

OAKLAND UNIVERSITY WILLIAM BEAUMONT SCHOOL OF MEDICINE

PUBLICATION LIST

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Abramson DH, Marr BP, Brodie SE, Dunkel IJ, Lin A, **Folberg R** and Gobin YP (2012). "Intraocular hemorrhage after intra-arterial chemotherapy for retinoblastoma in sickle cell trait." *Open Ophthalmology Journal* 6: 1-3.

[Full-Text](#)

Administration

Massive intraocular hemorrhage developed in a child with advanced unilateral retinoblastoma after intrarterial treatment with Melphalan and Topotecan. The child tested positive for sickle cell trait. Sickle cell trait may predispose such children to slower vascular transit time, hypoxia, sickling and vascular occlusion caused by catheter induced decreased flow. Enucliation confirmed the ultrasound and selective angiogram findings in addition to a completely calcified tumor. Clinicians should be on the lookout for the association of sickle-cell disease/trait and intraocular hemorrhages after intraarterial chemotherapy to fully understand its clinical significance.

Akerson VL, Buzzelli CA and **Eastwood JL** (2012). "Bridging the gap between preservice early childhood teachers' cultural values, perceptions of values held by scientists, and the relationships of these values to conceptions of nature of science." *Journal of Science Teacher Education* 23(2): 133-157.

[Full-Text](#)

Department of Biomedical Sciences

This study explored preservice teachers' views of their own cultural values, the cultural values they believed scientists hold, and the relationships of these views to their conceptions of nature of science (NOS). Parallel assignments in a foundations of early childhood education and a science methods course required preservice teachers to explore their own cultural backgrounds and their perceptions of the cultural backgrounds of scientists. The Schwartz Values Inventory was used to measure preservice teachers' personal cultural values and those they perceived of scientists. The Views of Nature of Science version B questionnaire and interviews assessed teachers' conceptions of NOS. Copies of student work were collected and sought for

themes indicating how preservice teachers perceived scientists' cultural values and how those perceptions changed over time. We found that from the beginning to the end of the semester, preservice teachers perceived fewer differences between their own cultural values and those they perceived scientists held, though they did not change their own cultural values. We found that preservice teachers' NOS conceptions improved, and that they were related to both their cultural values and those they perceived scientists held. Preservice teachers who indicated the fewest differences between their own cultural values and those they perceived scientists held the most informed conceptions of NOS.

Akerson VL, Donnelly LA, Riggs ML and **Eastwood J** (2012). "Developing a community of practice to support preservice elementary teachers' nature of science instruction." International Journal of Science Education 34(9): 1371-1392.

[Request Form](#)

Department of Biomedical Sciences

This study explored 'To what extent will preservice teachers with adequate nature of science (NOS) conceptions and who participate in a community supporting NOS instruction teach NOS in their internship settings?' Using a combination of focus group discussions and peer feedback, five preservice teachers met with university personnel bi-monthly during their internships to share NOS teaching and assessment ideas and ask questions. Field notes and voice recordings were used to track conversations at focus group settings and videotapes were made of science instruction in each internship setting. None of the preservice teachers had cooperating teachers who taught NOS, yet results showed that all five preservice teachers were able to explicitly teach NOS in their science lessons, albeit in different ways and to different degrees.

Aladily TN, Medeiros LJ, **Amin MB**, Haideri N, Ye D, Azevedo SJ, Jorgensen JL, de Peralta-Venturina M, Mustafa EB, Young KH, You MJ, Fayad LE, **Blenc AM** and Miranda RN (2012). "Anaplastic large cell lymphoma associated with breast implants: a report of 13 cases." American Journal of Surgical Pathology 36(7): 1000-1008.

