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PUBLICATION LIST  
January - March 2021

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Abdel Motaleb AA, Tawfik YM, El-Mokhtar MA, Elkady S, El-Gazzar AF, **ElSayed SK** and Awad SM (2021). "Cutaneous JAK expression in vitiligo." *Journal of Cutaneous Medicine and Surgery* 25(2): 157-162.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Background: The Janus kinase-signal transducer and activator of transcription signaling pathway has been suggested as a promising therapeutic target in vitiligo. However, limited data is available on the cutaneous expression of JAK in vitiligo. Aim: This study is designed to analyze the cutaneous expression patterns of JAK1, 2, and 3 in vitiligo and investigate their relation to the disease clinical parameters. Methods: This case-control study recruited 24 patients having active vitiligo and 20 age, sex, and skin type-matched healthy volunteers. Skin biopsies were obtained from patients (lesional, perilesional and nonlesional) and controls for assessment of JAK1, 2, and 3 expression using RT-PCR. Results: JAK1 and JAK3 were overexpressed in patients' skin compared to control skin and showed a stepwise pattern of upregulation from control to nonlesional, perilesional and lesional skin. However, JAK3 showed much stronger expression. In contrast JAK2 expression showed no significant difference in any of lesional, perilesional or nonlesional skin compared to control skin. JAK1 and JAK3 expression levels showed no correlation with neither the disease activity nor severity. Conclusion: JAK1 and more prominently JAK3 are upregulated in vitiliginous skin and possibly contribute to the pathogenesis of the disease. Accordingly, selective JAK3/1 inhibition may provide a favorable therapeutic opportunity for vitiligo patients.

**Al-Hadidi A**, Amine M, Batman A and Hakmeh W (2021). "Homemade cardiac and vein cannulation ultrasound phantoms for trauma management training in resource-limited settings." *Avicenna Journal of Medicine* 11(1): 42-45.

[Full Text](#)

*OUWB Medical Student Author*

Ultrasound has become an essential skill for trauma management in resource-limited areas. Prohibitive costs of commercial ultrasound phantoms limit the abilities of many hospitals to adequately train health-care providers. We assessed the utility of homemade phantoms in a wartime setting. Thirty physicians and technicians enrolled in a medical training course, sponsored by the Syrian American Medical Society (SAMS). Ultrasound simulation models were created onsite by using psyllium, gelatin, a hotel coffee maker, and Pyrex

dishes. Lamb hearts were used to teach visual diagnosis and subsequent drainage of pericardial effusions. Penrose drains were used to teach vein identification and cannulation under dynamic ultrasound guidance. Two phantoms with a total of 14 penrose drains were created, serving 30 health-care providers. Feedback from participants was positive and within one month of the course, two cases of pericardial tamponade were diagnosed and surgically treated in the largest trauma hospital operated by SAMS. Context: In resource-limited environments, ultrasound phantoms (models) are cost-prohibitive. AIMS: We assessed the utility of homemade phantoms in a resource-limited wartime setting to train Syrian physicians and technicians in vein cannulation and limited cardiac ultrasonography. Settings and Design: Thirty physicians and technicians enrolled in a medical training course, sponsored by SAMS. Methods: Ultrasound simulation models were created onsite by using psyllium, gelatin, a hotel coffee maker, and Pyrex dishes. Lamb hearts were used to teach visual diagnosis and subsequent drainage of pericardial effusions. Penrose drains were used to teach vein identification and cannulation under dynamic ultrasound guidance. Two phantoms with a total of 14 penrose drains were created, serving 30 health-care providers. Statistical Analysis Used: N/A. Results: Feedback from participants was positive and within one month of the course, two cases of pericardial tamponade were diagnosed and surgically treated in the largest trauma hospital operated by SAMS. Conclusions: Homemade ultrasound phantoms are a promising cost-effective means for meeting an educational gap in ultrasound training, particularly for resource-limited hospitals and possibly more broadly in residency education.

**Al-Hadidi A**, Lapkus M, **Karabon P**, **Akay B** and **Khandhar P** (2021). "Respiratory modalities in preventing reintubation in a pediatric intensive care unit." *Global Pediatric Health* 8: 2333794x21991531.

[Full Text](#)

*Department of Surgery*

*Department of Pediatrics*

*Department of Medical Education*

*OUIB Medical Student Author*

Post-extubation respiratory failure requiring reintubation in a Pediatric Intensive Care Unit (PICU) results in significant morbidity. Data in the pediatric population comparing various therapeutic respiratory modalities for avoiding reintubation is lacking. Our objective was to compare therapeutic respiratory modalities following extubation from mechanical ventilation. About 491 children admitted to a single-center PICU requiring mechanical ventilation from January 2010 through December 2017 were retrospectively reviewed. Therapeutic respiratory support assisted in avoiding reintubation in the majority of patients initially extubated to room air or nasal cannula with high-flow nasal cannula (80%) or noninvasive positive pressure ventilation (100%). Patients requiring therapeutic respiratory support had longer PICU LOS (10.92 vs 6.91 days, P-value = .0357) and hospital LOS (16.43 vs 10.20 days, P-value = .0250). Therapeutic respiratory support following extubation can assist in avoiding reintubation. Those who required therapeutic respiratory support experienced a significantly longer PICU and hospital LOS. Further prospective clinical trials are warranted.

Allam S, McDowell E, Heard B, Kim T, Luu E, Muto C, Mazimba S and **Mehta N** (2021). "A novel disinfection protocol using ATP testing for lead garments in the electrophysiology lab." *Journal of Interventional Cardiac Electrophysiology*. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

Purpose: Electrophysiology procedures pose infection risk and require surgical room sterility. Currently, there is no universally approved protocol for disinfecting lead garments in the electrophysiology laboratory. This study explores the feasibility of using ATP testing to assess the microbial burden of lead aprons and evaluates the impact of a sanitary intervention. Methods: Adenosine triphosphate (ATP) testing is a well-established hospital standard to quantify biological matter on a surface and, by proxy, the microbial burden. It is measured in RLU (relative light units). Pre-intervention ATP testing was performed on 34 lead garments after use for electrophysiology procedures. The thyroid collar, mid-chest vest, and left axillary areas of the garments were swabbed using a Hygiena SystemSure II luminometer with ATP swabs (Hygiena, Camarillo, CA). These sites were then disinfected with disinfectant wipes (PDI Super Sani-cloth Germicidal Disposable Wipe) and ATP testing was repeated. Results: The mean duration of garment wear was 213 min. The thyroid

collars had the highest mean RLU before intervention, followed by the mid-chest vest and the left axillary areas. The intervention was found to significantly decrease ATP readings for all three sites ( $p = 0.0002$ ,  $p = 0.0001$ ,  $p = 0.0002$  respectively). Linear regression modeling to assess the impact of intervention showed a significant correlation with pre-intervention ATP values for all three sites but no correlation with fluoroscopy time, fluoroscopy dose, or total time spent within the procedure. Conclusions: Lead garments harbor microbial contamination after use according to ATP testing. A sanitary intervention can decontaminate lead garments and potentially reduce rates of hospital infection.

**Allen M**, Meraj TS, **Oska S**, **Spillinger A**, **Folbe AJ** and Cramer JD (2021). "Acute epiglottitis: Analysis of U.S. mortality trends from 1979 to 2017." *American Journal of Otolaryngology* 42(2): 102882.

[Full Text](#)

*Department of Surgery*

*OUIB Medical Student Author*

Purpose: Evaluate trends in mortality due to acute epiglottitis before and after adoption of Haemophilus influenzae Type b vaccination (Hib) in pediatric and adult populations. Materials and Methods: Patients who died from acute epiglottitis from 1979 to 2017 identified using National Vital Statistics System. Mortality rates calculated using age-adjusted US census data expressed in rate per 100,000 individuals. Trends analyzed using the National Cancer Institute Joinpoint Regression Program (version 4.7.0; Bethesda, Maryland). Results: 1187 epiglottitis-related deaths were identified over thirty-nine years. Total deaths decreased from 65 in 1979 to 15 in 2017. Adult deaths accounted for 63.5% and decreased from 0.015 per 100,000 individuals (24 deaths) in 1979 to 0.006 per 100,000 individuals (14 deaths) in 2017. Best fitting log-linear regression model showed APC of -3.5% (95% CI, -4.2 to -2.7%) from 1979 to 2017. Pediatric and adolescent deaths accounted for 443 (37.3%) deaths, decreasing from 0.064 per 100,000 individuals (41 deaths) in 1979 to 0.001 per 100,000 individuals (1 death) in 2017. APC was -11.1% (95% CI, -13.8% to -8.3%) in 1979 to 1990; 46.5% (95% CI, -16.6% to 157.3%) in 1990 to 1993; -61.6% (95% CI, -88% to 23%) in 1993 to 1996; and 1.1% (95% CI, -2.4% to 4.7%) in 1996 to 2017. Conclusions: Mortality from acute epiglottitis decreased after widespread adoption of Hib vaccination in the US. Adults are now more likely than children to die of acute epiglottitis. Further research including multi-institutional cohort studies must be done to elucidate causative factors contributing to remaining cases of mortality.

Almahariq MF, Levitin R, Quinn TJ, **Chen PY**, **Dekhne N**, **Kiran S**, **Desai A**, Benitez P, **Jawad MS**, **Gustafson GS** and **Dilworth JT** (2021). "Omission of axillary lymph node dissection is associated with inferior survival in breast cancer patients with residual N1 nodal disease following neoadjuvant chemotherapy." *Annals of Surgical Oncology* 28(2): 930-940.

[Full Text](#)

*Department of Radiation Oncology*

*Department of Surgery*

*OUIB Medical Student Author*

Background: The appropriateness of substituting sentinel lymph node dissection (SLND) and regional nodal irradiation (RNI) for axillary lymph node dissection (ALND) in patients with residual lymph node (LN) disease following neoadjuvant chemotherapy (NAC) is unknown. We used the National Cancer Database (NCDB) to compare survival following SLND and ALND in breast cancer patients with residual LN disease. Methods: We analyzed NCDB patients, treated between 2006 and 2014, with cT1-3, cN1, cM0 breast cancer and residual disease in 1-3 axillary LNs (ypN1) following NAC. Patients were grouped into those who received SLND (defined as removal of  $\leq 4$  LNs) and RNI, or ALND and RNI. Patients were matched for all patient, tumor, and treatment characteristics. Results: We identified 1313 eligible patients in the ALND group and 304 patients in the SLND group. For the matched cohorts, SLND was associated with significantly lower survival in both univariate and doubly robust multivariable analyses (MVA) (HR 1.7, 95% CI 1.3-2.2,  $P < 0.001$  for MVA), with estimated 5-year OS of 71%, compared with 77% in the ALND group ( $P = 0.01$ ). Exploratory subgroup analyses showed that SLND was comparable with ALND in patients with luminal A or B tumors with a single metastatic LN (HR 1.03, 95% CI 0.59-1.8, ( $P = 0.91$ )). Conclusions: Our analysis suggests that, while an ALND may not be needed for patients with limited residual nodal burden and biologically favorable tumors, SLND should not be routinely substituted for ALND in patients with ypN1 disease following NAC until its efficacy is confirmed by prospective trials.

Almahariq MF, Quinn TJ, Arden JD, Roskos PT, **Wilson GD**, Marples B, **Grills IS**, **Chen PY**, **Krauss DJ**, **Chinnaiyan P** and **Dilworth JT** (2021). "Pulsed radiation therapy for the treatment of newly diagnosed glioblastoma." *Neuro-oncology* 23(3): 447-456.

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*Department of Radiation Oncology*

Background: Pulsed radiation therapy (PRT) has shown effective tumor control and superior normal-tissue sparing ability compared with standard radiotherapy (SRT) in preclinical models and retrospective clinical series. This is the first prospective trial to investigate PRT in the treatment of patients with newly diagnosed glioblastoma (GBM). Methods: This is a single-arm, prospective study. Patients with newly diagnosed GBM underwent surgery, followed by 60 Gy of PRT with concurrent temozolomide (TMZ). Each day, a 2-Gy fraction was divided into ten 0.2-Gy pulses, separated by 3-minute intervals. Patients received maintenance TMZ. Neurocognitive function (NCF) and quality of life (QoL) were monitored for 2 years using the Hopkins Verbal Learning Test-Revised and the European Organisation for Research and Treatment of Cancer QLQ-C30 QoL questionnaire. Change in NCF was evaluated based on a minimal clinically important difference (MCID) threshold of 0.5 standard deviation. Results: Twenty patients were enrolled with a median follow-up of 21 months. Median age was 60 years. Forty percent underwent subtotal resection, and 60% underwent gross total resection. One patient had an isocitrate dehydrogenase (IDH)-mutated tumor. Median progression-free survival (PFS) and overall survival (OS) were 10.7 and 20.9 months, respectively. In a post-hoc comparison, median OS for the prospective cohort was longer, compared with a matched cohort receiving SRT (20.9 vs 14 mo,  $P = 0.042$ ). There was no decline in QoL, and changes in NCF scores did not meet the threshold of an MCID. Conclusions: Treatment of newly diagnosed GBM with PRT is feasible and produces promising effectiveness while maintaining neurocognitive function and QoL. Validation of our results in a larger prospective trial warrants consideration.

Almahariq MF, Quinn TJ, Kesarwani P, Kant S, Miller CR and **Chinnaiyan P** (2021). "Inhibition of colony-stimulating factor-1 receptor enhances the efficacy of radiotherapy and reduces immune suppression in glioblastoma." *In Vivo* 35(1): 119-129.

[Full Text](#)

*Department of Radiation Oncology*

Aim: To use inhibition of colony-stimulating factor-1 receptor (CSF-1R) to target tumor-associated macrophages (TAMs) and improve the efficacy of radiotherapy in glioblastoma (GBM). Materials and Methods: The CSF-1R inhibitor BLZ-945 was used to examine the impact of CSF-1R inhibition on M2 polarization in vitro. Using an orthotopic, immunocompetent GBM model, mice were treated with vehicle, RT, BLZ-945, or RT plus BLZ-945. Results: BLZ-945 reduced M2 polarization in vitro. BLZ-945 alone did not improve median overall survival (mOS=29 days) compared to control mice (mOS=27 days). RT improved survival (mOS=45 days;  $p=0.02$ ), while RT plus BLZ-945 led to the longest survival (mOS=not reached;  $p=0.005$ ). Resected tumors had a relatively large population of M2 TAMs in GBM at baseline, which was increased in response to RT. BLZ-945 reduced RT-induced M2 infiltration. Conclusion: Inhibition of CSF-1R improved response to RT in the treatment of GBM and may represent a promising strategy to improve RT-induced antitumor immune responses.

**Alpay Savasan Z**, Kim SK, Oh KJ and **Graham SF** (2021). "Advances in cerebral palsy biomarkers." *Advances in Clinical Chemistry* 100: 139-169.

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*Department of Obstetrics & Gynecology*

Cerebral palsy (CP), defined as a group of nonprogressive disorders of movement and posture, is the most common cause of severe neurodisability in children. The prevalence of CP is the same across the globe, affecting approximately 17 million people worldwide. Cerebral Palsy is an umbrella term used to describe the disease due to its inherent heterogeneity. For instance, CP has multiple (1) causes; (2) clinical types; (3) patterns of neuropathology on brain imaging and (4) it's associated with several developmental pathologies such as intellectual disability, autism, epilepsy, and visual impairment. Understanding its physiopathology is crucial to developing protective strategies. Despite its importance, there is still insufficient progress in the areas of CP prediction, early diagnosis, treatment, and prevention. Herein we describe the current risk factors

and biomarkers used for the diagnosis and prediction of CP. With the advancement in biomarker discovery, we predict that our understanding of the etiopathophysiology of CP will also increase, leading to more opportunities for developing novel treatments and prognosis.

**Ang NB** and **Wasserman JA** (2021). "Prevalence of traumatic brain injury among the guests at a low-barrier homeless shelter." *BMC Research Notes* 14(1): 44.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

*OUWB Medical Student Author*

Objective: This study aimed at determining the prevalence of traumatic brain injuries (TBI) among guests staying at a low-barrier homeless shelter who represent an especially vulnerable subset of individuals experiencing homelessness. Results: A total of 21 out of 35 shelter guests participated in the survey. We found that 17 (81.0%) had experienced at least one traumatic brain injury in their lifetime and 15 (71.3%) had TBI associated with loss of consciousness. In addition, 7 (33.3%) of the participants had experienced TBIs rated as moderate to severe. Of the participants with head trauma history, 16 (94.1%) experienced their injury before their first onset of homelessness. Compared to both the general population and the broader population of individuals experiencing homelessness, those in this sample were significantly more likely to experience TBI (95% CI 0.0000:0.2857;  $p < 0.001$  and 95% CI 0.3333:0.7619;  $p < 0.015$ , respectively) and significantly more likely to experience severe TBI (95% CI 0.0000:0.09524;  $p < 0.001$ ).

Araya-Ramírez F, Moncada-Jiménez J, Grandjean PW and **Franklin BA** (2021). "Improved walk test performance and blood pressure responses in men and women completing cardiac rehabilitation: Implications regarding exercise trainability." *American Journal of Lifestyle Medicine*. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

Purpose: To evaluate changes in walk test performance and blood pressure (BP) responses following a 12-week exercise-based outpatient cardiac rehabilitation (CR) program. Methods: Six-Minute Walk Test (6MWT) and resting systolic BP (SBP), diastolic BP (DBP), post-6MWT heart rate (HR), and post-6MWT BPs were measured before and after CR in 311 (237 men, 74 women) patients. Using age as a covariate, 2 by 2 (Gender × Measurement) ANCOVAs were used to determine differences in 6MWT performance and hemodynamic variables. Results: After adjusting for age, men covered a greater 6MWT distance than women; pre-CR versus post-CR program values are as follows: men,  $429.3 \pm 94.6$  versus  $557.6 \pm 90.7$  m,  $P \leq .001$ ; women,  $374.9 \pm 100.7$  versus  $483.2 \pm 82.9$  m,  $P \leq .001$ . Both genders reduced resting DBP following the CR program (men:  $67.2 \pm 9.8$  vs  $65.6 \pm 8.5$  mm Hg,  $P = .034$ ; women:  $69.2 \pm 10.7$  vs  $65.0 \pm 8.0$  mm Hg,  $P = .001$ ) and increased HR following the 6MWT after the CR program (men:  $97.7 \pm 16.8$  vs  $112.7 \pm 21.3$  bpm,  $P \leq .001$ ; women:  $100.7 \pm 20.8$  vs  $110.2 \pm 22.0$  bpm,  $P \leq .001$ ). Similarly, SBP increased immediately following the 6MWT ( $122.8 \pm 18.5$  vs  $133.6 \pm 20.7$  mm Hg;  $P \leq .001$ ) in men but not in women. Conclusion: The present findings indicate similar relative improvements in 6MWT performance and BP responses in adherent men and women following an exercise-based CR program.

Arden JD, Rutka E, Ye H and **Robertson JM** (2021). "A personalized patient teaching session at the time of radiation simulation may improve patient satisfaction scores." *Advances in Radiation Oncology* 6(1): 100570.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: Radiation therapy simulation is an excellent time for patient education. We implemented a comprehensive personalized patient experience-focused (PX) teaching session at the time of simulation and assessed its effect using patient satisfaction scores. Methods and Materials: From February 2016 to June 2018, a single PX-trained radiation therapy therapist met patients at simulation to address and resolve all treatment-related questions. Results from a Centers for Medicare & Medicaid Services approved voluntary patient satisfaction tool were used to assess the effect of this intervention, using tools the patients received during the on-treatment period. Scores from patients contacted by the PX therapist were compared with those of noncontacted patients. Results: For the survey, 1369 patients were contacted (median contact duration, 23 minutes; range, 0-117). Of 732 surveys submitted during this time, 98 were from on-treatment patients (69 contacted, 29 not contacted). The majority of contacted patients and survey responders were

women (64% and 62%, respectively), patients with breast cancer (38%, 41%), and patients who had received curative therapy (82%, 69%). Scores from contacted patients were significantly higher for 10 of the 17 questions (registration helpfulness,  $P = .03$ ; registration wait time,  $P = .048$ ; facility way finding,  $P = .03$ ; facility cleanliness,  $P = .01$ ; treatment staff skill,  $P = .03$ ; treatment staff concern for questions,  $P = .003$ ; response to concerns,  $P = .01$ ; staff worked together,  $P = .01$ ; overall rating of care,  $P = .01$ ; and likelihood of recommending care,  $P = .04$ ) and 4 of the 5 domains (registration,  $P = .04$ ; facility,  $P = .03$ ; personal issues,  $P = .02$ ; overall assessment,  $P = .002$ ). Conclusions: Contact by a PX therapist was associated with higher patient satisfaction scores, including areas specifically addressed by the PX teaching session (concerns for questions, response to concerns) as well as other areas (cleanliness, registration wait time).

**Arianpour K**, Allen M, Ashman P and **Folbe AJ** (2021). "Perioperative analgesia in cranial and skull base surgery," In Svinder PF, Pashkova AA and Johnson AP (ed). Perioperative Pain Control: Tools for Surgeons: A Practical, Evidence-Based Pocket Guide. Cham: Springer International Publishing. pp: 207-222.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Surgery*

This chapter examines the approach to management of perioperative analgesia in cranial and skull base surgeries. The controversy of pain management in cranial surgery dates back many years, and current trends in the literature are discussed including further addressing previously underrecognized pain and a drive toward the use of multimodal and non-opioid modalities. The use of scalp blockade and systemic therapies in cranial surgery are discussed. The approach to the skull base has evolved drastically in the last few decades, evolving into minimally invasive techniques that have reduced morbidity and consequently pain burden. Given the diversity of these procedures and the numerous subspecialties involved, it is not surprising that there is a need for further high-quality procedure-specific randomized controlled trials and systematic evidence-based reviews on perioperative analgesia in cranial and skull base surgeries. The current status of training in perioperative pain management in otolaryngology and neurosurgical residents also remains to be elucidated.

Armas-Phan M, Keihani S, Agochukwu-Mmonu N, Cohen AJ, Rogers DM, Wang SS, Gross JA, Joyce RP, Hagedorn JC, Voelzke B, Moses RA, Sensenig RL, Selph JP, Gupta S, Baradaran N, Erickson BA, Schwartz I, Elliott SP, Mukherjee K, Smith BP, Santucci RA, **Burks FN**, Dodgion CM, Carrick MM, Askari R, Majercik S, Nirula R, Myers JB and Breyer BN (2021). "Clinical and radiographic factors associated with failed renal angioembolization: Results from the Multi-institutional Genitourinary Trauma Study (Mi-GUTS)." Urology 148: 287-291.

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*Department of Urology*

Objective: To find clinical or radiographic factors that are associated with angioembolization failure after high-grade renal trauma. Material and Methods: Patients were selected from the Multi-institutional Genito-Urinary Trauma Study. Included were patients who initially received renal angioembolization after high-grade renal trauma (AAST grades III-V). This cohort was dichotomized into successful or failed angioembolization. Angioembolization was considered a failure if angioembolization was followed by repeat angiography and/or an exploratory laparotomy. Results: A total of 67 patients underwent management initially with angioembolization, with failure in 18 (27%) patients. Those with failed angioembolization had a larger proportion of grade IV (72% vs 53%) and grade V (22% vs 12%) renal injuries. A total of 53 patients underwent renal angioembolization and had initial radiographic data for review, with failure in 13 cases. The failed renal angioembolization group had larger perirenal hematoma sizes on the initial trauma scan. Conclusion: Angioembolization after high-grade renal trauma failed in 27% of patients. Failed angioembolization was associated with higher injury grade and a larger perirenal hematoma. Likely these characteristics are associated with high-grade renal trauma that may be less amenable to successful treatment after a single renal angioembolization.

**Attardi SM**, Taylor TAH, **Lerchenfeldt S**, **Pratt RL** and **Sawarynski KE** (2021). "Adapting strategically to changing times in health professions education: A generational workshop for educators." MedEdPORTAL 17: 11084.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Introduction: Health professions classrooms are filled with a new generation of students: iGen/generation Z. Much is known about millennials' educational needs, but they no longer comprise the majority of student populations. Research indicates that curricular strategies once useful for millennials may be ineffective for iGen. Due to multiple and surprising generational differences including ubiquitous technology, verbal/social/reading skills, and attention spans, educators might struggle to reach iGen members and are encouraged to re-examine instructional methods with iGen in mind. Methods: We designed this 90-minute workshop to give educators an informed understanding of iGen and discuss curricular adaptations intended to maintain educational quality through a literature-based presentation, self-assessment activities, and case discussions. We delivered the session to multiple diverse groups of health professions educators and staff. The attendees evaluated the workshop's quality and its longitudinal impact using 5-point Likert-style agreement surveys. Results: Respondents deemed the topic crucial to professional development and rated the content highly relevant (100% agreement/strong agreement). Longitudinal respondents could recognize iGen and personal characteristics (79% agreement or strong agreement) and the majority (58%) agreed/strongly agreed they were able to implement new instructional strategies. Discussion: Although educators are aware of typical generational differences, many are surprised to learn the unique attributes of their iGen student population. Workshop participation allowed educators to better understand both iGen students as well as how their own generational characteristics might relate to iGen members. Gaining this perspective allows educators to more adeptly create and deliver content to current health professions students.

**Bahado-Singh RO**, Vishweswaraiah S, Aydas B, **Yilmaz A**, Metpally RP, Carey DJ, Crist RC, Berrettini WH, **Wilson GD**, **Imam K**, **Maddens M**, Bisgin H, **Graham SF** and **Radhakrishna U** (2021). "Artificial intelligence and leukocyte epigenomics: Evaluation and prediction of late-onset Alzheimer's disease." *PLoS One* 16(3) e0248375.

[Full Text](#)

*Department of Obstetrics and Gynecology*

*Department of Internal Medicine*

*Department of Radiation Oncology*

We evaluated the utility of leukocyte epigenomic-biomarkers for Alzheimer's Disease (AD) detection and elucidates its molecular pathogenesis. Genome-wide DNA methylation analysis was performed using the Infinium MethylationEPIC BeadChip array in 24 late-onset AD (LOAD) and 24 cognitively healthy subjects. Data were analyzed using six Artificial Intelligence (AI) methodologies including Deep Learning (DL) followed by Ingenuity Pathway Analysis (IPA) was used for AD prediction. We identified 152 significantly (FDR  $p < 0.05$ ) differentially methylated intragenic CpGs in 171 distinct genes in AD patients compared to controls. All AI platforms accurately predicted AD with AUCs  $\geq 0.93$  using 283,143 intragenic and 244,246 intergenic/extragenic CpGs. DL had an AUC = 0.99 using intragenic CpGs, with both sensitivity and specificity being 97%. High AD prediction was also achieved using intergenic/extragenic CpG sites (DL significance value being AUC = 0.99 with 97% sensitivity and specificity). Epigenetically altered genes included CR1L & CTSV (abnormal morphology of cerebral cortex), S1PR1 (CNS inflammation), and LTB4R (inflammatory response). These genes have been previously linked with AD and dementia. The differentially methylated genes CTSV & PRMT5 (ventricular hypertrophy and dilation) are linked to cardiovascular disease and of interest given the known association between impaired cerebral blood flow, cardiovascular disease, and AD. We report a novel, minimally invasive approach using peripheral blood leukocyte epigenomics, and AI analysis to detect AD and elucidate its pathogenesis.

**Bahl A**, Johnson S and Chen NW (2021). "Timing of corticosteroids impacts mortality in hospitalized COVID-19 patients." *Internal and Emergency Medicine*. ePub Ahead of Print.

[Full Text](#)

*Department of Emergency Medicine*

The optimal timing of initiating corticosteroid treatment in hospitalized patients is unknown. We aimed to assess the relationship between timing of initial corticosteroid treatment and in-hospital mortality in COVID-19 patients. In this observational study through medical record analysis, we quantified the mortality benefit of corticosteroids in two equally matched groups of hospitalized COVID-19 patients. We subsequently evaluated the timing of initiating corticosteroids and its effect on mortality in all patients receiving corticosteroids. Demographic, clinical, and laboratory variables were collected and employed for

multivariable regression analyses. 1461 hospitalized patients with confirmed COVID-19 were analyzed. Of these, 760 were also matched into two equal groups based on having received corticosteroid therapy. Patients receiving corticosteroids had a lower risk of death than those who did not (HR 0.67, 95% CI 0.67-0.90;  $p = 0.01$ ). Timing of corticosteroids was assessed for all 615 patients receiving corticosteroids during admission. Patients receiving first dose of corticosteroids > 72 h into hospitalization had a lower risk of death compared to patients with first dose at earlier time intervals (HR 0.56, 95% CI 0.38-0.82;  $p = 0.003$ ). There was a mortality benefit in patients with > 7 days of symptom onset to initiation of corticosteroids (HR 0.56, 95% CI 0.33-0.95;  $p = 0.03$ ). In patients receiving oxygen therapy, corticosteroids reduced risk of death in mechanically ventilated patients (HR 0.38, 95% CI 0.24-0.60;  $p < 0.001$ ) but not in patients on high-flow or other oxygen therapy (HR 0.46, 95% CI 0.20-1.07;  $p = 0.07$ ) and (HR 0.84, 95% CI 0.35-2.00;  $p = 0.69$ ), respectively. Timing of corticosteroids initiation was related to in-hospital mortality for COVID-19 patients. Time from symptom onset > 7 days should trigger initiation of corticosteroids. In the absence of invasive mechanical ventilation, corticosteroids should be initiated if the patient remains hospitalized at 72 h. Hypoxia requiring supplemental oxygen therapy should not be a trigger for initiation of corticosteroids unless the timing is appropriate.

**Baker EA**, Fleischer MM, Vara AD, Salisbury MR, **Baker KC**, Fortin PT and Friedrich CR (2021). "Local and systemic in vivo responses to osseointegrative titanium nanotube surfaces." *Nanomaterials* 11(3): 583.

[Full Text](#)

*Department of Orthopaedic Surgery*

Orthopedic implants requiring osseointegration are often surface modified; however, implants may shed these coatings and generate wear debris leading to complications. Titanium nanotubes (TiNT), a new surface treatment, may promote osseointegration. In this study, in vitro (rat marrow-derived bone marrow cell attachment and morphology) and in vivo (rat model of intramedullary fixation) experiments characterized local and systemic responses of two TiNT surface morphologies, aligned and trabecular, via animal and remote organ weight, metal ion, hematologic, and nondecalcified histologic analyses. In vitro experiments showed total adherent cells on trabecular and aligned TiNT surfaces were greater than control at 30 min and 4 h, and cells were smaller in diameter and more eccentric. Control animals gained more weight, on average; however, no animals met the institutional trigger for weight loss. No hematologic parameters (complete blood count with differential) were significantly different for TiNT groups vs. control. Inductively coupled plasma mass spectrometry (ICP-MS) showed greater aluminum levels in the lungs of the trabecular TiNT group than in those of the controls. Histologic analysis demonstrated no inflammatory infiltrate, cytotoxic, or necrotic conditions in proximity of K-wires. There were significantly fewer eosinophils/basophils and neutrophils in the distal region of trabecular TiNT-implanted femora; and, in the midshaft of aligned TiNT-implanted femora, there were significantly fewer foreign body giant/multinucleated cells and neutrophils, indicating a decreased immune response in aligned TiNT-implanted femora compared to controls.

**Baker N**, Chao J and Pearce ZD (2021). "Progressive eyelid swelling in a middle-aged man." *JAMA Ophthalmology* 139(1): 123-124.

[Full Text](#)

*Department of Ophthalmology*

*OUIB Medical Student Author*

**Barbat A**, Oska S, Partiali B, Folbe A and Jacob J (2021). "Gender and ethnic diversity in diagnostic and interventional radiology trainees, 2014-2019: Has the recently introduced integrated interventional radiology program changed anything?" *Academic Radiology* 28: 292-293.

[Request Form](#)

*Department of Surgery*

*OUIB Medical Student Author*

Relative to residency programs in other specialties, diagnostic radiology (DR) has historically been one of the least diverse in terms of female and minority representation. Interventional radiology (IR) has been even less diverse, a trend that is believed to be the result of multiple factors including lack of exposure to the field, longer training, demanding call schedule and fear of radiation exposure. In a study assessing gender-specific preferences influencing IR selection among medical students, radiation exposure was frequently cited as a

deterring factor for both males and females. For female medical students, male predominance and call responsibilities were a significant deterring factor, as compared to their male counterparts.

Bax AM, van Rosendael AR, Ma X, van den Hoogen IJ, Gianni U, Tantawy SW, Hollenberg EJ, Andreini D, Al-Mallah MH, Budoff MJ, Cademartiri F, **Chinnaiyan K**, Choi JH, Conte E, Marques H, de Araújo Gonçalves P, Gottlieb I, Hadamitzky M, Leipsic JA, Maffei E, Pontone G, Shin S, Kim YJ, Lee BK, Chun EJ, Sung JM, Lee SE, Virmani R, Samady H, Stone PH, Berman DS, Min JK, Narula J, Lin FY, Chang HJ and Shaw LJ (2021). "Comparative differences in the atherosclerotic disease burden between the epicardial coronary arteries: Quantitative plaque analysis on coronary computed tomography angiography." *European Heart Journal Cardiovascular Imaging* 22(3): 322-330.

[Full Text](#)

*Department of Internal Medicine*

Aims: Anatomic series commonly report the extent and severity of coronary artery disease (CAD), regardless of location. The aim of this study was to evaluate differences in atherosclerotic plaque burden and composition across the major epicardial coronary arteries. Methods and Results: A total of 1271 patients (age  $60 \pm 9$  years; 57% men) with suspected CAD prospectively underwent coronary computed tomography angiography (CCTA). Atherosclerotic plaque volume was quantified with categorization by composition (necrotic core, fibrofatty, fibrous, and calcified) based on Hounsfield Unit density. Per-vessel measures were compared using generalized estimating equation models. On CCTA, total plaque volume was lowest in the LCx ( $10.0 \pm 29.4$  mm<sup>3</sup>), followed by the RCA ( $32.8 \pm 82.7$  mm<sup>3</sup>;  $P < 0.001$ ), and LAD ( $58.6 \pm 83.3$  mm<sup>3</sup>;  $P < 0.001$ ), even when correcting for vessel length or volume. The prevalence of  $\geq 2$  high-risk plaque features, such as positive remodelling or spotty calcification, occurred less in the LCx (3.8%) when compared with the LAD (21.4%) or RCA (10.9%,  $P < 0.001$ ). In the LCx, the most stenotic lesion was categorized as largely calcified more often than in the RCA and LAD (55.3% vs. 39.4% vs. 32.7%;  $P < 0.001$ ). Median diameter stenosis was also lowest in the LCx (16.2%) and highest in the LAD (21.3%;  $P < 0.001$ ) and located more distal along the LCx when compared with the RCA and LAD ( $P < 0.001$ ). Conclusion: Atherosclerotic plaque, irrespective of vessel volume, varied across the epicardial coronary arteries; with a significantly lower burden and different compositions in the LCx when compared with the LAD and RCA. These volumetric and compositional findings support a diverse milieu for atherosclerotic plaque development and may contribute to a varied acute coronary risk between the major epicardial coronary arteries.

Beaudoin FL, Zhai W, Merchant RC, Clark MA, Kurz MC, Hendry P, **Swor RA**, Peak D, Pearson C, Domeier R, Ortiz C and McLean SA (2021). "Persistent and widespread pain among blacks six weeks after MVC: Emergency department-based cohort study." *Western Journal of Emergency Medicine: Integrating Emergency Care with Population Health* 22(2): 139-147.

[Full Text](#)

*Department of Emergency Medicine*

Introduction: Blacks in the United States experience greater persistent pain than non-Hispanic Whites across a range of medical conditions, but to our knowledge no longitudinal studies have examined the risk factors or incidence of persistent pain among Blacks experiencing common traumatic stress exposures such as after a motor vehicle collision (MVC). We evaluated the incidence and predictors of moderate to severe axial musculoskeletal pain (MSAP) and widespread pain six weeks after a MVC in a large cohort of Black adults presenting to the emergency department (ED) for care. Methods: This prospective, multi-center, cohort study enrolled Black adults who presented to one of 13 EDs across the US within 24 hours of a MVC and were discharged home after their evaluation. Data were collected at the ED visit via patient interview and self-report surveys at six weeks after the ED visit via internet-based, self-report survey, or telephone interview. We assessed MSAP pain at ED visit and persistence at six weeks. Multivariable models examined factors associated with MSAP persistence at six weeks post-MVC. Results: Among 787 participants, less than 1% reported no pain in the ED after their MVC, while 79.8 (95% confidence interval [CI], 77.1 -- 82.2) reported MSAP and 28.3 (95% CI, 25.5 -- 31.3) had widespread pain. At six weeks, 67% (95% CI, 64, 70%) had MSAP and 31% (95% CI, 28, 34%) had widespread pain. ED characteristics predicting MSAP at six weeks post-MVC (area under the curve = 0.74; 95% CI, 0.72, 0.74) were older age, peritraumatic dissociation, moderate to severe pain in the ED, feeling uncertain about recovery, and symptoms of depression. Conclusion: These data indicate that Blacks presenting to the ED for evaluation after MVCs are at high risk for persistent and widespread musculoskeletal pain. Preventive interventions are needed to improve outcomes for this high-

risk group.

Belovich AN, Bahner I, Bonaminio G, Brennenman A, Brooks WS, Chinn C, El-Sawi N, Haight M, Haudek SB, **McAuley RJ**, McKell D, Rowe R, **Taylor TAH**, Slivkoff MD and Vari RC (2021). "Admissions during the COVID-19 Pandemic: Navigating an altered landscape for successful selection of future healthcare providers." Medical Science Educator. ePub Ahead of Print.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

**Berger DA**, Chen N-W, Miller JB, Welch RD, Reynolds JC, Pribble JM and **Swor RA** (2021). "Substantial variation exists in post-cardiac arrest outcomes across Michigan hospitals." Resuscitation 159: 97-104.

[Full Text](#)

*Department of Emergency Medicine*

Aim: Resuscitation from out of hospital cardiac arrest (OHCA) requires success across the entire chain of survival. Using a large state-wide registry, we characterized variation in clinical outcomes at hospital discharge in Michigan hospitals. Methods: We utilized the Michigan Cardiac Arrest Registry to Enhance Survival (CARES) and included adult OHCA subjects with return of spontaneous circulation (ROSC) from 2014 - 2017 that survived to hospital admission. 39 Michigan hospitals were included which managed >30 cases during the study period. Multilevel logistic regression, controlling for both subject characteristics and clustering of subjects within hospitals, assessed variation across hospitals in survival to hospital discharge and survival with cerebral performance category (CPC 1-2). Results: There were 5,486 CARES subjects that survived to hospital admission, and 4,690 met inclusion for analysis. Of 39 included hospitals, median survival to discharge was 31.3% (range 12.5%-46.7%) and median survival to discharge with CPC 1-2 was 25.0% (range 5.2%-42.2%). We identified 12-fold variation in the utilization of TTM by hospital (median 47.9%, range 6.7%-80.0%) for all admitted subjects. Similarly, there was nearly an eight-fold variation in LHC for all post-arrest subjects (median 22.1%, range 5.4%-42.2%). In multivariable analyses, median adjusted survival to discharge was 26.9% (range 18.1%-42.1%) and median adjusted survival to discharge with CPC 1-2 was 21.3% (range 9.6%-32.1%). Conclusion: We observed substantial variation in clinical outcomes at discharge between Michigan hospitals, including a four-fold range of survival and eight-fold range of survival with CPC 1-2. This variation was ameliorated but still persisted in adjusted modeling. Variation in post arrest survival by hospital was not fully explained by available covariates, which suggests the possibility of improving post-arrest clinical outcomes at some hospitals via quality improvement activities.

Bergsma D, Griffith K, Jagsi R, Dominello M, Boike T, **Dilworth J**, Bhatt A, Vicini F, Grubb M, Moran J, Hayman J and Pierce L (2021). "Contemporary practice patterns for the use of regional nodal irradiation during post-lumpectomy radiotherapy for patients with N0/N1 breast cancer." Cancer Research 81(4): PD4-07.

[Full Text](#)

*Department of Radiation Oncology*

Bernstein PS, Cheung G, Kadosono K, Kim JE, **Mahmoud TH**, Querques G, Roca JA and Wu L (2021). "Retina around the world: Experts share the latest research and preferred techniques for macular holes, nonexudative macular neovascularization, myopic traction maculopathy, and more." Retina Today 2021: 34-38.

[Full Text](#)

*Department of Ophthalmology*

Bicoll PS, Goyal A, **Blatt NB** and **Freij BJ** (2021). "Eculizumab-associated moraxella iacunata bacteremia and systemic inflammatory response syndrome in a toddler with atypical hemolytic uremic syndrome." Clinical Medicine Insights: Pediatrics. ePub Ahead of Print.

[Full Text](#)

*Department of Pediatrics*

Moraxella lacunata, a low-virulence Gram-negative coccobacillus, is classically associated with conjunctivitis and upper respiratory tract infections; systemic infections such as sepsis have rarely been reported, especially in children. We describe a 28-month-old girl with atypical hemolytic uremic syndrome and stage II chronic kidney disease on long-term eculizumab therapy who presented with systemic inflammatory response

syndrome and was found to have *Moraxella lacunata* bloodstream infection. Eculizumab, a humanized monoclonal anti-C5 antibody, has been associated with susceptibility to infections with encapsulated bacteria, especially *Neisseria meningitidis*. This is the first report of an invasive bacterial infection with *Moraxella lacunata* in a pediatric eculizumab recipient.

**Black EH and Schlachter DM-B** (2021). "Forehead/brow ptosis," In Servat JJ, Black EH, Nesi FA, Gladstone GJ and Calvano CJ (ed). Smith and Nesi's Ophthalmic Plastic and Reconstructive Surgery. Cham: Springer International Publishing. pp: 351-357.

[Full Text](#)

*Department of Ophthalmology*

Descent of the upper face and brow area occurs frequently with age. With brow ptosis in particular, many patients complain of appearing tired, angry, or sad. Returning the brow, sub-brow fat, and forehead to an improved anatomic position is important to achieve an aesthetically pleasing appearance of the upper face and periorbital area. Numerous techniques exist to elevate the forehead and brow area, so a thorough evaluation and discussion will help determine which technique is appropriate for each patient.

Bobman J, Mayfield CK, Bolia IK, Kang HP, **Hinckel BB**, Gipsman A, Hatch GFR, Heckmann N and Weber AE (2021). "Conversion rates and timing to total knee arthroplasty following anterior cruciate ligament reconstruction: A US population-based study." European Journal of Orthopaedic Surgery & Traumatologie. ePub Ahead of Print.

