

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

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Abbas A, Sakwa M, Shannon F, Shenouda K, Bilollikar AN, Hanson ID, Safian R, Hanzel G and Wood F (2014). "Comparison of invasive and non-invasive data of the ratio between the effective and geometric aortic valve area in normal and low flow patients: Overestimation of aortic stenosis severity by doppler with low flow: A TAVR study." *Journal of the American College of Cardiology* 64(11): B197.

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Department of Internal Medicine

Department of Surgery

OUWB Medical Student Author

Background: The ratio between the effective orifice area (EOA) and the geometrical aortic orifice area (GOA) is known as the Coefficient of Contraction (CoC). The GOA is derived from planimetry of the valve orifice, while the EOA is highly dependent on flow and is obtained from both Doppler and Invasive measures. Patients undergoing TAVR undergo multi modality imaging as well as invasive studies. We sought to study CoC in patients undergoing TAVR in those with normal and low flow states as defined by echo (stroke volume index < 35 ml/m²). Methods: Patients undergoing catheterization, CTA, TTE and TEE prior to TAVR were included. GOA obtained from TEE planimetry, EOA from Doppler using continuity equation and cath using the Gorlin equation and CoC was calculated (EOA/GOA) in normal and low flow states by echo (SVI > or < 35 ml/m²). LVOT area derived from CTA was substituted into the echo equation for Hybrid EOA. Results: 21 patients were included in the analysis, 11 patients with normal flow and 10 patients with low flow (Table (1)). Compared to normal flow (SVI > 35 ml/m²), patients with low flow on echo (< 35 ml/m²), had similar cardiac output, similar mean gradients on catheter and echo, smaller EOA, larger discordance with catheter EOA, and smaller CoC. Conclusions: In this study, patients with echocardiographic evidence of low flow (SVI < 35 ml/m²) did not have low cardiac index on catheterization. Moreover, patients with normal flow have CoC of 1 by both Doppler and catheter suggesting that the EOA by either Doppler or Catheter are comparable and are both a good reflection of the true anatomical area of the aortic valve. However, with low flow on

Echo, the CoC is 0.8 by Catheter and 0.6 on Doppler, suggestive that echo underestimated the true GOA and overestimated the AS severity. In this setting, hybrid EOA derived from CTA and Doppler may help rectify some of the Doppler data. (Figure Presented).

Abbas AE, Franey LM, Lester S, Raff G, Gallagher MJ, Hanzel G, Safian RD and Pibarot P (2014). "The role of jet eccentricity in generating disproportionately elevated transaortic pressure gradients in patients with aortic stenosis." Echocardiography: 1-11. ePub Ahead of Print.

[Full-Text](#)

Department of Internal Medicine

In patients with aortic stenosis (AS) and eccentric transaortic flow, greater pressure loss occurs as the jet collides with the aortic wall together with delayed and diminished pressure recovery. This leads to the elevated transaortic valve pressure gradients noted on both Doppler and cardiac catheterization. Such situations may present a diagnostic dilemma where traditional measures of stenosis severity indicate severe AS, while imaging modalities of the aortic valve geometric aortic valve area (GOA) suggest less than severe stenosis. In this study, we present a series of cases exemplifying this clinical dilemma and demonstrate how color M-mode, 2D and 3D transthoracic (TTE) and transesophageal (TEE) echocardiography, cardiac computed tomography angiography (CTA), and magnetic resonance imaging (MRI), may be used to resolve such discrepancies. (copyright) 2014, Wiley Periodicals, Inc.

Abramowitz PW, Breland BD, Clegg CA, Feinberg DB, Fortier CR, Johnson TJ, Meyer GE, **Pawlicki KS**, Saenz R, Schultz KR, Shaverd Pharm DLS, Silvester JA, Slain D, Smith KM, Vanderpool HK, White SJ and Witmer DR (2014). "Report of the ASHP Task Force on Organizational Structure." American Journal of Health-System Pharmacy 71(12): 1049-1054.

[Full-Text](#)

Department of Biomedical Sciences (BHS)

Al-Faham Z, **Rydberg JN** and **Wong CYO** (2014). "Use of SPECT/CT with 99mTc-MDP bone scintigraphy to diagnose sacral insufficiency fracture." Journal of Nuclear Medicine Technology 42(3): 240-241.

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Department of Diagnostic Radiology and Molecular Imaging

Bone SPECT/CT offers additional information on pelvic insufficiency fractures, especially when there is incomplete formation of the H-sign on planar bone scanning.

Alsibai A and **Voytas J** (2014). "Use of electrical stimulation in treatment of dysphagia, a nursing home experience." Journal of the American Geriatrics Society 62: S37.

[Full-Text](#)

Department of Internal Medicine

Introduction/Objective Traditional Dysphagia therapy has focused on teaching compensatory postures and strategies, diet modification and use of exercise to improve strength and coordination. Neuromuscular electrical stimulation (NMES) is an adjunct modality that utilizes electrical currents to strengthen muscles in conjunction with exercise. While much research has been documented on the use of NMSE, the efficacy of this modality has not been well established. The goal of the study was to determine if the use of NMSE in the treatment of Dysphagia has resulted in improved swallow function as evidenced by advancement of diet in patients treated for dysphagia. Design/Methodology Data was collected on Beaumont Health system affiliated nursing facility residents from September 2010 through September 2011. Data Collected includes age, sex, admission diagnosis, number of treatment sessions, BIMS score (Brief interview of mental status), and the Pre and post FOIS score. The FOIS score :functional Oral Intake Scale is a seven point ordinal scale that assigns a number to the functional level of oral intake of food and liquid from 1 to 7; 1 being NPO and 7 being on regular diet without restrictions. Results Results and Statistics: A total of 51 patients ages 41 to 101 years old received Dysphagia therapy with NMES. The average number of treatments was 12.29. Of the 51 patients treated, 35 (68.62%) demonstrated a change in FOIS score resulting in an advancement of diet. Of those who responded to treatment: 16 (31.37%) improved their FOIS score by 1 point, 16 (31.37%) by two points, 2 (4%) by three points, 1 (2%) by 4 points. The most frequent diagnoses in the study group were CVA

(16 patients) with a positive response rate of 81.25%, pneumonia/aspiration pneumonia (12) with a response rate of 68.75%, and Parkinson's Disease (9) with a response rate of 81.25%. Patients who showed no response totaled 16 (31.37% of the total sample). Analysis of the data indicated a number of reasons for no change in diet ranging from severe cognitive impairment to severity of medical condition.

Conclusion/Discussion The study suggests that NMES in the treatment of dysphagia is a valuable treatment tool. Further research is needed to determine the true efficacy of this treatment modality by controlling for etiology, treatment techniques and having a control group.

Anderson K, Werner MD, Franasiak JM, Hong KH and Scott Jr RT (2014). "The impact of variations of TSH with the nulllow normal rangenull on euploid blastocyst implantation rate (IR)." Fertility and Sterility 102(3): e31-e32.

[Full-Text](#)

Department of Orthopedic Surgery

OBJECTIVE: Supplementation of thyroid hormone during the first trimester is recommended by the American Thyroid Association for TSH values >2.5mIU/L as they may be associated with adverse outcomes. This standard may also be applied to infertile patients attempting conception, but there has been no analysis on whether variation of TSH values within this nulllow normal rangenull have an impact on IR. The goal (Table Presented) of the present analysis is to determine if variation of TSH within this range has an impact on IR after the transfer of high quality euploid blastocysts. **DESIGN:** Retrospective. **MATERIALS AND METHODS:** Patients undergoing their first blastocyst transfer of euploid embryos were included for analysis between 2012-2014. TSH values were recorded at first pregnancy test, and patients with a prior medical history of thyroid disease were excluded. Cycles were arbitrarily grouped according to TSH values in increments of 0.5mIU/L. A sub-analysis was performed to determine if there was a difference in IR amongst euthyroid individuals on levothyroxine. Chi-Squared tests were used to compare categorical variables and a receiver operator characteristic curve (ROC) was generated to determine if there was a point of discrimination in relation to TSH values. **RESULTS:** 1286 transfer cycles were included for analysis with 371 fresh ETs and 915 frozen ETs. TSH categories were created as described in Table 1 with no difference in age between groups ($p=0.35$). No difference was noted in implantation ($p=0.72$) or miscarriage rates ($p=0.62$). A ROC of implantation rate approached 1, signifying that there was no difference in TSH values within the normal range. Similarly, no difference was noted in implantation for patients on levothyroxine (63.47% vs 65.4%, $p=0.69$). **CONCLUSION:** Variations of TSH values within the low normal range <2.5mIU/L had no impact on implantation or miscarriage rates. The present analysis is unique as it eliminates the variable of embryonic competence, by including the transfer of only high quality euploid blastocysts. While it still remains important to measure TSH values during early pregnancy for other reasons, variations within the nulllow normalnull range do not appear to impact implantation.

Anton-Martin P, Thompson MT, Sheeran PD, **Fischer AC**, Taylor D and Thomas JA (2014). "Extubation during pediatric extracorporeal membrane oxygenation: A single-center experience." Pediatric Critical Care Medicine. ePub Ahead of Print.

[Full-Text](#)

Department of Surgery

OBJECTIVES:: Describe aspects of one center's experience extubating infants and children during extracorporeal membrane oxygenation. **DESIGN::** Retrospective review of medical records. **SETTING::** Seventy-one-bed critical care service (PICU and cardiovascular ICU) in a large urban tertiary children's hospital. **PATIENTS::** Pediatric and neonatal patients supported on extracorporeal membrane oxygenation between 1996 and 2013 who were either not intubated or extubated greater than 24 hours during their extracorporeal membrane oxygenation course. **INTERVENTIONS::** None. **MEASUREMENTS AND MAIN RESULTS::** Sixteen of 511 patients on extracorporeal membrane oxygenation were extubated for at least 24 hours during their extracorporeal membrane oxygenation courses. Fourteen had respiratory failure and two had cardiac disease. Five patients died while on extracorporeal membrane oxygenation, but the cause of death was not related to complications associated with extubation. Extubated patients were supported a median of 19.7 days on extracorporeal membrane oxygenation, with a median extubation latency (time between cannulation and first extubation) of 6.2 days and a median extubation duration of 5.5 days. Mean

time extubated was 43% of the total time on extracorporeal membrane oxygenation. Two patients were reintubated briefly or had a laryngeal mask airway placed for decannulation (n = 1). The remaining patients were extubated within 5 days of decannulation, weeks afterward (n = 2), transferred to outside facilities (n = 2), or died during extracorporeal membrane oxygenation support (n = 5). We also observed no complications directly attributable to extubation and spontaneous re-aeration of consolidated lungs in acute respiratory distress syndrome in extubated patients on extracorporeal membrane oxygenation. CONCLUSION:: Extubation and discontinuation of mechanical ventilation appear feasible in patients requiring long-term extracorporeal membrane oxygenation. Emergency procedure planning may need to be modified in extubated patients on extracorporeal membrane oxygenation.

Armstrong K, **Dixon S**, May S and Patricolo GE (2014). "Anxiety reduction in patients undergoing cardiac catheterization following massage and guided imagery." Complementary Therapies in Clinical Practice. ePub Ahead of Print.

[Full-Text](#)

Department of Internal Medicine

Objective: This study aimed to evaluate the effectiveness of massage with or without guided imagery in reducing anxiety prior to cardiac catheterization. Method: A total of 55 inpatients and outpatients received massage, guided imagery, or massage with guided imagery prior to cardiac catheterization. Self-reported anxiety levels and blood pressure (BP) and heart rate (HR) were evaluated in participants and a matched comparison group. Results: Massage with and without guided imagery resulted in significant reductions in self-reported anxiety ($p < 0.0001$). Patients receiving intervention had lower diastolic BP and HR vs. the comparison group ($p < 0.0001$ and $p < 0.05$). Conclusions: Massage with or without guided imagery immediately reduced self-reported anxiety. This pilot study has certain limitations: a non-randomized, convenience sample and a matched control group that was created retrospectively. However, the study indicates a benefit to providing massage or massage with guided imagery prior to anxiety-inducing medical procedures such as cardiac catheterization. © 2014 Elsevier Ltd. All rights reserved.

Atallah PC, Kassir A and Powers S (2014). "IgG4-related disease with effusive-constrictive pericarditis, tamponade, and hepatopathy: A novel triad." International Journal of Cardiology 176(2): 516-518.

[Full-Text](#)

Department of Internal Medicine

Auer J, Sinzinger H, **Franklin B** and Berent R (2014). "Muscle- and skeletal-related side-effects of statins: Tip of the iceberg?" Eur J Prev Cardiol. ePub Ahead of Print.

[Full-Text](#)

Department of Internal Medicine

The clinical spectrum of muscle- and skeletal-related side-effects of statins includes varied myalgias and weakness, an asymptomatic increase in the concentration of creatine kinase and other biochemical parameters, myositis and rhabdomyolysis. Currently, there is no consensus on the definition of 'statin myopathy'. Evidence suggests that deleterious effects may also be associated with the volume or dosage of structured exercise and/or the intensity of physical activity. Moreover, non-muscle adverse effects on the joints and tendons are often overlooked and underemphasized. The incidence of myopathy associated with statin treatment typically ranges between 1.5% and 10%. Few data are available regarding the prevalence of muscle-related symptoms associated with different statins and the distribution of affected muscles. Furthermore, discrepancies between clinical trials and daily practice may emanate, in part, because of inconsistent definitions or exclusion criteria. The pathophysiology of statin-related myopathy is incompletely understood. A dose-dependent and proapoptotic effect, direct effects on mitochondria, drug interactions and genetic factors, or combinations thereof, may be involved. Recently, a rare immune-mediated myopathy triggered by statin use has been described. With the increasing number of patients treated with statins and with more patients being prescribed high doses of potent statins to achieve low-density lipoprotein targets, muscle-related side-effects will become more prevalent. Currently, the only effective treatment is the discontinuation of statin use. Further research is needed to develop alternative LDL-lowering drugs when

statins are not well tolerated and to establish additional effective strategies to manage lipids and lipoproteins.

Bannazadeh M, Forsyth A, Wilson B, Jenkins C, **Sakwa M, Altshuler J, Bis K and Brown OW** (2014). "Flap thickness in type B aortic dissection predicts aneurysmal expansion." *Journal of Vascular Surgery* 59(6): 375-385.

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Department of Surgery

Department of Diagnostic Radiology and Molecular Imaging

Objectives: We sought to demonstrate the prognostic implication of flap thickness (FT) in type B aortic dissection (TBAD). Methods: A retrospective review was undertaken of all patients with TBAD from June 2006 to June 2012. Demographics, hospital course, imaging, and follow-up visits were analyzed. FT on computed tomography angiography (CTA) was measured using full width at half maximum technique. Survival rates and predictors of outcome were determined using the Kaplan-Meier method with Cox proportional hazards. Results: Of 134 patients with TBAD, 101 (75%) had a classical dissection and 33 (24%) had atypical dissection (no dissection flap). FT analysis was available in 63 patients (38 men), with a mean age of 64 (plus or minus) 15 years. Median follow-up was 33 (0-135) months. Sixteen patients underwent surgical interventions, and 47 were managed non-operatively. Patients with FT >2.5 mm had higher rates of aneurysmal growth (2.7 vs 0.3 mm/y; P = .01). In addition, patients with FT >2.5 mm had worse survival (median survival, 61 vs 100 months; P = .03). However, multivariate analysis showed that only age (hazard ratio, 1.13; 95% confidence interval, 1.06-1.2; P < .000) and growth rate >2 mm were independent predictors of survival (hazard ratio, 0.1; 95% confidence interval, 0.02-0.5; P < .004; Fig). Conclusions: Flap thickness in TABD predicts aneurysmal expansion. (Figure presented).

Barnes G, Kaatz S, Gu X, Heung M, Haymart B, Kline-Rogers E, **Almany S**, Kozlowski J, Beasley D, Krol G, Ahsan S and Froehlich J (2014). "Development of renal dysfunction in atrial fibrillation patients: the Michigan Anticoagulation Quality Improvement Initiative (MAQI2) experience." *Journal of Thrombosis and Haemostasis* 12: 8.

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Department of Internal Medicine

Baschnagel AM, Stone BM, Thibodeau BJ, Fortier LE, Ahmed S, Geddes TJ, Ketelsen BE, Pruetz BL, **Jury RP and Wilson GD** (2014). "The effects of neoadjuvant chemoradiation on gene expression patterns of pancreatic ductal adenocarcinoma." *International Journal of Radiation Oncology Biology Physics* 90(1): S360-S361.

[Full-Text](#)

Department of Surgery

Department of Radiation Oncology

Purpose/Objective(s): To compare the gene expression patterns of pancreatic ductal adenocarcinoma (PDAC) treated with neoadjuvant chemoradiation therapy to non-treated PDAC. Materials/Methods: Six patient samples of PDAC that had undergone neoadjuvant chemoradiation, 10 patient samples of PDAC that had not undergone chemoradiation and 10 normal pancreatic tissue samples were identified from our institution's biobank. Neoadjuvant chemoradiation consisted of gemcitabine, erlotinib and radiation therapy in 5 patients and gemcitabine and radiation therapy in one patient. Radiation was given as either 30 Gy or 36 Gy in 15 fractions. All patients went on to have a pancreatectomy at which time fresh frozen tissue was collected. RNA was then isolated and gene expression analysis was performed using gene microarrays. Gene expression profiles were then compared among PDAC treated with neoadjuvant therapy, PDAC not treated, and normal pancreatic tissue. Differentially expressed genes were identified by ANOVA (p(less-than or equal to) 0.01) and 2.0-fold cutoff. Gene expression of two PDAC cell lines, Panc1 and MIAPaCa2, were also examined by PCR before and after radiation. Results: Overall the treated and non-treated PDAC were more similar to each other than to the normal pancreas tissue. There were 171 genes altered between the non-treated PDAC and the normal pancreas tissue and 397 genes altered between the treated PDAC compared to normal pancreas. There were 78 genes differentially expressed between the treated PDAC and the non-treated PDAC. This includes 58 genes upregulated in the treated samples and 20 genes downregulated. Of these 78 genes, 29 genes were also found to be differentially expressed between the

treated PDAC and the normal pancreas tissue. DPCR1 (19.7 fold) and CLDN18 (12.6 fold) were highly expressed in the treated PDAC compared to the non-treated PDAC and highly expressed when compared to normal pancreatic tissue. Other genes, including chromogranin A (CHGA), chromogranin B (CHGB), secretogranin II (SCG2), secretogranin III (SCG3), secretogranin V (SCG5) were up regulated in the treated PDAC compared to the untreated PDAC. CHGB and SCG2 were also highly upregulated in two PDAC cell lines after treatment with 2 Gy x 10. Highly regulated expression target subnetworks of interest included neuronal differentiation 1 (NEUROD1), hypoxia inducible factor 1 alpha (HIF1A), transforming growth factor alpha (TGFA) and fibroblast growth factor receptor 1 (FGFR1). Conclusions: This study demonstrates that neoadjuvant therapy alters the gene expression of pancreatic adenocarcinoma. Future studies are underway examining these genes and their signaling pathways as markers of chemoradiation resistance.

Baschnagel AM, Yadav S, Marina O, Parzuchowski A, Lanni TB, Warner JN, Parzuchowski JS, **Ignatius RT, Akervall J, Chen PY and Krauss DJ** (2014). "Toxicities and costs of placing prophylactic and reactive percutaneous gastrostomy tubes in patients with locally advanced head and neck cancers treated with chemoradiotherapy." Head and Neck 36(8): 1155-1161.

[Full-Text](#)

Department of Internal Medicine

Department of Biomedical Sciences (BHS)

Department of Radiation Oncology

Background We compared dependence rates, complications, toxicities, and costs associated with prophylactic versus reactive percutaneous endoscopic gastrostomy (PEG) tube placement. Methods One hundred ninety-three patients with locally advanced head and neck squamous cell carcinoma treated with concurrent chemoradiotherapy were retrospectively reviewed. Results The 1-year and 2-year actuarial PEG tube dependence rate of the entire cohort was 24% and 13%, respectively. There was no difference in the PEG tube dependence rates between those placed prophylactically versus reactively. Patients who received a PEG tube reactively had a significantly higher stricture rate ($p = .03$) and aspiration rate ($p < .001$) compared to the prophylactic group. There were significantly fewer hospitalizations in the prophylactic group compared to the reactive group ($p = .003$). When accounting for both PEG placement and hospitalizations, the prophylactic approach was found to be more cost effective. Conclusion PEG tubes placed prophylactically were associated with lower rates of strictures, aspirations, hospitalizations, and costs compared to those placed reactively. © 2013 Wiley Periodicals, Inc. Head Neck 36: 1155-1161, 2014 Copyright © 2013 Wiley Periodicals, Inc.

Bastani A, Vahedi M, Nouhan P, Barton M, Rosh A and Pople B (2014). "I'd rather take plumbum metallicum 30c: Emergency medicine residents' knowledge and experience with homeopathic remedies." Annals of Emergency Medicine 64(4): S120.

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Department of Emergency Medicine

Bastani A, Young E, Shaqiri B, Walch R, Manthena P, Weimer S and Kayyali H (2014). "Screening electroencephalograms are feasible in the emergency department." Journal of Telemedicine and Telecare 20(5): 259-262.

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Department of Emergency Medicine

Department of Neurology

We investigated the feasibility and quality of a wireless, four-channel screening electroencephalogram (EEG) device on patients presenting to the emergency department (ED) with a possible seizure disorder. A convenience sample was used of ED patients presenting with a preliminary diagnosis of syncope, potential partial-complex or generalized seizure disorder, head injury with prolonged symptoms or acute undiagnosed altered mental status. Study patients had a screening EEG in the ED, but the emergency physician and patient were blinded to the results of the EEG so that neither patient care nor disposition were affected by inclusion in the study. A total of 227 patients were enrolled, with a mean age of 56 years. EEG quality was

acceptable, i.e. a screening interpretation was able to be provided, in 208 of 227 cases (92%). The EEG interpretation was normal in 65%, identified generalized or focal slowing in 24% and identified sub-clinical epileptiform activity in 12% of patients. Screening EEGs performed in the ED are feasible, can be acquired with acceptable quality, and may identify sub-clinical seizure activity in a significant number of patients. © The Author(s) 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav.

Bauer ME, **Bauer ST**, Rajala B, MacEachern MP, Polley LS, Childers D and Aronoff DM (2014). "Maternal physiologic parameters in relationship to systemic inflammatory response syndrome criteria: A systematic review and meta-analysis." *Obstetrics and Gynecology* 124(3): 535-541.

[Full-Text](#)

Department of Obstetrics and Gynecology

OBJECTIVE: To establish the normal maternal range in healthy pregnant women for each component of the systemic inflammatory response syndrome (SIRS) criteria and compare these ranges with existing SIRS criteria. **DATA SOURCES:** PubMed, Embase, and ClinicalTrials.gov databases were searched to identify studies of healthy parturients from the first trimester through 12 weeks postpartum that reported maternal temperature, respiratory rate, PaCO₂, heart rate, white blood cell count data, or a combination of these. **METHODS OF STUDY SELECTION:** Data were extracted from studies providing maternal values for components of SIRS criteria. The mean, standard deviation, and two standard deviations from the mean for all criteria parameters published in the literature were reported. **TABULATION, INTEGRATION, AND RESULTS:** Eighty-seven studies met inclusion criteria and included 8,834 patients and 15,237 data points: temperature (10 studies and 2,367 patients), respiratory rate (nine studies and 312 patients), PaCO₂ (12 studies and 441 patients), heart rate (39 studies and 1,374 patients), and white blood cell count (23 studies and 4,553 patients). Overlap with SIRS criteria occurred in healthy pregnant women during the second trimester, third trimester, and labor for each of the SIRS criteria except temperature. Every mean value for PaCO₂ during pregnancy (and up to 48 hours postpartum) was below 32 mm Hg. Two standard deviations above the mean for temperature, respiratory rate, and heart rate were 38.1 degrees C, 25 breaths per minute, and 107 beats per minute, respectively. **CONCLUSION:** Current SIRS criteria often overlap with normal physiologic parameters during pregnancy and the immediate postpartum period; thus, alternative criteria must be developed to diagnose maternal sepsis.

Bellavia M, Rappa F, Bello MLO, Brecchia G, Tomasello G, Leone A, Spatola G, Uzzo ML, Bonaventura G, David S, Damiani P, **Hajj-Hussein I**, Zeenny MN, Jurjus A, Schembri-Wismayer P, Cocchi M, Zummo G, Farina F, Gerbino A, Cappello F and Traina G (2014). "Lactobacillus casei and Bifidobacterium lactis supplementation reduces tissue damage of intestinal mucosa and liver after 2,4,6-trinitrobenzenesulfonic acid treatment in mice." *Journal of Biological Regulators and Homeostatic Agents* 28(2): 251-261.

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Department of Biomedical Sciences (OU)

Probiotics (PB) are living microorganisms that act as a commensal population in normal intestines and confer numerous beneficial effects on the host. The introduction of probiotics in the treatment of inflammatory bowel disease (IBD) prolongs remission. The aim of this study was to investigate the intestinal and hepatic effects of PB supplementation in an experimental IBD model in mice induced by 2,4,6-trinitrobenzene sulfonic acid (TNBS). In the first step of the experimental procedure, CD-1 male mice, 5 to 6 weeks old, were randomly divided into 3 groups and inoculated intrarectally with, respectively, saline, alcohol, or TNBS to assess the experimental IBD model. In the second step, mice treated, or not, with TNBS inoculation, were treated with PB (*Lactobacillus Casei*, *Bifidobacterium Lactis*) for 1,2 or 3 weeks, on a daily basis. Large bowel (colon and rectum) and liver were processed for histological alterations, according to a scoring system. Large bowel was also assessed for apoptosis by TUNEL assay. TNBS induced, as expected, severe damage and inflammation in the large bowel, including nuclear alterations and apoptosis, and, to a lesser extent, to the liver. Administration of PB determined significant reduction of both histological alterations and apoptosis. PB administration in advance protects from inflammation. In conclusion, supplementation with *Lactobacillus casei*, *Bifidobacterium lactis* PB is able to ameliorate the colitis by reversing the histological changes caused by TNBS in mice. Experimentation in human subjects is needed to prove their efficacy in reducing

histological alterations that may be present in subjects with IBD. Copyright © by BIOLIFE, s.a.s.

Bernbeck M, **VanHulle R**, Hall M and **Emerson S** (2014). "Pediatric chest radiography dose monitoring by s values: An efficient way to indirectly monitor exposure indices at the PACS station." *Pediatric Radiology* 44: S210-S211.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Purpose or Case Report: The hazards of ionizing radiation, and the increased susceptibility of pediatric populations to them are well established. Although radiography accounts for the bulk of the imaging performed on pediatric patients, they are not as aggressively monitored as fluoroscopy or CT. Since DR radiography, there has been a tendency towards dose creep. The S value is reported by Konica X-ray machines, recorded on PACS, and is negatively correlated with radiation dose, and is a measure we proposed to use to control radiation dosing in our institution. **Methods & Materials:** First, x-ray phantoms of different thicknesses were constructed to establish if S value correlated with patient dosing, Fig. 1. Then, all two view chest x-rays and NICU chest x-rays obtained at our institution obtained in 1 month were analyzed for age, location, patient AP thickness and S value of the frontal x-ray. Subsequently, the technologists were trained to use and record new AP thickness based protocols, and a second month of data was collected. The 2 months were compared. After final discussions with x-ray technologists regarding how to improve compliance with the new protocols, a final month of data was collected and compared to the first month. **Results:** The first phase showed a correlation between S value and x ray exposure given a certain patient thickness. The second phase showed that although most of the S values were within the manufacture suggested range (100-600), a substantially smaller number of data points were found in our target range (300-600), Table 1. Between the first 2 months, there was an increased mean S value as well as decrease in deviation below our minimum S value in the majority of the subcategories, but only statistically significant in a few subcategories. With improved technologist compliance during the third month of the study, there was a statistically significant increase in average S value in the majority of the subcategories as well as the overall data set, as well as decreased deviation in data points below our target S value in all subcategories. **Conclusions:** S value, or its counterparts with other x-ray vendors, has proven to be a useful tool in x-ray dose monitoring. Its association with xray dose given a patient thickness makes it a useful parameter to guide xray dosing technique. A good working relationship with a program's technologists, with emphasis of the mutual goal of improving patient care, and other active reminders helped reduce radiation exposure at our institution. (Figure Presented).

Bezner SK, Bernstein IH, Oldham KT, Goldin AB, **Fischer AC** and Chen LE (2014). "Pediatric surgeons' attitudes toward regionalization of neonatal surgical care." *Journal of Pediatric Surgery* 49(10): 1475-1479.

[Full-Text](#)

Department of Surgery

BACKGROUND/PURPOSE: Research has suggested that high-risk pediatric surgical patients have better outcomes when treated in resource-rich children's environments. Surgical neonates are a particularly high-risk population and some suggest that regionalization might be a strategy to improve clinical outcomes in neonatal surgical patients. We conducted a national survey of pediatric surgeons in the United States to explore their attitudes toward regionalization of neonatal surgical care. **METHODS:** Members of the American Pediatric Surgical Association were asked to participate in an anonymous online survey to assess both attitudes toward regionalization, as well as perceptions of the importance of various resources in providing optimal care for surgical neonates. **RESULTS:** Overall, 56.2% of participants favored regionalization. Surgeons whose practice was part of a training program tended to favor regionalization more, as did those from larger group practices and those who practiced at free-standing children's hospital. In addition, surgeons from larger groups and those involved with training programs more strongly favored the premise that a higher level of resource commitment should be available to treat surgical neonates. **CONCLUSIONS:** The impact of any national strategy to improve neonatal surgical outcomes will be large and multi-faceted. While the majority of pediatric surgeons favor regionalization, our findings demonstrate variation in this view and highlight the necessity for surgeon involvement and education that will be critical in this effort.