[Full-Text](#)

Department of Pathology

We report 13 cases of anaplastic large cell lymphoma (ALCL) associated with breast implants. Patient age ranged from 39 to 68 years, and the interval from implant to ALCL was 4 to 29 years. All tumors were composed of large, pleomorphic cells that were CD30(+) and ALK1(-), and all 7 cases assessed had monoclonal T-cell receptor gamma-chain rearrangements. Two patient subgroups were identified. Ten patients presented with effusion surrounded by fibrous capsule without a grossly identifiable tumor mass. Nine patients had stage I and 1 had stage II disease. Eight patients underwent implant removal and capsulectomy. Four patients received chemotherapy and 4 radiation therapy. All patients were alive without disease at last follow-up. A second subgroup of 3 patients had effusion and a distinct mass adjacent to the implant. One patient had stage I and 2 stage II disease. One patient had a 3-year history of lymphomatoid papulosis, and 1 patient had a 1-year history of CD30(+) T-cell lymphoma adjacent to the breast before the diagnosis of ALCL associated with breast implant. Two patients received chemotherapy and 1 radiation therapy. Two patients died 2 and 12 years after diagnosis, respectively. We conclude that the clinical behavior of ALCL associated with breast implants is heterogeneous. Patients who present with effusion without a distinct mass have an indolent disease course, similar to CD30(+) lymphoproliferative disorder of skin. In contrast, patients who present with a distinct mass may have advanced stage or possibly systemic disease and have a poorer prognosis.

Albo ME, Litman HJ, Richter HE, Lemack GE, **Sirls LT**, Chai TC, Norton P, Kraus SR, Zyczynski H, Kenton K, Gormley EA and Kusek JW (2012). "Treatment success of retropubic and transobturator mid urethral slings at 24 months." Journal of Urology 188(6): 2281-2287.

[Request Form](#)

Department of Urology

PURPOSE: Longer term comparative efficacy information regarding transobturator and retropubic mid urethral slings is needed. We report 24-month continence rates, complications and symptom outcomes from

a randomized equivalence trial. MATERIALS AND METHODS: Primary outcomes were objective (negative stress test, negative pad test and no re-treatment for stress urinary incontinence) and subjective (no self-report of stress urinary incontinence symptoms, no leakage episodes on 3-day bladder diary and no re-treatment for stress urinary incontinence) success at 24 months. The predetermined equivalence margin was +/- 12%. RESULTS: Of 597 randomized participants 516 (86.4%) were assessed. Objective success rates for retropubic and transobturator mid urethral slings were 77.3% and 72.3%, respectively (95% CI for difference of 5.1% was -2.0, 12.1), and subjective success rates were 55.7% and 48.3%, respectively (CI for difference of 7.4% was -0.7, 15.5). Neither objective nor subjective success rates met the prespecified criteria for equivalence. Patient satisfaction (retropubic 86.3% vs transobturator 88.1%, $p = 0.58$), frequency of de novo urgency incontinence (retropubic 0% vs transobturator 0.3%, $p = 0.99$) and occurrence of mesh exposure (retropubic 4.4% vs transobturator 2.7%, $p = 0.26$) were not significantly different. The retropubic mid urethral sling group had higher rates of voiding dysfunction requiring surgery (3.0% vs 0%, $p = 0.002$) and urinary tract infections (17.1% vs 10.7%, $p = 0.025$), whereas the transobturator group had more neurological symptoms (9.7% vs 5.4%, $p = 0.045$). CONCLUSIONS: Objective success rates met the criteria for equivalence at 12 months but no longer met these criteria at 24 months. Subjective success rates remained inconclusive for equivalence. Patient satisfaction remained high and symptom severity remained markedly improved. Continued surveillance is important in women undergoing mid urethral sling surgery.

Al-Tahou K, **Jamil S**, Mody R, Knaus A, **Micale M** and **Huang J** (2012). "Secondary acute myelogenous leukemia (AML) with trisomy 10 and del(9q) following precursor B-cell acute lymphoblastic leukemia (ALL) with a hyperdiploid karyotype." Cancer Genetics 205(10): 533-536.

[Full-Text](#)

Department of Pediatrics

Department of Pathology

Acute myelogenous leukemia (AML) secondary to acute lymphoblastic leukemia (ALL) in children is uncommon and usually occurs within 10 years of completing therapy for ALL. A variety of recurrent cytogenetic abnormalities have been described, suggesting significant biological heterogeneity. We report a case of highly refractory secondary AML with trisomy 10 and del(9q) occurring in an adolescent female 12 years after she was treated successfully for precursor B-cell ALL with chemotherapy only.