[Full Text](#)

*Department of Orthopaedic Surgery*

Purpose: To define the rate of subsequent TKA following ACLR in a large US cohort and to identify factors that influence the risk of later undergoing TKA after ACLR. Methods: The California's Office of Statewide Health Planning and Development (OSHPD) database was queried from 2000 to 2014 to identify patients who underwent primary ACLR (ACL group). An age- and gender-matched cohort that underwent appendectomy was selected as the control group. The cumulative incidence of TKA was calculated and ten-year survival was investigated using Kaplan-Meier analysis with failure defined as conversion to arthroplasty. Univariate and multivariate analyses were performed to explore the risk factors for conversion to TKA following ACLR. Results: A total of 100,580 ACLR patients (mean age 34.48 years, 66.1% male) were matched to 100,545 patients from the general population. The ACL cohort had 1374 knee arthroplasty events; conversion rate was 0.71% at 2-year follow-up, 2.04% at 5-year follow-up, and 4.86% at 10-year follow-up. This conversion rate was higher than that of the control group at all time points, with an odds ratio of 3.44 ( $p < 0.001$ ) at 10-year follow-up. Decreasing survivorship following ACLR was observed with increasing age, female gender, and worker's compensation insurance, while increased survivorship was found in patients of Hispanic and Asian Pacific Islander racial heritage and those who underwent concomitant meniscal repair. Conclusions: In this US statewide study, the rate of TKA after ACLR is higher than reported elsewhere, with significantly increased odds when compared to a control group. Age, gender, concomitant knee procedures and other socioeconomic factors influence the rate of conversion to TKA following ACLR.

**Bojrab DI, Fritz CG**, Lin KF, **Schutt CA, Hong RS, Babu SC, Chen PY** and Maitz A (2021). "Fundal fluid cap is associated with hearing preservation in the radiosurgical treatment of vestibular schwannoma." Otology & Neurotology 42(1): 137-144.

[Full Text](#)

*Department of Surgery*

*OUIWB Medical Student Author*

Objective: To evaluate the relationship between fundal fluid and hearing outcomes after treatment of vestibular schwannoma (VS) with Gamma Knife radiosurgery (GKRS). Study Design: Retrospective case series. Setting: Tertiary neurotology referral center. Patients: Patients treated with GKRS for vestibular schwannoma between March 2007 and March 2017 were considered for this study. Exclusion criteria included pretreatment pure-tone average (PTA)  $> 90$  dB, neurofibromatosis type II, history of previous surgical resection, and follow-up less than 1 year. Main Outcome Measure(s): Hearing function was assessed both by preservation of serviceable hearing and by preservation of baseline hearing ( $\leq 20$  dB change in PTA) after GKRS. Hearing preservation comparisons were made between groups of patients with and without a fundal fluid cap. Results: Patients with a fundal cap had significantly higher rates of baseline hearing

preservation ( $\leq 20$  dB change in PTA) according to Kaplan-Meier survival analysis of all 106 patients ( $p = 0.006$ ). By the 3rd year posttreatment, 70.9% of patients with a fundal cap had maintained a  $\leq 20$  dB change in PTA, while only 43.6% of patients without a fundal fluid cap achieved this outcome ( $p = 0.004$ ). Conclusions: Fundal fluid present on pretreatment magnetic resonance imaging is predictive of improved baseline hearing preservation rates in patients undergoing GKRS for vestibular schwannoma when considering all patients with PTA  $\leq 90$  dB. Fundal fluid cap presence may serve as a favorable prognostic indicator to help set hearing expectations and guide patient selection efforts.

**Bojrab DI, Fritz CG, Lin KF, Schutt CA, Hong RS, Babu SC, Chen PY** and Maitz A (2021). "A protective cap: Fundal fluid cap facilitates a reduction in inner ear radiation dose in the radiosurgical treatment of vestibular schwannoma." *Otology & Neurotology* 42(2): 294-299.

[Full Text](#)

*Department of Surgery*

*OUWB Medical Student Author*

Objective: Assess inner ear radiation dose magnitude as it relates to fundal cap length and hearing outcomes in the radiosurgical treatment of vestibular schwannoma. Study Design: Retrospective case series. Setting: Tertiary neurotology referral center. Patients: Patients treated with Gamma Knife radiosurgery for vestibular schwannoma between March 2007 and March 2017 were considered for this study. Exclusion criteria included pretreatment pure-tone average (PTA)  $> 90$  dB, neurofibromatosis type II, history of previous surgical resection, and follow-up less than 1 year. Main Outcome Measures: Hearing function was assessed by maintenance of class A/B hearing level and maintenance of baseline hearing ( $\leq 20$  dB change in PTA following Gamma Knife radiosurgery). Results: Lower radiation doses delivered to the inner ear were associated with longer fundal cap lengths: mean cochlear dose ( $r = -0.130$ ;  $p = 0.184$ ), mean labyrinth dose ( $r = -0.406$ ;  $p < 0.001$ ), max cochlear dose ( $r = -0.326$ ;  $p = 0.001$ ), and max labyrinth dose ( $r = -0.360$ ;  $p < 0.001$ ). Kaplan-Meier analysis with log-rank testing revealed that patients with a mean labyrinth dose  $< 3$  Gy achieved higher rates of preserving baseline hearing ( $\leq 20$  dB change in PTA) following radiosurgery, compared to patients with a mean labyrinth dose  $\geq 3$  Gy ( $p < 0.001$ ). A fundal fluid cap length of 2.5 mm was associated with the 3 Gy mean labyrinth dose threshold. Conclusions: We report that fundal cap presence facilitated the creation of treatment plans with a lower dose delivered to the labyrinth. By affording this dose reduction, a fundal cap may be associated with a slight improvement in hearing outcomes.

**Bowers T and Goldstein JA** (2021). "Hemodynamic compromise in pulmonary embolism: "A tale of two ventricles"." *Catheterization and Cardiovascular Interventions* 97(2): 299-300.

[Full Text](#)

*Department of Internal Medicine*

In acute pulmonary embolism (PE), low cardiac output (CO)–hypotension results from disparate ventricular conditions: The left ventricle (LV) is under-filled and contracting vigorously, whereas the right ventricle (RV) is failing and dilated. The proximate cause of LV preload deprivation is thrombus-induced pulmonary vascular obstruction; abruptly increased pulmonary vascular resistance (PVR) induces acute RV systolic dysfunction which further compromises trans-pulmonary flow. "Escalation of Care" interventions (thrombolytics and aspiration thrombectomy) improve systemic hemodynamics by increasing LV preload delivery directly by reducing PVR and indirectly by relief of the strained failing RV.

Bradley CJ, **Williamson BD**, George J and **Haines DE** (2021). "Protocol driven periprocedural anticoagulation for left atrial ablation." *Journal of Cardiovascular Electrophysiology* 32(3): 639-646.

[Full Text](#)

*Department of Internal Medicine*

Introduction: A weight-based heparin dosing policy adjusted for preprocedural oral anticoagulation was implemented to reduce the likelihood of subtherapeutic dosing during left atrial catheter ablation procedures. We hypothesized that initiation of the protocol would result in a greater prevalence of therapeutic activated clotting time (ACT) values and decreased time to therapeutic ACT during left atrial ablation procedures. Methods: A departmental protocol was initiated for which subjects received intravenous unfractionated heparin (UFH) to achieve and maintain a goal of ACT  $> 300$  s. Initial bolus dose was adjusted for pre-procedure oral anticoagulation and weight as follows: 50 units/kg for those receiving warfarin, 75

units/kg for those not anticoagulated, and 120 units/kg for those on direct oral anticoagulants (DOACs). A UFH infusion was initiated at 10% of the bolus per hour. One hundred consecutive left atrial ablation procedures treated with Protocol Guided heparin dosing were compared with a retrospective consecutive cohort of Usual Care heparin dosing. Results: When the Usual Care and Protocol Guided cohorts were compared, significant findings were limited to those on pre-procedure DOAC. The initial UFH bolus increased from  $99.3 \pm 24.8$  to  $118.2 \pm 22.8$  units/kg ( $p < .001$ ), the proportion of therapeutic ACT on the first draw after heparin administration increased from 57.7% to 76.6% ( $p = .010$ ), and the time to therapeutic ACT after UFH administration decreased from  $37.8 \pm 19.8$  to  $30.2 \pm 16.4$  min ( $p = .032$ ). Conclusion: A weight-based protocol for periprocedural UFH administration resulted in a higher proportion of therapeutic ACT values and decreased the time to therapeutic ACT for those on pre-procedure DOAC.

**Brummett A** and Muaygil R (2021). "Phenomenology, Saudi Arabia, and an argument for the standardization of clinical ethics consultation." *Philosophy, Ethics, and Humanities in Medicine* 16(1): 1.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Background: The purpose of this study is to make a philosophical argument against the phenomenological critique of standardization in clinical ethics. We used the context of clinical ethics in Saudi Arabia to demonstrate the importance of credentialing clinical ethicists. Methods: Philosophical methods of argumentation and conceptual analysis were used. Results: We found the phenomenological critique of standardization to be flawed because it relies on a series of false dichotomies. Conclusions: We concluded that the phenomenological framing of the credentialing debate relies upon two extreme views to be navigated between, not chosen among, in the credentialing of clinical ethicists.

Bunevicius A, Kano H, Lee CC, Krsek M, Nabeel AM, El-Shehaby A, Karim KA, Martinez-Moreno N, Mathieu D, Lee JYK, **Grills I**, Kondziolka D, Martinez-Alvarez R, Reda WA, Liscak R, Su YH, Lunsford LD, Vance ML and Sheehan JP (2021).

"Early versus late Gamma Knife radiosurgery for Cushing's disease after prior resection: Results of an international, multicenter study." *Journal of Neurosurgery* 134(3): 807-815.

[Full Text](#)

*Department of Radiation Oncology*

Objective: The optimal time to perform stereotactic radiosurgery after incomplete resection of adrenocorticotropic hormone (ACTH)-producing pituitary adenoma in patients with Cushing's disease (CD) remains unclear. In patients with persistent CD after resection of ACTH-producing pituitary adenoma, the authors evaluated the association of the interval between resection and Gamma Knife radiosurgery (GKRS) with outcomes. Methods: Pooled data from 10 institutions participating in the International Radiosurgery Research Foundation were used in this study. Results: Data from 255 patients with a mean follow-up of  $65.59 \pm 49.01$  months (mean  $\pm$  SD) were analyzed. Seventy-seven patients (30%) underwent GKRS within 3 months; 46 (18%) from 4 to 6 months; 34 (13%) from 7 to 12 months; and 98 (38%) at  $> 12$  months after the resection. Actuarial endocrine remission rates were higher in patients who underwent GKRS  $\leq 3$  months than when treatment was  $> 3$  months after the resection (78% and 65%, respectively;  $p = 0.017$ ). Endocrine remission rates were lower in patients who underwent GKRS at  $> 12$  months versus  $\leq 12$  months after the resection (57% vs 76%, respectively;  $p = 0.006$ ). In multivariate Cox regression analyses adjusted for clinical and treatment characteristics, early GKRS was associated with increased probability of endocrine remission (hazard ratio [HR] 1.518, 95% CI 1.039–2.218;  $p = 0.031$ ), whereas late GKRS (HR 0.641, 95% CI 0.448–0.919;  $p = 0.015$ ) was associated with reduced probability of endocrine remission. The incidence of some degree of new pituitary deficiency ( $p = 0.922$ ), new visual deficits ( $p = 0.740$ ), and other cranial nerve deficits ( $p = 0.610$ ) was not significantly related to time from resection to GKRS.

Cakmak AS, Perez Alday EA, Da Poian G, Bahrami Rad A, Metzler TJ, Neylan TC, House SL, Beaudoin FL, An X, Stevens J, Zeng D, Linnstaedt SD, Jovanovic T, Germine LT, Bollen KA, Rauch SL, Lewandowski C, Hendry PL, Sheikh S, Storrow AB, Musey PI, Haran JP, Jones CW, Punches BE, **Swor RA**, Gentile NT, McGrath ME, Seamon MJ, Mohiuddin K, Chang AM, Pearson C, Domeier RM, Bruce SE, O'Neil BJ, Rathlev NK, Sanchez LD, Pietrzak RH, Joormann J, Barch DM, Pizzagalli D, Harte SE, Elliott JM, Koenen KC, Ressler KJ, Kessler R, Li Q, McLean SA and Clifford GD (2021).

"Classification and prediction of post-trauma outcomes related to PTSD using circadian rhythm changes measured via wrist-worn research watch in a large longitudinal cohort." *IEEE Journal of Biomedical and Health Informatics* PP: 1-1.

[Full Text](#)

*Department of Emergency Medicine*

Post-Traumatic Stress Disorder (PTSD) is a psychiatric condition resulting from threatening or horrifying events. We hypothesized that circadian rhythm changes, measured by a wrist-worn research watch are predictive of post-trauma outcomes. Approach: 1618 post-trauma patients were enrolled after admission to emergency departments (ED). Three standardized questionnaires were administered at week eight to measure post-trauma outcomes related to PTSD, sleep disturbance, and pain interference with daily life. Pulse activity and movement data were captured from a research watch for eight weeks. Standard and novel movement and cardiovascular metrics that reflect circadian rhythms were derived using this data. These features were used to train different classifiers to predict the three outcomes derived from week-eight surveys. Clinical surveys administered at ED were also used as features in the baseline models. Results: The highest cross-validated performance of research watch-based features was achieved for classifying participants with pain interference by a logistic regression model, with an area under the receiver operating characteristic curve (AUC) of 0.70. The ED survey-based model achieved an AUC of 0.77, and the fusion of research watch and ED survey metrics improved the AUC to 0.79. Significance: This work represents the first attempt to predict and classify post-trauma symptoms from passive wearable data using machine learning approaches that leverage the circadian desynchrony in a potential PTSD population. IEEE

Cami E, Tagami T, **Raff G**, **Gallagher MJ**, **Fan A**, Hafeez A, Willner SJ, Arce PS, George J, **Bilollikar A**, **Chinnaiyan K** and **Safian RD** (2021). "Importance of measurement site on assessment of lesion-specific ischemia and diagnostic performance by coronary computed tomography Angiography-Derived Fractional Flow Reserve." Journal of Cardiovascular Computed Tomography 15(2): 114-120.

[Request Form](#)

*Department of Internal Medicine*

Background: Values of fractional flow reserve (FFR(CT)) by coronary computed tomography angiography (CTA) decline from the ostium to the terminal vessel, irrespective of stenosis severity. The purpose of this study is to determine if the site of measurement of FFR(CT) impacts assessment of ischemia and its diagnostic performance relative to invasive FFR (FFR(INV)). Methods: 1484 patients underwent FFR(CT); 1910 vessels were stratified by stenosis severity (normal; <25%, 25-50%, 50-70%, and >70% stenosis). The rates of positive FFR(CT) ( $\leq 0.8$ ) were determined by measuring FFR(CT) from the terminal vessel and from distal-to-the-lesion. Reclassification rates from positive to negative FFR(CT) were calculated. Diagnostic performance of FFR(CT) relative to FFR(INV) was evaluated in 182 vessels using linear regression, Bland Altman analysis, and receiver operating characteristic (ROC) curves. Results: Positive FFR(CT) was identified in 24.9% of vessels using terminal vessel FFR(CT) and 10.1% using FFR(CT) distal-to-the-lesion ( $p < 0.001$ ). FFR(CT) obtained distal-to-the-lesion resulted in reclassification of 59.6% of positive terminal FFR(CT) to negative FFR(CT). Relative to FFR(INV), there were improvements in specificity (50% to 86%,  $p < 0.001$ ), diagnostic accuracy (65% to 88%,  $p < 0.001$ ), positive predictive value (50% to 78%,  $p < 0.001$ ), and area-under-the-curve (AUC, 0.83 to 0.91,  $p < 0.001$ ) when FFR(CT) was measured distal-to-the-lesion. Conclusion: FFR(CT) values from the terminal vessel should not be used to assess lesion-specific ischemia due to high rates of false positive results. FFR(CT) measured distal-to-the-lesion improves the diagnostic performance of FFR(CT) relative to FFR(INV), ensures that FFR(CT) values are due to lesion-specific ischemia, and could reduce the rate of unnecessary invasive procedures.

Chagpar A, Tsangaris T, Garcia-Cantu C, Howard-McNatt M, Chiba A, Berger A, Levine EA, Gass J, Gallagher KK, Lum S, Martinez R, Willis AI, Pandya S, **Brown EA**, Fenton A, Mendiola A, Murray M, Haddad V, Solomon N, Senthil M, Edmonson D, Lazar M, Namm J, Li F, Morris M, McGowan N, Avitan Y, Yoder B, Walters L, McPartland T and Dupont E (2021). "Are surgeons still doing sentinel node biopsies in older women?" Annals of Surgical Oncology 28(SUPPL 1): S67-S67.

[Full Text](#)

*Department of Surgery*

**Chancellor MB** and **Lamb LE** (2021). "Toward a validated diagnostic test with machine learning algorithm for interstitial cystitis." Urological Science 32(1): 2-7.

[Request Form](#)

#### *Department of Urology*

Diagnosing interstitial cystitis/bladder pain syndrome (IC/BPS) is difficult as there is no definitive test for IC/BPS. Instead, the diagnosis is based on urinary symptoms and cystoscopy may be recommended. However, cystoscopic diagnosis is associated with potentially exacerbating painful side effects and is highly subjective among physicians. Furthermore, IC/PBS symptoms overlap with symptoms of bladder cancer, urinary tract infection, or overactive bladder. As a result, many patients may go years without a correct diagnosis and proper disease management. The goal of our current IC/BPS research is to develop a simple diagnostic test based on several urine proteins called the IC-risk score (IC-RS). A machine learning (ML) algorithm uses this information to determine if a person has IC/BPS or not; if they have IC/BPS, whether their IC/BPS is characterized by Hunner's lesions. We are currently in the middle of a grant to collect urine samples from 1000 patients with IC/BPS and 1,000 normal controls from across the United States. We are using social media such as Twitter and Facebook and working with patient advocacy organizations to collect urine samples from across the country. We hope to validate the IC-RS and apply for regulatory approval. Having a validated diagnostic test for IC/BPS would be a major advancement to help urology patients. In addition, drug companies developing new drugs and therapies for IC/BPS would have a better way to determine who to include in their clinical trials, and possibly another way to measure if their drug or therapy is effective. We will hereby review the steps that have led us in urine biomarker discovery research from urine protein assessment to use crowdsourcing stakeholders participation to ML algorithm IC-RS score development.

**Chancellor MB** and Smith CP (2021). "Use of botulinum toxin in the genitourinary system," In J Barrett (ed). Handbook of Experimental Pharmacology. 263. pp: 171-184.

[Full Text](#)

#### *Department of Urology*

Botulinum toxin injection has been widely accepted by the urology and urogynecology medical communities as a safe and effective treatment for refractory urinary incontinence. There are two approved genitourinary indications for botulinum toxin. OnabotulinumtoxinA (onaBoNTA) 200 U for the treatment of urinary incontinence due to detrusor overactivity associated with a neurologic condition (e.g., spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an anticholinergic medication. In addition, onaBoNTA 100 U is used for the treatment of overactive bladder with symptoms of urinary incontinence, urgency, and frequency, in adult patients who have an inadequate response to or are intolerant of an anticholinergic medication. We will discuss the application of botulinum toxin for genitourinary indications with a focus on bladder injection and on potential use of BoNT use in the prostate and pelvic floor.

Chiari EF, Weiss W, **Simon MR**, Kiessig ST, Pulse M, Brown SC, Gerding HR, Mandago M, Gisch K and von Eichel-Streiber C (2021). "Oral immunotherapy with human secretory IgA improves survival in the hamster model of clostridioides difficile infection." Journal of Infectious Diseases. ePub Ahead of Print.

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#### *Department of Internal Medicine*

Co-administration of human secretory IgA (sIgA) together with subtherapeutic vancomycin significantly enhanced survival in the Clostridioides difficile infection (CDI) hamster model. Vancomycin (5 or 10 mg/kgx5 days) + healthy donor plasma sIgA/monomeric IgA (TIDx21 days) or hyperimmune sIgA/monomeric IgA (BIDx13 days) enhanced survival of CDI hamsters. Survival curves were significantly improved compared to vancomycin alone (p=0.018 and 0.039 by log-rank (Mantel-Cox) for healthy, and hyperimmune, sIgA, respectively. Passive immunization with sIgA made with recombinant human secretory component and IgA dimer/polymer from pooled human plasma can be administered orally, and prevents lethal infection in a partially treated CDI hamster model.

**Chinnaiyan KM**, Revankar R, Shapiro MD and Kalra A (2021). "Heart, mind, and soul: Spirituality in cardiovascular medicine." European Heart Journal ehab080.

[Full Text](#)

#### *Department of Internal Medicine*

Cho RI and **Kahana A** (2021). "Embryology of the orbit." Journal of Neurological Surgery, Part B: Skull Base 82(1): 2-6.

[Full Text](#)

*Department of Ophthalmology*

The orbit houses and protects the ocular globe and the supporting structures, and occupies a strategic position below the anterior skull base and adjacent to the paranasal sinuses. Its embryologic origins are inextricably intertwined with those of the central nervous system, skull base, and face. Although the orbit contains important contributions from four germ cell layers (surface ectoderm, neuroectoderm, neural crest, and mesoderm), a significant majority originate from the neural crest cells. The bones of the orbit, face, and anterior cranial vault are mostly neural crest in origin. The majority of the bones of the skull base are formed through endochondral ossification, whereas the cranial vault is formed through intramembranous ossification. Familiarity with the embryology and fetal development of the orbit can aid in understanding its anatomy, as well as many developmental anomalies and pathologic conditions that affect the orbit. © 2021 American Society of Civil Engineers (ASCE). All rights reserved.

Chowdhury EA, Noorani B, Alqahtani F, Bhalerao A, Raut S, Sivandzade F and **Cucullo L** (2021). "Understanding the brain uptake and permeability of small molecules through the BBB: A technical overview." Journal of Cerebral Blood Flow and Metabolism. ePub Ahead of Print.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

The brain is the most important organ in our body requiring its unique microenvironment. By the virtue of its function, the blood-brain barrier poses a significant hurdle in drug delivery for the treatment of neurological diseases. There are also different theories regarding how molecules are typically effluxed from the brain. In this review, we comprehensively discuss how the different pharmacokinetic techniques used for measuring brain uptake/permeability of small molecules have evolved with time. We also discuss the advantages and disadvantages associated with these different techniques as well as the importance to utilize the right method to properly assess CNS exposure to drug molecules. Even though very strong advances have been made we still have a long way to go to ensure a reduction in failures in central nervous system drug development programs.

Chuck RS, **Dunn SP**, Flaxel CJ, Gedde SJ, Mah FS, Miller KM, Wallace DK and Musch DC (2021). "Comprehensive adult medical eye evaluation preferred practice pattern®." Ophthalmology 128(1): P1-P29.

[Full Text](#)

*Department of Ophthalmology*

Clark-Sienkiewicz SM, Caño A, **Zeman LL**, Lumley MA and Gothe N (2021). "Development of a multicomponent intervention to initiate health behavior change in primary care: The Kickstart Health Program." Journal of Clinical Psychology in Medical Settings. ePub Ahead of Print.

[Full Text](#)

*Department of Family Medicine and Community Health*

There is a growing movement to integrate behavioral health specialists into primary care settings in order to better manage patients' health behaviors. Group interventions in healthcare settings can provide services to multiple individuals simultaneously; however, the participants' experiences taking part in these activities and the logistics of integrating them into clinical settings are largely under-studied. This article describes the development and implementation of a novel group intervention for health behavior change, The Kickstart Health Program, which integrates components of cognitive, behavioral, acceptance, and experiential therapies. Participant feasibility, acceptability, experiences, and treatment course were assessed. Acceptability among a small sample of attendees was high, and initial data on behavior change suggest there were benefits to patients who attended the program. Increases in mindfulness practice and decreases in exercise barriers from baseline to 10-week follow-up were detected as were improvements in overall perceived health and well-being. Participants expressed that the program was acceptable and successful at helping them reach their individual health goals; however, enrollment barriers negatively impacted the feasibility of the program in regard to attendance. Modification to the enrollment process such as embedding referrals into the electronic medical record, encouraging spouse or family co-enrollment, and peer coaching may address these barriers. The Kickstart Health Program has the potential to improve health behaviors and paves the way for unique studies of dissemination and implementation of efficacious behavioral health interventions

into real-world healthcare settings.

Claus CF, Tong D, Lytle E, Bahoura M, Garmo L, Li C, Park P, Carr DA, **Easton R**, Abdulhak M, Chang V, Houseman C, Bono P, Richards B and **Soo TM** (2021). "Age as a predictor for complications and patient-reported outcomes in multilevel transforaminal lumbar interbody fusions: Analyses from the Michigan Spine Surgery Improvement Collaborative (MSSIC)." *Spine* 46(6): 356-365.

[Full Text](#)

*Department of Orthopaedic Surgery*

*Department of Neurosurgery*

Study Design: Retrospective review of a multi-institutional data registry. Objective: The authors sought to determine the association between age and complications & patient-reported outcomes (PRO) in patients undergoing multilevel transforaminal interbody lumbar fusion (MTLIF). Summary of Background Data: Elderly patients undergoing MTLIF are considered high risk. However, data on complications and PRO are lacking. Additionally, safety of multilevel lumbar fusion in the elderly remains uncertain. Methods: Patients  $\geq 50$ -year-old who underwent MTLIF for degenerative lumbar spine conditions were analyzed. Ninety-day complications and PROs (baseline, 90-d, 1-y, 2-y) were queried using the MSSIC database. PROs were measured by back & leg visual analog scale (VAS), Patient-reported Outcomes Measurement Information System (PROMIS), EuroQoL-5D (EQ-5D), and North American Spine Society (NASS) Patient Satisfaction Index. Univariate analyses were used to compare among elderly and complication cohorts. Generalized estimating equation (GEE) was used to identify predictors of complications and PROs. Results: A total of 3120 patients analyzed with 961 (31%)  $\geq 70$ -y-o and 2159 (69%) between 50-69. A higher proportion of elderly experienced postoperative complications ( $P = .003$ ) including urinary retention ( $P < .001$ ) and urinary tract infection ( $P = .002$ ). Multivariate analysis demonstrated that age was not independently associated with complications. Number of operative levels was associated with any ( $P = .001$ ) and minor ( $P = .002$ ) complication. Incurring a complication was independently associated with worse leg VAS and PROMIS scores ( $P < .001$ ). Preoperative independent ambulation was independently associated with improved PROMIS, and EQ5D ( $P < .001$ ). Within the elderly, preoperative independent ambulation and lower BMI were associated with improved PROMIS ( $P < .001$ ). Complications had no significant effect on PROs in the elderly. Conclusions: Age was not associated with complications nor predictive of functional outcomes in patients who underwent MTLIF. Age alone, therefore, may not be an appropriate surrogate for risk. Furthermore, baseline preoperative independent ambulation was associated with better clinical outcomes and should be considered during preoperative surgical counseling.

Concepcion R, **Hafron J**, Hamilton J and **Handel J** (2021). "Upper tract transitional cell carcinoma: Diagnostic and therapeutic considerations." *Urology Times* 49: 22-23.

[Full Text](#)

*Department of Diagnostic Radiology and Molecular Imaging*

*Department of Urology*

The article presents the highlights of a virtual panel discussion on the diagnosis and therapeutic treatments of upper tract transitional cell carcinoma in January 2021. Topics include the role of genetic testing in a Lynch syndrome patient, genomic sequencing, and the use of ureteroscopy. Panelists include doctors Joelle Hamilton, Jeremy D. Handel, and Jason M. Hafron.

Conte E, Dwivedi A, Mushtaq S, Pontone G, Lin FY, Hollenberg EJ, Lee SE, Bax J, Cademartiri F, **Chinnaiyan K**, Chow BJW, Cury RC, Feuchtner G, Hadamitzky M, Kim YJ, Baggiano A, Leipsic J, Maffei E, Marques H, Plank F, **Raff GL**, van Rosendael AR, Villines TC, Weirich HG, Al'Aref SJ, Baskaran L, Cho I, Danad I, Han D, Heo R, Lee JH, Stuijzand WJ, Gransar H, Lu Y, Sung JM, Park HB, Al-Mallah MH, de Araújo Gonçalves P, Berman DS, Budoff MJ, Samady H, Shaw LJ, Stone PH, Virmani R, Narula J, Min JK, Chang HJ and Andreini D (2021). "Age- and sex-related features of atherosclerosis from coronary computed tomography angiography in patients prior to acute coronary syndrome: Results from the ICONIC study." *European Heart Journal Cardiovascular Imaging* 22(1): 24-33.

[Full Text](#)

*Department of Internal Medicine*

Aims: Although there is increasing evidence supporting coronary atherosclerosis evaluation by coronary computed tomography angiography (CCTA), no data are available on age and sex differences for

quantitative plaque features. The aim of this study was to investigate sex and age differences in both qualitative and quantitative atherosclerotic features from CCTA prior to acute coronary syndrome (ACS). Methods and Results: Within the ICONIC study, in which 234 patients with subsequent ACS were propensity matched 1:1 with 234 non-event controls, our current subanalysis included only the ACS cases. Both qualitative and quantitative advance plaque analysis by CCTA were performed by a core laboratory. In 129 cases, culprit lesions identified by invasive coronary angiography at the time of ACS were co-registered to baseline CCTA precursor lesions. The study population was then divided into subgroups according to sex and age (<65 vs. ≥ 65 years old) for analysis. Older patients had higher total plaque volume than younger patients. Within specific subtypes of plaque volume, however, only calcified plaque volume was higher in older patients ( $135.9 \pm 163.7$  vs.  $63.8 \pm 94.2$  mm<sup>3</sup>,  $P < 0.0001$ , respectively). Although no sex-related differences were recorded for calcified plaque volume, females had lower fibrous and fibrofatty plaque volume than males (Fibrofatty volume  $29.6 \pm 44.1$  vs.  $75.3 \pm 98.6$  mm<sup>3</sup>,  $P = 0.0001$ , respectively). No sex-related differences in the prevalence of qualitative high-risk plaque features were found, even after separate analyses considering age were performed. Conclusion: Our data underline the importance of age- and sex-related differences in coronary atherosclerosis presentation, which should be considered during CCTA-based atherosclerosis quantification.

Conway RM, Sugihara EM, **Lee DM**, Renker J, Sioshansi PC and **Babu SC** (2021). "Frequency-specific electrocochleography and traveling wave time as a clinical test for Menière's Disease." *Otology & Neurotology* 42(2): 290-293.

[Full Text](#)

*Department of Surgery*

*OUIB Medical Student Author*

**Cowan B, Oska S, Arianpour K**, Svider PF, **Bojrab D** and **Hong RS** (2021). "A systematic review of cochlear implantation in temporal bone fractures and the significance of otic capsule involvement." *Otology & Neurotology* 42(1): 1309-1315.

[Full Text](#)

*Department of Surgery*

*OUIB Medical Student Author*

Coyne CJ, Reyes-Gibby CC, Durham DD, Abar B, Adler D, **Bastani A**, Bernstein SL, Baugh CW, Bischof JJ, Grudzen CR, Henning DJ, Hudson MF, Klotz A, Lyman GH, Madsen TE, Pallin DJ, Rico JF, Ryan RJ, Shapiro NI, **Swor R**, Thomas CR, Jr., Venkat A, Wilson J, Yeung SJ and Caterino JM (2021). "Cancer pain management in the emergency department: A multicenter prospective observational trial of the Comprehensive Oncologic Emergencies Research Network (CONCERN)." *Support Care Cancer*. ePub Ahead of Print.

[Full Text](#)

*Department of Emergency Medicine*

Purpose: Many patients with cancer seek care for pain in the emergency department (ED). Prospective research on cancer pain in this setting has historically been insufficient. We conducted this study to describe the reported pain among cancer patients presenting to the ED, how pain is managed, and how pain may be associated with clinical outcomes. Methods: We conducted a multicenter cohort study on adult patients with active cancer presenting to 18 EDs in the USA. We reported pain scores, response to medication, and analgesic utilization. We estimated the associations between pain severity, medication utilization, and the following outcomes: 30-day mortality, 30-day hospital readmission, and ED disposition. Results: The study population included 1075 participants. Those who received an opioid in the ED were more likely to be admitted to the hospital and were more likely to be readmitted within 30 days (OR 1.4 (95% CI: 1.11, 1.88) and OR 1.56 (95% CI: 1.17, 2.07)), respectively. Severe pain at ED presentation was associated with increased 30-day mortality (OR 2.30, 95% CI: 1.05, 5.02), though this risk was attenuated when adjusting for clinical factors (most notably functional status). Conclusions: Patients with severe pain had a higher risk of mortality, which was attenuated when correcting for clinical characteristics. Those patients who required opioid analgesics in the ED were more likely to require admission and were more at risk of 30-day hospital readmission. Future efforts should focus on these at-risk groups, who may benefit from additional services including palliative care, hospice, or home-health services.

**Dekhou A, Oska N, Partiali B, Johnson J, Chung MT and Folbe A** (2021). "E-cigarette burns and explosions: What are the patterns of oromaxillofacial injury?" *Journal of Oral and Maxillofacial Surgery*. ePub Ahead of Print.

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*Department of Surgery*

*OUIB Medical Student Author*

Purpose: With the recent increase in popularity of electronic cigarette use in the United States, its harmful effects are not only limited to smoke inhalation, but also to the possibility of e-cigarette device malfunction. The purpose of this review is to characterize oromaxillofacial trauma secondary to electronic cigarette device explosion. Methods: For this systematic review, PubMed and Embase were searched in October 2019 using the following search terms: e-cigarette burns, e-cigarette injury, and e-cigarette explosions, which yielded 400 studies. Basic science research, animal studies, non-English studies, and reports of non-oromaxillofacial injuries were excluded. Study subject demographics, mechanism of trauma, injury type, treatment, and sequelae were recorded and analyzed. Results: Of all studies, 20 studies met inclusion criteria, including 14 case reports and 6 case series, with a total of 21 study subjects. For cases that reported sex, 100% were male (20) with a mean age of 29.5 years. Most common lacerations and/or burns involved the lips (10/21), tongue (8/21), soft palate and/or hard palate (4/21), and nose (5/21). Thirteen subjects underwent surgeries including oral-maxillofacial surgery or dental implants (7/13), bone graft repair (3/13), open reduction and internal fixation for preservation of sinus outflow tracts (2/13), foreign body removal from the cervical spine (1/13), and iridectomy (1/13). Reported complications included bone loss secondary to traumatic fracture, tinnitus and hearing loss, lip paralysis secondary to persistent edema, major depressive disorder/ post-traumatic stress disorder, persistent sinusitis, photophobia, and bilateral axillary and hand contractures. Conclusions: Electronic cigarette device malfunction and explosion carries great risk for acute oromaxillofacial trauma that may be disfiguring. With the increasing popularity of electronic cigarette use, clinicians and patients should be advised regarding dangers of electronic cigarette use.

**Derias N, Loftus S and Kamel-ElSayed S** (2021). "Threshold concepts in preclinical medical education: Students' perceptions." *Medical Science Educator* 31(2): 917-921.

[Full Text](#)

*OUIB Medical Student Author*

*Department of Foundational Medical Studies (OU)*

Threshold concepts are those ideas that learners often find difficult, but must understand in order to master a discipline. Nearly all research into threshold concepts has been from the perspective of teachers. We argue that the students' perspectives can also be helpful. In this commentary, we explore this issue and inform the debate by drawing on insights from a pilot study in which medical students articulated their own views on what constituted threshold concepts from recent learning experiences in physiology. Combining insights, from teachers and students, into candidate threshold concepts could be used to improve the medical curriculum.

Dioh W, Chabane M, Tourette C, Azbekyan A, Morelot-Panzini C, Hajjar LA, Lins M, **Nair GB**, Whitehouse T, Mariani J, Latil M, Camelo S, Lafont R, Dilda PJ, Veillet S and Agus S (2021). "Testing the efficacy and safety of BIO101, for the prevention of respiratory deterioration, in patients with COVID-19 pneumonia (COVA study): A structured summary of a study protocol for a randomised controlled trial." *Trials* 22: 1-5.

[Full Text](#)

*Department of Internal Medicine*

El-Zein ZS, Gehrke CK, Croley JS, Siljander MP, Mallow MA, **Flierl MA, Verner JJ and Baker EA** (2021). "Assessing taper geometry, head size, head material, and their interactions in taper fretting corrosion of retrieved total hip arthroplasty implants." *Journal of Arthroplasty*. ePub Ahead of Print.

[Request Form](#)

*Department of Orthopaedic Surgery*

Background: Decreased fretting and corrosion damage at the taper interface of retrieved ceramic-on-polyethylene total hip arthroplasty (THA) implants has been consistently reported; however, resultant fretting corrosion as a function of femoral head size and taper geometry has not been definitively explained.

Methods: Eight cohorts were defined from 157 retrieved THA implants based on femoral head composition (n = 95, zirconia-toughened alumina, ZTA vs n = 62, cobalt-chromium alloy, CoCr), head size (n = 56, 32mm vs n = 101, 36mm), and taper geometry (n = 84, 12/14 vs n = 73, V40). THA implants were evaluated and graded for taper fretting and corrosion. Data were statistically analyzed, including via a 2(3) factorial modeling. Results: Factorial-based analysis indicated the significant factors related to both resultant (summed) fretting and corrosion damage were head material and taper geometry; head material-taper geometry interaction was also a significant factor in resultant corrosion damage. Lower rates of moderate-to-severe fretting and corrosion damage were exhibited on ZTA heads (ZTA = 13%, CoCr = 38%), smaller heads (32mm = 18%, 36mm = 26%), and 12/14 tapers (12/14 = 13%, V40 = 35%). ZTA+32mm heads demonstrated the lowest rates of moderate-to-severe fretting and corrosion damage (12/14 = 2%, V40 = 7%), whereas CoCr heads with V40 tapers demonstrated the greatest rates of moderate-to-severe damage (32mm = 47%, 36mm = 59%). Conclusion: In this series, retrieved implants with ZTA, 32-mm heads paired with 12/14 tapers exhibited lower rates of moderate-to-severe damage. Factorial analysis showed head material, taper geometry, and their interactions were the most significant factors associated with resultant damage grades. Isolating implant features may provide additional information regarding factors leading to fretting and corrosion damage in THA.

Evans DG, Phillips KA, Milne RL, Fruscio R, Cybulski C, Gronwald J, Lubinski J, Huzarski T, Hyder Z, Forde C, Metcalfe K, Senter L, Weitzel J, Tung N, **Zakalik D**, Ekholm M, Sun P and Narod SA (2021). "Survival from breast cancer in women with a BRCA2 mutation by treatment." *British Journal of Cancer* 124(9): 1524-1532.

[Full Text](#)

*Department of Internal Medicine*

Background: The impact of various breast-cancer treatments on patients with a BRCA2 mutation has not been studied. We sought to estimate the impact of bilateral oophorectomy and other treatments on breast cancer-specific survival among patients with a germline BRCA2 mutation. Methods: We identified 664 women with stage I-III breast cancer and a BRCA2 mutation by combining five different datasets (retrospective and prospective). Subjects were followed for 7.2 years from diagnosis to death from breast cancer. Tumour characteristics and cancer treatments were patient-reported and derived from medical records. Predictors of survival were determined using Cox proportional hazard models, adjusted for other treatments and for prognostic features. Results: The 10-year breast-cancer survival for ER-positive patients was 78.9% and for ER-negative patients was 82.3% (adjusted HR = 1.23 (95% CI, 0.62-2.45, p = 0.55)). The 10-year breast-cancer survival for women who had a bilateral oophorectomy was 89.1% and for women who did not have an oophorectomy was 59.0% (adjusted HR = 0.45; 95% CI, 0.28-0.72, p = 0.001). The adjusted hazard ratio for chemotherapy was 0.83 (95% CI, 0.65-1.53; p = 0.56). Conclusions: For women with breast cancer and a germline BRCA2 mutation, positive ER status does not predict superior survival. Oophorectomy is associated with a reduced risk of death from breast cancer and should be considered in the treatment plan.

Feinberg DL, Rosner MS and **Rosner AJ** (2021). "Validation of the binocular vision dysfunction questionnaire (BVDQ)." *Otology & Neurotology* 42(1): e66-e74.

[Full Text](#)

*Department of Surgery*

Objective: Among patients presenting with dizziness, visual dysfunction must be considered, including vertical heterophoria (VH), a frequently under-identified form of binocular vision dysfunction where there is vertical discrepancy between the lines of sight of the eyes when at physiologic rest. Current self-rated screening measures do not account for complex VH symptomatology including dizziness/ambulation difficulties, nausea, headache, anxiety, neck pain, and reading impairment. VH must be differentiated from vestibular/otolithic etiologies, as their treatment frequently provides inadequate relief, yet treatment of the VH can reduce/eliminate symptoms. The objective of this study is to create a valid measurement tool (binocular vision dysfunction questionnaire) to assist in identifying VH among dizzy patients to aid in appropriate referral. Study Design: Retrospective case series. Setting: Tertiary referral center. Patients: One hundred twenty-six patients presenting to an optometric binocular vision subspecialist diagnosed with VH. Intervention: Psychometric study. The measurement tool's internal consistency and test-retest reliability was assessed. Confirmatory and exploratory factor analyses were performed. Validity was estimated through

correlations with a visual analog scale and validated instruments for headaches, dizziness, and anxiety. Main Outcome Measures/Results: Excellent reliability demonstrated including Cronbach's alpha of 0.91 and high test-retest reliability. Statistical correlations with established measurements established sound convergent/content validity. Analysis of participants who underwent treatment indicated change in BVDQ score correlates with perception of change in symptom burden. Conclusions: Results suggest the BVDQ is a valid, reliable screening tool to assist otologists in identifying VH among their dizzy patients. The BVDQ may also be useful for measuring changes with various treatments, and in identifying diverse symptoms associated with BVD/VH.

Fenton A, Dupont E, Tsangaris T, Garcia-Cantu C, Howard-McNatt M, Chiba A, Berger A, Levine E, Gass J, Gallagher K, Lum S, Martinez R, Willis A, Pandya S, **Brown E**, Mendiola A, Murray M, Solomon N, Senthil M, Ollila D, Edmonson D, Lazar M, Namm J, Li FY, Butler M, McGowan N, Herrera M, Avitan Y, Yoder B, **Walters L**, McPartland T, Haddad V, Ma HW, **Xie M** and Chagpar A (2021). "Does breast cancer subtype impact margin status in patients undergoing partial mastectomy?" Cancer Research 81(4).

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*Department of Pathology*

*Department of Surgery*

Ferrey AJ, Hanna R, Reddy UG, **Tantisattamo E**, Kalantar-Zadeh K and Amin AN (2021). "Novel therapeutic approaches for COVID-19 in chronic kidney disease and transplant." Current Opinion in Nephrology and Hypertension 30(1): 47-53.