Bickel RJ, Collins CD, Lucarotti RL, Stevenson JG, **Pawlicki K**, Baumann TJ and Pratt DM (2014). "Moving the pharmacy practice model initiative forward within a state affiliate." American Journal of Health-System Pharmacy 71(19): 1679-1685.

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Department of Biomedical Sciences (BHS)

Purpose. Efforts to advance the ASHP Pharmacy Practice Model Initiative (PPMI) in the Michigan Society of Health-System Pharmacists (MSHP) are described. **Summary.** After the Pharmacy Practice Model Summit in November 2010, the board of directors of MSHP began to strategize ways to help health-system pharmacists in Michigan achieve the vision and concepts envisioned by the PPMI. The ultimate goal was to develop a process for acting on recommendations developed by the PPMI to advance the practice of health-system pharmacy in Michigan. A task force was formed and reviewed the 147 national recommendations from the ASHP Pharmacy Practice Model Summit and grouped them into related areas of focus. Six focus areas were identified: acute care, ambulatory care, education and training, organizational affairs and leadership, pharmacy technicians, and technology and information systems. A PPMI Michigan conference was arranged in which focus groups would assess these six areas. Each focus group was limited to six or seven participants, with a member of the task force serving as the facilitator for the group. Individual focus groups then formulated recommendations MSHP could develop into actionable strategies to address the key issues identified during the morning session. A total of 56 recommendations were submitted by the focus groups for consideration by all conference participants. Over 80% of the recommendations were deemed to be high impact/high feasibility. **Conclusion.** A process for acting on recommendations of the ASHP PPMI to advance the practice of health-system pharmacy within the state of Michigan was developed.

Billinger SA, Arena R, Bernhardt J, Eng JJ, **Franklin BA**, Johnson CM, MacKay-Lyons M, Macko RF, Mead GE, Roth EJ, Shaughnessy M, Tang A, Amer Heart Assoc Stroke C, Council Cardiovasc Stroke N, Council Lifestyle Cardiometab H, Council Epidemiology P and Council Clinical C (2014). "Physical activity and exercise recommendations for stroke survivors: A statement for healthcare professionals from the American Heart Association/American Stroke Association." Stroke 45(8): 2532-2553.

[Full-Text](#)

Department of Internal Medicine

Purpose-This scientific statement provides an overview of the evidence on physical activity and exercise recommendations for stroke survivors. Evidence suggests that stroke survivors experience physical deconditioning and lead sedentary lifestyles. Therefore, this updated scientific statement serves as an overall guide for practitioners to gain a better understanding of the benefits of physical activity and recommendations for prescribing exercise for stroke survivors across all stages of recovery. **Methods-**Members of the writing group were appointed by the American Heart Association Stroke Council's Scientific Statement Oversight Committee and the American Heart Association's Manuscript Oversight Committee. The writers used systematic literature reviews, references to published clinical and epidemiology studies, morbidity and mortality reports, clinical and public health guidelines, authoritative statements, personal files, and expert opinion to summarize existing evidence and indicate gaps in current knowledge. **Results-**Physical inactivity after stroke is highly prevalent. The assessed body of evidence clearly supports the use of exercise training (both aerobic and strength training) for stroke survivors. Exercise training improves functional capacity, the ability to perform activities of daily living, and quality of life, and it reduces the risk for subsequent cardiovascular events. Physical activity goals and exercise prescription for stroke survivors need to be customized for the individual to maximize long-term adherence. **Conclusions-**The recommendation from this writing group is that physical activity and exercise prescription should be incorporated into the management of stroke survivors. The promotion of physical activity in stroke survivors should emphasize low-to moderate-intensity aerobic activity, muscle-strengthening activity, reduction of sedentary behavior, and risk management for secondary prevention of stroke.

Blas KG, Stone B, Marina O, Mangona V, Ye H, Avkshtol V, **Brabbins D, Chen P, Gustafson G** and **Krauss DJ** (2014). "Long-term clinical outcomes for patients treated with adjuvant versus early versus delayed salvage radiation therapy in the postprostatectomy setting." International Journal of Radiation Oncology Biology Physics 90(1): S454.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): To assess utility of salvage radiation therapy (SRT) in the post-prostatectomy setting and its impact on long-term clinical outcomes in the context of adjuvant versus early versus delayed postoperative radiation therapy (RT). Materials/Methods: From 1987-2013, 207 patients were treated with RT after prostatectomy via four-field box, three-dimensional conformal RT, or intensity-modulated RT. Patients were subdivided into cohorts based on pre-RT PSA. The adjuvant (aRT) treatment cohort consisted of patients with undetectable prostate-specific antigen (PSA), while patients with detectable PSAs, but less than 0.5 ng/mL, were categorized as early (eRT), and patients with PSA values equal to or greater to 0.5 ng/mL were defined as delayed (dRT). A subset of eRT patients were treated with salvage RT with a PSA value < 0.3 ng/mL was also evaluated in an attempt to define any benefit associated with very early salvage treatment. All clinical and pathologic records were reviewed to measure response between groups. Biochemical failure was defined as nadir plus 2 ng/mL or initiation of hormonal therapy. Results: The median follow-up time after SRT was 38 months, 33 months, and 86 months for the aRT, eRT, and dRT cohorts respectively. Thirty-six patients (17%) received aRT, 51 (25%) eRT, and 120 (58%) dRT. Median dose for aRT, eRT, and dRT patients was 67.5 Gy, 66.6 Gy, and 64.8 Gy, respectively (p = 0.01). On multivariate analysis pre-treatment PSA was predictive (HR 1.08, p < .001) whereas dose was not (p = .47). Five-year biochemical failure rates were 10% vs. 12.5% vs. 34% (p = 0.03) with disease-free survival rates of 95.2% vs. 81.1% vs. 76.1% (p = 0.03) favoring aRT vs. eRT vs. dRT, respectively. Within the aRT, eRT, and dRT cohorts there were no significant differences detected in local recurrence (0% vs. 8.2% vs. 14.7%, p = 0.16), distant metastasis (0% vs. 8.2% vs. 10.2%, p = 0.48), cause-specific survival (100% vs. 92.3% vs. 96.6%, p = 0.95), or overall survival (95.2% vs. 92.3% vs. 94.2%, p = 0.14), respectively. Thirty-four eRT patients (15%) with PSA < 0.3 ng/mL were compared to the aRT patients. No significant differences in clinical or biochemical outcomes were appreciated in this comparison. Conclusions: In this set of post-prostatectomy patients, adjuvant RT was associated with superior long-term biochemical control when compared to patients treated in the delayed salvage setting. There was no difference in biochemical control between patients undergoing very early salvage or adjuvant post-prostatectomy RT suggesting a need for further investigation into which group of patients is most likely to benefit from adjuvant postprostatectomy RT.

Blum E and **Burks FN** (2014). "Noninvasive bladder cancer: Diagnosis and management." Journal of Clinical Outcomes Management 21(9): 409-418.

[Request Form](#)

Department of Urology

Bortsov AV, Platts-Mills TF, Peak DA, Jones JS, **Swor RA**, Domeier RM, Lee DC, Rathlev NK, Hendry PL, Fillingim RB and McLean SA (2014). "Effect of pain location and duration on life function in the year after motor vehicle collision." Pain 155(9): 1836-1845.

[Request Form](#)

Department of Emergency Medicine

Persistent musculoskeletal pain is common after motor vehicle collision (MVC) and often results in substantial disability. The objective of this study was to identify distributions of post-MVC pain that most interfere with specific life functions and that have the greatest interference with aggregate life function. Study data were obtained from a prospective longitudinal multicenter emergency department-based cohort of 948 European Americans experiencing MVC. Overall pain (0-10 numeric rating scale [NRS]), pain in each of 20 body regions (0-10 NRS), and pain interference (Brief Pain Inventory, 0-10 NRS) were assessed 6 weeks, 6 months, and 1 year after MVC. After adjustment for overall pain intensity, an axial distribution of pain caused the greatest interference with most specific life functions (R(2)=0.15-0.28, association P values of <.001) and with overall function. Axial pain explained more than twice as much variance in pain interference as other pain distributions. However, not all patients with axial pain had neck pain. Moderate or severe low back pain

was as common as neck pain at week 6 (prevalence 37% for each) and overlapped with neck pain in only 23% of patients. Further, pain across all body regions accounted for nearly twice as much of the variance in pain interference as neck pain alone (60% vs 34%). These findings suggest that studies of post-MVC pain should not focus on neck pain alone.

Bowdon MM, **Franklin B, Boura J, Marcovitz P** and Billecke S (2014). "Effects of a 6-month exercise intervention in women at risk for cardiovascular disease." Medicine and Science in Sports and Exercise 46(5): 373-374.

[Full-Text](#)

Department of Internal Medicine

Department of Biomedical Sciences (BHS)

Cappell MS (2014). "Adverse patient consequences from inadequately trained endoscopists obtaining privileges for advanced endoscopic procedures: case reports suggesting a need for stricter enforcement of fellowship procedure certification & hospital privileging guidelines." Minerva Gastroenterologica e Dietologica 60(3): 202-203.

[Request Form](#)

Department of Internal Medicine

Cappell MS (2014). "Complaints against gastroenterology fellows." Gastrointestinal Endoscopy 80(1): 153-155.

[Request Form](#)

Department of Internal Medicine

Cappell MS, Mogrovejo E, Manickam P and **Batke M** (2014). "Endoclips to facilitate cannulation and sphincterotomy during ERCP in a patient with an ampulla within a large duodenal diverticulum: Case report and literature review." Digestive Diseases and Sciences. ePub Ahead of Print.

[Full-Text](#)

Department of Internal Medicine

Chancellor M, Yehoshua A, Corbell C, Globe D, Cheng I, Pulicharam R, Joshi M, Campbell K and Vasavada S (2014). "Health resource utilization and burden in overactive bladder patients treated with anticholinergics." International Urogynecology Journal and Pelvic Floor Dysfunction 25(1): S100-S101.

[Request Form](#)

Department of Urology

Introduction: Overactive bladder (OAB) is a common medical condition with significant economic and humanistic burden. Inadequately managed OAB may exacerbate or result in comorbidities such as depression, urinary tract infections (UTIs), and falls; all of which increase the burden to the healthcare system. Anticholinergics (ACHs) are the most commonly prescribed first-line pharmacotherapy (following behavioral therapy) in the treatment of OAB. While there has been a fair amount of research on the economic burden of OAB, the impact of ACHs on health resource utilization (HRU) and costs has not been well studied. Objective: The aim of this study was to compare comorbidities and HRU in a cohort of OAB patients with UI treated with ACH compared to matched controls. Methods: Retrospective claims data for patients seen through a California-based managed care organization were linked to a cross-sectional patient survey and used to compare HRU in a cohort of OAB cases and controls. Cases were patients with an ICD-9 code for OAB; (greater-than or equal to) 1 UI episodes/day based on self-report and who initiated anticholinergic therapy between January 2008 and May 2012. Controls were patients without an ICD-9 code for OAB who never received anticholinergic therapy and were matched to cases in a 3:1 ratio based on gender, age and observation time. The index date for cases was the date of anticholinergic initiation; for controls, the index date was the date of the medical claim that resulted in the same observation time as a matched case. Medical and pharmacy claims data were used to analyze patient comorbidities as well as track HRU (including outpatient visits, emergency room (ER) visits, hospitalizations and medication use) from the index date until the end of follow-up (May 2013). Results: A total of 655 patients with OAB and 1,965 controls were enrolled into the study. Mean age of the study population was 73.2 years; 79.2 % were female. The average follow up time was 3.1 years. OAB patients had an average of 3.56 UI episodes per day. Descriptive statistics

showed that compared to controls, this cohort of OAB cases who had initiated ACH therapy had a higher prevalence of falls and fractures (55.1 % vs. 47.3 %; $p < 0.001$), UTIs (49.6 % vs. 27.4 %; $p < 0.0001$), diabetes (40.2 % vs. 34.6 %; $p = 0.01$), and depression and/or anxiety (35.4 % vs. 23.1 %; $p < 0.0001$), during the follow-up period (Table 1). OAB cases also experienced higher HRU than controls (Table 2). The mean outpatient visits per year were 17.0 and 11.2 ($p < 0.0001$); mean ER visits per year were 2.0 and 1.4 ($p = 0.0008$), and mean inpatient admissions per year were 0.30 and 0.24 ($p = 0.0011$) in cases and controls respectively. Furthermore, OAB cases received more prescription fills per year than controls (7.8 vs. 4.6; $p < 0.0001$). There were no statistically significant differences observed in the mean skilled nursing facility admissions per year. Conclusion: Our analysis indicates that this cohort of OAB patients with UI, exposed to ACHs experienced more cases of depression, falls and fractures and UTIs than patients of similar age and gender without OAB. In addition, OAB cases had higher ER visits, outpatient visits and overall medication use than controls. A higher prevalence of comorbidities and resource utilization in OAB cases than controls appeared to occur despite the fact that OAB patients had all been initiated on ACH therapy. A higher burden in OAB patients despite ACH treatment suggests an unmet need for alternative therapies that have a greater impact on reducing total HRU. (Table Presented).

Chancellor MB (2014). "The overactive bladder progression to underactive bladder hypothesis." International Urology and Nephrology 46 Suppl 1: 23-27.

[Full-Text](#)

Department of Urology

The overactive bladder (OAB) is a well-known and common urologic condition. However, the apparent opposite syndrome to the OAB, the underactive bladder (UAB), remains an enigma. Underactive bladder syndrome is complex condition that shares symptoms with other prevalent urologic diagnoses. UAB is not a pure condition—it is not the result of any single factor, but rather, it is multifactorial. As a result, UAB may overlap with OAB, bladder outlet obstruction, or even occur with no symptoms or associated diseases. To make it yet more challenging, in the elderly, detrusor hyperreflexia/impaired contractility (DHIC) is a condition that has the pathological elements of both OAB and UAB and is also common. I hypothesize that UAB and OAB may not be an entirely separate disease entity. Instead, chronic untreated or treatment refractory OAB—due to neurological diseases such as diabetes, bladder outlet obstruction or aging sarcopenia and frailty—may progress to DHIC and, finally, UAB. The progression of OAB to UAB hypothesis suggests that early education, behavioral modification and medical treatment may alter and/or prevent progression to UAB.

Chancellor MB and **Diokno A** (2014). "CURE-UAB: shedding light on the underactive bladder syndrome." International Urology and Nephrology 46 Suppl 1: 1.

[Full-Text](#)

Department of Urology

Chancellor MB, **Levanovich P**, **Rajaganapathy BR** and **Vereecke AJ** (2014). "Optimum management of overactive bladder: Medication vs Botox® vs InterStim® vs Urgent® PC." Urology Practice 1(1): 7-12.

[Request Form](#)

Department of Urology

Introduction: Optimal management of the overactive bladder is changing quickly, and urology practices need to stay in the vanguard of offering safe and effective therapies when anticholinergics are not effective or not tolerated. Methods: We will review approved therapies for overactive bladder prescribed after behavioral therapy and anticholinergic medications have failed. Results: The treatment failure rate of anticholinergics is high and does not improve with the use of multiple drugs. Therefore, we propose a new treatment paradigm that will stop anticholinergic cycling. Conclusions: We believe that it is time to get patients off the anticholinergic cycle and move forward with effective alternative treatments to optimize overactive bladder therapy. © 2014 American Urological Association Education and Research, Inc.

Chehab M, Hlubocky J, Olariu E, **Bloom D** and **Nandalur K** (2014). "Comprehensive magnetic resonance enterography of Crohn's Disease in the pediatric population: Technique, interpretation, and management." Current Problems in Diagnostic Radiology. ePub Ahead of Print.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Magnetic resonance enterography (MRE) plays a critical role in the management of Crohn's disease in the pediatric population. The ability to provide dynamic assessment of disease burden, complications, and therapeutic response without ionizing radiation makes it an ideal tool for younger patients requiring frequent follow-up. With a growing array of available treatment options, a sound understanding of MRE is critical in directing management aimed at curbing the physical and emotional morbidity associated with the lifelong condition. The goal of this article is to provide a practical overview of MRE in the pediatric population. This includes a review of our technique, approach to interpretation, pictorial collection of findings, and discussion of the role MRE plays in management. © 2014 Mosby, Inc.

Chen N and Prada AE (2014). "Development of allele-specific multiplex PCR to determine the length of poly-T in intron 8 of CFTR." PeerJ 2: e468.

[Full-Text](#)

Department of Pathology

Cystic fibrosis transmembrane conductance regulator (CFTR) gene mutation analysis has been implemented for Cystic Fibrosis (CF) carrier screening, and molecular diagnosis of CF and congenital bilateral absence of the vas deferens (CBAVD). Although poly-T allele analysis in intron 8 of CFTR is required when a patient is positive for R117H, it is not recommended for routine carrier screening. Therefore, commercial kits for CFTR mutation analysis were designed either to mask the poly-T allele results, unless a patient is R117H positive, or to have the poly-T analysis as a standalone reflex test using the same commercial platform. There are other standalone assays developed to detect poly-T alleles, such as heteroduplex analysis, High Resolution Melting (HRM) curve analysis, allele-specific PCR (AS-PCR) and Sanger sequencing. In this report, we developed a simple and easy-to-implement multiplex AS-PCR assay using unlabeled standard length primers, which can be used as a reflex or standalone test for CFTR poly-T track analysis. Out of 115 human gDNA samples tested, results from our new AS-PCR matched to the previous known poly-T results or results from Sanger sequencing.

Chen N and Prada AE (2014). "Development of allele-specific multiplex PCR to determine the length of poly-T in intron 8 of CFTR." PeerJ 2(1): e468.

[Full-Text](#)

Department of Pathology

Cystic fibrosis transmembrane conductance regulator (CFTR) gene mutation analysis has been implemented for Cystic Fibrosis (CF) carrier screening, and molecular diagnosis of CF and congenital bilateral absence of the vas deferens (CBAVD). Although poly-T allele analysis in intron 8 of CFTR is required when a patient is positive for R117H, it is not recommended for routine carrier screening. Therefore, commercial kits for CFTR mutation analysis were designed either to mask the poly-T allele results, unless a patient is R117H positive, or to have the poly-T analysis as a standalone reflex test using the same commercial platform. There are other standalone assays developed to detect poly-T alleles, such as heteroduplex analysis, High Resolution Melting (HRM) curve analysis, allele-specific PCR (AS-PCR) and Sanger sequencing. In this report, we developed a simple and easy-to-implement multiplex AS-PCR assay using unlabeled standard length primers, which can be used as a reflex or standalone test for CFTR poly-T track analysis. Out of 115 human gDNA samples tested, results from our new AS-PCR matched to the previous known poly-T results or results from Sanger sequencing. (copyright) 2014 Chen and Prada.

Chen PY, Kamrava M, Kuske R, Anderson BM, Hayes JK, DeManes J, **Wang P**, Wang P, Veruttipong D and Snyder M (2014). "Outcomes of nullunsuitable patients by ASTRO guidelines treated with accelerated partial breast irradiation via interstitial multicatheter brachytherapy: A multi-institution collaborative study." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S135-S136.

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Department of Radiation Oncology

Department of Family Medicine

Purpose/Objective(s): To determine the clinical outcomes from 5 institutions of interstitial multi-catheter multi-planar brachytherapy in the treatment of select breast cancers in the ASTRO nullunsuitable unless on clinical trial category. Materials/Methods: Pooled data from five institutions with extensive experience delivering interstitial brachytherapy for accelerated partial breast irradiation (APBI) were collected for patients treated from 1992 to 2013. Each institution was asked to include all APBI patients, but most followed the common exclusion factors of tumors > 3 cm, > 3 positive nodes, extracapsular extension, or positive margins, with a small number of exceptions (included in this report). Of 938 patients who underwent APBI with interstitial brachytherapy, 849 had available follow-up information to assess for clinical outcomes. ASTRO Guidelines classified a total of 253 patients as nullunsuitable. All patients were treated with interstitial brachytherapy (I-125 LDR [50 Gy at 52 cGy/H x 96 hrs] or Iridium-192 HDR [32 or 34 Gy in 8 or 10 BID fractions]) with dose prescribed at 1.5 to 2 cm beyond the lumpectomy cavity. Results: Median age was 47. Median follow-up was 4.3 years. The most common factors for patients falling into the nullunsuitable group are age < 50 yrs (78%) or positive axillary nodes (26%). The other factors comprise only 2% of this group. Staging was Tis 26%, T1 63%, T2 11%, Nx 21%, N0 51%, Ni+ 1.6%, and N1 26%. With respect to disease control, 12 ipsilateral breast tumor recurrences (IBTR) were noted. The 5- and 10-year actuarial rates of local recurrence (LR) were 4.6% and 6.0%, regional recurrences [RR] 2.8% and 2.8%, distant metastases [DM] 1.8% and 4.4%, and contralateral breast failures [CBF] 2.6% and 6.5%. In the analyses of multiple clinical and pathological factors to determine the association with LR, RR, DM, and CBF, significance was only found for age less than 45 for higher local recurrence; specifically, for the unsuitable category patient less than 45 yrs of age, the 5 and 10-yr actuarial LR rates were 10.7% and 18.8%, respectively versus 3.2% actuarial at 5- and 10-years for those greater than 45 yrs (p = 0.03). No association with age was found for RR, DM and CBF. Conclusions: In this collaborative project of five institutions with expertise in delivering APBI with interstitial multi-catheter brachytherapy APBI, patients in the ASTRO nullunsuitable category had few ipsilateral breast tumor recurrences. In a detailed analysis of IBTR, the one significant factor associated with an increase in LR was age younger than 45. These results underscore the importance of a reevaluation of the Guidelines in light of emerging data.

Chen PY, Marina O, Liu Q, Limbacher A, Wallace M, Ye H, Wobb J, Jawad S, Pietron A, **Dekhne N**, **Grills I** and **Brabbins D** (2014). "Propensity score matched-pair analysis of interstitial multicatheter versus balloon-based accelerated partial breast irradiation, stratified by ASTRO guidelines." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S272.

[Full-Text](#)

Department of Radiation Oncology

Department of Surgery

Purpose/Objective(s): To determine if differing irradiated volumes affect the clinical outcomes and cosmesis with brachytherapy interstitial MultiCatheter-Accelerated Partial Breast Irradiation [MC-APBI] vs that of single-entry Balloon-APBI [BAL-APBI] stratified by the ASTRO Guidelines [ASTRO-G] from a single institution. Materials/Methods: From 1993-2008, 484 patients with early-stage breast CA were treated with APBI. Between 1993 and 2000, all eligible patients were treated with either I-125 low-dose-rate or Ir-192 high-dose-rate MCAPBI with dose prescribed at 2 to 3 cm beyond the lumpectomy. Between 2000 and 2008, the balloon applicator (BAL-APBI) was increasingly used. Dose prescription for balloon applicators was 1 cm from the balloon surface. Due to the differing dose prescriptions and thus irradiated volumes, we undertook a propensity-score matched-pair analysis to determine the outcomes of MC-APBI vs BAL-APBI stratified by ASTRO-G. Match criteria were age and ASTRO-G by propensity score; exact match of Tis/ T1/T2 stage and ER +/-; and minimal follow-up 3 yrs and tx info. Of the original 484 pts, 293 had information, yielding 90

matched pairs (ratio 1:1) totaling 180 patients for comparative analysis of clinical outcomes via Kaplan-Meier, stratified by ASTRO-G. Results: Median age for MC-APBI was 65 yrs (range 42-84) and BAL-APBI 63 (41-86) (p=0.82). Median follow-up was 9.0 yrs; MC-APBI 14.9 yrs and BAL-APBI 6.2 yrs (p < 0.001). The majority of tumors were T1 (93%) with median size 1.0 cm. ER + was found in 84% and 68% received endocrine Rx, with 69% MC-APBI and 66% BAL-APBI (p = 0.66). Chemotherapy was delivered in 15%, with 8% MC-APBI and 22% BAL-APBI (p=0.01). The irradiated volumes differed significantly, with median 154 cc (36-455) for MC-APBI vs 95 cc (61-168) for BAL-APBI (p<0.001). For disease control, MC-APBI had a 5 and 10 yr actuarial local recurrence rate of 1.2% & 3.8% vs BAL-APBI of 4.5% at both 5 & 10 yrs (p=0.45); true recurrence/marginal miss revealed 0% & 1.2% at 5 & 10 yrs for MC-APBI vs 1.1% at both for BAL-APBI (p = 0.74). No difference was noted for 10-yr actuarial rates of regional recurrence (0% for both, pZns)&distant metastases (2.2% & 4.7% for MC-APBI at 5 & 10 yrs, 2.2% for BAL-APBI, p = 0.69). The 10-yr actuarial cause specific survival (97% MC-APBI vs 96% BAL-APBI, p = 0.98), disease-free survival (92% vs 93%, p=0.75) and overall survival (81% vs 76%, p=0.68) were similar. When stratified by ASTRO-G, no difference in LR, DM, CSS, or DFS was noted between MC-APBI vs BAL-APBI. Cosmetic outcomes were good/ excellent in 95% of all patients. Conclusions: In comparing 2 differing APBI treatment techniques, with significantly different irradiated volumes, no difference in clinical outcomes or cosmesis were discernable, even when stratified by ASTRO-G. Further follow-up will be required for validation of long-term outcomes and cosmesis in such APBI patients.

Cho I, Chang HJ, B OH, Shin S, Sung JM, Lin FY, Achenbach S, Heo R, Berman DS, Budoff MJ, Callister TQ, Al-Mallah MH, Cademartiri F, Chinnaiyan K, Chow BJ, Dunning AM, DeLago A, Villines TC, Hadamitzky M, Hausleiter J, Leipsic J, Shaw LJ, Kaufmann PA, Cury RC, Feuchtner G, Kim YJ, Maffei E, **Raff G**, Pontone G, Andreini D and Min JK (2014). "Incremental prognostic utility of coronary CT angiography for asymptomatic patients based upon extent and severity of coronary artery calcium: results from the COronary CT Angiography EvaluationN For Clinical Outcomes InteRnational Multicenter (CONFIRM) Study." *European Heart Journal*. ePub Ahead of Print.

[Full-Text](#)

Department of Internal Medicine

AIM: Prior evidence observed no predictive utility of coronary CT angiography (CCTA) over the coronary artery calcium score (CACs) and the Framingham risk score (FRS), among asymptomatic individuals. Whether the prognostic value of CCTA differs for asymptomatic patients, when stratified by CACS severity, remains unknown. METHODS AND RESULTS: From a 12-centre, 6-country observational registry, 3217 asymptomatic individuals without known coronary artery disease (CAD) underwent CACS and CCTA. Individuals were categorized by CACS as: 0-10, 11-100, 101-400, 401-1000, >1000. For CCTA analysis, the number of obstructive vessels-as defined by the per-patient presence of a $\geq 50\%$ luminal stenosis-was used to grade the extent and severity of CAD. The incremental prognostic value of CCTA over and above FRS was measured by the likelihood ratio (LR) χ^2 , C-statistic, and continuous net reclassification improvement (NRI) for prediction, discrimination, and reclassification of all-cause mortality and non-fatal myocardial infarction. During a median follow-up of 24 months (25th-75th percentile, 17-30 months), there were 58 composite end-points. The incremental value of CCTA over FRS was demonstrated in individuals with CACS >100 (LR χ^2 , 25.34; increment in C-statistic, 0.24; NRI, 0.62, all P < 0.001), but not among those with CACS ≤ 100 (all P > 0.05). For subgroups with CACS >100, the utility of CCTA for predicting the study end-point was evident among individuals whose CACS ranged from 101 to 400; the observed predictive benefit attenuated with increasing CACS. CONCLUSION: Coronary CT angiography provides incremental prognostic utility for prediction of mortality and non-fatal myocardial infarction for asymptomatic individuals with moderately high CACS, but not for lower or higher CACS.

Copelan A, Chehab M, Cash C, **Korman H** and **Dixit P** (2014). "Endovascular management of ureteroarterial fistula: A rare potentially life threatening cause of hematuria." *Journal of Radiology Case Reports* 8(7): 37-45.

[Request Form](#)

Department of Urology

Department of Diagnostic Radiology and Molecular Imaging

Ureteroarterial fistula is a rare, potentially life-threatening cause of hematuria characterized by an abnormal

channel between a ureter and artery. The rarity of this condition, complexity of predisposing risk factors and intermittence of symptoms may delay or obscure its diagnosis. With a high index of suspicion and careful angiographic evaluation, embarking on this condition is not only possible but sets the stage for curative intervention. We report a case of a ureteroarterial fistula presenting with intermittent hematuria, successfully diagnosed at angiography and managed with endovascular stent graft placement.

de Jong MD, Ison MG, Monto AS, Metev H, **Clark C**, O'Neil B, Elder J, McCullough A, Collis P and Sheridan WP (2014). "Evaluation of intravenous peramivir for treatment of Influenza in hospitalized patients." [Clinical Infectious Diseases](#). ePub Ahead of Print.

