

Importance: Neovascular age-related macular degeneration (nvAMD) is a leading cause of vision loss. The optimal screening protocol to detect choroidal neovascularization (CNV) in fellow eyes of patients undergoing treatment for unilateral CNV has not been determined. Objective: To compare the visual outcomes of eyes with established, active nvAMD in index eyes with outcomes of fellow eyes that subsequently developed CNV during the management protocol. Design, Setting, and Participants: In this retrospective single-center case series conducted at a private vitreoretinal practice, data were collected for all patients treated for bilateral nvAMD between October 1, 2015, and October 1, 2016, for whom we could determine the date of index eye and fellow eye conversion to nvAMD (n = 1600). Per institutional protocol, patients were screened for new CNV in the fellow eye at every office visit. Patients were excluded if they had a condition that could result in marked asymmetric vision loss. Exposures: Development of nvAMD. Main Outcomes and Measures: Visual acuity (VA) at the time of diagnosis of nvAMD and at equivalent time points following conversion to nvAMD for both index eyes and fellow eyes. Results: A total of 264 patients met the inclusion criteria; 197 (74.6%) were women and 253 (95.8%) were white, and the mean (SD) age was 79.1 (8.2) years at time of index eye conversion to nvAMD and 80.6 (8.2) years at time of fellow eye conversion to nvAMD. Fellow eyes presented with better VA (mean VA, 20/50 [0.40 logMAR]) compared with index eyes (mean VA, 20/90 [0.67 logMAR]) at the time of conversion (difference, 14 letters [0.27 logMAR]; 95%CI, 10-17 [0.20-0.34]; P <.001). Index eyes did not achieve the same level of VA as fellow eyes after an equivalent

postconversion follow-up of approximately 20 months (mean VA: Index eye; 20/70 [0.56 logMAR]; fellow eye, 20/50 [0.40 logMAR]; difference, 8 letters [0.15 logMAR]; 95%CI, 4-11 [0.08-0.22]; P <.001). No difference was detected between the mean number of anti-vascular endothelial growth factor injections received by fellow eyes and index eyes (9.7 vs 10.0 injections, respectively). Conclusions and Relevance: This retrospective study suggests that fellow eyes of previously treated patients with nvAMD may achieve better VA than their index eye counterparts after an equivalent amount of follow-up. This may be because the CNV was detected and treated earlier and at a better level of VA, although it is unknown whether the frequent office visits, VA measurements, or optical coherence tomography testing was responsible for the detection at a better level of VA.

Stewart M and **Loftus S** (2018). "Sticks and stones: The impact of language in musculoskeletal rehabilitation." Journal of Orthopaedic & Sports Physical Therapy 48(7): 519-522.

[Full Text](#)

*Department of Foundational Medical Studies*

The article offers information on musculoskeletal rehabilitation and the impact that the words used by therapists can play in the clinical outcome. Topics discussed include the importance of effective communication by therapists in rehabilitation; the role of psychological factors as predictors of pain and disability levels; and the influence of language on pain perception of individuals.

**Sundram U** (9000). "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. ePub Ahead of Print.

[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.

Svider PF, **Arianpour K**, Guo E, Folbe E, Zuliani G, Lin H, Eloy JA and Folbe AJ (2018). "Opioid prescribing patterns among otolaryngologists: Crucial insights among the medicare population." Laryngoscope 128(7): 1576-1581.

[Full Text](#)

*OUWB Medical Student Author*

Objectives/Hypothesis: There has been growing recognition of the roles prescription drug misuse and diversion play in facilitating the ongoing opioid epidemic. Our objective was to evaluate opioid prescription patterns among practicing otolaryngologists. Study Design: Retrospective review of a CMS database. Methods: Medicare Part D beneficiary data (2015) were accessed for a list of otolaryngologists. Opioid prescription rates, amount, and supply were calculated. Factors including board certification, experience, gender, and location were obtained for the 9,068 unique otolaryngologists represented in this dataset. Results: In 2015, otolaryngologists wrote 133,779 opioid prescriptions for 922,806 days (6.9 days/per prescription). The majority was for hydrocodone-acetaminophen (64.0%). Most otolaryngologists (51.2%) prescribed ≤ 10 opioids; 6.1% offered > 50 opioid prescriptions. Men wrote more prescriptions on average. Opioid prescription rates were greatest in the Midwest (4.6%) and least in the Northeast (1.8%), and the highest/lowest rates were in Delaware (8.6%) and New York (1.3%). Midcareer (11 –20 years) otolaryngologists were most likely to write >50 prescriptions. The opioid prescription rate declined with greater experience. Conclusions: Opioid prescriptions written by otolaryngologists may play a significant role in the availability of these agents, as otolaryngologists wrote nearly 1 million days worth of opioids to