Anderson KS and Segars JH (2012). "Predicting fertility with antimüllerian hormone: Is a cutoff value adequate?" Fertility and Sterility 98(6): 1421-1422.

[Full-Text](#)

Department of Orthopedic Surgery

Anekstein Y, Mirovsky Y, Arnabitsky V, Gelfer Y, **Zaltz I** and **Smorgick Y** (2012). "Reversing the concept: correction of adolescent idiopathic scoliosis using the convex rod de-rotation maneuver." European Spine Journal 21(10): 1942-1949.

[Full-Text](#)

Department of Orthopedic Surgery

Department of Surgery

PURPOSE: To show the radiological results of adolescent idiopathic scoliosis (AIS) patients treated with posterior fusion using all-pedicle-screw construct with correction carried out using a convex rod reduction technique. METHODS: Between October 2004 and June 2007, 42 AIS patients were treated with posterior fusion using all-pedicle-screw construct with correction done through the convex side. Two patients were lost to follow-up and were not included in the study. Forty patients had a minimum follow-up of 2 years. Patients were evaluated for the deformity correction in coronal and sagittal planes and for spinal balance. RESULTS: The mean preoperative Cobb angle of the major curve and secondary minor curves was 60 degrees and 41 degrees, respectively. Immediate postoperative mean Cobb angle of the major curve and secondary minor curves was 17 degrees and 13 degrees, respectively. Postoperative 2-year average major curve loss of correction was 7%. Postoperative 2-year average minor curve loss of correction was 5%. Preoperative thoracic kyphosis of 28 degrees was changed to 22 degrees in 2-years follow-up. The loss of thoracic

kyphosis was most noted in hyperkyphotic patients. CONCLUSIONS: The correction of AIS by convex-sided pedicular screws yields a coronal correction comparable to what is described in the literature for segmental concave-sided screws.

Angoa-Perez M, Kane MJ, Briggs DI, Sykes CE, Shah MM, Francescutti DM, Rosenberg DR, **Thomas DM** and Kuhn DM (2012). "Genetic depletion of brain 5HT reveals a common molecular pathway mediating compulsivity and impulsivity." *Journal of Neurochemistry* 121(6): 974-984.

[Full-Text](#)

Department of Biomedical Sciences

Neuropsychiatric disorders characterized by behavioral disinhibition, including disorders of compulsivity (e.g. obsessive-compulsive disorder; OCD) and impulse-control (e.g. impulsive aggression), are severe, highly prevalent and chronically disabling. Treatment options for these diseases are extremely limited. The pathophysiological bases of disorders of behavioral disinhibition are poorly understood but it has been suggested that serotonin dysfunction may play a role. Mice lacking the gene encoding brain tryptophan hydroxylase 2 (Tph2^{-/-}), the initial and rate-limiting enzyme in the synthesis of serotonin, were tested in numerous behavioral assays that are well known for their utility in modeling human neuropsychiatric diseases. Mice lacking Tph2 (and brain 5HT) show intense compulsive and impulsive behaviors to include extreme aggression. The impulsivity is motor in form and not cognitive because Tph2^{-/-} mice show normal acquisition and reversal learning on a spatial learning task. Restoration of 5HT levels by treatment of Tph2^{-/-} mice with its immediate precursor 5-hydroxytryptophan attenuated compulsive and impulsive-aggressive behaviors. Surprisingly, in Tph2^{-/-} mice, the lack of 5HT was not associated with anxiety-like behaviors. The results indicate that 5HT mediates behavioral disinhibition in the mammalian brain independent of angiogenesis.

Angoa-Perez M, Kane MJ, Francescutti DM, Sykes KE, Shah MM, Mohammed AM, **Thomas DM** and Kuhn DM (2012). "Mephedrone, an abused psychoactive component of bath salts' and methamphetamine congener, does not cause neurotoxicity to dopamine nerve endings of the striatum." *Journal of Neurochemistry* 120(6): 1097-1107.