[Full-Text](#)

Department of Emergency Medicine

BACKGROUND: Seasonal influenza causes >200 000 annual hospitalizations in the United States. Current antiviral treatment options are limited to oral or inhaled agents. There is an urgent unmet need for intravenous antiviral treatments. METHODS: Patients hospitalized with suspected influenza were randomized to 5-day treatment with intravenous peramivir (600 mg once daily) or placebo; all received the institution's standard of care (SOC) treatment. Time to clinical resolution and change in viral shedding in nasopharyngeal specimens were the primary and key secondary end points. RESULTS: Influenza infection was confirmed in 338 of 405 enrolled patients. At the time of a preplanned interim analysis, the primary efficacy analysis population comprised 121 patients who did not receive a concurrent neuraminidase inhibitor as part of the SOC. The median (95% confidence interval) time to clinical resolution was 42.5 (34.0-57.9) hours for peramivir versus 49.5 (40.0-61.9) hours for placebo (P = .97). A larger treatment effect was observed in patients with history of symptoms <48 hours or admitted to an intensive care unit. Greater reductions in viral shedding, based on median tissue culture infective dose, were observed in patients who received peramivir than in placebo recipients, although this difference was not statistically significant. The incidence and severity of adverse events and laboratory abnormalities were similar between the 2 treatment groups. The study was terminated for futility after a preplanned interim analysis. CONCLUSIONS: A significant clinical benefit was not demonstrated for peramivir plus SOC compared with placebo plus SOC. Peramivir was generally safe and well tolerated. These findings highlight the challenges in designing studies to evaluate influenza antiviral agents in a hospitalized setting. Clinical Trials Registration. NCT00958776.

Diaz KM, Eckstrand KL, **Doo F** and Grace Wojcik M (2014). "Impact of LGBT Safe Space Training on school climate in medical education (iCollaborative)." MedEdPortal Resource ID 2321

[Full-Text](#)

Department of Biomedical Sciences (OU)

OUWB Medical Student Author

Attitudes and behaviors of administration, faculty, staff, and students in lesbian, gay, bisexual, and transgender (LGBT) education create the climate of a medical school. The Association of American Medical Colleges (AAMC) revealed in 2007 that medical students experience LGBT discrimination throughout their educational and clinical training. National medical regulatory bodies, including the AAMC, have called for improvement in the culture and climate of academic medical centers and medical schools towards LGBT individuals. To date, no specific programs have been developed to improve LGBT inclusivity. The purpose of this program is to highlight an innovative medically-relevant Safe Space program in academic medicine. Safe Space training is a program that promotes inclusivity and is primarily used to establish a network of LGBT allies. While available at many undergraduate university settings, there remain limited opportunities in Safe Space training in medical education. In response to the need for an inclusive climate for LGBT persons, Oakland University William Beaumont School of Medicine (OUWB) has adapted the LGBT Safe Space training program to enhance LGBT climate in academic medicine.

Dunn SP, Gal RL, Kollman C, Raghinaru D, Dontchev M, Blanton CL, Holland EJ, Lass JH, Kenyon KR, Mannis MJ, Mian SI, Rapuano CJ, Stark WJ and Beck RW (2014). "Corneal graft rejection 10 years after penetrating keratoplasty in the cornea donor study." Cornea 33(10): 1003-1009.

[Full-Text](#)

Department of Ophthalmology

PURPOSE: The aim of this study was to assess the effect of donor and recipient factors on corneal allograft rejection and evaluate whether a rejection event was associated with graft failure. METHODS: One thousand ninety subjects undergoing penetrating keratoplasty for a moderate risk condition (principally Fuchs dystrophy or pseudophakic corneal edema) were followed for up to 12 years. Associations of baseline recipient and donor factors with the occurrence of a rejection event were assessed in univariate and multivariate proportional hazards models. RESULTS: Among 651 eyes with a surviving graft at 5 years, the 10-year graft failure (+/-99% confidence interval) rates were 12% +/- 4% among eyes with no rejection events in the first 5 years, 17% +/- 12% in eyes with at least 1 probable, but no definite rejection event, and 22% +/- 20% in eyes with at least 1 definite rejection event. The only baseline factor significantly associated with a higher risk of definite graft rejection was a preoperative history of glaucoma, particularly when previous glaucoma surgery had been performed and glaucoma medications were being used at the time of transplant (10-year incidence 35% +/- 23% compared with 14% +/- 4% in eyes with no history of glaucoma/intraocular pressure treatment, P = 0.008). CONCLUSIONS: Patients who experienced a definite rejection event frequently developed graft failure raising important questions as to how we might change acute and long-term corneal graft management. Multivariate analysis indicated that previous use of glaucoma medications and glaucoma filtering surgery was a significant risk factor related to a definite rejection event.

Farria DM, Salcman J, Monticciolo DL, Monsees BS, **Rebner M** and Bassett LW (2014). "A survey of breast imaging fellowship programs: Current status of curriculum and training in the United States and Canada." Journal of the American College of Radiology 11(9): 894-898.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Purpose The Society of Breast Imaging and the Education Committee of the ACR Breast Commission conducted a survey of breast imaging fellowship programs to determine the status of fellowship curricula, help identify strengths and potential areas for improvement, and assess the current demand for fellowship programs. Methods In 2012, a two-part survey was emailed to breast imaging fellowship directors from 72 fellowship programs. Results Of the 66 respondents, a total of 115 positions were identified. There were 90 positions with 9-12 months of breast imaging, and 25 positions with 6 months focused on breast imaging. Approximately two-thirds of programs reported an increase in the number of fellowship applicants, with three-quarters having 3 or more applicants for each position. All programs offered digital mammography, breast MRI, and diagnostic ultrasound services, and nearly all provided experience with interventional procedures. Approximately one-third provided breast screening ultrasound training. More than two-thirds required at least a 1-day rotation with a breast surgeon. Important nonclinical areas of training were not addressed in many programs. Approximately 40% of programs did not offer training related to the practice audit, and one-third of programs did not provide formal training related to quality control. Conclusions Breast imaging fellowships are currently in higher demand than in the past. Most fellowship programs provide training in the key imaging modalities and interventional procedures. Potential gaps in training for many programs include the practice audit, quality control procedures, breast positioning, and mammography technical factors. (copyright) 2014 Published by Elsevier Inc. on behalf of American College of Radiology.

Fatima A and **Gibson DP** (2014). "Pneumatosis intestinalis associated with Henoch-Schonlein purpura." Pediatrics 134(3): e880-e883.

[Full-Text](#)

Department of Pediatrics

Department of Diagnostic Radiology and Molecular Imaging

Henoch-Schonlein purpura (HSP) is the most common vasculitis in children. It is a disorder of the inflammatory cascade leading to immunoglobulin A deposition and leukocytoclastic vasculitis of small vessels of skin, kidneys, joints, and gastrointestinal (GI) tract. A wide variety of GI manifestations are seen in ~50% to 75% of patients with HSP. Diffuse colicky abdominal pain is the most common GI symptom. The small bowel is the most frequently involved GI site. Intussusception is rare but is the most common surgical complication. We report the case of a 2-year-old girl with a 5-day history of abdominal pain followed by a palpable purpuric rash. Her urinalysis, complete blood cell count, and tests of renal function were normal. An acute abdominal series was unremarkable initially, and abdominal ultrasound imaging showed ascites and thickened small bowel loops. She was diagnosed with HSP. The abdominal pain worsened, and an abdominal computed tomography scan demonstrated distal small bowel wall thickening and pneumatosis intestinalis in the descending colon. She was started on total parenteral nutrition and antibiotics and placed on bowel rest. She was given 2 mg/kg of intravenous immunoglobulin. Her abdominal pain gradually improved over the next week, and a repeat computed tomography scan showed significant improvement of the small bowel wall thickening and pneumatosis. The purpuric rash improved, and her abdominal pain resolved. We report a case of HSP and pneumatosis intestinalis, an association that has not been reported previously.

Flynt L and **Balon HR** (2014). "17-year-old runner with shin pain." Journal of Nuclear Medicine Technology 42(3): 238-239.

[Request Form](#)

Department of Diagnostic Radiology and Molecular Imaging

Stress injury is a common cause of exercise-induced anterior shin pain. It is important to distinguish between the various causes of stress injury in a timely manner in order to optimize favorable treatment outcomes.

Here, we will discuss a case of medial tibial stress syndrome, or shin splints, as one of the causes of shin pain, as well as how to approach shin pain for a successful diagnosis.

Folberg R (2015). "The eye," In Kumar V, Abbas AK and Aster JC (ed). Robbins and Cotran Pathologic Basis of Disease Philadelphia, PA: Saunders. pp: 1319-1343.

[Full-Text](#)

Administration

Fortin PT (2014). "The midfoot is really deformed after hindfoot arthrodesis. How to salvage?" Foot and Ankle Clinics 19(3): 469-482.

[Request Form](#)

Department of Orthopedic Surgery

Concomitant hindfoot and midfoot deformity is common. Hindfoot fusion is associated with prolonged recovery and significant disability. Further surgery is often required to obtain a plantigrade foot.

Understanding normal structural and kinematic relationships between the midfoot and hindfoot, as well as recognizing common combined patterns of midfoot and hindfoot deformity, can minimize the unanticipated consequences of hindfoot fusion. Treatment of residual or resultant midfoot deformity requires a thorough analysis of the deformity and familiarity with a variety of operative techniques for correction. © 2014 Elsevier Inc.

Fossa A, Zhou M, Morganroth J, Ellis D, **Hartrick CT**, Watts R and Gan TJ (2014). "Cardiac safety of SABER(registered trademark) bupivacaine in patients undergoing abdominal surgery in the BESST trial." Anesthesia and Analgesia 118(5): S148.

[Request Form](#)

Department of Anesthesiology

INTRODUCTION: Bupivacaine is commonly used as a part of postsurgical multimodal pain management, but its use is limited by a short duration of action. SABER(registered trademark)-bupivacaine was developed to provide a sustained release formulation of bupivacaine for 72 hours in order to maximize analgesia during the period of maximal postoperative pain. To evaluate any clinical evidence of cardiovascular-related bupivacaine systemic toxicity with SABER(registered trademark)-bupivacaine treatment, cardiac safety was

assessed in the phase 3 Bupivacaine Effectiveness in SABER(registered trademark) Surgical Trial (BESST). METHODS: BESST was an international, multicenter, double-blind trial evaluating the safety and efficacy of SABER(registered trademark)-bupivacaine 5 mL (660 mg) instilled into surgical wounds prior to closing. Eligible patients were randomized into 3 cohorts depending on surgical procedure; cohort 1 (n = 48) for open laparotomy (long incisions; mean, 20 cm); cohort 2 (n = 50) for laparoscopic cholecystectomy (small incisions; mean, 4 cm); and cohort 3 (n = 207) for laparoscopic colectomy (medium incisions; mean, 8-9 cm). Control for cohorts 1 and 2 was bupivacaine HCl (150 mg); cohort 3 was placebo controlled. Safety assessments included treatment-emergent adverse events (TEAEs), laboratory monitoring, wound healing, vital signs, and physical exam. Cardiac safety was assessed by digital 12-lead Holter monitoring from 1 hour before surgery until 72 hours after surgery. A 24-hour baseline Holter was obtained on an ambulatory basis before surgery. ECGs and PK samples were taken before and 0.5, 1, 2, 4, 8, 12, 16, 24, 30, 48, and 72 hours after dose. ECGs extracted from the Holter recordings were assessed for changes in heart rate, RR, PR, QRS, QT, QTcF (Fridericia formula-corrected QT interval), QTcB (Bazett corrected QT interval), QTbtb (QT beat-to-beat) and percentage QTbtb outliers. The primary ECG end point was SABER(registered trademark)-placebo - corrected baseline-adjusted effect on QTcF ((Delta)(Delta)QTcF) for SABER(registered trademark)-bupivacaine in cohort 3. The relationship of plasma bupivacaine concentration to (Delta)(Delta)QTcF was also evaluated in cohort 3. Bupivacaine plasma concentration was assessed via a validated liquid chromatography/mass spectrometry (LC-MS/MS) method. RESULTS: Most patients reported at least 1 TEAE, most commonly gastrointestinal symptoms (nausea, vomiting, or constipation), likely to due to anesthetic, surgery, or opioid use. Cardiovascular and neurologic TEAEs were similar between treatments with no signs of bupivacaine toxicity. There were no consistent effects on any of the ECG intervals, including QTcF, observed in the Holter data. PK-PD modeling showed that SABER(registered trademark)-bupivacaine did not prolong the QT interval as the slope of the (Delta)(Delta)QTcF versus bupivacaine concentration regression was essentially flat. No proarrhythmic events were observed in any of the Holter recordings for all 3 cohorts. CONCLUSIONS: SABER(registered trademark)-bupivacaine (5 mL instilled into a variety of abdominal surgical wounds) was well tolerated, with no evidence of systemic bupivacaine cardiac toxicity, no effect on ECG intervals, and no ventricular arrhythmias.

Franey LM, Lester SJ, Marwick T, Maeder MT, Kaye DM, Vlahos AP, Serra W, Al-Azizi K, Schiller NB and **Abbas AE** (2014). "Doppler-derived pulmonary vascular resistance ratio: An assessment of pulmonary vascular or total pulmonary resistance?" *Journal of the American Society of Echocardiography* 27(6): B118.

[Request Form](#)

Department of Internal Medicine

Background: The ratio of peak tricuspid regurgitation velocity (TRV) to the time velocity integral of right ventricular outflow (TVIEVOT) distinguishes between normal and elevated pulmonary vascular resistance (PVR). Moreover, the equation $TRV/TVIEVOT_{null10} (PVR_{ccho})$ has been validated as a good estimate of invasive PVR (PVR_{cath}). A critique of $TKV/TVLRVOT$ is the lack of a variable reflective of left atrial pressure. As such, $TRV/TVIRVOT$ may be a better correlate of total pulmonary resistance (TPR) which does not include a determinant of left atrial pressure. We thus sought to assess whether $TRV/TVIRVOT$ and $TRV2/TVIRVOT$ correlate better with PVR or TPR. Methods: We collected data from 5 studies comparing PVR_{recho} to PVR_{cath}. Linear regression analyses were generated between $TRV/TVIRVOT$ and $TRV2/TVIRVOT$, and PVR_{cath} and TPR_{cath}. Using Bland Altman analysis, PVR_{recho} was compared to PVR_{cath}, TPR, (derived from a regression equation correlating TPR_{cath} to $TRV/TVIRVOT$) was compared to TPR_{cath}. Cutoff values for $TRV/TVIRVOT$ and $TRV2/TVIRVOT$ were obtained to predict $PVR > 3$ WU and $TPR > 5$ WU. Results: 143 patients were included for analysis. Linear regression revealed good correlation between PVR_{cath} and $TRV/TVIRVOT$ and $TRV2/TVIRVOT$ ($r = 0.76$, $p < 0.0001$ and $r = 0.79$, $p < 0.0001$, respectively) and poorer correlation between TPR_{cath} and $TRV/TVIRVOT$ and $TRV2/TVIRVOT$ ($r = 0.72$, $p < 0.0001$) under various hemodynamic states (Figure 1, Table 1). Using Bland Altman, $TRV/TVIRVOT$ compared better to PVR_{cath} than TPR_{cath}. Moreover, $TRV/TVIRVOT > 0.2$ had a higher sensitivity to predict PVR_{cath} > 3 WU than TPR_{cath} > 5 WU. Conclusions: $TRV/TVIRVOT$ and $TRV2/TVIRVOT$ correlate better and provide improved noninvasive comparisons of PVR_{cath}.than TPR_{cath}.

Goldin D, Reich S, George D, Bahoura L, **Emerson S, Campbell J** and **Savin M** (2014). "Carcinoembryonic antigen response after initial single- or multi-session radioembolization for colorectal cancer: Analysis of cumulative delivered radioactivity and dose." *Cardiovascular and Interventional Radiology* 37(2): S251-S252.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Purpose: To investigate whether administered radioactivity and dose correlate with changes in carcinoembryonic antigen (CEA) levels after initial radioembolization for metastatic colorectal cancer (mCRC). **Material and Methods:** Retrospective review of patients treated with radioembolization for liver-dominant mCRC between June 2009 and February 2013 was conducted. Multivariate analysis included age, sex, disease stage, number of prior chemotherapy lines, and initial presentation with stage IV disease. Multisession therapy variables were calculated including total radioactivity administered, lobe dose of most disease-burdened lobes, total radioactivity delivered to the tumor, multi-session liver, and tumor doses. Response variables included progression-free survival, absolute and relative changes of CEA levels at 4-6 weeks and 12 weeks after completion of initial radioembolization. Statistical correlations and robust regression models were used to investigate the significance of findings after therapy. **Results:** Thirty subjects treated with radioembolization for mCRC were included. CEA level follow-up was at 4-6 week (n=28) and 12 week (n=17) intervals. Analyzing the entire cohort, there were no significant correlations at $(\alpha)=0.05$; however, nearly significant correlations were observed in total radioactivity administered compared with progression-free survival ($p=0.055$) and total activity delivered to tumor compared with CEA change at 12 weeks ($p=0.064$). Total radioactivity delivered to tumor in liver-only mCRC patients (excluding extrahepatic patients) was significantly correlated with a decrease in CEA both at 4-6 and 12 weeks post radioembolization with estimated Spearman correlations of -0.66 ($p=0.01$) and -0.60 ($p=0.022$), respectively. **Conclusion:** Total radioactivity delivered to tumor in liver-only mCRC disease was the only variable correlated with change in CEA levels after radioembolization.

Gottschalk MB, Yoon ST, **Park DK**, Rhee JM and Mitchell P (2014). "Surgical training using three - dimensional simulation in placement of cervical lateral mass screws: A blinded randomized control trial." *Spine J*. ePub Ahead of Print.

[Full-Text](#)

Department of Orthopedic Surgery

BACKGROUND CONTEXT: The skills and knowledge that residents have to master has increased, yet the amount of hours that residents are allowed to work has been reduced. There is a strong need to improve training techniques to compensate for these changes. One approach is to use simulation-training methods to shorten the learning curve for surgeons in training. **PURPOSE:** To analyze the effect of surgical training using three-dimensional(3D) simulation on placement of lateral mass screws in the cervical spine on either cadavers or sawbones. **STUDY DESIGN / SETTING:** Blinded Randomized Control Study **METHODS:** The Cervical Spine Research Society provided funding in the amount of \$12,000 for this study. No other conflicts of interest were noted as our institution supplied financial support. Fifteen orthopaedic residents post-graduate year(PGY) 1-6 were asked to simulate Magerl lateral mass screw trajectories from C3-7 on cadavers using a navigated drill guide but with no feedback as to the actual trajectory within bone (Baseline1). This was repeated to determine baseline accuracy (Baseline2). They were then randomized into three groups: Group 1, Control, did not receive any training, while Groups 2 and 3 received 3D navigational feedback as to the intended drill trajectory on Sawbones and Cadavers, respectively. All three groups then performed final simulated drilling (FinalTest). All 3D images were de-identified and reviewed by a blinded single fellowship trained orthopaedic spine surgeon. Each image/screw was measured for starting site, caudad/cephalad angle, and medial/lateral angle to determine trajectory accuracy. **RESULTS:** The aggregate mean difference from a perfect screw was compiled for each session for each group. A negative difference shows improvement, while a positive difference shows regression. The difference between FinalTest and Baseline1 in the Control group was 2.4 degrees, suggesting regression. In contrast, the differences for groups Sawbone and Cadaver were -8.2 degrees and -7.2 degrees, respectively, suggesting improvement. When comparing the difference in aggregate sum angle for the Sawbones and Cadaver groups to the Control group, the difference was statistically significant ($p < .0001$). **CONCLUSIONS:** L: Training with 3D navigation

significantly improved the ability of orthopaedic residents to properly drill simulated lateral mass screws. As such, training with 3D navigation may be a useful adjunct in resident surgical education.

Gralow J, Barlow WE, Paterson AHG, Lew D, Stopeck A, Hayes DF, Hershman DL, Schubert M, Clemons M, Van Poznak CH, Claire Dees E, Ingle JN, Falkson CI, Elias AD, Messino MJ, **Margolis JH**, Dakhil SR, Chew HK, Livingston RB and Hortobagyi GN (2014). "SWOG S0307 phase III trial of bisphosphonates as adjuvant therapy in primary breast cancer: Comparison of toxicities and patient-stated preference for oral versus intravenous delivery." Journal of Clinical Oncology 32(15).

[Request Form](#)

Department of Internal Medicine

Background: Bone metastases are a common site of distant recurrence in breast cancer. Evidence from randomized trials, including a recent meta-analysis, suggests that adjuvant bisphosphonates can decrease recurrence and death. SWOG S0307 compares efficacy of 3 bisphosphonates in early stage breast cancer. Methods: Patients with stage I-III breast cancer receiving adjuvant systemic therapy were randomized to receive 3 years of clodronate (CLOD) (1600 mg po qd), ibandronate (IBAN) (50 mg po qd) or zoledronic acid (ZA) (4 mg IV q month x 6, then q3 months x 2.5 years). The primary endpoint is disease-free survival. Overall survival, sites of first recurrence, and adverse events are secondary endpoints. Results: Between Nov 2005 and Feb 2010 6,097 patients were enrolled. Survival data are maturing with 50% of the expected events occurring to date. Annual interim analyses are being conducted. 5,752 patients are assessable for toxicity. Median age was 53. 78% of tumors were ER positive, 16% HER2 positive, 16% triple negative. 34% were stage I, 45% stage II, and 21% stage III. Planned adjuvant treatment included chemotherapy in 80%, endocrine therapy in 76%, and both in 56%. 25 (0.4%) and 494 (8.6%) patients experienced grade 4 or 3 toxicities, respectively. The most common adverse events were musculoskeletal, pain, gastrointestinal, metabolic/laboratory (creatinine, calcium), and constitutional symptoms (acute phase reactions). There have been 40 reported cases of osteonecrosis of the jaw (ONJ): ZA 24/2094 (1.15%), CLOD 6/2151 (0.28%), and IBAN 10/1507 (0.66%) ($p=0.003$). Fractures have been reported in 4.5% of patients in ZA arm, 4.8% in CLOD arm, and 4.1% in IBAN arm ($p=ns$). Prior to randomization, 76% preferred oral medication versus 24% for intravenous if drugs proved equal in efficacy. Preferences changed little at completion of therapy, although some switched preference. Conclusions: Grade 3 and 4 toxicities were low in S0307. ONJ, a rare but serious complication, was statistically highest for ZA and lowest for CLOD. Fractures were equal across arms. The majority of patients indicated a preference for oral formulation.

Green KA, Coffey MP, **Wolf LJ** and **Miller BT** (2014). "Progesterone level at hCG trigger affects chemical pregnancy rate after IVF but not progression to clinical or ongoing pregnancy." Fertility and Sterility 102(3): e339.

[Full-Text](#)

Department of Obstetrics and Gynecology

OBJECTIVE: Evaluate IVF outcomes based on the progesterone (P) level at the time of hCG trigger. DESIGN: Retrospective analysis. MATERIALS AND METHODS: 681 fresh, autologous IVF cycles of 500 women from 2007 to 2014 were evaluated. Women were <35 years of age with FSH<10 and at least two follicles (greater-than or equal to)17 mm on the day of hCG trigger. The primary objective was to evaluate whether P level at hCG trigger differentially affected chemical, clinical (fetal cardiac motion), or ongoing pregnancy rates. The effect of P was examined using a four level variable: Group 1: P<1 ng/mL, Group 2: 1 to <1.5, Group 3: 1.5 to <2, and Group 4: (greater-than or equal to)2. Analyses used generalized linear models fit with GEE methodology to account for multiple IVF attempts. RESULTS: There were 442 chemical pregnancies in 681 cycles (64.9%). Chemical pregnancy rates for Groups 1, 2, 3, and 4 were 70.71, 68.47, 51.82, and 50.72%, respectively. Clinical pregnancy rates for Groups 1, 2, 3, and 4 were 60.35, 53.15, 40.00, and 40.58%, respectively. Ongoing pregnancy rates for Groups 1, 2, 3, and 4 were 53.21, 49.55, 36.36, and 36.23, respectively. P level on the day of hCG trigger significantly affected chemical pregnancy ($p=0.001$). The odds of chemical pregnancy with P<1.5 ng/mL were 2.14 times the odds with PR1.5 ng/mL (95%CI 1.49, 3.09). When chemical pregnancies were considered, P levels did not affect progression to clinical or ongoing pregnancy ($p=0.26$ and 0.76 , respectively). There was no difference in insemination method between P groups. P levels did not appear to differentially affect pregnancy in agonist versus antagonist cycles ($p=0.60$).

The effect of P on chemical pregnancy persisted when peak estradiol was added to the model ($p=0.0005$).
CONCLUSION: P level on the day of hCG trigger significantly affects chemical pregnancy rate but does not appear to influence progression to clinical or ongoing pregnancy. The effect of P is significant regardless of peak estradiol levels. These findings support the theory that the negative effect of elevated P may be related to endometrial receptivity. (Table Presented).

Grunberger G (2014). "Clinical utility of dipeptidyl peptidase-4 inhibitors: a descriptive summary of current efficacy trials." European Journal of Clinical Pharmacology 70(11): 1277-1289.

[Full-Text](#)

Department of Internal Medicine

Purpose To review efficacy and safety data of dipeptidyl peptidase-4 inhibitors used in treatment of patients with type 2 diabetes mellitus. Methods A search of MEDLINE(registered trademark)/PubMed(registered trademark), a service of the National Library of Medicine of the National Institutes of Health as well as of the original publications of individual trials with dipeptidyl peptidase-4 inhibitors was carried out. Results Dipeptidyl peptidase-4 inhibitors are orally administered medications indicated for improved glycemic control in patients with type 2 diabetes. They inhibit activity of the enzyme dipeptidyl peptidase-4 responsible for inactivating nutrient-released incretin hormones (mainly glucagon-like peptide-1 and glucose-dependent insulinotropic peptide). As a result, the effect of the incretin hormones is enhanced, leading to improved (beta)-cell function and inhibition of the glucagon secretion from the pancreatic islets. Patients can expect to see lowering of fasting and postprandial glucose levels (by 0.5-1 mmol/l and 2-3 mmol/l, respectively), leading to reduction of hemoglobin A1c by 0.5-0.9% (depending on the baseline hemoglobin A1c). Conclusion Dipeptidyl peptidase-4 inhibitors are generally well tolerated, with minimal risks of hypoglycemia or weight gain. Many postmarketing and surveillance studies are now conducted which focus on long-term safety and cardiovascular outcomes. (copyright) 2014 Springer-Verlag Berlin Heidelberg.

Grunberger G (2014). "Response to comment on Grunberger "Insulin analogs-are they worth it? Yes!" Diabetes Care 2014;37:1767-1770 and Davidson "Insulin analogs-is there a compelling case to use them? No!" Diabetes Care 2014;37:1771-1774." Diabetes Care 37(10): e232.

[Full-Text](#)

Department of Internal Medicine

Haines DE, Beheiry S, Akar JG, Baker JL, Beinborn D, Beshai JF, Brysiewicz N, Chiu-Man C, Collins KK, Dare M, Fetterly K, Fisher JD, Hongo R, Irefin S, Lopez J, Miller JM, Perry JC, Slotwiner DJ, Tomassoni GF and Weiss E (2014). "Heart Rhythm Society expert consensus statement on electrophysiology laboratory standards: Process, protocols, equipment, personnel, and safety." Heart Rhythm 11(8): e9-e51.

[Full-Text](#)

Department of Internal Medicine

Hanzel G, Berman A, Almany SL, Huber K, Kar S and Holmes D (2014). "Comparison of imputed placebo versus observed ischemic stroke rates in the Watchman Trials represents a significant reduction in risk." Journal of the American College of Cardiology 64(11): B52.

[Request Form](#)

Department of Internal Medicine

Background: Left atrial appendage closure (LAAC) is, intuitively, an attractive strategy to reduce stroke risk in atrial fibrillation. Although the PROTECT-AF trial demonstrated superiority of the WATCHMANTM LAAC device over warfarin at four years, there is little data regarding ischemic stroke protection of LAAC therapy in patients unable or unwilling to take warfarin. We sought to assess the effectiveness of the device for stroke risk reduction compared to the imputed placebo event rate, that is, the expected ischemic stroke rate without anticoagulation therapy, based on CHADS2 score, in three separate device trials. Methods: The imputed placebo event rate in the trials (PROTECT AF, CAP, PREVAIL) was calculated using the average CHADS2 score in each study. The expected event rate, which is well validated in the literature, was compared

with the observed ischemic stroke rate in the device arm of each individual trial. Results: Patients from PROTECT AF (n=463), CAP (n=566) and PREVAIL (n=407) were analyzed. The average CHADS2 score and imputed placebo event rate per 100 patient-years were 2.2 (5.6-5.7), 2.5 (6.4), and 2.6 (6.6-6.7) in PROTECT AF, CAP, and PREVAIL, respectively. The relative risk reduction for ischemic stroke was 77%, 83%, and 62%, respectively (Table). Conclusions: In this analysis, LAAC with WATCHMAN is associated with a significant reduction in ischemic stroke compared with an expected event rate derived from the CHADS2 score. The relative risk reduction is similar to that seen in the historical trials comparing warfarin to placebo, suggesting LAAC may provide a reduction in stroke risk for patients not receiving anticoagulation therapy. (Table Presented).

