

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

PUBLICATION LIST

July - September 2015

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Ahmed KA, Chinnaiyan P, Fulp WJ, Eschrich S, Torres-Roca JF and Caudell JJ (2015). "The radiosensitivity index predicts for overall survival in glioblastoma." [Oncotarget](#). ePub Ahead of Print.

[Full-Text](#)

Department of Internal Medicine

Department of Radiation Oncology

We have previously developed a multigene expression model of tumor radiosensitivity (RSI) with clinical validation in multiple cohorts and disease sites. We hypothesized RSI would identify glioblastoma patients who would respond to radiation and predict treatment outcomes. Clinical and array based gene expression (Affymetrix HT Human Genome U133 Array Plate Set) level 2 data was downloaded from the cancer genome atlas (TCGA). A total of 270 patients were identified for the analysis: 214 who underwent radiotherapy and temozolomide and 56 who did not undergo radiotherapy. Median follow-up for the entire cohort was 9.1 months (range: 0.04-92.2 months). Patients who did not receive radiotherapy were more likely to be older ($p < 0.001$) and of poorer performance status ($p < 0.001$). On multivariate analysis, RSI is an independent predictor of OS (HR = 1.64, 95% CI 1.08-2.5; $p = 0.02$). Furthermore, on subset analysis, radiosensitive patients had significantly improved OS in the patients with high MGMT expression (unmethylated MGMT), 1 year OS 84.1% vs. 53.7% ($p = 0.005$). This observation held on MVA (HR = 1.94, 95% CI 1.19-3.31; $p = 0.008$), suggesting that RT has a larger therapeutic impact in these patients. In conclusion, RSI predicts for OS in glioblastoma. These data further confirm the value of RSI as a disease-site independent biomarker.

Ali L, **Young MR**, Bayerl MG, Helm KF and Clarke LE (2015). "Gamma-Delta T-cell lymphoma arising in a long-standing cutaneous plaque." [Journal of Cutaneous Pathology](#). ePub Ahead of Print.

[Full-Text](#)

Department of Pathology

The precise classification and characterization of primary cutaneous gamma- delta T-cell lymphoma (PCGD-TCL) has been hindered by clinical and morphologic features that overlap with other lymphomas, especially subcutaneous panniculitis-like T cell lymphoma (SPTCL). The recent WHO / EORTC classification distinguishes the more aggressive PCGD-TCL from the usually indolent SPTCL, however. We report a 30 year

old woman with an indurated violaceous plaque on the left cheek that had been present for several years. Biopsies showed a dense lymphocytic infiltrate involving the subcutis and dermis that consisted mostly of small and medium sized lymphocytes, some with irregular nuclear contours and dense chromatin. These cells were positive for TIA-1, TCR-gamma and CD8, but negative for beta-F1 and Granzyme-B. Staging with PET/CT, CBC, and bone marrow with flow cytometry identified lymphadenopathy as well as blood and marrow involvement by an abnormal TCRgd-positive T-cell proliferation (Ann Arbor Stage IV). The patient's history of a long-standing lesion in this case is unusual, in that gamma-delta T-cell lymphomas are typically rapidly progressive neoplasms. As such, it raises the possibility of 'transformation' of a long-standing inflammatory process into an overt lymphoma.

Allegra CJ, Yothers G, O'Connell MJ, Beart RW, Wozniak TF, Pitot HC, Shields AF, Landry JC, Ryan DP, Arora A, Evans LS, Bahary N, Soori G, Eakle JF, **Robertson JM**, Moore DF, Jr., Mullane MR, Marchello BT, Ward PJ, Sharif S, Roh MS and Wolmark N (2015). "Neoadjuvant 5-FU or capecitabine plus radiation with or without oxaliplatin in rectal cancer patients: A phase III randomized clinical trial." Journal of the National Cancer Institute 107(11): 1-8.

[Full-Text](#)

Department of Radiation Oncology

BACKGROUND: National Surgical Adjuvant Breast and Bowel Project R-04 was designed to determine whether the oral fluoropyrimidine capecitabine could be substituted for continuous infusion 5-FU in the curative setting of stage II/III rectal cancer during neoadjuvant radiation therapy and whether the addition of oxaliplatin could further enhance the activity of fluoropyrimidine-sensitized radiation. METHODS: Patients with clinical stage II or III rectal cancer undergoing preoperative radiation were randomly assigned to one of four chemotherapy regimens in a 2x2 design: CVI 5-FU or oral capecitabine with or without oxaliplatin. The primary endpoint was local-regional tumor control. Time-to-event endpoint distributions were estimated using the Kaplan-Meier method. Hazard ratios were estimated from Cox proportional hazard models. All statistical tests were two-sided. RESULTS: Among 1608 randomized patients there were no statistically significant differences between regimens using 5-FU vs capecitabine in three-year local-regional tumor event rates (11.2% vs 11.8%), 5-year DFS (66.4% vs 67.7%), or 5-year OS (79.9% vs 80.8%); or for oxaliplatin vs no oxaliplatin for the three endpoints of local-regional events, DFS, and OS (11.2% vs 12.1%, 69.2% vs 64.2%, and 81.3% vs 79.0%). The addition of oxaliplatin was associated with statistically significantly more overall and grade 3-4 diarrhea ($P < .0001$). Three-year rates of local-regional recurrence among patients who underwent R0 resection ranged from 3.1 to 5.1% depending on the study arm. CONCLUSIONS: Continuous infusion 5-FU produced outcomes for local-regional control, DFS, and OS similar to those obtained with oral capecitabine combined with radiation. This study establishes capecitabine as a standard of care in the pre-operative rectal setting. Oxaliplatin did not improve the local-regional failure rate, DFS, or OS for any patient risk group but did add considerable toxicity.

Anthony G, Cunliffe A, Castillo R, Pham N, **Guerrero T**, Armato S and Al-Hallaq H (2015). "Incorporation of pre-therapy 18F-FDG uptake with CT texture features in a predictive model for radiation pneumonitis development." Medical Physics 42(6): 3324.

[Full-Text](#)

Department of Radiation Oncology

Bahado-Singh RO, Zaffra R, Albayarak S, Chelliah A, Bolinjar R, Turkoglu O and Radhakrishna U (2015). "Epigenetic markers for newborn congenital heart defect (CHD)." Journal of Maternal-Fetal & Neonatal Medicine: 1-7. ePub Ahead of Print.

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Department of Obstetrics and Gynecology

OBJECTIVE: Our objective was to determine whether there were significant differences in genome-wide DNA methylation in newborns with major congenital heart defect (CHD) compared to controls. We also evaluated methylation of cytosines in CpG motifs for the detection of these CHDs. METHODS: Genome-wide DNA methylation analysis was performed on DNA from 60 newborns with various CHDs, including hypoplastic left heart syndrome, ventricular septal deficit, atrial septal defect, pulmonary stenosis, coarctation of the aorta

and Tetralogy of Fallot, and 32 controls. RESULTS: Highly significant differences in cytosine methylation were seen in a large number of genes throughout the genome for all CHD categories. Gene ontology analysis of CHD overall indicated over-represented biological processes involving cell development and differentiation, and anatomical structure morphogenesis. Methylation of individual cytosines in CpG motifs had high diagnostic accuracy for the detection of CHD. For example, for coarctation one predictive model based on levels of particular cytosine nucleotides achieved a sensitivity of 100% and specificity of 93.8% (AUC = 0.974, $p < 0.00001$). CONCLUSION: Profound differences in cytosine methylation were observed in hundreds of genes in newborns with different types of CHD. There appears to be the potential for development of accurate genetic biomarkers for CHD detection in newborns.

Baschnagel AM, Wobb JL, **Dilworth JT**, Williams L, Eskandari M, **Wu D**, Pruetz BL and **Wilson GD** (2015). "The association of 18F-FDG PET and glucose metabolism biomarkers GLUT1 and HK2 in p16 positive and negative head and neck squamous cell carcinomas." *Radiotherapy and Oncology*. ePub Ahead of Print.

[Full-Text](#)

Department of Radiation Oncology

Department of Diagnostic Radiology and Molecular Imaging

Objectives: To investigate the relationship between FDG-PET maximum standard uptake value (SUVmax), p16, EGFR, GLUT1 and HK2 expression in head and neck squamous cell carcinomas (HNSCC). Materials and methods: Immunohistochemical staining of p16, EGFR, GLUT1 and HK2 was performed on primary tumor tissue from 97 locally advanced HNSCC patients treated with definitive chemoradiation. SUVmax along with p16, EGFR, GLUT1 and HK2 expression were analyzed for associations including local control, locoregional control and disease free survival. Results: Pretreatment SUVmax in primary tumors did not differ when stratified by p16, EGFR or GLUT1 expression but SUVmax was significantly higher in HK2 expressing tumors ($p = 0.021$) and in tumors with higher T-stage ($p = 0.022$). GLUT1 expression was significantly higher in p16 negative ($p < 0.001$) and EGFR positive tumors ($p < 0.01$). HK2 expressing tumors were associated with EGFR positive tumors ($p = 0.022$) but not with p16 or GLUT1 expression. EGFR positive, p16 negative and high GLUT1 expressing tumors were associated with worse local control and disease free survival on univariate analyses. After adjusting for patient and treatment characteristics p16 status was the only factor that predicted for outcome on multivariate analysis. Conclusions: High GLUT1 expression was associated with EGFR positive and p16 negative HNSCC tumors. GLUT1 maybe an important biomarker in HNSCC but its expression appears dependent on p16 status. © 2015 Elsevier Ireland Ltd.

Bauer ME, **Lorenz RP**, **Bauer ST**, Rao K and Anderson FWJ (2015). "Maternal deaths due to sepsis in the state of Michigan, 1999-2006." *Obstetrics and Gynecology* 126(4): 747-752.

[Full-Text](#)

Department of Obstetrics and Gynecology

OBJECTIVE: To identify maternal deaths due to sepsis in the state of Michigan, review the events leading to diagnosis, and evaluate treatment to identify areas for improvement. METHODS: A case series was collected for maternal deaths due to sepsis from a cohort of maternal deaths in the state of Michigan. The study period was 1999-2006 and included deaths during pregnancy and up to 42 days postpartum. Cases were identified using Maternal Mortality Surveillance records from the Michigan Department of Community Health. Each case was reviewed by all authors. RESULTS: Maternal sepsis was the cause of death in 15% (22/151) of pregnancy-related deaths. Of 22 deaths, 13 women presented to the hospital with sepsis, two developed sepsis during hospitalization, and seven developed sepsis at home without admission to the hospital for care. Review of available hospital records ($n=15$) revealed delays in initial appropriate antibiotic treatment occurred in 73% (11/15) of patients. Delay in escalation of care also occurred and was identified in 53% (8/15) of patients. CONCLUSION: Common elements in these deaths illustrate three key delays that may have contributed to the deaths: in recognition of sepsis, in administration of appropriate antibiotics, and in escalation of care.

Bedi DS, Krenzien F, Quante M, Uehara H, Edtinger K, Liu G, Denecke C, Jurisch A, Kim I, Li H, Yuan X, Ge X, ElKhal A and Tullius SG (2015). "Defective CD8 signaling pathways delay rejection in older recipients." Transplantation. ePub Ahead of Print.

[Full-Text](#)

Department of Surgery

CD8 T cells play a cardinal feature in response to alloantigens and are able to generate effector/memory T cells independently from CD4 T cells. To investigate the impact of aging on CD8 T cells, we used a fully mismatched mouse skin transplant model. Our findings showed a prolonged allograft survival in older recipients associated with a significant increase of CD4 and CD8CD44CD62L effector/memory T cells and a reduced systemic IFN γ production. When reconstituting young CBA Rag-1 mice that lack mature T and B cells with old CD8 T cells expressing clonal anti-H2K T cell receptor (TCR) alloreactive for MHC I, graft survival was significantly prolonged and comparable to those receiving young CD8 T cells. Moreover, our data showed that reduced systemic IFN γ levels observed in old recipients had been linked to a compromised expression of the IL-2R beta subunit (CD122) by old CD8 T cells. In addition, we observed an impaired IFN γ production on IL-2 receptor activation. At the same time, gene profiling analysis of old CD8 T cells demonstrated reduced chemokine ligand-3 and CD40L expression that resulted in compromised CD8 T cell/dendritic cell communication, leading to impaired migratory and phagocytic activity of CD11c cells. Collectively, our study demonstrated that aging delays allograft rejection. CD8 T cells play a critical role in this process linked to a compromised production of IFN γ , in addition to a defective IL-2 receptor signaling machinery and a defective communication between CD8 T cells and dendritic cells.

Benesh EC, Gill J, **Lamb LE** and Moley KH (2015). "Maternal obesity, cage density, and age contribute to prostate hyperplasia in mice." Reproductive Sciences. ePub Ahead of Print.

[Full-Text](#)

Department of Urology

Identification of modifiable risk factors is gravely needed to prevent adverse prostate health outcomes. We previously developed a murine precancer model in which exposure to maternal obesity stimulated prostate hyperplasia in offspring. Here, we used generalized linear modeling to evaluate the influence of additional environmental covariates on prostate hyperplasia. As expected from our previous work, the model revealed that aging and maternal diet-induced obesity (DIO) each correlated with prostate hyperplasia. However, prostate hyperplasia was not correlated with the length of maternal DIO. Cage density positively associated with both prostate hyperplasia and offspring body weight. Expression of the glucocorticoid receptor in prostates also positively correlated with cage density and negatively correlated with age of the animal. Together, these findings suggest that prostate tissue was adversely patterned during early life by maternal overnutrition and was susceptible to alteration by environmental factors such as cage density. Additionally, prostate hyperplasia may be acutely influenced by exposure to DIO, rather than occurring as a response to worsening obesity and comorbidities experienced by the mother. Finally, cage density correlated with both corticosteroid receptor abundance and prostate hyperplasia, suggesting that overcrowding influenced offspring prostate hyperplasia. These results emphasize the need for multivariate regression models to evaluate the influence of coordinated variables in complicated animal systems.

Berger DA, Ross MA, **Hollander JB**, **Ziadeh J**, **Chen C**, **Jackson RE** and **Swor RA** (2015). "Tamsulosin does not increase 1-week passage rate of ureteral stones in ED patients." American Journal of Emergency Medicine. ePub Ahead of Print

[Full-Text](#)

Department of Urology

Department of Emergency Medicine

Department of Pediatrics

OBJECTIVE: The objective of the study is to determine if tamsulosin initiated in the emergency department (ED) decreases the time to ureteral stone passage at 1 week or time to pain resolution, compared to placebo. **METHODS:** We performed a prospective, randomized, double-blinded, placebo-controlled trial of tamsulosin vs placebo in ED patients with ureterolithiasis on computed tomography. Patients were identified and

enrolled between April 2007 and February 2009 and were randomized to either 0.4 mg of tamsulosin or placebo for 1 week. We contacted participants using a telephone survey on post-ED visit days 1, 2, 3, and 7. The primary outcome was time to stone passage, with secondary outcomes being maximum pain score and amount of pain medication required. RESULTS: Of the 127 patients enrolled during this study, 15 were lost to follow-up, and 12 required surgical interventions before the 7-day mark, leaving 100 patients for analysis. Of the 100 patients, 53 received tamsulosin and 47 received placebo. There was no difference between groups in percentage of male, mean age, initial serum creatinine, average stone size, stone location, and history of prior stone. The probability that the patient did not pass a stone at 7 days was not different between tamsulosin and placebo, 62.1% (95% confidence interval, 49.1%-75.1%) vs 54.4% (95% confidence interval, 40.3%-68.6%; $P = .58$). There was no significant difference in the high pain score ($P = .12$) or hydrocodone/acetaminophen intake ($P = .76$) between treatment groups at any of the time points. CONCLUSION: This study reveals no difference in the proportion of stone passage or high pain score and pain medication utilization at 7 days between tamsulosin and placebo.

Brennan D, Schubert L, Diot Q, Castillo R, Castillo E, **Guerrero T**, Martel MK, Linderman D, Gaspar LE, Miften M, Kavanagh BD and Vinogradskiy Y (2015). "Clinical validation of 4-dimensional computed tomography ventilation with pulmonary function test data." International Journal of Radiation Oncology Biology Physics 92(2): 423-429.

[Full-Text](#)

Department of Radiation Oncology

Purpose A new form of functional imaging has been proposed in the form of 4-dimensional computed tomography (4DCT) ventilation. Because 4DCTs are acquired as part of routine care for lung cancer patients, calculating ventilation maps from 4DCTs provides spatial lung function information without added dosimetric or monetary cost to the patient. Before 4DCT-ventilation is implemented it needs to be clinically validated. Pulmonary function tests (PFTs) provide a clinically established way of evaluating lung function. The purpose of our work was to perform a clinical validation by comparing 4DCT-ventilation metrics with PFT data. Methods and Materials Ninety-eight lung cancer patients with pretreatment 4DCT and PFT data were included in the study. Pulmonary function test metrics used to diagnose obstructive lung disease were recorded: forced expiratory volume in 1 second (FEV1) and FEV1/forced vital capacity. Four-dimensional CT data sets and spatial registration were used to compute 4DCT-ventilation images using a density change-based and a Jacobian-based model. The ventilation maps were reduced to single metrics intended to reflect the degree of ventilation obstruction. Specifically, we computed the coefficient of variation (SD/mean), ventilation V20 (volume of lung <20% ventilation), and correlated the ventilation metrics with PFT data. Regression analysis was used to determine whether 4DCT ventilation data could predict for normal versus abnormal lung function using PFT thresholds. Results Correlation coefficients comparing 4DCT-ventilation with PFT data ranged from 0.63 to 0.72, with the best agreement between FEV1 and coefficient of variation. Four-dimensional CT ventilation metrics were able to significantly delineate between clinically normal versus abnormal PFT results. Conclusions Validation of 4DCT ventilation with clinically relevant metrics is essential. We demonstrate good global agreement between PFTs and 4DCT-ventilation, indicating that 4DCT-ventilation provides a reliable assessment of lung function. Four-dimensional CT ventilation enables exciting opportunities to assess lung function and create functional avoidance radiation therapy plans. The present work provides supporting evidence for the integration of 4DCT-ventilation into clinical trials.