[Full-Text](#)

Department of Biomedical Sciences

Mephedrone (4-methylmethcathinone) is a beta-ketoamphetamine with close structural analogy to substituted amphetamines and cathinone derivatives. Abuse of mephedrone has increased dramatically in recent years and has become a significant public health problem in the United States and Europe. Unfortunately, very little information is available on the pharmacological and neurochemical actions of mephedrone. In light of the proven abuse potential of mephedrone and considering its similarity to methamphetamine and methcathinone, it is particularly important to know if mephedrone shares with these agents an ability to cause damage to dopamine nerve endings of the striatum. Accordingly, we treated mice with a binge-like regimen of mephedrone (4 x 20 or 40 mg/kg) and examined the striatum for evidence of neurotoxicity 2 or 7 days after treatment. While mephedrone caused hyperthermia and locomotor stimulation, it did not lower striatal levels of dopamine, tyrosine hydroxylase or the dopamine transporter under any of the treatment conditions used presently. Furthermore, mephedrone did not cause microglial activation in striatum nor did it increase glial fibrillary acidic protein levels. Taken together, these surprising results suggest that mephedrone, despite its numerous mechanistic overlaps with methamphetamine and the cathinone derivatives, does not cause neurotoxicity to dopamine nerve endings of the striatum.

Asami T, Wong SC, Mitchell PC, Tokunaga CC, Chen YH, Dang L, Giblin FJ and **Trese MT** (2012). "A novel quadrupole needle with improved intravitreal drug dispersion." *Retina* 32(6): 1222-1225.

[Full-Text](#)

Department of Ophthalmology

Autologous plasmin enzyme has been shown to induce clinically relevant vitreous liquefaction and induce posterior vitreous detachment (PVD) through degradation of the vitreoretinal juncture and stimulation of collagenase activity.¹ Microplasmin (ThromboGenics Co, Ltd., NV, Leuven, Belgium) is a truncated

recombinant form of plasmin enzyme lacking kringle sites and has been shown to be efficacious in recent phase II, multicenter, randomized, controlled, clinical trials.^{2,3} It is our hypothesis that the technique of intravitreal delivery and dispersion of these enzymatic medications may affect clinical efficacy. We describe a novel technique of drug delivery within the vitreous cavity.

Bain EE, Apostol G, **Sangal RB**, Robieson WZ, McNeill DL, Abi-Saab WM and Saltarelli MD (2012). "A randomized pilot study of the efficacy and safety of ABT-089, a novel α 4 β 2 neuronal nicotinic receptor agonist, in adults with attention-deficit/hyperactivity disorder." Journal of Clinical Psychiatry 73(6): 783-789.

[Full-Text](#)

Department of Family Medicine

Objective: ABT-089, an α 4 β 2 neuronal nicotinic receptor partial agonist (generic name pozanicline), has demonstrated efficacy in adults with attention-deficit/hyperactivity disorder (ADHD) at doses of 40 mg once daily and 40 mg twice daily. The purpose of this exploratory pilot study was to obtain initial safety, tolerability, and efficacy data for an ABT-089 80-mg once-daily regimen to inform a decision of whether to include an 80-mg once-daily dose regimen in subsequent, definitive (phase 3) efficacy studies. **Method:** This phase 2, randomized, double-blind, parallel-group, placebo-controlled pilot study was conducted at 12 sites from March to August 2008. A screening/washout period of up to 4 weeks was followed by an 8-week double-blind treatment period. Eligible subjects met DSM-IV-TR criteria for ADHD and were randomized in a 1:1:1 ratio to ABT-089 40 mg once daily, ABT-089 80 mg once daily, or placebo. The primary efficacy variable was reduction from baseline to the final evaluation in the investigator-rated Conners' Adult ADHD Rating Scale for each active treatment group versus placebo. Safety assessments and pharmacokinetic sampling were also conducted. **Results:** A total of 160 subjects were randomized, with 137 (86%) completing the trial. No statistically significant treatment effects were observed with either ABT-089 dose for any efficacy measures. The most commonly reported adverse events in the active treatment groups were nasopharyngitis (6.6%), upper respiratory tract infection (6.6%), and somnolence (5.7%). The incidence of adverse events did not differ significantly between active groups and placebo. There were no clinically significant laboratory, electrocardiogram, or physical examination findings. **Conclusions:** ABT-089 was generally well tolerated at doses up to 80 mg. Because ABT-089 is a weak partial neuronal nicotinic receptor agonist, the results may not predict the potential efficacy for other, more potent neuronal nicotinic receptor agonists. **Trial Registration:** ClinicalTrials.gov identifier: NCT00640185. © Copyright 2012 Physicians Postgraduate Press, Inc

Band J (2012). Diagnosis of intravascular catheter-related infections, in Basow D. (ed). UpToDate: Wolters Kluwer Health.