Hendrickson KD, Heck M, **Franklin BA**, **Chinnaiyan KM**, **Boura J**, **James J** and **Rosenbaum L** (2014). "Predictors of computed tomographic-documented coronary disease during an executive physical." Medicine and Science in Sports and Exercise 46(5): 381.

[Full-Text](#)

Department of Internal Medicine

Department of Biomedical Sciences (BHS)

Hsu ICJ, Yamada Y, Assimos DG, D'Amico AV, Davis BJ, Frank SJ, Gottschalk AR, **Gustafson GS**, McLaughlin PW, Nguyen PL, Rosenthal SA, Taira A, Vapiwala N and Merrick G (2014). "A critical ACR Appropriateness Criteria omission response." Brachytherapy 13(5): 523-525.

[Request Form](#)

Department of Radiation Oncology

Hussein IH, Eid A, Maksoud R, Jambart S, Assi TB, Zgheib Z, Oueidat D, Chams N, Chams S, Diab R, Barada K, Jurjus R, Cappello F, Reimund J, Kreiker J, Leone A and Jurjus A (2014). "Estrogens control inflammation in experimental colitis." Journal of Biological Regulators and Homeostatic Agents 28(2): 213-224.

[Request Form](#)

Department of Biomedical Sciences (OU)

There is now a wealth of experimental evidence indicating that the deficit in endogenous estrogen facilitates the onset of inflammation that can be antagonized by estrogen replacement therapy. This work investigated the role of estrogen in the control of intestinal inflammation in a panel of colitis models, focusing on the morphological changes, the activity of mast cells, the expression of cytokines (IL-1 beta, IL-6, and TNF-alpha), fibronectin and reactive oxygen species. Two hundred adult male rats were divided into 4 groups: colitis was induced in Group I and Group II but only the latter was treated with estrogen; Group III received estrogen only, and Group IV saline. Colitis was induced in 4 models using: iodoacetamide; iodoacetamide + enteropathogenic E. coli; 2,4,6-Trinitrobenzene sulfonic acid; and dextran sulfate sodium salt. Macroscopic and microscopic evaluations of abdominal structures as well as molecular analysis were made on days 7, 14, 28 and 56. There was a significant improvement in the health condition of the estrogen-treated rats: the inflammation scores were reduced by at least 10-15%, the number of mast cells in the colon decreased by 30%, fibronectin expression was only 50% and reactive oxygen species decreased by 30%. In addition, there was a significant decrease in TNF-alpha, IL-6 and IL-1 beta expression by about 25%. In conclusion, there was an improvement in the inflammatory status in all estrogen-treated groups through the duration of the experiment at all-time points. In addition, there was less tissue necrosis as depicted by less fibronectin and a marked antioxidant effect.

Hymas RV, Jawad MS, Mangona VS, Zamdborg L, Wobb JL, Pietron A, Wallace M, **Chen PY**, **Grills IS**, **Brabbins DS** and Dilworth JT (2014). "Dosimetric predictors of toxicity and cosmesis in women treated with hypofractionated whole-breast irradiation." International Journal of Radiation Oncology Biology Physics 90(1): S270-S271.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): Large breast volume (BV) and distance of separation (DoS) have historically served as exclusionary criteria for hypofractionated whole breast irradiation (H-WBI). We investigate dosimetric

parameters impacting toxicity and cosmesis. Materials/Methods: 299 consecutive patients with early stage (T0-2, N0- 1, M0) breast cancer were treated with H-WBI at a single institution from 2007-2013. 4,256 cGy was delivered in 16 fractions via tangent photon beams utilizing inverse-planned intensity modulated radiation therapy, with objectives to limit the BV receiving 105% of the prescribed dose (V105) to 15%, the V110 to 2%, and the V115 to <0.1%. 227 patients with available treatment planning information and at least 6 months of follow-up were analyzed. 7% and 65% of patients received chemotherapy and endocrine therapy, respectively. Dosimetric parameters were correlated with acute ((less-than or equal to)6 months post-treatment) and chronic (>6 months posttreatment) toxicity and overall cosmesis. Proportions of toxicity grade and cosmesis score were compared with chi-square or Fisher exact test as appropriate. Results: With a median follow-up of 2.7 years (range 0.4-6.6 years), there were no local or regional recurrences, 1 distant failure, and one in-field angiosarcoma. Rates of any acute and chronic grade 1/2/3 toxicity were 47%/32%/9% and 53%/22%/7%, respectively (subdivided in the Table). Cosmesis (beyond 6 months) was reported as excellent, good, and fair in 45%, 55%, and <1% of patients, respectively. The V105 was the best predictor for cosmesis and chronic toxicity, with a V105(less-than or equal to)10% being associated with a better cosmesis (excellent vs fair/poor) and lower toxicity (grade 0 vs grade 1 vs grade 2/3) compared to a V105 > 10% (p = 0.09 and 0.03, respectively). The mean DoS was 22 cm (range 16-30 cm), with 22% and 3% of patients having a DoS greater than 25 cm and 28 cm, respectively. The mean BV was 1523 cc (range 299-3279 cc), with 19% and 5% having a BV greater than 2000 cc and 2500 cc, respectively. Neither a larger DoS nor a larger BV correlated with an inability to achieve a V105(less-than or equal to)10% (p = 0.37 and p = 0.13, respectively). Neither DoS nor BV predicted for worse acute toxicity, chronic toxicity, or cosmesis. Conclusions: Minimizing the V110 and V115 and limiting the V105 to (greater-than or equal to)10% are useful dosimetric objectives to achieve excellent or good cosmesis following H-WBI. Acceptable toxicity and excellent cosmesis is achievable in women with large DoS or BV, provided techniques to maximize dose homogeneity are employed.

Jacobs BL, Daignault S, Lee CT, Hafez KS, Montgomery JS, Montie JE, Humrich JE, Hollenbeck BK, **Wood DP, Jr.** and Weizer AZ (2014). "Prostate capsule sparing versus nerve sparing radical cystectomy for bladder cancer: Results from a randomized controlled trial." Journal of Urology. ePub Ahead of Print.

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Department of Urology

PURPOSE: Prostate capsule sparing and nerve sparing cystectomies are alternative procedures for bladder cancer that may reduce morbidity while achieving cancer control. However, the comparative effectiveness of these approaches has not been established. We sought to evaluate the functional and oncologic outcomes of patients undergoing these two procedures. MATERIAL AND METHODS: We performed a single-institution trial of bladder cancer patients who had a negative transurethral prostatic urethral biopsy and negative transrectal prostate biopsy. Men were randomized to prostate capsule sparing or nerve sparing cystectomy with neobladder creation. Patients were stratified by Sexual Health Inventory for Men (SHIM) scores (SHIM >21 or </=21). Our primary endpoint was 12-month overall urinary function as measured by the bladder cancer index (BCI). Secondary endpoints included sexual function, cancer control, and complications. RESULTS: Forty patients were enrolled in the study, with 20 patients in each arm. Urinary function at 12 months decreased by 13 and 28 points in the prostate capsule sparing and nerve sparing groups, respectively (p=0.10). Sexual function followed a similar pattern (p=0.06). There were no differences in recurrence-free, metastasis-free, or overall survival (all p>0.05). The rate of incidentally detected prostate cancer was similar (p=0.15). CONCLUSIONS: Our study provides a randomized comparison of prostate capsule sparing and nerve sparing cystectomy techniques. We found no differences in functional or oncologic outcomes between the two approaches, although our study was underpowered due to lack of patient accrual.

Jagsi R, Griffith K, Heimbürger D, Walker EM, Boike TP, **Grills IS**, Moran JM, Hayman J and Pierce LJ (2014). "Choosing wisely? Patterns and correlates of the use of hypofractionated whole breast radiation therapy in the state of Michigan." *International Journal of Radiation Oncology Biology Physics* 90(1): S134.

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Department of Radiation Oncology

Purpose/Objective(s): Hypofractionated whole breast radiation therapy (HRT) reduces the cost and burden of adjuvant RT for breast cancer and has equivalent outcomes to standard fractionation for appropriate patients. Recent studies have suggested that utilization of HRT is low and variable. We investigated patterns and correlates of HRT in a consortium of RT practices in Michigan to determine variation at the practice level and whether use reflects individualization based on potentially relevant patient characteristics (such as habitus, age, chemotherapy receipt, or laterality). Materials/Methods: We evaluated the proportion of whole breast RT administered with hypofractionated approaches in breast cancer patients receiving lumpectomy and RT at each practice participating in the Michigan Radiation Oncology Quality Consortium (MROQC). MROQC is an initiative that includes community and academic practices that collect detailed dosimetric, clinical, and patient-reported data on all breast cancer patients receiving adjuvant whole breast RT after lumpectomy at these sites, regardless of payor. We evaluated associations between HRT receipt and various patient characteristics. Results: Of 1475 patients registered by MROQC from October 2011 to December 2013, 919 had T1-2, N0 breast cancer. Of these 919, 284 (30.9%) received HRT, of whom 185 (72.8%) received a boost. Among the 13 practices, HRT use ranged from 2% to 80%. On multivariable analysis, HRT was more likely in patients who were older (OR = 1.04 per 1-yr increase, $p < 0.001$) and less likely with larger body habitus (OR = 0.92 per 1 cm increase in separation, $p=0.001$) and with chemotherapy receipt (OR = 0.42, $p < 0.001$). Use was not significantly associated with laterality ($p = 0.17$). HRT use was not higher in the last 6 months analyzed (29.5% from 6/13-12/13 vs 30.9% from 10/11-5/13; $p=0.70$). HRT use in other stage MROQC patients was 81 (26%) among 311 DCIS patients and 92 (19.8%) among 465 node-positive patients. Conclusions: HRT has been variably administered in the adjuvant setting in Michigan since the publication of the long-term results of the Canadian trial and after the initiation of the Choosing Wisely campaign. Use varies by patient characteristics but also varies substantially between practices, suggesting that differences in use may reflect differences in physician attitudes or knowledge. (Table Presented).

Jawad MS, Dilworth JT, Ye H, Wallace M, Martinez AA, **Chen PY**, **Gustafson GS** and **Krauss DJ** (2014). "Comparison of toxicity profiles associated with 3 high-dose-rate brachytherapy treatment schedules for favorable-risk prostate cancer." *International Journal of Radiation Oncology Biology Physics* 90(1): S211-S212.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): We report the acute and chronic toxicity profiles associated with 3 high-dose-rate (HDR) brachytherapy regimens used as monotherapy for favorable-risk prostate cancer. Materials/Methods: Four hundred ninety-four patients with T-stage (less-than or equal to) T2b, Gleason (less-than or equal to) 7, and pre-treatment PSA (less-than or equal to) 18 ng/mL underwent HDR brachytherapy as monotherapy from 1999-2013. Three hundred nineteen received 38 Gy/4 fractions, 79 received 24 Gy/2 fractions, and 96 received 27 Gy/2 fractions. Acute genitourinary (GU) and gastrointestinal (GI) toxicity was defined as side effects occurring (less-than or equal to) 6 mos post- RT. Chronic toxicity was defined as side effects > 6 mos post-RT. Toxicity was graded according to CTCAE v3.0. Time to toxicity was calculated from the date of RT completion. Variables were analyzed using chi-square analysis, and p -values < 0.05 were considered significant. Results: Median follow-up for all patients was 4 years. Maximal acute and chronic GU and GI toxicities are seen in the Table. The majority of GU symptoms were similar between groups, with overall acute/chronic grade 1 frequency/urgency, dysuria, and incontinence of 40%/37%, 23%/19%, and 3%/8%, respectively. Grade 1/2/3 chronic urethral stricture was similar between groups, with overall rates of 0.3%/2%/1%. Acute grade 1 hematuria was higher with 38 Gy vs 27 Gy (5% vs 0%, $p = 0.004$) but not statistically different from 24 Gy. No differences in grade 2/3 acute hematuria were seen. Chronic grade 1 retention was higher with 27 Gy (41%) vs both 24 Gy (17%, $p = 0.002$) and 38 Gy (19%, $p < 0.001$). There were no differences in grade 2/3 retention. No grade 4/5 acute/chronic GU toxicities were seen. All GI toxicities were similar between groups, with overall rates of acute/chronic grade 1 diarrhea, rectal

pain/tenesmus, rectal bleeding, and proctitis of 9%/8%, 4%/5%, 3%/7%, and < 1%/2%, respectively. Minimal grade 2 toxicity ((less-than or equal to) 2%) and no grade 3/4/5 toxicities were seen. All results were similar when excluding patients who received hormonal therapy. Time to maximal toxicity was similar between groups, with mean time to maximal GU and GI toxicity ranging from 1-1.5 years and 1-1.2 years, respectively. Overall clinical outcomes have been published previously and are similar among the groups. Conclusions: The acute and chronic GI and GU toxicity profiles associated with these 3 hypofractionated HDR brachytherapy schedules were similar and well tolerated. Acceptable rates of grade 2 toxicity were noted, with minimal grade 3 and no grade 4-5 toxicity. The favorable side effect profiles reported here suggest that further hypofractionation and/or dose escalation is feasible.

Jawad MS, Vance SM, **Grills IS**, Ye H, Prausa SK, Wloch J and **Yan D** (2014). "Variability of inter-fraction target motion during conventional and hypofractionated lung radiation therapy." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S141-S142.

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Department of Radiation Oncology

Purpose/Objective(s): Target excursion obtained from pre-treatment 4DCT has been used in planning for motion management of lung RT. However, excursion can change during RT delivery. This study is to investigate patterns of excursion variability ((Delta)E) during conventionally fractionated (CRT) or hypofractionated RT (HRT), effect of (Delta)E on dose reduction, and clinical factors correlated with (Delta)E. Materials/Methods: Eighty-four patients with primary or metastatic lung tumors underwent CRT (n=43) or HRT (n=41). All patients underwent planning with 4D-CT imaging. Online 4D-CBCT was performed weekly for CRT and pre/post-delivery for each HRT fraction. Respiratory-induced target excursion was quantified for each 4D-CBCT in 3 directions: anterior- posterior (AP), left-right (LR), and superior-inferior (SI). (Delta)E was calculated as the excursion difference between each 4D-CBCT and the planning 4D-CT. Target dose reduction caused by (Delta)E was calculated for tumors with (Delta)E (greater-than or equal to) 4 mm. Pearson correlation was performed to associate clinical factors with (Delta)E. Continuous variables were analyzed with an independent samples t-test and categorical variables with chi-square. Results: Eight hundred forty-four 4D-CBCT's were analyzed (495 CRT, 349 HRT). (Delta)E was largest in the SI direction overall, with mean (SD) of 0.5 ((plus or minus) 3) mm (-25 - 17). Mean (Delta)E (mm) in the SI direction was larger in HRT as compared to CRT, with smaller SD (1.1 ((plus or minus) 2.3) v 0.03 ((plus or minus) 3.3), p < 0.001). A similar trend was noted in the AP direction, and no difference was seen in the LR direction. Eleven percent of the 844 4D-CBCT's had (Delta)E > 4 mm (38% HRT, 62% CRT). For treatments with (Delta)E > 4 mm, overall mean target dose reduction was largest in the SI direction, -7.4 (plus or minus) 4.2%. The following factors were significantly correlated with (Delta)E: age, weight, tumor location, performance status (KPS), smoking history, pre-RT O2 use, and planning 4D-CT excursion. Tumor size and right v left lung did not correlate. Tumors with (greater-than or equal to) 4 mm(Delta)E in any direction were found in younger patients with higher weight and KPS, male gender, and lower lobe (LL) location (Table 1). Conclusions: The largest degree of (Delta)E is seen in the SI direction for both CRT and HRT, causing > 5% target dose reduction in 11% of daily RT deliveries. Target margins designed based only on pre-treatment 4D-CT without considering clinical variables could under compensate for target motion during treatment. Large (Delta)E seems predictable, and seen more in young patients with higher baseline weight, KPS, male gender, and LL tumors. Online 4D-CBCT provides a means to monitor excursion and adapt RT, and further analysis to optimize timing is underway. (Table Presented).

Johnson MD, Dilworth JT, Baschnagel AM, Maitz AH, Ye H, **Krauss DJ**, **Chen PY**, **Pieper DR**, **Olson RE** and **Grills IS** (2014). "Brain metastases treated with surgical resection followed by frame-based stereotactic radiosurgery."

[International Journal of Radiation Oncology Biology Physics](#) 90(1): S329-S330.

[Full-Text](#)

Department of Radiation Oncology

Department of Neurosurgery

Purpose/Objective(s): To evaluate outcomes and quality of life (QOL) for patients with brain metastases treated with surgical resection followed by frame based radiosurgery. Materials/Methods: 94 patients with

brain metastases were underwent surgical resection followed by frame based radiosurgery between 12/2006 and 6/2013. 56 patients were treated to the resection cavity only; 38 had synchronous lesions (median 3, 2-9) treated definitively with frame based radiosurgery along with the surgical bed. The most common histologies were non-small cell lung cancer (59%) and breast (18%). The median marginal dose was 18 Gy (12.5-18 Gy). Median resection cavity volume was 8.9 cc (0.5-41 cc); median treatment volume and conformity index (CI) were 17.6 cc and 1.9, respectively. Clinical endpoints were assessed using the Kaplan- Meier method; univariate(UVA) and multivariate(MVA) analyses using Cox proportional hazard regression models. QOL data was collected prospectively using the EORTC QLQ-C30 and BN20 questionnaires. Results: Median follow-up was 13 mos (1.5-79 mos). 6- and 12-mo actuarial local control rates (LC) for resected metastases were 86% and 78%, with a median time to local recurrence (LR) of 8.5 mos (2 - 55 mos). 6- and 12-month LC rates for unresected metastases were 97% and 93% with median time to LR of 6.1 mo (1.2-22 mo). 6- and 12-month freedom from elsewhere brain failure (EBF) were 65 and 50%, with a median time to EBF of 5.4 mos (1.5-49 mos). Median overall survival (OS) was 15 mos (1.5 - 79 mos). 28 patients (30%) received salvage whole brain RT; 35 (37%) underwent multiple frame based radiosurgery treatments (mean: 2.5, 2-5) for metachronous lesions. On UVA, marginal dose, cavity volume, max cavity dimension, pre-surgical lesion volume, CI, and tumor location did not predict for LR for resected cavities. While tumor volume, max linear dimension, and dose predicted LR for unresected lesions on UVA; max linear dimension remained significant on MVA (HR 8.05, $p = 0.02$). Compared to smaller resection cavities, larger cavities ($> 9.5 \text{ cm}^3$) had similar rates of LR but significantly higher rates of radionecrosis (RN) (20% versus 4%, $p=0.048$). Freedom from leptomeningeal failure (LMF) at 6- and 12- mos were 89% and 84%; LMF predicted for OS on UVA and MVA (HR 2.3; $p<.05$), as did controlled primary, extracranial disease and KPS. Compared to baseline, there was no significant difference was seen in global health status, fatigue, seizures or physical/motor/cognitive functioning 6 mos post-frame based radiosurgery; 6-mo nausea was worse ($p = 0.02$), related to chemotherapy. Conclusions: frame based radiosurgery achieves acceptable LC of resected brain metastases and synchronous lesions with no impact on QOL. Treatment of larger resection cavities increases RN risk. Identifying factors predictive of LMF may aid in patient selection. Future comparisons of post-resection radiosurgery versus whole brain RT with respect to QOL, patterns of failure and toxicity are warranted given these findings.

Jolepalem P, **Balon HR, Wong CYO** and **Wu D** (2014). "Complementary role of 18F-FDG PET and 123I-Ioflupane SPECT in the diagnosis of lewy body disease." *Journal of Nuclear Medicine Technology* 42(3): 233-234.

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Department of Diagnostic Radiology and Molecular Imaging

We present a case demonstrating how correlative imaging with 123I-ioflupane SPECT and 18F-FDG PET can be used to help make the diagnosis of Lewy body disease more specific.

Jolepalem P, Flynt L, **Rydberg J** and **Wong CY** (2014). "Implications of ambient glucose variation on the target-to-background ratio of hepatic tumors by 18FDG-PET imaging." *Journal of Clinical Imaging Science* 4(1).

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Objectives: To investigate the effects of ambient glucose on quantitative analysis of hepatic tumors on 2-deoxy-2-(18F)-fluoro-D-glucose (18FDG) positron emission tomography (PET) and to establish a method for glucose correction. Patients and Methods: Eighty-six patients with hepatic lesions identified on 18FDG PET/computed tomography (CT) were analyzed. The serum glucose level (Glc) was recorded prior to imaging, and the maximum standardized uptake value (SUV) in the hepatic tumors and the average SUV in normal liver were determined. The inverse relationship of SUV to glucose can be defined as $d(SUV)/d(Glc) = gFNx01SUV/(Glc)$, where g is the glucose sensitivity. Simulations using glucose level from 70 to 250 mg/dl were performed to evaluate the effects of Glc on the maximum SUV of malignant hepatic lesions and normal liver. Results: By logarithmic transformation and linear regression, g for metastasis was significantly higher than that for normal liver (-0.636 (plus or minus) 0.144 vs.-0.0536 (plus or minus) 0.0583; $P = 0.00092$). Simulation studies showed that the SUV in malignant lesions will decrease rapidly when Glc level is >120 mg/dl, while background liver remains relatively constant up to 250 mg/dl. Conclusion: The tumor FDG uptake is much more sensitive to ambient glucose level variation than the background liver. Therefore,

correction by the glucose sensitivity factor will result in more accurate SUV measurements and make semi-quantitative analysis of 18FDG PET scans more reliable.

Kim S, Chen D, Al-Rashdan AF, Elsaka R, Torres-Roca J, Haura E, Dilling TJ, Robinson L and **Stevens C** (2014). "A novel molecular signature for early-stage squamous cell carcinoma of the lung predicting locoregional recurrence following local therapy with surgery or stereotactic body radiation therapy (SBRT)." International Journal of Radiation Oncology Biology Physics 90(1): S78.

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Department of Radiation Oncology

Purpose/Objective(s): Early stage (T1-T2N0M0) squamous cell carcinoma (SCC) of the lung is managed by surgery or SBRT alone. Adjuvant therapy is typically not given in this group of node-negative patients. Unfortunately, 14% to 31% of patients recur loco-regionally following surgery. The purpose of this study was to develop a molecular signature to predict the risk for disease recurrence at the time of initial presentation, ultimately to intensify treatment with adjuvant radiation therapy or chemotherapy. Materials/Methods: Our institution has collected more than 40,000 tumor microarray databank linked to longitudinal clinical data to develop a platform for personalized medicine. We conducted a retrospective chart review of pathologic T1-T2N0 NSCLC patients in this database, and classified patients according to their recurrence pattern. Affymetrix microarray data from pathologic specimens were obtained, and gene expression profile was analyzed. Results: We identified a cohort of 59 SCC patients treated with surgical resection. 24 patients were without evidence of disease at least 3 years following surgery (Control cohort), 12 patients failed locally and in regional lymph nodes (Loco-regional failure cohort), and 23 patients developed distant metastasis (distant failure cohort). One hundred fortyeight genes were identified that showed significant differences in RNA expression level between control cohort vs loco-regional failure cohort. However, there was no gene was associated with distant metastasis. This may be a reflection of squamous histology associated with an increased risk for loco-regional failure in lung as well as other disease sites. Metacore pathway analysis demonstrated a subgroup of 12 immune genes within the molecular signature implying suppression of anti-tumor immune responses as one of possible mechanisms of loco-regional failure. Conclusions: We have identified a 148 gene signature and a 12 immune gene signature that predict loco-regional recurrence among surgically resected pT1-T2N0 SCC of the lung. We are currently developing the score system to classify these earliest stage lung SCC patients into 3 groups, low risk, intermediate risk, and high risk for loco-regional recurrence based on our gene signature. The outcome of this study will identify a select group of stage I-II lung SCC patients who will benefit from adjuvant loco-regional radiation therapy after surgery. Patients after SBRT may also benefit from mediastinal radiation therapy for the highrisk group. Ultimately, we are planning to translate these findings to a clinical trial.

Koreckij T, **Park DK** and **Fischgrund J** (2014). "Minimally invasive spine surgery in the treatment of thoracolumbar and lumbar spine trauma." Neurosurgical Focus 37(1): E11.

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Department of Orthopedic Surgery

Thoracolumbar and lumbar trauma account for the majority of traumatic spinal injuries. The mainstay of current treatments is still nonoperative therapy with bracing. Classic treatment algorithms reserved absolute surgical intervention for spinal trauma patients with neurological compromise or instability. Relative indications included incapacitating pain and obesity/body habitus making brace therapy ineffective. In the past decade, minimally invasive surgical (MIS) techniques for spine surgery have been increasingly used for degenerative conditions. These same minimally invasive techniques have seen increased use in trauma patients. The goal of minimally invasive surgery is to decrease surgical morbidity through decreased soft-tissue dissection while providing the same structural stability afforded by classic open techniques. These minimally invasive techniques involve percutaneous posterior pedicle fixation, vertebral body augmentation, and utilization of endoscopic and thoracoscopic techniques. While MIS techniques are somewhat in their infancy, an increasing number of studies are reporting good clinical and radiographic outcomes with these MIS techniques. However, the literature is still lacking high-quality evidence comparing these newer techniques to classic open treatments. This article reviews the relevant literature regarding minimally invasive

spine surgery in the treatment of thoracolumbar and lumbar trauma. © AANS, 2014.

Krauss DJ, Martinez AA, Ye H, **Chen PY**, Ghilezan MI and **Gustafson GS** (2014). "Favorable toxicity profiles for low-and intermediate-risk prostate cancer patients treated with single-fraction high-dose-rate brachytherapy." International Journal of Radiation Oncology Biology Physics 90(1): S412.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): High dose rate (HDR) brachytherapy as monotherapy has evolved with a trend toward decreasing number of treatment fractions so as to exploit the low alpha-beta ratio associated with prostate cancer, as well as to minimize patient inconvenience and cost in an era of value-based medicine. We report initial toxicity outcomes of single fraction HDR brachytherapy for patients with low- and intermediate-risk prostate cancer. Materials/Methods: Patients from a single institution were enrolled prospectively on an IRB-approved protocol testing the hypothesis that definitive radiotherapy could be safely and effectively administered in a single HDR fraction. Patients were eligible if they had clinical stage (less-than or equal to) T2b, pretreatment PSA < 15 ng/mL, and Gleason score (less-than or equal to) 7. Patients with Gleason score 7 with predominant pattern (greater-than or equal to) 4 were ineligible. The following served as exclusion criteria: prostate volume > 50cc, American Urologic Association (AUA) Symptom Score > 12, Adult Comorbidity Evaluation 27 (ACE-27) score > 1, on alpha blocker medications for urinary symptoms, and initial diagnosis > 18 months prior to study enrollment. Treatment consisted of transperineal prostate implant followed by delivery of 19 Gy in a single fraction via 192Ir HDR source. Treatment planning was done in real time using transrectal ultrasound imaging. Dose was prescribed to the margin of the prostate with no planning target volume expansion. Acute and chronic toxicities were defined by whether or not they occurred before or after 6 months post-treatment, respectively. Toxicity was scored according to CTCAE Version 3.0. Results: Fifty patients were available for evaluation at the time of this analysis. Median follow up was 1.5 years (range 0.3-2.7 years). 64% of patients were low risk by NCCN criteria and 36% intermediate risk. All patients had Gleason score 6 (70%) or 7 (30%) disease. 64% were clinical stage T1 and 36% T2. No patients received hormonal therapy. Acute grade 2 toxicity incidence was 10% (3 patients frequency/urgency and 2 patients dysuria) with no grade (greater-than or equal to) 3 acute toxicity. Grade (greater-than or equal to) 2 acute GI toxicity did not occur. Chronic grade 2 urinary toxicity occurred in 4 patients (8%) (3 frequency/urgency, dysuria) with no chronic grade (greater-than or equal to) 3 GU toxicity. There has been no chronic grade 2 GI toxicity, but a single patient developed grade 3 diarrhea. Grade (greater-than or equal to) 2 erectile dysfunction occurred in 15 patients (30%), ten patients grade 2 and five grade 3. Conclusions: Single fraction HDR brachytherapy to a dose of 19 Gy is safe and extremely well tolerated with minimal grade (greater-than or equal to) 2 acute or chronic toxicity. Additional follow up will be required to determine comparative efficacy with respect to established multi-fraction regimens.