Medicare beneficiaries in 2015. Although the majority of otolaryngologists write fewer than 11 prescriptions annually, those writing more prescriptions also write lengthier courses. There is significant geographic variation in prescribing patterns, highlighting a lack of consensus, and midcareer otolaryngologists are more aggressive in offering opioids. These findings highlight an urgent need for strengthening educational resources aimed at minimizing unnecessary prescriptions.

Svider PF, **Arianpour K, Nguyen B**, Hsueh WD, Langer PD, Eloy JA and Folbe AJ (2018). "Endoscopic and external approaches for orbital decompression: an analysis of trends from a U.S. perspective." International Forum of Allergy and Rhinology 8(8): 934-938.

[Full Text](#)

*OUWB Medical Student Author*

Background: Although the endoscopic approach has been increasingly utilized for a variety of sinonasal and skull base pathologies, there has been little inquiry into its adoption in the surgical management of orbital disease. Our objective was to evaluate nationwide temporal and geographic trends in approaches for orbital decompression. Methods: Data available from the Centers for Medicare and Medicaid Services (CMS) were evaluated, focusing on the use of open and endoscopic approaches for orbital decompression (CPT codes 67414, 67445, 31292, and 31293) among Medicare beneficiaries over a 10-year period. Regional data were also analyzed. Results: There were 8047 orbital decompressions billed to Medicare from 2007 to 2016. The number of external and endoscopic approaches increased by 73.0% and 29.2%, respectively, while the number of Medicare beneficiaries increased by 29.1%. Endoscopic decompression represented 23.5% of Medicare-billed orbital decompressions in 2016 (221 of 939), down from 29.2% in 2007 (171 of 586). The South had the greatest proportion of decompressions utilizing an endoscopic approach (30.2%). Conclusion: There has not been a clear movement toward the endoscopic approach for orbital decompression, with modest growth when compared with external approaches. Potential explanations include the specialty-exclusive nature of approaches, as well as a lack of consensus; the latter idea is further reinforced by geographic variation. High-quality prospective trials may clarify the role of endoscopic approaches in these patients.

Svider PF, **Nguyen B, Yuhan B**, Zuliani G, Eloy JA and Folbe AJ (2018). "Perioperative analgesia for patients undergoing endoscopic sinus surgery: an evidence-based review." International Forum of Allergy and Rhinology 8(7): 837-849.

[Full Text](#)

*OUWB Medical Student Author*

Background: Misuse and diversion of prescription opioids have been critical in facilitating the opioid epidemic. Our objective was to perform a systematic evidence-based review delineating perioperative regimens (including opioid alternatives) evaluated for endoscopic sinus surgery. Methods: PubMed/MEDLINE, Cochrane Library, and EmBase databases were evaluated for studies detailing analgesics employed after endoscopic sinus surgery. Studies were assessed for level of evidence. Bias risk was evaluated using the Cochrane Bias tool and GRADE criteria. Medication, administration, adverse effects, pain scores, and rescue analgesic consumption were evaluated. A summary of evidence detailing benefits, harm, and cost was prepared. Results: Thirty-two studies encompassing 1812 patients were included. The GRADE criteria determined the overall evidence to be of moderate quality. Perioperative acetaminophen had few adverse events and reduced immediate need for opioid rescue after sinus surgery; studies evaluating acetaminophen demonstrate a preponderance of benefit over harm. Nonsteroidal anti-inflammatory drugs (NSAIDs) also reduce postoperative opioid consumption, although a small portion of patients undergoing sinus surgery harbor the potential for NSAID intolerance. The aggregate level of evidence for studies evaluating NSAIDs was grade A, whereas the aggregate grade of evidence for several other agents was grade B. Conclusion: There is evidence supporting the use of NSAIDs and gabapentin for the control of pain after endoscopic sinus surgery. Acetaminophen,  $\alpha$ -agonists, and local anesthetics are also viable options for postoperative analgesia. Familiarity with these data is essential to facilitate the use of opioid alternatives. Further large-scale, multi-institutional, randomized trials are needed to provide conclusive recommendations for these perioperative analgesics.