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Department of Internal Medicine

Band J and Gaynes R (2012). Prevention of intravascular catheter-related infections, in Basow D. (ed). UpToDate: Wolters Kluwer Health.

[Full-Text](#)

Department of Internal Medicine

Barger RL, Jr. and **Nandalur KR** (2012). "Diagnostic performance of dual-time 18F-FDG PET in the diagnosis of pulmonary nodules: a meta-analysis." Academic Radiology 19(2): 153-158.

[Full-Text](#)

Department of Radiation Oncology

RATIONALE AND OBJECTIVE: Perform a comprehensive meta-analysis evaluating the diagnostic performance of dual time point deoxy-2-[(18)F]fluoro-D-glucose positron emission tomography (FDG-PET) in the diagnosis of pulmonary nodules. **MATERIALS AND METHODS:** MEDLINE, EMBASE, and PUBMED were queried between January 2000 and January 2011. Studies were included if they: 1) used dual time point FDG-PET as a diagnostic test for pulmonary nodules, 2) used pathology or clinical follow-up as the reference standard, and 3) reported absolute number of true-positive (TP), true-negative (TN), false-positive (FP), and false-negative (FN) results or stated sufficient data to derive these values. Summary sensitivity (SN), summary

specificity (SP), positive and negative likelihood ratios (LR+) and (LR-), and diagnostic odds ratio were calculated. Heterogeneity of the results was assessed using Forest plots and the value of inconsistency index (I(2)). RESULTS: Inclusion criteria were fulfilled by 10 articles with a total of 816 patients and 890 pulmonary nodules. The summary sensitivity was 85% (82%-89% at 95% confidence interval [CI]) and summary specificity was 77% (CI: 72%-81%), with a LR+ of 2.7 (CI: 1.4-5.2) and a LR- of 0.26 (CI: 0.14-0.49). Diagnostic odds ratio was 11 (CI: 3.8-32.2). Significant heterogeneity was found in the sensitivity (I(2) = 77%) and specificity (90.3%). CONCLUSION: Dual time point FDG-PET demonstrates similar sensitivity and specificity to single time point FDG-PET in the diagnosis of pulmonary nodules. The additive value of the dual time point FDG-PET is questionable, primarily because of the significant overlap of benign and malignant nodule FDG-PET characteristics and lack of consensus criteria for quantitative thresholds to define nodules as malignant.

Baschnagel A, Shah C, **Margolis J, Nadeau L, Stein J, Jury R and Robertson JM** (2012). "Survival after chemoradiation in resected pancreatic cancer: the impact of adjuvant gemcitabine." International Journal of Radiation Oncology Biology Physics 83(3): E331-E335.

[Full-Text](#)