Krueger SA, Schoenherr D, Galoforo S, **Wilson GD** and **Marples B** (2014). "Evaluating low-dose pulsed radiation therapy in murine model of neuroblastoma." International Journal of Radiation Oncology Biology Physics 90(1): S793-S794.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): Highly aggressive advanced-stage neuroblastoma is treated with a multimodality approach but survival remains poor. The aim of this study was to evaluate low-dose pulsed radiation therapy (PRT) as a novel treatment for neuroblastoma. Although the mechanism of PRT is not fully elucidated, it is thought to induce DNA damage below the activation threshold of ATM-dependent DNA detection, repair and cell cycle checkpoint mechanisms, and also protect tumor vasculature. Materials/Methods: Radiosensitivity of SK-N-BE(2), SK-N-SH, MCIXC, and SH-SY5Y neuroblastoma cells was determined by clonogenic assay. DNA repair was assessed by H2AX foci and apoptosis by caspase-3. Subcutaneous xenograft tumors were established from SK-N-SH, SK-NBE(2), or MC-IXC cells in female CB-17/SCID mice and irradiated with a total dose of 20 Gy given over 10 consecutive days (2 Gy/day) as either continuously-delivered standard RT (SRT) or PRT (10 x 0.2 Gy using a 3 minute inter-pulse interval). Tumor response was evaluated 3 times a week by caliper measurements. F18-FDG PET/CT was also performed 1 day

prior to and 2 days post RT. VEGF expression was assayed by ELISA. The study was approved by the Institutional IACUC. Results: In vitro, a single 2 Gy dose of PRT was not inferior to SRT in any of the 4 cell lines despite the prolonged delivery time. In vivo, PRT and SRT were equally effective at controlling MC-IXC and SK-N-SH subcutaneous tumors. However, significant differences in tumor volume and regrowth were evident for MYCN amplified SK-N-BE(2) tumors between PRT and SRT at 5 days ($p = 0.008$) and 21 days ($p = 0.014$) post treatment. Endpoint criteria was reached at 43 days for SRT but 56 days after PRT ($p = 0.012$). Furthermore, tumors treated with PRT demonstrated a significant increase in FDG PET maximum standardized uptake value after treatment (SUVmax = 1.13 SRT, 1.79 PRT, $p = 0.03$). This increase was also significant when compared to pre-treatment values for PRT (SUVmax PreTreatment = 1.04, $p = 0.009$). Quantitative immunohistochemistry identified differences in vascular density (CD34) and hypoxic markers (HIF1/CA-IX) between PRT and SRT. VEGF levels in the blood did not change after PRT tumor irradiation but increased after SRT. Conclusions: These data indicate that PRT may provide a new treatment regimen for MYCN amplified neuroblastoma. While the exact mechanism behind PRT is not known, changes in vascularity and cellular proliferation during treatment likely play vital roles. These data are currently being confirmed in an orthotopic SK-N-BE(2) model utilizing non-invasive PET imaging.

Laban MM and **Wang AM** (2014). "Engorgement of the cervical spinal epidural venous plexus simulating a spinal epidural mass." [American Journal of Physical Medicine and Rehabilitation](#) 93(7): 634-635.

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Department of Physical Medicine and Rehabilitation

Department of Diagnostic Radiology and Molecular Imaging

Lanni T, **Krauss D**, Marvin KS, **Gustafson G**, Ye H and **Chen P** (2014). "Comparing the cost-effectiveness of low-dose-rate brachytherapy, high-dose-rate brachytherapy, and hypofractionated intensity modulated radiation therapy for the treatment of low-/intermediate-risk prostate cancer." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S587-S588.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): To evaluate cost effectiveness of low dose rate (LDR) brachytherapy, hypofractionated IMRT (h-IMRT), and various high dose rate (HDR) brachytherapy regimens in low and intermediate risk prostate cancer patients. Materials/Methods: Eight hundred twenty patients with low or intermediate prostate cancer were treated with LDR ($n = 225$), HDR with 4 fractions ($n=321$), HDR with 2 fractions ($n=178$), HDR with 1 fraction ($n = 50$) or IMRT ($n = 46$) between January 1992 and December 2012. LDR patients were treated with palladium seeds to a median dose of 120 Gy while HDR patients were treated with one of the following regimens: 19.0 Gy (1 fraction), 24.0 Gy (2 fractions) and 38.0 Gy (4 fractions) respectively. h-IMRT patients received 64 Gy in twenty 3.2 Gy fractions on an in-house protocol. The cost of each treatment course was calculated using hospital-based 2014 Medicare Ambulatory Payment Classification (APC) and physician fee screen reimbursement rates for both the technical and professional components of therapy. Results: According to 2014 Medicare reimbursements, the reimbursement in our patient population for LDR, HDR with 4 fractions, HDR with 2 fractions, HDR with 1 fraction and h-IMRT was \$10,036, \$20,350, \$17,376, \$9,394, and \$18,220 respectively. Each brachytherapy regimen included the costs of anesthesia and any relevant hospital costs within the reimbursement scheme. HDR single fraction and LDR were statistically less costly than the other treatments ($p<0.001$). The analysis does not include any complications or readmissions for those patients receiving brachytherapy and does not account for the costs of toxicity, which can extend for 10-15 years after treatment. Conclusions: In this study of low and intermediate risk prostate cancer patients, the Medicare reimbursement for h-IMRT was similar to previously reported HDR techniques; however it was still higher than LDR and HDR single fraction regimens. While potentially attractive from a cost effectiveness standpoint, it must be emphasized that clinical outcomes from these regimens have yet to be formally compared, and it is only at that point that a formal assessment of comparative treatment value may be performed.

Lawrence PF, Klausner JQ, Harlander-Locke MP, Coleman DM, Stanley JC, Oderich GS, Inui TS, Mell MW, Humphries M, **Bove PG**, Abularrage CJ, Feezor RJ, Azarbal AF, Smeds MR, Ladowski JS, Hsiang YN, Dominguez JA and Morasch MD (2014). "The contemporary guidelines for asymptomatic renal artery aneurysms are too aggressive: A North American experience." *Journal of Vascular Surgery* 59(6): 24S-25S.

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Department of Surgery

Objectives: Most prior single-center series have recommended repair of asymptomatic renal artery aneurysms (RAA) >2 cm. This study evaluated the contemporary management of a large series of RAAs. Methods: Patients with RAAs were analyzed using a standardized database by a research consortium of 15 institutions. Results: A total of 614 RAAs were identified in 525 patients at 15 institutions (age, 61; male-to-female ratio = 1:2). Seventy-one percent of patients were asymptomatic. Symptomatic patients had severe hypertension (12%), flank pain (7%), abdominal pain (6%), and hematuria (4%). Aneurysm location included the main renal artery bifurcation (40%), main trunk (28%), primary branch (18%), secondary branch (7%), and pole artery (7%). Most RAAs were saccular (86%) and calcified (64%). Diameters were 1.8 (plus or minus) 0.1 cm for symptomatic RAAs and 1.5 (plus or minus) 0.1 cm for asymptomatic RAAs (P < .001). Aneurysms were observed (67%; diameter 1.3 (plus or minus) .1 cm) or surgically treated with open repair (OR; 28%; diameter 2.1 (plus or minus) .1 cm), or endovascularly (EV; 5%; diameter 2.3 (plus or minus) .2 cm). For OR vs EV, minor complications were 26% and 10%, respectively (P < .001), and major complications were 1% and 3%, respectively (P = .014). Only one death occurred, in an EV patient. Conservatively managed patients were observed for 41 (plus or minus) 4 months with no ruptures. Fifty-nine RAA >2 cm were treated non-OR (diameter 2.8 (plus or minus) .1 cm) with a mean follow-up time of 42 (plus or minus) 10 months. There were no ruptures. The growth rate for asymptomatic RAA, based on serial imaging, was 0.16 (plus or minus) 0.01 cm/y (calcified = 0.16 (plus or minus) 0.01 cm/y; noncalcified = 0.17 (plus or minus) 0.01 cm/y; P = .913). Conclusions: This largest study of RAA demonstrates that (1) asymptomatic RAA rarely rupture, even when >2 cm and not calcified, (2) open repair is associated with significant minor morbidity but rarely a major morbidity or mortality, (3) RAA growth rate is 0.16 (plus or minus) 0.01 cm/y and calcification does not protect against growth, (4) the current guideline of repairing asymptomatic RAA >2 cm is too aggressive.

Lee KC, Thibodeau BJ, Fortier LE, Pruetz BL, Galoforo S, Chunta J, **Wong C, Yan D, Marples B**, Huang J and **Wilson GD** (2014). "Glucose metabolism gene expression patterns and tumor uptake of 18F-FDG following radiation treatment." *International Journal of Radiation Oncology Biology Physics* 90(1): S795.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Department of Radiation Oncology

Purpose/Objective(s): To investigate whether radiation treatment influences the expression of glucose metabolism genes and compromises the potential use of 18F-fluorodeoxyglucose-positron emission tomography (FDG-PET) as a tool to monitor the early response of head neck cancer xenografts to radiation therapy (RT). Materials/Methods: Low passage head and neck squamous cancer cells (UT14) were injected to the flanks of female nu/nu mice to generate xenografts. After tumors reached a size of 500mm³, they were treated with either sham RT or 15 Gy in one fraction. At different time points, days 3, 9 and 16 for controls and days 4, 7, 12, 21, 30, 40 after irradiation, 2-3 mice were assessed with dynamic FDG-PET acquisition over 2 hours. Immediately after the FDG-PET, the tumors were harvested for global gene expression analysis and immunohistochemical evaluation of GLUT1 and hexokinase 2 (HK2). Different analytical parameters were used to process the dynamic PET data. Results: Radiation had no effect on key genes involved in FDG uptake and metabolism but did alter other genes in the HIF1-(alpha) and glucose transport related pathways. In contrast to the lack of effect on gene expression, changes in the protein expression patterns of the key genes GLUT1/ SLC2A1 and HK2 were observed following radiation treatment. The changes in GLUT1 protein expression showed some correlation with dynamic FDG-PET parameters such as the kinetic index (Ki). Conclusions: FDG-PET changes following RT represent an altered metabolic state and not a direct effect on the key genes regulating FDG uptake and metabolism. Further research is ongoing to characterize the biological significance of early changes in FDG-PET parameters to predict response to therapy.

Lewis LM, Graffeo C, Crosley P, Klausner HA, **Clark CL**, Frank A, Miner J, Iarrobino R and Chyung Y (2014). "Ecallantide for the acute treatment of angiotensin-converting enzyme inhibitor-induced angioedema: A multicenter, randomized, controlled trial." *Annals of Emergency Medicine*. ePub Ahead of Print.

[Full-Text](#)

Department of Emergency Medicine

Study objective: We compare the safety and efficacy of ecallantide with placebo in subjects undergoing assessment for acute angiotensin-converting enzyme inhibitor-induced angioedema (ACEIA) in an emergency department (ED). Methods: This was a multicenter, phase 2, double-blind study with subjects randomized to receive a single subcutaneous dose of ecallantide (10, 30, or 60 mg) or placebo plus physician-directed conventional therapy. The primary endpoint was defined as meeting predetermined discharge eligibility criteria within 6 hours of study drug administration. Discharge criteria included improvement of edema, stable vital signs, absence of stridor, absence of dyspnea or use of accessory muscles during respiration, absence of drooling, and ability to drink without difficulty. Results: An interim analysis showed that a high percentage of subjects met the primary endpoint, and the study was halted. Overall, 79 subjects were randomized and 76 had data for analysis. Most had mild (45%) or moderate (42%) ACEIA. The discharge eligibility endpoint was met by 72% of the placebo group and 85%, 89%, and 89% of the ecallantide 10-, 30-, and 60-mg groups, respectively. This difference in meeting discharge eligibility endpoint criteria between treatment groups was not statistically significant. The incidence of treatment-emergent adverse events was similar between placebo and active-treatment groups. Conclusion: The addition of ecallantide to standard therapy does not appear to improve angioedema compared with placebo in ED patients with ACEIA. Our data suggest that most ED patients presenting with mild to moderate ACEIA are likely to meet our discharge eligibility criteria within 6 hours of treatment, regardless of intervention. Further studies to assess the utility of ecallantide in patients with more severe angioedema may be useful. No new safety signals related to ecallantide administration were identified. (copyright) 2014 American College of Emergency Physicians.

Lorenz RP (2014). "What is new in bed rest in pregnancy? Best articles from the past year." *Obstetrics and Gynecology* 124(2 PART1): 377-378.

[Full-Text](#)

Department of Obstetrics and Gynecology

This month, we focus on current research in bed rest in pregnancy. Dr. Lorenz discusses four recent publications, and each is concluded with a "bottom line" that is the take-home message. The complete reference for each can be found in on this page, along with direct links to the abstracts. (copyright) 2014 by The American College of Obstetricians and Gynecologists. Published by Lippincott Williams & Wilkins.

Louwens LM, **Raofi V**, **Cohn S** and **Koffron A** (2014). "When surgical shunting is the best or only option: A case series." *HPB* 16: 65.

[Full-Text](#)

Department of Surgery

Background: Surgical portosystemic shunting (PSS) has become a less frequently used modality for control of portal hypertension (PHTN) in the era of transjugular intrahepatic portosystemic shunting (TIPS). In certain instances, however, TIPS may not be anatomically feasible or the best long-term management strategy. Objectives: To present a series of patients highlighting scenarios where surgical PSS may have a more favorable outcome compared to TIPS placement or medical management, reinforcing the role of surgical shunting in the post-TIPS era. Methods: Aretrospective review of surgical PSS performed at a tertiary care center from 2009-2011. Results: Six cases were selected to highlight circumstances wherein surgical shunting was the preferred or only available modality in complicated benign disease states. The underlying etiologies of PHTN included nodular regenerative hyperplasia, polycystic liver disease, chronic pancreatitis, non-alcoholic steatohepatitis, and alcoholic pancreatitis with left-sided PHTN. Detailed preoperative and operative descriptions provide enhanced understanding of the benefits of PSS in these situations. Conclusion: In this series, we highlight two groups where surgical shunting may still be the preferred, and in some cases the only approach. The first group is patients who will need long term patency of their shunt

given the fact that they are either well compensated cirrhotics or have non-cirrhotic portal hypertension. The second, and probably more important, are the patients with underlying aberrant anatomy which precludes or cannot be completely addressed by TIPS placement. We hope that by presenting these cases, we have reinforced the need to consider surgical shunting in appropriately selected patients. (Table Presented).

Lundbye J, Adams MP, **Sawyer K** and Klein D (2014). "Targeted temperature management in nursing care." Therapeutic Hypothermia and Temperature Management 4(3): 111-114.

[Request Form](#)

Department of Emergency Medicine

Madan I, Redman M, Bronsteen R, Bahado-Singh RO and Goncalves LF (2014). "The genetic sonogram." Fetal and Maternal Medicine Review 25(1): 12-41.

[Full-Text](#)

Department of Obstetrics and Gynecology

Maerz T, Newton MD, Kristof K, Motovylyak O, Fischgrund JS, Park DK and Baker KC (2014). "Three-dimensional characterization of in vivo intervertebral disc degeneration using EPIC-muCT." Osteoarthritis and Cartilage. ePub Ahead of Print.

[Full-Text](#)

Department of Surgery

Department of Obstetrics and Gynecology

Department of Orthopedic Surgery

OBJECTIVE: Small animal models are commonly employed to study progression of and potential treatment techniques for degenerative disc disease (DDD), but assessment using conventional imaging techniques is challenging due to resolution. The objective of this study was to employ equilibrium partitioning of an ionic contrast agent micro computed tomography (EPIC - muCT) to map three-dimensional (3D) degenerative changes in the rabbit intervertebral disc (IVD). MATERIALS AND METHODS: In vivo degeneration was induced surgically in 12 New Zealand White rabbits via percutaneous annular puncture and percutaneous nucleotomy. IVDs were harvested after 3 and 6 weeks. EPIC-muCT imaging was performed on fresh, IVDs before and after formalin fixation, and 3D IVD volumes were segmented. IVDs were histologically stained with Safranin-O/Fast-Green and Hematoxylin & Eosin (H&E). EPIC-muCT attenuation and 3D morphological measurements were assessed in healthy and degenerate IVDs and compared to qualitative grading and disc height measurement from histology. RESULTS: EPIC-muCT caused pronounced contrast enhancement of the IVD. Annular puncture and nucleotomy produced mild and severe degenerative changes, respectively. IVD attenuation following contrast enhancement increased significantly in nucleotomized discs at 3 and 6 weeks. IVD attenuation correlated significantly with histologic score and disc height measurements. Disc height decreased most extensively in the posterior and lateral aspects of the IVD. 3D morphological measurements correlated strongly to IVD attenuation and were more sensitive to degenerative changes than histologic measurements. Formalin fixation reduced the attenuation of IVDs by approximately 10%. CONCLUSION: EPIC-muCT is sensitive to in vivo DDD induced by nucleotomy and provides a high resolution 3D method for mapping degenerative changes in rabbit IVDs.

Maisels MJ, Clune S, Coleman K, Gendelman B, Kendall A, McManus S and Smyth M (2014). "The natural history of jaundice in predominantly breastfed infants." Pediatrics 134(2): e340-e345.

[Full-Text](#)

Department of Pediatrics

BACKGROUND AND OBJECTIVES: Breastfed newborns are more likely to develop prolonged hyperbilirubinemia than those fed formula, but the prevalence of prolonged hyperbilirubinemia in a largely white, North American breastfed population is unknown. In this population, we documented the natural history of jaundice and the prevalence of prolonged hyperbilirubinemia, and we evaluated the utility of assessing the cephalocaudal progression of jaundice in office-based practices. METHODS: We measured transcutaneous bilirubin (TcB) levels during the first month in 1044 predominantly breastfed infants

(greater-than or equal to)35 weeks of gestation and assigned a cephalocaudal zone score to each infant at the time of the TcB measurement. RESULTS: TcB level was (greater-than or equal to)5 mg/dL in 43% of infants at age 21 (plus or minus) 3 days and 34% were clinically jaundiced. At 28 (plus or minus) 3 days, the TcB was (greater-than or equal to)5 mg/dL in 34% and 21% were jaundiced. There was a strong correlation between the TcB level and the jaundice zone score, but there was a wide range of TcB levels associated with each score. CONCLUSIONS: Practitioners can be reassured that it is normal for 20% to 30% of predominantly breastfed newborns to be jaundiced at age 3 to 4 weeks and for 30% to 40% of these infants to have bilirubin levels (greater-than or equal to)5 mg/dL. The jaundice zone score does not provide an accurate assessment of the bilirubin level, but a score of zero (complete absence of jaundice) suggests that the level is unlikely to be >12.9 mg/dL, whereas a score of (greater-than or equal to)4 usually predicts a level of (greater-than or equal to)10 mg/dL. Copyright (copyright) 2014 by the American Academy of Pediatrics.

Maisels MJ and Watchko JF (2014). "Introduction." Seminars in Perinatology 38(7): 395-396.

[Full-Text](#)

Department of Pediatrics

Manickam P, Krishnamoorthi R, Kanaan Z, Gunasekaran PK and **Cappell MS** (2014). "Prognostic implications of recipient or donor hepatitis B seropositivity in thoracic transplantation: Analysis of 426 hepatitis B surface antigen-positive recipients." Transplant Infectious Disease 16(4): 597-604.

[Full-Text](#)

Department of Internal Medicine

Background: Prognostic data on survival of hepatitis B surface antigen-positive (HBsAg+) recipients and of hepatitis B core antibody-positive (HBcAb+) donors are limited in the thoracic transplantation (TT) cohort. Improved understanding of risks could potentially expand the recipient and donor pools. Methods: Post-hoc analysis of limited-access dataset of the United Network for Organ Sharing database from January 2000-September 2010 was performed. Analyses were performed for all TT, including single and bilateral lung, orthotopic heart, and simultaneous heart-lung transplants. The primary analyzed outcome was overall survival. A Cox proportional multivariate hazards model was used to adjust for significant risk predictors. Results: Of 24,817 patients included, 426 recipients were HBsAg+, of whom 106 (25%) died during a mean follow-up of 3.6 years. On multivariate analysis, recipient HBsAg+ (hazard ratio [HR] = 0.88, 95% confidence interval [CI]: 0.69-1.32; P = 0.80), and donor HBcAb+ (HR = 0.91, 95% CI: 0.68-1.22; P = 0.53) were not associated with increased overall mortality in the entire TT cohort, with similar results for each individual transplant cohort. Unadjusted survival analysis using Kaplan-Meier curves in individual transplant cohorts did not show significant differences between HBsAg+ and HBsAg- recipients. No statistically significant differences were found between causes of mortality in the 2 groups. Conclusion: HBsAg+ status of recipients or HBcAb+ status of donors does not significantly affect overall survival of TT recipients. These data add to the scant literature on this subject and could potentially increase the donor and recipient pools. (copyright) 2014 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.

Marina O, **Gustafson GS, Brabbins DS, Chen PY**, Wallace M, Ye H and **Krauss DJ** (2014). "Prognostic value of diagnostic prostate biopsy percent carcinoma volume (PCV) and percent positive cores (PPC) on treatment outcomes following radiation therapy (RT): A retrospective analysis of 1731 patients." International Journal of Radiation Oncology Biology Physics 90(1): S404-S405.

[Request Form](#)

Department of Radiation Oncology

Purpose/Objective(s): PPC and PCV are prognostic of outcomes after radiation therapy for prostate cancer, based on smaller series which included non-contemporary diagnostic biopsies (<6 core) or standard dose RT. Materials/Methods: Localized prostate cancer patients treated 1997-2012 with dose-escalated high-dose-rate brachytherapy boost (HDRB, 42-46 Gy external beam RT and 19-23 Gy/2 fx boost) or off-line image-guided adaptive RT (IGRT, 73.8-82.8 Gy) were reviewed. Exclusion criteria were <6 biopsy cores, insufficient pathology detail, or <0.5 y follow-up. Outcomes were compared by cumulative incidence (Gray's) and competing risks regression (Fine and Gray's). Results: Median clinical and PSA follow-up were 4.9 y

(0.5-15.1) and 3.4 y (0.5-14.5). A median of 10 (6-47) biopsy cores were sampled. ROC curves identified PPC(greater-than or equal to)36% and PCV(greater-than or equal to)16.5% as prognostic of Phoenix biochemical control (BC). Median (range) or percentages are shown (Table). Both cutoffs selected for worse pre-treatment characteristics and predicted 8-year BC (93% vs 80% by PPC, and 93% vs 77% by PCV cutoff, $p < 0.001$) and 10-year cause specific survival (CSS) (98% vs 96% by PPC, 99% vs 95% by PCV cutoff, $p \leq 0.01$). For BC multivariate analysis (MVA), higher PPC ($p = .04$), PCV ($p = .009$), PSA ($p < .001$), and risk group ($p < .005$), lower dose (< 77.4 Gy IGRT, $p = .03$), and an interaction of PPC, PCV and PSA ($p < .001$) were prognostic. For CSS MVA, higher PCV ($p < .001$), PSA ($p = .002$), risk group ($p < .001$), and an interaction of PCV and PSA ($p = .002$) were prognostic; PPC was prognostic only with PCV excluded ($p = .008$). Conclusions: PPC and PCV are similarly predictive of BC, while PCV is a stronger predictor of CSS, following contemporary prostate cancer RT. (Table Presented).

Marina O, Wloch J, Jawad MS, Mangona VS, **Grills IS, Yan D** and **Ionascu D** (2014). "On the dynamic variability of abdominal compression plate use on tumor motion during lung stereotactic body radiation therapy." International Journal of Radiation Oncology Biology Physics 90(1): S140-S141.

[Request Form](#)

Department of Radiation Oncology

Purpose/Objective(s): To determine the dynamic (4D) daily variability of lung tumors when an abdominal compression plate (CP) is used in the clinic in terms of amplitude change of lung tumor motion during stereotactic body radiation therapy (SBRT). CP use may add additional patient setup variability due to device positioning and pressure, and secondarily by emphasizing the effect of physiological states such as gastric filling. Materials/Methods: Patients who underwent 4D CT simulations and daily 4D cone-beam CTs (4DCBCT) before and after each treatment delivery for lung SBRT between 2011-2013 were reviewed. Among 47 total patients, there were 13 patients treated with SBRT with CP used and 36 with no CP used. There were 49 4DCT and 445 4DCBCT performed. CP use was at the discretion of the treating physician, selected when motion amplitude > 2.0 cm was noted and the patient tolerated its use. All patients underwent a 4DCBCT on the day of verification, and subsequently received 48 Gy in 4 or 45-60 Gy in 5 treatment fractions. The amplitude (A) of tumor motion along each direction ($A_x =$ lateral, $A_y =$ sup-inf, $A_z =$ ant-post) within each 4DCT/4DCBCT, and standard deviation (SD) of the tumor position with respect to the mean position used for treatment setup, were determined. Due to different numbers of repeat measures of 4DCBCT for each patient and an unbalanced number of patients, a general linear model (GLM) was used to identify significant predictors of variability. Results: Median patient age was 76 years (range 43-91) and 51% were male. Smokers (84% of patients) had a median 53 pack-year (10-160) smoking history. Median body mass index was 26 (17-39). Median tumor size was 2.4 cm (1.2- 4.2). The 4DCT A_x , A_y and A_z did not differ between groups, with a median of 0.15 cm (0.05-0.42) vs 0.11 (0.03-0.38) ($p = 0.10$, Wilcoxon rank-sum), 0.58 (0.09-1.24) vs 0.32 (0.04-1.7) ($p = 0.08$), and 0.23 (0.07-0.38) vs 0.19 (0.04- 0.54) ($p = 0.35$), respectively. On univariate GLM, CP use is a significant ($p < 0.15$) in each respective GLM. CP is likewise not a significant predictor of SD when the respective simulation 4DCT amplitude is included (p greater-than or equal to 0.10). The change in amplitude (ΔA) between the pre- and post-treatment 4DCBCT were not predicted by CP use in x and y; ΔA_z , however, was positively and significantly related to CP use, on univariate ($p = 0.02$) and multivariate ($p = 0.03$) GLM. Conclusions: CP use to limit tumor motion leads to increased tumor motion variability along the AP (z) direction, the direction in which CP does not restrict thoracic motion, following delivery of SBRT, and therefore, intrafractionally. On the other hand, the CP modality does not significantly impact intra-fractional sup-inf or lateral motion. Moreover, CP device use, despite variability in positioning, pressure, and patient gastric state, does not seem to significantly affect treatment setup reproducibility.

Markel K, Webb M, Aggarwal A and **Long G** (2014). "Outcomes analysis of the pluripotential antecubital vein dialysis fistula." Journal of Vascular Surgery 59(6): 60S.

[Request Form](#)

Department of Surgery

Objectives: To study the single surgeon outcomes of pluripotential antecubital vein fistulas (PAF) for patients with borderline basilic and cephalic vein diameters. Methods: This is a retrospective analysis of a single

surgeon experience with 115 PAFs created from April 2004 to November 2011, using a prospectively maintained patient database. Primary outcome was time to fistula release (TR) for dialysis access. Secondary outcomes were 1-year primary and primary assisted patency. Patient comorbidities were recorded. Borderline veins were defined as diameters 3 to 4 mm. PAF was defined as an arteriovenous fistula in the antecubital fossa with outflow through the upper arm cephalic and basilic veins via the connecting median cubital vein. Results: Of 115 PAFs, 18 (15.7%) were released for dialysis access after the first-stage procedure; a second-stage procedure was required in 82 (71.3%). Forty-nine (59.8%) were converted to basilic vein transposition, and 33 (40.2%) were converted to selective cephalic vein outflow. A total of 84.3% (97 of 115) fistulas were released for use after a mean of 89 (plus or minus) 70 days after the definitive procedure. Eleven (9.6%) underwent a second index procedure due to thrombosis in (5), failure to mature (3), body habitus (1), diseased outflow vein (1), and ligation secondary to persistent seroma with arm swelling (1). There was one death (0.9%), one who refused second stage procedure (0.9%), and five lost to follow up (4.3%) from PAF creation. One-year follow-up was documented in 68% of patients (66 of 97). Primary 1-year patency was 36.4% (24 of 66); assisted 1-year patency was 100%. Conclusions: PAF is a reasonable strategy that yields an acceptable percentage with a functional dialysis fistula. A substantial fraction will require secondary conversion to single-vein outflow and endovascular intervention to maintain patency in the first year. Further study is indicated with larger cohorts and longer follow-up to corroborate these findings.

Martel J, Oteng R, Mould-Millman NK, Bell SA, Zakariah A, Oduro G, **Kowalenko T** and Donkor P (2014). "The development of sustainable emergency care in Ghana: Physician, nursing and prehospital care training initiatives." *Journal of Emergency Medicine* 47(4): 462-468.

[Full-Text](#)

Department of Emergency Medicine

Background Ghana's first Emergency Medicine residency and nursing training programs were initiated in 2009 and 2010, respectively, at Komfo Anokye Teaching Hospital in the city of Kumasi in association with Kwame Nkrumah University of Science and Technology and the Universities of Michigan and Utah. In addition, the National Ambulance Service was commissioned initially in 2004 and has developed to include both prehospital transport services in all regions of the country and Emergency Medical Technician training. Over a decade of domestic and international partnership has focused on making improvements in emergency care at a variety of institutional levels, culminating in the establishment of comprehensive emergency care training programs. Objective We describe the history and status of novel postgraduate emergency physician, nurse, and prehospital provider training programs as well as the prospect of creating a board certification process and formal continuing education program for practicing emergency physicians. Discussion Significant strides have been made in the development of emergency care and training in Ghana over the last decade, resulting in the first group of Specialist-level emergency physicians as of late 2012, as well as development of accredited emergency nursing curricula and continued expansion of a national Emergency Medical Service. Conclusion This work represents a significant move toward in-country development of sustainable, interdisciplinary, team-based emergency provider training programs designed to retain skilled health care workers in Ghana and may serve as a model for similar developing nations.

Matuszak SA, Baker EA, Stewart CM and Fortin PT (2014). "Missed peritalar injuries: an analysis of factors in cases of known delayed diagnosis and methods for improving identification." *Foot Ankle Spec* 7(5): 363-371.