**Swanberg SM, Mi M, Engwall K and Bulgarelli N** (2018). "Community engagement at an emerging academic

medical library: A three-pronged outreach model." *Medical Reference Services Quarterly* 37(3): 234-248.

[Full Text](#)

*Department of Foundational Medical Studies*

*Medical Library*

The Oakland University William Beaumont School of Medicine's (OUWB) service-oriented mission and vision is reflected in all aspects of the school including its culture, curriculum, research, community engagement, and the OUWB Medical Library. Though starting informally, the OUWB Medical Library's outreach program has matured and now sustains a wide array of activities each year. This outreach program has blossomed into a three-pronged model that is inclusive of activities and endeavors engaging the institution and local community: integrate, partner, and create. Among its successes and challenges, the library's ongoing outreach efforts have showcased the value of libraries in promoting community health and meaningfully contributing to the institutional mission.

Tejeda-Franco CD, Valadez V, Hernandez-Lopez X, **Ysunza PA**, Mena-Ramirez ME, Garcia-Zalapa RA and Miranda-Duarte A (2018). "Hearing aid use and auditory verbal therapy improve voice quality of deaf children." *Journal of Voice*. ePub Ahead of Print.

[Full Text](#)

*Department of Physical Medicine & Rehabilitation*

Background: Adequate phonation is self-regulated by auditory feedback. Children with bilateral profound hearing loss (PHL) lack this feedback resulting in abnormal voice. Adequate hearing aid use and auditory-verbal therapy (AVT) may improve voice quality in deaf children. Objective: To study whether hearing aid use and AVT approach improve acoustic parameters of voice of children with bilateral PHL. Materials and Methods: Nineteen children with bilateral PHL were studied. Age range 2–5 years ( $X = 53.04$  months;  $SD = 9.54$ ). All children were fitted with hearing aids according to auditory testing and they underwent a 1-year auditory habilitation period using the AVT approach. Acoustic analysis of voice including F0, shimmer, and jitter was performed at the onset and at the end of the auditory habilitation period. Final acoustic data were compared to a matched control group of 19 children, age range 2–5 years ( $X = 52.85$ ;  $SD = 9.74$ ) with normal hearing. Results: Mean fundamental frequency (F0) was significantly increased after AVT intervention. Shimmer and jitter significantly ( $P < 0.05$ ) improved after the intervention period. However, despite the improvements, mean F0 at the end of the intervention period was still significantly ( $P < 0.05$ ) decreased as compared to controls. Also, mean shimmer and jitter at the end of the habilitation period were still significantly ( $P < 0.05$ ) higher as compared to controls. Conclusions: The results of this preliminary study suggest that hearing aid use and auditory habilitation with AVT approach improved acoustic voice parameters of children with PHL. However, acoustic parameters persisted abnormal as compared to matched normal hearing controls. AVT approach and regular hearing aid use seem to be safe and reliable clinical tools for improving voice quality of children with PHL.

Thomas AS and **Mahmoud TH** (2018). "Subretinal transplantation of an autologous retinal free flap for chronic retinal detachment with proliferative vitreoretinopathy with and without macular hole." *Retina* 38: S121-S124.

[Full Text](#)

*Department of Ophthalmology*

Purpose: To describe the surgical technique for subretinal transplantation of an autologous retinal free flap in cases of chronic retinal detachment with proliferative vitreoretinopathy with and without a macular hole. Methods: Descriptive case series. Results: Two patients with recurrent retinal detachment with proliferative vitreoretinopathy were referred for surgical evaluation. The first patient had high myopia and a macular hole. Acuity at the last time of sustained retinal reattachment was 20/400 for the first patient and counting fingers for the second patient and, in both cases, declined to light perception in the months after redetachment. Despite membrane/internal limiting membrane peeling, surgical repair required an inferior retinectomy in both cases. A retinal free flap was placed subfoveally. In the first patient, the flap was placed with the photoreceptors facing bare retinal pigment epithelium. In the second patient, the flap was inverted so its photoreceptors faced residual macular photoreceptors. The retina was flattened over the flap. Postoperatively, vision improved to 20/160 and 20/400 in the first and second patient respectively. Conclusion: Subretinal placement of a retinal flap is possible in eyes with retinal detachment and proliferative vitreoretinopathy with and without macular hole. Whether such a flap results in superior visual and

anatomical outcomes remains to be seen.