[Full Text](#)

*Department of Internal Medicine*

Purpose of Review: Severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) is the novel virus responsible for the current worldwide pandemic. The scientific and healthcare communities have made every effort to discover and implement treatment options at a historic pace. Patients with kidney disease are uniquely vulnerable to an infectious pandemic because of their need to be in frequent contact with the healthcare system for life-sustaining renal replacement therapy whether it be by dialysis or transplant. Recent Findings: The use of targeted viral therapies, extracorporeal therapies, immunosuppressive therapy and public health interventions are important in the management of patients with COVID-19 but require special consideration in patients with kidney disease because of the complexity of their condition. Summary: Here, we discuss some of the major efforts made to prevent spread and emerging treatment options for this virus, as they pertain to patients with kidney disease.

Fiani B, Runnels J, Taylor A, **Sekhon M**, Chacon D, McLarnon M, Houston R and Vereecken S (2021). "Prevalence of sports-related spinal injury stratified by competition level and return to play guidelines." Reviews in Neurosciences 32(2): 169-179.

[Full Text](#)

*OUIB Medical Student Author*

Spinal injury is among the most severe and feared injuries an athlete may face. We present an up-to-date review of the recent literature, stratifying recommendations based on injury location (cervical, thoracic, and lumbar spine) and type, as well as, the level of competitive play (high school, collegiate, professional). A literature search was completed to identify all publications reporting return to play guidelines for athletic injuries or injury-related surgery irrespective of the study design. Publication dates were not restricted by year. Search terms used included "return to play" and "spinal injury" on National Library of Medicine (PubMed) and Google Scholar. Selection criteria for literature included axial spine injury guidelines for athletic participation post-injury or post-surgery. Literature found from the search criteria was sorted based on level of competition and location of axial spine injury involved. It was found that professional athletes are more likely to suffer severe spinal injuries, require surgery, and necessitate a longer return to play (RTP), with high school and college athletes usually returning to play within days or weeks. Injuries occur mainly within contact sports and concordance exists between initial and subsequent spinal injuries. Adequate rest, rehabilitation, and protective equipment alongside the education of athletes and coaches are recommended. In conclusion, a multidisciplinary approach to patient management is required with consideration for the emotional, social, and perhaps financial impact that spinal injury may have upon the athlete. Consensus from

the literature states that in order for an athlete to safely return to play, that athlete should not be actively suffering from pain, should have a full range of motion, and complete return of their strength in the absence of neurological deficit.

Field JP, Zuckerwise LC, **DeMare AM**, Zhao S, Lipscomb BE, Raees MA, Walia S, Lovvorn HN and **Novotny NM** (2021). "Identifying prenatal ultrasound predictors and the ideal neonatal management of closing gastroschisis: The key is prevention." *Journal of Perinatology*. ePub Ahead of Print.

[Request Form](#)

*OUIB Medical Student Author*

*Department of Surgery*

Objective: To evaluate the optimal approaches to initial surgical management and the potential for prenatal ultrasound detection of patients with closing gastroschisis. Study Design: We performed a retrospective analysis of patients born with gastroschisis to determine clinical and surgical outcomes and the ability to determine prognosis by prenatal imaging. Data collected included operative findings and postoperative outcome, as well as prenatal imaging features from a subset of cases with and without closing gastroschisis. Statistical analyses were performed as appropriate. Results: We included 197 patients with gastroschisis. No statistical significance was seen in outcomes between closing gastroschisis patients undergoing resection versus intracorporeal parking (n = 18). Ultrasound review was performed on 33 of these patients, 11 with closing gastroschisis, and 22 without. Significantly more closing gastroschisis patients had imaging indicative of progressive defect narrowing and defect diameter  $\leq 8$  mm after 30 weeks of gestation versus non-closing patients (p = 0.002). Conclusion: Parking of extruded bowel offers potential for intestinal remodeling. In addition, prenatal ultrasound may be useful in detection of closing gastroschisis in utero.

Fonseka G, Bognanno E and **Rollinger K** (2021). "14-year-old girl • history of bullying • lack of social support • multiple linear scars on breasts • Dx?" *Journal of Family Practice* 70(2): 93-95.

[Full Text](#)

*Department of Family Medicine and Community Health*

**Franklin BA** (2021). "Physical activity strategies," In Wong ND, Amsterdam EA and Toth PP (ed). *ASPC Manual of Preventive Cardiology*. Cham: Springer International Publishing. pp: 99-118.

[Full Text](#)

*Department of Internal Medicine*

Numerous studies now suggest that cardiorespiratory fitness (CRF), expressed as metabolic equivalents (METs), is one of the strongest prognostic markers in persons with and without coronary heart disease (CHD), regardless of the level of coronary artery calcium or the coronary risk factor profile. Each 1-MET increase in CRF confers an ~15% decrease in mortality up to about 10 METs. In addition, physically active and/or fit people are more likely to have lower annual healthcare costs and rates of chronic disease, including incident heart failure. Accordingly, sedentary individuals should be counseled to become more physically active and/or fit by starting an endurance exercise program, increasing lifestyle activity, or both. When individuals can adopt this regimen comfortably, that is, moderate-intensity exercise, they should strive for the goal of more vigorous exercise over time, provided they remain asymptomatic. On the other hand, unaccustomed vigorous- to high-intensity physical activity (PA), especially in previously inactive/unfit individuals with known or occult CHD, can trigger acute cardiac events. Moreover, extreme endurance exercise training regimens are associated with potential cardiac maladaptations in some individuals, including accelerated coronary calcification and an increased likelihood to develop atrial fibrillation. This relationship has been increasingly described by a U- or reverse J-shaped dose-response curve. Despite these recent findings, the benefits of moderate-to-vigorous PA far outweigh the risks for the majority of the population.

**Freij BJ**, Hanrath AT, Chen R, Hambleton S and Duncan CJA (2021). "Life-threatening influenza, hemophagocytic lymphohistiocytosis and probable vaccine-strain varicella in a novel case of homozygous STAT2 deficiency." *Frontiers in Immunology* 11: 624415.

[Full Text](#)

*Department of Pediatrics*

STAT2 is a transcription factor that plays an essential role in antiviral immunity by mediating the activity of type I and III interferons (IFN-I and IFN-III). It also has a recently established function in the negative regulation of IFN-I signaling. Homozygous STAT2 deficiency is an ultra-rare inborn error of immunity which provides unique insight into the pathologic consequence of STAT2 dysfunction. We report here a novel genetic cause of homozygous STAT2 deficiency with several notable clinical features. The proband presented aged 12 months with hemophagocytic lymphohistiocytosis (HLH) closely followed by clinical varicella, both occurring within three weeks of measles, mumps, and rubella (MMR) and varicella vaccinations. There was a history of life-threatening influenza A virus (IAV) disease 2 months previously. Genetic investigation uncovered homozygosity for a novel nonsense variant in STAT2 (c. 1999C>T, p. Arg667Ter) that abrogated STAT2 protein expression. Compatible with STAT2 deficiency, dermal fibroblasts from the child demonstrated a defect of interferon-stimulated gene expression and a failure to mount an antiviral state in response to treatment with IFN-I, a phenotype that was rescued by lentiviral complementation by wild type STAT2. This case significantly expands the phenotypic spectrum of STAT2 deficiency. The occurrence of life-threatening influenza, which has not previously been reported in this condition, adds STAT2 to the list of monogenetic causes of this phenotype and underscores the critical importance of IFN-I and IFN-III to influenza immunity. The development of probable vaccine-strain varicella is also a novel occurrence in STAT2 deficiency, implying a role for IFN-I/III immunity in control of attenuated varicella zoster virus in vivo and reinforcing the susceptibility to pathologic effects of live-attenuated viral vaccines in disorders of IFN-I immunity. Finally, the occurrence of HLH in this case reinforces emerging links to hyperinflammation in patients with STAT2 deficiency and other related defects of IFN-I signaling—highlighting an important avenue for further scientific enquiry.

Fucinari J, Zaiem F, **Daboul R**, Elshaikh M, Ruterbusch J, Cote M, Schultz D, Dyson G, Naaman J, Bandyopadhyay S and Ali-Fehmi R (2021). "The prognostic value of pelvic wash cytology on uterine serous carcinoma outcomes." Laboratory Investigation 101(SUPPL 1): 681-682.

[Full Text](#)

*OUWB Medical Student Author*

**Gannon J**, Pollock AJ, Allen DB and Kling PJ (2021). "A practical screening tool to predict early childhood obesity risk: Examining a birth cohort." Clinical Pediatrics 60(3): 178-183.

[Full Text](#)

*OUWB Medical Student Author*

Children obese at the age of 5 years are at greater risk of lifelong obesity. Because certain risks of obesity can be identified in early infancy, a tool for obesity risk prediction in early life would be clinically useful. We investigated predictors of obesity risk in a novel, prospectively collected healthy birth cohort recruited for demographic risks to develop iron deficiency at 1 year, a cohort leveraged because risk factors for iron deficiency and obesity overlap. Obesity at the age of 5 years was defined as age- and sex-specific body mass index Z -score (z BMI) >2SD. For each child, obesity risk factors were summed. Of 10 total risk factors, the following 4 key risks were identified: maternal obesity, maternal diabetes, large for gestational age, or breastfeeding <6 months. Childhood obesity was predicted by either  $\geq 3$  total number of risks (P <.033), any key risk (P <.002), or summing key risks (P <.0001). In clinical practice, summing early life risk factors may be a useful strategy for preemptive counseling.

Gasteratos K, Alser O, Hart J and **Chaiyasate K** (2021). "Palliative reconstructive surgery for advanced maxillofacial osteosarcoma in the peak of COVID-19 pandemic: A matter of ethical decision-making." Plastic and Reconstructive Surgery-Global Open 9(3): e3545.

[Full Text](#)

*Department of Surgery*

The coronavirus disease 2019 posed an unprecedented strain to plastic surgery services. The scarcity of validated guidelines—at the beginning of this healthcare crisis—to direct clinical, ethical, transparent decision-making for head and neck cancer patients requiring palliative reconstructive surgery was a difficult situation. We report a 15-year-old girl with an advanced chemoresistant rare radiotherapy-induced mandibular osteosarcoma during the early phase of the pandemic in the United States in mid-March 2020, when official

recommendations for triage were still developing. Local guidelines suggested canceling all elective procedures, and allowed operating emergency and/or nonelective cases only. Many surgeons declined surgery due to patient's poor prognosis and high perioperative risk, but her mother pursued different professional opinions elsewhere. However, upon Beaumont hospital approval, the patient underwent radical en bloc resection of the tumor, hemimandibulectomy, zygomatic resection, maxillectomy, and hemipalate resection followed by reconstruction with free fibula osteocutaneous and anterolateral thigh flaps. The challenging decision to proceed with surgery was based on evidence-based and objective risk-stratifying scores, available at the time, and ethical recommendations from emerging reliable published literature. Despite a favorable postoperative outcome, the patient expired due to cardiac complications of the disease. Our patient taught us that ethical decision-making, sound clinical judgment, and a patient-centered individualized approach remain pivotal aspects of the medical profession. Although the surgery will not provide a cure for the disease, we have found that palliative reconstructive surgery can greatly improve patient's quality of life, and help family cope with the advancing stages of disease.

**Ghandour M, Shereef H, Homida H, Revankar S and Zachariah MS (2021).** "Disseminated nocardiosis in a renal transplant recipient." *Cureus* 13(1): 12497.

[Full Text](#)

*OUWB Medical Student Author*

Nocardiosis is an uncommon opportunistic Gram-positive bacterial infection caused by aerobic actinomycetes in the genus *Nocardia*. *Nocardia* can cause localized or systemic suppurative diseases involving eyes, kidneys, skin, lungs, bone, and central nervous system. Disseminated nocardiosis is a rare condition, seen among immunocompromised patients. We report the case of a 55-year-old African American, kidney transplant male recipient on maintenance immunosuppression, who was diagnosed with cutaneous and pulmonary nocardiosis. Presenting symptoms were shortness of breath, and bilateral lower extremities pain and swelling. Tissue culture grew Gram-positive bacilli specified as *Nocardia farcinica* from thigh and gluteal abscesses. CT thorax showed bilateral reticulonodular opacities. The patient was managed with immunosuppression reduction and specific treatment with high-dose trimethoprim-sulfamethoxazole (TMP-SMX) in conjunction with linezolid. Combination antibiotics were continued for four weeks, and thereafter, TMP-SMX alone was continued for 12 months, at which point all lesions had healed. Nocardiosis with systemic involvement carries a poor prognosis. However, early diagnosis and appropriate antibiotic coverage had a favorable outcome in a renal transplant recipient. Recommended treatment duration is 6 to 12 months.

Gibbons AT, Hanke RE, Berazaluce AMC, Abdulhai S, Glenn IC, McNinch NL, Endo M, Shah S, Yada K, Wolak P, Leys CM, Aranda A, Miyano G, Midulla P, Patkowski D, **Novotny NM** and Ponsky TA (2021). "Recurrence after laparoscopic high ligation in adolescents: A multicenter international retrospective study of ten hospitals." *Journal of Pediatric Surgery* 56(1): 126-129.

[Request Form](#)

*Department of Surgery*

Purpose: Inguinal hernia repairs are among the most common operations performed by pediatric surgeons. Laparoscopic high ligation is a popular technique, but its recurrence rate in adolescents is unknown. We hypothesized that recurrence after laparoscopic high ligation in adolescents would be similar to open repair (1.8%-6.3%). Methods: We evaluated adolescent patients (12-18 years old at the time of surgery) who underwent laparoscopic high ligation across eleven hospitals. At least six months postoperatively, they were contacted by telephone for follow-up. Variables analyzed included demographics, operative details, recurrence, and other complications. Results: A total of 144 patients were enrolled. One hospital (n=9) had a recurrence rate of 44.4%, compared to 3.0% (4/135) for the other hospitals. By accounting for 50.0% of recurrences, it represented a statistical outlier and was excluded, leaving 135 patients for analysis. The median age was 14 years, and 63.7% were male. Recurrence with the excluded center was 5.6% (8/144). Use of absorbable suture (OR 42.67, CI 4.41-412.90, p <0.01) and braided suture (OR 12.10, CI 1.54-95.25, p =0.02) was weakly associated with recurrence. Recurrence was not significantly different from published results. Conclusion: Laparoscopic high ligation of adolescent inguinal hernias has a recurrence rate similar to open repair when performed by experienced surgeons.

Gill I, Antonios B, Imam Z and **Ghaith G** (2021). "Self-Expanding Metal Stent (SEMS) placement to treat bleeding from late radiation esophagitis." Case Reports in Gastrointestinal Medicine 2021: 6678139.

[Full Text](#)

*Department of Internal Medicine*

Radiation esophagitis is a serious complication occurring in patients receiving radiotherapy for head and neck cancers. Current treatment with proton pump inhibitors and mucosal protectants provides symptomatic relief with few studies showing improvement in erosive esophagitis or ulceration. Use of self-expandable metal stents (SEMS) in cases of erosive radiation esophagitis refractory to medical therapy has not been studied. We report a case of a patient presenting with recurrent hematemesis from late (chronic) radiation esophagitis with bleeding esophageal ulceration successfully treated with SEMS placement after failure of conservative medical management, proposing a possible utility for SEMS in this setting.

Gill I, Shaheen AA, Edhi AI, **Amin M, Rana K** and **Cappell MS** (2021). "Novel case report: A previously reported, but pathophysiologically unexplained, association between collagenous colitis and protein-losing enteropathy may be explained by an undetected link with collagenous duodenitis." Digestive Diseases and Sciences. ePub Ahead of Print.

[Full Text](#)

*Department of Pathology*

*Department of Internal Medicine*

Collagenous colitis (CC) is associated with non-bloody, watery diarrhea, which is pathophysiologically reasonable because normal colonic absorption (or excretion) of water and electrolytes can be blocked by the abnormally thick collagen layer in CC. However, CC has also been associated with six previous cases of protein-losing enteropathy (PLE), with no pathophysiologic explanation. The colon does not normally absorb (or excrete) amino acids/proteins, which is primarily the function of the small bowel. Collagenous duodenitis (CD) has not been associated with PLE. This work reports a novel case of CD (and CC) associated with PLE; a pathophysiologically reasonable mechanism for CD causing PLE (by the thick collagen layer of CD blocking normal intestinal amino acid absorption); and a novel association of PLE with severe COVID-19 infection (attributed to relative immunosuppression from hypoproteinemia, hypoalbuminemia, hypogammaglobulinemia, and malnutrition from PLE).

**Gladstone GJ** and Kim JM (2021). "Endoscopic conjunctivodacryocystorhinostomy," In Servat JJ, Black EH, Nesi FA, Gladstone GJ and Calvano CJ (ed). Smith and Nesi's Ophthalmic Plastic and Reconstructive Surgery. Cham: Springer International Publishing. pp: 577-582.

[Full Text](#)

*Department of Ophthalmology*

The evaluation of a patient with excess tears involves investigating causes of excess lacrimation as well as lacrimal outflow obstruction. There are many causes of excess lacrimation, including dry eye syndrome, entropion, trichiasis, and other causes of ocular irritation. Idiopathic hypersecretion, although a diagnosis of exclusion, is an important consideration.

Golan S, Zoumalan CI, **Nesi FA** and Lelli GJ (2021). "Basic principles of ophthalmic plastic surgery," In Servat JJ, Black EH, Nesi FA, Gladstone GJ and Calvano CJ (ed). Smith and Nesi's Ophthalmic Plastic and Reconstructive Surgery. Cham: Springer International Publishing. pp: 65-85.

[Full Text](#)

*Department of Ophthalmology*

Ophthalmic plastic and reconstructive surgery combines the precision of ophthalmic microsurgery with plastic and reconstructive surgical principles, allowing for subspecialized care of the eyelid, orbital, and lacrimal system. A foundation in ophthalmology grants the oculoplastic surgeon the knowledge and skills to safely and successfully protect the globe while achieving functional and aesthetic results. Certain basic ophthalmic and plastic surgical considerations form the necessary framework for the successful practice of oculoplastic surgery.

Golan S, Zoumalan CI, **Nesi FA** and Lelli GJ (2021). "Instrumentation in ophthalmic plastic surgery," In Servat JJ, Black EH, Nesi FA, Gladstone GJ and Calvano CJ (ed). Smith and Nesi's Ophthalmic Plastic and Reconstructive Surgery. Cham: Springer International Publishing. pp: 105-118.

[Full Text](#)

*Department of Ophthalmology*

The use of proper instrumentation in ophthalmic plastic surgery is an essential element to successful surgical outcomes. However, the surgeon must be aware that without proper adherence to the basic surgical principles, surgical outcomes will be suboptimal. The surgeon must have an intimate knowledge of the eyelid, orbital, and facial anatomy. Furthermore, an understanding of the anatomy and the natural tissue planes allows the surgeon to surgically dissect the tissue planes as atraumatically as possible with the aid of appropriate and adequate instrumentation.

Golas VL, Lao KM, Misuraca MS, **Li W**, Marrone MG, **Kanaan HD** and **Zhang PL** (2021). "The clinical features of overlap syndrome (ANCA-associated crescentic glomerulonephritis [AACGN] and immune complex-mediated glomerulonephritis) are similar to those of AACGN alone." *International Urology and Nephrology* 53(3): 515-521.

[Full Text](#)

*Department of Pathology*

The overlap syndromes of anti-neutrophil cytoplasmic antibodies (ANCA)-associated crescentic glomerulonephritis (AACGN) and variants of immune complex mediated glomerulopathy (ICMGN) have been reported. But very few have compared AACGN alone with the overlap syndromes (AACGN plus ICMGN). The aim of this retrospective study was to make that comparison, following serum creatinine (sCr) to determine whether the two groups (AACGN-only group versus overlap group) would behave differently over time. We identified 14 cases with dual diagnoses of AACGN and various ICMGN in the overlap group. Data were collected and compared with 15 randomly selected AACGN-only cases over the similar period of time. The overlap syndrome represented 0.35% of our overall biopsies (14/4049). All 14 patients were ANCA positive and had crescentic formation. The percentage of crescents in the biopsies ranged from 10 to 78%. ICMGN included the following: membranoproliferative glomerulonephritis, post-infectious glomerulonephritis, membranous glomerulopathies, idiopathic mesangial proliferative glomerulonephritis, lupus nephritis, and IgA nephropathy. With the exception one biopsy revealing lupus nephritis class III, most of the ICMGN were mild. When compared to the AACGN-only group, there were no significant differences in clinical and histologic indices including age, percent of crescents, and sCr (on biopsy days, and over the follow-up periods), although the numbers of follow-up cases were limited over time. Our findings suggest that AACGN was the dominant disease process in the majority of overlap syndromes between AACGN and ICMGN, similar to the clinical processes of AACGN-only disease, therefore, the AACGN in overlap syndrome cases should be the main target for clinical management.

Gormley M, **Dabrowski E**, Tilton A, Christian A, Evans SH, Maisonobe P and Wietek S (2021). "Efficacy and safety of abobotulinumtoxinA in pediatric lower limb spasticity (PLLS): 2nd interim results from a phase IV, prospective, observational, multicenter study." *Toxicon* 190: S28-S28.

[Full Text](#)

*Department of Physical Medicine and Rehabilitation*

**Gould DJ** and Hammond M (2021). "Leadership institute for faculty development." *Medical Science Educator* 31:787-793.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

The purpose of the present project is to describe a cohort-based intradepartmental leadership program at our medical school. Leadership development programs are becoming popular in academic medicine as institutions seek solutions to problems. We developed and implemented a cohort-based leadership program within the Department of Foundational Medical Studies at our medical school in order to not only develop our next cadre of leaders but also to spread and disseminate the principles of leadership and enhance the recognition by all departmental members of the various leadership roles each holds.

Goyal VK, **Spillinger A**, Peterson EI and Craig JR (2021). "Odontogenic sinusitis publication trends from 1990 to 2019: A systematic review." *European Archives of Otorhinolaryngology*. ePub Ahead of Print.

[Full Text](#)

*OUWB Medical Student Author*

Purpose: Odontogenic sinusitis (ODS) is underrepresented in the literature compared to other forms of rhinosinusitis, specifically in sinusitis guidelines and position statements. ODS publication characteristics could help explain why ODS has received less attention in sinusitis guidelines and position statements. The purpose of this study was to explore trends in the quantity and quality of ODS studies over 3 decades from 1990 to 2019. Methods: A systematic review was performed to identify all ODS studies from 1990 to 2019. The following variables from all ODS studies were compared between and across the 3 decades: authors' specialties, journal specialties, authors' geographic origins (continents), study topics, study designs, and evidence levels. Results: From 1990 to 2019, there were 254 ODS studies that met inclusion criteria. Numbers of publications increased each decade, with 161 being published from 2010 to 2019. Otolaryngologists and dental authors published over 75% of ODS studies each decade, with 60-75% of ODS articles being published in otolaryngology or dental journals. European and Asian authors published the most ODS studies each decade. Overall, 92-100% of ODS publications per decade were level 4 and 5 evidence, with no significant changes between or across decades. Conclusion: While numbers of ODS publications increased each decade from 1990 to 2019, evidence levels remained low without significant changes over time. Otolaryngologists and dental authors published the majority of ODS studies each decade, with a minority of these studies being multidisciplinary. More ODS studies are needed across all aspects of the condition, and future projects would benefit from improved study designs and multidisciplinary collaboration.

Grace ZT, Magdich AR, Barinsky GL, Chen T, Karim M, Benson B, **Folbe AJ** and Svider PF (2021). "Assessing the academic influence of otolaryngologists on sinus and allergy research." International Forum of Allergy & Rhinology. ePub Ahead of Print.

[Full Text](#)

*Department of Surgery*

Grzywacz V, Quinn TJ, Wilson T, **Reitemeier P**, Navin M, **Hamstra D**, **Anderson J**, **Chinnaiyan P**, **Stevens C** and **Kabolizadeh P** (2021). "Ethical allocation of proton therapy and the insurance review process." Practical Radiation Oncology. ePub Ahead of Print.

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*Department of Foundational Medical Studies (BH)*

*Department of Radiation Oncology*

*Department of Internal Medicine*

Purpose: The purpose of this study was to delineate a scoring system to maximize the ethical allocation of proton beam therapy (PBT) and determine what factors are associated with receipt of PBT, including the role of specific insurance providers. Methods and Materials: Our scoring system was developed in collaboration with a multidisciplinary panel of experts. Patients submitted for PBT consideration were assigned a score by committee at a weekly peer-reviewed session at a time when our center was operating at capacity. Univariate analysis and multivariable analysis of initial and final insurance response were performed. Results: One hundred ninety-seven patients were prospectively reviewed. Ninety-three percent of patients with Medicaid coverage, 88% of patients with Medicare, and 78% of patients with private insurance were ultimately approved for PBT. Median time to final insurance response was 12 days (interquartile range, 9-18 days) for patients who were ultimately denied PBT coverage. Having primary provider C (odds ratio [OR], 14; 95% confidence interval [CI], 1.20-1.96; P = .033) or third party providers A (OR, 4.22; 95% CI, 1.71-10.9; P = .002) or B (OR, 5.28; 95% CI, 1.56-17.2; P = .006) was significantly associated with final insurance denial for PBT on univariate analysis. Total score (OR, 0.79; 95% CI, 0.67-0.90; P = .002) and having coverage through third party provider A (OR, 24.2; 95% CI, 9.51-68.9; P < .001) were associated with final insurance response on multivariable analysis. Conclusions: Our scoring system was significantly associated with receipt of proton beam therapy. Certain insurance providers are less likely to approve PBT for patients, all else being equal. Such a scoring system could be implemented effectively at other PBT facilities, and additional work is needed in ensuring patients with the most to gain from PBT will be approved by their insurance providers.

**Guina J**, Audu AK, Cameron J, Lemmen A, Mamidipaka A and Kletzka N (2021). "Prevalence of traumas and PTSD among individuals adjudicated not guilty by reason of insanity." Journal of the American Academy of Psychiatry and the Law. ePub Ahead of Print.

[Full Text](#)

*Department of Psychiatry*

Trauma and posttraumatic stress disorder (PTSD) are common among psychiatric and criminal populations, yet there have been few studies among forensic psychiatric populations and no known studies have specifically examined insanity acquittees. This study aimed to identify the prevalence of trauma and to assess recognition of PTSD in forensic settings. Using a cross-sectional self-report survey methodology, we examined traumas, adverse childhood experiences (ACEs), and PTSD in insanity acquittees (n = 107). Most insanity acquittees experienced trauma (86%, averaging 11 events) and ACEs (76%, averaging 3 types). The most commonly experienced traumas were sudden death of a loved one, witnessed death or serious injury, adult physical assault, and motor vehicle accident. Women were significantly more likely to experience any ACE (especially witnessing domestic violence, household members with mental illness, emotional abuse, and emotional neglect) and adult sexual assault. PTSD prevalence was 25 percent, with 97 percent of cases being previously undiagnosed. Sexual traumas and younger age were significantly associated with PTSD. These results suggest that insanity acquittees have high levels of trauma, ACEs, and PTSD. While PTSD was about seven times more common than in previous findings in the general population, it frequently goes undiagnosed in forensic settings. Potential explanations and implications of our findings are discussed.

Gupta R, Madanat L, Jindal V and **Gaikazian S** (2021). "Celiac plexus block complications: A case report and review of the literature." *Journal of Palliative Medicine*. ePub Ahead of Print.

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*Department of Internal Medicine*

Celiac plexus block (CPB) has been widely used as a treatment option for chronic intractable abdominal pain resulting from intra-abdominal malignancies as well as benign conditions. Complications resulting from CPB have been long reported and include diarrhea, back pain, paraplegia, postural hypotension, pneumothorax, and local anesthesia toxicity. Diarrhea and postural hypotension are two most common complications with studies reporting incidences occurring in 44% to 60% and 10% to 52% of patients, respectively. Diarrhea is most often transient, resolving within 48 hours; however, literature reports cases in which diarrhea was chronic, debilitating, and in some instances life threatening. Persistent diarrhea proves difficult to treat. We report a case of a 76-year-old male with unresectable pancreatic adenocarcinoma who underwent computed tomography-guided CBP complicated by persistent diarrhea and fecal incontinence. After conventional antidiarrheal failed to improve the symptoms, octreotide proved to be beneficial and the patient reported significant improvement in symptoms.

Guzzardo G and **Gowans LK** (2021). "A 21-year-old with right lower extremity edema." *Clinical Pediatrics* 60(2): 99.

[Full Text](#)

*Department of Pediatrics*

**Halalau A**, Fuller W and Wheeler S (2021). "Canagliflozin reduces the risk of kidney failure in patients with type 2 diabetes mellitus and nephropathy: The CREDENCE randomized trial." *Journal of General Internal Medicine*. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

Halalmeh DR and **Perez-Cruet MJ** (2021). "Use of local morselized bone autograft in minimally invasive transforaminal lumbar interbody fusion: Cost analysis." *World Neurosurgery* 146: E544-E554.

[Full Text](#)

*Department of Neurosurgery*

Objective: Few studies have investigated the financial influence of surgical site local morselized bone autograft (LMBA) on the overall cost of spinal arthrodesis procedures. The purpose of this study is to evaluate the potential savings from introducing LMBA in spinal fusion procedures compared with no LMBA use. Methods: Retrospectively, cost analysis was conducted on a single-center data collected from 266 patients who underwent minimally invasive transforaminal lumbar interbody fusion (MI-TLIF) ranging from L1 through S1 during a period of approximately 4 years. Cost data were obtained from individual patient invoices from the distributor. Sensitivity analyses were also conducted for different costs of allograft and LMBA. Results: A total of 282 levels were grafted in 266 subjects. The total quantity of LMBA harvested was

2433.5 mL, and a total of 1610 mL of allograft (Trinity Elite, ORTHOFIX, Lewisville, Texas, USA) were used. The overall cost savings from introducing LMBA in MI-TLIF surgery were \$1,094,931 over the 4-year period with mean direct cost saving of \$4116.28 per patient based on reduction in allograft. Results for cost savings per patient were sensitive to different direct costs of allograft and LMBA. A >95% fusion rate was achieved based on dynamic radiographs evaluated by an independent radiologist. Conclusions: LMBA is a cost-saving bone graft extender option in MI-TLIF procedures while achieving high fusion rates. The savings are mainly achieved by reducing the amount of allograft needed and subsequent reduction in the total bone graft costs. Further research needs to be performed regarding long-term economic benefit.

Hamera JA, **Bryant NB**, Shievitz MS and **Berger DA** (2021). "Systemic thrombolysis for refractory cardiac arrest due to presumed myocardial infarction." *American Journal of Emergency Medicine* 40: 226.e223-226.e225.

[Full Text](#)

*Department of Emergency Medicine*

The empiric usage of systemic thrombolysis for refractory out of hospital cardiac arrest (OHCA) is considered for pulmonary embolism (PE), but not for undifferentiated cardiac etiology [1, 2]. We report a case of successful resuscitation after protracted OHCA with suspected non-PE cardiac etiology, with favorable neurological outcome after empiric administration of systemic thrombolysis. A 47-year-old male presented to the emergency department (ED) after a witnessed OHCA with no bystander cardiopulmonary resuscitation (CPR). His initial rhythm was ventricular fibrillation (VF) which had degenerated into pulseless electrical activity (PEA) by ED arrival. Fifty-seven minutes into his arrest, we gave systemic thrombolysis which obtained return of spontaneous circulation (ROSC). He was transferred to the coronary care unit (CCU) and underwent therapeutic hypothermia. On hospital day (HD) 4 he began following commands and was extubated on HD 5. Subsequent percutaneous coronary intervention (PCI) revealed non-obstructive stenosis in distal LAD. He was discharged home directly from the hospital, with one-month cerebral performance category (CPC) score of one. He was back to work three months post-arrest. Emergency physicians (EP) should be aware of this topic since we are front-line health care professionals for OHCA. Thrombolytics have the advantage of being widely available in ED and therefore offer an option on a case-by-case basis when intra-arrest PCI and ECPR are not available. This case report adds to the existing literature on systemic thrombolysis as salvage therapy for cardiac arrest from an undifferentiated cardiac etiology. The time is now for this treatment to be reevaluated.

Han E, Killinger KA, Turner KM, **Gilleran J**, Tenney D and **Peters KM** (2021). "Small fiber polyneuropathy in hunner lesion and non-hunner lesion interstitial cystitis/bladder pain syndrome." *Female Pelvic Medicine and Reconstructive Surgery* 27(1): E91-E95.

[Full Text](#)

*Department of Urology*

Objective: This study aimed to determine whether small fiber polyneuropathy (SFPN) diagnosis differs between Hunner lesion interstitial cystitis/bladder pain syndrome (HL IC/BPS) and non-Hunner lesion IC/BPS (NHL IC/BPS). Methods: This was a pilot study of 20 women with IC/BPS. Results from baseline questionnaires, such as Genitourinary Pain Index, Interstitial Cystitis Symptom Index/Interstitial Cystitis Problem Index (ICSI/ICPI), Patient Health Questionnaire-2, were collected. Two punch biopsies were performed on each patient: distal leg and thigh. The samples were evaluated for intraepidermal nerve fiber density. One intraepidermal nerve fiber density less than the fifth percentile, regardless of site, indicated a positive SFPN diagnosis. Results: Twenty patients were enrolled; 10 HL IC/BPS and 10 NHLIC/BPS. The HL IC/BPS group was found to be significantly older than the NHL IC/ BPS group (63 vs 48 years, P = 0.007). No significant differences were found in employment or relationship statuses, or in levels of education or comorbidities between the 2 groups. Sixty percent (6/10) of patients had SFPN in the NHL IC/BPS group compared with 40% (4/10) in the HL IC/BPS group. No significant differences were seen in SFPN positivity (P = 0.3) or Genitourinary Pain Index, Patient Health Questionnaire-2, or Interstitial Cystitis Symptom Index/Interstitial Cystitis Problem Index scores between the NHL and HL IC/BPS groups. Conclusions: Similar to previously published studies, 60% of NHL IC/ BPS patients in this cohort were positive for SFPN compared with only 40% of the HL IC/BPS patients. Larger studies may be needed to realize the full impact of SFPN in IC/BPS.

Hanna A, Gjeorgjievski M, **Amin M** and **Cappell MS** (2021). "Novel case report of hypopharyngeal, extraesophageal cancer first visualized and diagnosed by a gastroenterologist at esophagogastroduodenoscopy with endoscopic biopsies." *ACG Case Reports Journal* 8(3): 1-3.

[Full Text](#)

*Department of Pathology*

*Department of Internal Medicine*

Hanna NH, Robinson AG, Temin S, Baker S, Brahmer JR, Ellis PM, Gaspar LE, Haddad RY, Hesketh PJ, Jain D, **Jaiyesimi I**, Johnson DH, Leighl NB, Moffitt PR, Phillips T, Riely GJ, Rosell R, Schiller JH, Schneider BJ, Singh N, Spigel DR, Tashbar J and Masters G (2021). "Therapy for stage IV non-small-cell lung cancer with driver alterations: ASCO and OH (CCO) joint guideline update." *Journal of Clinical Oncology* 39(9): 1040-1091.

[Full Text](#)

*Department of Internal Medicine*

Purpose: To provide evidence-based recommendations updating the 2017 ASCO guideline on systemic therapy for patients with stage IV non-small-cell lung cancer (NSCLC) with driver alterations. A guideline update for systemic therapy for patients with stage IV NSCLC without driver alterations was published separately. Methods: The American Society of Clinical Oncology and Ontario Health (Cancer Care Ontario) NSCLC Expert Panel updated recommendations based on a systematic review of randomized controlled trials (RCTs) from December 2015 to January 2020 and meeting abstracts from ASCO 2020. Results: This guideline update reflects changes in evidence since the previous update. Twenty-seven RCTs, 26 observational studies, and one meta-analysis provide the evidence base (total 54). Outcomes of interest included efficacy and safety. Additional literature suggested by the Expert Panel is discussed. Recommendations: All patients with nonsquamous NSCLC should have the results of testing for potentially targetable mutations (alterations) before implementing therapy for advanced lung cancer, regardless of smoking status recommendations, when possible, following other existing high-quality testing guidelines. Most patients should receive targeted therapy for these alterations: Targeted therapies against ROS-1 fusions, BRAF V600e mutations, RET fusions, MET exon 14 skipping mutations, and NTRK fusions should be offered to patients, either as initial or second-line therapy when not given in the first-line setting. New or revised recommendations include the following: Osimertinib is the optimal first-line treatment for patients with activating epidermal growth factor receptor mutations (exon 19 deletion, exon 21 L858R, and exon 20 T790M); alectinib or brigatinib is the optimal first-line treatment for patients with anaplastic lymphoma kinase fusions. For the first time, to our knowledge, the guideline includes recommendations regarding RET, MET, and NTRK alterations. Chemotherapy is still an option at most stages.

Harmon DJ, **Attardi SM**, **Barremkala M**, Bentley DC, Brown KM, Dennis JF, Goldman HM, Harrell KM, Klein BA, Ramnanan CJ, Richtsmeier JT and Farkas GJ (2021). "An analysis of anatomy education before and during Covid-19: May-August 2020." *Anatomical Sciences Education* 14(2): 132-147.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Coronavirus disease 2019 (Covid-19) created unparalleled challenges to anatomy education. Gross anatomy education has been particularly impacted given the traditional in-person format of didactic instruction and/or laboratory component(s). To assess the changes in gross anatomy lecture and laboratory instruction, assessment, and teaching resources utilized as a result of Covid-19, a survey was distributed to gross anatomy educators through professional associations and listservs. Of the 67 survey responses received for the May-August 2020 academic period, 84% were from United States (US) institutions, while 16% were internationally based. Respondents indicated that in-person lecture decreased during Covid-19 (before: 76%, during: 8%,  $P < 0.001$ ) and use of cadaver materials declined (before: 76 +/- 33%, during: 34 +/- 43%,  $P < 0.001$ ). The use of cadaver materials in laboratories decreased during Covid-19 across academic programs, stand-alone and integrated anatomy courses, and private and public institutions ( $P \leq 0.004$ ). Before Covid-19, cadaveric materials used in laboratories were greater among professional health programs relative to medical and undergraduate programs ( $P \leq 0.03$ ) and among stand-alone relative to integrated anatomy courses ( $P \leq 0.03$ ). Furthermore, computer-based assessment increased ( $P < 0.001$ ) and assessment materials changed from cadaveric material to images ( $P < 0.03$ ) during Covid-19, even though assessment structure was not different ( $P > 0.05$ ). The use of digital teaching resources increased during Covid-19 ( $P <$

0.001), with reports of increased use of in-house created content, BlueLink, and Complete Anatomy software ( $P < 0.05$ ). While primarily representing US institutions, this study provided evidence of how anatomy educators adapted their courses, largely through virtual mediums, and modified laboratory protocols during the initial emergence of the Covid-19 pandemic.

Harnett NG, van Rooij SJH, Ely TD, Lebois LAM, Murty VP, Jovanovic T, Hill SB, Dumornay NM, Merker JB, Bruce SE, House SL, Beaudoin FL, An X, Zeng D, Neylan TC, Clifford GD, Linnstaedt SD, Germine LT, Bollen KA, Rauch SL, Lewandowski C, Hendry PL, Sheikh S, Storrow AB, Musey PI, Jr., Haran JP, Jones CW, Panches BE, **Swor RA**, McGrath ME, Pascual JL, Seamon MJ, Mohiuddin K, Chang AM, Pearson C, Peak DA, Domeier RM, Rathlev NK, Sanchez LD, Pietrzak RH, Joormann J, Barch DM, Pizzagalli DA, Sheridan JF, Harte SE, Elliott JM, Kessler RC, Koenen KC, McLean S, Ressler KJ and Stevens JS (2021). "Prognostic neuroimaging biomarkers of trauma-related psychopathology: Resting-state fMRI shortly after trauma predicts future PTSD and depression symptoms in the AURORA study." *Neuropsychopharmacology*. ePub Ahead of Print.

[Full Text](#)

*Department of Emergency Medicine*

Neurobiological markers of future susceptibility to posttraumatic stress disorder (PTSD) may facilitate identification of vulnerable individuals in the early aftermath of trauma. Variability in resting-state networks (RSNs), patterns of intrinsic functional connectivity across the brain, has previously been linked to PTSD, and may thus be informative of PTSD susceptibility. The present data are part of an initial analysis from the AURORA study, a longitudinal, multisite study of adverse neuropsychiatric sequelae. Magnetic resonance imaging (MRI) data from 109 recently (i.e., ~2 weeks) traumatized individuals were collected and PTSD and depression symptoms were assessed at 3 months post trauma. We assessed commonly reported RSNs including the default mode network (DMN), central executive network (CEN), and salience network (SN). We also identified a proposed arousal network (AN) composed of a priori brain regions important for PTSD: the amygdala, hippocampus, mamillary bodies, midbrain, and pons. Primary analyses assessed whether variability in functional connectivity at the 2-week imaging timepoint predicted 3-month PTSD symptom severity. Left dorsolateral prefrontal cortex (DLPFC) to AN connectivity at 2 weeks post trauma was negatively related to 3-month PTSD symptoms. Further, right inferior temporal gyrus (ITG) to DMN connectivity was positively related to 3-month PTSD symptoms. Both DLPFC-AN and ITG-DMN connectivity also predicted depression symptoms at 3 months. Our results suggest that, following trauma exposure, acutely assessed variability in RSN connectivity was associated with PTSD symptom severity approximately two and a half months later. However, these patterns may reflect general susceptibility to posttraumatic dysfunction as the imaging patterns were not linked to specific disorder symptoms, at least in the subacute/early chronic phase. The present data suggest that assessment of RSNs in the early aftermath of trauma may be informative of susceptibility to posttraumatic dysfunction, with future work needed to understand neural markers of long-term (e.g., 12 months post trauma) dysfunction. Furthermore, these findings are consistent with neural models suggesting that decreased top-down cortico-limbic regulation and increased network-mediated fear generalization may contribute to ongoing dysfunction in the aftermath of trauma.

Hawkes CP, Roy SM, **Dekelbab B**, Frazier B, Grover M, Haidet J, Listman J, Madsen S, Roan M, Rodd C, Sopher A, Tebben P and Levine MA (2021). "Hypercalcemia in children using the ketogenic diet: A multicenter study." *Journal of Clinical Endocrinology & Metabolism* 106(2): E485-E495.

[Full Text](#)

*Department of Pediatrics*

Context: The ketogenic diet is associated with progressive skeletal demineralization, hypercalciuria, and nephrolithiasis. Acute hypercalcemia has been described as a newly recognized complication of this treatment. Objective: To describe the clinical characteristics of acute hypercalcemia in children on the ketogenic diet through analysis of the presentation, response to treatment, and natural history in a large cohort of patients. Design: A multicenter case series was performed including children who developed acute hypercalcemia while treated with the ketogenic diet. Information on clinical presentation, treatment, and course of this complication was collated centrally. Results: There were 14 patients (median (range) age 6.3 (0.9 to 18) years) who developed hypercalcemia 2.1 (range, 0.2-12) years after starting the ketogenic diet. All had low levels of parathyroid hormone and levels of 1,25-dihydroxyvitamin D were low in all except one.