Capone A, Jr. (2015). "Individualizing therapy for DME: Disease features as well as individual patient needs and preferences should drive treatment choices." Retina Today 2015(July): 79-80,84.

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Department of Ophthalmology

Cappell MS (2015). "Gastroenterology endoscopy nurses as important evaluators of gastroenterology fellow performance: A proposed model evaluation form." Gastroenterology Nursing 38(4): 313-316.

[Full-Text](#)

Department of Internal Medicine

Cappell MS (2015). "List predatory journal publications separately from genuine scholarly publications as standard for CVs." BMJ (Clinical research ed.) 350: h2470.

[Full-Text](#)

Department of Internal Medicine

Cappell MS, Mogrovejo E and Manickam P (2015). "Acute liver failure caused by metastatic breast cancer: Can we expect some results from chemotherapy? Reply." Digestive Diseases and Sciences 60(8): 2542-2543.

[Full-Text](#)

Department of Internal Medicine

Castillo R, Pham N, Castillo E, Aso-Gonzalez S, Ansari S, Hobbs B, Palacio D, Skinner H and **Guerrero TM** (2015). "Pre-radiation therapy fluorine 18 fluorodeoxyglucose PET helps identify patients with esophageal cancer at high risk for radiation pneumonitis." Radiology 275(3): 822-831.

[Full-Text](#)

Department of Radiation Oncology

Purpose: To examine the association between pre-radiation therapy (RT) fluorine 18 fluorodeoxyglucose (FDG) uptake and post-RT symptomatic radiation pneumonitis (RP). Materials and Methods: In accordance with the retrospective study protocol approved by the institutional review board, 228 esophageal cancer patients who underwent FDG PET/CT before chemotherapy and RT were examined. RP symptoms were evaluated by using the Common Terminology Criteria for Adverse Events, version 4.0, from the consensus of five clinicians. By using the cumulative distribution of standardized uptake values (SUVs) within the lungs, those values greater than 80%-95% of the total lung voxels were determined for each patient. The effect of prechemotherapy and RT FDG uptake, dose, and patient or treatment characteristics on RP toxicity was studied by using logistic regression. Results: The study subjects were treated with three-dimensional conformal RT (n = 36), intensity-modulated RT (n = 135), or proton therapy (n = 57). Logistic regression analysis demonstrated elevated FDG uptake at pre-chemotherapy and RT was related to expression of RP symptoms. Study subjects with elevated 95% percentile of the SUV (SUV >95) were more likely to develop symptomatic RP (P < .000012); each 0.1 unit increase in SUV >95 was associated with a 1.36-fold increase in the odds of symptomatic RP. Receiver operating characteristic (ROC) curve analysis resulted in area under the ROC curve of 0.676 (95% confidence interval: 0.58, 0.77), sensitivity of 60%, and specificity of 71% at the 1.17 SUV >95 threshold. CT imaging and dosimetric parameters were found to be poor predictors of RP symptoms. Conclusion: The SUV >95 , a biomarker of pretreatment pulmonary metabolic activity, was shown to be prognostic of symptomatic RP. Elevation in this pretreatment biomarker identifies patients at high risk for posttreatment symptomatic RP.

Castillo SJ, Castillo R, Castillo E, Pan T, Ibbott G, Balter P, Hobbs B and **Guerrero T** (2015). "Evaluation of 4D CT acquisition methods designed to reduce artifacts." Journal of Applied Clinical Medical Physics 16(2): 23-32.

[Request Form](#)

Department of Radiation Oncology

Four-dimensional computed tomography (4D CT) is used to account for respiratory motion in radiation treatment planning, but artifacts resulting from the acquisition and postprocessing limit its accuracy. We investigated the efficacy of three experimental 4D CT acquisition methods to reduce artifacts in a prospective institutional review board approved study. Eighteen thoracic patients scheduled to undergo radiation therapy received standard clinical 4D CT scans followed by each of the alternative 4D CT acquisitions: 1) data oversampling, 2) beam gating with breathing irregularities, and 3) rescanning the clinical acquisition acquired during irregular breathing. Relative values of a validated correlation-based artifact metric (CM) determined the best acquisition method per patient. Each 4D CT was processed by an extended phase sorting approach that optimizes the quantitative artifact metric (CM sorting). The clinical acquisitions were also postprocessed by phase sorting for artifact comparison of our current clinical implementation with the experimental methods. The oversampling acquisition achieved the lowest artifact presence among all acquisitions, achieving a 27% reduction from the current clinical 4D CT implementation (95% confidence

interval = 34-20). The rescan method presented a significantly higher artifact presence from the clinical acquisition (37%; $p < 0.002$), the gating acquisition (26%; $p < 0.005$), and the oversampling acquisition (31%; $p < 0.001$), while the data lacked evidence of a significant difference between the clinical, gating, and oversampling methods. The oversampling acquisition reduced artifact presence from the current clinical 4D CT implementation to the largest degree and provided the simplest and most reproducible implementation. The rescan acquisition increased artifact presence significantly, compared to all acquisitions, and suffered from combination of data from independent scans over which large internal anatomic shifts occurred.

Chapman R, Sabina R and Thomas D (2015). "Skin signs of systemic disease TBL (Peer Reviewed)." MedEdPortal Publication No. 10184

[Full-Text](#)

Department of Internal Medicine

Department of Biomedical Sciences (OU)

Department of Medical Education

Teaching dermatology to medical students and interns poses unique challenges but provides an excellent learning experience because many skin diseases look similar to the untrained eye. Enhancing observational skills through fine art has been used to help train new dermatology residents at Yale Medical School. Years of practice are generally needed before a new practitioner learns to integrate memorized facts with history and physical findings. In the upcoming age of telemedicine, the practitioner will need to be able to ask pertinent questions and develop a diagnostic and treatment ladder based on photographs and history. This resource was designed to enable learners to recognize common skin signs of disease, such as hair loss, and how it may be the initial manifestation of an autoimmune connective tissue disorder. This team-based learning (TBL) module relies on application of knowledge gained from written material and applied to a changing clinical picture designed to simulate clinical practice. It requires drawing knowledge from multiple sources (lectures, online reading, and basic science) and applying it to develop a logical diagnosis and treatment strategy.

Chehab M, **Savin M, Campbell J**, Cash C, **Wong C** and **Schultz C** (2015). "5: 27 PM, Abstract No. 239-Yttrium-90 infusion: Incidence and outcomes of delivery system occlusions." *Journal of Vascular and Interventional Radiology* 26(2): S110.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Chehab M and **Wilseck J** (2015). "E-086 non-ischemic etiologies by CT perfusion." *Journal of Neurointerventional Surgery* 7(Suppl 1): A79.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Chehab M and **Wilseck J** (2015). "E-087 negative predictive value of CT perfusion in excluding lesions amenable to endovascular reperfusion." *Journal of Neurointerventional Surgery* 7(Suppl 1): A79.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Chen L, Khan M, Alapati K, **Hsieh M** and **Barry K** (2015). "Evaluation of image quality and radiation dose of various unenhanced head CT protocols." *Medical Physics* 42(6): 3237.

[Full-Text](#)

Department of Pathology

Department of Diagnostic Radiology and Molecular Imaging

Copelan A, Bahoura L, Tardy F, **Kirsch M, Sokhandon F** and Kapoor B (2015). "Etiology, diagnosis, and management of bilomas: A current update." Techniques in Vascular and Interventional Radiology. ePub Ahead of Print.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

A biloma is a well-demarcated collection of bile outside the biliary tree. Traumatic and iatrogenic injuries, most commonly secondary to cholecystectomy, are the usual causes. Although bilomas are relatively uncommon, this pathologic entity may lead to significant morbidity and mortality if not promptly diagnosed and properly managed. As clinical signs and symptoms of bilomas are often nonspecific and laboratory values may be unremarkable, imaging modalities including ultrasound, computed tomography, magnetic resonance imaging, and hepatobiliary cholescintigraphy play a crucial role in the diagnosis of this condition. It is paramount that interventional radiologists not only be well versed in the management of bilomas but also be knowledgeable in the diagnosis as well as key imaging findings that dictate the interventional management. The purpose of this article is to review the etiology, pathophysiology, and clinical presentation of bilomas to primarily focus on the relevant multimodal imaging findings and the minimally invasive management options.

Counselman FL, Carius ML, **Kowalenko T**, Battaglioli N, Hobgood C, Jagoda AS, Lovell E, Oshva L, Patel A, Shayne P, Tabas JA and Reisdorff EJ (2015). "The American Board of Emergency Medicine Maintenance of Certification Summit." Journal of Emergency Medicine. ePub Ahead of Print.

[Full-Text](#)

Department of Emergency Medicine

Background: The American Board of Emergency Medicine (ABEM) convened a summit of stakeholders in Emergency Medicine (EM) to critically review the ABEM Maintenance of Certification (MOC) Program. Objective: The newly introduced American Board of Medical Specialties (ABMS) 2015 MOC Standards require that the ABMS Member Boards, including ABEM, "engage in continual quality monitoring and improvement of its Program for MOC. ." ABEM sought to have the EM community participate in the quality improvement process. Discussion: A review of the ABMS philosophy of MOC and requirements for MOC were presented, followed by an exposition of the ABEM MOC Program. Roundtable discussions included strengths of the program and opportunities for improvement; defining, teaching, and assessing professionalism; identifying and filling competency gaps; and enhancing relevancy and adding value to the ABEM MOC Program. Conclusions: Several suggestions to improve the ABEM MOC Program were discussed. ABEM will consider these recommendations when developing its next revision of the ABEM MOC Program.

D'Andrea K, Dreyer J and **Fahim DK** (2015). "Utility of preoperative MRI co-registered with intraoperative CT scan for the resection of complex tumors of the spine." World Neurosurgery. ePub Ahead of Print.

[Full-Text](#)

Department of Neurosurgery

BACKGROUND: Complete surgical resection is known to provide the best prognosis when treating complex tumors of the spine. The anatomy of the cervical spine and the extensive involvement often present by the time these lesions are discovered can make total resection challenging. A novel technique combining preoperative and intraoperative imaging for intraoperative navigation can serve as an additional tool for facilitating tumor resection. METHODS: Preoperative MRI was co-registered with intraoperative CT for accurate, real-time, intraoperative navigation for complete resection of complex tumors of the cervical spine. This new technique is demonstrated. The potential advantages and challenges are discussed. RESULTS: Preoperative MRI co-registered and merged with intraoperative CT allows for accurate visualization of tumor boundaries, osseous anatomy, and surrounding soft tissue structures. Total resection of extensive spinal tumors involving the anterior and posterior elements can be facilitated by this technique. CONCLUSIONS: Preoperative MRI co-registered and merged with intraoperative CT may serve as a useful intraoperative imaging modality for facilitating safe and complete resection of complex spine tumors.

Dave CN, Chaus F, **Chancellor MB**, Lajness M and **Peters KM** (2015). "Innovative use of intravesical tacrolimus for hemorrhagic radiation cystitis." International Urology and Nephrology 47(10): 1679-1681.

[Full-Text](#)

Department of Urology

Hemorrhagic cystitis is a rare and severe late complication of pelvic radiation, and there is no regulatory-approved drug treatment. We present an 81-year-old man with a history of localized prostate cancer, which was treated with external beam radiation therapy and subsequently developed severe hemorrhagic radiation cystitis for which he has failed several treatments. We present the novel use of intravesical tacrolimus for the treatment of refractory radiation cystitis and gross hematuria. The patient tolerated the treatment well, and it resulted in the resolution of his gross hematuria without further consideration for formalin instillation or cystectomy and diversion. Intravesical tacrolimus is a safe, minimally invasive, and promising treatment option for radiation hemorrhagic cystitis.

Dhanota H, Pinkas D, Josserand D, **Wiater BP**, Koueiter DM and **Wiater JM** (2015). "Use of a topical thrombin-based hemostatic agent in shoulder arthroplasty." American Journal of Orthopedics (Belle Mead, N.J.) 44(8): E262-E267.

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Department of Orthopedic Surgery

Shoulder arthroplasty is associated with significant blood loss, often requiring blood transfusion. Hemostatic agents are used in various surgical specialties to minimize blood loss, but to date few studies have examined their efficacy in shoulder arthroplasty. We retrospectively reviewed 211 consecutive shoulder arthroplasty cases performed by a single surgeon. Our hypothesis was that patients treated with a topical thrombin prepared with a hemostatic matrix (Surgiflo) would have decreased perioperative blood loss. Patients with humeral fractures or preexisting blood disease were excluded. Control patients were managed December 2012 through April 2013. Study patients were managed May 2013 through August 2013 using the same surgical technique with the additional application of the hemostatic agent before closure. Charts were reviewed for demographics, estimated blood loss, drain output, transfusion rates, and complications. Hidden blood loss was calculated using a validated method. There were no differences in estimated blood loss ($P = .301$), drain output ($P = .906$), or hidden blood loss ($P = .601$) between groups. There was no increased incidence of transfusion between study (25%) and control (20%) groups ($P = .407$). No increased complications resulted from use of the hemostatic agent ($P = .764$). On the basis of these results, we cannot conclude that this topical hemostatic agent is effective as a blood loss management tool in shoulder arthroplasty.

Dhou S, Cai W, Hurwitz M, Williams C, Cifter F, Myronakis M, **Ionascu D** and Lewis J (2015). "Day-to-day variations in fraction-specific motion modeling using patient 4DCBCT images." Medical Physics 42(6): 3299.

[Full-Text](#)

Department of Radiation Oncology

Dhou S, Cai W, Hurwitz M, Williams C, Rottmann J, **Mishra P**, Myronakis M, Cifter F, Berbeco R, **Ionascu D** and Lewis J (2015). "3D fluoroscopic image generation from patient-specific 4DCBCT-based motion models derived from physical phantom and clinical patient images." Medical Physics 42(6): 3697.

[Full-Text](#)

Department of Internal Medicine

Department of Radiation Oncology

Dukkipati SR, Cuoco F, **Kutinsky I**, Aryana A, Bahnson TD, Lakkireddy D, Woollett I, Issa ZF, Natale A and Reddy VY (2015). "Pulmonary vein isolation using the visually guided laser balloon a prospective, multicenter, and randomized comparison to standard radiofrequency ablation." Journal of the American College of Cardiology 66(12): 1350-1360.

[Full-Text](#)

Department of Internal Medicine

Background Balloon catheters have been designed to facilitate pulmonary vein (PV) isolation in patients with paroxysmal atrial fibrillation (AF). The visually guided laser balloon (VGLB) employs laser energy to ablate

tissue under direct visual guidance. Objectives This study compared the efficacy and safety of VGLB ablation with standard irrigated radiofrequency ablation (RFA) during catheter ablation of AF. Methods Patients with drug-refractory paroxysmal AF were enrolled in a multicenter, randomized controlled study of PV isolation using either the VGLB or RFA (control). The primary efficacy endpoint was freedom from protocol-defined treatment failure at 12 months, including symptomatic AF occurring after the 90-day blanking period. The primary efficacy and safety endpoints were powered for noninferiority. Results A total of 353 patients (178 VGLB, 175 control) were randomized at 19 clinical sites. The mean procedure, ablation, and fluoroscopy times were longer with VGLB compared with controls. The primary efficacy endpoint was met in 61.1% in the VGLB group versus 61.7% in controls (absolute difference -0.6%; lower limit of 95% confidence interval [CI]: -9.3%; $p = 0.003$ for noninferiority). The primary adverse event rate was 11.8% in the VGLB group versus 14.5% in controls (absolute difference -2.8%; upper limit of 95% CI: 3.5; $p = 0.002$ for noninferiority), and was mainly driven by cardioversions. Diaphragmatic paralysis was higher (3.5% vs. 0.6%; $p = 0.05$), but PV stenosis was lower (0.0% vs. 2.9%; $p = 0.03$) with VGLB. Conclusions Despite minimal prior experience, the safety and efficacy of VGLB ablation proved noninferior to RFA for the treatment of paroxysmal AF. (Pivotal Clinical Study of the CardioFocus Endoscopic Ablation System-Adaptive Contact [EAS-AC] [HeartLight] in Patients With Paroxysmal Atrial Fibrillation [PAF] [HeartLight]; NCT01456000)

Dukkupati SR, Woollett I, McElderry HT, Böhmer MC, **Doshi SK**, Gerstenfeld EP, Horton R, D'Avila A, **Haines DE**, Valderrabano M, Mangrum JM, Ruskin JN, Natale A and Reddy VY (2015). "Pulmonary vein isolation using the visually guided laser balloon: Results of the U.S. feasibility study." *Journal of Cardiovascular Electrophysiology* 26(9): 944-949.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Department of Internal Medicine

Visually Guided PV Isolation Introduction Visually guided laser balloon (VGLB) ablation is unique in that the operator delivers ablative energy under direct visual guidance. In this multicenter study, we sought to determine the feasibility, efficacy, and safety of performing pulmonary vein isolation (PVI) using this VGLB. Methods Patients with symptomatic, drug-refractory paroxysmal atrial fibrillation (AF) underwent PVI using the VGLB with the majority of operators conducting their first-ever clinical VGLB cases. The primary effectiveness endpoint was defined as freedom from treatment failure that included: Occurrence of symptomatic AF episodes ≥ 1 minutes beyond the 90-day blanking, the inability to isolate 1 superior and 2 total PVs, occurrence of left atrial flutter or atrial tachycardia, or left atrial ablation/surgery during follow-up. Results A total of 86 patients (mean age 56 ± 10 years, 67% male) were treated with the VGLB at 10 US centers. Mean fluoroscopy, ablation, and procedure times were 39.8 ± 24.3 minutes, 205.2 ± 61.7 minutes, and 253.5 ± 71.3 minutes, respectively. Acute PVI was achieved in 314/323 (97.2%) of targeted PVs. Of 84 patients completing follow-up, the primary effectiveness endpoint was achieved in 50 (60%) patients. Freedom from symptomatic or asymptomatic AF was 61%. The primary adverse event rate was 16.3% (8.1% pericarditis, phrenic nerve injury 5.8%, and cardiac tamponade 3.5%). There were no cerebrovascular events, atrioesophageal fistulas, or significant PV stenosis. Conclusions This multicenter study of operators in the early stage of the learning curve demonstrates that PVI can be achieved with the VGLB with a reasonable safety profile and an efficacy similar to radiofrequency ablation.