Todorich B, Stem MS, Kooragayala K, Thanos A, **Faia LJ, Williams GA, Hassan TS**, Woodward MA and **Wolfe JD** (2018). "Structural analysis and comprehensive surgical outcomes of the sutureless intrascleral fixation of secondary intraocular lenses in human eyes." *Retina* 38: S31-S40.

[Full Text](#)

*Department of Ophthalmology*

Purpose: To describe surgical outcomes and structural characteristics of intraocular lenses (IOLs) implanted with transconjunctival sutureless intrascleral (SIS) fixation in human eyes. Design: Retrospective interventional surgical case series involving live and cadaveric human eyes. Methods: In this study, we investigated the surgical outcomes and structural anatomy of secondary IOLs implanted with the SIS technique in human eyes. All cases involving SIS IOL fixation performed at a single academic center from January 1, 2012, through July 30, 2016, were reviewed to describe the surgical technique, common indications, clinical outcomes, and the rate of common operative complications. To investigate the structure of SIS-fixated IOLs in vivo, slit-lamp biomicroscopy, ultrasound biomicroscopy, and intraoperative endoscopy were analyzed to describe anatomical outcomes. The primary anatomical outcomes were the optic pupillary centration and location of haptic externalization. Results were correlated with cadaveric human eyes that underwent the SIS-IOL technique. Cadaveric eyes were imaged and analyzed using high-resolution photography for centration, stress measurements at the haptic-optic junction, and qualitative descriptors of IOL optic and haptic position. Results: A total of 122 consecutive patients who underwent IOL placement using SIS technique were included in the study with mean follow-up of 1.52 years (range, 0.4-4.5 years). The majority (75%) of patients received a new 3-piece IOL for primary aphakia or after IOL exchange. The other patients (25%) had a dislocated 3-piece IOL that was rescued using the SIS technique. Preoperative mean Snellen visual acuity was 20/633 (logarithm of the minimum angle of resolution = 1.501). At the final visit, the mean best-corrected visual acuity was 20/83 (logarithm of the minimum angle of resolution = 0.6243) and final mean spherical equivalent was -0.57 diopters. The most common complications were vitreous hemorrhage (22% of eyes), which resolved spontaneously in most cases, and cystoid macular edema. The rates of IOL dislocation, IOL decentration, haptic erosion, IOL tilting, iris capture, and endophthalmitis were low. Intraoperative endoscopy and ultrasound biomicroscopy demonstrated a securely fixated IOL and well-centered optic without iris or ciliary body touch. Structural study of cadaveric eyes confirmed IOL optic and haptic anatomy observed during live human surgery. The ab interno haptic insertion was the anterior pars plana, away from the iris, ciliary processes and ora serrata. The degree of haptic externalization was correlated with the degree of strain on the haptic-optic junction. The angle of the haptic-optic junction in SIS-fixated IOLs (33.97°) was not significantly different compared with overlaid native nonfixated IOL (32.93°) but increased slightly with degree of haptic tip externalization (36.26 and 39.16 for 2 and 3 mm haptic externalizations, respectively). Conclusion: In this comprehensive study, we demonstrate the surgical outcomes achieved with SIS fixation of IOLs. Surgical and postoperative complications do occur, albeit at a low rate, and can effectively be managed with excellent anatomical and visual outcomes. The structural and anatomical data in this study may help guide SIS placement and optimize long-term surgical results.

Tominna M and **Al-Katib S** (2018). "Mass-like ground-glass opacities in sarcoidosis: A rare presentation not previously described." *Case Reports in Radiology* 2018: 5686915-5686915.

[Full Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

Various typical and atypical imaging findings for pulmonary sarcoidosis have been described in the literature. Ground-glass opacities are one of the atypical manifestations, reported as diffuse or patchy ill-defined opacities frequently associated with additional findings and interstitial nodules. We performed a literature review to determine if our case had previously been described. The literature describes cases of mass-like consolidations, but there are no reports of mass-like ground-glass opacities. The appearance of the ground-glass opacities in our case is unique, appearing as discrete well-defined mass-like ground-glass opacities in a peribronchovascular distribution without additional parenchymal findings typically seen in sarcoidosis.

**Vakharia PP, Lee DE** and Khachemoune A (2018). "Efficacy and safety of noncultured melanocyte-keratinocyte transplant procedure for vitiligo and other leukodermas: a critical analysis of the evidence." *International Journal of*

Dermatology 57(7): 770-775.