Seven (50%) had impaired renal function at presentation. All except the 2 oldest had low alkaline phosphatase levels for age. Once normocalcemia was achieved, hypercalcemia recurred in only 2 of these patients over observation of up to 9.8 years. One patient discontinued the ketogenic diet prior to achieving normocalcemia while 4 more stopped the diet during follow-up after resolution of hypercalcemia. Conclusions: Ketotic hypercalcemia can occur years after starting the ketogenic diet, especially in the setting of renal impairment. The mechanism is unknown but appears to be due to reduced osteoblast activity and impaired bone formation. We recommend close attention to optimizing bone health in these children, and screening for the development of ketotic hypercalcemia.

Hiller SC, Qi J, Leavitt D, Frontera JR, **Jafri SM**, Hollingsworth JM, Dauw CA and Ghani KR (2021). "Ureteroscopy in patients taking anticoagulant or antiplatelet therapy: Practice patterns and outcomes in a surgical collaborative." [The Journal of Urology](#) 205(3): 833-840.

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*Department of Urology*

Purpose: AUA guidelines recommend ureteroscopy as first line therapy for patients on anticoagulant or antiplatelet therapy and advocate using a ureteral access sheath. We examined practice patterns and unplanned health care use for these patients in Michigan. Materials and Methods: Using the Michigan Urological Surgery Improvement Collaborative (MUSIC) clinical registry we identified ureteroscopy cases from 2016 to 2019. We assessed outcomes and adherence to guidelines based on therapy at time of ureteroscopy: 1) anticoagulant: continuous warfarin or novel oral agent therapy; 2) antiplatelet: continuous clopidogrel or aspirin therapy; 3) control: not on anticoagulant/antiplatelet therapy. We fit multivariate models to assess anticoagulant or antiplatelet therapy association with emergency department visits, hospitalization and ureteral access sheath use. Results: In total, 9,982 ureteroscopies were performed across 31 practices with 3.1% and 7.8% on anticoagulant and antiplatelet therapy, respectively. There were practice (0% to 21%) and surgeon (0% to 35%) variations in performing ureteroscopy on patients on anticoagulant/antiplatelet therapy regardless of volume. After adjusting for risk factors, anticoagulant or antiplatelet therapy was not associated with emergency department visits. Hospitalization rates in anticoagulant, antiplatelet and control groups were 4.3%, 5.5% and 3.2%, respectively, and significantly increased with antiplatelet therapy (OR 1.48, 95% CI 1.02-2.14). Practice-level ureteral access sheath use varied (23% to 100%) and was not associated with anticoagulant/antiplatelet therapy. Limitations include inability to risk stratify between type/dosage of anticoagulant/antiplatelet therapy. Conclusions: We found practice-level and surgeon-level variation in performing ureteroscopy while on anticoagulant/antiplatelet therapy. Ureteroscopy on anticoagulant is safe. However, antiplatelet therapy increases the risk of hospitalization. Despite guideline recommendations, ureteral access sheath use is not associated with anticoagulant/antiplatelet therapy.

**Hinckel BB**, Thomas D, Vellios EE, Hancock KJ, Calcei JG, Sherman SL, Eliasberg CD, Fernandes TL, Farr J, Lattermann C and Gomoll AH (2021). "Algorithm for treatment of focal cartilage defects of the knee: Classic and new procedures." [Cartilage](#) 1947603521993219.

[Full Text](#)

*Department of Orthopaedic Surgery*

Objective: To create a treatment algorithm for focal grade 3 or 4 cartilage defects of the knee using both classic and novel cartilage restoration techniques. Design: A comprehensive review of the literature was performed highlighting classic as well as novel cartilage restoration techniques supported by clinical and/or basic science research and currently being employed by orthopedic surgeons. Results: There is a high level of evidence to support the treatment of small to medium size lesions (<2-4 cm<sup>2</sup>) without subchondral bone involvement with traditional techniques such as marrow stimulation, osteochondral autograft transplant (OAT), or osteochondral allograft transplant (OCA). Newer techniques such as autologous matrix-induced chondrogenesis and bone marrow aspirate concentrate implantation have also been shown to be effective in select studies. If subchondral bone loss is present OAT or OCA should be performed. For large lesions (>4 cm<sup>2</sup>), OCA or matrix autologous chondrocyte implantation (MACI) may be performed. OCA is preferred over MACI in the setting of subchondral bone involvement while cell-based modalities such as MACI or particulated juvenile allograft cartilage are preferred in the patellofemoral joint. Conclusions: Numerous techniques exist for the orthopedic surgeon treating focal cartilage defects of the knee. Treatment strategies

should be based on lesion size, lesion location, subchondral bone involvement, and the level of evidence supporting each technique in the literature.

**Huynh KA**, Yoon AP, Zhou Y and Chung KC (2021). "Bayesian statistics to estimate diagnostic probability of scaphoid fractures from clinical examinations: A meta-analysis." *Plastic and Reconstructive Surgery*: 424E-435E.

[Full Text](#)

*OUWB Medical Student Author*

Background: Management of suspected scaphoid fractures includes repeated evaluation and casting in symptomatic patients with nondiagnostic radiographs. In this systematic review and meta-analysis, the authors compare the diagnostic accuracy of clinical examinations for scaphoid fractures and create a decision guide using Bayesian statistics. Methods: The MEDLINE, Embase, and Cumulative Index to Nursing and Allied Health Literature databases were queried for studies that evaluated clinical index tests and their diagnostic accuracies for scaphoid fracture. Summary estimates were achieved by a bivariate random effects model and used in Bayes' theorem. The authors varied the scaphoid fracture prevalence for sensitivity analysis. Results: Fourteen articles with 22 index tests and 1940 patients were included. Anatomical snuffbox pain/tenderness (11 studies, 1363 patients), pain with axial loading (eight studies, 995 patients), and scaphoid tubercle tenderness (five studies, 953 patients) had sufficient data for pooled analysis. Anatomical snuffbox pain/tenderness was the most sensitive test (0.93; 95 percent CI, 0.87 to 0.97), and pain with axial loading was the most specific test (0.66; 95 percent CI, 0.41 to 0.85), but all three tests had lower estimated specificities compared with sensitivities. In the base case, the probability of fracture was approximately 60 percent when a patient presented with all three findings after acute wrist injury. Conclusions: The posttest probability of scaphoid fracture was sensitive to both prevalence and diagnostic accuracy of individual clinical index tests. In a population with a fracture prevalence of 20 percent, patients presenting with concurrent anatomical snuffbox pain/tenderness, pain on axial loading, and scaphoid tubercle tenderness may benefit from early advanced imaging to rule out scaphoid fractures if initial radiographs are nondiagnostic.

Hwang D, Kim HJ, Lee SP, Lim S, Koo BK, Kim YJ, Kook W, Andreini D, Al-Mallah MH, Budoff MJ, Cademartiri F, **Chinnaiyan K**, Choi JH, Conte E, Marques H, de Araújo Gonçalves P, Gottlieb I, Hadamitzky M, Leipsic JA, Maffei E, Pontone G, Raff GL, Shin S, Lee BK, Chun EJ, Sung JM, Lee SE, Berman DS, Lin FY, Virmani R, Samady H, Stone PH, Narula J, Bax JJ, Shaw LJ, Min JK and Chang HJ (2021). "Topological data analysis of coronary plaques demonstrates the natural history of coronary atherosclerosis." *JACC: Cardiovascular Imaging*. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

Objectives: This study sought to identify distinct patient groups and their association with outcome based on the patient similarity network using quantitative coronary plaque characteristics from coronary computed tomography angiography (CTA). Background: Coronary CTA can noninvasively assess coronary plaques quantitatively. Methods: Patients who underwent 2 coronary CTAs at a minimum of 24 months' interval were analyzed (n = 1,264). A similarity Mapper network of patients was built by topological data analysis (TDA) based on the whole-heart quantitative coronary plaque analysis on coronary CTA to identify distinct patient groups and their association with outcome. Results: Three distinct patient groups were identified by TDA, and the patient similarity network by TDA showed a closed loop, demonstrating a continuous trend of coronary plaque progression. Group A had the least coronary plaque amount (median 12.4 mm<sup>3</sup> [interquartile range (IQR): 0.0 to 39.6 mm<sup>3</sup>]) in the entire coronary tree. Group B had a moderate coronary plaque amount (31.7 mm<sup>3</sup> [IQR: 0.0 to 127.4 mm<sup>3</sup>]) with relative enrichment of fibrofatty and necrotic core (32.6% [IQR: 16.7% to 46.2%] and 2.7% [IQR: 0.1% to 6.9%] of the total plaque, respectively) components. Group C had the largest coronary plaque amount (187.0 mm<sup>3</sup> [IQR: 96.7 to 306.4 mm<sup>3</sup>]) and was enriched for dense calcium component (46.8% [IQR: 32.0% to 63.7%] of the total plaque). At follow-up, total plaque volume, fibrous, and dense calcium volumes increased in all groups, but the proportion of fibrofatty component decreased in groups B and C, whereas the necrotic core portion decreased in only group B (all p < 0.05). Group B showed a higher acute coronary syndrome incidence than other groups (0.3% vs. 2.6% vs. 0.6%; p = 0.009) but both group B and C had a higher revascularization incidence than group A (3.1% vs. 15.5% vs. 17.8%; p < 0.001). Incorporating group information from TDA demonstrated increase of model fitness for predicting acute coronary syndrome or revascularization compared with that incorporating clinical

risk factors, percentage diameter stenosis, and high-risk plaque features. Conclusions: The TDA of quantitative whole-heart coronary plaque characteristics on coronary CTA identified distinct patient groups with different plaque dynamics and clinical outcomes.

Ichkhanian Y, Barawi M, Seoud T, Thakkar S, Kothari TH, Halabi ME, Ullah A, Edris W, Aepli P, Kowalski T, Shinn B, Shariaha RZ, Mahadev S, Mosko JD, Andrisani G, Di Matteo FM, Albrecht H, Giap AQ, Tang SJ, Naga YM, Van Geenen E, Friedland S, Tharian B, Irani S, Ross AS, **Jamil LH**, Lew D, Nett AS, Farha J, Runge TM, Jovani M and Khashab MA (2021). "Endoscopic full-thickness resection of polyps involving the appendiceal orifice: A multicenter international experience." *Endoscopy*. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

Background: Endoscopic resection of lesions involving the appendiceal orifice remains a challenge. We aimed to report outcomes with the full-thickness resection device (FTRD) for the resection of appendiceal lesions and identify factors associated with the occurrence of appendicitis. Methods: This was a retrospective study at 18 tertiary-care centers (USA 12, Canada 1, Europe 5) between November 2016 and August 2020. Consecutive patients who underwent resection of an appendiceal orifice lesion using the FTRD were included. The primary outcome was the rate of R0 resection in neoplastic lesions, defined as negative lateral and deep margins on post-resection histologic evaluation. Secondary outcomes included the rates of: technical success (en bloc resection), clinical success (technical success without need for further surgical intervention), post-resection appendicitis, and polyp recurrence. Results: 66 patients (32 women; mean age 64) underwent resection of colonic lesions involving the appendiceal orifice (mean [standard deviation] size, 14.5 (6.2) mm), with 40 (61%) being deep, extending into the appendiceal lumen. Technical success was achieved in 59/66 patients (89%), of which, 56 were found to be neoplastic lesions on post-resection pathology. Clinical success was achieved in 53/66 (80%). R0 resection was achieved in 52/56 (93%). Of the 58 patients in whom EFTR was completed who had no prior history of appendectomy, appendicitis was reported in 10 (17%), with six (60%) requiring surgical appendectomy. Follow-up colonoscopy was completed in 41 patients, with evidence of recurrence in five (12%). Conclusions: The FTRD is a promising non-surgical alternative for resecting appendiceal lesions, but appendicitis occurs in 1/6 cases.

Imam Z, Hanna A, **Jomaa D**, Khasawneh M, Abonofal A and Murad MH (2021). "Hypercalcemia of malignancy and acute pancreatitis." *Pancreas* 50(2): 206-213.

[Full Text](#)

*OUWB Medical Student Author*

Objectives: Hypercalcemia of malignancy confers a poor prognosis. This systematic review evaluated published cases of hypercalcemia of malignancy presenting with acute pancreatitis (AP), in terms of clinical presentation and outcomes. Methods: A comprehensive review of PubMed and Embase until March 18, 2020, was conducted. Studies were included if they reported on patients with hypercalcemia of malignancy and AP with attempts to exclude other etiologies of hypercalcemia and AP. Two independent reviewers selected and appraised studies using the Murad tool. Results: Thirty-seven cases were identified. Mean (standard deviation) age was 44.8 (2.46) years. Mean (standard deviation) presenting corrected calcium was 14.5 (0.46) mg/dL. Parathyroid carcinoma (21.6%) and multiple myeloma (21.6%) were the most common malignancies. Cases were classified as severe (37.8%), mild (21.6%), and moderately severe (18.9%), whereas 21.6% did not report severity. Necrotizing pancreatitis developed in 21.6% of cases. Most cases were treated with intravenous hydration and bisphosphonates or calcitonin/calcitonin analogues. Mortality was 32.4% during the same presentation of AP. Among mortality cases, 10 of 12 had severe AP, and 5 of 12 had necrotizing pancreatitis. Degree of hypercalcemia did not influence mortality. Conclusion: Acute pancreatitis associated with hypercalcemia of malignancy is rare. One in 3 patients with this presentation may not survive AP.

Ionescu F, **Jaiyesimi I**, Petrescu I, Lawler PR, **Castillo E**, Munoz-Maldonado Y, Imam Z, Narasimhan M, **Abbas AE**, Konde A and **Nair GB** (2021). "Association of anticoagulation dose and survival in hospitalized COVID-19 patients: A retrospective propensity score-weighted analysis." *European Journal of Haematology* 106(2): 165-174.

[Full Text](#)

*Department of Internal Medicine*

*Department of Radiation Oncology*

Background: Hypercoagulability may contribute to COVID-19 pathogenicity. The role of anticoagulation (AC) at therapeutic (tAC) or prophylactic doses (pAC) is unclear. Objectives: We evaluated the impact on survival of different AC doses in COVID-19 patients. Methods: Retrospective, multi-center cohort study of consecutive COVID-19 patients hospitalized between March 13 and May 5, 2020. Results: A total of 3480 patients were included (mean age, 64.5 years [17.0]; 51.5% female; 52.1% black and 40.6% white). 18.5% (n = 642) required intensive care unit (ICU) stay. 60.9% received pAC (n = 2121), 28.7% received  $\geq 3$  days of tAC (n = 998), and 10.4% (n = 361) received no AC. Propensity score (PS) weighted Kaplan-Meier plot demonstrated different 25-day survival probability in the tAC and pAC groups (57.5% vs 50.7%). In a PS-weighted multivariate proportional hazards model, AC was associated with reduced risk of death at prophylactic (hazard ratio [HR] 0.35 [95% confidence interval {CI} 0.22-0.54]) and therapeutic doses (HR 0.14 [95% CI 0.05-0.23]) compared to no AC. Major bleeding occurred more frequently in tAC patients (81 [8.1%]) compared to no AC (20 [5.5%]) or pAC (46 [2.2%]) subjects. Conclusions: Higher doses of AC were associated with lower mortality in hospitalized COVID-19 patients. Prospective evaluation of efficacy and risk of AC in COVID-19 is warranted.

Jae SY, Heffernan K, Kurl S, Kunutsor SK, **Franklin BA**, Savonen K and Laukkanen JA (2021). "Chronotropic response to exercise testing and the risk of stroke." *American Journal of Cardiology* 143: 46-50.

[Full Text](#)

*Department of Internal Medicine*

Although the chronotropic response to exercise testing, defined as an inadequate heart rate response to incremental exercise to volitional fatigue, is associated with adverse cardiovascular outcomes, it remains unclear whether this response is related to the future risk of cerebrovascular events. We tested the hypothesis that the chronotropic response to exercise is associated with an increased risk of stroke in a general population. This prospective study was based on a population sample of 2,036 men aged 42 to 60 years in the Kuopio Ischemic Heart Disease cohort study. Chronotropic response to exercise was defined as the percentage of chronotropic index ( $[(\text{maximum heart rate} - \text{resting heart rate}) / (220 - \text{age} - \text{resting heart rate})] \times 100$ ). Incident strokes were obtained from the Finnish national hospital discharge registry. During a median 27-year follow-up, 343 incident stroke (289 ischemic and 66 hemorrhagic) events occurred. Twelve events were diagnosed as both ischemic and hemorrhagic stroke. Comparing the bottom versus top quintile of chronotropic reserve, there was an increased risk of stroke (hazard ratio [HR] 1.73, 95% confidence Interval [CI]: 1.09 to 2.75) and ischemic stroke (HR 1.72, 95% CI, 1.04 to 2.85), but not hemorrhagic stroke (HR 2.23, 95% CI, 0.77 to 6.46) in analyses that adjusted for potential risk factors. These results suggest that an impaired chronotropic response to exercise is independently associated with a higher risk of total and ischemic stroke events in middle-aged men. The role of chronotropic incompetence during exercise testing as a potential prognostic indicator for stroke risk needs further investigation.

**James E** and **Salahou A** (2021). "Medical students and issues of social change: Gender inclusion in student organizations." *Medical Science Educator* 31(2): 315-316.

[Full Text](#)

*OUIB Medical Student Author*

In order to promote the mentality of inclusion and highlight the importance of inclusion more broadly in medicine, we provided summaries of primary research data to first- and second-year medical students in response to the lack of gender variation amongst the leadership boards of our student organizations.

**James E**, **Salahou A** and **Seawright K** (2021). "An innovative way to welcome medical students during this unprecedented time." *Academic Medicine* 96(1): 17.

[Full Text](#)

*OUIB Medical Student Author*

Jin HY, Weir-McCall JR, Leipsic JA, Son JW, Sellers SL, Shao M, Blanke P, Ahmadi A, Hadamitzky M, Kim YJ, Conte E, Andreini D, Pontone G, Budoff MJ, Gottlieb I, Lee BK, Chun EJ, Cademartiri F, Maffei E, Marques H, de Araujo Goncalves P, Shin S, Choi JH, Virmani R, Samady H, Stone PH, Berman DS, Narula J, Shaw LJ, Bax JJ, **Chinnaiyan K**, **Raff G**, Al-Mallah MH, Lin FY, Min JK, Sung JM, Lee SE and Chang HJ (2021). "The relationship between coronary

calcification and the natural history of coronary artery disease." *JACC: Cardiovascular Imaging* 14(1): 233-242.

[Full Text](#)

*Department of Internal Medicine*

**Objectives:** The aim of the current study was to explore the impact of plaque calcification in terms of absolute calcified plaque volume (CPV) and in the context of its percentage of the total plaque volume at a lesion and patient level on the progression of coronary artery disease. **Background:** Coronary artery calcification is an established marker of risk of future cardiovascular events. Despite this, plaque calcification is also considered a marker of plaque stability, and it increases in response to medical therapy. **Methods:** This analysis included 925 patients with 2,568 lesions from the PARADIGM (Progression of Atherosclerotic Plaque Determined by Computed Tomographic Angiography Imaging) registry, in which patients underwent clinically indicated serial coronary computed tomography angiography. Plaque calcification was examined by using CPV and percent CPV (PCPV), calculated as  $(\text{CPV}/\text{plaque volume}) \times 100$  at a per-plaque and per-patient level (summation of all individual plaques). **Results:** CPV was strongly correlated with plaque volume ( $r = 0.780$ ;  $p < 0.001$ ) at baseline and with plaque progression ( $r = 0.297$ ;  $p < 0.001$ ); however, this association was reversed after accounting for plaque volume at baseline ( $r = -0.146$ ;  $p < 0.001$ ). In contrast, PCPV was an independent predictor of a reduction in plaque volume ( $r = -0.11$ ;  $p < 0.001$ ) in univariable and multivariable linear regression analyses. Patient-level analysis showed that high CPV was associated with incident major adverse cardiac events (hazard ratio: 3.01; 95% confidence interval: 1.58 to 5.72), whereas high PCPV was inversely associated with major adverse cardiac events (hazard ratio: 0.529; 95% confidence interval: 0.229 to 0.968) in multivariable analysis. **Conclusions:** Calcified plaque is a marker for risk of adverse events and disease progression due to its strong association with the total plaque burden. When considered as a percentage of the total plaque volume, increasing PCPV is a marker of plaque stability and reduced risk at both a lesion and patient level.

Jue TL, Storm AC, Naveed M, Fishman DS, Qumseya BJ, McRee AJ, Truty MJ, Khashab MA, Agrawal D, Al-Haddad M, Amateau SK, Buxbaum JL, Calderwood AH, DeWitt J, DiMaio CJ, Fujii-Lau LL, Gurudu SR, **Jamil LH**, Kwon RS, Law JK, Lee JK, Pawa S, Sawhney MS, Thosani NC, Yang J and Wani SB (2021). "ASGE guideline on the role of endoscopy in the management of benign and malignant gastroduodenal obstruction." *Gastrointestinal Endoscopy* 93(2): 309-+.

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*Department of Internal Medicine*

This American Society for Gastrointestinal Endoscopy guideline provides evidence-based recommendations for the endoscopic management of gastric outlet obstruction (GOO). We applied the Grading of Recommendations, Assessment, Development and Evaluation methodology to address key clinical questions. These include the comparison of (1) surgical gastrojejunostomy to the placement of self-expandable metallic stents (SEMS) for malignant GOO, (2) covered versus uncovered SEMS for malignant GOO, and (3) endoscopic and surgical interventions for the management of benign GOO. Recommendations provided in this document were founded on the certainty of the evidence, balance of benefits and harms, considerations of patient and caregiver preferences, resource utilization, and cost-effectiveness.

Kadri AN, Bernardo M, Assar SZ, Werns S and **Abbas AE** (2021). "Surgical versus transcatheter aortic valve replacement in patients with malignancy." *Cardiovascular Revascularization in Medicine* 23: 59-65.

[Full Text](#)

*Department of Internal Medicine*

**Background:** Patients with aortic stenosis (AS) and malignancy experience poor clinical outcomes with challenging decisions regarding aortic valve replacement (AVR). We sought to compare the outcomes of transcatheter (TAVR) versus surgical (SAVR) AVR in patients with AS and malignancy. **Methods:** Based on the Nationwide Readmission Database, we compared all patients with malignancy who underwent isolated SAVR vs. TAVR in 2016 for severe AS. We performed univariate and multivariate analyses for baseline characteristics and clinical outcomes. A total of 2566 patients were included, 1952 (76%) had TAVR and the remaining 614 (24%) had isolated SAVR. Patients who underwent TAVR were older (82 vs 72 years,  $p < .001$ ), had more metastasis (19 vs 14%,  $p = .004$ ), heart failure (72% vs 34%,  $p < .001$ ), coronary artery disease (72% vs 52%,  $p < .001$ ), anemia (28% vs 22%,  $p = .006$ ), chronic lung (30% vs 22%,  $p < .001$ ) and renal disease (35% vs 14%,  $p < .001$ ), and shorter length of stay (3 vs 7 days,  $p < .001$ ). **Results:** In multivariate regression, TAVR and SAVR had similar in-patient mortality (HR = 1.08; 95%CI 0.61 \_ 1.94) and 30-day readmission

(HR = 1.26; 95%CI 0.95\_ 1.67). TAVR was associated with lower vascular complications (HR = 0.59; 95%CI 0.41\_ 0.86), acute deep venous thrombosis (HR = 0.25, 95%CI 0.1\_ 0.59), acute kidney injury (HR = 0.24, 95%CI 0.17\_ 0.33), blood transfusion (HR = 0.22, 95%CI 0.16\_ 0.3), cardiogenic shock (HR = 0.48, 95%CI 0.26\_ 0.89), and respiratory complications (HR = 0.26, 95%CI 0.2\_ 0.35). Conclusions: In patients with malignancy, TAVR is a viable and safe option compared to SAVR with better clinical outcomes, especially thromboembolic events.

Kadri AN, Zawit M, Al-Adham R, **Hader I**, Nusairat L, Almahmoud MF, Senussi M, Altibi A, Barakat A, Hernandez AV and Masri A (2021). "Prevalence of venous thromboembolism in admissions and readmissions with and without syncope: A nationwide cohort study." *European Heart Journal Quality Care & Clinical Outcomes* 7(1): 52-58.

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*Department of Internal Medicine*

Aims: The Pulmonary Embolism in Syncope Italian Trial reported 17.3% prevalence of pulmonary embolism (PE) in patients admitted with syncope. We investigated the prevalence of venous thromboembolism [VTE, including PE and deep vein thrombosis (DVT)] in syncope vs. non-syncope admissions and readmissions, and if syncope is an independent predictor of VTE. Methods and Results: We conducted an observational study of index admissions of the 2013-14 Nationwide Readmission Database. We excluded patients <18 years, December discharges, died during hospitalization, hospital transfers, and missing length of stay. Encounters were stratified by the presence or absence of DVT/PE and syncope diagnoses. Multivariable logistic regression analysis was used to evaluate the association between syncope and VTE. There were 38 655 570 admissions, of whom 285 511 had syncope. In the overall cohort, syncope occurred in 1.6% of VTE and 1.8% in non-VTE admissions. In a multivariable model, syncope was associated with a lower prevalence of VTE [odds ratio (OR) 0.76, 95% confidence interval (CI) 0.75-0.78; P < 0.001]. In index syncope vs. non-syncope admissions, the prevalence of DVT, PE, and VTE were 0.4 ± 0.06% vs. 1.3 ± 0.12%, 0.2 ± 0.04% vs. 1.2 ± 0.11%, and 0.5 ± 0.07% vs. 2.1 ± 0.14% (all P < 0.001), respectively. At 30 days, the prevalence of DVT, PE, and VTE in syncope vs. non-syncope were 2.2 ± 0.14% vs. 2.1 ± 0.14% (P = 0.38), 1.4 ± 0.12% vs. 1.2 ± 0.11% (P = 0.01), and 2.6 ± 0.17% vs. 3.0 ± 0.17% (P = 0.99), respectively. Conclusion: Syncope admissions were associated with a lower prevalence of VTE as compared to non-syncope admissions. Syncope should not trigger an automatic PE workup, rather, should be put into context of patient presentation.

Kelsch RD, **Nolan DA** and **Krishnan A** (2021). "Unusual case of biotin-thiamine responsive encephalopathy without basal ganglia involvement." *Pediatric Radiology* 51(3): 485-488.

[Full Text](#)

*Department of Pediatrics*

*Department of Diagnostic Radiology and Molecular Imaging*

Khan JM, Babaliaros VC, Greenbaum AB, Spies C, Daniels D, Depta JP, Oldemeyer JB, Whisenant B, McCabe JM, Muhammad KI, George I, Mahoney P, Lanz J, Laham RJ, Shah PB, Chhatrwalla A, Yazdani S, **Hanzel G**, Pershad A, Leonardi RA, Khalil R, Tang GHL, Herrmann HC, Agarwal S, Fail PS, Zhang M, Pop A, Lisko J, Perdoncin E, Koch RL, Ben-Dor I, Satler LF, Zhang C, Cohen JE, Lederman RJ, Waksman R and Rogers T (2021). "Preventing coronary obstruction during transcatheter aortic valve replacement results from the multicenter international BASILICA Registry." *JACC - Cardiovascular Interventions* 14(9): 941-948.

[Request Form](#)

*Department of Internal Medicine*

Objectives: This study sought to determine the safety of the BASILICA (bioprosthetic or native aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction) procedure. Background: Transcatheter aortic valve replacement causes coronary artery obstruction in 0.7% of cases, with 40% to 50% mortality. BASILICA is a procedure to prevent coronary obstruction. Safety and feasibility in a large patient cohort is lacking. Methods: The international BASILICA registry was a retrospective, multicenter, real-world registry of patients at risk of coronary artery obstruction undergoing BASILICA and transcatheter aortic valve replacement. Valve Academic Research Consortium-2 definitions were used to adjudicate events. Results: Between June 2017 and December 2020, 214 patients were included from 25 centers in North America and Europe; 72.8% had bioprosthetic aortic valves and 78.5% underwent solo BASILICA. Leaflet traversal was successful in 94.9% and leaflet laceration in 94.4%. Partial or complete coronary artery obstruction was seen

in 4.7%. Procedure success, defined as successful BASILICA traversal and laceration without mortality, coronary obstruction, or emergency intervention, was achieved in 86.9%. Thirty-day mortality was 2.8% and stroke was 2.8%, with 0.5% disabling stroke. Thirty-day death and disabling stroke were seen in 3.4%. Valve Academic Research Consortium-2 composite safety was achieved in 82.8%. One-year survival was 83.9%. Outcomes were similar between solo and doppio BASILICA, between native and bioprosthetic valves, and with the use of cerebral embolic protection. Conclusions: BASILICA is safe, with low reported rates of stroke and death. BASILICA is feasible in the real-world setting, with a high procedure success rate and low rates of coronary artery obstruction.

Khanna AK, Saager L, Bergese SD, Jungquist CR, Morimatsu H, Uezono S, Ti LK, **Soto R**, Jiang W and Buhre W (2021). "Opioid-induced respiratory depression increases hospital costs and length of stay in patients recovering on the general care floor." *BMC Anesthesiology* 21(1): 88.

[Full Text](#)

*Department of Anesthesiology*

Background: Opioid-induced respiratory depression is common on the general care floor. However, the clinical and economic burden of respiratory depression is not well-described. The PRediction of Opioid-induced respiratory Depression In patients monitored by capnoGraphY (PRODIGY) trial created a prediction tool to identify patients at risk of respiratory depression. The purpose of this retrospective sub-analysis was to examine healthcare utilization and hospital cost associated with respiratory depression. Methods: One thousand three hundred thirty-five patients (N = 769 United States patients) enrolled in the PRODIGY trial received parenteral opioids and underwent continuous capnography and pulse oximetry monitoring. Cost data was retrospectively collected for 420 United States patients. Differences in healthcare utilization and costs between patients with and without  $\geq 1$  respiratory depression episode were determined. The impact of respiratory depression on hospital cost per patient was evaluated using a propensity weighted generalized linear model. Results: Patients with  $\geq 1$  respiratory depression episode had a longer length of stay ( $6.4 \pm 7.8$  days vs  $5.0 \pm 4.3$  days,  $p = 0.009$ ) and higher hospital cost ( $\$21,892 \pm \$11,540$  vs  $\$18,206 \pm \$10,864$ ,  $p = 0.002$ ) compared to patients without respiratory depression. Patients at high risk for respiratory depression, determined using the PRODIGY risk prediction tool, who had  $\geq 1$  respiratory depression episode had higher hospital costs compared to high risk patients without respiratory depression ( $\$21,948 \pm \$9128$  vs  $\$18,474 \pm \$9767$ ,  $p = 0.0495$ ). Propensity weighted analysis identified 17% higher costs for patients with  $\geq 1$  respiratory depression episode ( $p = 0.007$ ). Length of stay significantly increased total cost, with cost increasing exponentially for patients with  $\geq 1$  respiratory depression episode as length of stay increased. Conclusions: Respiratory depression on the general care floor is associated with a significantly longer length of stay and increased hospital costs. Early identification of patients at risk for respiratory depression, along with early proactive intervention, may reduce the incidence of respiratory depression and its associated clinical and economic burden.

Khatri IA, Aljwair S, Alammam H, Altariq A, Masud N, Al Malik Y and **Kojan S** (2021). "Social anxiety and obsessive-compulsive disorder are common among persons with multiple sclerosis at King Abdulaziz Medical City, Riyadh." *Cureus* 13(2): e13619.

[Full Text](#)

*Department of Neurology*

Background: Multiple sclerosis (MS) is associated with a physical disability and disturbed psychosocial functioning in young people. Many psychological and psychiatric comorbidities have been reported in MS. Objective To determine the frequency of social anxiety disorder (SAD) and obsessive-compulsive disorder (OCD) among MS patients and their relation to MS severity. Methods: A cross-sectional survey was conducted in an adult MS cohort. Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and Social Phobia Inventory (SPIN) were used to determine the presence and severity of OCD and SAD. The Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corp., Armonk, NY) was used for statistical analysis. The Mann-Whitney U test and logistic regression were used to assess the association of the two diseases with the severity of MS. Results: A total of 145 persons with MS (pwMS) were studied. The mean age was 33.5 (+/- 8.5) years; the mean duration of MS was 7.2 (+/- 5.1) years. The majority (74.1%) were women; 57.3% were married; 63% had a college education; 50% belonged to the higher middle-class socioeconomic strata. Relapsing-remitting multiple sclerosis was the most common type of MS (92.2%). The mean Expanded

Disability Status Scale (EDSS) score was 2.24 (+/- 2.19). SAD was reported by 26.9%, and OCD was reported by 31% of the cohort. PwMS with walking difficulty but not wheelchair-bound had a statistically significant increased risk of SAD ( $p = 0.036$ ). There was no direct association between MS-related disability and OCD. However, pwMS with SAD were more likely to have concomitant OCD ( $t=4.68$ ,  $p$ -value  $<0.001$ , 95% CI: 0.47-1.16). Increasing disability was associated with higher chances of developing social anxiety and, in turn, OCD ( $t=3.39$ ,  $p$ -value  $<0.001$ , 95% CI: 0.66-2.52). Conclusions: Social anxiety and obsessive-compulsive disorders were present in nearly one-third of pwMS. Impaired walking but not wheelchair dependence was associated with social anxiety. PwMS with SAD were more likely to have obsessive-compulsive disorder.

**Khatter NJ**, Mark JA, Forlenza G and Triolo TM (2021). "Retrospective analysis of total pancreatectomy with islet auto transplantation outcomes in pediatric patients with chronic pancreatitis." *Journal of Investigative Medicine* 69(1): 147-147.

[Request Form](#)

*OUWB Medical Student Author*

Killinger KA, **Henrichsen JL**, Han E, **Dai YL**, Nguyen L, **Gilleran J**, Odabachian L, Boura JA, **Peters KM** and **Sirls LT** (2021). "Symptom and quality of life improvements after pelvic floor physical therapy in a clinical population of women with pelvic pain and other symptoms." *Female Pelvic Medicine and Reconstructive Surgery* 27(1): e18-e21.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Urology*

Objectives: This study aimed to evaluate changes in validated symptom scores at intake and discharge in women undergoing pelvic floor physical therapy (PFPT) for pain and other pelvic floor symptoms. Methods: Consecutive women starting PFPT during 1 year were reviewed. History, demographics, and Pelvic Floor Distress Inventory Questionnaire - Short Form 20 (PFDI) total and domain scores (Pelvic Organ Prolapse Distress Inventory-6, Urogenital Distress Inventory-6, Colorectal-Anal Distress Inventory-8), Pelvic Floor Impact Questionnaire (PFIQ-7), and pain levels on a numeric rating scale (NRS) were collected at intake and discharge. Data were analyzed with descriptive statistics and sign tests. Results: Of 474 women, mean age was  $50.3 \pm 16.7$  years (range, 18-87 years) and the most common indication for PFPT was pelvic pain (208/474; 43.9%). In women with complete data, pretreatment to posttreatment median scores improved on the PFDI (77.3 vs 41.8;  $P < 0.0001$ ), Urogenital Distress Inventory (37.5 vs 16.0;  $P < 0.0001$ ), and PFIQ (58.0 vs 19.0;  $P < 0.0001$ ), and the minimal clinically important difference was met for the PFDI, PFIQ, and Colorectal-Anal Distress Inventory. Women with primarily pelvic pain ( $n = 208$ ) achieved significant improvements in PFDI, PFIQ, and NRS scores ( $P < 0.0001$  for all) as well as the minimal clinically important difference for these measures. Pain patients with a history of pelvic surgery ( $n = 50$ ) also had significant improvements in PFIQ and NRS but not PFDI scores. Conclusions: Most women referred to PFPT demonstrated symptom improvements as measured by validated instruments.

Kim SJ, Sonmez K, Swan R, Campbell JP, Ostmo S, Chan RVP, Nagiel A, **Drenser KA**, Berrocal AM, Horowitz JD, Li X, Chen YDI, Taylor KD, Simmons C, Rotter JI and Chiang MF (2021). "Identification of candidate genes and pathways in retinopathy of prematurity by whole exome sequencing of preterm infants enriched in phenotypic extremes." *Scientific Reports* 11(1): 4966.

[Full Text](#)

*Department of Ophthalmology*

Retinopathy of prematurity (ROP) is a vasoproliferative retinal disease affecting premature infants. In addition to prematurity itself and oxygen treatment, genetic factors have been suggested to predispose to ROP. We aimed to identify potentially pathogenic genes and biological pathways associated with ROP by analyzing variants from whole exome sequencing (WES) data of premature infants. As part of a multicenter ROP cohort study, 100 non-Hispanic Caucasian preterm infants enriched in phenotypic extremes were subjected to WES. Gene-based testing was done on coding nonsynonymous variants. Genes showing enrichment of qualifying variants in severe ROP compared to mild or no ROP from gene-based tests with adjustment for gestational age and birth weight were selected for gene set enrichment analysis (GSEA). Mean BW of included infants with pre-plus, type-1 or type 2 ROP including aggressive posterior ROP ( $n = 58$ ) and mild or no ROP ( $n = 42$ ) were 744 g and 995 g, respectively. No single genes reached genome-wide

significance that could account for a severe phenotype. GSEA identified two significantly associated pathways (smooth endoplasmic reticulum and vitamin C metabolism) after correction for multiple tests. WES of premature infants revealed potential pathways that may be important in the pathogenesis of ROP and in further genetic studies.

Klein M, Bacher J, Barth S, Atzadeh F, Siebenhaller K, Ferreira I, Beisken S, Posch AE, Carroll KC, Wunderink RG, Qi C, Wu F, Hardy DJ, Patel R and **Sims MD** (2021). "Multicenter evaluation of the unyvero platform for testing bronchoalveolar lavage fluid." *Journal of Clinical Microbiology* 59(3): JCM.02497-20.

[Full Text](#)

*Department of Internal Medicine*

Bronchoalveolar lavage (BAL) culture is a standard, though time-consuming, approach for identifying microorganisms in patients with severe lower respiratory tract (LRT) infections. The sensitivity of BAL culture is relatively low, and prior antimicrobial therapy decreases the sensitivity further, leading to overuse of empirical antibiotics. The Unyvero LRT BAL Application (Curetis GmbH, Germany) is a multiplex molecular panel that detects 19 bacteria, 10 antibiotic resistance markers, and a fungus, *Pneumocystis jirovecii*, in BAL fluid in 4.5h. Its performance was evaluated using 1,016 prospectively collected and 392 archived specimens from 11 clinical trial sites in the United States. Overall positive and negative percent agreements with culture results for identification of bacteria that grow in routine cultures were 93.4% and 98.3%, respectively, with additional potential pathogens identified by Unyvero in 21.7% of prospectively collected specimens. For detection of *P. jirovecii*, the positive percent agreement with standard testing was 87.5%. Antibiotic resistance marker results were compared to standard antibiotic susceptibility test results to determine positive predictive values (PPVs). PPVs ranged from 80 to 100%, based on the microorganism and specific resistance marker(s). The Unyvero LRT BAL Application provides accurate detection of common agents of bacterial pneumonia and of *P. jirovecii*. The sensitivity and rapidity of this panel suggest significant clinical value for choosing appropriate antibiotics and for antibiotic stewardship.

Kline JA, Camargo CA, Courtney DM, Kabrhel C, Nordenholz KE, Aufderheide T, Baugh JJ, Beiser DG, Bennett CL, Bledsoe J, Castillo E, Chisolm-Straker M, Goldberg EM, House H, House S, Jang T, Lim SC, Madsen TE, McCarthy DM, Meltzer A, Moore S, Newgard C, Pagenhardt J, Pettit KL, Pulia MS, Puskarich MA, Southerland LT, Sparks S, **Turner-Lawrence D**, Vrablik M, Wang A, Weekes AJ, Westafer L and Wilburn J (2021). "Clinical prediction rule for SARS-CoV-2 infection from 116 US emergency departments 2-22-2021." *PLoS One* 16(3): e0248438.

[Full Text](#)

*Department of Emergency Medicine*

**Objectives:** Accurate and reliable criteria to rapidly estimate the probability of infection with the novel coronavirus-2 that causes the severe acute respiratory syndrome (SARS-CoV-2) and associated disease (COVID-19) remain an urgent unmet need, especially in emergency care. The objective was to derive and validate a clinical prediction score for SARS-CoV-2 infection that uses simple criteria widely available at the point of care. **Methods:** Data came from the registry data from the national REgistry of suspected COVID-19 in EmeRgency care (RECOVER network) comprising 116 hospitals from 25 states in the US. Clinical variables and 30-day outcomes were abstracted from medical records of 19,850 emergency department (ED) patients tested for SARS-CoV-2. The criterion standard for diagnosis of SARS-CoV-2 required a positive molecular test from a swabbed sample or positive antibody testing within 30 days. The prediction score was derived from a 50% random sample (n = 9,925) using unadjusted analysis of 107 candidate variables as a screening step, followed by stepwise forward logistic regression on 72 variables. **Results:** Multivariable regression yielded a 13-variable score, which was simplified to a 13-point score: +1 point each for age >50 years, measured temperature >37.5 degrees C, oxygen saturation <95%, Black race, Hispanic or Latino ethnicity, household contact with known or suspected COVID-19, patient reported history of dry cough, anosmia/dysgeusia, myalgias or fever; and -1 point each for White race, no direct contact with infected person, or smoking. In the validation sample (n = 9,975), the probability from logistic regression score produced an area under the receiver operating characteristic curve of 0.80 (95% CI: 0.79-0.81), and this level of accuracy was retained across patients enrolled from the early spring to summer of 2020. In the simplified score, a score of zero produced a sensitivity of 95.6% (94.8-96.3%), specificity of 20.0% (19.0-21.0%), negative likelihood ratio of 0.22 (0.19-0.26). Increasing points on the simplified score predicted higher probability of infection (e.g., >75% probability with +5 or more points). **Conclusion:** Criteria that are available at the point

of care can accurately predict the probability of SARS-CoV-2 infection. These criteria could assist with decisions about isolation and testing at high throughput checkpoints.