[Full-Text](#)

Department of Orthopedic Surgery

Because of the complex anatomy of the foot, rarity of fractures of the foot, and subtle radiographic cues, foot injuries are commonly overlooked and mis/undiagnosed. This study seeks to investigate a patient population whose peritalar injuries, including fractures and dislocations, were missed on initial examination, in order to analyze factors of known, missed injuries and provide insight into methods for reducing the incidence of missed diagnoses. Surgical cases between January 1999 and May 2011 were queried and retrospectively reviewed to identify missed peritalar injuries. Of 1682 surgical cases reviewed, 27 patients with missed peritalar injury(ies), which were subsequently confirmed by imaging studies, were identified. Using the Orthopaedic Trauma Association classification, fracture and dislocation subtypes were classified. A

medical record review was performed to assess demographic and surgical data elements. In this study population, 7 types of peritalar injuries (talus, calcaneal, navicular, and cuboid fractures as well as subtalar, calcaneocuboid, and talonavicular joint dislocations) were diagnosed in 27 patients. All patients required surgical intervention. Talus fractures were the most commonly missed injury. In patients with multiple peritalar injuries, there was a strong correlation between talus and navicular fractures ($r = -0.60$; $P < .01$) as well as a moderate correlation between talus fractures and calcaneocuboid dislocations ($r = -0.46$; $P = .02$). The presence of a calcaneal fracture significantly decreased the time to definitive diagnosis ($P = .01$). Male patients' diagnoses were delayed an average of 324 days and females 105 days ($P = .04$). A moderate correlation was found between patient age at injury and time to diagnosis ($r = -0.47$; $P = .04$), with a decreased time to diagnosis as patient age increased. Significant factors were identified in this patient population, including patient sex and age, which may contribute to missed or delayed diagnosis in the clinical setting. Prompt and accurate diagnosis of peritalar injuries may improve long-term outcomes. LEVELS OF EVIDENCE: Care Management, Level V.

McCullough PA (2014). "Untitled." Reviews in Cardiovascular Medicine 15(2): 1.

[Request Form](#)

Department of Internal Medicine

Meyer K, Maitz A, Ye H, Manders M and **Grills IS** (2014). "Predictors of symptomatic edema after treatment of intracranial meningiomas with single-fraction stereotactic radiosurgery." International Journal of Radiation Oncology Biology Physics 90(1): S296.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): Stereotactic radiosurgery (SRS) provides a 10 year local control (LC) rate of up to 99% for intracranial meningiomas, but may be associated with higher post-treatment symptomatic edema rates. Prior reports have combined single and multi-fraction SRS when analyzing edema rates. The objective was to determine factors predictive of posttreatment edema after single fraction SRS alone to identify patients who may require either surgery or fractionated RT. Materials/Methods: Seventy-five patients with radiographic evidence of intracranial meningioma underwent gamma knife (GK) SRS alone at a single institution between 10/2007-7/2013. Those with prior surgical resection, radiation, multiple meningiomas or malignancy were excluded. All patients had pre- and post-GK MRIs, typically 6 mo, and 12 mo post- GK then annually thereafter; all pre- and post-GK MRIs were reviewed for analysis. Tumor volume (TV) was contoured on the GK treatment T1 Gdenhanced MRI; treatment volume (TxV), defined as the volume receiving the prescribed dose, was calculated. Peri-tumoral edema was defined as the T2 FLAIR or equivalent volume less both TV and any pre-GK edema. TV, TxV, max linear dimension, age, sex, location of tumor, and marginal dose were evaluated for association with edema and symptomatic edema using chi-square and t-test. Results: Median age was 65 years (41 - 90); 7 male and 68 female. Median follow-up was 22 mo (3 - 60 mo). Median TV was 3.2 cc (0.25 - 23.8 cc); median TxV was 5.2 cc (0.47 - 37.9 cc). The median marginal dose was 13 Gy (10 - 17 Gy) prescribed to a median isodose line of 50% (30- 60%). 33 patients (44%) had pre-GK symptoms attributed to tumor; 9 (12%) had pre-GK edema on MRI. Symptoms improved or resolved after GK in 45% of these patients. 25 patients (33%) developed post-GK edema. 9 (12%) were symptomatic; 5 (6.6%) were treated with steroids. One had resection for steroid-refractory symptoms. LC was 100%. On univariate analysis, increasing TV (OR = 1.2, $p < 0.001$), TxV (OR = 1.2, $p = 0.001$), and max linear dimension (OR = 1.8, $p = 0.01$) were associated with increased edema. There was no association for edema with or without symptoms for sex, location, or marginal dose. ROC analysis of tumor volume and edema found a cut point of 3.1 cc with sensitivity of 85% and specificity of 61%. Symptomatic edema was predicted by both TV ($p = 0.01$) and edema volume ($p < 0.001$), with an edema volume of 2.1 cc predicting for symptoms (sensitivity 89% and specificity 100%) and TV of 5.2 cc predicting for symptoms (sensitivity 73% and specificity 70%). Conclusions: Larger tumor and treatment volumes were associated with higher rates of edema after SRS. Tumor volume greater than 5.2 cc was associated with an increased risk of symptomatic edema and edema volumes of at least 2.1 cc were more likely to be symptomatic. Patients with tumors larger than this size should be advised of this risk with a consideration for alternative therapies.

Mi M, Stefaniak J and Afonso N (2014). "Community needs assessment to reach out to an underserved population." Medical Reference Services Quarterly 33(4): 375-390.

[Full-Text](#)

Medical Library

Department of Biomedical Sciences (OU)

A community-based participatory research project was conducted to identify health information needs of clients (an underserved population) at a homeless shelter. Staff at the shelter, medical students, and public librarians were sought as outreach partners; their needs and challenges in accessing health information resources to serve underserved populations were also assessed. The community needs assessment yielded results that helped shape a medical library's efforts in supporting medical students' service-learning activities related to humanistic education. The resulting data also informed library decisions on health information education outreach programs tailored to vulnerable, underserved populations and community partners serving the specific populations in the communities.

Millis MB and **Zaltz I** (2014). "Current perspectives on the pediatric hip: Selected topics in hip dysplasia, perthes disease, and chondrolysis: Synopsis of the hip subspecialty session at the POSNA Annual Meeting, May 1, 2013, Toronto." Journal of Pediatric Orthopedics 34 Suppl 1: S36-S43.

[Full-Text](#)

Department of Orthopedic Surgery

The following are proceedings from the Hip Breakout Session held at the 2013 annual meeting of the Pediatric Orthopaedic Society of North America in Toronto, Canada. The organizer's goal of the meeting was to gather experts with years of clinical experience to discuss topics based upon both experience and current clinical evidence. The topics that were selected represented the most commonly encountered pathology where there are wide variations of clinical practice. The invited speakers were asked to summarize both their clinical experience and the current scientific evidence and to summarize areas that require further scientific investigation.

Mogrovejo E, **Nojkov B, Cannon M and Cappell MS** (2014). "Endoscopic hemoclips to immediately close gastric perforation from a failed attempt at PEG in a morbidly obese patient." Surgery for Obesity and Related Diseases 10(4): 757-758.

[Request Form](#)

Department of Internal Medicine

Muslimani A, Chisti MM, **Margolis J, Nadeau L, Ye H, Micale M, Huang J and Jaiyesimi I** (2014). "Pulmonary infiltrates in acute myeloid leukemia during induction treatment: How much do we know?" American Journal of Clinical Oncology: Cancer Clinical Trials 37(4): 377-383.

[Full-Text](#)

Department of Internal Medicine

Department of Pathology

BACKGROUND: During induction treatment, acute myeloid leukemia patients may develop pulmonary infiltrates due to infectious or noninfectious etiologies. The risk association and the clinical outcome of such pulmonary infiltrates are poorly characterized in the literature. **METHODS:** We retrospectively reviewed 363 cases of acute myeloid leukemia patients who received induction therapy as inpatients over a period of 11 years at William Beaumont Health System. Of these 363 patients, 120 developed pulmonary infiltrates during induction therapy, those patients were divided into 2 groups based on distribution of the infiltrate presenting as localized or diffuse in nature. Data on patients characteristics, leukemia subtype, cytogenetic risk, microorganism type, white blood cell count at diagnosis, neutrophil count at the time the infiltrate was reported, response to antibiotic and/or antifungal therapy, using respiratory support, and mortality rate were retrieved through chart review. **RESULTS:** Thirty-three percent of patients developed pulmonary infiltrates during their induction therapy. Sixty-three patients (52.5%) had a localized infiltrates and 57 patients (47.5%) had diffuse infiltrates. Of the 120 patients with pulmonary infiltrates, 48 (40%) had at least 1 pathogenic

microorganism identified, and 58 (48.7%) required intubation and ventilatory support. Patients with localized pulmonary infiltrates were more likely to have positive pathogenic microorganisms (68.3% vs. 8.8%, $P < 0.001$), to be neutropenic (96.8% vs. 21%, $P < 0.001$), and tended to have potentially reversible infiltrates after treatment (87.3% vs. 21%, $P < 0.001$). Whereas patients with diffuse infiltrates were more likely to require intubation (78.9% vs. 21%, $P < 0.001$), to have leukocytosis (white blood cell > 100 billions/L) at diagnosis (54.4% vs. 0%, $P < 0.001$), and had a higher mortality rate (70.2% vs. 9.5%, $P < 0.001$). CONCLUSIONS: The radiologic patterns of pulmonary infiltrates showed specific etiological and prognostic associations. Diffuse infiltrates are an unfavorable characteristic with overall dismal outcome. Copyright (copyright) 2012 by Lippincott Williams & Wilkins.

Nguyen PL, Aizer A, Assimos DG, D'Amico AV, Frank SJ, Gottschalk AR, **Gustafson GS**, Hsu ICJ, McLaughlin PW, Merrick G, Rosenthal SA, Showalter TN, Taira AV, Vapiwala N, Yamada Y and Davis BJ (2014). "ACR appropriateness criteria (R) definitive external-beam irradiation in stage T1 and T2 prostate cancer." *American Journal of Clinical Oncology-Cancer Clinical Trials* 37(3): 278-288.

[Full-Text](#)

Department of Radiation Oncology

Purpose: To present the most updated American College of Radiology consensus guidelines formed from an expert panel on the appropriate use of external-beam radiation to manage stage T1 and T2 prostate cancer. Methods: The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed every 2 years by a multidisciplinary expert panel. The guideline development and review include an extensive analysis of current medical literature from peer-reviewed journals and the application of a well-established consensus methodology (modified Delphi) to rate the appropriateness of imaging and treatment procedures by the panel. In those instances where evidence is lacking or not definitive, expert opinion may be used to recommend imaging or treatment. Results: The panel summarized the most recent and relevant literature on the topic and voted on 3 clinical variants illustrating the appropriate dose, techniques, and use of adjuvant hormone therapy with external-beam radiation for low-risk, intermediate-risk, and high-risk prostate cancer. Numerical rating and commentary reflecting the panel consensus was given for each treatment approach in each variant. Conclusions: External-beam radiation is a key component of the curative management of T1 and T2 prostate cancer. By combining the most recent medical literature and expert opinion, this guideline can aid clinicians in the appropriate use of external-beam radiation for prostate cancer.

Nirmal J, **Tyagi P**, Chuang YC, Lee WC, Yoshimura N, Huang CC, Rajaganapathy B and **Chancellor MB** (2014). "Functional and molecular characterization of hyposensitive underactive bladder tissue and urine in streptozotocin-induced diabetic rat." *PLoS One* 9(7): e102644.

[Full-Text](#)

Department of Urology

Background: The functional and molecular alterations of nerve growth factor (NGF) and Prostaglandin E2 (PGE2) and its receptors were studied in bladder and urine in streptozotocin (STZ)-induced diabetic rats. Methodology/Principal Findings: Diabetes mellitus was induced with a single dose of 45 mg/kg STZ Intraperitoneally (i.p) in female Sprague-Dawley rats. Continuous cystometrograms were performed on control rats and STZ treated rats at week 4 or 12 under urethane anesthesia. Bladder was then harvested for histology, expression of EP receptors and NGF by western blotting, PGE2 levels by ELISA, and detection of apoptosis by TUNEL staining. In addition, 4-hr urine was collected from all groups for urine levels of PGE2, and NGF assay. DM induced progressive increase of bladder weight, urine production, intercontraction interval (ICI) and residual urine in a time dependent fashion. Upregulation of Prostaglandin E receptor (EP)1 and EP3 receptors and downregulation of NGF expression, increase in urine NGF and decrease levels of urine PGE2 at week 12 was observed. The decrease in ICI by intravesical instillation of PGE2 was by 51% in control rats and 31.4% in DM group at week 12. Conclusions/Significance: DM induced hyposensitive underactive bladder which is characterized by increased inflammatory reaction, apoptosis, urine NGF levels, upregulation of EP1 and EP3 receptors and decreased bladder NGF and urine PGE2. The data suggest that EP3 receptor are potential targets in the treatment of diabetes induced underactive bladder. (copyright) 2014 Nirmal et al.

Ogunyemi T, Siadat MR, **Diokno AC**, Arslanturk S and Killinger K (2014). "Bayesian prediction of incontinence among older women using an experimental design template." ICISA 2014 - 2014 5th International Conference on Information Science and Applications. ePub Ahead of Print.

[Request Form](#)

Department of Urology

In this study, a Bayesian predictor of urinary incontinence (UI) is devised for screening older women. Risk factors identified from an epidemiological survey data as significant for UI, are utilized. The proposed Bayesian method combines an experimental design template with relevant information to construct a predictive index in terms of posterior probabilities. The computations are carried out on a longitudinal data called the Medical, Epidemiological and Social Aspects of Aging (MESA). The index is applied to the baseline and follow-up portions of the MESA data. The results show that, the percentage of the absolute relative change between the prior and posterior probabilities can be used as a decision tool to make conclusions on credibility of the class labels on continence and incontinence. The proposed index can be applied for immediate screening and for predicting future urinary incontinence in older women of comparable demographics as those presented in the MESA data. © 2014 IEEE.

Okada H, **Tyagi P**, Kawamorita N, Majima T, **Chancellor MB** and Yoshimura N (2014). "A novel animal model of chronic urothelial injury and bladder pain hypersensitivity induced by intermittent infusion of protamine sulphate into the bladder in rats: The involvement of prostaglandin E2 and EP1 receptor activation." Neurourology and Urodynamics 33(6): 800-801.

[Full-Text](#)

Department of Urology

O'Keefe JH, **Franklin B** and Lavie CJ (2014). "Exercising for health and longevity vs peak performance: Different regimens for different goals." Mayo Clinic Proceedings 89(9): 1171-1175.

[Request Form](#)

Department of Internal Medicine

Pamplona MC, **Ysunza A** and Morales S (2014). "Strategies for treating compensatory articulation in patients with cleft palate." International Journal of Biomedical Science 10(1): 43-51.

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Department of Physical Medicine and Rehabilitation

Patients with cleft palate frequently show compensatory articulation (CA). CA requires a prolonged period of speech intervention. Some scaffolding strategies can be useful for correcting placement and manner of articulation in these cases. The purpose of this paper was to study whether the use of specific strategies of speech pathology can be more effective if applied according to the level of severity of CA. Ninety patients with CA were studied in two groups. One group was treated using strategies specific for their level of severity of articulation, whereas in the other group all strategies were used indistinctively. The degree of severity of CA was compared at the end of the speech intervention. After the speech therapy intervention, the group of patients in which the strategies were used selectively, showed a significantly greater decrease in the severity of CA, as compared with the patients in whom all the strategies were used indistinctively. An assessment of the severity of CA can be useful for selecting the strategies, which can be more effective for correcting the compensatory errors. (copyright) 2014 Maria del Carmen Pamplona et al.

Parish K and **Mulhem E** (2014). "What is the appropriate duration of treatment for bacteremia from a UTI?" Evidence-Based Practice 17(9): 8-9.

[Request Form](#)

Department of Family Medicine

Peers S, Moravek JE, Budge MD, Newton MD, **Kurdziel MD, Baker KC** and **Wiater JM** (2014). "Wear rates of highly cross-linked polyethylene humeral liners subjected to alternating cycles of glenohumeral flexion and abduction." Journal of Shoulder and Elbow Surgery. ePub Ahead of Print.

[Full-Text](#)

Department of Surgery

Department of Orthopedic Surgery

Background: Although short-term outcomes of reverse total shoulder arthroplasty have been promising, long-term success may be limited due to device-specific complications, including scapular notching. Scapular notching has been explained primarily as mechanical erosion; however, the generation of wear debris may lead to further biologic changes contributing to the severity of scapular notching. Methods: A 12-station hip simulator was converted to a reverse total shoulder arthroplasty wear simulator subjecting conventional and highly cross-linked ultra-high-molecular-weight polyethylene humeral liners to 5 million cycles of alternating abduction-adduction and flexion-extension loading profiles. Results: Highly cross-linked polyethylene liners (36.5(plus or minus)10.0mm³/million cycle) exhibited significantly lower volumetric wear rates compared with conventional polyethylene liners (83.6(plus or minus)20.6mm³/million cycle; P<.001). The flexion-extension loading profile exhibited significantly higher wear rates for conventional (P<.001) and highly cross-linked polyethylene (P<.001) compared with the abduction-adduction loading profile. Highly cross-linked wear particles had an equivalent circle diameter significantly smaller than wear particles from conventional polyethylene (P<.001). Conclusions: Highly cross-linked polyethylene liners significantly reduced polyethylene wear and subsequent particle generation. More favorable wear properties with the use of highly cross-linked polyethylene may lead to increased device longevity and fewer complications but must be weighed against the effect of reduced mechanical properties. (copyright) 2014 Journal of Shoulder and Elbow Surgery Board of Trustees.

Perez AG, Lopez XH, Jimenez VMV, Martinez AM and **Ysunza PA** (2014). "Synchronous electrical stimulation of laryngeal muscles: An alternative for enhancing recovery of unilateral recurrent laryngeal nerve paralysis." Journal of Voice 28(4): 7.

[Full-Text](#)

Department of Physical Medicine and Rehabilitation

Background. Although electrical stimulation of the larynx has been widely studied for treating voice disorders, its effectiveness has not been assessed under safety and comfortable conditions. This article describes design, theoretical issues, and preliminary evaluation of an innovative system for transdermal electrical stimulation of the larynx. The proposed design includes synchronization of electrical stimuli with laryngeal neuromuscular activity. Objective. To study whether synchronous electrical stimulation of the larynx could be helpful for improving voice quality in patients with dysphonia due to unilateral recurrent laryngeal nerve paralysis (URLNP). Materials and Methods. A 3-year prospective study was carried out at the Instituto Nacional de Rehabilitacion in the Mexico City. Ten patients were subjected to transdermal current electrical stimulation synchronized with the fundamental frequency of the vibration of the vocal folds during phonation. The stimulation was triggered during the phase of maximum glottal occlusion. A complete acoustic voice analysis was performed before and after the period of electrical stimulation. Results. Acoustic analysis revealed significant improvements in all parameters after the stimulation period. Conclusion. Transdermal synchronous electrical stimulation of vocal folds seems to be a safe and reliable procedure for enhancing voice quality in patients with (URLNP).

Pershad A, Fraij G, Massaro JM, David SW, Kleiman NS, Denktas AE, Wilson BH, **Dixon SR**, Ohman EM, Douglas PS, Moses JW and O'Neill WW (2014). "Comparison of the use of hemodynamic support in patients (greater-than or equal to)80 years versus patients <80 years during high-risk percutaneous coronary interventions (from the multicenter protect II randomized study)." American Journal of Cardiology 114(5): 657-664.

[Full-Text](#)

Department of Internal Medicine

The outcomes of hemodynamic support during high-risk percutaneous coronary intervention in the very elderly are unknown. We sought to compare outcomes between the patients (greater-than or equal to)80

years versus patients <80 years enrolled in the PROTECT II (Prospective Randomized Clinical Trial of Hemodynamic Support with the Impella 2.5 versus Intra-Aortic Balloon Pump in Patients undergoing High Risk Percutaneous Coronary Intervention) randomized trial. Patients who underwent high-risk percutaneous coronary intervention with an unprotected left main or last patent conduit and a left ventricular ejection fraction (less-than or equal to)35% or with 3-vessel disease and a left ventricular ejection fraction (less-than or equal to)30% were randomized to receive an intra-aortic balloon pump or the Impella 2.5; 90-day (or the longest follow-up) outcomes were compared between patients (greater-than or equal to)80 years (n = 59) and patients <80 years (n = 368). At 90 days, the composite end point of major adverse events and major adverse cerebral and cardiac events were similar between patients (greater-than or equal to)80 and <80 years (45.6% vs 44.1%, p = 0.823, and 23.7% vs 26.8%, p = 0.622, respectively). There were no differences in death, stroke, or myocardial infarction rates between the 2 groups, but fewer repeat revascularization procedures were required in patients (greater-than or equal to)80 years (1.7% vs 10.4%, p = 0.032). Bleeding and vascular complication rates were low and comparable between the 2 age groups (3.4% vs 2.4%, p = 0.671, and 6.8% vs 5.4%, p = 0.677, respectively). Multivariate analysis confirmed that age was not an independent predictor of major adverse events (odds ratio = 1.031, 95% confidence interval 0.459-2.315, p = 0.941), whereas Impella 2.5 was an independent predictor for improved outcomes irrespective of age (odds ratio = 0.601, 95% confidence interval 0.391-0.923, p = 0.020). In conclusion, the use of percutaneous circulatory support is reasonable and feasible in a selected octogenarian population with similar outcomes as those of younger selected patients. Irrespective of age, the use of Impella 2.5 was an independent predictor of favorable outcomes. (copyright) 2014 Elsevier Inc. All rights reserved.

Peters KM, Hasenau D, Killinger KA, **Chancellor MB**, Anthony M and Kaufman J (2014). "Liposomal bladder instillations for IC/BPS: An open-label clinical evaluation." International Urology and Nephrology. ePub Ahead of Print.
[Full-Text](#)

Department of Urology

PURPOSE: Intravesical instillation of liposomes is a potentially new therapeutic option for subjects with interstitial cystitis/bladder pain syndrome (IC/BPS). The aim of this study was to explore the safety and clinical outcomes of 4 weekly instillations of sphingomyelin liposomes in an open-label cohort of subjects with IC/BPS. **METHODS:** Fourteen symptomatic IC/BPS subjects were treated with intravesical liposomes once a week for 4 weeks. Safety measurements included laboratory specimen collection, vital signs, post-void residual, and assessment of adverse events (AEs). Efficacy measurements included pain visual analog scales (VAS), voiding diaries, global response assessments (GRAs), and O'Leary-Sant Interstitial Cystitis Symptom and Problem Indices (ICSI and ICPI). **RESULTS:** No treatment-related AEs were reported at any time over the course of the study. Urgency VAS scores significantly decreased at 4 weeks (p = 0.0029) and 8 weeks (p = 0.0112) post-treatment. Pain VAS scores significantly decreased at 4 weeks post-treatment (p = 0.0073). Combined ICSI and ICPI scores improved significantly at 4 and 8 weeks (p = 0.002 for both time points) post-treatment. Responses to GRA showed improvement at 4 weeks post-instillation. No significant decrease in urinary frequency was found. **CONCLUSIONS:** Sphingomyelin liposome instillations were well tolerated in subjects with IC/BPS with no AEs attributed to the test article. Treatment was associated with improvements in pain, urinary urgency, and overall symptom scores. Placebo-controlled clinical trials are needed to assess this potential therapy for IC/BPS.

Peters KM, Killinger KA, **Jaeger C** and **Chen C** (2014). "Pilot study exploring chronic pudendal neuromodulation as a treatment option for pain associated with pudendal neuralgia." LUTS: Lower Urinary Tract Symptoms. ePub Ahead of Print.

[Full-Text](#)

Department of Urology

OUWB Medical Student Author

Department of Pediatrics

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 54.8years, 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) 2.95years: 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) 4.42years 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. (copyright) 2014 Wiley Publishing Asia Pty Ltd.

Raff GL, Chinnaiyan KM, Cury RC, Garcia MT, Hecht HS, Hollander JE, O'Neil B, Taylor AJ and Hoffmann U (2014). "SCCT guidelines on the use of coronary computed tomographic angiography for patients presenting with acute chest pain to the emergency department: A report of the Society of Cardiovascular Computed Tomography Guidelines Committee." Journal of Cardiovascular Computed Tomography 8(4): 254-271.

[Full-Text](#)

Department of Internal Medicine

Rice CM, Yadav S, **Boyanton B**, Subedi P and **Band J** (2014). "A creeping suspicion." New England Journal of Medicine 371(1): 68-73.

[Full-Text](#)

Department of Pathology

Department of Internal Medicine

Rodenbaugh HR, Lujan HL, **Rodenbaugh DW** and DiCarlo SE (2014). "Having fun and accepting challenges are natural instincts: jigsaw puzzles to challenge students and test their abilities while having fun!" Advances in Physiology Education 38(2): 185-186.

[Full-Text](#)

Department of Biomedical Sciences (OU)

Sacks RL, **Franklin B**, **Boura J** and Van Loon J (2014). "Accuracy of the heart rate index equation to assess oxygen consumption in obese patients." Medicine and Science in Sports and Exercise 46(5): 169-170.

[Full-Text](#)

Department of Internal Medicine

Department of Biomedical Sciences (BHS)

Saith SA, Brock D and Daaleman T (2014). "An exploratory study of peer support and advance care planning in African American elders with serious illness." Journal of the American Geriatrics Society 62: S279.

[Full-Text](#)

OUWB Medical Student Author

Background: Advance care planning (ACP) - the process of reflection, discussion, and communication of treatment preferences prior to the end-of-life - is a major goal of quality end-of-life care, but the process is often difficult to initiate and complete in minority populations. Interventions to enhance ACP have been limited; however, a peer mentoring approach, that incorporates community members who work in association with health care systems and share ethnicity, language, and socioeconomic status with their mentees, may be an effective strategy for African-American patients. Peer mentors enhance linkages to care and attend to the dynamic and evolving conditions associated with chronic illness by sharing a knowledge and an experience that others, including professional health care staff, do not have. We explored the

feasibility of peer support ACP interventions in community dwelling African American elders with serious chronic illness and their caregivers. Methods: Qualitative semi-structured interviews and editing analysis of community-dwelling African-American elders and caregivers in North Carolina Results: There were several themes that were identified. First, participants and their caregivers seemed to recognize the importance of advance care planning and were generally receptive to the idea of a peer support system even if there was no need for additional help in their particular situation. Participants had varied recommendations for the preferred peers and the frequency of communication and meetings, but agreed that it was important to involve faith communities and to make the meeting locations accessible, such as homes or churches. Finally, some participants were cautious of peer support due to a fear of loss of confidentiality or a fear of discussing terminal care and advance wishes. Conclusions: Preliminary results suggest that seriously ill African American elders are mixed about the feasibility of peer support to help them with advance care planning.

Sams S, Grichnik K and **Soto R** (2014). "Preoperative evaluation of the vascular surgery patient." [Anesthesiology Clinics](#) 32(3): 599-614.

[Request Form](#)

Department of Anesthesiology

Patients undergoing vascular surgery present a myriad of perioperative challenges due to the complex comorbidities affecting them in conjunction with high-risk surgical procedures. Additionally, advances in endovascular technology have enabled surgical procedures to be performed on patients who would not have been considered surgical candidates in the past. This combination of increasing patient morbidity and evolving surgical technique requires a well-planned preoperative assessment and close communication with surgical and perioperative colleagues. This article outlines an appropriate approach by first considering each organ system, followed by review of considerations unique to various surgical procedures, and then an overall assessment of risk. (copyright) 2014 Elsevier Inc.

Seymour EM, Warber SM, Kirakosyan A, Noon KR, Gillespie B, **Uhley VE**, Wunder J, Urcuyo DE, Kaufman PB and Bolling SF (2014). "Anthocyanin pharmacokinetics and dose-dependent plasma antioxidant pharmacodynamics following whole tart cherry intake in healthy humans." [Journal of Functional Foods](#). ePub Ahead of Print.

[Full-Text](#)

Department of Biomedical Sciences (OU)

Anthocyanin-rich tart cherries may impart health benefits for oxidative stress and inflammation. Anthocyanin (ACN) pharmacokinetic studies often sample plasma and urine within hours of ingestion; these approaches do not reveal enterohepatic metabolites that may be critical for pharmacodynamic bioactivity. This study investigated ACN pharmacokinetics in healthy humans following intake of Montmorency tart cherries (*Prunus cerasus*). Using a within-subject crossover design, subjects (n = 12) ingested whole frozen tart cherries (45 or 90 cherries), and blood and urine samples were collected over 12 hours. LC-MS/MS identified two unmodified ACN in plasma and two ACN metabolites in urine. Intake of 45 cherries caused a biphasic antioxidant response, while 90 cherries caused a prolonged elevation over the 12 h period. The broad antioxidant peak beyond 8 h suggests that enterohepatic metabolites contribute to antioxidant pharmacodynamics. These findings should encourage extended pharmacokinetic studies with ACN-rich foods to reveal their breadth of bioavailability and bioactivity. © 2014.

Smythe MA, Forsyth LL, Warkentin TE, **Smith MD**, Sheppard JAI and Shannon F (2014). "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](#). ePub Ahead of Print.

[Request Form](#)

Department of Biomedical Sciences (BHS)

Department of Pediatrics

Smythe MA, Koerber JM, **Forsyth LL** and Tuchscherer RM (2014). "Implications of heparin-induced thrombocytopenia overdiagnosis." [Annals of Pharmacotherapy](#) 48(10): 1394-1395.