Engwall K (2015). "Exploring information security and shared encrypted spaces in libraries." *Code4Lib* 2015(29).

[Full-Text](#)

Medical Library

Libraries are sensitive to the need to protect patron data, but may not take measures to protect the data of the library. However, in an increasingly collaborative online environment, the protection of data is a concern that merits attention. As a follow-up to a new patron privacy policy, the Oakland University William Beaumont Medical Library evaluated information security tools for use in day-to-day operations in an attempt to identify ways to protect private information in communication and shared storage, as well as a means to manage passwords in a collaborative team environment. This article provides an overview of encryption measures, outlines the Medical Library's evaluation of encryption tools, and reflects on the benefits and challenges in their adoption and use.

Fawole AA, Ogunleye FN, Rana J, Isaac D, **Ibrahim M, Huben MT, Wasvary H, Anderson JM, Gaikazian SS, Zakalik D, Robertson JM** and **Jaiyesimi IA** (2015). "Colorectal cancer in patients 50 years and younger: The Beaumont Health System experience." Journal of Clinical Oncology 33(15): e14583.

[Request Form](#)

Department of Internal Medicine

Department of Surgery

Department of Radiation Oncology

Background: Colorectal cancer (CRC) is a common and lethal disease. Age is a major risk factor for developing sporadic CRC. CRC is uncommon before 50 years of age, and it is often discovered at later stages. These factors may explain why there are limited studies in this age group. Although the incidence of CRC has been decreasing over the past three decades, the incidence in people younger than 50 years has been on the rise. The declining incidence of CRC in individuals older than 50 years has been attributed to early detection and intervention through screening studies. Methods: After obtaining IRB approval, the Beaumont Hospital's oncologic database was used to identify patients 18 to 50 years of age with histologically confirmed adenocarcinoma of the colon and/or rectum between 2008 and 2010. Results: Charts of 159 patients were included for the final analysis. Their ages ranged from 21-50 years, with a median age of 46 years. Only 3.7% of all patients had preexisting colonic polyps or inflammatory bowel disease. Twenty-eight (17.6%) of 159 patients had a family history of predisposing conditions such as colonic polyps, CRC, and/or endometrial carcinoma prior to CRC diagnosis. Among patients with a family history of predisposing conditions, only four (14.3%) had screening colonoscopy. Stage IV CRC was diagnosed at presentation in 36 (22.6%) patients. CRC was located in the sigmoid colon and the rectum in 103 (64.8%) patients in this cohort. Conclusions: One in five young adults with CRC already had advanced stage cancer at presentation. The majority of young patients with CRC had no family history of predisposing conditions. Most young adults considered at increased risk of CRC were not being screened by colonoscopy. In this cohort, CRC was most commonly located in sigmoid colon and rectum.

Franklin BA, Brinks J and Hendrickson K (2015). "Counseling strategies for health-fitness professionals." ACSM's Health & Fitness Journal 19(5): 23-30.

[Full-Text](#)

Department of Internal Medicine

Franklin BA and Lavie CJ (2015). "Impact of statins on physical activity and fitness: Ally or adversary?" Mayo Clinic Proceedings 90(10): 1314-1319.

[Full-Text](#)

Department of Internal Medicine

Garg L, Yadav D and **Shoichet S** (2015). "Hypermucovirulent klebsiella pneumoniae: An emerging threat in the United States." Infectious Diseases in Clinical Practice 23(5): 278.

[Full-Text](#)

Department of Internal Medicine

Gjeorgjievski M, Purohit T, **Amin MB**, Kurtin PJ and **Cappell MS** (2015). "Upper gastrointestinal bleeding from gastric amyloidosis in a patient with smoldering multiple myeloma." Case Rep Gastrointest Med 2015: 320120.

[Full-Text](#)

Department of Pathology

Department of Internal Medicine

Amyloidosis is a common complication of patients with monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM), and multiple myeloma (MM). This proteinaceous material can be deposited intercellularly in any organ system, including the gastrointestinal (GI) tract. In the GI tract, amyloidosis affects the duodenum most commonly, followed by the stomach and colorectum. Gastric amyloidosis causes symptoms of nausea, vomiting, early satiety, abdominal pain, and GI bleeding. A

case of upper GI bleeding from gastric amyloidosis is presented in a patient with SMM. Esophagogastroduodenoscopy (EGD) revealed a gastric mass. Endoscopic biopsies revealed amyloid deposition in the lamina propria, consistent with gastric amyloidosis. Liquid chromatography tandem mass spectrometry performed on peptides extracted from Congo red-positive microdissected areas of paraffin-embedded stomach specimens revealed a peptide profile consistent with AL- (lambda-) type amyloidosis. Based on this and multiple other case reports, we recommend that patients with GI bleeding and MGUS, SMM, or MM undergo EGD and pathologic examination of endoscopic biopsies of identified lesions using Congo red stains for amyloidosis for early diagnosis and treatment.

Goncalves LF, Lee W, Mody S, Shetty A, Sangi-Haghpeykar H and Romero R (2015). "Diagnostic accuracy of ultrasonography and magnetic resonance imaging for the detection of fetal anomalies - a blinded case-control study." *Ultrasound in Obstetrics and Gynecology*. ePub Ahead of Print.

[Full-Text](#)

Department of Obstetrics and Gynecology

PURPOSE: To compare the accuracy of two-dimensional ultrasound (2DUS), three-dimensional ultrasound (3DUS) and MRI to diagnose congenital anomalies without knowledge of indications and prior imaging findings. **MATERIAL AND METHODS:** Prospective blinded case-control study. 2DUS, 3DUS and MRI were performed in one institution. Different examiners at a collaborating institution performed image interpretation. Sensitivity and specificity were calculated for individual anomalies based on postnatal imaging and/or autopsy. Diagnostic confidence was graded on a 4-point Likert scale. **RESULTS:** 157 fetuses (67 cases and 90 controls) were enrolled. Nine cases were excluded due to incomplete outcome. Among cases, 13 (22.4%) had CNS anomalies, 40 (69.0%) had non-CNS anomalies, and 5 (8.6%) had both CNS and non-CNS anomalies. **MAIN RESULTS:** 1) MRI was more sensitive than 3DUS to diagnose CNS anomalies [MRI 88.9% (16/18), 3DUS 66.7% (12/18), 2DUS 72.2%; (13/18); McNemar's test: MRI vs. 3DUS $p = 0.046$]; 2) MRI provided additional information affecting prognosis and/or counseling in 22.2% (4/18) of CNS anomalies; 3) 2DUS, 3DUS, and MRI had similar sensitivity to diagnose non-CNS anomalies; 4) specificity was higher for 3DUS [MRI 85.6% (77/90), 3DUS 94.4% (85/90), 2DUS 92.2% (83/90); McNemar's test: MRI vs. 3DUS $p = 0.03$]; 5) MRI confidence was lower to rule out certain CNS abnormalities (usually questionable cortical dysplasias or hemorrhage) not confirmed after delivery. **CONCLUSION:** MRI was more sensitive than ultrasonography and provided additional information that changed prognosis, counseling or management in 22.2% of fetuses with CNS anomalies. False-positives for subtle CNS findings were higher by MRI.

Greenlee H, Lew D, Hershman DL, Pierce JP, Hansen LK, Newman VA, Korner J, **Sayegh A**, Fehrenbacher L, Lo SS, Klemp JR, Rinn K, **Robertson JM**, Unger JM, Gralow J, Albain KS, Krouse RS and Fabian CJ (2015). "Phase II feasibility study of a physical activity and dietary change weight loss intervention in a subset analysis of breast cancer survivors (SWOG S1008)." *Journal of Clinical Oncology* 33(15): 9572.

[Request Form](#)

Department of Family Medicine

Department of Radiation Oncology

Background: Weight loss among overweight and obese breast and colorectal cancer survivors is hypothesized to be associated with improved diseasefree survival. Phase III trials are needed to test effective and implementable weight loss interventions in breast and colorectal cancer survivors. **Methods:** We conducted a feasibility study of a 12-month communitysituated physical activity and telephonebased dietary change weight loss intervention in female breast and colorectal cancer survivors. We report the primary outcomes for the breast cancer (BC) cohort. Sedentary postmenopausal women with prior Stage III BC and BMI ≥ 25 kg/m² were eligible. Primary objectives were to assess feasibility and weight loss at 12 months. Target accrual was 25 BC participants (ppts). Ppts were assigned a telephone counselor and given a 12-month membership to a local Curves fitness center, which offers a 30minute circuitbased exercise program. Ppts were counseled 14 times over 12 months and were instructed to exercise 150 minutes/week, walk 10,000 steps/day, and decrease caloric intake by 500 kcal/day. The intervention would be considered feasible if full accrual was met within 10 months, $\geq 68\%$ of ppts met minimum goals for exercise (attend ≥ 2 exercise sessions/week for ≥ 36 weeks) and diet (reduce caloric intake by ≥ 100 kcal/day and/or increase

fruit/vegetable intake by ≥ 1 serving/day) (adherence), and $\geq 68\%$ of ppts provided anthropometric measures at 12 months (retention). Results: Among 25 evaluable ppts, median age was 57.3 years with median BMI 37.5 kg/m² (range 27.7-54.6), 64% Stage I, and median 2.1 years from diagnosis. Accrual occurred in 10 months, 80% of ppts provided anthropometric measures at 12 months, 96% of ppts met the diet goal, and 28% of ppts met the exercise goal. Thus feasibility goals were met, with the exception of exercise adherence as defined a priori. At 12 months, average weight loss was 7.6% (95% CI -3.9%, 19.2%) with median weight loss of 7.1%. Conclusions: It is feasible to recruit and retain BC survivors in a multi-center weight loss trial using dietary change plus physical activity to achieve clinically meaningful weight loss over 12 months.

Hans SS, Catanescu I, **Bove P, Long G, Khoury M, Uzieblo M**, Rimar S and Brown W (2015). "Rupture of abdominal aortic and iliac aneurysms in patients with and without antecedent endovascular repair." Journal of Vascular Surgery 62(3): 830.

[Full-Text](#)

Department of Surgery

Department of Internal Medicine

Hanson ID, David SW, **Dixon SR**, Metzger DC, Génereux P, Maehara A, Xu K and Stone GW (2015). "Optimized" delivery of intracoronary supersaturated oxygen in acute anterior myocardial infarction: A feasibility and safety study." Catheterization and Cardiovascular Interventions 86: S51-S57.

[Full-Text](#)

Department of Internal Medicine

Objectives We sought to evaluate the feasibility and safety of catheter-based supersaturated oxygen (SSO²) delivery via the left main coronary artery (LMCA) following primary percutaneous coronary intervention (PCI). **Background:** In the multicenter, randomized AMIHOT-II trial, SSO² delivered into the proximal or mid left anterior descending (LAD) artery via an indwelling intracoronary infusion catheter in patients with acute anterior ST-segment elevation myocardial infarction (STEMI) following primary PCI significantly reduced infarct size but resulted in a numerically higher incidence of safety events. **Methods:** Patients with acute anterior STEMI presenting within 6 hr of symptom onset were enrolled at three centers. Following successful LAD stenting, SSO² was infused into the LMCA via a diagnostic catheter for 60 min. The primary safety endpoint was the 30-day rate of target vessel failure (composite of death, reinfarction, or target vessel revascularization). Cardiac magnetic resonance imaging (cMRI) was performed at 3-5 and 30 days to assess infarct size. **Results:** Twenty patients with acute anterior STEMI were enrolled. The infarct lesion was located in the proximal LAD in 7 cases (35%) and the mid LAD in 13 cases (65%). Following primary PCI, SSO² was delivered successfully in all cases. Target vessel failure within 30 days occurred in 1 patient (5%). Median [interquartile range] infarct size was 13.7% [5.4-20.6%] at 3-5 days and 9.6% [2.1-14.5%] at 30 days. **Conclusions:** Following primary PCI in acute anterior STEMI, infusion of SSO² via the LMCA is feasible, and is associated with a favorable early safety and efficacy profile.

Hanson ID, **Goldstein JA, Dixon SR** and Stone GW (2015). "Comparison of coronary artery lesion length by NIRS-IVUS versus angiography alone." Coronary Artery Disease 26(6): 484-489.

[Full-Text](#)

Department of Internal Medicine

Background Intravascular ultrasound (IVUS) studies analyzing target lesion plaque burden (PB) have established that invasive coronary angiography commonly underestimates lesion length, predisposing to 'geographic miss' during a percutaneous coronary intervention, which has been associated with adverse outcomes. Plaque composition may also influence stent outcome. The present study used near-infrared spectroscopy and IVUS (NIRS-IVUS) to assess the prevalence of PB and lipid-core plaque (LCP) extending beyond angiographic borders of target lesions. **Methods** Fifty-eight patients (58 lesions) undergoing NIRS-IVUS were identified. By invasive coronary angiography, target lesion length and minimum lumen diameter were measured. Plaque, defined as NIRS-IVUS atheroma (either PB $>40\%$ or LCP), was identified adjacent to the angiographic-defined lesion margins. **Results** By NIRS-IVUS, atheroma (either PB $>40\%$ or

LCP) was identified beyond angiographic lesion margins in 52/58 (90%) lesions. The mean lesion length was 13.4±5.9 mm by angiography and 19.8±7.0 mm (P<0.0001) by NIRS-IVUS. LCP extending beyond the angiographic border was observed in 30/58 (52%) lesions. Conclusion NIRS-IVUS imaging shows that target lesion length is commonly underestimated by angiography alone. This finding may have implications for stent length selection and avoidance of geographic miss.

Hawasli A, Bush A, Hare B, Meguid A, Thatimatla N and Szpunar S (2015). "Laparoscopic management of severe reflux after sleeve gastrectomy, in selected patients, without conversion to roux-en-Y gastric bypass." Journal of Laparoendoscopic and Advanced Surgical Techniques 25(8): 631-635.

[Request Form](#)

Department of Surgery

Background: Treatment of severe reflux after laparoscopic sleeve gastrectomy (LSG) may require conversion to Roux-en-Y gastric bypass (RYGB). We conducted a pilot study to evaluate the feasibility and effectiveness of performing laparoscopic anterior fundoplication with posterior crura approximation (LAF/pCA), in selected patients, to correct the reflux without conversion to RYGB. Patients and Methods: From October 2012 to April 2013, 6 patients with confirmed severe de novo reflux after LSG were treated with LAF/pCA. Results: All patients were females with a mean age of 41.5±14.2 years. All patients had lost weight after initial LSG. The percentage excess body mass index (BMI) loss (%EBL) was 61.2±33.2%. The mean time from the initial LSG to LAF/pCA was 33.2±12.5 months. Four patients had reduction of gastric fundus size. One patient required resleeving. Reflux resolved immediately in all patients with a follow-up of 18.5±2.7 months. All patients continued to lose weight, with %EBL reaching 75.5±22.9% and a mean BMI of 32±7.3 kg/m². Conclusions: LAF/pCA with reduction of gastric fundus size, when needed, may be considered an alternative option to correct severe reflux after LSG in selected patients.

Hills A and **Al-Hakim M** (2015). "Lhermitte sign as a presenting symptom of thoracic spinal pathology: A case study." Case Rep Neurol Med 2015: 707362.

[Full-Text](#)

OUWB Medical Student Author

Department of Neurology

A 54-year-old male with ankylosing spondylitis presented with complaints of progressively worsening bilateral leg weakness and difficulty ambulating of 2-week duration. He also felt a sharp, electric, shock-like sensation radiating from his lower back into his legs upon flexing the trunk. There was no history of trauma or other inciting events within the 2 weeks prior to presentation. Thoracic MRI at this visit showed a three-column fracture at T11-T12. He underwent spinal fusion surgery and within 2 days after surgery the radiating electrical sensation with spinal flexion had completely resolved.

Hoffman JL, Aneese NJ, Schmidt KJ, Chaben AC and **Smythe MA** (2015). "Optimizing anticoagulation management through the use of a hospital engagement network metric for inpatient anticoagulant-associated hemorrhage." Annals of Pharmacotherapy. ePub Ahead of Print.