[Full Text](#)

*OUWB Medical Student Author*

Vitiligo is an acquired pigmentary skin of depigmentation occurring secondary to melanocyte destruction. Vitiligo and other leukodermas have a profound impact on quality of life. Current therapies include medical options, such as phototherapy, topical and systemic corticosteroids, topical calcineurin inhibitors, immunomodulators, and antioxidants, and surgical options. Surgical options provide melanocytic cells to previously depigmented areas and use either tissue grafting or cellular grafting methods. Topical treatments are often insufficient, and many of the current surgical procedures have shown variable response rates. In this review, we discuss the process of the cellular grafting melanocyte-keratinocyte transplantation procedure (MKTP) and critically analyze its efficacy and safety in the treatment of vitiligo and other leukodermas. PubMed was searched for studies (2001-2017) describing the use of MKTP in patients with vitiligo or other leukodermas. Articles or trials discussing the use of MKTP for these patients were selected for in-depth review. Clinically relevant results regarding efficacy and safety of MKTP in vitiligo and leukoderma patients were analyzed. Numerous trials and case series/reports have demonstrated tolerability and efficacy of MKTP with repigmentation for patients with refractory, stable vitiligo. However, the response rates have been variable, likely influenced by vitiligo type and affected areas. Future research and clinical reporting will provide more insight on which phenotypes may benefit from MKTP.

**Vercellone J, Cohen L, Mansuri S, Zhang PL and Kellerman PS** (2018). "Bartonella endocarditis mimicking crescentic glomerulonephritis with PR3-ANCA positivity." Case Reports in Nephrology 2018: 9607582-9607582.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Internal Medicine*

*Department of Pathology*

*Bartonella henselae* is a fastidious organism that causes cat scratch disease, commonly associated with fever and lymphadenopathy but, in rare instances, also results in culture-negative infectious endocarditis. We describe a patient who presented with flank pain, splenic infarct, and acute kidney injury with an active urinary sediment, initially suspicious for vasculitis, which was subsequently diagnosed as *B. henselae* endocarditis. *Bartonella* endocarditis may present with a crescentic glomerulonephritis (GN) and elevated PR3-ANCA antibody titers, mimicking ANCA-associated GN, with 54 cases reported in the literature. Unique to our case in this series is a positive PR3-ANCA antibody despite a negative IIF-ANCA. Thus, the presentation of *Bartonella* can mimic ANCA-associated GN, and renal biopsy showing immune complex deposition is critical for diagnosis and appropriate treatment.

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 WL (2018). "Appropriate use criteria in dermatopathology: Initial recommendations from the American Society of Dermatopathology." Journal of Cutaneous Pathology 45(8): 563-580.

[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," 52 (25%) "rarely appropriate" and 43 (20%) "uncertain appropriateness.". Limitations: The methodology requires a focus on appropriateness without comparison between tests and irrespective of cost. Conclusions: The ultimate decision of when to order specific test rests with the physician and is one where the expected benefit exceeds the negative consequences. This publication outlines the recommendations of appropriateness—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.

Wa CA, Walsh MK, Stem M, Todorich B and **Wolfe JD** (2018). "The efficacy and safety of flanged needleless sutureless intrascleral intraocular lens fixation." *Investigative Ophthalmology & Visual Science* 59(9): 4431.

[Full Text](#)