Department of Internal Medicine

Department of Urology

Department of Surgery

Department of Radiation Oncology

Purpose: To evaluate survival in patients with resected pancreatic cancer treated with concurrent chemoradiation with or without adjuvant gemcitabine (Gem). Methods and Materials: From 1998 to 2010, 86 patients with pancreatic adenocarcinoma who underwent resection were treated with adjuvant concurrent chemoradiation. Thirty-four patients received concurrent 5-fluorouracil-based chemoradiation (5-FU/RT) with traditional field radiation (range, 45-61.2 Gy; median, 50.4 Gy) without further adjuvant therapy. Thirty patients received traditional field 5-FU/RT (range, 45-60.4 Gy; median, 50.4 Gy) with Gem (1,000 mg/m² weekly) either before and after radiotherapy or only after radiotherapy. Twenty-two patients received concurrent full-dose Gem (1,000 mg/m² weekly)-based chemoradiation (Gem/RT), consisting of involved-field radiation (range, 27-38 Gy; median, 36 Gy) followed by further adjuvant Gem. Results: The median age of the cohort was 65 years (range, 40-80 years). Of the patients, 58 had T3 tumors (67%), 22 had T2 tumors (26%), and 6 had T1 tumors (7%). N1 disease was present in 61 patients (71%), whereas 18 patients (21%) had R1 resections. Performance status, lymph node status, and margin status were all similar among the treatment groups. Median follow-up was 19.0 months. Median overall survival (OS) (19.2 months, 19.0 months, and 21.0 months) and 3-year OS rates (26.5%, 27.2%, and 32.1%) were similar among patients with 5-FU/RT with no adjuvant Gem, those with 5-FU/RT with adjuvant Gem, and those with Gem/RT with adjuvant Gem, respectively (p = 0.88). Patients who received adjuvant Gem had a similar median OS (22.1 months) and 3-year OS rate (29%) compared to patients who did not (19.2 months and 26.5%, respectively) (p = 0.62). There was a trend for improved 3-year OS rates in patients with R0 vs. R1 resections (28.1% vs. 14.2%, p = 0.06) and in patients with T1 and T2 vs. T3 tumors (38% vs. 20%, p = 0.09). Node-negative patients had an improved 3-year OS rate (30.1%) when compared with patients with N1 disease (16.2%) (p = 0.02). Conclusion: In our cohort of patients with resected pancreatic cancer, Gem chemotherapy did not improve OS after chemoradiotherapy. (C) 2012 Elsevier Inc.

Baschnagel AM, Shah C, Wilkinson JB, **Dekhne N, Arthur DW and Vicini FA** (2012). "Failure rate and cosmesis of immediate tissue expander/implant breast reconstruction after postmastectomy irradiation." Clinical Breast Cancer 12(6): 428-432.

[Full-Text](#)

Department of Surgery

Department of Internal Medicine

Postmastectomy radiation therapy (PMRT) can increase the rate of breast reconstruction complications and failures. There are limited data on immediate breast reconstruction with tissue expanders (TEs)/implants followed by irradiation. We report on a large cohort of women who received immediate breast

reconstruction with TEs/implants and then were treated with irradiation. Good cosmesis was achieved in the majority of women, with an acceptable risk of expander or implant loss. Background: This study reports the rate of breast reconstruction failure and cosmetic outcomes after postmastectomy radiation therapy (PMRT) with temporary tissue expanders (TEs) or implants in place. Patients and Methods: Ninety-four patients underwent mastectomy (93 unilateral, 1 bilateral; 95 cases total) and immediate TE reconstruction followed by PMRT. Ninety TEs and 5 permanent implants were irradiated. All patients received a dose of 5400 cGy given in 180-cGy fractions to the reconstructed breast. Twenty-one patients (22%) received tangents alone and 74 patients (78%) were treated with tangents and a supraclavicular field using a monoisocentric technique. Bolus was used in 91 patients (96%). Eighty-eight patients (93%) received chemotherapy and 78 patients (82%) received endocrine therapy. Results: With a median follow-up of 24.1 months, 19 patients (20%) experienced failure of reconstruction. The 1-, 2-, and 3-year actuarial rate of reconstruction failure was 9.7%, 19.3%, and 25.5%, respectively. Infection was the most common cause of failure. Of the 19 failures, 8 patients underwent salvage procedures with flap reconstruction. Univariate analysis was performed examining age, chemotherapy use, hormone therapy use, use of a supraclavicular field, smoking status, diabetes, hypertension, and menopausal status. No risk factors were found to be associated with reconstruction failure. In patients who did not experience reconstruction failure, good/excellent cosmesis was observed in 75% of patients. Conclusion: In the current series of women with a high risk of locoregional recurrence, PMRT with a TE/implant in place provides good cosmesis in the majority of women, with an acceptable risk of expander or implant loss.

Bastani A, Galens S, Rocchini A, Walch R, Shaqiri B, Palomba K, Milewski AM, Falzarano A, Loch D and Anderson W (2012). "ED identification of patients with severe sepsis/septic shock decreases mortality in a community hospital." [American Journal of Emergency Medicine](#) 30(8): 1561-1566.