Knill C, Sandhu R, Halford R, **Snyder M** and **Seymour Z** (2021). "Commissioning cranial single-isocenter multi-target radiosurgery for the Versa HD." *Journal of Applied Clinical Medical Physics* 22(4): 108-114.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: Brainlab's Elements Multiple Brain Mets SRS (MBMS) is a dedicated treatment planning system for single-isocenter multi-target (SIMT) cranial stereotactic radiosurgery (SRS) treatments. The purpose of this study is to present the commissioning experience of MBMS on an Elekta Versa HD. Methods: MBMS was commissioned for 6 X, 6 FFF, and 10 FFF. Beam data collected included: output factors, percent depth doses (PDDs), diagonal profiles, collimator transmission, and penumbra. Beam data were processed by Brainlab and resulting parameters were entered into the planning system to generate the beam model. Beam model accuracy was verified for simple fields. MBMS plans were created on previously treated cranial SRS patient data sets. Plans were evaluated using Paddick inverse conformity (ICI), gradient indices (GI), and cumulative volume of brain receiving 12 Gy. Dosimetric accuracy of the MBMS plans was verified using microDiamond, Gafchromic film, and SRS Mapcheck measurements of absolute dose and dose profiles for individual targets. Finally, an end-to-end (E2E) test was performed with a MR-CT compatible phantom to validate the accuracy of the simulation-to-delivery process. Results: For square fields, calculated scatter factors were within 1.0% of measured, PDDs were within 0.5% past dmax, and diagonal profiles were within 0.5% for clinically relevant off-axis distances (<10 cm). MBMS produced plans with ICIs < 1.5 and GIs < 5.0 for targets > 10 mm. Average point doses of the MBMS plans, measured by microDiamond, were within 0.31% of calculated (max 2.84%). Average per-field planar pass rates were 98.0% (95.5% minimum) using a 2%/1 mm/10% threshold relative gamma analysis. E2E point dose measurements were within 1.5% of calculated and Gafchromic film pass rates were 99.6% using a 5%/1 mm/10% threshold gamma analysis. Conclusion: The experience presented can be used to aid the commissioning of the Versa HD in the Brainlab MBMS treatment planning system, to produce safe and accurate SIMT cranial SRS treatments.

Korman A, **Ramanathan S**, Korman J, Ramanathan S, Balaraman S, Luke N, Dewar R, Wojno K, **Sirls L** and **Korman H** (2021). "Innovative workflow to collect home urine samples from symptomatic patients sheltered in place during COVID-19." *Neurourology and Urodynamics* 40: S46-S47.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Urology*

Kryklywy JH, **Roach VA** and Todd RM (2021). "Assessing the efficacy of tablet-based simulations for learning pseudo-surgical instrumentation." *PLoS One* 16(1): e0245330.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Nurses and surgeons must identify and handle specialized instruments with high temporal and spatial precision. It is crucial that they are trained effectively. Traditional training methods include supervised practices and text-based study, which may expose patients to undue risk during practice procedures and lack motor/haptic training respectively. Tablet-based simulations have been proposed to mediate some of these limitations. We implemented a learning task that simulates surgical instrumentation nomenclature encountered by novice perioperative nurses. Learning was assessed following training in three distinct conditions: tablet-based simulations, text-based study, and real-world practice. Immediately following a 30-minute training period, instrument identification was performed with comparable accuracy and response times following tablet-based versus text-based training, with both being inferior to real-world practice. Following a week without practice, response times were equivalent between real-world and tablet-based practice. While tablet-based training does not achieve equivalent results in instrument identification accuracy as real-world practice, more practice repetitions in simulated environments may help reduce performance decline. This project has established a technological framework to assess how we can implement simulated educational environments in a maximally beneficial manner. © 2021 Kryklywy et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted

use, distribution, and reproduction in any medium, provided the original author and source are credited.

Kumar S, **Schwartz J**, **Amin M**, Kilbourn J, Vue H, **Daraiseh S** and **Jabbar K** (2021). "ILLUMINA TruSight Oncology 500 Sequencing Panel validation at a large community based hospital." Laboratory Investigation 101(SUPPL 1): 1066-1067.

[Full Text](#)

*Department of Pathology*

**Ledvina A**, **Otero R**, Hamilton J, **Clark C**, **Bastani A**, **Ziadeh J**, **Ditkoff J** and **Swor R** (2021). "Preliminary report of drive-through screening COVID-19 screening process in a large suburban community." International Journal of Emergency Medicine 14(1): 1-5.

[Full Text](#)

*Department of Emergency Medicine*

*OUWB Medical Student Author*

**Lee DM**, **Berger DA**, Wloszczynski PA, **Karabon P**, **Qu L** and **Burla MJ** (2021). "Assessing the impact of resuscitation residents on the treatment of cardiopulmonary resuscitation patients." American Journal of Emergency Medicine 41: 46-50.

[Full Text](#)

*Department of Emergency Medicine*

*Department of Medical Education*

*Department of Foundational Medical Studies (BH)*

*OUWB Medical Student Author*

Background: The management of cardiac arrest patients receiving cardiopulmonary resuscitation (CPR) is an essential aspect of emergency medicine (EM) training. At our institution, we have a 1-month Resuscitation Rotation designed to augment resident training in managing critical patients. The objective of this study is to compare 30-day mortality between cardiac arrest patients with resuscitation resident (RR) involvement versus patients without. Our secondary outcome is to determine if RR involvement altered rates of initiating targeted temperature management (TTM). Methods: This study was conducted at a single site tertiary care Level-1 trauma center with an Emergency Department (ED) census of nearly 130,000 visits per year. Data was collected from 01/01/2015 to 01/01/2018 using electronic medical records via query. Patients admitted with cardiac arrest were separated into two groups, one with RR involvement and one without. Initial rhythm of ventricular fibrillation/tachycardia (VFIB/VTACH), 30-day mortality, history of coronary artery disease (CAD), and initiation of TTM were compared. Statistical analysis was performed. Results: Out of 885 patient encounters, 91 (10.28%) had RR participation. There was no statistical difference in 30-day mortality between patients with RR involvement compared to those without (71.42% vs 66.36%;  $P = 0.3613$ ). However, TTM was initiated more in the RR group (20.70% vs 8.86%;  $P = 0.0025$ ). Patients who received TTM also had a lower 30-day mortality compared to those without TTM (52.94% vs 70.87%;  $P = 0.0020$ ). Patients who were older and had no history of CAD were also noted to have a statistically significant higher 30-day mortality. All other variables were not statistically significant. Conclusion: Resuscitation resident involvement with the care of cardiac arrest patients had no impact in 30-day mortality. However, the involvement of RR was associated with a statistically significant increase in the initiation of TTM. One limitation is that RR participated in 10.28% of the cases analyzed herein, thus the two arms are unbalanced in size. Future work may investigate if the increase in TTM in the RR involved cases may portend improved rates of neurologically intact survival or more rapid achievement of goal temperatures.

Levine WN and **Fischgrund JS** (2021). "JAAOS rebranding completed and other achievements." Journal of the American Academy of Orthopaedic Surgery 29(1): 1-2.

[Full Text](#)

*Department of Orthopaedic Surgery*

Li P, Killinger BA, Ensink E, Beddows I, **Yilmaz A**, Lubben N, Lamp J, Schilthuis M, Vega IE, Woltjer R, Pospisilik JA, Brundin P, Brundin L, **Graham SF** and Labrie V (2021). "Gut microbiota dysbiosis is associated with elevated bile acids in Parkinson's Disease." Metabolites 11(1): 29.

[Full Text](#)

*Department of Obstetrics & Gynecology*

The gut microbiome can impact brain health and is altered in Parkinson's disease (PD). The vermiform appendix is a lymphoid tissue in the cecum implicated in the storage and regulation of the gut microbiota. We sought to determine whether the appendix microbiome is altered in PD and to analyze the biological consequences of the microbial alterations. We investigated the changes in the functional microbiota in the appendix of PD patients relative to controls (n = 12 PD, 16 C) by metatranscriptomic analysis. We found microbial dysbiosis affecting lipid metabolism, including an upregulation of bacteria responsible for secondary bile acid synthesis. We then quantitatively measure changes in bile acid abundance in PD relative to the controls in the appendix (n = 15 PD, 12 C) and ileum (n = 20 PD, 20 C). Bile acid analysis in the PD appendix reveals an increase in hydrophobic and secondary bile acids, deoxycholic acid (DCA) and lithocholic acid (LCA). Further proteomic and transcriptomic analysis in the appendix and ileum corroborated these findings, highlighting changes in the PD gut that are consistent with a disruption in bile acid control, including alterations in mediators of cholesterol homeostasis and lipid metabolism. Microbially derived toxic bile acids are heightened in PD, which suggests biliary abnormalities may play a role in PD pathogenesis.

Lin KF, **Bojrab DI, Fritz CG, Schutt CA, Hong RS, Babu SC** and **Bojrab DI** (2021). "Hearing outcomes with a novel total ossicular replacement prosthesis." *Otology & Neurotology* 42(3): 447-454.

[Full Text](#)

*Department of Surgery*

*OUWB Medical Student Author*

Introduction: A total ossicular replacement prosthesis (TORP) is used to reconstruct the ossicular chain in the absence of the stapes suprastructure. The Wildcat prosthesis is a novel TORP that eliminates the need for a separate footplate shoe prosthesis and aims to improve ease-of-use and stability. This study evaluates hearing outcomes using the Wildcat prosthesis. Study Design: Case series with chart review. Setting: Tertiary neurotology referral center. Methods: Retrospective chart review of 64 patients undergoing ossicular chain reconstruction using the Wildcat TORP. Hearing outcomes after surgery were assessed with air conduction pure-tone average, bone conduction pure-tone average, air-bone gap (ABG), speech recognition threshold, and word recognition score as primary outcome measures. The stability of hearing outcomes was evaluated on subsequent long-term follow-up. Results: At mean short-term follow-up of  $4.4 \pm 2.7$  months, ABG improved from  $31.0 \pm 13.0$  dB preoperatively to  $22.5 \pm 10.0$  dB ( $p < 0.001$ ) with 51.6% achieving ABG less than 20 dB. No significant difference in any primary outcome measures was found when analyzing outcomes by initial versus revision surgery, use of cartilage graft, or type of mastoidectomy. The only exception was a smaller reduction in ABG of 4.2 dB for patients with canal wall down mastoidectomy compared with a 13.7 dB ABG closure in patients with canal wall up mastoidectomy ( $p = 0.039$ ). Conclusion: Total ossicular chain reconstruction using the Wildcat demonstrates versatility in challenging cases to provide hearing outcomes that are comparable to published data using TORPs.

Lodise TP, Van Wart S, Sund ZM, Bressler AM, Khan A, Makley AT, Hamad Y, Salata RA, Silveira FP, **Sims MD**, Kabchi BA, Saad MA, Brown C, Oler RE, Fowler V and Wunderink RG (2021). "Pharmacokinetic and pharmacodynamic profiling of minocycline for injection following a single infusion in critically ill adults in a phase IV open-label multicenter study (ACUMIN)." *Antimicrobial Agents and Chemotherapy* 65(3): AAC.01809-20.

[Full Text](#)

*Department of Internal Medicine*

Intravenous (i.v.) minocycline is increasingly used to treat infections caused by multidrug-resistant (MDR) *Acinetobacter baumannii*. Despite its being approved nearly 50 years ago, published information on its pharmacokinetic (PK) profile is limited. This multicenter study examined the PK and probability of pharmacokinetic-pharmacodynamic (PK-PD) target attainment profile of i.v. minocycline in critically ill patients, with suspected or documented infection with Gram-negative bacteria. The PK study population included 55 patients who received a single 200-mg i.v. dose of minocycline. Plasma PK samples were collected predose and 1, 4, 12, 24, 36, and 48 h after initiation of minocycline. Total and unbound minocycline concentrations were determined at each time point. Probabilities of achieving the PK-PD targets associated with stasis and 1-log killing (free area under the curve above the MIC [fAUC:MIC] of 12 and 18, respectively) in an immunocompetent animal pneumonia infection model of *A. baumannii* were evaluated. A two-compartment population PK model with zero-order i.v. input and first-order elimination, which

estimated a constant fraction unbound ( $f_{ub}$ ) for minocycline, best characterized the total and unbound plasma minocycline concentration-time data. The only two covariates retained in the final PK model were body surface area (associated with central volume of distribution) and albumin (associated with  $f_{ub}$ ). In the PK-PD probability of target attainment analyses, minocycline 200 mg i.v. every 12 h (Q12H) was predicted to result in a suboptimal PK PD profile for patients with *A. baumannii* infections with MIC values of > 1 mg/liter. Like all PK PD profiling studies of this nature, these findings need clinical confirmation.

**Lozano D**, Porter E and **Guerrero T** (2021). "Deriving pulmonary perfusion images from 4DCT using deep learning." *Journal of Thoracic Oncology* 16(3): S137-S137.

[Full Text](#)

*Department of Radiation Oncology*  
*OUIB Medical Student Author*

Lucas JP, **Allen M**, Siegel B and Gonik N (2021). "Diagnosis and management of congenital floor of mouth masses: A systematic review." *International Journal of Pediatric Otorhinolaryngology* 140: 110541.

[Full Text](#)

*OUIB Medical Student Author*

**Objectives:** Determine the utility of preoperative imaging and the optimal course of management for congenital floor of mouth (FOM) cysts in infants. **Methods:** A systematic review of the literature was performed conforming to PRISMA guidelines. Pubmed, Embase and Cochrane Library databases were queried to identify cases of infants with congenital floor of mouth masses. Patient demographics, presenting findings, imaging, management, complications, and outcomes were determined. **Results:** 85 patients were evaluated. 98% of patients presented at 16 months of age or younger. The most common presenting symptom was submental mass or swelling, 31.3%. Among the patients that underwent imaging, the suspected diagnosis obtained from imaging findings was consistent with the final pathologic diagnosis 59% of the time reported and inaccurate 34% of the time. There were multiple definitive treatment modalities described in the literature review including surgical excision, 82.3%, marsupialization, 12.9%, chemical injection 2.3%, sclerotherapy 1.2%, and radiation, 1.2%. Recurrence rate after initial definitive treatment was as follows, surgical excision, 8.8%, marsupialization, 80%, sclerotherapy, 100%, chemical injection, 50%, and radiation, 100%. **Conclusion:** Preoperative imaging studies should not be relied upon alone to determine suspected pathology and subsequent management in pediatric patients with FOM masses. It may be beneficial for these patients to undergo primary surgical excision regardless of imaging studies or suspected pathology. Needle aspiration offers limited addition to pathologic diagnosis and should only be performed in the setting of acute symptomatic management. Surgical excision should be considered as definitive treatment modality in all patients with FOM masses, regardless of the suspected diagnosis of ranula. Further multi-institutional cohort studies could be invaluable to elucidate definitive treatment guidelines in this patient population.

Lupher V, Lynch A and **Zalesin KC** (2021). "Health, weight loss, and surgery beliefs: Why patients choose to undergo bariatric surgery and what influences their choice of surgery procedure." *Bariatric Surgical Practice and Patient Care*. ePub Ahead of Print.

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*Department of Internal Medicine*

**Introduction:** The purpose of this study was to determine what factors influence an individual's decision to have bariatric surgery, including why they choose a particular surgery type. **Methods:** Thirty bariatric surgery patients (11 gastric bypass [GB] and 19 sleeve gastrectomy [SG]) participated in qualitative interviews pre- and postsurgery. Interviews questioned why patients chose bariatric surgery, their specific procedure choice, timing, and expectations for surgery. Verbatim transcripts were coded using a constant comparative method and a grounded theory approach. Analysis focused on surgery motivations, personal influences, and choice of procedure. **Results:** Five themes emerged regarding the decision to have bariatric surgery: Health, Activity and Lifestyle Interference, Frustration with Weight, Social Influences, and Body Image. Most participants selected GB surgery based on beliefs about weight loss outcomes. Rationales for choosing a SG centered on surgery effects, including perceptions that the sleeve was less invasive or allowed for less restrictive eating habits postsurgery. Surgery veterans emerged as an important influence on the choice of surgery procedure.

Conclusion: Patients consider multiple factors in their decision to undergo bariatric surgery. Health care professionals should take these factors into account to help patients make informed decisions and to clarify existing misconceptions.

Madanat L, **Schoenherr D, Wey E** and Gupta R (2021). "Rasburicase-induced haemolysis and methemoglobinemia: An ongoing issue." *BMJ Case Reports* 14: e240967.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Pathology*

We report a case of a 91-year-old Caucasian woman with a history of chronic lymphocytic leukaemia who developed acute hypoxic respiratory failure (AHRF) requiring intubation for less than 24 hours after receiving rasburicase. Laboratory workup was significant for methemoglobinemia and acute anaemia, and blood film demonstrated evidence of oxidative haemolysis with bite cells. The patient was given a presumptive diagnosis of glucose-6-phosphate dehydrogenase (G6PD) deficiency and was managed conservatively with successful resolution of AHRF and stabilisation of haemoglobin level. Seven days after admission, she passed away due to subsequent complications; hence, follow-up G6PD level could not be obtained. Haemolytic anaemia and methemoglobinemia in the setting of recent rasburicase administration should raise clinical suspicion for G6PD deficiency. In non-emergent cases, patients should be screened prior to receiving rasburicase regardless of risk factors. Because rasburicase is often needed emergently, patients at high risk of tumour lysis syndrome should be screened early for G6PD deficiency.

Maerz T, Nepple JJ, Bedi A, **Zaltz I**, Belzile É, Beaulé PE, Sink EL, Clohisy JC and Group A (2021). "Sex differences in clinical outcomes following surgical treatment of femoroacetabular impingement." *The Journal of Bone and Joint Surgery* 103(5): 415-423.

[Full Text](#)

*Department of Orthopaedic Surgery*

Background: Sex-based differences in clinical outcomes following surgical treatment of femoroacetabular impingement remain largely uncharacterized; this prospective, multicenter study evaluated these differences both directly and adjusted for covariates. Methods: Hips undergoing surgical treatment of symptomatic femoroacetabular impingement were prospectively enrolled in a multicenter cohort. Patient demographics, radiographic parameters, intraoperatively assessed disease severity, and history of surgical procedures, as well as patient-reported outcome measures, were collected preoperatively and at a mean follow-up of 4.3 years. A total of 621 (81.6%) of 761 enrolled hips met the minimum 1 year of follow-up and were included in the analysis; 56.7% of analyzed hips were female. Univariate and multivariable statistics were utilized to assess the direct and adjusted differences in outcomes, respectively. Results: Male hips had greater body mass index and larger  $\alpha$  angles. Female hips had significantly lower preoperative and postoperative scores across most patient-reported outcome measures, but also had greater improvement from preoperatively to postoperatively. The preoperative differences between sexes exceeded the threshold for the minimal clinically important difference of the modified Harris hip score (mHHS) and all Hip disability and Osteoarthritis Outcome Score (HOOS) domains except quality of life. Preoperative sex differences in mHHS, all HOOS domains, and Short Form-12 Health Survey physical function component score were greater than the postoperative differences. A greater proportion of female hips achieved the minimal clinically important difference for the mHHS, but male hips were more likely to meet the patient acceptable symptom state for this outcome. After adjusting for relevant covariates with use of multiple regression analysis, sex was not identified as an independent predictor of any outcome. Preoperative patient-reported outcome scores were a strong and highly significant predictor of all outcomes. Conclusions: Significant differences in clinical outcomes were observed between sexes in a large cohort of hips undergoing surgical treatment of femoroacetabular impingement. Despite female hips exhibiting lower baseline scores, sex was not an independent predictor of outcome or reoperation.

Mahatanan R, **Tantisattamo E**, Charoenpong P and Ferrey A (2021). "Outcomes of C difficile infection in solid-organ transplant recipients: The National Inpatient Sample (NIS) 2015-2016." *Transplant Infectious Disease* 23(1): e13459.

[Full Text](#)

*Department of Internal Medicine*

Background: Clostridioides (formerly Clostridium) difficile infection (CDI) is one of the leading causes of morbidity and mortality worldwide. Solid organ transplant (SOT) recipients are at an increased risk for CDI. A recent study showed an overall improvement in mortality amongst hospitalized individuals with CDI, but it is unclear if this benefit extends to SOT recipients. Methods: We scrutinized the 2015 and 2016 National Inpatient Sample (NIS), the largest all-payer inpatient database in the United States for CDI data in patients with SOT. SOT was defined as any recipient who had received a heart, lung, liver, intestinal, kidney, pancreas, or combined thoracic and/or abdominal organ transplantation. Baseline characteristics, comorbidities, and concomitant diagnosis of pneumonia or urinary tract infection were adjusted for in our analysis. Primary outcomes included inpatient mortality, hospital length of stay and total hospital charges. Results: A total of 105 780 hospital discharges of SOT recipients were included. The incidence of CDI was 3554 (3.36%) among SOTs. CDI was associated with a higher inpatient mortality (OR 1.85, 95% CI 1.56-2.20,  $P < .01$ ), longer length of hospital stay (mean difference 5.07 days, 95% CI 4.43-5.71,  $P < .01$ ) and higher total hospital charges (mean difference 43 958 US dollars,  $P < .01$ ). Conclusion: Our study found that CDI is associated with poorer overall outcomes among hospitalized SOT recipients. However, there was a possible improving trend of the outcomes when compare to previous studies.

**Mankuzhy NP**, Almahariq MF, Siddiqui ZA, Thompson AB, **Grills IS**, **Guerrero TM**, Lee KC, **Stevens CW** and Quinn TJ (2021). "The role of postoperative radiation therapy for pN2 non-small-cell lung cancer." *Clinical Lung Cancer* 22(1): e5-e17.

[Full Text](#)

*Department of Radiation Oncology*

*OUIB Medical Student Author*

Background: The role for postoperative radiation therapy (PORT) for patients with non-small-cell lung cancer (NSCLC) with mediastinal lymph node (LN) involvement (pN2 disease) is controversial. We compared surgery alone with PORT among patients with pN2 NSCLC. We then performed subset analyses to better delineate patients that might benefit from PORT. Patients and Methods: We conducted a propensity score (PS)-matched, inverse probability of treatment weighting (IPTW) Surveillance, Epidemiology, and End Results (SEER) analysis of patients with pN2 disease from 1989 to 2016 with surgery alone or PORT. Multiple imputation with chained equations was used for missing LN data. Results: A total of 8631 patients were included in this analysis; 4579 underwent surgery alone, and 4052 underwent PORT. Following PS matching and IPTW, there was no difference in overall survival (OS) (hazard ratio [HR], 0.99;  $P = .76$ ). However, PORT improved OS among a subset of patients with a LN positive to sampled ratio  $\geq 50\%$  (HR, 0.90;  $P = .01$ ). Moreover, there was a trend towards improved OS among this subset, even with chemotherapy (HR, 0.91;  $P = .09$ ). Conclusion: PORT is not associated with an improvement or detriment in OS for all patients with pN2 NSCLC. However, patients with a positive to sampled LN ratio  $\geq 50\%$  may benefit, regardless of chemotherapy status. Nevertheless, PORT will remain the standard of care as we await the results of the ongoing LUNG ART trial.

Mann GE, Flamer SZ, Nair S, Maher JN, **Cowan B**, Streiff A, Adams D and Shaparin N (2021). "Opioid-free anesthesia for adenotonsillectomy in children." *International Journal of Pediatric Otorhinolaryngology* 140: 110501.

[Full Text](#)

*OUIB Medical Student Author*

Introduction: Opioids are administered during the intraoperative and postoperative periods in pediatric adenotonsillectomy and tonsillectomy. Non-opioid analgesics are often used as an analgesic during pediatric adenotonsillectomy and tonsillectomy. In this hypothesis generating study, we are evaluating safety and efficacy of stand-alone opioid analgesia for adenotonsillectomy and tonsillectomy. Methods: This is a single-center retrospective chart review of patients ages 2 to 13 who underwent elective adenotonsillectomy and tonsillectomy. We used a convenience sampling method to select patients who received intraoperative intravenous fentanyl, acetaminophen, ibuprofen, or any combination thereof. The following outcomes were analyzed in this study: (i) the length of Post Anesthesia Care Unit stay, (ii) administration of postoperative opioids; (iii) postoperative opioid equivalents required; (iv) administration of postoperative non-opioid analgesics; and (v) inpatient admission from ED within 30 days. We used univariate analysis to compare the data points. Results: We analyzed data from 323 patients who underwent adenotonsillectomy and tonsillectomy. The Post Anesthesia Care Unit length stay was similar for the intraoperative opioid-free and

intraoperative opioid groups, 146.68 ( $\pm 67.35$ ) and 143.18 ( $\pm 37.85$ ) minutes, respectively ( $p = 0.586$ ). Additionally, 102 patients (73.4%) in the intraoperative opioid-free group and 184 patients (83.2%) in the intraoperative opioid group did not receive any postoperative opioids ( $p = 0.033$ ). The incidence of adverse events was similar between the intraoperative opioid-free and intraoperative opioid groups 3 (2.2%) and 5 (2.7%) respectively,  $p$ -value 0.749. A subgroup analysis comparing extracapsular 235 (72.8%) versus intracapsular 88 (27.2%) tonsillectomy yielded similar results. Conclusion: In this study, our data indicates that American Society of Anesthesiologists I– II pediatric patients undergoing adenotonsillectomy and tonsillectomy can be efficiently and safely managed with an opioid-free intraoperative and postoperative analgesic regimen. Due to the explained limitations, our study results should be interpreted cautiously.

McConachie SM, Hanni CM, Raub JN, Mohammad RA and **Wilhelm SM** (2021). "The impact of multiple renal Estimates on pharmacist dosing recommendations: A randomized trial." *Annals of Pharmacotherapy* 55(1): 25-35.

[Full Text](#)

*OUWB Medical Student Author*

Background: Numerous equations are used for estimation of renal function, and many electronic medical records report multiple clearance estimates to assist with drug dosing. It is unknown whether the presence of multiple clearance estimates affects clinical decision-making. Objective: To determine whether the presence of multiple renal clearance estimates affects pharmacist drug dosing decisions. Methods: A randomized trial in the form of an electronic survey including 4 clinical vignettes was delivered to hospital pharmacists. Vignettes consisted of a patient presenting with an acute pulmonary embolism requiring enoxaparin therapy. Pharmacists were randomized to receive a single estimate of renal function or multiple estimates for all vignettes. The primary outcome was deviation from approved recommendations on at least 1 vignette. The  $\chi^2$  test was used to detect differences in deviation rates between groups. Logistic regression was performed to adjust for the effects of potentially confounding variables. Results: A total of 154 studies were completed (73 in the multiple-estimate group and 81 in the single-estimate group). Pharmacists presented with multiple renal estimates were significantly more likely to deviate from recommended dosing regimens than pharmacists presented with a single estimate (54.7% vs 38.2%;  $P = 0.04$ ). The results were driven primarily by the 2 vignettes that included discordance among Cockcroft-Gault equation creatinine clearance estimates. Logistic regression identified multiple estimates as the only independent predictor of deviation ( $P = 0.04$ ). Conclusion and Relevance: Pharmacists provided with a single renal clearance estimate were more likely to adhere to approved dosing recommendations than pharmacists provided with multiple estimates.

**Mehta NK**, Morgaenko K, **Haines D**, Rojas-Pena E, Heard B, Malhotra R, Darby A, Mangrum JM, Mason P, Campbell C and Bilchick K (2021). "Baseline incision characteristics and early scar maturation indices following cardiac device implantation." *Journal of Arrhythmia* 37(2): 400-406.

[Full Text](#)

*Department of Internal Medicine*

Aims: Dermatologic evaluation for cardiac implantable electronic devices (CIEDs) has not been established. We sought to ascertain baseline wound scar features using quantifiable surgical tools and scar scales on post-CIED patients. Methods: A single-center, prospective observational case-control study was performed where 92 study subjects (40 healthy volunteers and 52 post-CIED patients) completed the study. Durometer was used to quantify skin pliability before CIED placement, postprocedure, and 2 weeks postprocedure. Higher durometer readings signified reduced skin pliability. Durometer readings were compared to the patients' contralateral pectoral skin and to a healthy volunteer's cohort skin within the prepectoral region. Patient wounds were observed and graded using the Patient Observer Scar Assessment Scale (POSAS) and Manchester Scar Scale (MSS). Results: Baseline pectoral skin pliability readings were similar in healthy volunteers and CIED patient population. In comparison to preprocedural measurements, surgical site skin pliability decreased in postprocedural and 2 weeks follow-up time points ( $P$ -value .004 and  $<.001$ , respectively). The increases in durometer readings were higher in the older population (age  $>75$  over time,  $P = .008$ ). POSAS evaluations showed on average a thin painless hypopigmented scar with moderate stiffness. MSS scar evaluation showed a palpable scar with slight contour differences and color mismatch and appeared to be slightly better in the African American population. There was no difference in scar characteristics with preprocedural use of antiplatelet or anticoagulation or staple closure or gender. Conclusions: Serial measurements could be of value for development of new strategies for cosmesis and

improved wound healing.

**Memon AM** (2021). "Transcranial magnetic stimulation in treatment of adolescent attention deficit/hyperactivity disorder: A narrative review of literature." *Innovations in Clinical Neuroscience* 18(1-3): 43-46.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Attention deficit/hyperactivity disorder (ADHD), one of the most common neurodevelopmental disorders, affected 3.3 million adolescents in the United States (US) in 2016. Ten to 30 percent of these patients do not respond to standard pharmacotherapy and, as a result, suffer adverse physical/mental health and socioeconomic consequences. Despite being approved by the US Food and Drug Administration (FDA) for treatment of adult depression, with evidence suggesting positive outcomes in children and adults in treatment of ADHD and good safety and tolerability records, there is no existent literature reviewing the efficacy, safety, and feasibility of use of transcranial magnetic stimulation (TMS) in the treatment of adolescent ADHD. Thus, We have conducted this review for which a thorough literature search was conducted on PubMed and PsycInfo databases using a combination of MeSH terms that yielded 32 articles, five of which satisfied the inclusion criteria. We observed objective improvements in ADHD treatment outcomes in adolescent patients who participated in a randomized, sham-controlled, crossover pilot study that assessed the safety and efficacy of TMS. The study participants did not suffer any major adverse events, which was also supported by findings from other studies. However, since only one study out of five included in the review is an interventional study with limited number of study participants, there is a need to conduct large-scale clinical trials that recruit a greater number of study participants to explore the clinical efficacy and safety of TMS in the treatment of adolescent ADHD patients who do not respond to or tolerate standard pharmacotherapy based on the preliminary data extracted to this end.

Milman T, Eiger-Moscovich M, Henry RK, **Folberg R**, Coupland SE, Grossniklaus HE, Mudhar HS, Eberhart CG, Heegaard S, Auw-Hädrich C, Herwig-Carl MC, Löffler KU, Cherepanoff S, Zhang Q, Sharpe JE, See TRO, Shields CL and Eagle RC, Jr. (2021). "Validation of the newly proposed World Health Organization classification system for conjunctival melanocytic intraepithelial lesions: A comparison with the C-MIN and PAM classification schemes." *American Journal of Ophthalmology* 223: 60-74.

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*Department of Ophthalmology*

Purpose: We sought to compare the sensitivity, specificity, accuracy, and interobserver agreement of the two most commonly used classification systems for conjunctival melanocytic intraepithelial lesions with the new World Health Organization (WHO) classification. Design: Retrospective case series and evaluation of classification systems. Methods: We reviewed the pathology and medical records of all patients who underwent a primary biopsy procedure for conjunctival primary acquired melanosis (PAM) at Wills Eye Hospital between 1974 and 2002 who had  $\geq 36$  months of follow-up. Data collected included age, sex, clinical findings, recurrence, and progression to melanoma. Twelve ophthalmic pathologists analyzed scanned hematoxylin and eosin-stained virtual microscopic slides using 3 classification systems: PAM, conjunctival melanocytic intraepithelial neoplasia, and the WHO 4th edition classification of conjunctival melanocytic intraepithelial lesions. Observer agreement, sensitivity, specificity, and diagnostic accuracy of each classification system were assessed. Results: There were 64 patients who underwent 83 primary excisions with cryotherapy for conjunctival PAM who had adequate tissue for histopathologic evaluation. The interobserver agreement in distinction between the low- and high-grade lesions was 76% for PAM, 67% for conjunctival melanocytic intraepithelial neoplasia, and 81% for WHO classification system. Low-grade lesions provided the greatest interpretative challenge with all 3 classification systems. The 3 classification systems had comparable accuracy of 81%-83% in their ability to identify lesions with potential for recurrence. Conclusions: This study highlights the comparable strengths and limitations of the 3 classification systems for conjunctival melanocytic intraepithelial lesions and suggests that the simplified WHO classification scheme is appropriate for evaluation of these lesions.

Moghadami M, Amini M, Moghadami M, **Dalal B** and Charlin B (2021). "Teaching clinical reasoning to undergraduate medical students by illness script method: A randomized controlled trial." *BMC Medical Education* 21(1): 87.

[Full Text](#)

#### *Department of Internal Medicine*

Background: The illness script method employs a theoretical outline (e.g., epidemiology, pathophysiology, signs and symptoms, diagnostic tests, interventions) to clarify how clinicians organized medical knowledge for clinical reasoning in the diagnosis domain. We hypothesized that an educational intervention based on the illness script method would improve medical students' clinical reasoning skills in the diagnosis domain. Methods: This study is a randomized controlled trial involving 100 fourth-year medical students in Shiraz Medical School, Iran. Fifty students were randomized to the intervention group, who were taught clinical reasoning skills based on the illness script method for three diseases during one clinical scenario. Another 50 students were randomized to the control group, who were taught the clinical presentation based on signs and symptoms of the same three diseases as the intervention group. The outcomes of interest were learner satisfaction with the intervention and posttest scores on both an internally developed knowledge test and a Script Concordance Test (SCT). Results: Of the hundred participating fourth-year medical students, 47 (47%) were male, and 53 (53%) were female. On the knowledge test, there was no difference in pretest scores between the intervention and control group, which suggested a similar baseline knowledge in both groups; however, posttest scores in the intervention group were ( $15.74 \pm 2.47$  out of 20) statistically significantly higher than the control group ( $14.38 \pm 2.59$  out of 20,  $P = 0.009$ ). On the SCT, the mean score for the intervention group ( $6.12 \pm 1.95$  out of 10) was significantly higher than the control group ( $4.54 \pm 1.56$  out of 10;  $P = 0.0001$ ). Learner satisfaction data indicated that the intervention was well-received by students. Conclusion: Teaching with the illness script method was an effective way to improve students' clinical reasoning skills in the diagnosis domain suggested by posttest and SCT scores for specific clinical scenarios. Whether this approach translates to improved generalized clinical reasoning skills in real clinical settings merits further study.

Moore SR, Menon SS, **Cortes C** and Ferreira VP (2021). "Hijacking factor H for complement immune evasion." *Frontiers in Immunology* 12: 602277.

[Full Text](#)

#### *Department of Foundational Medical Studies (OU)*

The complement system is an essential player in innate and adaptive immunity. It consists of three pathways (alternative, classical, and lectin) that initiate either spontaneously (alternative) or in response to danger (all pathways). Complement leads to numerous outcomes detrimental to invaders, including direct killing by formation of the pore-forming membrane attack complex, recruitment of immune cells to sites of invasion, facilitation of phagocytosis, and enhancement of cellular immune responses. Pathogens must overcome the complement system to survive in the host. A common strategy used by pathogens to evade complement is hijacking host complement regulators. Complement regulators prevent attack of host cells and include a collection of membrane-bound and fluid phase proteins. Factor H (FH), a fluid phase complement regulatory protein, controls the alternative pathway (AP) both in the fluid phase of the human body and on cell surfaces. In order to prevent complement activation and amplification on host cells and tissues, FH recognizes host cell-specific polyanionic markers in combination with complement C3 fragments. FH suppresses AP complement-mediated attack by accelerating decay of convertases and by helping to inactivate C3 fragments on host cells. Pathogens, most of which do not have polyanionic markers, are not recognized by FH. Numerous pathogens, including certain bacteria, viruses, protozoa, helminths, and fungi, can recruit FH to protect themselves against host-mediated complement attack, using either specific receptors and/or molecular mimicry to appear more like a host cell. This review will explore pathogen complement evasion mechanisms involving FH recruitment with an emphasis on: (a) characterizing the structural properties and expression patterns of pathogen FH binding proteins, as well as other strategies used by pathogens to capture FH; (b) classifying domains of FH important in pathogen interaction; and (c) discussing existing and potential treatment strategies that target FH interactions with pathogens. Overall, many pathogens use FH to avoid complement attack and appreciating the commonalities across these diverse microorganisms deepens the understanding of complement in microbiology.

Moysidis SN, Koulisis N, Rao P, Govindaraju VK, **Gamsky S, Mahmoud TH, Randhawa S, Faia LJ, Wolfe JD, Dreiser KA, Ruby AJ, Garretson BR, Hassan TS, Williams GA, Trese MT** and **Capone A, Jr.** (2021). "Peripheral retinal angiographic findings in macular telangiectasis type 2." *Retina* 41(3): 480-486.

[Full Text](#)

*Department of Ophthalmology*  
*OUWB Medical Student Author*

Purpose: To evaluate the retinal periphery in patients with idiopathic juxtafoveal telangiectasis or macular telangiectasis Type 2 (MacTel2), using widefield fluorescein angiography. Methods: Single-center, retrospective, observational case series of 50 eyes of 50 patients with MacTel2 and 50 eyes of 50 age-matched controls. Results: Thirty-seven eyes in the MacTel2 group (74%) showed peripheral capillary nonperfusion or dropout, compared with 37 eyes in the control group (74%,  $P = 1.0$ ). Morphologically, the MacTel2 group trended toward having a higher proportion of pruning-type capillary dropout (44%) compared with controls (28%), but this was not statistically significant ( $P = 0.12$ ). Patients with MacTel2 had a higher incidence of microaneurysms compared with controls (MacTel2 56%; controls 42%;  $P = 0.048$ ), independent of age or systemic risk factors. There was no difference in the incidence of venous-venous shunts (MacTel2 10%; controls 10%;  $P = 1.0$ ), arteriovenous shunts (MacTel2 14%; controls 18%;  $P = 0.60$ ), venous tortuosity (MacTel2 60%; controls 66%;  $P = 0.58$ ), or arterial tortuosity (MacTel2 54%; controls 68%;  $P = 0.20$ ), which was mild in most cases. Conclusion: We note a high incidence of peripheral vascular and retinal findings in both patients with MacTel2 and age-matched controls, using widefield fluorescein angiography. Patients with MacTel2 had significantly more microaneurysms, independent of age or other systemic risk factors.

Muccio P, Schueller J, Boas MV, Howe N, **Dabrowski E** and Durrant D (2021). "Therapeutic effectiveness of AxioBionics Wearable Therapy Pain Management System in patients with chronic lower back pain." *Clinical Medicine Insights- Arthritis and Musculoskeletal Disorders* 14: 1179544121993778.

[Full Text](#)

*Department of Physical Medicine & Rehabilitation*

Chronic lower back pain is one of the most common medical conditions leading to a significant decrease in quality of life. This study retrospectively analyzed whether the AxioBionics Wearable Therapy Pain Management (WTPM) System, a customized and wearable electrical stimulation device, alleviated chronic lower back pain, and improved muscular function. This study assessed self-reported pain levels using the visual analog scale before and during the use of the AxioBionics WTPM System when performing normal activities such as sitting, standing, and walking ( $n = 69$ ). Results showed that both at-rest and activity-related pain were significantly reduced during treatment with the AxioBionics WTPM System (% reduction in pain: 64% and 60%, respectively;  $P < .05$ ). Thus, this study suggests that the AxioBionics WTPM System is efficacious in treating chronic lower back pain even when other therapies have failed to sufficiently decrease reported pain levels.

**Nair GB, Al-Katib S, Turner-Lawrence D, Khasawneh M, Myziuk N, Guerrero T, Podolsky R and Castillo E** (2021). "A prospective study to validate pulmonary blood mass changes on non-contrast 4DCT in pulmonary embolism patients." *Clinical Imaging* 78: 179-183.

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*Department of Internal Medicine*

*Department of Diagnostic Radiology and Molecular Imaging*

*Department of Emergency Medicine*

*Department of Radiation Oncology*

Purpose: Limited diagnostic options exist for patients with suspected pulmonary embolism (PE) who cannot undergo CT-angiogram (CTA). CT-ventilation methods recover respiratory motion-induced lung volume changes as a surrogate for ventilation. We recently demonstrated that pulmonary blood mass change, induced by tidal respiratory motion, is a potential surrogate for pulmonary perfusion. In this study, we examine blood mass and volume change in patients with PE and parenchymal lung abnormalities (PLA). Methods: A cross-sectional analysis was conducted on a prospective, cohort-study with 129 consecutive PE suspected patients. Patients received 4DCT within 48 h of CTA and were classified as having PLA and/or PE. Global volume change (VC) and percent global pulmonary blood mass change (PBM) were calculated for each patient. Associations with disease type were evaluated using quantile regression. Results: 68 of 129 patients were PE positive on CTA. Median change in PBM for PE-positive patients (0.056; 95% CI: 0.045, 0.068; IQR: 0.051) was smaller than that of PE-negative patients (0.077; 95% CI: 0.064, 0.089; IQR: 0.056), with an estimated difference of 0.021 (95% CI: 0.003, 0.038;  $p = 0.0190$ ). PLA was detected in 57 (44.2%) patients.

Median VC for PLA-positive patients (1.26; 95% CI: 1.22, 1.30; IQR: 0.15) showed no significant difference from PLA-negative VC (1.25; 95% CI: 1.21, 1.28; IQR: 0.15). Conclusions: We demonstrate that pulmonary blood mass change is significantly lower in PE-positive patients compared to PE-negative patients, indicating that PBM derived from dynamic non-contrast CT is a potentially useful surrogate for pulmonary perfusion.

**Nair GB**, Galban CJ, **Al-Katib S**, Podolsky R, van den Berge M, **Stevens C** and **Castillo E** (2021). "An assessment of the correlation between robust CT-derived ventilation and pulmonary function test in a cohort with no respiratory symptoms." *British Journal of Radiology* 94(1118): 20201218.

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*Department of Internal Medicine*

*Department of Radiation Oncology*

Objective: To evaluate CT-ventilation imaging (CTVI) within a well-characterized, healthy cohort with no respiratory symptoms and examine the correlation between CTVI and concurrent pulmonary function test (PFT). Methods: CT scans and PFTs from 77 Caucasian participants in the NORM dataset (clinicaltrials.gov NCT00848406) were analyzed. CTVI was generated using the robust Integrated Jacobian Formulation (IJF) method. IJF estimated total lung capacity (TLC) was computed from CTVI. Bias-adjusted Pearson's correlation between PFT and IJF-based TLC was computed. Results: IJF- and PFT-measured TLC showed a good correlation for both males and females [males: 0.657, 95% CI (0.438-0.797); females: 0.667, 95% CI (0.416-0.817)]. When adjusting for age, height, smoking, and abnormal CT scan, correlation moderated [males: 0.432, 95% CI (0.129-0.655); females: 0.540, 95% CI (0.207-0.753)]. Visual inspection of CTVI revealed participants who had functional defects, despite the fact that all participant had normal high-resolution CT scan. Conclusion: In this study, we demonstrate that IJF computed CTVI has good correlation with concurrent PFT in a well-validated patient cohort with no respiratory symptoms. ADVANCES IN KNOWLEDGE: IJF-computed CTVI's overall numerical robustness and consistency with PFT support its potential as a method for providing spatiotemporal assessment of high and low function areas on volumetric non-contrast CT scan.