[Full-Text](#)

Department of Biomedical Sciences (BHS)

BACKGROUND: The University HealthSystem Consortium (UHC), a national hospital engagement network (HEN), establishes health-system metrics to assess and improve quality of care. In 2012, a metric for inpatient anticoagulant hemorrhage was developed. The utility of this metric to improve anticoagulation care has not been assessed. OBJECTIVE: To identify opportunities to improve anticoagulation safety through the use of a HEN metric for inpatient anticoagulant-associated hemorrhage. METHODS: This was a single-center, retrospective, observational study of metric identified patients with presumed inpatient anticoagulant hemorrhage. Records were reviewed to confirm anticoagulant hemorrhage and identify bleed site and severity. A structured process was used to assess bleed preventability and subsequently identify opportunities for improving care. Each bleed was reviewed by 2 investigators. RESULTS: Anticoagulant hemorrhage was confirmed in 85.9% (61/71) with heparin infusion the most common anticoagulant. Patients were primarily medical, with a mean age of 72.7 +/- 15 years. The most common bleed sites were

gastrointestinal (24.6%) and retroperitoneal (21.3%). Major bleeding occurred in 60.7% (37/61). Anticoagulant hemorrhage was preventable in 18% (11/61) of cases with heparin protocol noncompliance the most common cause of a preventable bleed. Several opportunities for improving heparin infusion therapy were recognized and protocol changes were implemented. CONCLUSIONS: The UHC metric accurately captures inpatient anticoagulant-associated hemorrhage the majority of time. The UHC metric on anticoagulant-associated hemorrhage can be a useful part of a health system's overall plan for the safe use of anticoagulants in the hospital setting.

Holtrop P, Swails T and Riggs T (2015). "Hypertriglyceridemia in extremely low birth weight infants receiving lipid emulsions." Journal of Neonatal-Perinatal Medicine 8(2): 133-136.

[Request Form](#)

Department of Pediatrics

OBJECTIVE: To determine the prevalence of high TG levels in extremely low birth weight (ELBW) infants and what the risk factors are for high TG levels. STUDY DESIGN: We performed a prospective observational study of triglyceride concentrations in extremely low birth weight infants receiving lipid infusions. Lipid infusions were begun at 0.5 grams/kg/day at age one day and the dose advanced by 0.5 grams/kg/day. Triglyceride concentrations were drawn when the dose reached 1 and 2 grams/kg/day. We compared infants with normal triglyceride levels (<200 mg/dl) with those with elevated triglyceride levels (>200 mg/dl) with univariate and multivariate analysis. RESULTS: There were 75 infants included in the analysis. Twenty (26.7%, 95% CI = 16.6-36.7%) had triglyceride levels >200 mg/dl. On multiple logistic regression analysis, lower birth weight was associated with the risk of an elevated triglyceride level. Triglyceride levels >200 mg/dl did not predict future mortality or morbidity. CONCLUSION: Elevated TG levels occur commonly in ELBW infants and are associated with a lower birth weight.

Honaker M, Edwards C, **Ballouz S** and **Wasvary H** (2015). "Multidisciplinary tumor clinic results in improved five year overall and disease-free survival in patients with colorectal cancer." Journal of Clinical Oncology 33(15): e14672.

[Request Form](#)

Department of Internal Medicine

Department of Surgery

Background: Colorectal cancer remains a significant cause of cancer related mortality. The introduction of a colorectal multidisciplinary tumor clinic at our institution revealed better adherence to NCCN guidelines in a 2009 study. The purpose of this study was to determine if the implementation of a multidisciplinary clinic resulted in improved five year survival outcomes. Methods: Patients treated in a multidisciplinary colorectal cancer clinic were compared to patients cared for outside of the tumor clinic. Patient outcomes were followed for five years and included recurrence rates, overall and disease-free survival. Stage for stage, clinic patients were compared to non-clinic patients with regards demographics and outcomes using appropriate statistical analysis. A two-tailed p-value of less than 0.05 was considered statistically significant. Results: 78 patients were identified who had been cared for in the tumor clinic and 177 patients were cared for outside of the tumor clinic. The clinic group by cancer stage included; stage I (n = 17), stage II (n = 20), stage III (n = 22) and stage IV (n = 19). In the group of patients treated outside of the clinic, the number of patients by stage included; stage I (n = 51), stage II (n = 52), stage III (n = 42) and stage IV (n = 32). The only significant difference between the two groups was an increased number of female patients treated in the clinic for stage III colorectal cancer (86% vs. 42%; p = 0.0008). Recurrence rates were similar across all stages regardless of the site of treatment. When overall five year survival was examined, there was a statistically significant improvement for patients treated in the clinic with stage III disease (81% vs 53.8%; p = 0.0377). There was also a statistically significant increase in the length of disease-free survival (mean 35 vs 25.7 months; p = 0.0326) and overall survival (mean 33.3 vs 25 months; p = 0.0214) in patients with stage III disease in the clinic group compared with those patients treated outside of the clinic. Conclusions: Five year survival, overall survival, and disease-free survival are significantly improved in patients with stage III disease when cared for at a multidisciplinary colorectal tumor clinic.

Jae SY, **Franklin B**, Choi YH and Fernhall B (2015). "Metabolically healthy obesity and carotid intima-media thickness effects of cardiorespiratory fitness." Mayo Clinic Proceedings 90(9): 1217-1224.

[Full-Text](#)

Department of Internal Medicine

Objective To test the hypothesis that cardiorespiratory fitness modifies the association between metabolically healthy obesity (MHO) phenotype and carotid intima-media thickness. Patients and Methods We evaluated 3838 men (mean age, 51±6 years) who participated in the general health examination program at Samsung Medical Center, Seoul, South Korea, between January 2, 2008, and December 31, 2008. Participants were divided into 4 groups on the basis of body habitus and metabolic health status using the Asia-Pacific criteria. On the basis of Asian criteria, MHO was defined as body mass index greater than or equal to 25 kg/m² with less than 3 metabolic abnormalities. Cardiorespiratory fitness (fitness) was directly measured by using peak oxygen uptake and divided into unfit (lower tertile of fitness) and fit (middle and upper tertiles of fitness) categories on the basis of age-specific peak oxygen uptake percentiles. The prevalence of subclinical carotid atherosclerosis was defined as a mean carotid intima-media thickness greater than the 75th percentile. Results Compared with metabolically healthy normal weight (MHNW), MHO was associated with a higher prevalence of subclinical carotid atherosclerosis (odds ratio, 1.39; 95% CI, 1.12-1.72) after adjusting for potential confounding variables. Using multivariate logistic regression analysis, we found that the MHO unfit group had 2.00 times (95% CI, 1.48-2.73) and the metabolically unhealthy obesity unfit group had 1.84 times (95% CI, 1.26-2.67) higher risk of subclinical carotid atherosclerosis as compared with the MHNW fit group (reference group). However, MHO fit (OR, 1.25; 95% CI, 0.97-1.62) and metabolically unhealthy obesity fit (OR, 1.31; 95% CI, 0.90-1.92) groups had odds ratios for subclinical carotid atherosclerosis similar to those of the MHNW fit group. Conclusion Metabolically healthy obesity was associated with a higher prevalence of subclinical carotid atherosclerosis, but this association was attenuated by increasing levels of cardiorespiratory fitness.

Kaza RK, Al-Hawary MM, **Sokhandon F**, Shirkhoda A and Francis IR (2015). "Pitfalls in pancreatic imaging." Seminars in Roentgenology. ePub Ahead of Print.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Kazanji N, Gjeorgjievski M, Yadav S, Mertens AN and **Lauter C** (2015). "Monomicrobial vs polymicrobial clostridium difficile bacteremia: A case report and review of the literature." American Journal of Medicine 128(9): e19-e26.

[Full-Text](#)

Department of Internal Medicine

Kilic ID, Caiazzo G, Fabris E, Serdoz R, Abou-Sherif S, Madden S, Moreno PR, **Goldstein J** and Di Mario C (2015). "Near-infrared spectroscopy-intravascular ultrasound: Scientific basis and clinical applications." European Heart Journal Cardiovascular Imaging. ePub Ahead of Print.

[Full-Text](#)

Department of Internal Medicine

Coronary angiography underestimates the magnitude of the atherosclerotic burden and cannot detect the presence of disease in the early phases. Recognition of these inherent limitations of angiography has been an impetus for the development of other coronary imaging techniques. The novel near-infrared spectroscopy-intravascular ultrasound (NIRS-IVUS) catheters can detect and quantify the presence of lipid core in the atherosclerotic plaque and associate it with other features such as lumen size and plaque architecture. Lipid-rich plaques are known to pose a higher risk of distal embolization during interventions and plaque disruption. The aim of this manuscript is the review of the potential clinical and research applications of this technology as highlighted by recent studies.

Klingenstein A, Schaumberger MM, Freeman WR, **Folberg R**, Mueller AJ and Schaller UC (2015). "MuSIC report III: Tumour microcirculation patterns and development of metastasis in long-term follow-up of melanocytic uveal tumours." Acta Ophthalmol. ePub Ahead of Print.

[Full-Text](#)

Administration

PURPOSE: To statistically determine differences in microcirculation patterns between nevi and uveal melanomas and the influence of these patterns on metastatic potential in the long-term follow-up of 112 patients with melanocytic uveal tumours. In vivo markers indicating malignancy and metastatic potential have implications for treatment decision. METHODS: Primary diagnosis and work-up included clinical examination, fundus photography, standardized A and B scan echography as well as evaluation of tumour microcirculation patterns via confocal fluorescein and indocyanine green angiography (ICGA). Patient data were collected from the patient files, the tumour registry or personal contact. Statistical analysis was performed with spss 22.0 using chi-square, Fisher's exact test and Kaplan-Meier survival analysis. RESULTS: Forty-three uveal melanocytic lesions remained untreated and were retrospectively classified as benign nevi, whereas 69 lesions were malignant melanomas (T1: 32, T2: 28, T3: 6 and T4: 3). 'Silent' and 'arcs without branching' were found significantly more often in nevi ($p = 0.001$ and $p = 0.010$), whereas 'parallel with cross-linking' and 'networks' were significantly more frequent in melanomas ($p = 0.022$ and $p = 0.029$). The microcirculation pattern 'parallel with cross-linking' proved significantly more frequent in patients who developed metastases ($p = 0.001$). CONCLUSIONS: Certain microcirculation patterns may guide us in differentiating uveal nevi from malignant melanomas. A non-invasive prognostic marker can be of great value for borderline lesions in which cytology is less likely taken. 'Parallel with cross-linking' did not only indicate malignancy, but it was also associated with later tumour metastasis.

LaBan MM (2015). "Re: "Review of secondary health conditions in post-polio syndrome" by McNalley TE, Jenson MP, Truitt AR, Schomer KG, Baylor C, Molton IR: Am J Phys Med Rehabil 2015;94:139-45." American Journal of Physical Medicine and Rehabilitation 94(10): e92.

[Full-Text](#)

Department of Physical Medicine and Rehabilitation

LaBan MM, Jones M and Lenger A (2015). "Mechanical compression of the iliopsoas muscle by a large vertebral osteophyte, presenting with abdominal and lumbar pain." American Journal of Physical Medicine and Rehabilitation 94(8): e75.

[Full-Text](#)

Department of Physical Medicine and Rehabilitation

Ladkany R, Marinos A, Pereira-Rodrigues O, Khaddour L, Isaac D, Yadav S and **Zakalik D** (2015). "Trends in the incidence and survival of ovarian cancer: An analysis of the SEER database." Journal of Clinical Oncology 33(15): e16587.

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Department of Internal Medicine

Background: Ovarian cancer is the leading cause of gynecologic cancer related deaths as well as the fifth overall cause of cancer deaths among American women. The vast majority of cases are diagnosed at an advanced stage, for which the 5year survival rate is less than 30%. Methods: Data obtained from The National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) Program was reviewed. Adult women diagnosed with ovarian cancer between the years of 2000 and 2011 were included. The analysis focused on histologic type, histologic grade, disease stage and cause specific survival. The patients were stratified by age into three groups: patients 18 to 44 years old (Group A), patients 45 to 74 years old (Group B) and patients 75 years old and older (Group C). Results: A histologic diagnosis was available for 57 759 patients. The mean age of diagnosis was 60.7 years, with the majority of patients (67.4%) being in group B. Eighty five percent of the subjects were Caucasian. Epithelial tumors comprised 91.8% of all the cases and were the most prevalent type in all age groups. Germ cell tumors were more frequent in group A (14.0%) compared to groups B and C (0.3% and 0.1% respectively). Overall, most of the patients were diagnosed at

stage III (34.5%); however there was a difference between younger and older subjects in this regard. Fifty three percent of patients in group A were diagnosed at stage I or II while 64.6% of subjects in group C were diagnosed at stage III or IV. Lastly, the 5year cause specific survival was 75% in group A, 52% in group B and 27% in group C ($p < 0.001$). Conclusions: This study demonstrated that women in the younger age group were generally diagnosed at an earlier stage, which may account for the better survival compared to older patients who are diagnosed at a later stage. Although the current data does not directly address the reason for earlier diagnosis in younger patients, we can hypothesize that one of the related factors is a close gynecological follow up in women of childbearing age.

Lavie C, **Franklin B** and Mittleman M (2015). "Acute cardiac events and the preventive role of regular exercise." The Medical Roundtable General Medicine Edition 1(1): 17-27.

[Request Form](#)

Department of Internal Medicine

Ledbetter KA, **Shetty M** and Myers DT (2015). "Hysterosalpingography: An imaging Atlas with cross-sectional correlation." Abdominal Imaging 40(6): 1721-1732.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Hysterosalpingography (HSG) provides a unique combination of both fallopian tube and uterine cavity evaluation. A comprehensive understanding of both HSG and correlative cross-sectional imaging findings are essential radiologic skills. This article will review the spectrum of technical artifacts, anatomic variants, congenital uterine anomalies, uterine and tubal pathology, and postsurgical findings as they appear on HSG. Additionally, correlation with MR and ultrasound images is provided. This review article serves as a reference for residents new to HSG as well as staff who perform and interpret HSG infrequently.

Linnstaedt SD, Hu JM, Bortsov AV, Soward AC, **Swor R**, Jones J, Lee D, Peak D, Domeier R, Rathlev N, Hendry P and McLean SA (2015). "Mu-opioid receptor gene A118 g variants and persistent pain symptoms among men and women experiencing motor vehicle collision." Journal of Pain 16(7): 637-644.

[Full-Text](#)

Department of Emergency Medicine

The mu-opioid receptor 1 (OPRM1) binds endogenous opioids. Increasing evidence suggests that endogenous OPRM1 agonists released at the time of trauma may contribute to the development of posttraumatic musculoskeletal pain (MSP). In this prospective observational study, we evaluated the hypothesis that individuals with an AG or GG genotype at the OPRM1 A118 G allele, which results in a reduced response to opioids, would have less severe MSP 6 weeks after motor vehicle collision (MVC). Based on previous evidence, we hypothesized that this effect would be sex-dependent and most pronounced among women with substantial peritraumatic distress. European American men and women ≥ 18 years of age presenting to the emergency department after MVC and discharged to home after evaluation ($N = 948$) were enrolled. Assessments included genotyping and 6-week evaluation of overall MSP severity (0-10 numeric rating scale). In linear regression modeling, a significant A118 G Allele x Sex interaction was observed: an AG/GG genotype predicted reduced MSP severity among women with substantial peritraumatic distress ($\beta = -.925$, $P = .014$) but not among all women. In contrast, men with an AG/GG genotype experienced increased MSP severity at 6 weeks ($\beta = .827$, $P = .019$). Further studies are needed to understand the biologic mechanisms mediating observed sex differences in A118 G effects. Perspective: These results suggest a sex-dependent mechanism by which an emotional response to trauma (distress) contributes to a biologic mechanism (endogenous opioid release) that increases MSP in the weeks after stress exposure. These results also support the hypothesis that endogenous opioids influence pain outcomes differently in men and women. (C) 2015 by the American Pain Society

Liu HT, Chen SH, **Chancellor MB** and Kuo HC (2015). "Presence of cleaved synaptosomal-associated protein-25 and decrease of purinergic receptors p2x3 in the bladder urothelium influence efficacy of botulinum toxin treatment for overactive bladder syndrome." *PLoS One* 10(8): 1-12.

[Full-Text](#)

Department of Urology

Objectives To evaluate whether botulinum toxin A (BoNT-A) injection and Lipotoxin (liposomes with 200 U of BoNT-A) instillation target different proteins, including P2X3, synaptic vesicle glycoprotein 2A, and SNAP-25, in the bladder mucosa, leading to different treatment outcomes. **Materials and Methods** This was a retrospective study performed in a tertiary teaching hospital. We evaluated the clinical results of 27 OAB patients treated with intravesical BoNT-A injection (n = 16) or Lipotoxin instillation (n = 11). Seven controls were treated with saline. Patients were injected with 100 U of BoNT-A or Lipotoxin in a single intravesical instillation. The patients enrolled in this study all had bladder biopsies performed at baseline and one month after BoNT-A therapy. Treatment outcome was measured by the decreases in urgency and frequency episodes at 1 month. The functional protein expressions in the urothelium were measured at baseline and after 1 month. The Wilcoxon signed-rank test and ordinal logistic regression were used to compare the treatment outcomes. **Results** Both BoNT-A injection and Lipotoxin instillation treatments effectively decreased the frequency of urgency episodes in OAB patients. Lipotoxin instillation did not increase postvoid residual volume. BoNT-A injection effectively cleaved SNAP-25 (p < 0.01). Liposome-encapsulated BoNT-A decreased urothelial P2X3 expression in the five responders (p = 0.04), while SNAP-25 was not significantly cleaved. **Conclusions** The results of this study provide a possible mechanism for the therapeutic effects of BoNT-A for the treatment of OAB via different treatment forms. BoNT-A and Lipotoxin treatments effectively decreased the frequency of urgency episodes in patients with OAB.