*Department of Ophthalmology*

Purpose: The placement or repositioning of intraocular lenses (IOL) in the absence of capsular support can be difficult. The aim of this study was to evaluate the efficacy and safety of a novel surgical technique using flanged needleless sutureless intrascleral (SIS) fixation of a sulcus IOL. Methods : A retrospective chart review was performed for 52 patients who underwent pars plana vitrectomy with IOL repositioning, exchange, or secondary placement with flanged needleless SIS fixation. Trocar cannulas were used to make scleral tunnels instead of needles. Average follow-up was 6 months. Main outcome measures were best corrected visual acuity (BCVA), stable anatomic placement of IOL, and any intra- or post-operative complications. Results : The indications for SIS were dislocated crystalline lens (2 patients, 3.7%), aphakia (7, 13%), and pseudophakia with dislocated IOL (45, 83.3%). A total of 9 eyes (16.7%) underwent secondary IOL placement, 19 eyes (35.2%) underwent IOL exchange, and 26 (48.1%) underwent IOL repositioning. BCVA improved from pre-operative  $0.93 \pm 0.74$  logMAR (Snellen equivalent 20/170) to post-operative  $0.34 \pm 0.35$  logMAR (Snellen equivalent 20/44) ( $P < 0.001$ ). Intra-operatively, one case of retinal tear, one case of serous choroidal effusion with a retinal tear, and one case of limited suprachoroidal hemorrhage were noted. The most common post-operative issues were transient IOP elevation (22.2%), CME (20.4%), reverse pupillary block (11.1%), and IOL tilt or decentration (11.1%). All patients with IOP elevation and CME responded to topical medications. Reverse pupillary block resolved after laser peripheral iridotomy. IOL tilt was mild and did not require reoperation. One eye with mild iris capture developed increased IOP at postoperative month 4, so the IOL was repositioned at the slit lamp with complete resolution of symptoms. There were no cases of endophthalmitis or retinal detachments. Of the 52 patients, 2 patients (3.8%) underwent reoperation for recurrent dislocation for a total of 54 surgeries. Conclusions : Our study demonstrated that a flanged needleless SIS fixation technique was effective with improved BCVA and minimal transient complications. Additionally, an intra-operative peripheral iridectomy may prevent the occurrence of reverse pupillary block. This combination offers a new approach in the surgical repair of dislocated lenses, especially in the absence of capsular support.

Wagner TH, Scott JY, Newman DK, Miller JM, Kirk K, DiCamillo MA, Raghunathan TE, **Diokno AC** and Sampsel CM (2018). "Costs and sustainability of a behavioral intervention for urinary incontinence prevention." *Urology Practice* 5(4): 266-271.

[Full Text](#)

*Department of Urology*

Introduction: Many women choose behavioral interventions as first line treatment for urinary incontinence. We developed a 20-minute abbreviated video, which proved to be similar to a 2-hour in-person class in a randomized trial. This study examines economic end points for the 20-minute video relative to the 2-hour class. Methods: We randomized 332 participants to the 2-hour class and 315 to the 20-minute video. We estimated the cost for the 2-hour class, the 20-minute video and followup health care utilization. Participants were followed for 3, 12 and 24 months, and asked about health care utilization, quality of life and lost productivity. To measure perceived value, we queried each participant regarding willingness to pay. Regression analysis was used for statistical comparisons. Results: The estimated per participant cost for a 2-hour class was \$38, which was more than the marginal cost of the video (\$0). We found no significant differences between the treatment groups at each followup for quality of life, lost productivity or health care utilization. Women were willing to pay \$26, \$21 and \$30 for a copy of the DVD, video on the Web and in-person class, respectively, all of which were less than the average cost of the in-person class (\$38). Conclusions: Poor adherence remains a challenge for many behavioral interventions designed to prevent urinary incontinence. The 20-minute video is less expensive than the 2-hour class and is equally effective. Distributing the video on the Internet will improve access and will be easier to sustain than in-person classes.

**Wasserman JA**, Navin MC and Krug EF (2018). "The value of parental permission in pediatric practice." [JAMA Pediatrics](#) 172(7): 613-614.

[Full Text](#)

*Department of Foundational Medical Studies*

This viewpoint provides clinical illustrations showing how taking parental permission seriously can help clinicians deliver better care to pediatric patients and addresses frustrations with parent requests for what may seem to be suboptimal interventions.

**Weiner AJ**, Rao P and **Williams G** (2018). "Large traumatic retinal dialysis associated with prominent vitreous base avulsion." [Ophthalmic Surgery, Lasers & Imaging Retina](#) 49(9): 731-731.

[Request Form](#)

*OUIWB Medical Student Author*

*Department of Ophthalmology*

A 13-year-old female with a history of regressed retinopathy of prematurity presented with new-onset floaters after sustaining blunt force trauma to her left eye. Best-corrected visual acuity was 20/20 in both eyes (OU), with an intraocular pressure of 14 mm Hg and 15 mm Hg in the right eye (OD) and left eye (OS), respectively. Exam under anesthesia revealed an unremarkable anterior segment OU, including no hyphema or subluxated crystalline lens. Scleral depression OS demonstrated a retinal dialysis superotemporally (1-o'clock to 3-o'clock) and nasally (7-o'clock to 10-o'clock) associated with a prominent vitreous base avulsion but no subretinal fluid (Figure). Scleral depression OD was unremarkable. Both areas of retinal dialysis OS were treated with three rows of indirect green laser photocoagulation posterior to the edge of the dialysis.