**Nair GB** and Niederman MS (2021). "Updates on community acquired pneumonia management in the ICU." *Pharmacology & Therapeutics* 217: 107663.

[Full Text](#)

*Department of Internal Medicine*

While the world is grappling with the consequences of a global pandemic related to SARS-CoV-2 causing severe pneumonia, available evidence points to bacterial infection with *Streptococcus pneumoniae* as the most common cause of severe community acquired pneumonia (SCAP). Rapid diagnostics and molecular testing have improved the identification of co-existent pathogens. However, mortality in patients admitted to ICU remains staggeringly high. The American Thoracic Society and Infectious Diseases Society of America have updated CAP guidelines to help streamline disease management. The common theme is use of timely, appropriate and adequate antibiotic coverage to decrease mortality and avoid drug resistance. Novel antibiotics have been studied for CAP and extend the choice of therapy, particularly for those who are intolerant of, or not responding to standard treatment, including those who harbor drug resistant pathogens. In this review, we focus on the risk factors, microbiology, site of care decisions and treatment of patients with SCAP.

Navin M, **Wasserman JA**, Stahl D and Tomlinson T (2021). "The capacity to designate a surrogate is distinct from decisional capacity: Normative and empirical considerations." *Journal of Medical Ethics*. ePub Ahead of Print.

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*Department of Foundational Medical Studies (OU)*

The capacity to designate a surrogate (CDS) is not simply another kind of medical decision-making capacity (DMC). A patient with DMC can express a preference, understand information relevant to that choice, appreciate the significance of that information for their clinical condition, and reason about their choice in light of their goals and values. In contrast, a patient can possess the CDS even if they cannot appreciate their condition or reason about the relative risks and benefits of their options. Patients who lack DMC for many or most kinds of medical choices may nonetheless possess the CDS, particularly since the complex means-ends reasoning required by DMC is one of the first capacities to be lost in progressive cognitive diseases (eg, Alzheimer's disease). That is, patients with significant cognitive decline or mental illness may still understand

what a surrogate does, express a preference about a potential surrogate, and be able to provide some kind of justification for that selection. Moreover, there are many legitimate and relevant rationales for surrogate selection that are inconsistent with the reasoning criterion of DMC. Unfortunately, many patients are prevented from designating a surrogate if they are judged to lack DMC. When such patients possess the CDS, this practice is ethically wrong, legally dubious and imposes avoidable burdens on healthcare institutions. © Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.

Nous F, Budde RPJ, Fairbairn TA, Akasaka T, Nørgaard BL, Berman DS, **Raff G**, Hurwitz-Koweek LM, Pontone G, Kawasaki T, Sand NPR, Jensen JM, Amano T, Poon M, Øvrehus KA, Sonck J, Rabbat MG, Mullen S, De Bruyne B, Rogers C, Matsuo H, Bax JJ, Leipsic J, Patel MR and Nieman K (2021). "Temporal changes in FFR(CT)-guided management of coronary artery disease - Lessons from the ADVANCE Registry." *Journal of Cardiovascular Computed Tomography* 15(1): 48-55.

[Full Text](#)

*Department of Internal Medicine*

Background: The ADVANCE registry is a large prospective study of outcomes and resource utilization in patients undergoing coronary computed tomography angiography (CCTA) and CT-based fractional flow reserve (FFR(CT)). As experience with new technologies and practices develops over time, we investigated temporal changes in the use of FFR(CT) within the ADVANCE registry. Methods: 5083 patients with coronary artery disease (CAD) on CCTA were prospectively enrolled in the ADVANCE registry and were divided into 3 equally sized cohorts based on the temporal order of enrollment per site. Demographics, CCTA and FFR(CT) findings, and clinical outcomes through 1-year follow-up, were recorded and compared between tertiles. Results: The number of patients with a  $\geq 70\%$  stenosis on CCTA was similar over time (33.6%, 30.9%, and 33.8% for cohort 1-3). The rate of positive FFR(CT)  $\leq 0.80$  was higher for cohorts 2 (67.3%) and 3 (74.6%) than for cohort 1 (57.1%,  $p < 0.001$ ). Invasive FFR rates decreased from 25.8% to 22.4% between cohort 1 and 3 ( $p = 0.023$ ). Moreover, patients with a FFR(CT)  $\leq 0.80$  were less frequently referred for invasive coronary angiography (ICA) (from 62.9% to 52.9%,  $p < 0.001$ ), and underwent fewer revascularizations between cohort 1 and 3 (from 41.9% to 32.0%,  $p < 0.001$ ). The prevalence of major events was low (1.2%) and similar between cohorts. Conclusions: Growing experience with FFR(CT) improved the likelihood of identifying hemodynamically significant CAD and safely reduced the need for ICA and revascularization in patients with anatomically significant disease even in the instance of an abnormal FFR(CT.)

O'Connell TF, Bradley CJ, **Abbas AE**, **Williamson BD**, Rusia A, Tawney AM, Gaines R, Schott J, Dmitrienko A and **Haines DE** (2021). "Hydroxychloroquine/Azithromycin therapy and QT prolongation in hospitalized patients with COVID-19." *JACC: Clinical Electrophysiology* 7(1): 16-25.

[Full Text](#)

*Department of Internal Medicine*

Objectives: This study aimed to characterize corrected QT (QTc) prolongation in a cohort of hospitalized patients with coronavirus disease-2019 (COVID-19) who were treated with hydroxychloroquine and azithromycin (HCQ/AZM). Background: HCQ/AZM is being widely used to treat COVID-19 despite the known risk of QT interval prolongation and the unknown risk of arrhythmogenesis in this population. Methods: A retrospective cohort of COVID-19 hospitalized patients treated with HCQ/AZM was reviewed. The QTc interval was calculated before drug administration and for the first 5 days following initiation. The primary endpoint was the magnitude of QTc prolongation, and factors associated with QTc prolongation. Secondary endpoints were incidences of sustained ventricular tachycardia or ventricular fibrillation and all-cause mortality. Results: Among 415 patients who received concomitant HCQ/AZM, the mean QTc increased from  $443 \pm 25$  ms to a maximum of  $473 \pm 40$  ms (87 [21%] patients had a QTc  $\geq 500$  ms). Factors associated with QTc prolongation  $\geq 500$  ms were age ( $p < 0.001$ ), body mass index  $< 30$  kg/m<sup>2</sup> ( $p = 0.005$ ), heart failure ( $p < 0.001$ ), elevated creatinine ( $p = 0.005$ ), and peak troponin ( $p < 0.001$ ). The change in QTc was not associated with death over the short period of the study in a population in which mortality was already high (hazard ratio: 0.998;  $p = 0.607$ ). No primary high-grade ventricular arrhythmias were observed. Conclusions: An increase in QTc was seen in hospitalized patients with COVID-19 treated with HCQ/AZM. Several clinical factors were associated with greater QTc prolongation. Changes in QTc were not associated with increased risk of death.

Oleszek J, Tilton A, Carranza J, Dursun N, Bonikowski M, **Dabrowski E**, Regnault B and Delgado MR (2021). "Dosing from a phase 3 pivotal study of abobotulinumtoxinA injection in upper-limb muscles in pediatric patients with cerebral palsy." Toxicon 190: S53-S53.

[Full Text](#)

*Department of Physical Medicine and Rehabilitation*

**Oska S**, Bedford LM and Potts GA (2021). "Alopecia totalis following hand-foot-and-mouth disease." Pediatric Dermatology. ePub Ahead of Print.

[Full Text](#)

*OUIB Medical Student Author*

We present a case of a 13-month-old male patient with alopecia totalis that began two months after an episode of hand-foot-and-mouth disease. It is hypothesized that the viral infection triggered an autoimmune response, which led to production of lymphocytes targeting an antigen present in the hair bulb. Future research is necessary to determine whether and how the pathophysiology of alopecia totalis may be triggered by viral infection.

Ozcan A, Ahn T, **Akay B** and **Menoch M** (2021). "Imaging for pediatric blunt abdominal trauma with different prediction rules: Is the outcome the same?" Pediatric Emergency Care. ePub Ahead of Print.

[Request Form](#)

*Department of Surgery*

*Department of Emergency Medicine*

Background: Computerized tomography (CT) of the abdomen and pelvis is the standard imaging modality to diagnose intra-abdominal injury (IAI). Clinicians must weigh the risk-benefit of CT compared with the degree of clinical suspicion for an IAI. Pediatric Emergency Care Applied Research Network (PECARN), Streck, and blunt abdominal trauma in children (BATiC) prediction rules have been published to help guide evaluation of these patients. Pediatric Emergency Care Applied Research Network uses history and physical examination findings, whereas Streck and BATiC use examination plus laboratory and imaging findings. At the time of the study, there was not a protocol that was more routinely sited. Our goal was to compare these different prediction rules. Methods: This was a retrospective electronic chart review of all children younger than 18 years presenting for either level 1 or 2 trauma activations at our pediatric emergency department (ED) between June 1, 2015, to June 30, 2017. Charts were manually reviewed for a mechanism concerning for abdominal trauma, and demographic data, history and physical examination findings, laboratory and imaging results per prediction rules, and revisits in 7 days were collected. The prediction rules were applied to all charts that had all data necessary. For study purposes, a score of zero for PECARN and Streck, and score of  $\leq 5$  for modified BATiC (mBATiC) were defined as "low risk." Patients with no CT, negative CT, and no new injury found on revisit were classified as "no IAI identified," and patients with positive CT or revisit with injury found as "IAI identified." The results were compared via Fisher exact test. Results: A total of 249 patients met the inclusion criteria with a median age of 12 years. Of the low-risk patients, 119 (98.7%) of 121 in PECARN group, 21 (100%) of 21 in Streck, and 48 (85.7%) of 56 in mBATiC group had no IAI identified. None of the low-risk patients required any intra-abdominal intervention. No missed IAI was identified during revisit review. Negative predictive values of all 3 rules were significant for PECARN, Streck, and mBATiC (98.35%, 100%, and 85.71%, respectively). Overall, 27 patients had positive CT results for IAI. Conclusions: The PECARN and Streck rules have high negative predictive values to predict low-risk patients who do not require CT. When laboratory studies are not obtained, PECARN is an effective means of excluding IAI for low-risk patients. When laboratory tests were obtained, the Streck rule performed well. Overall, the results are similar to the past individual studies done on each individual rule. History and physical examination findings are of high importance in pediatric trauma. This study supports limited imaging when no abnormal findings are present in children with blunt torso trauma. This is the only study found in the literature that has compared 3 different prediction rules.

**Page TP**, Werner L, Ellis N and Heczko JB (2021). "'S' means stop! Critical examination of capsular tension ring movements with Miyake-Apple video analysis." Journal of Cataract and Refractive Surgery 47(3): 379-384.

[Full Text](#)

#### *Department of Ophthalmology*

Purpose: To examine capsular tension ring (CTR) implantation to establish whether there are predictable movements of the CTR during deployment, indicating complicated vs uneventful implantation. Setting: Intermountain Ocular Research Center, John A. Moran Eye Center, University of Utah, Salt Lake City, Utah. Design: Experimental study. Methods: Nine cadaver eyes were prepared using standard Miyake-Apple protocol with digital video recording. A 4 o'clock zonular dialysis was created, followed by a capsulorhexis and hydrodissection. In 4 eyes, a suture-guided CTR (SGCTR) injector and 8-0 nylon suture through the leading eyelet served as a visible tracer for the CTR. In 5 eyes, a standard CTR was used. The movements of the CTR during implantation were observed. Results: In all eyes, SGCTR and CTR movements were predictable during implantation. All CTRs displayed cardinal movements within the injector, initially adjacent to the side of the inner diameter of the CTR. As the CTR made contact with lens or capsule, it shifted first to the center and then to the opposite side of the injector lumen. The appearance of an S-curve in the surgeon's view coincided with an obstruction of the leading eyelet and stress on the zonular fibers, as viewed with Miyake-Apple analysis. Conclusions: Traumatic CTR implantation might be avoided by understanding the characteristics of uneventful insertion vs an insertion complicated by entrapment or entanglement of the CTR. By recognizing the abnormal movements of the CTR associated with an obstruction, a surgeon might avoid iatrogenic complications.

Park P, Chang V, Yeh HH, Schwalb JM, Nerenz DR, Schultz LR, Abdulhak MM, **Easton R, Perez-Cruet M**, Kashlan ON, Oppenlander ME, Szerlip NJ, Swong KN and Aleem IS (2021). "Impact of Michigan's new opioid prescribing laws on spine surgery patients: Analysis of the Michigan Spine Surgery Improvement Collaborative." Journal of Neurosurgery: Spine 34(3): 531-536.

[Request Form](#)

#### *Department of Orthopaedic Surgery*

#### *Department of Neurosurgery*

Objective: In 2017, Michigan passed new legislation designed to reduce opioid abuse. This study evaluated the impact of these new restrictive laws on preoperative narcotic use, short-term outcomes, and readmission rates after spinal surgery. Methods: Patient data from 1 year before and 1 year after initiation of the new opioid laws (beginning July 1, 2018) were queried from the Michigan Spine Surgery Improvement Collaborative database. Before and after implementation of the major elements of the new laws, 12,325 and 11,988 patients, respectively, were treated. Results: Patients before and after passage of the opioid laws had generally similar demographic and surgical characteristics. Notably, after passage of the opioid laws, the number of patients taking daily narcotics preoperatively decreased from 3783 (48.7%) to 2698 (39.7%;  $p < 0.0001$ ). Three months postoperatively, there were no differences in minimum clinically important difference (56.0% vs 58.0%,  $p = 0.1068$ ), numeric rating scale (NRS) score of back pain (3.5 vs 3.4,  $p = 0.1156$ ), NRS score of leg pain (2.7 vs 2.7,  $p = 0.3595$ ), satisfaction (84.4% vs 84.7%,  $p = 0.6852$ ), or 90-day readmission rate (5.8% vs 6.2%,  $p = 0.3202$ ) between groups. Although there was no difference in readmission rates, pain as a reason for readmission was marginally more common (0.86% vs 1.22%,  $p = 0.0323$ ). Conclusions: There was a meaningful decrease in preoperative narcotic use, but notably there was no apparent negative impact on postoperative recovery, patient satisfaction, or short-term outcomes after spinal surgery despite more restrictive opioid prescribing. Although the readmission rate did not significantly increase, pain as a reason for readmission was marginally more frequently observed.

Parzen JS, Quinn TJ, Thompson AB, Chang P, Collins SP, Suy S, Michalski JM, Mantz CA, **Seymour Z** and **Hamstra DA** (2021). "Evaluating the correlation between early and late quality-of-life declines using the Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP) after definitive stereotactic body radiotherapy, intensity-modulated radiotherapy, or brachytherapy for prostate cancer." Journal of Clinical Oncology 39(6 SUPPL): 214.

[Full Text](#)

#### *Department of Radiation Oncology*

Background: Multiple authorities including an NCI Taskforce have recommended routine evaluation of patient reported outcomes (PRO) in cancer care. The Expanded Prostate Cancer Index Composite for Clinical Practice (EPIC-CP) is a single-page quality-of-life (QOL) tool which is easily integrated into routine clinical practice. The EPIC-CP has 5 domains (each scored 0-12). The present study evaluated whether early clinically significant changes in EPIC-CP were correlated with later changes in patients undergoing definitive

radiotherapy (RT) for prostate cancer. Methods: A cohort of 979 patients including the PROSTQA study and 3 other institutions with prospective QOL data pooled for analysis were evaluated for patient-reported outcomes. Patients were treated with definitive low-dose rate brachytherapy (n=284), intensity-modulated RT (n=251), or stereotactic body RT (n=444). EPIC-CP scores were derived based upon responses to the EPIC-26. Data were evaluated using minimal clinically important difference (MCID) thresholds to compare QOL at 1-2 months and 24 months from baseline. Univariate analysis was used to assess the correlation between early and late MCID changes. Results: On univariate analysis, early  $\geq 1$  MCID change from baseline was strongly associated with a late  $\geq 1$  MCID across all 5 domains (urinary incontinence, urinary irritation/obstruction, bowel, sexual, and vitality/hormonal) within EPIC-CP and for the overall EPIC-CP score (Table). When MCID was instead defined as 1 or 3, early toxicity remained predictive of late toxicity for all domains and the overall EPIC-CP score. Conclusions: The EPICCP is an easy-to-use QOL assessment with clinically relevant outcomes. Early QOL decline was strongly associated with late QOL decline in patients undergoing definitive RT for prostate cancer across all EPIC-CP domains. Patients with early QOL decline may be candidates for early QOL-based interventions to alleviate their late toxicity burden from treatment.

**Pastewski J**, Baker D, Somerset A, **Leonard K**, Azzie G, **Roach VA**, **Ziegler K** and **Brahmamdam P** (2021). "Analysis of instrument motion and the impact of residency level and concurrent distraction on laparoscopic skills." *Journal of Surgical Education* 78(1): 265-274.

[Full Text](#)

*Department of Surgery*

*Department of Foundational Medical Studies (OU)*

*OUWB Medical Student Author*

Objective: Using a laparoscopic box trainer fitted with motion analysis trackers and software, we aim to identify differences between junior and senior residents performing the peg transfer task, and the impact of a distracting secondary task on performance. Design: General surgery residents were asked to perform the laparoscopic peg transfer task on a trainer equipped with a motion tracker. They were also asked to perform the laparoscopic task while completing a secondary task. Extreme velocity and acceleration events of instrument movement in the 3 rotational degrees of freedom were measured during task completion. The number of extreme events, defined as velocity or acceleration exceeding 1 SD above or below their own mean, were tabulated. The performance of junior residents was compared to senior residents. Setting: Simulation learning institute, Beaumont Hospital, Royal Oak, Michigan. Participants: Thirty-seven general surgery residents from Beaumont Hospital, Royal Oak. Results: When completing the primary task alone, senior residents executed significantly fewer extreme motion events specific to acceleration in pitch (16.63 vs. 20.69,  $p = 0.04$ ), and executed more extreme motion events specific to velocity in roll (16.14 vs. 15.11,  $p = 0.038$ ), when compared to junior residents. With addition of a secondary task, senior residents had fewer extreme acceleration events specific to pitch, (14.69 vs. 22.22,  $p < 0.001$ ). Conclusions: While junior and senior residents completed the peg transfer task with similar times, motion analysis identified differences in extreme motion events between the groups, even when a secondary task was added. Motion analysis may prove useful for real-time feedback during laparoscopic skill acquisition.

Patel A, Wietek S and **Dabrowski E** (2021). "Development of the Hygiene Extension Limb Position Pain (HELP) tool to monitor waning of clinical efficacy in patients with spasticity or cervical dystonia treated with botulinum toxins." *Toxicon* 190: S57-S57.

[Full Text](#)

*Department of Physical Medicine and Rehabilitation*

Patel SN, **Mahmoud TH**, Kazahaya M and Todorich B (2021). "Autologous neurosensory retinal transplantation: Bridging the gap." *Retina*. ePub Ahead of Print.

[Full Text](#)

*Department of Ophthalmology*

Purpose: To review the autologous retinal transplantation (ART) surgical technique, indications, rationale, and current outcomes of data published to date. Methods: Review of surgical technique, pre- and postoperative best-corrected visual acuity (BCVA), and macular hole (MH) closure rate in studies with at least 5 eyes. Results: The weighted average MH closure rate is 88% with a MH closure rate ranging from 66.7-100%. The

weighted average BCVA improved from mean logMAR of 1.35 (Snellen equivalent of 20/450) preoperatively to mean logMAR 1.02 (Snellen equivalent of 20/210) postoperatively. From the largest ART case series, 37% of patients gained 3 or more lines of visual acuity after ART for primary or refractory MHs and 74% gained 3 or more lines of visual acuity after ART for MH-retinal detachments. Functional improvement including negative Watzke-Allen sign and conversion from positive to negative scotoma was reported in large case series. Conclusion: ART is a promising technique for closure of large and refractory MHs otherwise difficult to repair with conventional techniques. This technique may allow for replacement of neural tissue in the macula through cell rehabilitation and regeneration through presumed ectopic synaptogenesis, retinal progenitor cell differentiation and integration, and/or retinal progenitor cell material transfer to host neurons.

**Pathangey G**, Fadadu PP, **Hospodar AR** and **Abbas AE** (2021). "Angiotensin-converting enzyme 2 and COVID-19: Patients, comorbidities, and therapies." *American Journal of Physiology - Lung Cellular and Molecular Physiology* 320(3): L301-L330.

[Full Text](#)

*Department of Internal Medicine*

*OUWB Medical Student Author*

On March 11, 2020, the World Health Organization declared coronavirus disease 2019 (COVID-19) a pandemic, and the reality of the situation has finally caught up to the widespread reach of the disease. The presentation of the disease is highly variable, ranging from asymptomatic carriers to critical COVID-19. The availability of angiotensin-converting enzyme 2 (ACE2) receptors may reportedly increase the susceptibility and/or disease progression of COVID-19. Comorbidities and risk factors have also been noted to increase COVID-19 susceptibility. In this paper, we hereby review the evidence pertaining to ACE2's relationship to common comorbidities, risk factors, and therapies associated with the susceptibility and severity of COVID-19. We also highlight gaps of knowledge that require further investigation. The primary comorbidities of respiratory disease, cardiovascular disease, renal disease, diabetes, obesity, and hypertension had strong evidence. The secondary risk factors of age, sex, and race/ genetics had limited-to-moderate evidence. The tertiary factors of ACE inhibitors and angiotensin II receptor blockers had limited- to-moderate evidence. Ibuprofen and thiazolidinediones had limited evidence.

Pendell Meyers H, Bracey A, Lee D, Lichtenheld A, Li WJ, Singer DD, **Rollins Z**, Kane JA, Dodd KW, Meyers KE, Shroff GR, Singer AJ and Smith SW (2021). "Accuracy of OMI ECG findings versus STEMI criteria for diagnosis of acute coronary occlusion myocardial infarction." *International Journal of Cardiology Heart & Vasculature* 33: 100767.

[Full Text](#)

*OUWB Medical Student Author*

Objective: In the STEMI paradigm of Acute Myocardial Infarction (AMI), many NSTEMI patients have unrecognized acute coronary occlusion MI (OMI), may not receive emergent reperfusion, and have higher mortality than NSTEMI patients without occlusion. We have proposed a new OMI vs. Non-Occlusion MI (NOMI) paradigm shift. We sought to compare the diagnostic accuracy of OMI ECG findings vs. formal STEMI criteria for the diagnosis of OMI. We hypothesized that blinded interpretation for predefined OMI ECG findings would be more accurate than STEMI criteria for the diagnosis of OMI. Methods: We performed a retrospective case-control study of patients with suspected acute coronary syndrome. The primary definition of OMI was either 1) acute TIMI 0-2 flow culprit or 2) TIMI 3 flow culprit with peak troponin T  $\geq$  1.0 ng/mL or I  $\geq$  10.0 ng/mL. Results: 808 patients were included, of whom 49% had AMI (33% OMI; 16% NOMI). Sensitivity, specificity, and accuracy of STEMI criteria vs Interpreter 1 using OMI ECG findings among 808 patients were 41% vs 86%, 94% vs 91%, and 77% vs 89%, and for Interpreter 2 among 250 patients were 36% vs 80%, 91% vs 92%, and 76% vs 89%. STEMI(-) OMI patients had similar infarct size and mortality as STEMI(+) OMI patients, but greater delays to angiography. Conclusions: Blinded interpretation using predefined OMI ECG findings was superior to STEMI criteria for the ECG diagnosis of Occlusion MI. These data support further investigation into the OMI vs. NOMI paradigm and suggest that STEMI(-) OMI patients could be identified rapidly and noninvasively for emergent reperfusion using more accurate ECG interpretation.

Pezzella A, McCrery R, Lane F, Benson K, Taylor C, Padron O, Blok B, de Wachter S, Gruenenfelder J, Pakzad M, Perrouin-Verbe MA, van Kerrebroeck P, Mangel J, **Peters K**, Kennelly M, Shapiro A, Lee U, Comiter C, Mueller M and

Goldman HB (2021). "Two-year outcomes of the ARTISAN-SNM study for the treatment of urinary urgency incontinence using the Axonics rechargeable sacral neuromodulation system." *Neurourology and Urodynamics* 40(2): 714-721.

[Full Text](#)

*Department of Urology*

Aims: Sacral neuromodulation (SNM) is a guideline-recommended treatment with proven therapeutic benefit for urinary urgency incontinence (UUI) patients. The Axonics (R) System is the first Food and Drug Administration-approved rechargeable SNM system and is designed to deliver therapy for a minimum of 15 years. The ARTISAN-SNM study was designed to evaluate UUI participants treated with the Axonics System. Two-year follow-up results are presented. Methods: One hundred and twenty-nine UUI participants underwent implantation with the Axonics System. Therapeutic response rate, participant quality of life (QoL), and satisfaction were determined using 3-day voiding diaries, ICIQ-OABqol, and satisfaction questionnaires. Participants were considered responders if they had a 50% or greater reduction in UUI episodes post-treatment. As-treated and Completers analyses are presented. Results: At 2 years, 93% of the participants (n = 121 Completers at 2 years) were therapy responders, of which 82% achieved  $\geq 75\%$  reduction in UUI episodes and 37% were dry (100% reduction). Daily UUI episodes reduced from 5.6  $\pm$  0.3 at baseline to 1.0  $\pm$  0.2 at 2 years. Statistically significant improvements in ICIQ-OABqol were reported. All participants were able to recharge their device and 94% of participants reported that the recharging frequency and duration were acceptable. Participant demographics nor condition severity were correlated with clinical outcomes or recharging experience. No unanticipated or serious device-related adverse events occurred. Conclusions: At 2 years, participants treated with the Axonics System demonstrated sustained safety and efficacy, high levels of satisfaction with therapy and recharging. Participant-related factors were not associated with efficacy or recharging outcomes, indicating the reported results are applicable to a diverse population.

Purohit E, **Karimipour D** and Madder RD (2021). "Multiple cutaneous cancers in an interventional cardiologist: Predominance in unprotected skin nearest the radiation source." *Cardiovascular Revascularization Medicine*. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

A 70 year-old interventional cardiologist, who worked in the cardiac catheterization laboratory for  $>35$  years, developed multiple skin cancers in regions not conventionally covered by protective lead apparel. The majority of lesions were left-sided, representing cutaneous regions in closest proximity to the radiation source. Although skin not covered by lead apparel often receives frequent sun exposure, a known risk factor for skin cancer, malignancies resulting exclusively from sun exposure would not in most cases be expected to have a left-sided predominance. Additional research is warranted to study the potential link between occupational radiation exposure and skin cancer risk.

**Radhakrishna U**, Vishweswaraiah S, Uppala LV, Szymanska M, **Macknis J**, Kumar S, **Saleem-Rasheed F**, Aydas B, Forray A, Muvvala SB, Mishra NK, Guda C, Carey DJ, Metpally RP, Crist RC, Berrettini WH and **Bahado-Singh RO** (2021). "Placental DNA methylation profiles in opioid-exposed pregnancies and associations with the neonatal opioid withdrawal syndrome." *Genomics* 113(3): 1127-1135.

[Full Text](#)

*Department of Pathology*

*Department of Obstetrics and Gynecology*

*Department of Pediatrics*

Opioid abuse during pregnancy can result in Neonatal Opioid Withdrawal Syndrome (NOWS). We investigated genome-wide methylation analyses of 96 placental tissue samples, including 32 prenatally opioid-exposed infants with NOWS who needed therapy (+Opioids/+NOWS), 32 prenatally opioid-exposed infants with NOWS who did not require treatment (+Opioids/-NOWS), and 32 prenatally unexposed controls (-Opioids/-NOWS, control). Statistics, bioinformatics, Artificial Intelligence (AI), including Deep Learning (DL), and Ingenuity Pathway Analyses (IPA) were performed. We identified 17 dysregulated pathways thought to be important in the pathophysiology of NOWS and reported accurate AI prediction of NOWS diagnoses. The DL had an AUC (95% CI) = 0.98 (0.95-1.0) with a sensitivity and specificity of 100% for distinguishing NOWS from the +Opioids/-NOWS group and AUCs (95% CI) = 1.00 (1.0-1.0) with a sensitivity and specificity of 100%

for distinguishing Nows versus control and + Opioids/-Nows group versus controls. This study provides strong evidence of methylation dysregulation of placental tissue in Nows development.

Rahi MS, Jindal V, Reyes S-P, Gunasekaran K, Gupta R and **Jaiyesimi I** (2021). "Hematologic disorders associated with COVID-19: A review." *Annals of Hematology* 100(2): 309-320.

[Full Text](#)

*Department of Internal Medicine*

Coronavirus disease 2019 is caused by severe acute respiratory syndrome coronavirus 2. Primarily an infection of the lower respiratory tract, it is now well known to cause multisystem abnormalities. Hematologic manifestations constitute a significant area of concern. Severe acute respiratory syndrome coronavirus 2 infects monocytes and endothelial cells leading to a complex downstream cascade, cytokine storm, and eventual intravascular thrombosis. Coronavirus disease 2019 causes lymphopenia, neutrophilia, and thrombocytopenia. Prophylactic anticoagulation is vital in patients with coronavirus disease 2019, as its effect on the coagulation system is associated with significant morbidity and mortality. The disease can cause both arterial and venous thromboses, especially pulmonary embolism and pulmonary microthrombi. A high index of suspicion is indispensable in recognizing these complications, and timely institution of therapeutic anticoagulation is vital in treating them. Virus-induced disseminated intravascular coagulation is uncommon but shares some similarities to sepsis-induced disseminated intravascular coagulation. Marked elevations in hematologic biomarkers such as lactate dehydrogenase, D-dimer, ferritin, and C-reactive protein are associated with worse outcomes. Understanding the pathophysiology and recognizing factors associated with poor prognosis are crucial in improving patient outcomes with coronavirus disease 2019.

**Ramanathan S**, Ramanathan S, Korman A, **Ballouz S**, Ghilezan M, **Levin M**, Wojno K, Martinez A, **Korman H** and Balaraman S (2021). "The positive impact of implementing an onsite guideline-based genetic testing procedure for prostate cancer in a multidisciplinary uro-oncology clinic." *Journal of Clinical Oncology* 39(6 SUPPL): 234.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Internal Medicine*

*Department of Urology*

Background: Prior to the guidelines set forth by the 2017 Philadelphia consensus conference, genetic testing for prostate cancer was conducted based on personal and family history of malignancies pursuant to NCCN recommendations. The 2017 guidelines expanded testing criteria to include age at diagnosis, metastatic disease, and tumor sequencing. In spite of these advancements, limited literature is available regarding successful implementation of a streamlined system for genetic testing in prostate cancer. This paper explores the benefits of implementing an on-site guideline-based genetic testing process for prostate cancer patients treated at a multi-disciplinary uro-oncology practice. Methods: Data was retrospectively reviewed for 561 prostate cancer patients seen in a multi-disciplinary uro-oncology clinic since January 2017. Prior to January 1, 2019 genetic testing was recommended to patients based on NCCN guidelines, and swabs for testing were procured off-site less than 1 mile from the clinic (n=107). After January 1, 2019 genetic testing was recommended based on the guidelines set forth by the Philadelphia consensus conference, and swabs for testing were procured at the clinic itself (n=454). Results: A statistically significant increase in compliance with genetic testing was observed after the implementation of an on-site, guideline-based testing process. Patient compliance with genetic testing increased from 33.6% to 96.5%. The time to receive the genetic test results (calculated as the time between referral for genetic testing and obtaining the test results) was also significantly improved from 38 days to 21 days. Conclusions: The implementation of an onsite, guideline-based genetic testing model for prostate cancer patients significantly improved compliance with genetic testing to 96.5% and decreased the time to receive genetic test results by 17 days. Overall, adopting a guideline based model with on-site genetic testing has the potential to significantly improve the detection rate for pathogenic and actionable mutations, increase the utilization of targeted therapies, and increase cascade testing to include at-risk family members.

Rao P, Kaiser R, Lum F, Atchison E, Parke DW and **Williams GA** (2021). "Reoperation rates of patients undergoing primary noncomplex retinal detachment surgery in a cohort of the IRIS Registry." *American Journal of Ophthalmology* 222: 69-75.

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### *Department of Ophthalmology*

Purpose: To present the reoperation rates of patients who underwent a primary noncomplex RD repair in a cohort of the American Academy of Ophthalmology IRIS Registry. Design: Retrospective, nonrandomized comparative clinical study. Methods: This was a retrospective, nonrandomized cohort study of patients who underwent a primary noncomplex RD repair with either a scleral buckle (SB) or vitrectomy with or without scleral buckle (PPV±SB) between 2013 and 2016. The primary outcome was the odds of reoperation within 12 months. Results: Of 24,068 patients, 2,937 patients (12.2%) underwent an SB and 21,131 patients (87.8%) a PPV ± SB. The overall reoperation rate was 12.2% for SB and 11.6% for PPV ± SB. After multivariate adjustment for age and initial RD diagnosis, the PPV ± SB group exhibited a lower odds of reoperation within 12 months compared with SB only (OR 0.84, 95% CI 0.75-0.96, P = .007). However, there was an age interaction. Patients ≤50 years old with PPV ± SB exhibited a higher odds of reoperation (OR 1.46, 95% CI 1.14-1.88, P = .003) compared to SB only. Patients >50 years with PPV ± SB had a lower odds of reoperation (OR 0.73, 95% CI 0.63-0.84, P < .0001). Conclusion: The odds of reoperation of PPV ± SB compared with SB only varies depending on the patient's age. Further subset analyses are required to determine if there are clinically relevant differences with respect to RD configuration or other RD repair types (PPV only vs PPV with SB).

Ray TN, Lanni DJ, Parkhill MR, **Duong TV**, Pickett SM and Burgess-Proctor AK (2021). "Interpersonal violence victimization among youth entering college: A preliminary analysis examining the differences between LGBTQ and non-LGBTQ youth." *Violence and Gender*. ePub Ahead of Print.

## [Request Form](#)

### *OUWB Medical Student Author*

Evidence from the literature suggests that lesbian, gay, bisexual, transgender, and queer (LGBTQ) people are at greater risk of experiencing sexual victimization (SV) and intimate partner physical violence (IPPV) than their heterosexual and cisgender peers. Although there has been a plethora of recent research investigating the victimization experiences among LGBTQ adults, little research has examined victimization among LGBTQ youth. The current study consists of a preliminary analysis that compares the prevalence rates of SV and IPPV between LGBTQ and non-LGBTQ youth entering college. First-year students at a large Midwestern university were asked to complete an online questionnaire containing comprehensive measures of SV and IPPV. Results suggested that LGBTQ youth (n = 41) experienced higher rates of nearly every type of violent victimization when compared with their non-LGBTQ peers (n = 350). These results support previous research, which suggests LGBTQ people are at increased risk to be sexually and physically victimized. The results also extended the extant literature by utilizing a subsample of LGBTQ youth, among whom there is a particular dearth of research, relative to adults. This research is a step toward understanding the types of victimization experiences encountered by LGBTQ youth and provides descriptive details that may help to inform future research, school policy, and interventions aimed at improving the safety, health, and well-being of the LGBTQ community.

**Rebner M** and **Pai VR** (2021). "Breast cancer screening recommendations: African American women are at a disadvantage." *Journal of Breast Imaging* 3(2): 262-262.

## [Full Text](#)

### *Department of Diagnostic Radiology and Molecular Imaging*

Since 1990, breast cancer mortality has decreased by 40% in white women but only 26% in African American women. The age at diagnosis of breast cancer is younger in black women. Breast cancer diagnosed before age 50 represents 23% of all breast cancers in African American women but only 16% of all breast cancers in white women. White women have a higher incidence of breast cancer over the age of 60. Tumor subtypes also vary among racial and ethnic groups. The triple-negative (TN) subtype, which has a poorer outcome and occurs at a younger age, represents 21% of invasive breast cancers in black women but only 10% of invasive breast cancers in white women. The hormone receptor-positive subtype, which is more common in older women and has the best outcome, has a higher incidence in white women (70%) than in black women (61%). The BRCA2 mutation is also more common in black women than in white women (other than those who are of Ashkenazi Jewish ancestry). There are also many barriers to screening. Major ones include the lack of contact with a primary health care provider as well as a decreased perceived risk of having breast cancer in

the African American population. Given the younger age of onset and the higher incidence of the TN molecular subtype, following breast cancer screening guidelines that do not support screening before the age of 50 may disadvantage black women.

Reynolds WS, Suskind AM, Anger JT, Brucker BM, Cameron AP, Chung DE, Daignault-Newton S, Lane G, Lucioni A, Mourtzinou AP, **Padmanabhan P**, Reyblat PX, Smith AL and Lee UJ (2021). "Incomplete bladder emptying and urinary tract infections after onabotulinumtoxin A injection for overactive bladder in men and women: Multi-institutional collaboration from the Sufu Research Network." *Neurourology and Urodynamics* 40: S72-S72.

[Full Text](#)

*Department of Urology*

Roberts LH, Volin J, McCartney T, Vollstedt A and **Peters K** (2021). "Stimwave(R) for pudendal neuralgia." *Neurourology and Urodynamics* 40: S154-S155.

[Full Text](#)

*Department of Urology*

Romero R, Pacora P, Kusanovic JP, Jung E, Panaitescu B, Maymon E, Erez O, Berman S, Bryant DR, Gomez-Lopez N, Theis KR, Bhatti G, Kim CJ, Yoon BH, Hassan SS, Hsu CD, Yeo L, Diaz-Primera R, Marin-Concha J, Lannaman K, **Alhousseini A**, Gomez-Roberts H, Varrey A, Garcia-Sanchez A and Gervasi MT (2021). "Clinical chorioamnionitis at term X: Microbiology, clinical signs, placental pathology, and neonatal bacteremia - Implications for clinical care." *Journal of Perinatal Medicine* 49(3): 275-298.

[Full Text](#)

*Department of Obstetrics & Gynecology*

**Objectives:** Clinical chorioamnionitis at term is considered the most common infection-related diagnosis in labor and delivery units worldwide. The syndrome affects 5-12% of all term pregnancies and is a leading cause of maternal morbidity and mortality as well as neonatal death and sepsis. The objectives of this study were to determine the (1) amniotic fluid microbiology using cultivation and molecular microbiologic techniques; (2) diagnostic accuracy of the clinical criteria used to identify patients with intraamniotic infection; (3) relationship between acute inflammatory lesions of the placenta (maternal and fetal inflammatory responses) and amniotic fluid microbiology and inflammatory markers; and (4) frequency of neonatal bacteremia. **Methods:** This retrospective cross-sectional study included 43 women with the diagnosis of clinical chorioamnionitis at term. The presence of microorganisms in the amniotic cavity was determined through the analysis of amniotic fluid samples by cultivation for aerobes, anaerobes, and genital mycoplasmas. A broad-range polymerase chain reaction coupled with electrospray ionization mass spectrometry was also used to detect bacteria, select viruses, and fungi. Intra-amniotic inflammation was defined as an elevated amniotic fluid interleukin-6 (IL-6) concentration  $\geq 2.6$  ng/mL. **Results:** (1) Intra-amniotic infection (defined as the combination of microorganisms detected in amniotic fluid and an elevated IL-6 concentration) was present in 63% (27/43) of cases; (2) the most common microorganisms found in the amniotic fluid samples were *Ureaplasma* species, followed by *Gardnerella vaginalis*; (3) sterile intra-amniotic inflammation (elevated IL-6 in amniotic fluid but without detectable microorganisms) was present in 5% (2/43) of cases; (4) 26% of patients with the diagnosis of clinical chorioamnionitis had no evidence of intra-amniotic infection or intra-amniotic inflammation; (5) intra-amniotic infection was more common when the membranes were ruptured than when they were intact (78% [21/27] vs. 38% [6/16];  $p=0.01$ ); (6) the traditional criteria for the diagnosis of clinical chorioamnionitis had poor diagnostic performance in identifying proven intra-amniotic infection (overall accuracy, 40-58%); (7) neonatal bacteremia was diagnosed in 4.9% (2/41) of cases; and (8) a fetal inflammatory response defined as the presence of severe acute funisitis was observed in 33% (9/27) of cases. **Conclusions:** Clinical chorioamnionitis at term, a syndrome that can result from intra-amniotic infection, was diagnosed in approximately 63% of cases and sterile intra-amniotic inflammation in 5% of cases. However, a substantial number of patients had no evidence of intra-amniotic infection or intra-amniotic inflammation. Evidence of the fetal inflammatory response syndrome was frequently present, but microorganisms were detected in only 4.9% of cases based on cultures of aerobic and anaerobic bacteria in neonatal blood.

Ross JR, Clohisy JC, Bedi A and **Zaltz I** (2021). "Why does hip arthroscopy fail? Indications and PEARLS for revision

success." [Sports Medicine and Arthroscopy Review](#) 29(1): 44-51.

[Full Text](#)

*Department of Orthopaedic Surgery*

The surgical treatment of femoroacetabular impingement has been shown to have successful early and mid-term clinical outcomes. Despite these favorable clinical outcomes that have been published in the literature, there is a subgroup of patients that present with continued or recurrent symptoms after surgical treatment. Not only has there been an increase in the number of hip arthroscopy procedures, but also there has been a corresponding increase in the number of revision hip arthroscopy and hip preservation surgeries. Previous studies have reported residual deformity to be the most common reason for revision hip arthroscopy. However, chondral, labral, and capsular considerations also are important when addressing patients not only in the primary but also, the revision setting. In this review, we outline the evaluation and treatment of the patient that presents with continued hip and groin pain after undergoing a hip.

Rund JM, **Hinckel BB** and Sherman SL (2021). "Acute patellofemoral dislocation: Controversial decision-making." [Current Reviews in Musculoskeletal Medicine](#) 14(1): 82-87.

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*Department of Orthopaedic Surgery*

Purpose of Review: The topic of acute patella dislocations is controversial. Discussions revolve around which individuals need early surgery, identification of risk factors, and rehabilitation protocol. The purpose of this review is to discuss the current recommendations for non-operative and/or operative management of first-time dislocators. Recent Findings: Recent studies have made it clear that not all patellar dislocations are the same, not all patients do well with conservative treatment, and risk stratification can identify individuals at high risk of recurrence who would benefit from early surgical intervention. Risk factors that have been identified include younger age, skeletally immature, contralateral instability, trochlear dysplasia, patella alta, increased tibial tubercle-trochlear groove distance, and increased patella tilt. The PAPI (Pediatric and Adolescent Patellar Instability) RCT study and JUPITER (Justifying Patellar Instability Treatment by Early Results) prospective cohort study have been carefully developed, are under way, and will provide further guidance. In summary, the management of acute patellar dislocations is evolving. Surgery for patients with osteochondral loose bodies should include fixation as well as soft tissue stabilization. The standard of care for patients with an acute patellar dislocation without osteochondral loose bodies or fracture is non-operative treatment. However, imaging for all first-time dislocators is indicated to stratify risks and determine risk profile. If an individual is at high risk, soft tissue stabilization may be considered. Still, most patients will be treated non-operatively.