Maerz T, Newton MD, Matthew HW and **Baker KC** (2015). "Surface roughness and thickness analysis of contrast-enhanced articular cartilage using mesh parameterization." *Osteoarthritis and Cartilage*. ePub Ahead of Print.

[Full-Text](#)

Department of Surgery

Department of Orthopedic Surgery

OBJECTIVE: Articular cartilage (AC) morphology is an important metric for characterizing degeneration. We propose a novel morphologic analysis using mesh parameterization, enabling the use of surface roughness and thickness metrics to characterize degeneration in a rodent model of post-traumatic osteoarthritis. **METHODS:** Six rats underwent anterior cruciate ligament transection (ACL-T) and six were controls (Control). At 4-weeks, femora and tibiae were harvested and imaged using contrast-enhanced μ CT. Cartilage surfaces were manually outlined, and 2-dimensional thickness maps were generated using mesh parameterization and analyzed by thickness and surface roughness (Sa). The parameterization technique was validated against the direct-distance transform (DDT) and histologic AC thickness from sagittal Safranin-O/Fast-Green sections. Parameterization and DDT measurements were also validated using known, virtual shapes with zero, one, and two planes of curvature. **RESULTS:** Parameterization had 0.00%-6.26% error and DDT had 5.06%-12.02% error in determining thicknesses of known shapes. Parameterization thickness correlated highly to DDT thickness (femur: r=0.978, P<0.001; tibia: r=0.992, P<0.001) and histologic thickness (femur: r=0.952, P<0.001; tibia: r=0.959, P<0.001). Thickness maps enabled visualization and quantification of AC degeneration. ACL-T samples displayed general thickening of cartilage, with adjacent regions of thickening and thinning on the medial femoral condyle. Compared to Control, ACL-T thickness was higher in the whole femur, whole tibia, and all compartments and sub-compartments. Sa was higher in the whole femur and medial and lateral condyle, and the whole tibia and medial and lateral plateau. The largest increases in Sa were observed on the medial femoral condyle. **CONCLUSIONS:** Cartilage analysis using parameterization effectively characterized early degeneration in AC, including sub-compartmental thickening/thinning, and is a powerful tool for assessing degeneration in preclinical osteoarthritis.

Majima T, Tyagi P, Dogishi K, Kadekawa K, Kashyap M, Wada N, Takai S, Shimizu T, Gotoh M, **Chancellor M** and Yoshimura N (2015). "The effect of intravesical liposome-based NGF antisense therapy on bladder overactivity and nociception in a rat model of cystitis induced by hydrogen peroxide." Neurourology and Urodynamics 34: S201-S203.

[Full-Text](#)

Department of Urology

Martins da Silva C, **Chancellor MB**, Smith CP and Cruz F (2015). "Use of botulinum toxin for genitourinary conditions: What is the evidence?" Toxicon. ePub Ahead of Print.

[Full-Text](#)

Department of Urology

Botulinum toxin A is licensed for the treatment of urinary incontinence due to neurogenic detrusor overactivity (NDO) and overactive bladder (OAB). Only onabotulinumtoxinA has at this moment such approval, in NDO at a dose of 200U and in OAB at a dose of 100U. Regulatory phase 3 trials have been carried out in both conditions. In NDO it was shown to decrease urinary incontinence, to improve urodynamic parameters and to increase quality of life in multiple sclerosis and spinal cord injured patients. Adverse events included urinary tract infections and necessity of de novo clean intermittent catheterization, which occurred mainly in patients with multiple sclerosis. In OAB patients with urge incontinence, onabotulinumtoxinA decreased urinary incontinence and micturition frequency while improving quality of life. Again, main adverse events were urinary tract infections and transient urinary retentions. Long-term studies in both NDO and OAB demonstrate the efficacy and safety of the treatment. Available phase 3 trials of onabotulinumtoxinA in benign prostatic hyperplasia did not show any relevant efficacy in improving lower urinary tract symptoms.

McKenney S, Bevins N, **Olariu E** and Flynn M (2015). "A six-year longitudinal evaluation of the DICOM GSDF conformance stability of LCD monitors." Medical Physics 42(6): 3670.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Mirza FG, **Bauer ST**, Van Der Veer A and Simpson LL (2015). "Gastroschisis: Incidence and prediction of growth restriction." Journal of Perinatal Medicine 43(5): 605-608.

[Request Form](#)

Department of Obstetrics and Gynecology

Fetuses with gastroschisis are at increased risk of intrauterine growth restriction (IUGR). However, there is a tendency for underestimation of fetal abdominal circumference and hence fetal weight, leading to overdiagnosis of IUGR. Our objective was to evaluate the accuracy of ultrasound for the prediction of being small for gestational age (SGA) at birth in these cases. Methods: A retrospective study of prenatally diagnosed cases of gastroschisis was conducted at a tertiary center. Fetal weight was estimated using the formula of Hadlock. IUGR was defined as an estimated fetal weight ≤ 10 th percentile for gestational age. SGA at the time of birth was defined as a birth weight ≤ 10 th percentile for gestational age. The incidence of IUGR on last ultrasound and that of SGA at birth were calculated, and the precision of ultrasound in predicting SGA was determined. Results: IUGR was reported on the last ultrasound prior to delivery in 9/25 cases (36%). Postnatally, 13/25 newborns (52%) were SGA. All sonographically suspected cases of IUGR based on the last ultrasound were SGA at birth. The positive predictive value of the last ultrasound in identifying SGA was 100%. Conclusions: At least half of the infants affected by gastroschisis were SGA at birth. Sonographic estimation of fetal weight within 1 month of birth reliably predicted SGA in infants with gastroschisis.

Miyazato M, Kitta T, Kaiho Y, Oshiro T, Saito S, **Chancellor MB**, De Groat WC and Yoshimura N (2015). "Effects of duloxetine on urethral continence reflex and bladder activity in rats with cerebral infarction." Journal of Urology 194(3): 842-847.

[Full-Text](#)

Department of Urology

Purpose We investigated the effect of duloxetine, a norepinephrine and serotonin reuptake inhibitor, on the

sneeze induced continence reflex and on bladder function in rats with cerebral infarction. Materials and Methods Using urethane anesthesia the effect of duloxetine (1 mg/kg intravenously) on the amplitude of urethral responses during sneezing as well as urethral baseline pressure at the mid urethra was evaluated in normal female adult rats and cerebral infarction rats. Tilt leak point pressure was also measured. In normal and cerebral infarction rats continuous cystometry was evaluated before and after duloxetine injection. Results In cerebral infarction rats urethral baseline pressure was 43% lower than in normal rats but the amplitude of urethral responses during sneezing did not differ in the 2 groups. Duloxetine increased the amplitude of urethral responses during sneezing and urethral baseline pressure by 31% and 21%, respectively, in normal rats but did not affect either in cerebral infarction rats. Also, in cerebral infarction rats leak point pressure was 29% lower compared with normal rats. Duloxetine increased leak point pressure in normal rats but not in cerebral infarction rats. Cerebral infarction reduced intercontraction intervals without affecting the amplitude of bladder contractions compared with normal rats. Duloxetine prolonged intercontraction intervals in cerebral infarction rats but not in normal rats. Conclusions These results suggest that cerebral infarction induces not only bladder overactivity but also stress urinary incontinence, which may account for mixed incontinence in patients with cerebral infarction. After cerebral infarction duloxetine reduced bladder overactivity but failed to enhance active urethral closure mechanisms during sneezing, suggesting that disorganization of the brain network after cerebral infarction might influence the effect of duloxetine on lower urinary tract function.

Mori K, Noguchi M, Tobu S, Sato F, Mimata H, Tyagi P, **Chancellor MB** and Yoshimura N (2015). "Age-related changes in bladder function with altered angiotensin II receptor mechanisms in rats." Neurourology and Urodynamics. ePub Ahead of Print.

[Full-Text](#)

Department of Urology

Aims: To examine alterations in expression of angiotensin II type 1 receptors (AT1R) which induce organ tissue remodeling, angiotensin II type 2 receptors (AT2R) which protect against it, and related molecules in the bladder of matured rats with bladder dysfunction. Methods: Female SD rats of three different ages were used: 8 weeks old (8W; n=5), 9 months old (9M; n=5), and 15 months old (15M; n=5). After cystometry, the expression levels of AT1R, connexin43 (Cx43), MAP kinase (MAPK), collagen1, AT2R, PPAR- γ , adiponectin (Adipo), and adiponectin receptor (Adipo-R) were investigated in the bladder. Results: Pressure threshold, post-void residual volume and the number of non-voiding contractions were significantly increased in 15M versus 8W rats ($P < 0.01$). Maximum voiding pressure was significantly decreased in 15M versus 8W rats ($P < 0.05$). There was no significant difference in CMG parameters between 8W and 9M rats. In the bladder, the mRNA expression of AT1R, Cx43, MAPK, collagen 1, AT2R, PPAR- γ , Adipo, and Adipo-R were significantly higher in 15M than in 8W rats. The relative expression ratio of AT1R protein against AT2R protein in the mucosa and detrusor was significantly increased in 15M versus 8W rats. Conclusions: These results indicate that matured rats exhibit not only bladder overactivity but also impaired voiding, which are associated with upregulation of AT1R. The upregulation of AT2R also may play a significant role in the suppressing of AT1R induced remodelling. However, because AT1R upregulation is more dominant than AT2R increases, AT2R activation may not be sufficient to suppress AT1R stimulation in matured rats. © 2015 Wiley Periodicals, Inc.

Mukthapuram S, **Dewar D** and **Maisels MJ** (2015). "Extreme hyperbilirubinemia and G6PD deficiency with no laboratory evidence of hemolysis." Clinical Pediatrics. ePub Ahead of Print.

[Full-Text](#)

Department of Pediatrics

Ogunleye F, **Huang J**, **Mohammed I**, Allen E, Brennan N and **Jaiyesimi I** (2015). "Diagnostic significance of screening for BCR-ABL1 by PCR in patients with neutrophilia. The William Beaumont Hospital experience." Clinical Lymphoma Myeloma and Leukemia 15(Sup 2): S33.

[Full-Text](#)

Department of Pathology

Department of Internal Medicine

Oliver-McNeil S, Templin TN and **Haines DE** (2015). "Predicting readmission after implantable cardioverter defibrillator using a risk model." *Cardiology (Switzerland)* 131: 208.

[Request Form](#)

Department of Internal Medicine

Objectives: The goal of this study was to implement the ICD risk stratification model developed through NCDR data to determine if patients could be identified for 30-day readmission. Background: Previous analysis of the National Cardiovascular Data Registry (NCDR) ICD database identified clinical risk factors for procedure-related complications. Methods: Patients scheduled to undergo ICD implantation were prospectively identified. Preoperative NCDR ICD risk score was calculated by assigning points for age > 70 years; female sex; prior valve surgery; chronic lung disease; dual or biventricular device; history of atrial fibrillation/flutter; NYHA class II-IV heart failure; non-elective hospitalization; and BUN >30; and re-implantation other than elective generator change. A logistic regression model determined the association of variables and pre-procedure risk to all-cause 30-day readmission rate. Results: 182 consecutive patients undergoing ICD implantation were assessed. Mean age was 69 years (SD=11.00), with 72% (n=131) of the group consisting of men. The 30-day readmission rate was 17.6%. Four variables from the ICD Adverse Outcome Risk Model, (BUN >30, history of lung disease, NYHA Class IV and device implant during an inpatient hospital stay) were identified as predictive of 30-day readmission. Patients with a combination of 2 or more out of the 4 risks were more likely to be readmitted (Hosmer-Lemeshow test (χ^2 (8) = 5.20, P = .74), c-statistic = .71, and Nagelkerke R square = 0.15). Conclusion: In a typical group of patients receiving ICD implant, the four variables were predictive of all-cause 30-day readmission rate. The risk factors identified were similar to previous studies.

Oliver-McNeil S, Templin TN and **Haines DE** (2015). "Using a risk model to predict 30-day readmission after implantable cardioverter defibrillator." *Journal of Cardiac Failure* 21(8): S60-S61.

[Full-Text](#)

Department of Internal Medicine

Paesmans M, Garcia C, **Wong CO**, Patz EF, Jr., Komaki R, Eschmann S, Govindan R, Vansteenkiste J, Meert AP, de Jong WK, Altorki NK, Higashi K, Van Baardwijk A, Borst GR, Ameye L, Lafitte JJ, Berghmans T, Flamen P, Rami-Porta R and Sculier JP (2015). "Primary tumour standardised uptake value is prognostic in nonsmall cell lung cancer: A multivariate pooled analysis of individual data." *European Respiratory Journal*. ePub Ahead of Print.

[Request Form](#)

Department of Diagnostic Radiology and Molecular Imaging

¹⁸F-fluoro-2-deoxy-d-glucose positron emission tomography (PET) complements conventional imaging for diagnosing and staging lung cancer. Two literature-based meta-analyses suggest that maximum standardised uptake value (SUVmax) on PET has univariate prognostic value in nonsmall cell lung cancer (NSCLC). We analysed individual data pooled from 12 studies to assess the independent prognostic value of binary SUVmax for overall survival. After searching the published literature and identifying unpublished data, study coordinators were contacted and requested to provide data on individual patients. Cox regression models stratified for study were used. Data were collected for 1526 patients (median age 64 years, 60% male, 34% squamous cell carcinoma, 47% adenocarcinoma, 58% stage I-II). The combined univariate hazard ratio for SUVmax was 1.43 (95% CI 1.22-1.66) and nearly identical if the SUV threshold was calculated stratifying for histology. Multivariate analysis of patients with stage I-III disease identified age, stage, tumour size and receipt of surgery as independent prognostic factors; adding SUV (HR 1.58, 95% CI 1.27-1.96) improved the model significantly. The only detected interaction was between SUV and stage IV disease. SUV seems to have independent prognostic value in stage I-III NSCLC, for squamous cell carcinoma and for adenocarcinoma.

Page TP (2015). "Suture-guided capsular tension ring insertion to reduce risk for iatrogenic zonular damage." Journal of Cataract and Refractive Surgery 41(8): 1564-1567.

[Full-Text](#)

Department of Ophthalmology

The capsular tension ring (CTR) is a useful device for managing a zonular dialysis. However, insertion of the CTR has potential complications. The CTR can damage zonular fibers during deployment into the capsular bag. Also, the angle and point of initial contact of the CTR with the capsular bag relative to the orientation of the dialysis must be considered to avoid damage to the zonular fibers. Adequate fill of the capsular bag with an ophthalmic viscosurgical device is important to minimize the risk for capsule entanglement with the leading eyelet of the CTR. A simple technique is described to prevent these complications. The technique can be used with both standard and modified CTRs. Financial Disclosure Dr. Page is a consultant to Bausch & Lomb, Inc. and Abbott Medical Optics, Inc. He has no financial or proprietary interest in any material or method mentioned.

Pamplona MDC, **Ysunza PA**, Sarre P, Morales S and Sterling M (2015). "The effectiveness of mentoring speech and language pathology students when they face patients with cleft palate." International Journal of Pediatric Otorhinolaryngology 79(10): 1708-1713.

[Full-Text](#)

Department of Physical Medicine and Rehabilitation

Introduction: Mentoring programs can boost Speech & Language (SL) pathologists' satisfaction about their clinical skills, increasing their professional competence. A quality induction program provides a bridge for an efficient and comfortable transition between theoretical knowledge and clinical practice in front of clients. This transition can be especially difficult when the SL pathologist confronts patients with cleft palate. Objective: To study whether a mentoring program can improve SL Pathology students' performance for treating patients with cleft palate. Materials and methods: 18 SL Pathology students coursing the third year of a SL Pathology graduate program volunteered for participating in the study. The students were divided in two groups. All SL students from both groups were equally supervised. The students were followed for two semesters during their participation in the SL Pathology intervention for patients with cleft palate. The only difference between the students from each group was that one group (active group) was mentored by an experienced SLP who had previously received specific training to become a mentor. All SL students were assessed at the onset and at the end of the study. The assessment was performed through an analysis according to a previously validated scale (Learning Continuum of Speech & Language pathologists). Results: A Wilcoxon test demonstrated a significant improvement ($P < .05$) in the levels of The Learning Continuum of Speech & Language Pathologists at the end of the follow-up period in both groups of students. When the levels of performance at the end were compared between groups, a Mann Whitney test demonstrated a significant difference ($P < .05$). The students included in the active group who were receiving additional mentoring besides the usual clinical supervision, showed a greater improvement as compared with the students from the control group. Conclusions: Learning how to conduct an adequate and effective intervention in cleft palate patients from an integral stand point is not easy for SL students. The support and guidance of an experienced mentor seems to enhance self-confidence and improve students' performance confronting patients with cleft palate.

Paugh TA, Dickinson TA, Martin JR, **Hanson EC**, Fuller J, Heung M, Zhang M, Shann KG, Prager RL and Likosky DS (2015). "Impact of ultrafiltration on kidney injury after cardiac surgery: The Michigan experience." Annals of Thoracic Surgery. ePub Ahead of Print.