White JL, Chang AM, Hollander JE, Su E, Weiss RE, Yagapen AN, Malveau SE, Adler DH, **Bastani A**, Baugh CW, Caterino JM, **Clark CL**, Diercks DB, Nicks BA, Nishijima DK, Shah MN, Stiffler KA, Storrow AB, Wilber ST and Sun BC (2018). "QTc prolongation as a marker of 30-day serious outcomes in older patients with syncope presenting to the Emergency Department." [The American Journal of Emergency Medicine](#). ePub Ahead of Print.

[Full Text](#)

*Department of Anesthesiology*

*Department of Emergency Medicine*

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

Wood EH, Rao P, Moysidis SN, Dedania VS, Elman MJ, **Drenser KA**, **Capone A** and **Trese MT** (2018). "Fellow eye anti-VEGF 'crunch' effect in retinopathy of prematurity." [Ophthalmic Surgery Lasers and Imaging Retina](#) 49(9): e102-e104.

[Request Form](#)

*Department of Ophthalmology*

Background and Objective: Anti-vascular endothelial growth factor (VEGF) therapy is increasing in popularity for treatment of retinopathy of prematurity (ROP). Despite many technical benefits, issues remain prompting further investigation. Patients and Methods: Retrospective case report and literature review. Results: A 42-week-old postmenstrual age female with gestational age of 28 weeks and birth weight of 990 g presented with prominent progression of peripapillary purely tractional atypical stage 4A ROP in both eyes following

intravitreal bevacizumab therapy in the right eye only. Conclusion: The authors present the first reported case, to their knowledge, of a "crunch" phenomenon tractional retinal detachment from fellow eye administration of bevacizumab.

Wright M, Harks E, Deladi S, Fokkenrood S, Brink R, Belt H, Kolen AF, Rankin D, Stoffregen W, Cockayne DA, Cefalu J and **Haines DE** (2018). "Characteristics of radiofrequency catheter ablation lesion formation in real time in vivo using near field ultrasound imaging." *JACC: Clinical Electrophysiology* 4(8): 1062-1072.

[Full Text](#)

*Department of Internal Medicine*

Objectives: Visualizing myocardium with near field ultrasound (NFUS) transducers in the tip of the catheter might provide an image of the evolving pathological lesion during energy delivery. Background: Radiofrequency (RF) catheter ablation has been effective in arrhythmia treatment, but no technology has allowed lesion formation to be visualized in real time in vivo. Methods: RF catheter ablations were performed in vivo with the goal to create transmural atrial lesions and large ventricular lesions. RF lesion formation was imaged in real time using M-mode, tissue Doppler, and strain rate information from the NFUS open irrigated RF ablation catheter incorporating 4 ultrasound transducers (1 axial and 3 radial), and growth kinetics were analyzed. Nineteen dogs underwent ablation in the right and left atria (n = 185), right ventricle (n = 67), and left ventricle (n = 66). Lesions were echolucent with tissue strain rate by NFUS. Results: Lesion growth frequently progressed from epicardium to endocardium in thin-walled tissue. The half time of lesion growth was  $5.5 \pm 2.8$  s in thin-walled and  $9.7 \pm 4.3$  s in thick-walled tissue. Latency of lesion onset was seen in 57% of lesions ranging from 1 to 63.8 s. Tissue edema (median 25% increased wall thickness) formed immediately upon lesion formation in 83%, and intramyocardial steam was seen in 71% of cases. Conclusions: NFUS was effective in imaging RF catheter ablation lesion formation in real time. It was useful in assessing the dynamics of lesion growth and could visualize impending steam pops. It may be a useful technology to improve both safety and efficacy of RF catheter ablation.

Yadav S, Jinna S, Pereira-Rodrigues O, Reeves A, Campian S, Sufka A and **Zakalik D** (2018). "Impact of preoperative BRCA1/2 testing on surgical decision making in patients with newly diagnosed breast cancer." *Breast Journal* 24(4): 541-548.