**Safian RD** (2021). "Renal artery stenosis." [Progress in Cardiovascular Diseases](#). ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

Renal artery stenosis is the most common secondary cause of hypertension and predominantly caused by atherosclerosis. In suspected patients, a non-invasive diagnosis with ultrasound is preferred. Asymptomatic, incidentally found RAS does not require revascularization. In symptomatic patients requiring revascularization, renal artery stenting is the preferred therapy. Selecting appropriate patients for revascularization requires careful consideration of lesion severity and is optimized with a multidisciplinary team. All patients with atherosclerotic RAS should be treated with guideline-directed medical therapy, including hypertension control, diabetes control, statins, antiplatelet therapy, smoking cessation and encouraging activity.

**Saleh ES** (2021). "Pediatric obturator internus muscle myxoma." [Journal of the American Academy of Orthopaedic Surgeons](#) 5(1) e20.00099.

[Full Text](#)

*Department of Orthopaedic Surgery*

Intramuscular myxoma is a rare benign tumor that presents as a slow-growing, deeply seated mass confined within a skeletal muscle. Histologically, these lesions most resemble umbilical cord tissue. They mostly occur in people between 40 and 70 years old, with a 57% female predilection. These tumors are very rare in children. Only one pediatric intramuscular myxoma case is reported in the literature. The goal of this study is

to report the case of a 13-year-old girl who presented to our hospital emergency department in 2018 with right hip pain, elevated inflammatory markers, and fever; her initial differential diagnosis was hip septic arthritis, pelvic osteomyelitis, and pelvic abscess. A pelvic MRI revealed a well-defined enhancing round lesion in the right obturator internus muscle. The diagnosis was conformed with a CT-guided core biopsy. The patient's symptoms improved with conservative management, and she continues to be doing well 2 years later. Pediatric pelvic intramuscular myxomas are extremely rare; however, they can have a presentation that mimic a more serious condition such as hip septic arthritis, pelvic osteomyelitis, and pelvic abscess and should be considered in the differential diagnosis in a pediatric patient presenting with hip pain.

Salita A, Rosado M, Mack K, **Pui J**, Zekman R and Dinnan K (2021). "Metastatic lobular carcinoma of the breast found incidentally on pathology following cholecystectomy for chronic cholecystitis: A case report." *International Journal of Surgery Case Reports* 80: 105612.

[Full Text](#)

*Department of Pathology*

Background: Traditional oncologic pattern of spread of breast cancer is metastasis to axillary lymph nodes, lung, liver and bone (Doval et al., 2006 [1]). Here we present a case of unknown synchronous breast cancer in a patient that was revealed on histopathologic assessment following elective cholecystectomy. Case Summary: A 57 year old female presented for an elective laparoscopic cholecystectomy secondary to biliary colic. Histopathologic assessment of the gallbladder revealed metastatic adenocarcinoma with signet ring features, consistent with metastatic lobular carcinoma. The patient went on to have a complete oncologic workup that revealed invasive ductal carcinoma with components of high grade ductal carcinoma in situ in the left breast, lobular carcinoma in the right breast, and metastatic lobular carcinoma to left and right axillary lymph nodes as well as diffuse osseous metastatic disease. Conclusions: Metastatic disease to the gallbladder found incidentally on elective cholecystectomy is a rare presentation of synchronous breast cancer.

**Sangal RB** (2021). "Efficacy and safety of esmirzapine in adult insomnia: Unsupported statements about residual daytime effects." *Journal of Clinical Sleep Medicine* 17(2): 341.

[Full Text](#)

*Department of Family Medicine and Community Health*

Sarva H, **Patino GA**, Rashid M, Owens JWM, Robbins MS and Sandrone S (2021). "The status of neurology fellowships in the United States: Clinical needs, educational barriers, and future outlooks." *BMC Medical Education* 21(1): 108.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

The need for subspecialty-trained neurologists is growing in parallel with increasing disease burden. However, despite the immense burden of neurological diseases, like headache and neurodegenerative disorders, recruitment into these subspecialties remains insufficient in the United States. In this manuscript, a group of educators from the American Academy of Neurology's A.B. Baker Section on Neurological Education sought to review and discuss the current landscape of neurology fellowships in the United States, the factors driving fellowship recruitment and the educational barriers. Moreover, suggestions to potentially improve recruitment for under-selected fellowships, which can contribute towards an alignment between neurological education and neurological needs, and future educational scenarios are discussed.

**Schlachter DM-B** and **Black EH** (2021). "Transcanalicular Laser-assisted dacryocystorhinostomy," In Servat JJ, Black EH, Nesi FA, Gladstone GJ and Calvano CJ (ed). *Smith and Nesi's Ophthalmic Plastic and Reconstructive Surgery*. Cham: Springer International Publishing. pp: 589-591.

[Full Text](#)

*Department of Ophthalmology*

Advances in endoscopic and fiberoptic technology have led to the development of innovative, minimally invasive approaches for lacrimal surgery. Lacrimal endoscopy, endocanalicular drilling, trephination, electrocauterization, and endocanalicular laser-assisted dacryocystorhinostomy (ELADCR) are techniques being used to treat nasolacrimal duct obstruction. In the endocanalicular laser-assisted DCR, a laser fiberoptic probe (Fig. 40.1) is inserted in the punctum and advanced along the canaliculus to the

nasolacrimal sac. Once in the sac, the laser is used to make the osteotomy between the sac and middle meatus. Advantages of the ELADCR approach include avoidance of an external scar, improved hemostasis, limited intranasal instrumentation and tissue dissection, decreased operative time, and presumably faster recovery. A variety of lasers have been used in this method, including the argon laser, the holmium (HO):YAG laser, the potassium titanyl phosphate (KTP):YAG laser, the neodymium (Nd):YAG laser, the erbium (Er):YAG laser, and more recently, the diode laser. The diode laser, with a 600-micron fiberoptic probe, is a portable, semiconductor contact laser of 810 nm wavelength that achieves efficient tissue dissection and instant vaporization. The laser coagulates blood vessels with minimal damage to adjacent structures, giving surgeons an alternative method for DCR surgery.

**Sellers T, Ghannam M, Asantey K, Klei J, Olive E and Roach VA** (2021). "An early introduction to surgical skills: Validating a low-cost laparoscopic skill training program purpose built for undergraduate medical education." *American Journal of Surgery* 221(1): 95-100.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Foundational Medical Studies (OU)*

Background: Medical student exposure to laparoscopy is limited to observation despite the prevalence of minimally invasive techniques in practice. The high cost of laparoscopic simulation equipment, commonly called "box trainers", limits undergraduate exposure to skill training. Methods: Students at a Midwestern medical school were recruited to participate in an experimental laparoscopic skill training program. One cohort (n = 17) used a DIY box trainer design freely available on MedEdPORTAL. A second cohort (n = 17) used a commercially available equivalent. Pre- and post-training attempts for four tasks were scored and the difference was calculated. The average differences for each cohort were then contrasted statistically. Results: Significant performance improvements (pre- and post-training) were demonstrated regardless of group allocation. The difference in performance between the cohorts was not significant for any task (p > 0.05). Conclusions: This low-cost training program using DIY box trainers is as effective as commercially available equivalent box trainers for introducing laparoscopic skills to medical students.

Serena TJ, Schnurr CAS, **Pui JC** and Gerken JR (2021). "Surgical excision of sclerosing mesenteritis, exploration of an unknown mesenteric mass." *Cureus* 13(1) e12546.

[Full Text](#)

*Department of Pathology*

Sclerosing mesenteritis is a rare and often benign condition characterized as a fibrotic disease consisting of non-suppurative inflammation of adipose tissue. Through mass effect, sclerosing mesenteritis can compromise the gastrointestinal lumen as well as mesenteric vessel integrity. There is a poor understanding of this disorder and its pathogenesis, which presents with various symptomatology and often without identification of inciting factors. Patients with sclerosing mesenteritis exhibit gastrointestinal and systemic manifestations including weight loss, fever, nausea, vomiting, diarrhea, and abdominal pain. This case presents a patient with a seven-month history of chronic, epigastric abdominal pain following laparoscopic surgery for acute uncomplicated appendicitis. The patient underwent work-up with computed tomography and magnetic resonance enterography that confirmed the presence of a mesenteric mass of unknown etiology located in the mid-epigastrium. Due to the inability to safely sample the mass, the patient underwent diagnostic laparoscopy, which was subsequently converted to an open procedure where excision of the mesenteric lesion was performed. Surgical pathology revealed fat necrosis with fibrosis, granulomatous inflammation, and dystrophic calcifications consistent with sclerosing mesenteritis. The patient was seen in follow-up with the resolution of her epigastric abdominal pain. This case report demonstrates a unique presentation of a symptomatic patient with a mesenteric mass not amenable to non-invasive biopsy. Complete excision of this lesser sac mass revealed sclerosing mesenteritis as the pathological cause.

Shaheen AA, Gill I, Edhi AI, **Amin M** and **Cappell MS** (2021). "Pancreatic ganglioneuroma presenting in an octogenarian." *ACG Case Reports Journal* 8(3): 1-4.

[Full Text](#)

*Department of Pathology*

*Department of Internal Medicine*

Pancreatic ganglioneuromas occur mostly in children and rarely in young adults, with no cases reported in adults older than 60 years. An 86-year-old-woman, with active advanced multiple myeloma, presented with epigastric pain for 2 days. Abdominal and pelvic computed tomography demonstrated a distended gallbladder, mildly dilated biliary tree, and a 13 × 8-mm hypodense mass in pancreatic body, without extrapancreatic invasion at endoscopic ultrasound. Fine-needle endoscopic ultrasound-guided core biopsy revealed characteristic histopathology of ganglioneuroma, as confirmed by immunohistochemical positivity for S100, SOX-10, and synaptophysin. This demonstrates novel finding of pancreatic ganglioneuroma occurring in the elderly. Lesion inclusion in the differential diagnosis may mandate tissue for pathologic diagnosis and complete lesion resection.

**Shannon FL** (2021). "Appreciation of the lifelong repercussions of postoperative atrial fibrillation." *Annals of Thoracic Surgery* 111(2): 554-555.

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*Department of Surgery*

**Sharrak A, Bergsman C and Hamstra D** (2021). "Six-year-old male with acute eye swelling and drainage." *Contemporary Pediatrics* 38: 14-16.

[Full Text](#)

*Department of Pediatrics*

*Department of Radiation Oncology*

*OUIB Medical Student Author*

The article presents a case of a 6-year-old boy who was rushed to his pediatrician due to clear drainage from his left eye for two days. He developed clear nasal drainage and slight redness of his bulbar conjunctiva after treatment of antibiotic eyedrops. He was previously diagnosed by an eye clinic with conjunctivitis and was prescribed with eyedrop containing dexamethasone and antibiotics. He was eventually diagnosed with preseptal cellulitis of the left eye and acute maxillary sinusitis.

**Sharrak A, Jamil M, Bazzi M, Timar R, Kovacevic N and Atiemo H** (2021). "Disparity in female pelvic examination in the evaluation of lower urinary tract symptoms." *Neurourology and Urodynamics* 40: S95-S96.

[Full Text](#)

*OUIB Medical Student Author*

**Sharrak A, Roberts LH, Vollstedt A, Fischer M and Han E** (2021). "Parental leave satisfaction in physicians compared to non-physicians." *Neurourology and Urodynamics* 40: S20-S20.

[Full Text](#)

*OUIB Medical Student Author*

*Department of Urology*

Sheikh MA, Kong X, Haymart B, Kaatz S, Krol G, Kozlowski J, Dahu M, Ali M, **Almany S**, Alexandris-Souphis T, Kline-Rogers E, Froehlich JB and Barnes GD (2021). "Comparison of temporary interruption with continuation of direct oral anticoagulants for low bleeding risk procedures." *Thrombosis Research* 203: 27-32.

[Request Form](#)

*Department of Internal Medicine*

Introduction: Limited data is available on the rates of bleeding and thromboembolic events for patients undergoing low bleeding risk procedures while taking direct oral anticoagulants (DOAC). Methods: Adults taking DOAC in the Michigan Anticoagulation Quality Improvement Initiative (MAQI(2)) database who underwent a low bleeding risk procedure between May 2015 and Sep 2019 were included. Thirty-day bleeding (of any severity), thromboembolic events, and death were compared between DOAC temporarily interrupted and continued uninterrupted groups. Adverse event rates were compared using an inverse probability weighting propensity score. Results: There were 820 patients who underwent 1412 low risk procedures. DOAC therapy was temporarily interrupted in 371 (45.2%) patients (601 [42.6%] procedures) and continued uninterrupted in 449 (54.8%) patients (811 [57.4%] procedures). DOAC patients with temporary interruptions were more likely to have diabetes, prior stroke or TIA, prior bleeding, higher CHA2DS2-VASc,

and higher modified HAS-BLED scores. DOAC interruption was common for gastrointestinal endoscopy, electrophysiology device implantation, and cardiac catheterization while it was less common for cardioversion, dermatologic procedures, and subcutaneous injection. After propensity score adjustment, bleeding risk was lower in the DOAC temporary interruption group (OR 0.62, 95% CI 0.41-0.95) as compared to the group with continuous DOAC use. Rates of thromboembolic events and death did not differ significantly between the two groups. Conclusions: DOAC-treated patients undergoing low bleeding risk procedures may experience lower rates of bleeding when DOAC is temporarily interrupted. Prospective studies focused on low bleeding risk procedures are needed to identify the safety DOAC management strategy.

Sherman SL, Rund JM, **Hinckel BB** and Farr J (2021). "Patellar instability," In Brittberg M and Slynarski K (ed). Lower Extremity Joint Preservation: Techniques for Treating the Hip, Knee, and Ankle. Cham: Springer International Publishing. pp: 231-254.

[Full Text](#)

*Department of Orthopaedic Surgery*

The evaluation and management of patellofemoral instability is complex and multifactorial. Variability in patient symptoms and the pathology of the underlying bony and soft tissue make it difficult to form precise treatment guidelines and recommendations for individual patients. Risk stratification through recognition of key anatomic and biomechanical factors, functional ability, and patient-specific goals is critical for selection of nonoperative versus operative treatment. This chapter presents a comprehensive approach to the work-up and treatment of patellofemoral instability. Our goal is to integrate anatomy, biomechanics, clinical examination, and imaging studies to guide physicians toward evidence-based recommendations.

Shields RA, Cheng OT and **Wolfe JD** (2021). "Iatrogenic vitreous hemorrhage, subretinal hemorrhage, and branch retinal vein occlusion after YAG laser vitreolysis for symptomatic vitreous floaters." Ophthalmology 128(4): 616.

[Full Text](#)

*Department of Ophthalmology*

Shields RA, Lee IJ, **Brown MM**, Dong LK, Lee R, Wa CA and **Hassan TS** (2021). "Clinical course and characteristics of eyes with recurrent episodes of endophthalmitis." Ophthalmology Retina 5(1): 10-15.

[Request Form](#)

*OUWB Medical Student Author*

*Department of Ophthalmology*

Purpose: Infectious endophthalmitis is a devastating, yet rare, complication after intraocular surgery, trauma, and systemic illness. Given its rare incidence, few patients would be expected to experience more than 1 episode of infectious endophthalmitis in their lifetime. We reviewed our patients who were diagnosed with and treated for at least 2 separate episodes of endophthalmitis. Design: A retrospective, consecutive case series was conducted of patients managed at Associated Retinal Consultants PC (Royal Oak, Michigan) from January 2013 through December 2019. Participants: Patients were identified with the diagnosis of endophthalmitis by International Classification of Diseases, Ninth and Tenth Editions, codes. Methods: Those diagnosed and then treated either with a vitreous tap and intravitreal injection of antibiotics or with pars plana vitrectomy at least twice were included. Those treated multiple times for the same episode of endophthalmitis were excluded. Main Outcome Measures: Cause and risk factors for recurrent endophthalmitis. Results: Charts of 535 patients were reviewed, and 12 patients met inclusion criteria. The median age at initial presentation was 72.5 years, and 33.3% were men. Eight of the 12 patients (66%) experienced recurrent endophthalmitis in the same eye, and 4 of the 12 patients (33%) experienced separate episodes in different eyes. The average time between episodes was 604 days (range, 90–2366 days). The average follow-up from the second episode was 492 days (range, 119–1185 days). The most common cause for both the first and second episodes was recent intravitreal injection (50% and 58.3%, respectively) followed by surgery associated (41.6% and 33.3%, respectively). The cause was the same for the first and second episodes of 8 patients (75%). Of the 24 recorded episodes of endophthalmitis, culture results were positive in 41.6%, with coagulase-negative Staphylococcus being the most common bacteria identified. Conclusions: Recurrent endophthalmitis is rare and seen most commonly after intravitreal injections. Most patients in this series showed culture-negative results. Each successive episode of endophthalmitis was

associated with a worse final visual outcome. The cumulative number of intravitreal injections may be an independent risk factor for recurrent postinjection endophthalmitis.

Shikhare AR, Iqbal RM, **Tariq R, Turner DR, Gebara BM and Freij BJ** (2021). "Diversity of cardiac and gastrointestinal presentations of multisystem inflammatory syndrome in children (MIS-C) Associated with COVID-19: A case series." Global Pediatric Health 8: 2333794x21996613.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Pediatrics*

COVID-19 is generally a benign or asymptomatic infection in children, but can occasionally be severe or fatal. Delayed presentation of COVID-19 with hyperinflammation and multi-organ involvement was recently recognized, designated the Multisystem Inflammatory Syndrome in Children (MIS-C). Six children with MIS-C with molecular and serologic evidence of SARS-CoV-2 infection were admitted to our hospital between May 5, 2020 and June 25, 2020. All had fever and weakness; 4/6 presented with gastrointestinal symptoms. Two children had features of complete Kawasaki disease, 3 had incomplete Kawasaki disease, while 1 had terminal ileitis with delayed onset of circulatory shock. Treatment consisted of intravenous immunoglobulin and aspirin for Kawasaki-like disease. Remdesivir, corticosteroids, and infliximab were used when indicated. Median hospitalization was 7 days. Immediate treatment resulted in rapid clinical improvement. In children presenting with hyperinflammatory syndromes without cardiac manifestations, testing for SARS-CoV-2 RNA and antibodies, with close cardiac monitoring should be pursued due to the manifold presentations of SARS-CoV-2 infection in children.

Siddens JD, Kim JM and **Gladstone GJ** (2021). "Acquired ptosis: Classification and evaluation," In Servat JJ, Black EH, Nesi FA, Gladstone GJ and Calvano CJ (ed). Smith and Nesi's Ophthalmic Plastic and Reconstructive Surgery. Cham: Springer International Publishing. pp: 295-306.

[Full Text](#)

*Department of Ophthalmology*

Blepharoptosis, or ptosis, is a unilateral or bilateral droop of the upper eyelid with the patient's head in the fully upright position and eyes in primary gaze. Patients often seek medical attention because of visual obstruction or cosmetic deformity caused by ptotic lids. Ptosis is often recognized by friends or family but some cases may be seen only by a physician. Ptosis may be an isolated condition, or it may occur from a number of different causes.

Siddens JD, Kim JM and **Gladstone GJ** (2021). "Management of acquired ptosis," In Servat JJ, Black EH, Nesi FA, Gladstone GJ and Calvano CJ (ed). Smith and Nesi's Ophthalmic Plastic and Reconstructive Surgery. Cham: Springer International Publishing. pp: 307-322.

[Full Text](#)

*Department of Ophthalmology*

Ptosis repair is one of the most challenging problems faced by oculoplastic surgeons. There is no single procedure that will suffice for every case, and there is a considerable difference of opinion as to which procedure is the best. Many different techniques have been discussed and tried, and it appears that the procedure of choice rests with the experience of the surgeon and the needs of the patient. In this chapter, the four most common surgical methods of approaching ptosis—frontalis suspension, levator advancement, the Fasanella-Servat operation, and Müller's muscle-conjunctival resection—are discussed.

**Sims M**, Podolsky RH, **Maine GN, Kennedy RH and Homayouni R** (2021). "Reply to authors." Clinical Infectious Diseases. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

*Department of Foundational Medical Studies (OU)*

*Department of Pathology*

Sivandzade F and **Cucullo L** (2021). "Regenerative stem cell therapy for neurodegenerative diseases: An overview." International Journal of Molecular Science 22(4): 2153.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Neurodegenerative diseases resulting from the progressive loss of structure and/or function of neurons contribute to different paralysis degrees and loss of cognition and sensation. The lack of successful curative therapies for neurodegenerative disorders leads to a considerable burden on society and a high economic impact. Over the past 20 years, regenerative cell therapy, also known as stem cell therapy, has provided an excellent opportunity to investigate potentially powerful innovative strategies for treating neurodegenerative diseases. This is due to stem cells' capability to repair injured neuronal tissue by replacing the damaged or lost cells with differentiated cells, providing a conducive environment that is in favor of regeneration, or protecting the existing healthy neurons and glial cells from further damage. Thus, in this review, the various types of stem cells, the current knowledge of stem-cell-based therapies in neurodegenerative diseases, and the recent advances in this field are summarized. Indeed, a better understanding and further studies of stem cell technologies cause progress into realistic and efficacious treatments of neurodegenerative disorders.

**Smith JT**, Jee Y, Daley E, Koueiter DM, Beck M and **Zaltz I** (2021). "Can the Femoro-Epiphyseal Acetabular Roof (FEAR) Index be used to distinguish dysplasia from impingement?" *Clinical Orthopaedics and Related Research* 479(5): 962-971.

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*Department of Orthopaedic Surgery*

*OUWB Medical Student Author*

Background: Classifying hips with structural deformity on the spectrum from impingement to dysplasia is often subjective and frequently inexact. Currently used radiographic measures may inaccurately predict a hip's morphological stability in borderline hips. A recently described radiographic measure, the Femoro-Epiphyseal Acetabular Roof (FEAR) index, has demonstrated an ability to predict stability in the borderline hip. This measure is attractive to clinicians because procedures can be used on the basis of a hip's pathomechanics. This study was designed to further validate and characterize the FEAR index in a skeletally immature population, in hips with dysplasia/femoroacetabular impingement (FAI), and in asymptomatic hips. Questions/Purposes: (1) What are the characteristics of the FEAR index in children and how does the index change with skeletal maturation? (2) How does the FEAR index correlate with clinical diagnosis and surgical treatment in a large cohort of symptomatic hips and asymptomatic controls? (3) How does the FEAR index correlate with clinical diagnosis in the borderline hip (lateral center-edge angle [LCEA] 20°-25°) group? Methods: A total of 220 participants with symptomatic investigational hips with a clinical diagnosis of dysplasia or FAI between January 2008 and January 2018 were retrospectively collected from the senior author's practice. Investigational hips were excluded if they had any femoral head abnormalities preventing LCEA measurement (for example, Perthes disease), Tönnis osteoarthritis grade greater than 1, prior hip surgery, or prior femoral osteotomy. In the 220 participants, 395 hips met inclusion criteria. Once exclusion criteria were applied, 15 hips were excluded due to prior hip surgery or prior femoral osteotomy, and 12 hips were excluded due to femoral head deformity. A single hip was then randomly selected from each participant, resulting in 206 investigational hips with a mean age of 13 ± 3 years. Between January 2017 and December 2017, 70 asymptomatic control participants were retrospectively collected from the senior author's institutional trauma database. Control hips were included if the AP pelvis film had the coccyx centered over the pubic symphysis and within 1 to 3 cm of the superior aspect of the symphysis. Control hips were excluded if there was any fracture to the pelvis or ipsilateral femur or the participant had prior hip/pelvis surgery. After exclusion criteria were applied, 16 hips were excluded due to fracture. One hip was then randomly selected from each participant, resulting in 65 control hips with a mean age of 16 ± 8 years. Standardized standing AP pelvis radiographs were used to measure the FEAR index, LCEA, and Tönnis angle in the investigational cohort. Standardized false-profile radiographs were used to measure the anterior center-edge angle (ACEA) in the investigational cohort. Two blinded investigators measured the FEAR index with an intraclass correlation coefficient of 0.92 [95% CI 0.84 to 0.96]. Question 1 was answered by comparing the above radiographic measures in age subgroups (childhood: younger than 10 years; adolescence: 10 to 14 years old; maturity: older than 14 years) of dysplastic, FAI, and control hips. Question 2 was answered by comparing the radiographic measures in all dysplastic, FAI, control hips, and a subgroup of operatively or nonoperatively managed dysplasia and FAI hips. Question 3 was answered by comparing the radiographic measures in borderline (LCEA 20°-25°) dysplastic, FAI, and control hips. Results: The FEAR index

was lower in older dysplastic hips (younger than 10 years,  $6^\circ \pm 9^\circ$ ; 10 to 14 years,  $4^\circ \pm 10^\circ$ ; older than 14 years,  $5^\circ \pm 9^\circ$ ;  $p < 0.001$ ) and control hips (younger than 10 years,  $-6^\circ \pm 5^\circ$ ; 10 to 14 years,  $-15^\circ \pm 4^\circ$ ; older than 14 years,  $-16^\circ \pm 7^\circ$ ;  $p < 0.001$ ). The diagnosis and age groups were independently correlated with the FEAR index ( $p < 0.001$ ). The relationship between the FEAR index and diagnosis remained consistent in each age group ( $p = 0.11$ ). The FEAR index was higher in all dysplastic hips (mean  $5^\circ \pm 10^\circ$ ) than in asymptomatic controls (mean  $-13^\circ \pm 7^\circ$ ;  $p < 0.001$ ) and FAI hips (mean  $-10^\circ \pm 11^\circ$ ;  $p < 0.001$ ). Using  $-1.3^\circ$  as a cutoff for FAI/control hips and dysplastic hips, 81% (112 of 139) of hips with values below this threshold were FAI/control, and 89% (117 of 132) of hips with values above  $-1.3^\circ$  were dysplastic. The receiver operator characteristics area under the curve (ROC-AUC) was 0.91. Similarly, the FEAR index was higher in borderline dysplastic hips than in both asymptomatic borderline controls ( $p < 0.001$ ) and borderline FAI hips ( $p < 0.001$ ). Eighty-nine percent (33 of 37) of hips with values below this threshold were FAI/control, and 90% (37 of 41) of hips with values above  $-1.3^\circ$  were dysplastic. The ROC-AUC for borderline hips was 0.86. Conclusion: The FEAR index was associated with the diagnosis of hip dysplasia and FAI in a patient cohort with a wide age range and with varying degrees of acetabular deformity. Specifically, a FEAR index greater than  $-1.3^\circ$  is associated with a dysplastic hip and a FEAR index less than  $-1.3^\circ$  is associated with a hip displaying FAI. Using this reliable, developmentally based radiographic measure may help hip preservation surgeons establish a correct diagnosis and more appropriately guide treatment.

Snajdar E, Ajo AR, Rosen K, Miller R, Mohammed S, Gordon C, **Pui JC** and McIntosh G (2021). "Primary malignant melanoma of the urinary bladder." *Cureus* 13(3) e14067.

[Full Text](#)

*Department of Pathology*

There are only 30 reported cases of primary malignant melanoma of the bladder in the literature so far. Of those, 17 cases were reported as deceased within three years of presentation. Our case reported here is that of a 78-year-old female who presented with a new-onset incontinence and intermittent hematuria. She had no evidence of primary melanoma anywhere else in her body. The patient was treated with cystectomy and ileal conduit with plans for adjuvant chemotherapy. Unfortunately, the patient succumbed to her disease with diffuse metastatic involvement within 16 months of presentation.

**Snyder M**, Vadas J, Musselwhite J, Halford R, **Wilson G**, **Stevens C** and **Yan D** (2021). "Technical note: FLASH radiotherapy monitor chamber signal conditioning." *Medical Physics* 48(2): 791-795.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: Recent studies of ultra-high dose rate FLASH radiotherapy show a substantial reduction of damage to normal tissue cells when compared with conventional radiotherapy. Most, if not all, of these FLASH studies have taken place using either custom research equipment or heavily modified linacs with external dosimetric control. To simplify our preclinical research efforts, we wish to deliver FLASH with a minimally modified linac using the internal dosimetric system. Methods: To enable the built-in monitor chambers to terminate a FLASH beam, we reversibly modified an Elekta linear accelerator previously fit with a high dose rate electron (HDRE) system to include additional resistance in the signal path from the monitor chambers to the dose control system. To produce the FLASH beam, we altered the energy calibration tables of a decommissioned HDRE beam to functionally produce a photon mode beam current exiting through the electron window of the linac. We then used the machine modifications to assist in beam tuning and to calibrate the monitor chambers for FLASH delivery. We employed a radiochromic film for external dosimetry and preliminary tests of monitor chamber dosimetric stability. Results: We identified attenuation values and distributions that reduced the overall signal from the monitor chambers to the dose control system such that the system could terminate the beam without input from external monitoring circuits. Calibration of the control system resulted in 12 MU per second, constituting roughly 180 Gy at the mylar window. Preliminary tests indicate a linear MU to dose relationship at FLASH dose rates, but we encountered challenges in both dose resolution and repeatability of beam termination. Conclusions: The addition of attenuation in the control system path from the monitor chambers is fundamentally identical to current HDRE system design and was achieved without significant modification of the accelerator. Preliminary results indicate that current-generation monitor chambers could potentially govern FLASH radiotherapy, but overall beam and monitor chamber stability issues may necessitate machine modifications to achieve desired dosimetric

accuracy.

Sonmez Ince M and **Banka A** (2021). "Syndrome of inappropriate antidiuretic hormone secretion in a patient with pituitary apoplexy." *BMJ Case Reports* 14(2) e236787.

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*Department of Internal Medicine*

Pituitary apoplexy (PA) is an endocrine emergency presenting with headache, visual and hormonal disturbances. Syndrome of inappropriate antidiuretic hormone secretion (SIADH) is rare after PA. A 64-year-old woman presented with acute frontal headache and nausea with normal neurological examination. Labs included normal sodium and creatinine. Echo showed new-onset congestive heart failure (CHF) and MRI of the brain revealed PA. She had normal cortisol levels and low thyroid stimulating hormone with normal thyroxine (T4) levels. During her hospitalisation, patient developed hyponatraemia. Initially, this was attributed to CHF and she was treated with tolvaptan with normalisation of sodium. One week later, she was readmitted with diarrhoea and hyponatraemia. She was euvoelaemic on examination indicating compensated CHF. Despite fluid challenge, patient had no improvement of sodium levels. The diagnosis of SIADH was made. Clinicians should suspect SIADH in patients with hyponatraemia in the setting of PA with normal T4 and cortisol levels.

Starr MR, Hsu J, Yonekawa Y, Mittra RA, Ryan C, Forbes NJ, Ammar M, Patel LG, Obeid A, **Capone A**, Emerson GG, Joseph DP, Elliott D, Gupta OP, Regillo CD and Ryan EH (2021). "Surgical techniques for primary rhegmatogenous retinal detachments between surgeons with high versus low single surgery success rates." *Acta Ophthalmologica*. ePub Ahead of Print.

[Full Text](#)

*Department of Ophthalmology*

Background/Aims: To identify differences in preoperative characteristics and intraoperative approaches between surgeons with higher versus lower single surgery success rates (SSSR) for repair of rhegmatogenous retinal detachments (RRDs). Methods: This study is a sub-analysis of subjects who underwent RRD repair in the Primary Retinal Detachment Outcomes (PRO) study, a multi-institutional, retrospective comparative interventional study. The PRO study examined consecutive primary RRD surgeries from January 1, 2015 through December 31, 2015. The primary outcome was variations in surgical approach to different types of RRDs with secondary analyses of pre and intraoperative metrics for surgeons with SSSR > 90% compared to those <80% who performed at least 40 operations during the study period. Results: A total of 689 surgeries were included in the analysis. The mean SSSR was 94% for the higher tier and 75% for the lower tier ( $p < 0.0001$ ). Surgeons with >90% SSSR were more likely to have graduated fellowship more recently ( $p = 0.0025$ ), use less perfluorocarbon liquid ( $p < 0.0001$ ), perform less 360 degree laser retinopexy ( $p < 0.0001$ ), and perform a higher percentage of primary buckles and combined PPV/SB ( $p < 0.0001$ ). For pseudophakic eyes there was no difference between PPV and PPV/SB use ( $p = 0.6211$ ). Conclusion: Surgeons with high SSSR typically performed SB as well as combination PPV/SB for more RRDs. Similar numbers of PPV and PPV/SB were performed for pseudophakic eyes, suggesting that the difference in SSSR between the two groups may be related to a combination of preoperative and intraoperative decisions as well as differences in technique.

Starr MR, Obeid A, Ryan EH, Ryan C, Ammar M, Patel LG, Forbes NJ, **Capone A**, Emerson GG, Joseph DP, Elliott D, Gupta OP, Regillo CD, Hsu J and Yonekawa Y (2021). "Retinal detachment with inferior retinal breaks: Primary vitrectomy versus vitrectomy with scleral buckle." *Retina* 41(3): 525-530.

[Full Text](#)

*Department of Ophthalmology*

Introduction: Rhegmatogenous retinal detachments with inferior retinal breaks are believed to have a higher risk of recurrent rhegmatogenous retinal detachment. This study compared anatomic and visual outcomes between primary pars plana vitrectomy (PPV) and combination PPV with scleral buckle (PPV/SB) for rhegmatogenous retinal detachments with inferior retinal breaks. Methods: This is an analysis of the Primary Retinal Detachment Outcomes study, a multi-institutional cohort study of consecutive primary rhegmatogenous retinal detachment surgeries from January 1, 2015, through December 31, 2015. The primary outcome was single-surgery success rate. Only eyes with inferior retinal breaks (one break in the

detached retina between five and seven o'clock) were included. Results: There were 238 eyes that met the inclusion criteria, 95 (40%) of which underwent primary PPV and 163 (60%) that underwent combined PPV/SB. The single-surgery success rate was 76.8% for PPV and 87.4% for PPV/SB ( $P = 0.0355$ ). This remained significant on multivariate analysis ( $P = 0.01$ ). Subgroup analysis showed that a superior single-surgery success rate of PPV/SB was especially noted in phakic eyes (85.2% vs. 68.6%;  $P = 0.0464$ ). Conclusion: Retinal detachment with inferior retinal breaks had a higher single-surgery success rate if treated with PPV/SB compared with PPV alone, particularly in phakic eyes.

Starr MR, Yoshihiro Y, Obeid A, Ryan EH, Ryan C, Ammar M, Patel LG, Forbes NJ, **Capone Jr A**, Emerson GG, Joseph DP, Elliott D, Regillo CD, Hsu J, Gupta OP and Kuriyan AE (2021). "Comparison of visual and anatomic outcomes following RRD surgery using 23-gauge versus 25-gauge vitrectomy: PRO study report no. 12." *Ophthalmic Surgery, Lasers & Imaging Retina* 52(2): 70-76.

[Full Text](#)

*Department of Ophthalmology*

Background and Objective: Most surgeons now utilize small-gauge (23- or 25-gauge) pars plana vitrectomy (PPV) with or without scleral buckling for repair of rhegmatogenous retinal detachments (RRD), in addition to primary scleral buckle (SB), but comparative data between the two gauges are limited. Patients and Methods: This study is an analysis of primary RRD repairs comparing 23- versus 25-gauge vitrectomy for PPV or combination PPV/SB from January 1, 2015, through December 31, 2015, across multiple institutions. The primary outcome was single-surgery success and secondary outcomes included postoperative complications. Results: There were 1,932 eyes that met inclusion criteria. There was no statistically significant difference in single-surgery success (82.9% vs. 83.8%;  $P = 0.6329$ ). There were similar rates of postoperative hypotony, endophthalmitis, vitreous hemorrhage, and choroidal detachment. The findings were similar when analyzing only eyes that underwent primary PPV without SB. Conclusion: Both 23- and 25-gauge vitrectomy systems have similar anatomic and visual outcomes in the primary repair of RRD.

**Staudt MD**, Pouratian N, Miller JP, Hamani C, Raviv N, McKhann GM, Gonzalez-Martinez JA and Pilitsis JG (2021). "Congress of Neurological Surgeons systematic review and evidence-based guidelines for deep brain stimulations for obsessive-compulsive disorder: Update of the 2014 guidelines." *Neurosurgery* 88(4): 710-712.

[Full Text](#)

*Department of Neurosurgery*

Background: In 2020, the Guidelines Task Force conducted another systematic review of the relevant literature on deep brain stimulation (DBS) for obsessive-compulsive disorder (OCD) to update the original 2014 guidelines to ensure timeliness and accuracy for clinical practice. Objective: To conduct a systematic review of the literature and update the evidence-based guidelines on DBS for OCD. Methods: The Guidelines Task Force conducted another systematic review of the relevant literature, using the same search terms and strategies as used to search PubMed and Embase for relevant literature. The updated search included studies published between 1966 and December 2019. The same inclusion/exclusion criteria as the original guideline were also applied. Abstracts were reviewed and relevant full-text articles were retrieved and graded. Of 864 articles, 10 were retrieved for full-text review and analysis. Recommendations were updated according to new evidence yielded by this update. Results: Seven studies were included in the original guideline, reporting the use of bilateral DBS as more effective in improving OCD symptoms than sham treatment. An additional 10 studies were included in this update: 1 class II and 9 class III. Conclusion: Based on the data published in the literature, the following recommendations can be made: (1) It is recommended that clinicians utilize bilateral subthalamic nucleus DBS over best medical management for the treatment of patients with medically refractory OCD (level I). (2) Clinicians may use bilateral nucleus accumbens or bed nucleus of stria terminalis DBS for the treatment of patients with medically refractory OCD (level II). There is insufficient evidence to make a recommendation for the identification of the most effective target.

Sutton NR, Seth M, Madder RD, Sukul D, **Dixon SR**, Cannon LA and Gurm HS (2021). "Comparative safety of bioabsorbable polymer everolimus-eluting, durable polymer everolimus-eluting, and durable polymer zotarolimus-eluting stents in contemporary clinical practice." *Circulation Cardiovascular Interventions* 14(3): e009850.

[Full Text](#)

*Department of Internal Medicine*

Tagami T, Almahariq MF, Balanescu DV, Quinn TJ, **Dilworth JT, Franklin BA** and **Bilolikar A** (2021). "Usefulness of coronary computed tomographic angiography to evaluate coronary artery disease in radiotherapy-treated breast cancer survivors." American Journal of Cardiology 143: 14-20.

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*Department of Internal Medicine*

*Department of Radiation Oncology*

Breast cancer is the most commonly diagnosed cancer in women and radiotherapy is a widely used treatment approach. However, there is an increased risk of coronary artery disease and cardiac death in women treated with radiotherapy. The present study was undertaken to clarify the relation between radiotherapy and coronary disease in women with previous breast irradiation using coronary computed tomographic angiography (CCTA). We conducted a retrospective analysis of women with a history of right or left-sided breast cancer (RBC; LBC) treated with radiotherapy who subsequently underwent CCTA. RBC patients who had reduced radiation doses to the myocardium served as controls. Patients (n = 6,593) with a history of nonmetastatic breast cancer treated with radiotherapy were screened for completion of CCTA; 49 LBC and 45 RBC women were identified. Age and risk factor matched patients with LBC had higher rates of coronary disease compared with RBC patients; left anterior descending (LAD) coronary artery (76% vs 31% [p < 0.001]), left circumflex (33% vs. 6.7% [p = 0.004]), and right coronary artery (37% vs 13% [p = 0.018]). Mean LAD radiation dose and mean heart dose strongly correlated with coronary disease, with a 21% higher incidence of disease in the LAD per Gy for mean LAD dose and a 95% higher incidence of disease in the LAD per Gy for mean heart dose. In conclusion, LBC patients treated with radiotherapy have a significantly higher incidence of coronary disease when compared with a matched group of patients treated for RBC. Radiation doses correlated with the incidence of coronary disease.

**Tantisattamo E** and Kalantar-Zadeh K (2021). "Editorial: Novel therapeutic approaches in chronic kidney disease, uremia and kidney transplantation: past, present and future." Current Opinion in Nephrology and Hypertension 30(1): 1-4.

[Full Text](#)

*Department of Internal Medicine*

**Tantisattamo E**, Kalantar-Zadeh K, Halleck F, Duettmann W, Naik M and Budde K (2021). "Novel approaches to sarcopenic obesity and weight management before and after kidney transplantation." Current Opinion in Nephrology and Hypertension 30(1): 14-26.

[Full Text](#)

*Department of Internal Medicine*

Purpose of Review: Although a widely recognized and complex pathophysiological condition, sarcopenic obesity remains less appreciated and may elude diagnosis and workup in both kidney transplant waitlisted candidates and kidney transplant recipients. The lack of consensus definition, and practical diagnostic tools for evaluating waitlisted candidates and transplant recipients are barriers to early detect and initiate therapeutic management for sarcopenic obesity. Although sarcopenia leads to poor clinical outcomes, posttransplant obesity yields conflicting results. Exercise and nutritional managements are common therapies for sarcopenic obese patients; however, surgery weight loss or bariatric surgery in both transplant candidates and potential living kidney donors shows promising benefits for kidney transplant access in waitlist obese candidates but may require to be selected for appropriate patients. Recent Findings: Pathogenesis and management for sarcopenia and obesity are interconnected. The benefits of exercise to improve muscle mass and function is clear in waitlist kidney transplant candidates and transplant recipients. However, there are several barriers for those to increase exercise and improve physical activity including patient, provider, and healthcare or environmental factors. The advantages of fat mass reduction to lose weight can promote muscle mass and strength. However, epidemiological data regarding the obesity paradox in dialysis-dependent patients when overnutrition provides survival benefits for this population should be taken into account when performing weight loss especially bariatric surgery. Summary: Barriers in providing optimal care to kidney transplant waitlisted candidates and transplant recipients may partly result from underdiagnosis of sarcopenic obesity; notwithstanding that this entity has increasingly been more

recognized. Mechanistic studies to better understand pathogenesis of sarcopenic obesity will help determine pathogenesis and clinical tools for diagnosis of this entity, which can facilitate further studies related to the outcomes and weight management to ultimately improve kidney transplant outcomes.

**Tantisattamo E**, Leventhal JR, Mathew JM and Gallon L (2021). "Chimerism and tolerance: Past, present and future strategies to prolong renal allograft survival." *Current Opinion in Nephrology and Hypertension* 30(1): 63-74.