[Full-Text](#)

Department of Surgery

Background: This study examines the relationship between the use and volume of conventional ultrafiltration (CUF) and the risk of acute kidney injury (AKI) after isolated on-pump coronary artery bypass graft surgery. Methods: A total of 6,407 consecutive patients underwent isolated on-pump coronary artery bypass graft surgery between 2010 and 2013 at 21 medical centers participating in the PERFusion Measures and Outcomes (PERForm) registry. We assessed the effect of CUF use on AKI and other postoperative sequelae

using a generalized linear mixed-effect model with a logit link. We also modeled the effect of increasing volume of CUF per weight on AKI, and tested for any modification by a patient's preoperative kidney function. Results: Patients having CUF were more likely to have diabetes, vascular disease, chronic obstructive pulmonary disease, congestive heart failure, history of a myocardial infarction, or an intraaortic balloon pump ($p < 0.05$). They had lower preoperative and nadir hematocrits, creatinine clearance, and ejection fraction ($p < 0.05$). Patients exposed to CUF had higher adjusted risk of AKI (adjusted odds ratio, 1.36; $p = 0.002$), although similar rates of death, stroke, and reoperation for bleeding ($p > 0.05$). The risk of AKI was modified by a patient's preoperative kidney function ($p < 0.0004$). Among patients with a creatinine clearance of less than 99.6 mL/min (95% confidence interval, 67.6 to 137.5), increasing volume of CUF was associated with a higher risk of AKI. Conclusions: Patients exposed to CUF had a higher adjusted risk of AKI. Clinical teams should consider lower volumes of CUF among patients with low creatinine clearance to minimize the risk of AKI. © 2015 The Society of Thoracic Surgeons.

Peebles C, Simon R, **Nagar S**, Ahmed S and Thibodeau B (2015). "Using cancer gene profiling to distinguish benign from malignant follicular thyroid lesions." The Journal of Endocrinology and Metabolic Disorders 1(2): 1-5.

[Full-Text](#)

Department of Surgery

Perdoncin E, Seth M, **Dixon S**, Cannon L, Khandelwal A, Riba A, David S, Wohns D and Gurm H (2015). "The comparative efficacy of bivalirudin is markedly attenuated by use of radial access: Insights from Blue Cross Blue Shield of Michigan Cardiovascular Consortium." European Heart Journal. ePub Ahead of Print.

[Full-Text](#)

Department of Internal Medicine

AIM: The purpose of our study was to evaluate the relative impact of bivalirudin on bleeding outcomes associated with trans-radial interventions (TRI) in real world practice. METHODS AND RESULTS: Data for patients undergoing percutaneous coronary intervention (PCI) between January 2010 and March 2014 at the 47 hospitals participating in the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2) were utilized. Propensity matching was used within cohorts defined by access site. The impact of bivalirudin use on in-hospital outcomes was evaluated with Fisher's exact tests. Among patients undergoing trans-femoral interventions (TFI), use of bivalirudin was associated with a reduction in bleeding compared with both glycoprotein IIb/IIIa inhibitors (GPI; 1.67 vs. 3.46%, absolute risk reduction (ARR) 1.79%, odds ratio, OR, 0.47, confidence interval, CI, 0.41-0.54, number needed to treat, NNT 56, $P < 0.001$) and heparin (1.26 vs. 1.76%, ARR 0.5%, OR 0.71, CI 0.61-0.82, NNT 197, $P < 0.001$). Among patients undergoing TRI, there was a more modest absolute reduction in bleeding with bivalirudin compared with GPI (0.79 vs. 1.41%, ARR 0.62%, OR 0.56, CI 0.34-0.90, NNT 161, $P = 0.016$) and no difference in bleeding compared with heparin (0.46 vs. 0.46%, OR 1, CI 0.54-1.84, $P = 1$). CONCLUSION: Bivalirudin is markedly efficacious in reducing bleeding in patients undergoing TFI. The reduction in bleeding associated with bivalirudin use is minimal to absent in patients undergoing TRI. Given its lower cost and comparable outcomes, heparin should be the preferred anticoagulation strategy in those undergoing radial PCI.

Peters KM, Killinger KA, **Jaeger C** and **Chen C** (2015). "Pilot study exploring chronic pudendal neuromodulation as a treatment option for pain associated with pudendal neuralgia." LUTS: Lower Urinary Tract Symptoms 7(3): 138-142.

[Full-Text](#)

Department of Urology

OUWB Medical Student Author

Department of Radiation Oncology

Objectives: Pudendal neuralgia can cause significant voiding and pain symptoms. We explored the effects of chronic pudendal neuromodulation (CPN) and nerve blocks on pain associated with pudendal neuralgia. Methods: Patients with pudendal neuralgia and tined lead placed at the pudendal nerve were reviewed. History and initial improvement after lead placement were collected from medical records. Demographics, symptom characteristics and changes after various treatments were assessed by mailed survey. Descriptive statistics were performed. Results: Of 19 patients (mean age 54.8 years, 63% female), 6/19 (32%) had

previous sacral neuromodulation. Before CPN, 18 patients had 77 nerve blocks (median six blocks per patient); most blocks (60/77; 78%) provided at least some relief. After lead placement, pain relief was complete in three patients, almost complete in three, significant/remarkable in 10, and small/slight in three. All 19 patients had a permanent generator placed. Five were ultimately explanted at (mean) 2.95 years: one had total symptom resolution, one had stopped using the device, and three lost efficacy. Survey respondents (n = 10) indicated that they had been experiencing pain for (median) 4.42 years before CPN. The most helpful pain treatment cited was medication for 6/10 and neuromodulation for 4/10; 8/9 rated neuromodulation as more helpful than nerve block, while one subject felt that the two treatments were equally helpful. Compared to sacral neuromodulation, 3/4 rated CPN as more effective for pain. Overall, 8/10 were satisfied with CPN; only 1/9 was mildly satisfied with nerve block. Conclusions: Chronic pudendal neuromodulation can improve pain in patients with pudendal neuralgia.

Pinkas D, **Wiater B** and **Michael Wiater J** (2015). "The glenoid component in anatomic shoulder arthroplasty." Journal of the American Academy of Orthopaedic Surgeons 23(5): 317-326.

[Full-Text](#)

Department of Orthopedic Surgery

Ideal management of the glenoid in anatomic shoulder arthroplasty remains controversial. Glenoid component loosening remains a common source of clinical concern and, in young, active patients, implantation of a glenoid prosthesis is often avoided. Efforts to decrease glenoid loosening have resulted in changes to prosthetic design and implantation techniques. Currently, a wide variety of glenoid component options are available, including metal-backed or all-polyethylene, bone ingrowth or ongrowth, inset, and augmented designs. Additionally, several alternatives are available for the young, active patient, including hemiarthroplasty, nonprosthetic resurfacing, and tissue interposition. Many recent clinical and biomechanical studies have examined these implant options. A thorough knowledge of glenoid anatomy, pathology, implant options, indications, and principles of implantation is necessary to optimize the outcome following anatomic shoulder arthroplasty. © the American Academy of Orthopaedic Surgeons. Unauthorized reproduction of this article is prohibited.

Pololi LH, Evans AT, Civian JT, Vasiliou V, Coplit LD, **Gillum LH**, Gibbs BK and Brennan RT (2015). "Mentoring faculty: A US national survey of its adequacy and linkage to culture in academic health centers." Journal of Continuing Education in the Health Professions 35(3): 176-184.

[Full-Text](#)

Administration

Introduction: The aims of this study were to (1) describe the quantity and quality of mentoring faculty in US academic health centers (AHCs), (2) measure associations between mentoring and 12 dimensions that reflect the culture of AHCs, and (3) assess whether mentoring predicts seriously contemplating leaving one's institution. Methods: During 2007-2009, our National Initiative on Gender, Culture and Leadership in Medicine (C - Change) conducted a cross-sectional study of faculty from 26 representative AHCs in the United States using the 74-item C - Change Faculty Survey to assess relationships of faculty characteristics and various aspects of the institutional culture (52% response rate). Among the 2178 eligible respondents (assistant, associate, and full professors), we classified their mentoring experience as either inadequate, neutral, or positive. Results: In this national sample, 43% of the 2178 respondents had inadequate mentoring; only 30% had a positive assessment of mentoring. There was no statistical difference by sex, minority status, or rank. Inadequate mentoring was most strongly associated with less institutional support, lower self-efficacy in career advancement, and lower scores on the trust/relationship/inclusion scale. The percent of faculty who had seriously considered leaving their institution was highest among those who had inadequate mentoring (58%), compared to those who were neutral (28%) or had positive mentoring (14%) (all paired comparisons, $p < .001$). Discussion: In a national survey of faculty of US AHCs, mentoring was frequently inadequate and this was associated with faculty contemplating leaving their institutions. Positive mentoring, although less prevalent, was associated with many other positive dimensions of AHCs. © 2015 The Alliance for Continuing Education in the Health Professions, the Society for Academic Continuing Medical Education, and the Council on CME, Association for Hospital Medical Education.

Prabhu A, Sarcar B, Miller CR, Kim SH, Nakano I, Forsyth P and **Chinnaiyan P** (2015). "Ras-mediated modulation of pyruvate dehydrogenase activity regulates mitochondrial reserve capacity and contributes to glioblastoma tumorigenesis." Neuro-Oncology 17(9): 1220-1230.

[Full-Text](#)

Department of Radiation Oncology

Background. Even though altered metabolism representing a hallmark of cancer was proposed nearly a century ago, recent technological advances have allowed investigators to continue uncovering a previously unrecognized complexity of metabolic programs that drive tumorigenesis beyond that of aerobic glycolysis. Methods. The bioenergetic state of a diverse panel of glioblastoma models, including isogenic lines derived from a genetically engineered adult astrocytic mouse model and patient-derived glioblastoma stem cells, was determined at baseline and in stressed conditions. Mechanisms contributing to the discovered metabolic phenotypes were determined through molecular and chemical perturbation, and their biological consequences were evaluated in vivo and in patient samples. Results. Attenuated mitochondrial reserve capacity was identified as a common metabolic phenotype in glioblastoma lines. This phenotype was linked mechanistically with the capacity of Ras-mediated signaling to inhibit pyruvate dehydrogenase (PDH) activity through downregulation of PDH phosphatase (PDP) expression. PDP1 repression was validated clinically in patient-derived samples, suggesting that aberrant cellular signaling typical of glioblastoma actively modulates PDH activity. This phenotype was reversed through both chemical and molecular perturbation. Restoration of PDH activity through stable expression of PDP1-impaired tumorigenic potential. Conclusions. These findings support the central role that PDH regulation plays as a downstream consequence of aberrant signaling associated with gliomagenesis and the scientific rationale to continue to develop and test clinical strategies designed to activate PDH as a form of anticancer therapy in glioblastoma.

Putnam A, Gu X, Haymart B, Kline-Rogers E, **Almany S**, Kozlowski J, Krol GD, Kaatz S, Froehlich JB and Barnes GD (2015). "The changing characteristics of atrial fibrillation patients treated with warfarin." Journal of Thrombosis and Thrombolysis 40(4): 488-493.

[Full-Text](#)

Department of Internal Medicine

It has been suggested that direct oral anticoagulants are being preferentially used in low risk atrial fibrillation (AF) patients. Understanding the changing risk profile of new AF patients treated with warfarin is important for interpreting the quality of warfarin delivery through an anticoagulation clinic. Six anticoagulation clinics participating in the Michigan Anticoagulation Quality Improvement Initiative enrolled 1293 AF patients between 2010 and 2014 as an inception cohort. Abstracted data included demographics, comorbidities, medication use and all INR values. Risk scores including CHADS₂, CHA₂DS₂-VASc, HAS-BLED, SAME-TT₂R₂, and Charlson comorbidity index (CCI) were calculated for each patient at the time of warfarin initiation. The quality of anticoagulation was assessed using the Rosendaal time in the therapeutic range (TTR) during the first 6 months of treatment. Between 2010 and 2014, patients initiating warfarin therapy for AF had an increasing mean CHADS₂ (2.0 ± 1.1 to 2.2 ± 1.4 , $p = 0.02$) and CCI (4.7 ± 1.8 to 5.1 ± 2.0 , $p = 0.03$), and a trend towards increasing mean CHA₂DS₂-VASc, HAS-BLED, and SAME-TT₂R₂ scores. The actual TTR remained unchanged over the study period (62.6 ± 18.2 to 62.7 ± 17.0 , $p = 0.98$), and the number of INR checks did not change (18.9 ± 5.2 to 18.5 ± 5.1 , $p = 0.06$). Between 2010 and 2014, AF patients newly starting warfarin had mild increases in risk for stroke and death with sustained quality of warfarin therapy.

Qadri YJ, Bortsov AV, Orrey DC, **Swor RA**, Peak DA, Jones JS, Rathlev NK, Lee DC, Domeier RM, Hendry PL and McLean SA (2015). "Genetic polymorphisms in the dopamine receptor 2 predict acute pain severity after motor vehicle collision." Clinical Journal of Pain 31(9): 768-775.

[Full-Text](#)

Department of Emergency Medicine

Objectives: Dopaminergic signaling is implicated in nociceptive pathways. These effects are mediated largely

through dopamine receptors and modulated in part by dopamine transporters. This study tested the hypothesis that genetic variants in the genes encoding dopamine receptor 2 (DRD2) and the dopamine active transporter (SLC6A3) influence acute pain severity after motor vehicle collision. Materials and Methods: European Americans presenting to the emergency department after motor vehicle collision were recruited. Overall pain intensity in emergency department was assessed using a 0 to 10 numeric rating scale. DNA was extracted from blood samples and genotyping of single-nucleotide polymorphisms (SNPs) in the DRD2 and SLC6A3 gene was performed. Results: A total of 948 patients completed evaluation. After correction for multiple comparisons, SNP rs6276 at DRD2 showed significant association with pain scores, with individuals with the A/A genotype reporting lower mean pain scores (5.3; 95% confidence interval [CI], 5.1-5.5) than those with A/G (5.9; 95% CI, 5.6-6.1) or G/G (5.7; 95% CI, 5.2-6.2) genotypes (P=0.0027). Secondary analyses revealed an interaction between sex and DRD2 SNPs rs4586205 and rs4648318 on pain scores: females with 2 minor alleles had increased pain intensity, whereas males with 2 minor alleles had less pain than individuals with a major allele (interaction P=0.0019). Discussion: Genetic variants in DRD2 are associated with acute pain after a traumatic stressful event. These results suggest that dopaminergic agents may be useful for the treatment of individuals with acute posttraumatic pain as part of a multimodal opioid-sparing analgesic regimen.

Rao P, Abbey AM, Yonekawa Y, Shah AR, **Capone A, Trese MT and Drenser KA** (2015). "Macular cavernous hemangioma associated with peripheral vascular anomalies and nonperfusion." [Ophthalmic Surgery Lasers and Imaging Retina](#) 46(7): 764-767.

[Request Form](#)

Department of Ophthalmology

Retinal cavernous hemangiomas are benign vascular anomalies that are typically unilateral and located outside of the macula. Fluorescein angiography findings include an early slow-filling, non-leaking lesion with late intermixed lobules of hyperfluorescence and hypofluorescence secondary to plasma and erythrocyte sedimentation. We present a novel case of unilateral macular cavernous hemangioma with bilateral peripheral vascular anomalies and nonperfusion. This may represent a phenotypic variation of hemangiomas that, in conjunction with recent histopathologic and genetic findings, may aid in future therapies for a disease that has been traditionally observed due to slow progression.

Riofrio D, **Zhou J**, Ma L and Luan S (2015). "Optimizing the number of catheter implants and their tracks for prostate HDR brachytherapy." [Medical Physics](#) 42(6): 3594.

[Full-Text](#)

Department of Radiation Oncology

Safian RD (2015). "Carotid artery stenting: Optimizing patient selection and technique." [Catheterization and Cardiovascular Interventions](#) 86(3): 490-491.

[Full-Text](#)

Department of Internal Medicine

Safian RD (2015). "Cerebral embolization the cost of doing invasive business." [JACC: Cardiovascular Interventions](#) 8(9): 1235-1237.

[Full-Text](#)

Department of Internal Medicine

Sandhu R, **Qin A and Yan D** (2015). "Evaluation of adaptive MLC morphing for online correction of prostate cancer radiotherapy." [Medical Physics](#) 42(6): 3279.

[Full-Text](#)

Department of Radiation Oncology

Sankar WN, Beaulé PE, Clohisy JC, Kim YJ, Millis MB, Peters CL, Podeszwa DA, Schoenecker PL, Sierra RJ, Sink EL, Sucato DJ and **Zaltz I** (2015). "Labral morphologic characteristics in patients with symptomatic acetabular dysplasia." *American Journal of Sports Medicine* 43(9): 2152-2156.

[Full-Text](#)

Department of Orthopedic Surgery

Background: The morphologic characteristics of the labrum in patients with symptomatic acetabular dysplasia have been described to some extent in smaller retrospective series, but the need remains to further define these disease characteristics and their importance as a diagnostic feature of hip instability. Purpose: To (1) characterize the morphologic characteristics of the labrum in patients with symptomatic acetabular dysplasia and (2) test the relationships between specific labral variants, severity of dysplasia, and duration of symptoms. Study Design: Cross-sectional study; Level of evidence, 3. Methods: Thirteen surgeons from 10 centers enrolled patients undergoing periacetabular osteotomy (PAO) for symptomatic acetabular dysplasia from 2008 to 2014. Patient demographics, presenting characteristics, preoperative radiographic data, operative data, and intraoperative findings were prospectively collected and retrospectively reviewed. Results: A total of 942 patients (972 hips) met the initial inclusion criteria, with a mean age of 25.2 years (range, 9-51 years; 84% female, 16% male). In addition to having PAO, 52.6% of hips had an anterior arthrotomy and 19.8% had a hip arthroscopy either to perform an osteochondroplasty of the femoral head-neck junction or to address labral pathologic changes. Of these 553 hips in which the labrum was visualized, labral morphologic status was graded as hypertrophic in 50%, normal in 45%, hypoplastic in 4%, and ossified in less than 1%. Decreased lateral center-edge angle and anterior center-edge angle and increased acetabular inclination were associated with labral hypertrophy, but chronicity of symptoms was not. Of the 553 hips, 64% had tears of the labrum, with the majority being degenerative-type tears. Conclusion: Labral pathologic changes are common in patients with symptomatic acetabular dysplasia. Labral hypertrophy, however, is not a universal finding, particularly in hips with mild dysplasia, and therefore should not be considered a reliable diagnostic criterion for instability. © 2015 The Author(s).