[Request Form](#)

Department of Biomedical Sciences (BHS)

Spottswood SE, Pfluger T, Bartold SP, Brandon D, Burchell N, Delbeke D, **Fink-Bennett DM**, Hodges PK, Jolles PR, Lassmann M, Maurer AH, Seabold JE, Stabin MG, Treves ST and Vlajkovic M (2014). "SNMMI and EANM practice guideline for Meckel diverticulum scintigraphy 2.0." [Journal of Nuclear Medicine Technology](#) 42(3): 163-169.

[Request Form](#)

Department of Diagnostic Radiology and Molecular Imaging

Stone BM, Baschnagel AM, Thibodeau B, Fortier LE, Geddes T, Pruetz BL, Ketelsen BE, **Jury RP** and **Wilson GD** (2014). "Gene expression patterns in pancreatic neuroendocrine tumors suggest resistance to radiation therapy." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S768.

[Full-Text](#)

Department of Surgery

Department of Radiation Oncology

Purpose/Objective(s): The objective of this study was to examine the gene expression patterns of pancreatic neuroendocrine tumors (NET) compared to normal pancreatic tissue and pancreatic ductal adenocarcinomas (PDAC). Materials/Methods: Ten prospectively collected patient samples from each of the study groups (NETs, normal pancreatic tissue, and PDACs) were studied. Patients did not receive any type of neoadjuvant therapy prior to resection. RNA was isolated from fresh frozen tissue and gene expression analysis was performed using gene-expression microarrays. Differentially expressed genes were identified by ANOVA (p(plus or minus) 0.01) and 1.5-fold cutoff. Results: 1584 genes were found to be differentially expressed between the NET and normal pancreas tissue whilst only 171 differed in the PDAC group compared to controls. In the NETs, genes associated with apoptosis (BAX, JNK pathway), pathologic neovascularization (NOTCH1, HIF1A, EGFR, IGFBP3), cell cycle control (MYC, FOS, JUN, TGFB1) and DNA repair (TP53BP1, ABCB1, GADD45G, XRCC1, EGR1, CDK2, CCNG1, CDK6) were represented whilst in the PDACs a different set of genes associated with apoptosis (BCL2, CASP8, CASP3, APAF1) and cell cycle control (DNA replication pathway) were identified. Interestingly, relatively few genes associated with pathologic neovascularization were found to be deregulated in PDACs (6 genes) compared to NETs (37 genes). Similarly, relatively few genes associated with DNA repair were found to be deregulated in PDACs (11 genes) compared to NETs (118 genes). Several growth factor-related expression target pathways including the fibroblast growth factor 2/signal transducers and activators of transcription (FGF2/ STAT) were highly regulated in both NETs and PDACs but they were universally downregulated in NETs and upregulated in PDACs. Conclusions: In keeping with traditional thinking, this study suggests pancreatic neuroendocrine tumors are relatively radioresistant. This is supported by our findings of numerous upregulated genes associated with DNA repair and down regulation of genes associated with cell cycle progression. The larger number of highly regulated genes involved with pathologic neovascularization in NET supports clinical findings that the tyrosine kinase inhibitor, sunitinib, can improve overall survival in NETs. This is in contrast to PDACs where multiple VEGF targeting drugs (bevacizumab, aflibercept, and axitinib) have failed to demonstrate an overall survival benefit. The combination of highly regulated genes in cell cycle control in the NET samples make these tumors less likely to respond to EGFR therapy. Future studies are underway examining novel targeted agents to treat NETs and PDACs.

Sun BC, McCreath H, Liang LJ, Bohan S, Baugh C, Ragsdale L, Henderson SO, **Clark C**, **Bastani A**, Keeler E, An R and Mangione CM (2014). "Randomized clinical trial of an emergency department observation syncope protocol versus routine inpatient admission." [Annals of Emergency Medicine](#) 64(2): 167-175.

[Full-Text](#)

Department of Emergency Medicine

Study objective Older adults are frequently hospitalized from the emergency department (ED) after an episode of unexplained syncope. Current admission patterns are costly, with little evidence of benefit. We

hypothesize that an ED observation syncope protocol will reduce resource use without adversely affecting patient-oriented outcomes. **Methods** This randomized trial at 5 EDs compared an ED observation syncope protocol to inpatient admission for intermediate-risk adults ((greater-than or equal to)50 years) presenting with syncope or near syncope. Primary outcomes included inpatient admission rate and length of stay. Secondary outcomes included 30-day and 6-month serious outcomes after hospital discharge, index and 30-day hospital costs, 30-day quality-of-life scores, and 30-day patient satisfaction. **Results** Study staff randomized 124 patients. Observation resulted in a lower inpatient admission rate (15% versus 92%; 95% confidence interval [CI] difference -88% to -66%) and shorter hospital length of stay (29 versus 47 hours; 95% CI difference -28 to -8). Serious outcome rates after hospital discharge were similar for observation versus admission at 30 days (3% versus 0%; 95% CI difference -1% to 8%) and 6 months (8% versus 10%; 95% CI difference -13% to 9%). Index hospital costs in the observation group were \$629 (95% CI difference -\$1,376 to -\$56) lower than in the admission group. There were no differences in 30-day quality-of-life scores or in patient satisfaction. **Conclusion** An ED observation syncope protocol reduced the primary outcomes of admission rate and hospital length of stay. Analyses of secondary outcomes suggest reduction in index hospital costs, with no difference in safety events, quality of life, or patient satisfaction. Our findings suggest that an ED observation syncope protocol can be replicated and safely reduce resource use. (copyright) 2013 by the American College of Emergency Physicians.

Sura K, Johnson MD, Ye H, Glick A, Mangona VS and **Grills IS** (2014). "Matched pair analysis of high dose versus standard dose definitive chemoradiation therapy for locally advanced non-small cell lung cancer." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S146.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): To compare survival outcomes and failure patterns of locally advanced non-small cell lung cancer with high dose (HD) (> 64 Gy) vs standard dose (SD) (<=64 Gy) concurrent chemoradiation using a matched pair analysis. **Materials/Methods:** One hundred seventy-eight patients with Stage IIB-III B (T1-4, N1-3, M0) received definitive concurrent chemoradiation for non-small cell lung cancer (NSCLC) between April 2000 and December 2012. A change in practice pattern corresponded with a change in the NCCN guidelines to allow 74 Gy for advanced NSCLC in later years. A matched pair analysis was done to compare HD vs SD RT using age +/- 5 years, gender, stage, use of chemotherapy, and tumor size +/- 2 cm yielding a total of 88 patients (44 matched pairs). Ninety-one percent had staging PET in the SD group v 100% for HD (p=0.116). Pre-RT Brain MRI or CT were done in 55% of SD group v 84% for HD (p=0.005). Mean RT prescription dose was 62.3 Gy (range 58- 64) for SD and 72.8 Gy for HD (p < 0.001) (range 68.3-74.31). 77% of SD patients underwent 3DCRT and 23% IMRT v 0% 3DCRT and 100% IMRT in the HD group (p < 0.001). Independent t-test and chi-square were used to compare HD and SD groups. Clinical endpoints were assessed using the Kaplan-Meier method; univariate (UVA) analyses using Cox proportional hazard regression models. UVA of factors predicting survival and recurrence outcomes was performed considering age, gender, dose, tumor size, tumor location, baseline PET staging, baseline SUV, mean lung dose, lung V20, mean heart dose, heart V20, V30, and V40, IMRT versus 3DCRT, GTV volume, and pre-treatment brain imaging. **Results:** The mean follow-up time was 22.4 for the entire cohort (31.5mo SD; 15.2mo HD, p=0.577). There was a significant difference in RT dose but no differences in gender, follow-up time, pathology, grade, stage, tumor size, chemotherapy, or tumor location between the matched pairs. HD patients had a significantly longer overall survival (OS) [median SD 12 vs HD 23 months, p = 0.003] and lower rate of distant metastasis (DM) than SD patients. There were no significant differences in cause-specific survival (CSS), local recurrence (LR), regional recurrence (RR). The 1y OS rate was 52% for SD versus 79% for HD; the 2y OS rate was 31% for SD vs 49% for HD (p = 0.003), including a clear separation of survival curves. The 1 and 2y DM rates were 40% and 59% for SD and 26% and 35% for HD (p = 0.038). Baseline staging PET was predictive of lower local recurrence (HR = 0.218, p = 0.007). UVA of factors related to OS showed multiple heart dose parameters to be predictive, including lower mean heart dose, heart V20, V30, and V40 associated with longer survival. The UVA of distant metastasis showed only significant predictor as dose. **Conclusions:** In this matched pair analysis, definitive HD (> 64 Gy) chemoradiation was associated with improved OS and decreased DM for locally advanced NSCLC. OS was significantly associated with the mean heart dose, and

heart V20, V30, and V40.

Swanberg S and **Dereski M** (2014). "Structured abstracts: Best practices in writing and reviewing abstracts for publication and presentation (Peer Reviewed)." MedEdPortal Publication No. 9908

[Full-Text](#)

Medical Library

Department of Biomedical Sciences (OU)

Medical, nursing, and other allied health professional education institutions are expected by national accrediting bodies and associations to emphasize not only basic science and clinical knowledge and skills in the curriculum, but also research and scholarship. It is assumed that students entering the profession already know how to conduct and submit research for presentation and publication. Teaching of research methods usually takes the form of a research component or track within the curriculum, Capstone or scholarly concentration project, or dissertation or thesis. However, the practical skills of publishing including authorship responsibilities, writing abstracts and manuscripts, and peer review is often learned on the fly rather than formally taught as part of the curriculum. This experiential educational intervention teaches best practices in writing and peer reviewing scientific abstracts and affords students the opportunity to practice drafting and evaluating abstracts on their own research projects.

Thompson PM, Stein JL, Medland SE, Hibar DP, Vasquez AA, Renteria ME, Toro R, Jahanshad N, Schumann G, Franke B, Wright MJ, Martin NG, Agartz I, Alda M, Alhusaini S, Almasy L, Almeida J, Alpert K, Andreasen NC, Andreassen OA, Apostolova LG, Appel K, Armstrong NJ, Aribisala B, Bastin ME, Bauer M, Bearden CE, Bergmann O, Binder EB, Blangero J, Bockholt HJ, Boen E, Bois C, Boomsma DI, Booth T, Bowman JJ, Bralten J, Brouwer RM, Brunner HG, Brohawn DG, Buckner RL, Buitelaar J, Bulayeva K, Bustillo JR, Calhoun VD, Cannon DM, Cantor RM, Carless MA, Caseras X, Cavalleri GL, Chakravarty MM, Chang KD, Ching CRK, Christoforou A, Cichon S, Clark VP, Conrod P, Coppola G, Crespo-Facorro B, Curran JE, Czisch M, Deary IJ, de Geus EJC, den Braber A, Delvecchio G, Depondt C, de Haan L, de Zubicaray GI, Dima D, Dimitrova R, Djurovic S, Dong H, Donohoe G, Duggirala R, Dyer TD, Ehrlich S, Ekman CJ, Elvsashagen T, Emsell L, Erk S, Espeseth T, Fagerness J, Fears S, Fedko I, Fernandez G, Fisher SE, Foroud T, Fox PT, Francks C, Frangou S, Frey EM, Frodl T, Frouin V, Garavan H, Giddaluru S, Glahn DC, Godlewska B, Goldstein RZ, Gollub RL, Grabe HJ, Grimm O, Gruber O, Guadalupe T, Gur RE, Gur RC, Goring HHH, Hagenaars S, Hajek T, Hall GB, Hall J, Hardy J, Hartman CA, Hass J, Hatton SN, Haukvik UK, Hegenscheid K, Heinz A, Hickie IB, Ho BC, Hoehn D, Hoekstra PJ, Hollinshead M, Holmes AJ, Homuth G, Hoogman M, Hong LE, Hosten N, Hottenga JJ, Hulshoff Pol HE, **Hwang KS**, Jack Jr CR, Jenkinson M, Johnston C, Jonsson EG, Kahn RS, Kasperaviciute D, Kelly S, Kim S, Kochunov P, Koenders L, Kramer B, Kwok JBJ, Lagopoulos J, Laje G, Landen M, Landman BA, Lauriello J, Lawrie SM, Lee PH, Le Hellard S, Lemaitre H, Leonardo CD, Li CS, Liberg B, Liewald DC, Liu X, Lopez LM, Loth E, Lourdasamy A, Luciano M, Macciardi F, Machielsen MWJ, MacQueen GM, Malt UF, Mandl R, Manoach DS, Martinot JL, Matarin M, Mather KA, Mattheisen M, Mattingsdal M, Meyer-Lindenberg A, McDonald C, McIntosh AM, McMahon FJ, McMahon KL, Meisenzahl E, Melle I, Milanesechi Y, Mohnke S, Montgomery GW, Morris DW, Moses EK, Mueller BA, Munoz Maniega S, Muhleisen TW, Muller-Myhsok B, Mwangi B, Nauck M, Nho K, Nichols TE, Nilsson LG, Nugent AC, Nyberg L, Olvera RL, Oosterlaan J, Ophoff RA, Pandolfo M, Papalampropoulou-Tsiridou M, Pampmeyer M, Paus T, Pausova Z, Pearlson GD, Penninx BW, Peterson CP, Pfennig A, Phillips M, Pike GB, Poline JB, Potkin SG, Putz B, Ramasamy A, Rasmussen J, Rietschel M, Rijkema M, Risacher SL, Roffman JL, Roiz-Santianez R, Romanczuk-Seiferth N, Rose EJ, Royle NA, Rujescu D, Ryten M, Sachdev PS, Salami A, Satterthwaite TD, Savitz J, Saykin AJ, Scanlon C, Schmaal L, Schnack HG, Schork AJ, Schulz SC, Schur R, Seidman L, Shen L, Shoemaker JM, Simmons A, Sisodiya SM, Smith C, Smoller JW, Soares JC, Sponheim SR, Sprooten E, Starr JM, Steen VM, Strakowski S, Strike L, Sussmann J, Samann PG, Teumer A, Toga AW, Tordesillas-Gutierrez D, Trabzuni D, Trost S, Turner J, Van den Heuvel M, van der Wee NJ, van Eijk K, van Erp TGM, van Haren NEM, van 't Ent D, van Tol MJ, Valdes Hernandez MC, Veltman DJ, Versace A, Volzke H, Walker R, Walter H, Wang L, Wardlaw JM, Weale ME, Weiner MW, Wen W, Westlye LT, Whalley HC, Whelan CD, White T, Winkler AM, Wittfeld K, Woldehariat G, Wolf C, Zilles D, Zwiers MP, Thalamuthu A, Schofield PR, Freimer NB, Lawrence NS and Drevets W (2014). "The ENIGMA Consortium: Large-scale collaborative analyses of neuroimaging and genetic data." Brain Imaging and Behavior 8(2): 153-182.

[Full-Text](#)

OUWB Medical Student Author

The Enhancing NeuroImaging Genetics through Meta-Analysis (ENIGMA) Consortium is a collaborative network of researchers working together on a range of large-scale studies that integrate data from 70 institutions worldwide. Organized into Working Groups that tackle questions in neuroscience, genetics, and medicine, ENIGMA studies have analyzed neuroimaging data from over 12,826 subjects. In addition, data from 12,171 individuals were provided by the CHARGE consortium for replication of findings, in a total of 24,997 subjects. By meta-analyzing results from many sites, ENIGMA has detected factors that affect the brain that no individual site could detect on its own, and that require larger numbers of subjects than any individual neuroimaging study has currently collected. ENIGMA's first project was a genome-wide association study identifying common variants in the genome associated with hippocampal volume or intracranial volume. Continuing work is exploring genetic associations with subcortical volumes (ENIGMA2) and white matter microstructure (ENIGMA-DTI). Working groups also focus on understanding how schizophrenia, bipolar illness, major depression and attention deficit/hyperactivity disorder (ADHD) affect the brain. We review the current progress of the ENIGMA Consortium, along with challenges and unexpected discoveries made on the way. (copyright) 2014 The Author(s).

Tonlaar NY, Wobb JL, Wallace M, Pietron A, Ye H, **Gustafson GS**, Dilworth JT, **Brabbins DS**, **Grills IS** and **Chen PY** (2014). "Outcomes of African American women undergoing APBI for early-stage breast cancer: A matched pair analysis." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S277.

[Request Form](#)

Department of Radiation Oncology

Purpose/Objective(s): There are little data evaluating outcomes with the use of APBI for breast conservation therapy in African American women. This matched pair analysis compares the long-term outcomes of African American versus white women who underwent APBI at our institution. Materials/Methods: One hundred fifty-six patients with DCIS (33%) or stage I/II invasive breast cancer (77%) who underwent APBI at our institution between 1993 and 2013 were included in this matched pair analysis. 39 African American and 117 white patients underwent a 1:3 match according to age (+/- 5 years), T-stage (Tis vs T1 vs T2), and estrogen receptor (ER) status (+/-). Clinical outcomes were compared using the Kaplan-Meier method. Results: The median follow-up was 76 months. All patients received 34 Gy (brachytherapy) or 38.5 Gy (3D-CRT) in 10 B.I.D fractions. No significant differences were seen in tumor size, age at diagnosis, T-stage, N-stage, grade, margin status, ER/PR/HER 2 status, treatment type (interstitial, balloon-based, or 3D-CRT), adjuvant chemotherapy, or use of adjuvant hormone therapy by race (all $P > 0.05$). Local recurrence was higher for African American compared to white, with 5-year rate of 7.9% vs 1.1% ($p = 0.03$). Regional recurrence was also higher in African American, with 5-year rate of 5.8% vs 0% ($p = 0.02$). The 5-year contralateral breast failure and distant metastasis rates were 0% vs 0% ($p = 0.6$) and 2.7% vs 2.0% ($p = 0.99$), respectively. At 5 years, there were no statistically significant differences in OS (93% vs 88%, $p = 0.27$), CSS (96% vs 99%, $p = 0.20$), or DFS (92% vs 97%, $p = 0.16$) between the African American and white patients, respectively. On univariate analysis, age ($p = 0.034$) and tumor size ($p = 0.025$) were predictive for IBTR while nodal status ($p = 0.049$) and grade ($p = 0.027$) were predictive for regional recurrence in African American patients. No factors were predictive for white patients. On multivariate analysis, tumor size ($p=0.045$) and age ($p = 0.024$) remained independent predictors of IBTR for African American patients. Conclusions: Our results show similar overall, cause-specific, and diseasefree survival for African American patients undergoing APBI for breast conservation compared to matched White counterparts. In this small matched cohort, there was increased risk of locoregional recurrence in the African American patients and further study is needed to explore the biological, molecular, socioeconomic, and treatment related factors accounting for this difference. (Table Presented).

Totonchi S, Elgin R, Monahan M and **Johnston IWK** (2014). "Upper quadrant port placement for robot-assisted renal surgery: Implementation of the floating arm and the XL prototype." Journal of Endourology 28(8): 900-905.

[Request Form](#)

Department of Surgery

Background and Purpose: Placement of the fourth arm (4th arm) in the lower quadrant (LQ) is commonly described for robot-assisted renal surgical procedures but has anatomic restrictions and limited ergonomics. An alternative, upper quadrant (UQ) location is desirable, but patient habitus and spacing may restrict robotic attachment. We investigate current trends in 4th arm port placement and propose an alternative method at attaching the robot - the "Floating Arm" (FLA). Methods: Robotic surgeons from the Endourological Society were surveyed. A 20-cm extra-long (XL Prototype) da Vinci instrument was developed for the FLA technique. A dry lab allowed quantitative comparison of spacing and ranges of motion for standard da Vinci ports (dVP), bariatric dVP, telescoping dVP, and FLA. Results: There were 108 respondents who participated. Half of the respondents avoid using the 4th arm (30% lack of need and 20% because of interference). The majority (90%) typically positions the 4th arm in the LQ, but many reported limitations in this location. Few (5%) place 4th arm in the UQ, while most (73%) have never heard of UQ placement. Existing techniques may increase shoulder height clearance but inversely shorten the working length of the instrument intracorporeally. Alternatively, the XL Prototype significantly increased the shoulder length and maintained available working distances intracorporeally. Adjacent arm interference angle was essentially identical (27 degrees) for all ports except a greater range of movement for the XL Prototype (35 degrees). Conclusion: Few surgeons are using an UQ positioning or use techniques to improve attachment of the 4th arm. The greatest freedom may be obtained by implementing the FLA, but this necessitates production of a longer instrument. Copyright (copyright) 2014, Mary Ann Liebert, Inc.

Troeller A, Sohn M, **Grills IS, Ionascu D**, Guckenberger M, Klement R, Belderbos J, Sonke J, Hope AJ, Bissonnette J, Werner-Wasik M, Xiao Y and **Yan D** (2014). "Are lung NTCP models different in hypofractionated and standard fractionated radiotherapy?" International Journal of Radiation Oncology Biology Physics 90(1): S41-S42.

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Department of Radiation Oncology

Purpose/Objective(s): NTCP modeling of radiation induced lung pneumonitis in hypo-fractionated SBRT has resulted in a much higher MLD50 compared to the standard, 2 Gy, fractionated RT (SFRT). Although the LQ model is the most popular method in clinical use, it has been shown to be inaccurate for very low and high doses per fraction. Here we investigate the use of the low-dose hyper-radiosensitivity (LD-HRS) model as an alternative to adjust for fractionation effects in hypo-fractionated RT. The aim of this study is to show that the lung NTCP model in hypofractionated SBRT is similar to the one in the SFRT, as long as the correct radiation-induced lung cell survival model is used. Materials/Methods: Lung DVHs and CTCAE toxicity scores of 409 patients from 5 institutions treated with hypo-fractionated SBRT in 3-10 fractions were investigated in this study. The physical DVHs of SBRT were converted to biologically equivalent DVHs of SFRT using the LD-HRS model. This model has 4 parameters: α determines sensitivity to radiation in the low-dose regime, d_c is the threshold dose for induced repair, and a and b as in the LQ-model. The latter three were fixed to the same previously published in vitro values throughout the study, while the parameter α was variable to be determined. Optimal NTCP parameters of the Lyman model for grade (greater-than or equal to) 2 pneumonitis were then determined based on the mean lung dose (MLD) for all values as within a pre-selected interval using the corresponding biologically equivalent DVHs. Maximum likelihood estimation was used for the parameter optimization. Results: Twenty-nine (7.1%) of the patients investigated experienced pneumonitis of grade (greater-than or equal to) 2. Optimal values for the slope parameter m were stable within the range (0.55 - 0.57) for different α s, while the MLD50 inversely correlated to the α s. Values for MLD50 ranged from 20.0 Gy to 64.0 Gy for the values of α as investigated. All models had similar loglikelihoods, and thus described the dataset equally well. Comparing to the α as reported in vitro for human lung cell line, a higher value can be selected to obtain an identical lung NTCP model for both SBRT and SFRT. Conclusions: If the low-dose sensitivity parameter is properly selected, SBRT and SFRT can share an identical NTCP model to describe radiation-induced lung toxicity. Therefore, the LD-HRS cell survival model has the potential to resolve fractionation issues in NTCP modeling uncertainty for lung cancer RT.

Tyagi N, Yang K and Yan D (2014). "Comparing measurement-derived (3DVH) and machine log file-derived dose reconstruction methods for VMAT QA in patient geometries." *Journal of Applied Clinical Medical Physics* 15(4): 54-66.
[Request Form](#)

Department of Radiation Oncology

The purpose of this study was to compare the measurement-derived (3DVH) dose reconstruction method with machine log file-derived dose reconstruction method in patient geometries for VMAT delivery. A total of ten patient plans were selected from a regular fractionation plan to complex SBRT plans. Treatment sites in the lung and abdomen were chosen to explore the effects of tissue heterogeneity on the respective dose reconstruction algorithms. Single- and multiple-arc VMAT plans were generated to achieve the desired target objectives. Delivered plan in the patient geometry was reconstructed by using ArcCHECK Planned Dose Perturbation (ACPD) within 3DVH software, and by converting the machine log file to Pinnacle3 9.0 treatment plan format and recalculating dose with CVSP algorithm. In addition, delivered gantry angles between machine log file and 3DVH 4D measurement were also compared to evaluate the accuracy of the virtual inclinometer within the 3DVH. Measured ion chamber and 3DVH-derived isocenter dose agreed with planned dose within $0.4\% \pm 1.2\%$ and $-1.0\% \pm 1.6\%$, respectively. 3D gamma analysis showed greater than 98% between log files and 3DVH reconstructed dose. Machine log file reconstructed doses and TPS dose agreed to within 2% in PTV and OARs over the entire treatment. 3DVH reconstructed dose showed an average maximum dose difference of $3\% \pm 1.2\%$ in PTV, and an average mean difference of $-4.5\% \pm 10.5\%$ in OAR doses. The average virtual inclinometer error (VIE) was $-0.65^\circ \pm 1.6^\circ$ for all patients, with a maximum error of $-5.16^\circ \pm 4.54^\circ$ for an SRS case. The time averaged VIE was within 1° - 2° , and did not have a large impact on the overall accuracy of the estimated patient dose from ACPDP algorithm. In this study, we have compared two independent dose reconstruction methods for VMAT QA. Both methods are capable of taking into account the measurement and delivery parameter discrepancy, and display the delivered dose in CT patient geometry rather than the phantom geometry. The dose discrepancy can be evaluated in terms of DVH of the structures and provides a more intuitive understanding of the dosimetric impact of the delivery errors on the target and normal structure dose.

Ulirsch JC, Weaver MA, Bortsov AV, Soward AC, **Swor RA**, Peak DA, Jones JS, Rathlev NK, Lee DC, Domeier RM, Hendry PL and McLean SA (2014). "No man is an island: Living in a disadvantaged neighborhood influences chronic pain development after motor vehicle collision, and this effect is moderated by common genetic variation influencing HPA axis function." *Pain* 155(10): 2116-2123.

[Full-Text](#)

Department of Emergency Medicine

Living in a lower socioeconomic status neighborhood has been shown to alter stress system function and is associated with a number of adverse health outcomes, but its influence on musculoskeletal pain (MSP) outcomes after traumatic stress exposures such as motor vehicle collision (MVC) has not been assessed. We performed a multicenter, prospective study that enrolled 948 European-American individuals within 24 hours of MVC who were discharged home after emergency department evaluation. Follow-up evaluations were completed via telephone or Internet survey 6 weeks, 6 months, and 1 year after MVC on 91%, 89%, and 91% of participants, respectively. A robust aggregate measure of census tract neighborhood disadvantage was derived, and individual-level characteristics assessed included socioeconomic and demographic characteristics, pain prior to MVC, litigation status, and opioid use. MSP was assessed in the emergency department; MSP and pain interference with daily activity were assessed at 6 weeks, 6 months, and 1 year. After adjustment for individual-level factors, living in more disadvantaged neighborhoods was associated with increased MSP ($P = 0.0009$) and increased pain interference with daily function ($P < 0.0001$). The relationship between neighborhood disadvantage and MSP was moderated by a common single nucleotide polymorphism, rs2817038, 5' of the gene encoding FKBP5, a functional regulator of glucocorticoid receptor sensitivity (interaction P -value = 0.0015). These data support the hypothesis that low neighborhood socioeconomic status increases the likelihood of worse MSP outcomes after traumatic stress exposures such as MVC, and that this influence is mediated in part via its influence on stress system function. (copyright) 2014 International Association for the Study of Pain.

Vanhecke TE, Weber JE, Ebinger M, Bonzheim K, Tilli F, Rao S, Osman A, Silver M, Fliegner K, **Almany S** and **Haines D** (2014). "Implementation of ultraportable echocardiography in an adolescent sudden cardiac arrest screening program." *Clinical Medicine Insights: Cardiology* 8: 87-92.

[Full-Text](#)

Department of Internal Medicine

BACKGROUND: Over a 12-month period, adolescent heart-screening programs were performed for identifying at-risk adolescents for sudden cardiac death (SCD) in our community. Novel to our study, all adolescents received an abbreviated, ultraportable echocardiography (UPE). In this report, we describe the use of UPE in this screening program. **METHODS AND RESULTS:** Four hundred thirty-two adolescents underwent cardiac screening with medical history questionnaire, physical examination, 12-lead electrocardiogram (ECG), and an abbreviated transthoracic echocardiographic examination. There were 11 abnormalities identified with uncertain/varying clinical risk significance. In this population, 75 adolescents had a murmur or high ECG voltage, of which only three had subsequent structural abnormalities on echocardiography that may pose risk. Conversely, UPE discovered four adolescents who had a cardiovascular structural abnormality that was not signaled by the 12-lead ECG, medical history questionnaire, and/or physical examination. **CONCLUSIONS:** The utilization of ultraportable, handheld echocardiography is feasible in large-scale adolescent cardiovascular screening programs. UPE appears to be useful for finding additional structural abnormalities and for risk-stratifying abnormalities of uncertain potential of adolescents' sudden death.

Wasserman JA, Fitzgerald JE, Sunny MA, Cole M, Suminski RR and Dougherty JJ (2014). "Nonmedical use of stimulants among medical students." *Journal of the American Osteopathic Association* 114(8): 643-653.