[Full Text](#)

*Department of Internal Medicine*

Purpose of Review: Immunological factors are a major cause of kidney allograft loss. Calcineurin inhibitors (CNIs) have improved short-term kidney allograft survival; however, they in turn contribute to long-term kidney allograft loss from chronic CNI nephrotoxicity. Tolerance induction in transplantation can avoid the long-term adverse effects of immunosuppressive medications. This review aims to critically discuss recent efforts in inducing transplantation tolerance. Recent Findings: Tolerance induction mediated by chimerism has shown some promise in minimizing or even complete withdrawal of immunosuppressive treatments in kidney allograft recipients. There has been a number of approaches as varied as the number of centres conducting these trials. However, they can be grouped into those mediated by transient microchimerism and those facilitated by more stable macro or full donor chimerism. The success rates in terms of long-term drug-free graft survival has been limited in microchimerism-mediated tolerance induction approaches. Mixed macrochimerism of less than 50% donor may be unstable with mostly the recipient's native immune system overpowering the donor chimeric status. Tolerance induction leading to chimerism has been limited to living donor kidney transplantation and additional long-term outcomes are required. Furthermore, immune monitoring after tolerance induction has faced a limitation in studying due to a lack of sufficient study participants and appropriate study controls. Summary: Tolerance induction is one of several strategies used to prolong kidney allograft survival, but it has not been routinely utilized in clinical practice. However, future applications from the trials to clinical practice remain limited to living donor kidney transplantation. Once further data regarding tolerance inductions exist and practicality becomes widely accepted, tolerance induction may shift the paradigm in the field of kidney transplantation to achieve the best possible outcome of 'One Organ for Life'.

**Taranikanti V** (2021). "Hyperhomocysteinemia and risk of atherosclerosis, cardiovascular disease and cancer: A concise update," In Waly MI (ed). *Nutritional Management and Metabolic Aspects of Hyperhomocysteinemia*. Cham: Springer International Publishing. pp: 157-165.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Homocysteine is a sulfur-containing amino acid obtained from the metabolism of methionine. Dietary methionine is converted to S-adenosylmethionine and is demethylated to S-adenosylhomocysteine and homocysteine. Under conditions of protein deficient diet, intracellularly homocysteine is metabolized by one of two pathways: re-methylation and trans-sulfuration where vitamin B12 and folic acid participate as cofactors respectively. In the folate cycle, the enzyme methionine synthase and vitamin B12 as well as the enzyme 5,10-methylenetetrahydrofolate reductase are required. Folate enters the re-methylation cycle and is converted to 5-methyltetrahydrofolate, an important methyl donor in the conversion of homocysteine to methionine. Remethylation reactions also occur in the liver in which the enzyme betaine homocysteine methyltransferase, transfers a methyl group to homocysteine via the demethylation of betaine to dimethylglycine [1]. Therefore, disruption of S-adenosylmethionine -dependent transmethylation reactions leads to high concentrations of homocysteine in the blood and has been associated with deleterious effects. The normal level of homocysteine ranges between 5–15  $\mu\text{M}$ , however in diseased conditions it can range from 50  $\mu\text{M}$  in mild cases to 500  $\mu\text{M}$  in severe cases [2]. The etiology of cancer is multifactorial. Studies have established a close association between cancer and hyperhomocysteinemia [3]. Genetic & environmental factors play an important role in its pathogenesis. High levels of homocysteine are found in epigenetic regulation of DNA silencing and posttranslational modification of histones [3]. Specifically, the carcinogenic potential of hyper homocysteinemia is dependent on the detoxification pathways in homocysteine metabolism, venous thromboembolism, deficiency of folate and/or polymorphisms. In this chapter, the role of homocysteine on atherosclerosis, cardiovascular disease and cancer is discussed.

Tariq T, **Karabon P**, Irfan FB, Sieloff EM, **Patterson R** and Desai AP (2021). "National trends and outcomes of nonautoimmune hemolytic anemia in alcoholic liver disease: Analysis of the Nationwide Inpatient Sample." Journal of Clinical Gastroenterology 55(3): 258-262.

[Full Text](#)

Department of Medical Education  
OUWB Medical Student Author

Ternacle J, **Abbas AE** and Pibarot P (2021). "Prosthesis-patient mismatch after transcatheter aortic valve replacement has it become obsolete?" JACC - Cardiovascular Interventions 14(9): 977-980.

[Full Text](#)

Department of Internal Medicine

Ternacle J, Guimaraes L, Vincent F, Côté N, Côté M, Lachance D, Clavel M-A, **Abbas AE**, Pibarot P and Rodés-Cabau J (2021). "Reclassification of prosthesis-patient mismatch after transcatheter aortic valve replacement using predicted vs. measured indexed effective orifice area." European Heart Journal - Cardiovascular Imaging 22(1): 11-20.

[Full Text](#)

Department of Internal Medicine

Aims: The objective was to compare the incidence and impact on outcomes of measured (PPMM) vs. predicted (PPMP) prosthesis-patient mismatch following transcatheter aortic valve replacement (TAVR). Methods and Results: All consecutive patients who underwent TAVR between 2007 and 2018 were included. Effective orifice area (EOA) was measured by Doppler-echocardiography using the continuity equation and predicted according to the normal reference for each model and size of valve. PPM was defined using EOA indexed (EOAi) to body surface area as moderate if  $\leq 0.85 \text{ cm}^2/\text{m}^2$  and severe if  $\leq 0.65 \text{ cm}^2/\text{m}^2$  (respectively,  $\leq 0.70$  and  $\leq 0.55 \text{ cm}^2/\text{m}^2$  if body mass index  $\geq 30 \text{ kg}/\text{m}^2$ ). The outcome endpoints were high residual gradient ( $\geq 20 \text{ mmHg}$ ) and the composite of cardiovascular mortality and hospital readmission for heart failure at 1 year. Overall, 1088 patients underwent a TAVR (55% male, age  $79.1 \pm 8.4$  years, and STS score  $6.6 \pm 4.7\%$ ); balloon-expandable device was used in 83%. Incidence of moderate (10% vs. 27%) and severe (1% vs. 17%) PPM was markedly lower when defined by predicted vs. measured EOAi ( $P < 0.001$ ). Balloon-expandable device implantation (OR: 1.90,  $P = 0.029$ ) and valve-in-valve procedure ( $n = 118$ ; OR: 3.21,  $P < 0.001$ ) were the main factors associated with PPM occurrence. Compared with measured PPM, predicted PPM showed stronger association with high residual gradient. Severe measured or predicted PPM was not associated with clinical outcomes. Conclusion: The utilization of the predicted EOAi reclassifies the majority of patients with PPM to no PPM following TAVR. Compared with measured PPM, predicted PPM had stronger association with haemodynamic outcomes, while both methods were not associated with clinical outcomes.

Thapa SB, Kakar TS, Mayer C and **Khanal D** (2021). "Clinical outcomes of in-hospital cardiac arrest in COVID-19." JAMA Internal Medicine 181(2): 279-281.

[Full Text](#)

Department of Internal Medicine

Tieger MG, Rodriguez M, Wang JC, Obeid A, Ryan C, Gao X, Kakulavarapu S, Mardis PJ, Madhava ML, Maloney SM, Adika AZ, Peddada KV, Sioufi K, Stefater JA, Forbes NJ, **Capone A**, Emerson GG, Joseph DP, Regillo C, Hsu J, Gupta O, Elliott D, Ryan EH and Yonekawa Y (2021). "Impact of contact versus non-contact wide-angle viewing systems on outcomes of primary retinal detachment repair (PRO study report number 5)." British Journal of Ophthalmology 105(3): 410-413.

[Request Form](#)

Department of Ophthalmology

Background/Aims: Vitrectomy to repair retinal detachment is often performed with either non-contact wide-angle viewing systems or wide-angle contact viewing systems. The purpose of this study is to assess whether the viewing system used is associated with any differences in surgical outcomes of vitrectomy for primary non-complex retinal detachment repair. Methods: This is a multicenter, interventional, retrospective, comparative study. Eyes that underwent non-complex primary retinal detachment repair by either pars plana vitrectomy (PPV) alone or in combination with scleral buckle/PPV in 2015 were evaluated. The viewing

system at the time of the retinal detachment repair was identified and preoperative patient characteristics, intraoperative findings and postoperative outcomes were recorded. Results: A total of 2256 eyes were included in our analysis. Of those, 1893 surgeries used a non-contact viewing system, while 363 used a contact lens system. There was no statistically significant difference in single surgery anatomic success at 3 months ( $p=0.72$ ), or final anatomic success ( $p=0.40$ ). Average postoperative visual acuity for the contact-based cases was logMAR 0.345 (20/44 Snellen equivalent) compared with 0.475 (20/60 Snellen equivalent) for non-contact ( $p=0.001$ ). After controlling for numerous confounding variables in multivariable analysis, viewing system choice was no longer statistically significant ( $p=0.097$ ). Conclusion: There was no statistically significant difference in anatomic success achieved for primary retinal detachment repair when comparing non-contact viewing systems to contact lens systems. Postoperative visual acuity was better in the contact-based group but this was not statistically significant when confounding factors were controlled for.

**Topf JM** and Williams PN (2021). "COVID-19, social media, and the role of the public physician." Blood Purification. ePub Ahead of Print.

[Full Text](#)

*Department of Internal Medicine*

The COVID-19 pandemic has resulted in an avalanche of information, much of it false or misleading. Social media posts with misleading or dangerous opinions and analyses are often amplified by celebrities and social media influencers; these posts have contributed substantially to this avalanche of information. An emerging force in this information infodemic is public physicians, doctors who view a public presence as a large segment of their mission. These physicians bring authority and real-world experience to the COVID-19 discussion. To investigate the role of public physicians, we interviewed a convenience cohort of physicians who have played a role in the infodemic. We asked the physicians about how their roles have changed, how their audience has changed, what role politics plays, and how they address misinformation. The physicians noted increased audience size with an increased focus on the pandemic. Most avoided confronting politics, but others found it unavoidable or that even if they tried to avoid it, it would be brought up by their audience. The physicians felt that confronting and correcting misinformation was a core part of their mission. Public physicians on social media are a new occurrence and are an important part of fighting online misinformation.

**Tram J, Pressman A**, Chen N-W, **Berger DA**, Miller J, Welch RD, Reynolds JC, Pribble J, **Hanson I** and **Swor R** (2021). "Percutaneous mechanical circulatory support and survival in patients resuscitated from out of hospital cardiac arrest: A study from the CARES surveillance group." Resuscitation 158: 122-129.

[Full Text](#)

*Department of Emergency Medicine*

*OUBB Medical Student Author*

*Department of Internal Medicine*

Introduction: Maintenance of cardiac function is required for successful outcome after out-of-hospital cardiac arrest (OHCA). Cardiac function can be augmented using a mechanical circulatory support (MCS) device, most commonly an intra-aortic balloon pump (IABP) or Impella®. Objective: Our objective is to assess whether the use of a MCS is associated with improved survival in patients resuscitated from OHCA in Michigan. Methods: We matched cardiac arrest cases during 2014-2017 from the Cardiac Arrest Registry to Enhance Survival (CARES) in Michigan and the Michigan Inpatient Database (MIDB) using probabilistic linkage. Multilevel logistic regression tested the association between MCS and the primary outcome of survival to hospital discharge. Results: A total of 3790 CARES cases were matched with the MIDB and 1131 (29.8%) survived to hospital discharge. A small number were treated with MCS, an IABP ( $n = 183$ ) or Impella® ( $n = 50$ ). IABP use was associated with an improved outcome (unadjusted OR = 2.16, 95%CI [1.59, 2.93]), while use of Impella® approached significance (OR = 1.72, 95% CI [0.96, 3.06]). Use of MCS was associated with improved outcome (unadjusted OR = 2.07, 95% CI [1.55, 2.77]). In a multivariable model, MCS use was no longer independently associated with improved outcome (OR<sub>adj</sub> = 0.95, 95% CI [0.69, 1.31]). In the subset of subjects with cardiogenic shock ( $N = 725$ ), MCS was associated with improved survival in univariate (unadjusted OR = 1.84, 95% CI [1.24, 2.73]) but not multi-variable modeling (OR<sub>adj</sub> = 1.14, 95% CI [0.74, 1.77]). Conclusion: Use of MCS was infrequent in patients resuscitated from OHCA and was not independently associated with improvement in post arrest survival after adjusting for covariates.

**Trese M, Schimmel O and Gupta C** (2021). "Extensive autoimmune keratolysis with subsequent corneal perforation managed with tectonic endothelial keratoplasty." *American Journal of Ophthalmology Case Reports* 21: 101031.

[Full Text](#)

*Department of Ophthalmology*  
*OUWB Medical Student Author*

Purpose: To report a case of corneal perforation secondary to an extensive rheumatologic corneal melt, that was successfully managed via systemic immunosuppression and internal tectonic endothelial keratoplasty (TEK). Observations: A 55-year-old male with undiagnosed rheumatoid arthritis presented with a progressively enlarging area of peripheral ulcerative keratitis with extensive keratolysis which subsequently perforated despite treatment with oral steroids. The structural integrity of the globe was restored via a combination of cyanoacrylate glue and tectonic endothelial keratoplasty (TEK). This technique provided long term structural support and improved visual acuity. Conclusions and Importance: TEK grafts represent a viable treatment option in a subset of patients with corneal perforation secondary to an extensive corneal melt. The familiarity and relative ease of the surgical technique along with a lack of corneal sutures represents an alternate technique when compared to full thickness or lamellar keratoplasty. Further, through the use of anterior segment spectral domain optical coherence tomography (SD-OCT) we demonstrate that the donor graft integrated within the host cornea. To our knowledge, this represents the first case in the literature of corneal perforation secondary to an inflammatory corneal melt that was successfully managed with internal tectonic endothelial keratoplasty.

van Rosendaal AR, Lin FY, van den Hoogen IJ, Ma X, Gianni U, Al Hussein Alawamlh O, Al'Aref SJ, Peña JM, Andreini D, Budoff MJ, Cademartiri F, **Chinnaiyan K**, Choi JH, Conte E, Marques H, de Araújo Gonçalves P, Gottlieb I, Hadamitzky M, Leipsic J, Maffei E, Pontone G, Raff GL, Shin S, Kim YJ, Lee BK, Chun EJ, Sung JM, Lee SE, Han D, Berman DS, Virmani R, Samady H, Stone P, Narula J, Bax JJ, Shaw LJ, Min JK and Chang HJ (2021). "Progression of whole-heart atherosclerosis by coronary CT and major adverse cardiovascular events." *Journal of Cardiovascular Computed Tomography*. ePub Ahead of Print.

[Request Form](#)

*Department of Internal Medicine*

Background: The current study aimed to examine the independent prognostic value of whole-heart atherosclerosis progression by serial coronary computed tomography angiography (CCTA) for major adverse cardiovascular events (MACE). Methods: The multi-center PARADIGM study includes patients undergoing serial CCTA for symptomatic reasons,  $\geq 2$  years apart. Whole-heart atherosclerosis was characterized on a segmental level, with co-registration of baseline and follow-up CCTA, and summed to per-patient level. The independent prognostic significance of atherosclerosis progression for MACE (non-fatal myocardial infarction [MI], death, unplanned coronary revascularization) was examined. Patients experiencing interval MACE were not omitted. Results: The study population comprised 1166 patients (age  $60.5 \pm 9.5$  years, 54.7% male) who experienced 139 MACE events during 8.2 (IQR 6.2, 9.5) years of follow up (15 death, 5 non-fatal MI, 119 unplanned revascularizations). Whole-heart percent atheroma volume (PAV) increased from 2.32% at baseline to 4.04% at follow-up. Adjusted for baseline PAV, the annualized increase in PAV was independently associated with MACE: OR 1.23 (95% CI 1.08, 1.39) per 1 standard deviation increase, which was consistent in multiple subpopulations. When categorized by composition, only non-calcified plaque progression associated independently with MACE, while calcified plaque did not. Restricting to patients without events before follow-up CCTA, those with future MACE showed an annualized increase in PAV of 0.93% (IQR 0.34, 1.96) vs 0.32% (IQR 0.02, 0.90),  $P < 0.001$ . Conclusions: Whole-heart atherosclerosis progression examined by serial CCTA is independently associated with MACE, with a prognostic threshold of 1.0% increase in PAV per year.

**Vanood A**, Owen R, Maraskine M, **Schreiber A**, Pokharel R and **Cohen L** (2021). "Collapsing FSGS with concurrent class 2 and 3 lupus nephritis: A case report and review of the literature." *Case Reports in Nephrology and Dialysis* 11(1): 16-25.

[Full Text](#)

*OUWB Medical Student Author*  
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Lupus nephritis (LN) and the collapsing variant of focal segmental glomerulosclerosis (cFSGS) are separate histologic diagnoses that are generally thought to have separate etiologies. We describe the presentation of a 20-year-old African American female with advanced renal failure (creatinine 7.16 mg/dL), nephrotic-range proteinuria, and a 30-pound weight loss. Renal biopsy demonstrated class 2 and 3 LN as well as cFSGS. A review of the current literature demonstrates that the dual diagnosis of LN and cFSGS may not be as rare as previously understood. Whether the presence of one of these pathophysiologic processes predisposes a patient to the development of the other, or whether genetic variation increases the risk for development of both conditions, remains unclear. Currently there is no standard therapy to manage these patients, and overall renal prognosis is poor.

**Vanood A, Santhakumar S and Said A** (2021). "Repeat intravenous r-tPA administration four days after initial thrombolytic therapy for recurrent ischemic stroke: A case report and review of literature." Interdisciplinary Neurosurgery: Advanced Techniques and Case Management 23: 100937.

[Full Text](#)

*OUWB Medical Student Author*

*Department of Internal Medicine*

*Department of Neurology*

Stroke is a significant source of morbidity and mortality within the United States. The current standard of care for treatment of acute ischemic stroke is intravenous recombinant tissue-type plasminogen activator (IV r-tPA). However, IV r-tPA is contraindicated within 3 months of a previous stroke due to concern for symptomatic intracerebral hemorrhage (sICH). We describe the case of a 77-year-old female who developed aphasia and right-sided quadrantanopsia and was found to have a calcified embolus in the M3 branch of her left middle cerebral artery. She was given IV r-tPA with subsequent symptom resolution and no MRI evidence of acute or subacute infarct. 4 days after index stroke, she had recurrence of her symptoms, receiving a second dose of IV r-tPA. She improved clinically. Non-contrast CT 24 hours afterwards showed minimal foci of intraparenchymal hemorrhage without midline shift or mass effect. She remained neurologically stable and improved significantly with inpatient rehabilitation.

**Vanood A, Sharrak A, Karabon P and Fahim DK** (2021). "Industry-sponsored research payments in neurosurgery - Analysis of the Open Payments Database from 2014 to 2018." Neurosurgery 88(3): E250-E258.

[Request Form](#)

*OUWB Medical Student Author*

*Department of Neurosurgery*

Background: The Open Payments Database (OPD) started in 2013 to combat financial conflicts of interest between physicians and medical industry. OBJECTIVE: To evaluate the first 5 yr of the OPD regarding industry-sponsored research funding (ISRF) in neurosurgery. Methods: The Open Payments Research Payments dataset was examined from 2014 to 2018 for payments where the clinical primary investigator identified their specialty as neurosurgery. Results: Between 2014 and 2018, a \$106.77 million in ISRF was made to 731 neurosurgeons. Fewer than 11% of neurosurgeons received ISRF yearly. The average received \$140 000 in total but the median received \$30,000. This was because the highest paid neurosurgeon received \$3.56 million. A greater proportion ISRF was made to neurosurgeons affiliated with teaching institutions when compared to other specialties (26.74% vs 20.89%, P = .0021). The proportion of the total value of ISRF distributed to neurosurgery declined from 0.43% of payments to all specialties in 2014 to 0.37% in 2018 (P < .001), but no steady decline was observed from year to year. Conclusion: ISRF to neurosurgeons comprises a small percentage of research payments made to medical research by industry sponsors. Although a greater percentage of payments are made to neurosurgeons in teaching institutions compared to other specialties, the majority is given to neurosurgeons not affiliated with a teaching institution. A significant percentage of ISRF is given to a small percentage of neurosurgeons. There may be opportunities for more neurosurgeons to engage in industry-sponsored research to advance our field as long as full and complete disclosures can always be made.

Vayntraub A, Quinn TJ, Thompson AB, **Chen PY, Gustafson GS, Jawad MS and Dilworth JT** (2021). "Left anterior descending artery avoidance in patients receiving breast irradiation." Medical Dosimetry 46(1): 57-64.

[Full Text](#)

*Department of Radiation Oncology*

Purpose: Dose to the left anterior descending artery (LAD) may be significant in patients receiving left-sided irradiation for breast cancer. We investigated if prospective contouring and avoidance of the LAD during treatment planning were associated with lower LAD dose. Methods and Materials: We reviewed dosimetric plans for 323 patients who received left whole breast or chest wall irradiation with or without internal mammary node (IMLN) coverage between 1/2014 and 1/2019 at a single institution. The LAD was contoured prospectively for 155 cases, and techniques were utilized to minimize LAD dose. Dose-volume-histograms from these patients were compared to those of 168 patients for whom the LAD was contoured retrospectively after treatment completion. EQD2 was calculated to account for fractionation differences. Results: Compared to cases where the LAD was contoured retrospectively (n = 126), prospective LAD contouring (n = 124) was associated with lower unadjusted median max and mean LAD doses for 250 patients receiving whole-breast irradiation (WBI) without IMLN coverage: 8.5 Gy vs 5.2 Gy (p < 0.0001) and 3.6 Gy vs 2.7 Gy (p < 0.0001), respectively. EQD2 median max and mean LAD doses were also lower with prospective LAD contouring: 5.2 Gy vs 3.0 Gy (p < 0.0001) and 1.9 Gy vs 1.5 Gy (p < 0.0001), respectively. Compared to cases where the LAD was contoured retrospectively (n = 42), prospective LAD contouring (n = 31) was associated with lower max LAD doses for 73 patients with IMLN coverage: 20.4 Gy vs 14.3 Gy (p = 0.042). There was a nonsignificant reduction in median mean LAD dose: 6.2 Gy vs 6.1 Gy (p = 0.33). LAD doses were reduced while maintaining IMLN coverage (mean V90%(Rx) >90%). Conclusions: Prospective contouring and avoidance of the LAD were associated with lower max and mean LAD doses in patients receiving WBI and with lower max LAD doses in patients receiving IMLN treatment. Further reduction in LAD dose may require stricter optimization weighting or compromise in IMLN coverage.

Vollstedt A, Tennyson L, Rezaee M, Hoang L, **Sirls L**, **Padmanabhan P** and **Peters K** (2021). "Fractional carbon dioxide vaginal laser for the treatment of urinary symptoms: Preliminary short-term results." Neurourology and Urodynamics 40: S225-S226.

[Full Text](#)

*Department of Urology*

Vollstedt A, Wang DK, Luke N, Baunoch D, Wojno K, Cline K, Belkoff L, Milbank A, Sherman N, Haverkorn R, Gaines N, Yore L, Shore N, Opel M, Korman H, Huang SG, Zhao HN, Penaradnda M, **Jafri M**, Wenzler D, **Burks F**, Cacdac P and **Sirls L** (2021). "Are consortia polymicrobial urinary tract infections more symptomatic than monomicrobial? Results from a multi-institutional study." Neurourology and Urodynamics 40: S26-S27.

[Full Text](#)

*Department of Urology*

Vollstedt A, Wang DK, Luke N, Baunoch D, Wojno K, Cline K, Belkoff L, Milbank A, Sherman N, Haverkorn R, Gaines N, Yore L, Shore N, Opel M, **Korman H**, Huang SG, Zhao HN, Penaranda M, **Jafri M**, Wenzler D, **Burks F**, Cacdac P and **Sirls L** (2021). "Concordance between antibiotic resistance genes by multiplex polymerase chain reaction and antibiotic susceptibility by pooled antibiotic sensitivity testing in symptomatic patients with urinary tract infection." Neurourology and Urodynamics 40: S27-S28.

[Full Text](#)

*Department of Urology*

Vollstedt A, Wang DK, Luke N, Baunoch D, Wojno K, Cline K, Belkoff L, Milbank A, Sherman N, Haverkorn R, Gaines N, Yore L, Shore N, Opel M, Korman H, Huang SG, Zhao HN, Penaranda M, **Jafri M**, Wenzler D, **Burks F**, Cacdac P and **Sirls L** (2021). "Defining and detecting bacterial consortia within urine samples of patients with symptomatic urinary tract infection." Neurourology and Urodynamics 40: S31-S32.

[Full Text](#)

*Department of Urology*

Vollstedt AJ, Han E, Nguyen L, Tennyson L, Beck D and **Sirls L** (2021). "Placement of mid-urethral mesh slings at the time of vaginal prolapse repair does not affect post-operative sexual function or orgasm." International Urogynecology Journal 32(3): 639-645.

[Full Text](#)

*Department of Urology*

Introduction and Hypothesis: Because of the relationship between the clitoral neurovascular supply and the urethra, the dissection for placement of mid-urethral slings (MUS) may negatively impact orgasmic function. We aimed to analyze the role of MUS in orgasmic and overall sexual function in patients undergoing prolapse surgery. Methods: A single institution retrospective review was performed on 157 patients undergoing prolapse surgery with and without MUS from 2008 to 2014. Pelvic Organ Prolapse Incontinence Sexual Questionnaires (PISQ-12) scores at baseline, 6, and 12 months post-operatively were compared. The difference in overall mean post-operative PISQ-12 scores at 6 and 12 months in those undergoing POP with or without MUS placement was assessed using Wilcoxon rank tests. Results: Of 157 women who underwent prolapse surgery, 81 (52%) had concomitant MUS. Mean baseline PISQ-12 scores were 32 in both groups ( $p = 0.98$ ). Post-operative PISQ-12 scores between the two groups did not differ at 6 ( $p = 0.96$ ) or 12 months ( $p = 0.65$ ). Within the MUS group, mean overall PISQ-12 scores improved at 6 ( $p = 0.05$ ) and 12 months ( $p < 0.01$ ). Mean overall PISQ-12 scores did not improve in patients who did not have slings placed at 6 ( $p = 0.10$ ) or 12 months ( $p = 0.15$ ). Orgasm frequency and intensity did not differ between the two groups at 6 ( $p = 0.39$ ,  $p = 0.91$ , respectively) or 12 months ( $p = 0.11$ ,  $p = 0.44$ , respectively). Conclusion: MUS at the time of prolapse repair did not affect orgasmic or overall sexual function. PISQ-12 scores improved after prolapse surgery with concomitant MUS placement. Our findings may help counsel patients regarding the risk of MUS placement affecting sexual function.

Warkentin TE, **Smythe MA**, Ali MA, **Aslam N**, Sheppard JAI, Smith JW, Moore JC, Arnold DM and Nazy I (2021). "Serotonin-release assay-positive but platelet factor 4-dependent enzyme-immunoassay negative: HIT or not HIT?" *American Journal of Hematology* 96(3): 320-329.

[Full Text](#)

*Department of Foundational Medical Studies (BH)*

*Department of Internal Medicine*

IgG-specific and polyspecific PF4-dependent enzyme-immunoassays (EIAs) have exceptionally high sensitivity ( $\geq 99\%$ ) for diagnosis of heparin-induced thrombocytopenia (HIT), a drug reaction caused by platelet-activating antibodies detectable by serotonin-release assay (SRA). The IgG-specific EIAs are recommended for screening, as their high sensitivity is accompanied by relatively high specificity vis-à-vis polyspecific EIAs. We investigated the frequency of SRA-positive/EIA-negative (SRA+/EIA-) HIT, prompted by referral to our reference HIT laboratory of serial blood samples from a patient ("index case") with false-negative IgG-specific EIAs. Despite initial clinical suspicion for HIT, repeat negative IgG-specific EIAs prompted heparin resumption, which triggered recurrent thrombocytopenia and near-fatal cardiac arrest, indicating likely post-heparin HIT-associated anaphylactoid reaction. Further investigations revealed a strong-positive SRA, whether performed with heparin alone, PF4 alone, or PF4/heparin, with inhibition by Fc receptor-blocking monoclonal antibody (indicating IgG-mediated platelet activation); however, five different IgG-specific immunoassays yielded primarily negative (or weak-positive) results. To investigate the frequency of SRA+/EIA- HIT, we reviewed the laboratory and clinical features of patients with this serological profile during a 6-year period in which our reference laboratory investigated for HIT using both SRA and IgG-specific EIA. Although  $\sim 0.2\%$  of 8546 patients had an SRA+/EIA- profile, further review of 15 such cases indicated clerical/laboratory misclassification or false-positive SRA in all, with no SRA+/EIA- HIT case identified. We conclude that while SRA+/EIA- HIT is possible—as shown by our index case—this clinical picture is exceptionally uncommon. Moreover, the requirement for a positive EIA is a useful quality control maneuver that reduces risk of reporting a false-positive SRA result.

**Wasserman JA** and **Browne BJ** (2021). "On triggering and being triggered: Civil society and building brave spaces in medical education." *Teaching and Learning in Medicine*. ePub Ahead of Print.

[Full Text](#)

*Department of Foundational Medical Studies (OU)*

Issue: How educators should respond to student reports of intense emotional reactions to curricular content—i.e., being triggered—invites intense debate. There are claims of insensitivity on one side and calls to "toughen up" on the other. These polemics aside, such instances sometimes represent a true dilemma, particularly within medical education where engaging highly sensitive content is essential to future patient care and where managing one's own emotions is a core competency. Parsing this convoluted and emotional

debate into these domains illustrates how medical educators can simultaneously legitimize the lived experiences of students, engage in honest dialogue, and maintain a shared commitment to education. Evidence: While substantial energy has been spent debating the legitimacy of students' emotional reactions, the discourse lacks a clear conceptual framework and we often end up talking past each other. The concept of brave spaces offers an important alternative where sensitive subject matter can be engaged with civility. Implications: This paper offers a model for building brave spaces within medical education by clarifying the rights and responsibilities of both teachers and learners in each of three intersecting domains: intrapersonal, interpersonal, and civic. This model is exemplified in a case where students reported being triggered by course content. By parsing this case across the three domains, we can clarify how responses are multifaceted and we can simultaneously avoid indictment of another's lived experiences while preserving the pedagogical integrity of the curriculum.

Weber DJ, Talbot TR, Weinmann A, **Mathew T**, Heil E, Stenehjem E, Duncan R, Gross A, Stinchfield P, Baliga C, Wagner J, Schaffner W, Echevarria K, and Drees M (2021). "Policy statement from the Society for Healthcare Epidemiology of America (SHEA): Only medical contraindications should be accepted as a reason for not receiving all routine immunizations as recommended by the Centers for Disease Control and Prevention." [Infection Control and Hospital Epidemiology](#) 42(1): 1-5.

[Full Text](#)

*Department of Internal Medicine*

SHEA endorses adhering to the recommendations by the CDC and ACIP for immunizations of all children and adults. All persons providing clinical care should be familiar with these recommendations and should routinely assess immunization compliance of their patients and strongly recommend all routine immunizations to patients. All healthcare personnel (HCP) should be immunized against vaccine-preventable diseases as recommended by the CDC/ACIP (unless immunity is demonstrated by another recommended method). SHEA endorses the policy that immunization should be a condition of employment or functioning (students, contract workers, volunteers, etc) at a healthcare facility. Only recognized medical contraindications should be accepted for not receiving recommended immunizations.

**Weiner AJ, Weiner Y** and Weiner A (2021). "Corneal parameters after tube-shunt implantation through the ciliary sulcus." [Ophthalmology. Glaucoma](#) 4(1): 32-41.

[Full Text](#)

*Department of Ophthalmology*

Purpose: To monitor bilateral corneal parameters after unilateral Baerveldt 350 tube-shunt implantation (Advanced Medical Optics, Santa Ana, CA) through the ciliary sulcus. Design: Retrospective, interventional case series. Participants: Patients from 1 private glaucoma practice with severe uncontrolled glaucoma treated with sulcus tube-shunt implantation in 1 pseudophakic eye. Methods: Specular microscopy data were collected before and after unilateral sulcus tube-shunt implantation from the surgical and the glaucomatous fellow eyes. Main Outcome Measures: Central corneal endothelial cell density (CECD), coefficient of variation (CV), percent of hexagonal cells, central corneal thickness (CCT), intraocular pressure (IOP), IOP-lowering medications, visual acuity, and complications. RESULTS: Forty-six patients (mean age, 69.9 years; standard deviation [SD], 4.6 years; range, 20-88 years; male gender, 41.3%) were identified. After surgery, IOP and the number of IOP-lowering medications decreased significantly by 42.3% ( $P < 0.0001$ ) and 32.1% ( $P < 0.0001$ ), respectively, in the surgical eye group. Preoperative CECD measured 1807 cells/mm<sup>2</sup> (SD, 172 cells/mm<sup>2</sup>) and 1825 cells/mm<sup>2</sup> (SD, 172 cells/mm<sup>2</sup>) in the surgical and fellow eyes, respectively ( $P = 0.92$ ), and compared with baseline, it decreased by 8.6% ( $P = 0.17$ ) and 3.1% ( $P = 0.65$ ), respectively, by 24 months. Preoperative CV, percent of hexagonal cells, and CCT were similar in both groups and remained stable. All corneal parameters remained unchanged in a subgroup of 15 patients with low preoperative CECD (1273 cells/mm<sup>2</sup>; SD, 99 cells/mm<sup>2</sup>). Best-corrected visual acuity remained stable in both groups. Hyphema occurred in 23.9% of the surgical eyes and resolved with no intervention. We found no sight-threatening complications or corneal failures during follow-up. Conclusions: Tube-shunt implantation through the ciliary sulcus in pseudophakic eyes appears relatively safe to the corneal endothelium, demonstrating a small and nonsignificant decline in central CECD compared with baseline and with glaucomatous fellow eyes. No significant disruption to corneal endothelial cell morphologic features, increased corneal thickness, or corneal failures were found during the 24-month follow-up period. A prospective head-to-head comparison

to assess the effects of the various methods of tube-shunt implantation on the corneal endothelium is needed.

Willis BL, Radford NB, Barlow CE, Leonard D, **Franklin BA** and DeFina LF (2021). "Divergent association of high levels of physical activity with cardiac versus noncardiac arterial calcification." [American Heart Journal](#) 233: 10-13.

[Full Text](#)

*Department of Internal Medicine*

**Wilson GD**, Wilson TG, Hanna A, Dabjan M, Buelow K, Torma J, Marples B and Galoforo S (2021). "Dacomitinib and gedatolisib in combination with fractionated radiation in head and neck cancer." [Clinical and Translational Radiation Oncology](#) 26: 15-23.

[Full Text](#)

*Department of Radiation Oncology*

**Background and Purpose:** There has been little success targeting individual genes in combination with radiation in head and neck cancer. In this study we investigated whether targeting two key pathways simultaneously might be more effective. **Materials and Methods:** We studied the effect of combining dacomitinib (pan-HER, irreversible inhibitor) and gedatolisib (dual PI3K/MTOR inhibitor) with radiation in well characterized, low passage xenograft models of HNSCC in vitro and in vivo. **Results:** Dacomitinib showed differential growth inhibition in vitro that correlated to EGFR expression whilst gedatolisib was effective in both cell lines. Neither agent radiosensitized the cell lines in vitro. In vivo studies demonstrated that dacomitinib was an effective agent alone and in combination with radiation whilst the addition of gedatolisib did not enhance the effect of these two modalities despite inhibiting phosphorylation of key genes in the PI3K/MTOR pathway. **Conclusions:** Our results showed that combining two drugs with radiation provided no added benefit compared to the single most active drug. Dacomitinib deserves more investigation as a radiation sensitizing agent in HNSCC.

Won KB, Heo R, Park HB, Lee BK, Lin FY, Hadamitzky M, Kim YJ, Sung JM, Conte E, Andreini D, Pontone G, Budoff MJ, Gottlieb I, Chun EJ, Cademartiri F, Maffei E, Marques H, de Araújo Gonçalves P, Leipsic JA, Lee SE, Shin S, Choi JH, Virmani R, Samady H, **Chinnaiyan K**, Berman DS, Narula J, Shaw LJ, Bax JJ, Min JK and Chang HJ (2021). "Atherogenic index of plasma and the risk of rapid progression of coronary atherosclerosis beyond traditional risk factors."

[Atherosclerosis](#) 324: 46-51.

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*Department of Internal Medicine*

**Background and Aims:** The atherogenic index of plasma (AIP) has been suggested as a marker of plasma atherogenicity. This study aimed to assess the association between AIP and the rapid progression of coronary atherosclerosis using serial coronary computed tomography angiography (CCTA). **Methods:** A total of 1488 adults (60.9 ± 9.2 years, 58.9% male) who underwent serial CCTA with a median inter-scan period of 3.4 years were included. AIP was defined as the base 10 logarithm of the ratio of the concentrations of triglyceride to high-density lipoprotein cholesterol. Rapid plaque progression (RPP) was defined as the change of percentage atheroma volume (PAV) ≥1.0%/year. All participants were divided into three groups based on AIP tertiles. **Results:** Baseline total PAV (median [interquartile range (IQR)]) (%) (group I [lowest]: 1.91 [0.00, 6.21] vs. group II: 2.82 [0.27, 8.83] vs. group III [highest]: 2.70 [0.41, 7.50]), the annual change of total PAV (median [IQR]) (%/year) (group I: 0.27 [0.00, 0.81] vs. group II: 0.37 [0.04, 1.11] vs. group III: 0.45 [0.06, 1.25]), and the incidence of RPP (group I: 19.7% vs. group II: 27.3% vs. group III: 31.4%) were significantly different among AIP tertiles (all p < 0.05). In multiple logistic regression analysis, the risk of RPP was increased in group III (odds ratio: 1.52, 95% confidence interval: 1.02-2.26; p = 0.042) compared to group I after adjusting for clinical factors and baseline total PAV. **Conclusions:** Based on serial CCTA findings, AIP is an independent predictive marker for RPP beyond traditional risk factors.

**Yan D**, Chen S, **Krauss DJ**, **Deraniyagala R**, **Chen P**, Ye H and **Wilson G** (2021). "Inter/intra-tumoral dose response variations assessed using FDG-PET/CT feedback images: Impact on tumor control and treatment dose prescription." [Radiotherapy and Oncology](#) 154: 235-242.

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*Department of Radiation Oncology*

Purpose: To quantify inter/intra-tumoral variations of baseline metabolic activity and dose response. To evaluate their impact on tumor control and treatment dose prescription strategies. Methods and Materials: Tumor voxel baseline metabolic activity, SUV0, and dose response matrix, DRM, quantified using the pre-treatment and weekly FDG-PET/CT imaging feedback for each of 34 HNSCC patients (25 HPV+ and 9 HPV-) were evaluated. Inter/intra-tumoral variations of tumor voxel (SUV0, DRM) for each of the HPV- and HPV+ tumor groups were quantified and used to evaluate the variations of individual tumor control probabilities and the efficiency of uniform vs non-uniform treatment dose prescription strategies. Results: Tumor voxel dose response variation of all tumor voxels assessed using FDG-PET/CT imaging feedback had the mean(CV) = 0.47(47%), which was consistent with those of previously published in vitro tumor clonogenic assay. The HPV- tumors had the mean(CV) dose response, 0.53(49%), significantly larger than those of the HPV+ tumors, 0.45(43%). However, their baseline SUVs were opposite, 6.5(56%) vs 7.7(65%). Comparing to the inter-tumoral variations, both HPV-/+ tumor groups showed larger intra-tumoral variations, (53%, 58%) vs (20%, 31%) for the baseline SUV and (38%, 37%) vs (31%, 21%) for the dose response. Due to the large dose response variations, treatment dose to control the tumor voxels has very broad range with CV of TCD50 = 97% for the HPV- and 67% for the HPV+ tumor group respectively. As a consequence, heterogeneous prescription dose could potentially reduce the treatment integral dose for 92% of the HPV+ tumors and 78% of the HPV- tumors. Conclusions: The study demonstrates that tumor dose response assessed using FDG-PET/CT feedback images had a similar distribution to those assessed conventionally using in vitro tumor clonogenic assay. Inter-tumoral dose response variation seems larger for HPV- tumors, but intra-tumoral dose response variations are similar for both HPV groups. These variations cause very large variation on the individual tumor control probability and limit the efficacy of dose escalation and de-escalation in conventional clinical practice. On the other hand, heterogeneous dose prescription guided by metabolic imaging feedback has a potential advantage in radiotherapy.

Yan Y, Basij M, Garg A, Varrey A, **Alhousseini A**, Hsu R, Hernandez-Andrade E, Romero R, Hassan SS and Mehrmohammadi M (2021). "Spectroscopic photoacoustic imaging of cervical tissue composition in excised human samples." *PLoS One* 16(3): e0247385.

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*Department of Obstetrics and Gynecology*

Objective: Cervical remodeling is an important component in determining the pathway of parturition; therefore, assessing changes in cervical tissue composition may provide information about the cervix's status beyond the measurement of cervical length. Photoacoustic imaging is a non-invasive ultrasound-based technology that captures acoustic signals emitted by tissue components in response to laser pulses. This optical information allows for the determination of the collagen-to-water ratio (CWR). The purpose of this study was to compare the CWR evaluated by using spectroscopic photoacoustic (sPA) imaging in cervical samples obtained from pregnant and non-pregnant women. Methods: This cross-sectional study comprised cervical biopsies obtained at the time of hysterectomy (n = 8) and at the scheduled cesarean delivery in pregnant women at term who were not in labor (n = 8). The cervical CWR was analyzed using a fiber-optic light-delivery system integrated to an ultrasound probe. The photoacoustic signals were acquired within the range of wavelengths that cover the peak absorption of collagen and water. Differences in the CWR between cervical samples from pregnant and non-pregnant women were analyzed. Hematoxylin and eosin and Sirius Red stains were used to compare the collagen content of cervical samples in these two groups. Results: Eight cervix samples were obtained after hysterectomy, four from women <41 years of age and four from women ≥43 years of age; all cervical samples (n = 8) from pregnant women were obtained after 37 weeks of gestation at the time of cesarean section. The average CWR in cervical tissue samples from pregnant women was 18.7% (SD 7.5%), while in samples from non-pregnant women, it was 55.0% (SD 20.3%). There was a significantly higher CWR in the non-pregnant group compared to the pregnant group with a p-value <0.001. A subgroup analysis that compared the CWR in cervical samples from pregnant women and non-pregnant women ≤41 years of age (mean 46.3%, SD 23.1%) also showed a significantly higher CWR (p <0.01). Lower collagen content in the pregnancy group was confirmed by histological analysis, which revealed the loss of tissue composition, increased water content, and collagen degradation. Conclusion: The proposed bimodal ultrasound and sPA imaging system can provide information on the biochemical composition of cervical tissue in pregnant and non-pregnant women. Photoacoustic imaging showed a higher collagen content in cervical samples from non-pregnant women as compared to those from pregnant women, which matched

with the histological analysis. This novel imaging method envisions a new potential for a sensitive diagnostic tool in the evaluation of cervical tissue composition.

Yau TT, Sparks MA and **Topf JM** (2021). "Eight years of AJKD blog-lessons learned and what lies ahead." [American Journal of Kidney Diseases](#). ePub Ahead of Print.

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