Sen A, Heredia N, Senut MC, Land S, Hollocher K, Lu X, **Dereski MO** and Ruden DM (2015). "Multigenerational epigenetic inheritance in humans: DNA methylation changes associated with maternal exposure to lead can be transmitted to the grandchildren." *Scientific Reports* 5: 14466.

[Full-Text](#)

Department of Biomedical Sciences (OU)

We report that the DNA methylation profile of a child's neonatal whole blood can be significantly influenced by his or her mother's neonatal blood lead levels (BLL). We recruited 35 mother-infant pairs in Detroit and measured the whole blood lead (Pb) levels and DNA methylation levels at over 450,000 loci from current blood and neonatal blood from both the mother and the child. We found that mothers with high neonatal BLL correlate with altered DNA methylation at 564 loci in their children's neonatal blood. Our results suggest that Pb exposure during pregnancy affects the DNA methylation status of the fetal germ cells, which leads to altered DNA methylation in grandchildren's neonatal dried blood spots. This is the first demonstration that an environmental exposure in pregnant mothers can have an epigenetic effect on the DNA methylation pattern in the grandchildren.

Setty P, D'Andrea K P, Stucken EZ, Babu S, Larouere MJ and **Pieper DR** (2015). "Fully endoscopic resection of cerebellopontine angle meningiomas." *Journal of Neurological Surgery, Part A: Central European Neurosurgery*. ePub Ahead of Print.

[Request Form](#)

Department of Neurosurgery

Objective To describe our operative technique and results from patients who underwent fully endoscopic resection of cerebellopontine angle (CPA) meningiomas. Design Prospective observational study. Setting A single academic institution that includes both neurosurgery and neuro-otology. Participants Eleven consecutive patients who underwent fully endoscopic resection of a CPA meningioma. Main Outcome Measures Hearing preservation, based on the American Association of Otolaryngology-Head and Neck Surgeons score as well as facial nerve preservation base on the House-Brackmann (HB) score. In addition, the

extent of resection and complication rates was studied. Results All 11 patients underwent successful gross total resection, Simpson grade 2, of their meningioma, seen both intraoperatively and on postoperative imaging. Overall, 100% of patients maintained normal facial nerve function (HB 1/6). Audiometric testing revealed that 10 of 11 patients maintained either stable or improved hearing postoperatively based on Committee on Hearing and Equilibrium Guidelines for the Evaluation of Hearing Preservation in Acoustic Neuroma grade with the remaining patient retaining serviceable hearing. Tumor size ranged from 0.5 to 2.5 cm (mean: 1.54 cm). Mean operative time was 166 minutes (range: 122–207 minutes); estimated blood loss averaged 54.5 mL. Hospital length of stay ranged from 2 to 6 days (mean: 3.1 days), and a superficial wound infection was the only complication seen in one patient. Conclusion Fully endoscopic techniques can be used in CPA meningioma resection with excellent clinical results as an alternative to the traditional open microscopic approach.

Shanley CJ, Park YJ and Henke PK (2015). "Hospital variation in 30-day stroke outcomes for patients undergoing carotid endarterectomy for asymptomatic disease in Michigan." Journal of Vascular Surgery 62(3): 830.

[Full-Text](#)

Department of Surgery

Sheeran PD, Anton-Martin P, Thompson MT, **Fischer AC**, Taylor D and Thomas JA (2015). "Extubation during pediatric extracorporeal membrane oxygenation: Is it always safe? Reply." Pediatric Critical Care Medicine 16(5): 494-495.

[Full-Text](#)

Department of Surgery

Shi G, Lilo M, Fischer M, Lough D, **Fischer AC** and Tufaro AP (2015). "Identification of HPV molecular triggers in cutaneous squamous cell carcinoma." Journal of Clinical Oncology 33(15): e20084.

[Request Form](#)

Department of Surgery

Background: Cutaneous squamous cell carcinoma (SCC) a malignant tumor derived from epidermal keratinocytes and occurs predominately in sun-exposed skin. Organ transplant recipients have 60-250 times more likely to develop SCC than the immunocompetent population and the risk of SCC development increases with time posttransplant. Cutaneous SCC is the second most common skin cancer, affecting 700,000 people each year and up to 8,800 people died from the disease in 2012. Human papillomavirus (HPV) is a DNA virus from the papillomavirus family, with more than 100 HPV genotypes characterized. Although the significance of specific types of HPV is well recognized in cervical and anogenital SCC, as well as a subset of oropharyngeal SCC, its contributing role in cutaneous SCC oncogenesis is still being debated. A retrospective study was undertaken to study the oncogenesis of HPV presence and its types in aggressive cutaneous SCC. Methods: Formalin-fixed paraffin embedded (FFPE) archival patient tissue blocks with a clear aggressive cutaneous SCC history were deparaffinized and underwent DNA isolation and regular HPV-PCR with HPV specific primers: GP5+, 5'- TTTGTTACTGTGGTAGATACTAC-3' and GP6+, 5'- GAAAAATAAACTGTAAATCATATTC-3' to identify HPV presence. HPV positive PCR products were cloned into T4-Vectors and underwent DNA sequencing to identify HPV genotypes in cutaneous SCC. Results: Total 36 aggressive cutaneous SCC blocks were tested by HPV-PCR, among which 15 blocks were HPV-16, 1 block was HPV-10 and 15 blocks were HPV test negative. HPV positive blocks account for 51.6%, among which HPV-16 accounts for 48.4% and HPV-10 accounts for 3.2%. HPV negative blocks account for 48.4%. Conclusions: (i) HPV infection is very popular in aggressive cutaneous SCC patients and HPV-16 is the most prevalent HPV type, accounting for 93.8% HPV infections. HPV infection may not only be a risk factor but also a contributing factor to aggressive cutaneous SCC oncogenesis; (ii) HPV-10 was first identified in an aggressive cutaneous SCC patient, which may co-relate to the oncogenesis of aggressive cutaneous SCC.

Silber TC, Tweet MS, Bowman MJ, Hayes SN and Squires RW (2015). "Cardiac rehabilitation after spontaneous coronary artery dissection." Journal of Cardiopulmonary Rehabilitation and Prevention 35(5): 328-333.

[Full-Text](#)

OUWB Medical Student Author

PURPOSE: Although cardiac rehabilitation (CR) improves outcomes in patients after atherosclerotic myocardial infarctions, little is known of the CR benefit among patients with spontaneous coronary artery dissection (SCAD), who are primarily young, otherwise healthy women. The purpose of this study was to describe SCAD patient outcomes in phase 2 outpatient CR. METHODS: Patients with SCAD who enrolled in CR were retrospectively identified. Patients participated in standard CR, which included supervised and independent flexibility, stretching, aerobic, and strength training exercises. Patients received counseling regarding nutrition, weight and stress management. Assessments at baseline and program completion included cardiopulmonary exercise testing or 6-Minute Walk Test, body composition using plethysmography, depression (Patient Health Questionnaire-9), and stress (a scale of 1-10) scores. RESULTS: Nine patients, all women, enrolled in CR an average of 12.3 days (range, 7-21 days) after their SCAD event, with one enrolling again after a recurrence. Cardiac rehabilitation was well received, with participants completing an average of 28 CR sessions (range, 5-39 sessions). Patients did not report cardiac symptoms and there were no adverse events during exercise testing or training. Peak oxygen uptake increased by an average of 18% (n = 4) and 6-minute walk distance increased 22% (n = 4). Average body mass decreased 1.1 kg, fat mass decreased 1.6 kg, and lean mass increased 0.4 kg. Depression and stress scores improved by an average of 2.3 and 1.3 points, respectively. CONCLUSIONS: Standard CR beginning 1 to 2 weeks after SCAD seems to be feasible and safe and results in improved aerobic capacity, body composition, and measures of depression and stress. Because of these benefits, we recommend that patients with SCAD participate in CR.

Smorgick Y, **Baker KC** and **Fischgrund JS** (2015). "Hidden blood loss during posterior spine fusion surgery: In response to the letter by ZhiNan et al." Spine Journal 15(9): 2114-2115.

[Full-Text](#)

Department of Orthopedic Surgery

Smythe MA, **Forsyth LL**, Warkentin TE, **Smith MD**, Sheppard JA and **Shannon F** (2015). "Progressive, fatal thrombosis associated with heparin-induced thrombocytopenia after cardiac surgery despite "therapeutic" anticoagulation with argatroban: Potential role for PTT and ACT confounding." Journal of Cardiothoracic and Vascular Anesthesia 29(5): 1319-1321.

[Full-Text](#)

Department of Biomedical Sciences (BHS)

Department of Pathology

Department of Surgery

Stefaniak J and Joyce B (2015). "Complex learning: Promoting complex learning through the promotion of contextually relevant learning experience for the health sciences," In Halupa C (ed). Transformative Curriculum Design in Health Sciences Hershey, Penn.: IGI Global. pp: 193-223.

[Request Form](#)

Stone B, Mangona VS, Johnson MD, Ye H and **Grills IS** (2015). "Changes in pulmonary function following image guided stereotactic lung radiotherapy: Neither lower baseline or post-SBRT pulmonary function are associated with worse overall survival." Journal of Thoracic Oncology. ePub Ahead of Print.

[Full-Text](#)

Department of Radiation Oncology

INTRODUCTION: To determine changes in pulmonary function brought about by lung SBRT. METHODS: 127 patients were treated with lung stereotactic body radiation therapy (SBRT) using 48-60Gy in 4 to 5 fractions on a prospective trial. We obtained pulmonary function tests (PFTs) at baseline, 6 weeks, 3 months, 6 months, 9 months, 12 months, and 24 months after SBRT. Group mean PFT parameter values are reported. RESULTS: At baseline forced expiratory volume in the first second (FEV1) was 1.5 L (67% predicted, range: 0.4

- 3.4 L), corrected diffusing capacity for carbon monoxide (DLCO) was 12.2 ml/min/mmHg (50.8% predicted, range: 3.3 - 27.2 ml/min/mmHg), and total lung capacity (TLC) was 5.7 L (102.4% predicted, range: 3.1-9.1 L). At 12 months there was decline in FEV1 (-4.1%, P=0.01), corrected DLCO (-5.2%, P=0.027), forced vital capacity (FVC) (-5.7%, P=0.004), and TLC (-3.6%, P=0.039). Declines in FEV1 (-7.6%, P=0.001) and FVC (-8.9%, P=0.001) persisted at 24 months. Rates of pneumonitis were 3.1% and 0.8% for grades 2 and 3 respectively. There were no grade 3 PFT toxicities at 12 months. Lower PFTs at baseline and one year after SBRT did not predict for worse overall survival (OS). CONCLUSIONS: As the largest cohort of patients with prospective follow-up PFT evaluation after lung SBRT, this supports the safety of SBRT in this population of predominantly medically inoperable patients. While statistically significant, nearly all declines in PFTs would be rated as a grade 1 on the RTOG scale, demonstrating safety. PFT declines were not associated with worse overall survival.

Swanberg S, Abuelroos D, Dabaja E, Jurva S, Martin K, McCarron J, Reed-Hendon C, Yeow R and Harriott M (2015). "Partnership for diversity: A multidisciplinary approach to nurturing cultural competence at an emerging medical school." Medical Reference Services Quarterly 34(4). (accepted for publication).

[Request Form](#)

Medical Library

Swanberg S, Engwall K and Mi M (2015). "Continuing education for medical students: A library model." Journal of the Medical Library Association 103(4): 203-207.

[Full-Text](#)

Medical Library

Tao CJ, Yi JL, Chen NY, Ren W, Cheng J, Tung S, Kong L, Lin SJ, Pan JJ, Zhang GS, Hu J, Qi ZY, Ma J, Lu JD, **Yan D** and Sun Y (2015). "Multi-subject atlas-based auto-segmentation reduces interobserver variation and improves dosimetric parameter consistency for organs at risk in nasopharyngeal carcinoma: A multi-institution clinical study." Radiotherapy and Oncology 115(3): 407-411.

[Full-Text](#)

Department of Radiation Oncology

Background and purpose: To assess whether consensus guideline-based atlas-based auto-segmentation (ABAS) reduces interobserver variation and improves dosimetric parameter consistency for organs at risk (OARs) in nasopharyngeal carcinoma (NPC). Materials and methods: Eight radiation oncologists from 8 institutes contoured 20 OARs on planning CT images of 16 patients via manual contouring and manually-edited ABAS contouring. Interobserver variation [volume coefficient of variation (CV), Dice similarity coefficient (DSC), three-dimensional isocenter difference (3D-ICD)] and dosimetric parameters were compared between the two methods of contouring for each OAR. Results: Interobserver variation was significant for all OARs in manual contouring, resulting in significant dosimetric parameter variation ($P < 0.05$). Edited ABAS significantly improved multiple metrics and reduced dosimetric parameter variation for most OARs; brainstem, spinal cord, cochleae, temporomandibular joint (TMJ), larynx and pharyngeal constrictor muscle (PCM) obtained most benefit (range of mean DSC, volume CV and main ICD values was 0.36-0.83, 12.1-84.3%, 2.2-5.0 mm for manual contouring and 0.42-0.86, 7.2-70.6%, 1.2-3.5 mm for edited ABAS contouring, respectively; range of dose CV reduction: 1.0-3.0%). Conclusion: Substantial objective interobserver differences occur during manual contouring, resulting in significant dosimetric parameter variation. Edited ABAS reduced interobserver variation and improved dosimetric parameter consistency, particularly for brainstem, spinal cord, cochleae, TMJ, larynx and PCM. (C) 2015 Elsevier Ireland Ltd. All rights reserved.

Thibodeau BJ, Geddes TJ, Fortier LE, Ahmed S, Pruetz BL, Wobb J, **Chen P, Wilson GD** and **Akervall JA** (2015). "Gene expression characterization of HPV positive head and neck cancer to predict response to chemoradiation." [Head and Neck Pathology](#) 9(3): 345-353.

[Full-Text](#)

Department of Radiation Oncology

Department of Biomedical Sciences (BHS)

Human papillomavirus (HPV) has been shown to have a causal role in the development of head and neck squamous cell carcinoma. While HPV-positive head and neck cancer is associated with a better response to treatment in the majority of patients, there is a subset who does not respond favorably to current therapy. Identification of these patients could prevent unnecessary morbidity and indicate the need for alternative therapeutic options. Tissue samples were obtained from 19 patients with HPV-positive head and neck squamous carcinoma treated with chemoradiation therapy. HPV status was confirmed by polymerase chain reaction analysis through detection of HPV16 E7 in both DNA and RNA. RNA was isolated from tissue samples and subjected to microarray gene expression analysis. In addition to identification of potential genetic biomarkers (including LCE3D, KRTDAP, HMOX1, KRT19, MDK, TSPAN1), differentially expressed genes associated with genomic stability, cell cycle, and DNA damage were detected between responders and non-responders. These results were further validated with publicly available gene expression studies. This pilot study suggests prospective biomarkers that predict response to therapy. The importance of genes involved with genomic stability is highlighted in both development and progression of head and neck squamous cell carcinoma but also recurrence. Potential development of an assay may prove beneficial to clinicians, assisting them to provide alternative care sooner thus lowering morbidity.

Thomas BJ, Yonekawa Y, **Ruby AJ** and **Capone A** (2015). "Aggressive surgical therapy with early vitrectomy, panretinal photocoagulation, and silicone oil tamponade for streptococcus mitis endophthalmitis." [Ophthalmic Surgery Lasers and Imaging Retina](#) 46(8): 893-895.

[Request Form](#)

Department of Ophthalmology

An 87-year-old woman presented with acute, painful vision loss in her right eye after intravitreal injection. Examination disclosed hypopyon and vitritis, as well as discrete inflammatory collections in the vitreous and widespread retinal hemorrhages. The patient underwent vitrectomy with injection of intravitreal antibiotics. Vitreous cultures were positive for *Streptococcus mitis*, a pathogen associated with severe tissue damage and poor clinical outcomes. Clinical deterioration prompted repeat vitrectomy with silicone oil tamponade and panretinal photocoagulation two weeks later, resulting in more favorable anatomic and visual outcomes. Endophthalmitis caused by exotoxin-producing bacterial species such as *S. mitis* is often associated with severe vision loss or loss of the eye. Aggressive surgical intervention - prompted by concerning clinical findings and vitreous cultures - may play a role in improving outcomes in these patients.

Trapani AJ, **Goncalves LF**, Trapani TF, Franco MJ, Galluzzo RN and Pires MM (2015). "Comparison between transdermal nitroglycerin and sildenafil citrate in intrauterine growth restriction: Effect on uterine, umbilical and fetal middle cerebral artery pulsatility index." [Ultrasound in Obstetrics and Gynecology](#). ePub Ahead of Print.