[Full Text](#)

*Department of Internal Medicine*

The utility and benefit of integrating germ-line genetic testing into the management of newly diagnosed breast cancer is not fully understood. This study evaluates the impact of preoperative genetic testing on surgical decision making in patients with newly diagnosed breast cancer. Women with newly diagnosed breast cancer were classified into preoperative or postoperative genetic testing group, depending on whether they received their genetic testing results prior to or after their first surgery. Demographics, tumor characteristics, surgical treatment, and results of genetic testing were retrospectively collected. A total of 997 patients were evaluated, 531 (53.3%) in the preoperative genetic testing group and 466 (46.7%) in the postoperative group. Majority (87.2%) of BRCA-positive women in the preoperative group underwent bilateral mastectomy as first surgery. Majority (70.6%) of BRCA-positive women in postoperative group underwent partial mastectomy as first surgery prior to receiving their genetic testing result. Nearly half (41.2%) of these women in the postoperative group with partial mastectomy underwent bilateral mastectomy after receiving their BRCA-positive result. Time from diagnosis to first surgery was longer in the preoperative genetic testing group. Younger age, bilateral cancer, BRCA1/2- positive results, and preoperative genetic testing were significant predictors of bilateral mastectomy at first surgery. Preoperative genetic testing impacts initial surgical treatment in BRCA1/2-positive patients and reduces the need for additional surgeries.

Yaldou B, Cooper M and **Soto R** (2018). "Inter-rater reliability and reception of the Michigan Opioid Safety score." *Journal of Perianesthesia Nursing* 33(4): 412-419.

[Full Text](#)

*Department of Anesthesiology*

Purpose: The Michigan Opioid Safety Score (MOSS) combines health risk, respiratory rate, and sedation measurement to guide safe opioid administration. This study was designed to assess reliability and nursing

acceptance of the MOSS tool. Design: Cross-sectional survey. Methods: Nurses without prior exposure to the tool were asked to participate in an online survey. In part I, raters utilized the MOSS to answer questions based on four fictional case scenarios. In part II, anonymous opinion of the tool was queried. Finding: Participants correctly scored 58.1% of patient scenarios, while appropriate clinical action was 80.5%. The intraclass correlation coefficient was 0.83. In terms of opinion, a majority of raters agreed the tool positively impacted patient safety (59.2%), improved confidence in opioid therapy (59.2%), and was easy to use (53%). Conclusions: Participants interpreted case scenarios with excellent inter-rater reliability and had a generally positive opinion. These study findings suggest the MOSS is a reliable safety instrument.

Zhou D, Quan H, **Yan D**, Chen S, **Qin A**, Stanhope C, Lachaine M and Liang J (2018). "A feasibility study of intrafractional tumor motion estimation based on 4D-CBCT using diaphragm as surrogate." Journal of Applied Clinical Medical Physics 19(5): 525-531.

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*Department of Radiation Oncology*

Purpose: To investigate the intrafractional stability of the motion relationship between the diaphragm and tumor, as well as the feasibility of using diaphragm motion to estimate lung tumor motion. Methods: Eighty-five paired (pre and posttreatment) daily 4D-CBCT images were obtained from 20 lung cancer patients who underwent SBRT. Bony registration was performed between the pre- and post-CBCT images to exclude patient body movement. The end-exhalation phase image of the pre-CBCT image was selected as the reference image. Tumor positions were obtained for each phase image using contour-based translational alignments. Diaphragm positions were obtained by translational alignment of its apex position. A linear intrafraction model was constructed using regression analysis performed between the diaphragm and tumor positions manifested on the pretreatment 4D-CBCT images. By applying this model to posttreatment 4D-CBCT images, the tumor positions were estimated from posttreatment 4D-CBCT diaphragm positions and compared with measured values. A receiver operating characteristic (ROC) test was performed to determine a suitable indicator for predicting the estimate accuracy of the linear model. Results: Using the linear model, per-phase position, mean position, and excursion estimation errors were  $1.12 \pm 0.99$  mm,  $0.97 \pm 0.88$  mm, and  $0.79 \pm 0.67$  mm, respectively. Intrafractional per-phase tumor position estimation error, mean position error, and excursion error were within 3 mm 95%, 96%, and 99% of the time, respectively. The residual sum of squares (RSS) determined from pretreatment images achieved the largest prediction power for the tumor position estimation error (discrepancy < 3 mm) with an Area Under ROC Curve (AUC) of 0.92 ( $P < 0.05$ ). Conclusion: Utilizing the relationship between diaphragm and tumor positions on the pretreatment 4D-CBCT image, intrafractional tumor positions were estimated from intrafractional diaphragm positions. The estimation accuracy can be predicted using the RSS obtained from the pretreatment 4D-CBCT image.