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Department of Biomedical Sciences (OU)

Context: Proliferation of the use of psychopharmacologic drugs for the treatment of individuals with attention and behavior disorders has promoted discussion of the illicit use of such drugs to enhance academic performance. Previous research has focused on the use of such drugs by undergraduate students; however, inquiry into the nonmedical use of prescription stimulants by medical students is warranted because of the unique qualities of the medical school environment (including academic pressure, stress, and competition with peers) and the demographic characteristics common to many medical students. **Objective:** To examine the nonmedical use of prescription stimulants among osteopathic medical students, focusing on such key associated variables as academic stress, social network connections, and use of other substances. **Methods:** In 2012, first- and second-year students at a large osteopathic medical school were surveyed on the nonmedical use of prescription stimulants, stress, social networks, perceptions of drug use, and related topics. Data were compared with national data and assessed using analysis of variance and χ^2 statistical tests. **Results:** A total of 380 students completed the survey. Of those, 56 (15.2%) reported using prescription stimulants nonmedically to help them study in medical school. This percentage is significantly higher than the national estimated rate of diagnosis of attention-deficit/hyperactivity disorder in similar populations ($t=3.72$, $P<.001$). Both positive perceptions of the nonmedical use of stimulants ($F=14.89$, $P<.001$) and the use of other substances ($\chi^2=18.00$, $P<.001$) were positively associated with the nonmedical use of stimulants. Social network connections did not positively predict use by medical students, and certain types of social connectivity had a negative association with use. **Conclusion:** In contrast with research on undergraduate populations, addressing academic stress and feelings of competitiveness may not be viable strategies for mitigating nonmedical use of stimulants among medical students. © 2014 American Osteopathic Association.

Watchko JF and **Maisels MJ** (2014). "The enigma of low bilirubin kernicterus in premature infants: Why does it still occur, and is it preventable?" *Seminars in Perinatology* 38(7): 397-406.

[Full-Text](#)

Department of Pediatrics

Low bilirubin kernicterus in preterm neonates, though rare, remains an unpredictable and refractory form of brain injury. Hypoalbuminemia, co-morbid CNS insult(s), infection, and inflammation are contributing causes that, in many cases, appear to interact in potentiating bilirubin neurotoxicity. Despite compulsive attention to serum bilirubin levels, and clinical and laboratory indices of neurotoxicity risk, low bilirubin kernicterus continues to be seen in contemporary NICUs. While efforts to refine and improve current treatment guidelines are certainly needed, such revision(s) will also have to take into account the risks and benefits of any intervention, including phototherapy.

Wenzler DL, **Burks FN**, Cooney M and **Peters KM** (2014). "Proof of concept trial on changes in current perception threshold after sacral neuromodulation." *Neuromodulation*. ePub Ahead of Print.

[Full-Text](#)

Department of Urology

Objectives: Sacral neuromodulation (SNM) is theorized to alter the neural pathways that mediate bladder and urethral sensation. We hypothesize that SNM affects current perception thresholds (CPTs) of afferent sensory nerve pathways. Materials and Methods: Eight women were enrolled and completed pre and postoperative testing. A CPT device was used to measure CPT at 5Hz (C-fibers), 250Hz (A(delta)-fibers), and 2000Hz (A(beta)-fibers) on the urethra and bladder prior to and one month after SNM. Index finger readings at 2000Hz served as controls. Results: SNM had the greatest effect on the bladder at 250 and 2000Hz, suggesting reduced bladder sensitivity. Significant changes in CPT were seen in the bladder at 2000Hz with a decrease in sensitivity ($p = 0.033$). CPT testing was well tolerated, and no adverse events were identified. Conclusions: With a measurable change in CPT values for A(delta)-fibers and A(beta)-fibers, these findings suggest that SNM modulates large myelinated afferent fibers in the bladder. Notably, little or no changes were found in the C-fiber CPT measurements. More research is needed with a larger sample size to determine the significance of these findings. (copyright) 2014 International Neuromodulation Society.

Williams GA (2014). "High-deductible health plans: Implications for the retina specialist: Retina specialists need to adjust to the growing number of patients enrolled in high-deductible health plans to ensure that their offices run smoothly." *Retina Today* JUL/AUG: 22-24.

[Request Form](#)

Department of Ophthalmology

Wobb JL, Baschnagel AM, Dilworth JT, Lee K, Williams L, Eskandari M, **Wu D** and **Wilson GD** (2014). "The significance of 18FDG PET and related glucose metabolism biomarkers in HPV-positive and-negative head and neck squamous cell carcinomas." *International Journal of Radiation Oncology Biology Physics* 90(1): S815.

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Department of Diagnostic Radiology and Molecular Imaging

Department of Radiation Oncology

Purpose/Objective(s): The multidisciplinary treatment of locally advanced head neck squamous cell carcinoma (LAHNSCC) utilizes 18FDG PET for staging, treatment planning, restaging, and long-term follow-up. The objective of this study was to investigate if 18FDG PET is informative in both HPV positive (HPVpos) and negative (HPVneg) tumors and whether glucose metabolism biomarkers differ between these two etiologies and their response to chemoradiation. Materials/Methods: Tissue from 107 LAHNSCC patients treated with definitive chemoradiation therapy was retrieved and used to generate a tissue microarray. Immunohistochemical staining of the HPV surrogate p16, GLUT1, HK2, and HIF1(alpha) was performed and intensity scored by a pathologist. Pretreatment 18FDG PET data was available for primary (P) tumors in 80 patients; of these, 68 also had data on nodal (N) uptake. 18FDG PET SUV values 1 to 3 months post-RT were available in 48 primary tumors and nodes. Analyses were performed using ANOVA or independent T-test for categorical and continuous variables, Spearman's for correlations, and the Kaplan-Meier method for local

failure (LF). Results: Pretreatment SUVs in P tumors were not different between HPVpos and HPVneg tumors ($p = 0.69$), but SUVs were significantly higher in HK2 positive tumors ($p = 0.001$) and to a lesser extent in GLUT1 ($p = 0.04$) positive tumors. With respect to N disease, SUVs were higher in HPVpos (10.9 (plus or minus) 1.12) versus HPVneg (7.7 (plus or minus) 1.4), trending towards significance ($p = 0.08$). Post-treatment SUVs in the P dropped significantly more ($p = 0.007$) in HPVpos (1.49 (plus or minus) 0.8) versus HPVneg (4.84 (plus or minus) 0.87) but there were no differences in N disease ($p = 0.58$). In terms of the individual P/N reduction in SUV before and after treatment, there were no differences as a function of HPV status but a significant association in HK2 expression ($p = 0.006$) and a trend towards a steeper slope in HPVneg P. HPVpos tumors demonstrated lower GLUT1 positivity ($p = 0.001$), higher HK2 positivity ($p = 0.07$) and lower HIF1(alpha) ($p = 0.001$) staining compared to HPVneg tumors. Overall, higher pretreatment SUVs were associated with worse LF ($p = 0.07$). The association was stronger in HPVneg ($p = 0.11$) compared to HPVpos tumors ($p = 0.82$). Of the glucose metabolism-related genes, only GLUT1 showed an association with local control; this was independent of HPV status ($p = 0.03$). Conclusions: 18FDG PET parameters differed between HPVpos and HPVneg tumors. Some of these differences were associated with response to chemoradiation, but also with altered expression of glucose metabolism proteins. Taken together, glucose metabolism proteins may be important biomarkers in the context of HPV status for predicting local control in patients with LAHNSCC.

Wobb JL, Jawad MS, Wallace M, Shah CS, Ye H, Pietron A, **Grills IS** and **Chen PY** (2014). "Comparison of chronic toxicities between brachytherapy-based accelerated partial breast irradiation and whole-breast intensity modulated radiation therapy." *International Journal of Radiation Oncology Biology Physics* 90(1): S273.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): Brachytherapy-based accelerated partial breast irradiation (bAPBI) is a technique that shortens the treatment duration of adjuvant radiation to one week or less. While prospective studies and matched pair analyses have demonstrated excellent long term clinical outcomes, documentation of late toxicities for APBI is sparse when compared with whole breast radiation therapy (WBI). Therefore, the purpose of this study is to compare the chronic toxicity rates for patients treated with bAPBI versus WBI. Materials/Methods: A total of 489 patients receiving WBI with IMRT from 2000 to 2013 and 545 patients receiving bAPBI (interstitial, 40% or applicator-based, 60%) from 1993 to 2013 were treated at a single institution. Chronic toxicity was evaluated (greater-than or equal to) 6 months following treatment. Scoring was done utilizing CTCAE version 3.0 and cosmesis was evaluated using the Harvard scale. Analysis was performed using the Pearson Chi-Square test for categorical variables and the independent samples Ttest for continuous variables. Results: Median follow-up was 4.6 years (range 0.1-13.4) for WBI v. 6.7 years (range 0.1-20.1) for bAPBI. Rates of grade 2 or higher toxicity are presented in the table. No difference in rates of Grade 3 or higher hyperpigmentation (2.6% vs 0%), breast pain (0.8% vs 1.6%), induration/fibrosis (0.3% vs 0.7%), volume reduction (0% vs 0.2%), or telangiectasia (1.4% vs 2.3%) were noted between WBI and bAPBI (all $p > 0.05$). There were higher rates of seroma formation (2.9% vs 14.4%, $p < 0.001$) and fat necrosis (3.6% vs 10.2%, $p < 0.001$) in the bAPBI group. Infection rates were similar (1.3% vs 3.3%, $p = 0.07$). No difference in cosmesis was noted with respect to rates of fair (4.1% vs 6.1%, $p = 0.30$) or poor (0.5% vs 0.2%, $p = NS$) cosmesis with WBI and bAPBI, respectively. At 5 and 10 years, local recurrence (LR) rates were 2.6% and 4.8% with WBI and 2.2% and 4.6% with bAPBI, respectively ($p = 0.64$). No differences in mastectomy rates for LR (3.1% for WBI and 1.2% for bAPBI, $p = 0.06$), or for reasons other than LR (0.8% and 0.6%, $p = 0.60$) were noted. Conclusions: With long term follow-up, no differences in the rates of chronic toxicity were noted between WBI delivered with IMRT and bAPBI, with the exception of seroma formation, fat necrosis, and telangiectasias, which were slightly higher in bAPBI and hyperpigmentation, which was higher with WBI. These data further support the utilization of bAPBI as a modality to deliver adjuvant radiation in a safe as well as efficacious modality. (Table Presented).

Wobb JL, **Krueger SA**, Kane J, **Grills IS**, **Wilson G** and **Marples B** (2014). "Pulsed radiation therapy maintains tumor oxygenation in a murine model of head and neck squamous cell carcinoma." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S194.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): Despite multimodal therapy, local recurrence for advanced head and neck squamous cell carcinoma (HNSCC) remains high with overall 5-year survival of about 50%. Tumor hypoxia has been identified as a significant source of radioresistance and is associated with poor clinical outcomes. The aim of this study was to determine if tumor response and radiation-induced hypoxia are altered following fractionated standard radiation therapy (SRT) or pulsed radiation therapy (PRT) in murine xenograft model of HNSCC. Materials/Methods: Subcutaneous xenografts were established in female NIH III HO mice using a HNSCC cell line (UT14). Tumors grew to 300- 500 mm³ before a sub-curative 20 Gy total dose (2 Gy/day) was delivered via SRT or PRT. SRT was continuously-delivered and PRT was given as 10 x 0.2 Gy pulses separated by 3 minutes. 18F-FDG (n = 68) and 18FFMISO (n = 42) PET/CT scans were acquired pre-, mid-, and posttreatment using a trimodality system. The tumor maximum standardized uptake value (SUVmax) for each scan was calculated and normalized to pre-treatment values. Sixteen animals were treated and tumors allowed to regrow to 2000 mm³ (n = 8/RT scheme). Twelve additional animals (n = 6/RT scheme) were treated with SRT or PRT to 10 Gy or 20 Gy and sacrificed immediately for histological hypoxia analysis. Animal experiments were conducted with the approval and oversight of Institutional IACUC. Results: Analysis of individual tumor regrowth demonstrated that PRT and SRT were equally effective (~31 days growth inhibition for both SRT and PRT). 18FMISO PET imaging indicated a significant increase in the level of hypoxia following SRT treatment when compared to PRT (normalized SUVmax PRT = 1.55, SRT = 0.96, p-value = 0.03). Furthermore, a sizeable increase in hypoxia was noted only in tumors undergoing SRT (pvalue = 0.04). 18FDG imaging data was less conclusive, although there was a significant increase in FDG tumor SUVmax at 10 Gy in the SRT group (p-value = 0.01). Histological analysis of pimonidazole stained tumor samples mimicked 18FMISO imaging data, showing an increase in hypoxia in SRT tumors but not PRT tumors. Ongoing immunohistochemical studies are examining vascular markers to search for the mechanism behind the stabilization of tumor oxygenation levels following PRT. A second study using a more hypoxic HNSCC mouse model (UT15) is currently underway and preliminary data support the conclusions from the UT14 tumors. Conclusions: A significant increase in tumor hypoxia was seen following SRT but not PRT. Overall these data suggest that pulsed radiation therapy may be associated with lower levels of treatment-induced tumor hypoxia, which may translate to better tumor control and improved overall survival in patients given curative treatments.

Yan D, **Yang K**, Liang J, **Krauss D** and **Chen P** (2014). "Evaluation of image guidance and adaptive radiation therapy techniques for H&N cancer." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S860-S861.

[Full-Text](#)

Department of Radiation Oncology

Department of Internal Medicine

Purpose/Objective(s): It has been controversial whether or not additional adaptive planning is needed in the daily CBCT guided radiation therapy for H&N cancer. In this study, two treatment techniques, daily IGRT and hybrid IGRT/Adaptation, were evaluated and compared to address the uncertainty. Materials/Methods: Pre-treatment planning CT and daily treatment CBCT images of 12 oropharynx patients were used in this study. For each patient, pre-treatment IMRT plan with dose 70Gy in 35 fractions prescribed to (greater-than or equal to) 95% of the primary CTV1, while 60Gy to (greater-than or equal to) 95% of the nodal CTV2, was created using the planning CT with 0 mm CTV-to-PTV margin. Two treatment techniques: 1. Daily-IGRT: daily CBCT guided patient position localization, correction, and delivery; 2. Hybrid-ART: Daily-IGRT + additional adaptive planning performed using the same dose prescription on the 11th and 21th treatment days, were applied and evaluated. Treatment dose to each patient was reconstructed using deformable image registration on the daily CBCT images for each technique. Treatment DVH parameters used in the evaluation included the following: minimal dose (D99%) and high dose (V110%) for CTV1 and CTV2; the mean dose Dm for parotids, and the maximum dose D1% for cord, brain stem & mandible. Results: Table shows the

mean(plus or minus)SD of organ DVH parameters obtained and the %changes of the treatment dose from the pre-treatment plan. Daily-IGRT maintained the planned dose in CTV1, but had treatment dose reduction >5% in CTV2 for 33% patients. In addition, hot spot in the targets had >10% increase for 17% patients. The delivered dose to parotids was increased significantly, 50% patients had parotid mean dose increase >10%. Comparing to Daily-IGRT, the Hybrid-ART largely reduced parotids dose, and 57% patients had parotid dose reduction >3Gy including >5Gy reduction for 17% patients. In addition, there was >10% hot spot reduction in the targets for 33% patients. Conclusions: Daily IGRT cannot fully ensure the treatment delivery accuracy with 0 mm CTV-to-PTV margin. Both target dose heterogeneity and parotids dose are also increased from the pre-treatment plan. With the biweekly adaptive planning modification, all dose volume criteria can be largely or moderately improved. (Table Presented).

Ye H, Baschnagel AM, Rizvi S, Ducharme ER, **Chen PY**, Manders MD, **Krauss DJ**, Maitz AH, **Pieper DR** and **Grills IS** (2014). "Quality of life in patients with brain metastasis treated with gamma knife radiosurgery alone using the EORTC QLQ-C30 and QLQ-BN20." International Journal of Radiation Oncology Biology Physics 90(1): S704.

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Department of Radiation Oncology

Department of Neurosurgery

Purpose/Objective(s): To prospectively assess QOL endpoints in patients with brain metastases before and after Gamma Knife (GK) Stereotactic RS alone. Materials/Methods: One hundred sixty-one patients received GK alone (no surgery, no upfront whole brain RT) from January 2007 to August 2013 for brain metastases. The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-C30) and the EORTC Brain Cancer Module (EORTC QLQ-BN20) questionnaire were administered to prospectively assess the QOL of patients before, 3-, 6-, and 12-months post-GK. All of the scales and symptoms measures range from 0 to 100, which were transformed to a standardized score. Linear regression analysis was applied to assess changes in QOL scores over time and to examine the associations between the QLQ-C30 and QLQ-BN20 scales. Associations between the QLQ-C30 and QLQ-BN20 scales were evaluated using Spearman correlation. Baseline QLQ-C30 and QLQ-BN20 scales were compared among RTOG recursive partitioning analysis (RPA) classes. Results: All 161 patients completed baseline QOL questionnaires. Mean age was 62.5 y (24 - 87y), the median KPS was 100, and the median follow-up time was 6 months (range 0 - 44.8 months). Among them, there were 64 (40%), 39 (24%), and 28 (17%) who completed 3- month, 6-month, and 12-month post-GK QOL questionnaires. The 1- year overall survival and elsewhere brain failure rates for the cohort 161 patients and 64 patients completed 3-month QOL was 42%/50% and 66%/48%. Fatigue, insomnia, and future uncertainty were the most prominent symptoms at both baseline and 3 mos follow-up. Insomnia ($p = 0.001$) and future uncertainty ($p = 0.065$) improved from baseline to 3mos. Insomnia at 3 mos improved by minimal clinical importance difference (MCID) of 10 points. Physical functioning ($p = 0.010$), nausea/vomiting ($p = 0.011$), appetite loss ($p = 0.007$), financial difficulties ($p = 0.012$), and drowsiness ($p = 0.010$) were found statistically declined from baseline to 3-month follow up, however, only appetite loss reached MCID of 10 points. Patients who received chemotherapy before GK had worse QOL scores in most function scales and symptoms scales than patients without chemotherapy. Baseline KPS was positively correlated with all baseline QLQ-C30 functioning scales, and negatively correlated with all baseline symptom scales. Patients with KPS >70 had better functioning scales and lowest symptoms scales comparing to KPS = 70 and KPS <70. Only 3-mo social functioning ($p = 0.027$) was higher in patients with baseline KPS >70, with no other differences in 3-mo QOL scores according to KPS. Conclusions: GK radiosurgery alone for brain metastases had good QOL maintenance for nearly all QOL scores at 3 mos, independent of baseline KPS or RPA with only appetite loss of MCID and related to post-GK chemotherapy. Insomnia and future uncertainty were prominent at baseline and improved with time.

Ysunza A, Chaiyasate K, Micale MA, McBrien M, Bloom DA, Gibson DP and Weinhouse E (2014). "22q11.2 deletion detected by endoscopic observation of pharyngeal pulsations in a child with submucous cleft palate and persistent velopharyngeal insufficiency." [International Journal of Pediatric Otorhinolaryngology](#) 78(10): 1789-1794.
[Full-Text](#)

Department of Physical Medicine and Rehabilitation

Department of Surgery

Department of Pathology

Department of Diagnostic Radiology and Molecular Imaging

Department of Pediatrics

22q11.2 microdeletion syndrome (22q11.2DS) is the most common syndrome associated with cleft palate and velopharyngeal insufficiency (VPI). Over 180 clinical features have been described. Most common features include: cardiac malformations, cleft palate, velopharyngeal insufficiency, characteristic facial features, hypotonia, behavioral disorders, and musculoskeletal disorders among several other phenotypical features. A case of 22q11.2DS confirmed by cytogenomic analysis is presented with review of the literature. Main clinical features were a submucous cleft palate (SMCP) with persistent VPI after palatoplasty, an ectopic left internal carotid artery and a prominent aortic root. VPI was corrected with a pharyngeal flap, tailored according to findings of videonasopharyngoscopy, videofluoroscopy and neck CT scan with contrast.
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Zamdborg L, Jawad MS, Wobb JL, Pietron A, Benedetti LA, Dilworth JT, **Yan D** and **Grills IS** (2014). "Dosimetric predictors of cosmesis in whole-breast irradiation: A novel clinically applicable constraint." [International Journal of Radiation Oncology Biology Physics](#) 90(1): S249-S250.

[Full-Text](#)

Department of Radiation Oncology

Purpose/Objective(s): Whole breast irradiation (WBI) with a boost to the surgical cavity, when indicated, is an integral component of breast-conserving therapy for women with breast cancer. Overall breast dose heterogeneity is known to impact cosmesis. Recently, there has been increased interest in defining metrics of dose heterogeneity that are readily calculated from treatment planning dose volume histograms (DVHs), and that serve as good proxies for the distribution of dose within a treatment volume. The purpose of this analysis is to identify specific dosimetric predictors that can be controlled to improve cosmetic outcomes, and be readily integrated into existing clinical workflows. Materials/Methods: A total of 232 consecutive patients were treated with WBI at a single institution between 2011 and 2013. Median whole breast dose was 4500 cGy in 25 fractions, followed by a median boost dose of 1600 cGy in 10 fractions. One hundred twenty-nine patients received an electron boost and 103 received a photon boost, with identical median doses. Cosmesis was physician-rated during follow-up visits using the Harvard scale. Dose heterogeneity was calculated from the differential DVH as the standard deviation of the dose. Controllable dosimetric variables were analyzed to identify significant predictors of cosmesis and determine thresholds for these variables to help guide treatment planning. Results: Median age at diagnosis was 61. Median follow-up was 27 weeks. Median breast volume was 1812.4 cc. Median absolute biopsy cavity volume was 32.6 cc. Median biopsy cavity volume relative to breast volume was 1.97%. Post-boost whole-breast dose heterogeneity was a significant predictor of cosmesis ($p = 0.0003$). The 25th percentile of dose heterogeneity in patients with fair or poor cosmesis was 14%. This was a significant predictor of fair or poor cosmesis, with an odds ratio of 4.79 ($p = 0.02$). Biopsy cavity dose heterogeneity was not a significant predictor of cosmesis ($p = 0.7$) but biopsy cavity volume relative to breast volume was ($p = 0.04$). Total breast volume was not a significant predictor ($p = 0.5$). There was no significant association between boost type and cosmesis ($p = 0.13$). Conclusions: Patients whose post-boost whole-breast dose heterogeneity was below 14% had significantly improved cosmesis relative to those that did not. This constraint is readily usable within existing treatment planning systems, and may be rapidly implemented in a typical clinical workflow, using either forward or inverse planning.

Zaryanov AV, **Park DK**, **Khalil JG**, **Baker KC** and **Fischgrund JS** (2014). "Cement augmentation in vertebral burst fractures." Neurosurgical Focus 37(1): E5.

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Department of Orthopedic Surgery

As a result of axial compression, traumatic vertebral burst fractures disrupt the anterior column, leading to segmental instability and cord compression. In situations with diminished anterior column support, pedicle screw fixation alone may lead to delayed kyphosis, nonunion, and hardware failure. Vertebroplasty and kyphoplasty (balloon-assisted vertebroplasty) have been used in an effort to provide anterior column support in traumatic burst fractures. Cited advantages are providing immediate stability, improving pain, and reducing hardware malfunction. When used in isolation or in combination with posterior instrumentation, these techniques theoretically allow for improved fracture reduction and maintenance of spinal alignment while avoiding the complications and morbidity of anterior approaches. Complications associated with cement use (leakage, systemic effects) are similar to those seen in the treatment of osteoporotic compression fractures; however, extreme caution must be used in fractures with a disrupted posterior wall.
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Zhang PL and **Hafron JM** (2014). "Progenitor/stem cells in renal regeneration and mass lesions." International Urology and Nephrology 46(11): 2227-2236.

[Full-Text](#)

Department of Pathology

Department of Urology

Adult kidneys have limited regenerative capacity following a prominent acute kidney injury. As understanding regenerative mechanisms is the key to discovering therapeutic strategies for preventing and treating renal diseases, in recent years, researchers have hotly debated whether progenitor/stem cells offer a support system for renal repair. The Romagnani-led group identified CD133 stem cells in the parietal epithelium and renal tubules, and their data indicate that these progenitor/stem cells support renal repair in the glomeruli and renal tubules. The Humphreys and Bonventre group used the lineage-tracing technique. They observed no contribution of progenitor cells to tubular repair, but they later reported that the differentiated tubular cells responsible for tubular repair actually gained some characteristics of progenitor cells. This review article will focus on major updates regarding the controversial progenitor/stem cells in renal regeneration and highlight some new progenitor cell issues in renal mass lesions. (copyright) 2014 Springer Science+Business Media Dordrecht.

Zhou J, **Jawad MS**, **Harb JG**, **Yee S**, **Yan D** and **Grills IS** (2014). "Quantifying follow-up T2-weighted MR image in local failure spinal tumors after stereotactic body radiation therapy (SBRT)." International Journal of Radiation Oncology Biology Physics 90(1): S6.

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Department of Radiation Oncology

Department of Diagnostic Radiology and Molecular Imaging

Purpose/Objective(s): To identify and quantify local control (LC) / local failure (LF) predictors in follow-up T2-weighted MR image for patients undergoing stereotactic body radiation therapy (SBRT) for spinal tumors. Materials/Methods: Sixty-seven spinal tumors were treated with SBRT at our institution between February 2008 and January /2012. The median prescription dose was 18 Gy (8-35 Gy), delivered in 1-5 fractions. All MR images were acquired with T2-weighted (TR 3200-6600 ms; TE 75-132 ms) sequences. LC and LF were retrospectively assessed by a neuroradiologist. Ten of twelve LF tumors having MR image follow-up were included in failure group and 12 LC tumors with > 8 mos follow-up were chosen as control group. The T2-weighted MR images at failure (for the LF group) and at the last follow-up (for the LC group) were evaluated by a neuroradiologist. Reading results were ranked by tumor heterogeneity (homogeneous / heterogeneous) and intensity (increased / decreased) and compared to unaffected normal spine. The MR images were also fused to the planning CT. Image intensity and heterogeneity of the GTV in T2-weighted MR was evaluated using the mean T2-weighted signal ratio (intensity in GTV / intensity in normal vertebrae) and the coefficient of variation (COV). The mean ratio was ranked to 1 when (less-than or equal to) 1 and 0 when

< 1 and compared to neuroradiologist's reading. ANOVA and chi-square were used for statistical analysis. Correlation of the T2-weighted signal ratio with follow-up time was also calculated. Results: Median follow-up was 24.1 mos (range, 8.4-39.8 mos) and 8.7 mos (range, 1.5-36.5 mos) for LC and LF groups, respectively. Two thirds and half of tumors were heterogeneous in the LC and LF groups, respectively ($p = 0.36$). Two of 12 and 9 of 10 tumors showed increased T2-weighted signal in the LC and the LF groups, respectively ($p = 0.002$). While mean T2-weighted signal ratio in the LF group is significantly higher than that in the LC group (1.23 (plus or minus) 0.52 vs. 0.76 (plus or minus) 0.30, $p = 0.02$), the COV in the LC group is significantly higher for that in the LF group (0.57 vs. 0.39, $p = 0.02$). Three of 12 and 8 of 10 patients have a ranked T2-weighted signal ratio (greater-than or equal to) 1 for the LC and the LF groups, respectively ($p = 0.03$). Fifteen of 22 T2-weighted signal ratio ranks matched the neuroradiologist readings. No correlation was found between T2-weighted signal ratio and follow-up time (Pearson's $r = 0.16$). Conclusions: Increased T2-weighted signal is a predictor of local failure while decreased signal mostly predicts local control after spinal SBRT. The quantification of intensity and variation of GTV in the T2-weighted MR image can be used to predict LC and LF: higher ratio and lower variation in the T2-weighted MR image indicate LF. These results can be further studied and validated with large multi-institutional data.

Zimmern P, Litman H, Nager C, **Sirls L**, Kraus SR, Kenton K, Wilson T, Sutkin G, Siddiqui N, Vasavada S and Norton P (2014). "Pre-operative urodynamics in women with stress urinary incontinence increases physician confidence, but does not improve outcomes." *Neurourology and Urodynamics* 33(3): 302-306.

[Full-Text](#)

Department of Urology

AIMS: To determine if pre-operative urodynamic testing (UDS) affects physicians' diagnostic confidence and if physician confidence affects treatment outcomes at 1 year. **METHODS:** The Value of Urodynamic Evaluation (ValUE) trial randomized 630 women with predominant stress urinary incontinence (SUI) to office evaluation (OE) or OE plus UDS prior to surgery. After OE, physicians completed a checklist of five clinical diagnoses: SUI, overactive bladder (OAB) wet and dry, voiding dysfunction (VD), and intrinsic sphincter deficiency (ISD), and reported their confidence in each. Responses ranged from 1 to 5 with; 1 = "not very confident (<50%)" to 5 = "extremely confident (95 + %)." After UDS, investigators again rated their confidence in these five clinical diagnoses. Logistic regression analysis correlated physician confidence in diagnosis with treatment success. **RESULTS:** Of 315 women who received OE plus UDS, 294 had complete data. Confidence improved after UDS in patients with baseline SUI (4.52-4.63, $P < 0.005$), OAB-wet (3.55-3.75, $P < 0.001$), OAB-dry (3.55-3.68 $P < 0.005$), VD (3.81-3.95, $P < 0.005$), and suspected ISD (3.63-3.92, $P < 0.001$). Increased confidence after UDS was not associated with higher odds of treatment success although mean changes in confidence were slightly higher for those who achieved treatment success. Physician diagnoses shifted more from not confident to confident for ISD and OAB-wet after UDS (McNemar's P -value < 0.001 for both). **CONCLUSIONS:** In women undergoing UDS for predominant SUI, UDS increased physicians' confidence in their clinical diagnoses; however, this did not correlate with treatment success.