[Request Form](#)

Department of Obstetrics and Gynecology

OBJECTIVES: To evaluate the effect of transdermal nitroglycerin (GTN) and sildenafil citrate on Doppler velocity waveforms of the uterine, umbilical and fetal middle cerebral arteries in patients with intrauterine growth restriction (IUGR). METHODS: This was a prospective study of 35 singleton pregnancies (gestational age range: 24-31 weeks) with IUGR and abnormal uterine and umbilical artery Doppler waveforms. We compared maternal arterial blood pressure as well as Z-scores for the pulsatility index (PI) of the uterine, umbilical and fetal middle cerebral arteries (MCA) before and after application of either a transdermal nitroglycerin patch (average dose 0.4 mg/h), oral sildenafil citrate (50 mg) or placebo. Statistical analysis was performed using ANOVA for paired samples. RESULTS: There was a significant decrease in uterine artery PI with both GTN (21.3%) and sildenafil citrate (20.2%). A significant reduction in umbilical artery PI was also observed for both GTN (19.2%) and sildenafil citrate (18.4%). No difference in Doppler PI was observed for

uterine and umbilical arteries when GTN and sildenafil groups were compared. No Doppler velocimetry changes were observed for the placebo group. No significant change in MCA PI was observed in any of the groups. Maternal arterial blood pressure decreased with both GTN and sildenafil citrate. CONCLUSION: The use of transdermal nitroglycerin or sildenafil citrate in patients with IUGR is associated with a significant reduction uterine and umbilical artery Doppler PI, as well as of maternal arterial blood pressure. Neither drug affected MCA Doppler PI.

Trese MT (2015). "Subjectivity in retinopathy of prematurity screening." [American Journal of Ophthalmology](#) 160(3): 406-407.

[Full-Text](#)

Department of Ophthalmology

Troeller A, Soehn M, **Grills I**, Guckenberger M, Bederbos J, Sonke J, Hope A, Werner-Wasik M, Xiao Y and **Yan D** (2015). "Investigation of fractionation issues in NTCP modeling of pneumonitis: An analysis of common NTCP models for hypo-fractionated and standard-fractionated data." [Medical Physics](#) 42(6): 3701-3702.

[Full-Text](#)

Department of Radiation Oncology

Vereecke A and **Chancellor M** (2015). "Building momentum toward underactive bladder research and education." [International Urology and Nephrology](#) 47(10): 1593-1594.

[Full-Text](#)

Department of Urology

Vilchez GA, Dai J, Hoyos LR, Gill N, **Bahado-Singh R** and Sokol RJ (2015). "Labor and neonatal outcomes after term induction of labor in gestational diabetes." [Journal of Perinatology](#). ePub Ahead of Print.

[Request Form](#)

Department of Obstetrics and Gynecology

OBJECTIVE: To identify the optimal gestational age (GA) for induction of labor (IOL) at term among patients with gestational diabetes (GDMA) according to perinatal outcomes. STUDY DESIGN: The US Natality Database from 2007 to 2010 was reviewed. Inclusion criteria were singleton delivery, IOL at 37 to 42 weeks and GDMA. Exclusion criteria included congenital anomalies, pre-gestational diabetes, hypertensive disorders, previous cesarean, breech presentation and rupture of membranes. Controls were non-GDMA cases delivered in geographic and temporal proximity. Delivery mode, macrosomia and perinatal complications were analyzed. Logistic regression adjusted for confounders was used to calculate odds ratios by GA using 39 weeks non-GDMA as reference. RESULTS: In all, 96 964 cases and 176 079 controls were included. Increased risk for all adverse outcomes among GDMA cases was found. The nadir for intrapartum and neonatal complications was 38 and 40 weeks, respectively, whereas for cesarean and macrosomia was 39 weeks. CONCLUSION: The optimal timing for IOL at term in GDMA appears to be 39 to 40 weeks. [Journal of Perinatology](#) advance online publication, 27 August 2015; doi:10.1038/jp.2015.103.

Vinekar A, Jayadev C, Mangalesh S, Kiran Kumar A, Bauer N, **Capone A**, Trese M and Shetty B (2015). "Comparing the outcome of single versus multiple session laser photocoagulation of flat neovascularization in zone 1 aggressive posterior retinopathy of prematurity: A prospective randomized study." [Retina](#) 35(10): 2130-2136.

[Full-Text](#)

Department of Ophthalmology

Purpose: To compare single versus 2-session laser photocoagulation for flat neovascularization in cases with Zone 1 aggressive posterior retinopathy of prematurity. Methods: Twenty-nine Asian Indian infants with aggressive posterior retinopathy of prematurity were randomized; each eye received 1 of 2 methods (29 each in Group A or B) proposed by the PHOTO-ROP group. Group A underwent single session laser to the avascular retina underlying the flat neovascularization by direct laser over the fronds. Group B underwent laser in 2 sessions; first, laser was delivered to the avascular periphery up to the flat neovascularization and 7 days later to the avascular bed exposed by the retraction of the fronds. Outcome and complications between

the two groups were compared. Results: Mean birthweight and gestational ages were 1,276 g and 30.1 weeks, respectively. All eyes showed favorable outcome at a minimum 12-month follow-up. Hemorrhages after laser (41.4% vs. 17.2%, $P < 0.001$) were more common in the single laser group. Large hemorrhages (>1 disk diameter) seen in Group A took longer than 8 weeks to resolve and developed focal fibrosis. Conclusion: This study demonstrates that the two-staged laser procedure produces fewer and smaller hemorrhages and no fibrosis compared with a single session. Both methods have comparable favorable outcomes in Asian Indian infants.

Vinogradskiy Y, Waxweiler T, Diot Q, Castillo R, **Guerrero T**, Castillo E, Kavanagh B, Schubert L and Miften M (2015). "Developing clinical and quantitative guidelines for a 4DCT-ventilation functional avoidance clinical trial." Medical Physics 42(6): 3196-3197.

[Full-Text](#)

Department of Radiation Oncology

Wall M, Falardeau J, Fletcher WA, **Granadier RJ**, Lam BL, Longmuir RA, Patel AD, Bruce BB, He H and McDermott MP (2015). "Risk factors for poor visual outcome in patients with idiopathic intracranial hypertension." Neurology 85(9): 799-805.

[Full-Text](#)

Department of Ophthalmology

OBJECTIVES: Determine potential risk factors for progressive visual field loss in the Idiopathic Intracranial Hypertension Treatment Trial, a randomized placebo-controlled trial of acetazolamide in patients with idiopathic intracranial hypertension and mild visual loss concurrently receiving a low sodium, weight reduction diet. **METHODS:** Logistic regression and classification tree analyses were used to evaluate potential risk factors for protocol-defined treatment failure (>2 dB perimetric mean deviation [PMD] change in patients with baseline PMD -2 to -3.5 dB or >3 dB PMD change with baseline PMD -3.5 to -7 dB). **RESULTS:** Seven participants (6 on diet plus placebo) met criteria for treatment failure. The odds ratio for patients with grades III to V papilledema vs those with grades I and II was 8.66 (95% confidence interval [CI] 1.65-infinity, $p = 0.025$). A 1-unit decrease in the number of letters correct on the ETDRS (Early Treatment Diabetic Retinopathy Study) chart at baseline was associated with an increase in the odds of treatment failure by a factor of 1.16 (95% CI 1.04-1.30, $p = 0.005$). Compared with female participants, the odds ratio for male participants was 26.21 (95% CI 1.61-433.00, $p = 0.02$). The odds of treatment failure were 10.59 times higher (95% CI 1.63-116.83, $p = 0.010$) for patients with >30 transient visual obscurations per month vs those with ≤ 30 per month. **CONCLUSIONS:** Male patients, those with high-grade papilledema, and those with decreased visual acuity at baseline were more likely to experience treatment failure. All but one of these patients were treated with diet alone. These patients should be monitored closely and be considered for aggressive treatment of their idiopathic intracranial hypertension.

Wasserman JA, Stevenson SL, Claxton C and **Krug EF, 3rd** (2015). "Moral reasoning among HEC members: An empirical evaluation of the relationship of theory and practice in clinical ethics consultation." The Journal of Clinical Ethics 26(2): 108-117.

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OUWB Medical Student Author

In light of the ongoing development and implementation of core competencies in bioethics, it is important to proceed with a clear sense of how bioethics knowledge is utilized in the functioning of hospital ethics committees (HECs). Without such an understanding, we risk building a costly edifice on a foundation that is ambiguous at best. This article examines the empirical relationship between traditional paradigms of bioethics theory and actual decision making by HEC members using survey data from HEC members. The assumption underlying the standardization of qualifications and corresponding call for increased education of HEC members is that they will base imminent case decisions on inculcated knowledge. Our data suggest, however, that HEC members first decide intuitively and then look for justification, thereby highlighting the need to re-examine the pedagogical processes of ethics education in the process of standardizing and improving competencies. Copyright 2015 The Journal of Clinical Ethics. All rights reserved.

Welton KL, Gomberawalla MM, Gagnier JJ, **Fischgrund JS**, Graziano GP and Patel RD (2015). "Patient impressions of reimbursement for orthopedic spine surgeons." Spine Journal. ePub Ahead of Print.

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Department of Orthopedic Surgery

Williams GA (2015). "From SGR to MACRA: Out of the frying pan and into the fire?: The new legislation replaces multiple quality reporting systems with a new, single system." Retina Today 2015(September2015): 12-17.

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Department of Ophthalmology

Wolfe JD, Shah AR, Yonekawa Y, Faran AA, Franklin MS, Abbey AM and **Capone A** (2015). "Receiver operating characteristic curve to predict anti-VEGF resistance in retinal vein occlusions and efficacy of Ozurdex." European Journal of Ophthalmology. ePub Ahead of Print.

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Department of Ophthalmology

PURPOSE: Current treatment paradigms for macular edema associated with retinal vein occlusions (RVO) often involve initial treatment with anti-vascular endothelial growth factor (VEGF) agents, then switching to intravitreal dexamethasone implant (IDI; Ozurdex, Allergan, Parsippany, NJ) for poor responders. However, many patients undergo multiple injections prior to being declared a nonresponder. We devised a method for prediction of poor anti-VEGF response after one injection, and show that these patients subsequently respond well to IDI. METHODS: This study is a retrospective consecutive interventional case series of patients with RVO receiving anti-VEGF agents that were switched to IDI. Patients were categorized as nonresponders to anti-VEGF agents (edema did not improve) or responders (edema improved, but switched to IDI for longer treatment duration). Receiver operating characteristics (ROC) curve analysis was used to determine cutoffs of reduction in central retinal thickness (CRT) to predict poor response to anti-VEGF treatment. RESULTS: Twenty-three patients met inclusion criteria. There were 14 nonresponders and 9 responders. The ROC curve analysis found that the maximal sensitivity and specificity in correctly identifying responders to anti-VEGF therapy was those with $\geq 25\%$ reduction in CRT 1 month after 1 anti-VEGF treatment (sensitivity 0.89, specificity 0.79, area under the curve 0.93). After IDI placement, anti-VEGF nonresponders showed significant improvement in visual acuity (VA) ($p = 0.02$) and CRT ($p = 0.01$). CONCLUSIONS: In patients with macular edema secondary to RVOs, a reduction in CRT by $\leq 25\%$, 1 month after 1 anti-VEGF injection, is predictive of poor response to anti-VEGF treatment. These patients may benefit from earlier conversion to IDI treatment, which in our study, resulted in improved VA and CRT.

Wong SC and **Capone A** (2015). "Illumination techniques for complex pediatric anterior retinal detachment and associated retrolental plaque." Retina 35(9): 1905-1907.

[Full-Text](#)

Department of Ophthalmology

Yadavalli S (2015). "Radiologic evaluation of musculoskeletal soft tissue infections: A pictorial review." Current Radiology Reports 3(10): 39-40.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Musculoskeletal soft tissues infections are among the commonly encountered diagnoses in the outpatient as well as hospital settings. Often patients present with vague symptoms making it difficult to distinguish infectious causes from other diagnoses by clinical examination alone and laboratory studies may also prove inconclusive. In such cases, it is important to recognize imaging features of soft tissue infections on radiologic studies that may be obtained as part of the work-up. Imaging studies often play an important role in leading to the correct diagnosis and in delineating extent of disease. Recognizing the imaging characteristics of infectious processes such as cellulitis, necrotizing fasciitis, pyomyositis and bursitis using various modalities is crucial in reaching an early diagnosis in order to prevent significant morbidity and even

mortality in some cases. Image-guided intervention also has a prominent role in treatment of soft tissue infections. This article reviews various types of musculoskeletal soft tissue infections that may be encountered and their imaging features utilizing different imaging modalities, including radiography, computed tomography, ultrasound and magnetic resonance imaging.

Yonekawa Y, Thomas BJ, **Drenser KA, Trese MT** and Capone A (2015). "Acquired combined hamartoma of the retina and retinal pigment epithelium." JAMA Ophthalmology 133(9): 1085-1086.

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Department of Ophthalmology

Yonekawa Y, Thomas BJ, **Drenser KA, Trese MT** and Capone A (2015). "Familial exudative vitreoretinopathy. Spectral-domain optical coherence tomography of the vitreoretinal interface, retina, and choroid." Ophthalmology. ePub Ahead of Print.

[Full-Text](#)

Department of Ophthalmology

Purpose: The in vivo microstructural features of familial exudative vitreoretinopathy (FEVR) have not been well described. We present new anatomic features of FEVR with functional and genetic correlations. Design: Consecutive, retrospective, observational case series. Participants: Patients with FEVR treated from 2009 to 2014. Methods: We identified 346 patients with FEVR. Those imaged with spectral-domain optical coherence tomography (SD OCT) with or without enhanced depth imaging (EDI) were included, and images were correlated with best-corrected visual acuity (BCVA), widefield angiography, fundus autofluorescence (AF), and wnt signaling pathway mutations. Main Outcome Measures: Exploratory SD OCT findings and BCVA. Results: A total of 225 imaging sessions were acquired in 74 eyes from 41 patients. Mean age was 19.0 years. Sixty-seven eyes (91%) had interpretable images, of which 50 (75%) had anomalous microstructural findings; all eyes with FEVR severity of stage 2 or greater had abnormalities. A broad spectrum of features were identified: various forms of posterior hyaloidal organization, vitreomacular traction (VMT), vitreopapillary traction, vitreo-fold traction, vitreo-laser scar adhesion, diminished foveal contour, persistent fetal foveal architecture, cystoid macular edema (CME), intraretinal exudates and subretinal lipid aggregation, dry or edematous radial folds, and disruption of the ellipsoid zone. Mean foveal, central macular, and choroidal thicknesses were $305 \pm 145 \mu\text{m}$, $337 \pm 160 \mu\text{m}$, and $216 \pm 64 \mu\text{m}$, respectively. In stages 1 to 2, greater foveal and central macular thicknesses ($Rho = 0.493, 0.544$, respectively; both $P < 0.001$) correlated with poorer BCVA, but not choroidal thickness ($Rho = 0.032$; $P = 0.868$). Posterior hyaloidal organization ($P < 0.001$), VMT ($P < 0.001$), CME ($P < 0.001$), exudation ($P < 0.001$), and disruption of the ellipsoid zone ($P < 0.001$) were associated with poorer BCVA. Disruption of the ellipsoid zone ($\beta = 0.699$; $P < 0.001$) and posterior hyaloidal organization ($\beta = 0.289$; $P = 0.011$) retained significance in multivariate modeling ($R^2 = 0.627$; $P < 0.001$). Spectral-domain OCT detected all cases of angiographic edema and areas of outer retinal dysfunction that were hypoautofluorescent on AF. Microstructural-genetic associations were not identified. Conclusions: Spectral-domain OCT imaging identified microstructural anomalies in the majority of patients with FEVR. © 2015 American Academy of Ophthalmology.

Yonekawa Y and **Wolfe JD** (2015). "Dexamethasone intravitreal implant: Pharmacology and clinical update." Retina Today 2015(September 2015): 54-58.

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Department of Ophthalmology

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Department of Physical Medicine and Rehabilitation

Zarif JC, **Lamb LE**, Schulz VV, Nollet EA and Miranti CK (2015). "Androgen receptor non-nuclear regulation of prostate cancer cell invasion mediated by SRC and matriptase." [Oncotarget](#) 6(9): 6862-6876.

[Full-Text](#)

Department of Urology

Castration-resistant prostate cancers still depend on nuclear androgen receptor (AR) function despite their lack of dependence on exogenous androgen. Second generation anti-androgen therapies are more efficient at blocking nuclear AR; however resistant tumors still develop. Recent studies indicate Src is highly active in these resistant tumors. By manipulating AR activity in several different prostate cancer cell lines through RNAi, drug treatment, and the use of a nuclear-deficient AR mutant, we demonstrate that androgen acting on cytoplasmic AR rapidly stimulates Src tyrosine kinase via a non-genomic mechanism. Cytoplasmic AR, acting through Src enhances laminin integrin-dependent invasion. Active Matriptase, which cleaves laminin, is elevated within minutes after androgen stimulation, and is subsequently shed into the medium. Matriptase activation and shedding induced by cytoplasmic AR is dependent on Src. Concomitantly, CDCP1/gp140, a Matriptase and Src substrate that controls integrin-based migration, is activated. However, only inhibition of Matriptase, but not CDCP1, suppresses the AR/Src-dependent increase in invasion. Matriptase, present in conditioned medium from AR-stimulated cells, is sufficient to enhance invasion in the absence of androgen. Thus, invasion is stimulated by a rapid but sustained increase in Src activity, mediated non-genomically by cytoplasmic AR, leading to rapid activation and shedding of the laminin protease Matriptase.