[Full-Text](#)

Department of Emergency Medicine

STUDY OBJECTIVES: Our objective was to quantify the mortality difference between patients with severe sepsis/septic shock (SS/SS) identified in the emergency department (EDI) vs those not identified in the emergency department (NEDI) within our community hospital. METHODS: We conducted a retrospective review of all patients with SS/SS from July 2007 to January 2010 who were admitted to the intensive care unit within our community hospital. Our primary outcome measure was the difference in mortality rates of patients with SS/SS between the EDI and NEDI cohorts. Our secondary outcome measures included the final disposition, the length of stay, and direct cost (DC) for both groups. The data were analyzed using a 2 x 2 contingency table and the Fisher exact test for significance to compare the mortality rates between groups. Lengths of stay and DC between both groups were reported as medians, and significance was calculated using the Mann-Whitney U test. RESULTS: A total of 267 patients with SS/SS were identified during the 31-month study period. Of these patients, 155 were EDI patients with a mortality rate of 27.7%, and 112 were NEDI patients with a mortality rate of 41.1%. This represents an absolute difference in mortality rates of 13.4% between the 2 groups (P = .0257). The median length of stay between both groups was 7 days for the EDI group and 12.5 days for the NEDI group, translating to median DCs of \$9861.01 vs \$16 031.07. CONCLUSIONS: Emergency department identification of patients with SS/SS in the community hospital significantly improves mortality.

Bee M, McAuley R and Montante J (2012). "Upper limb bone video for gross human anatomy." Retrieved Video/DVD, from <https://www.mededportal.org/publication/9217>

[Full-Text](#)

Department of Biomedical Sciences

This 12-minute video provides a tutorial on the bones of the upper limb. It includes the scapula, clavicle, humerus, ulna, radius, carpals, metacarpals, and phalanges. Important structures on each bone are described along with mnemonics that aid with learning the complicated regions.

Bee MT, Diven A, Kalnasy K, Koettters E and Ottenbreit M (2012). "External laryngeal morphology: gender differences." FASEB Journal 26(Meeting Abstract Supplement): 722.724.

[Full-Text](#)

Department of Biomedical Sciences

The larynx is an important part of the respiratory system and has great clinical relevance. While many medical procedures involve manipulation or accessing different areas of the larynx, few studies quantify the distances within and between these cartilaginous structures. Our study investigated the size and distance of the hyoid bone, thyroid cartilage and cricoid cartilage and the distances between these structures on human cadavers (n=37). Surprisingly, a significant difference in the size of the cartilaginous structures was not identified in most parameters between genders (p=0.318). However, the distances of the fibrous gaps that lie between the hyoid bone the cartilaginous structures were higher in females than males (p<0.05). Knowledge of this variability has a significant impact on clinical processes like tracheostomies and cricothyrotomies of different genders.

Bee MT, Montante JM, Grabowski G and **Forbes WC** (2012). "Getting crafty in the classroom: reinforcing students' knowledge of muscular attachments and positions with fabric muscles." FASEB Journal 26((Meeting Abstract Supplement): 529.527.

[Full-Text](#)

Department of Biomedical Sciences

Helping students to visualize the origin, insertion, position and relationships of muscles is a challenge. We present a visual, interactive exercise to reinforce student understanding in this area. Students were asked to place precut two-dimensional felt models of the muscles on a life sized skeleton or disarticulated bones matching the correct bony origins and insertions. In order to assess the impact of this approach on student learning, the students were split into two groups. The first group spent 15 minutes utilizing the felt leg muscles while the second group spent 15 minutes reading their books to study the muscular attachments of the leg muscles. A pre-test and a post-test covering the material were administered to both groups. Students who worked with the felt muscles showed a greater improvement relative to the students who studied independently (p<0.05). The groups switched activities when studying the foot muscles and similar results were found. Student satisfaction was assessed with a survey administered after each unit. The majority of students indicated that the activity was fun and felt that the activity was an effective way to learn the material. We advocate the use of this type of activity to engage the students and to provide an opportunity for the students to reinforce their understanding of muscular attachments.

Bee MT, Montante JM and **McAuley B** (2012). "Cadaver dissection videos as an effective lab instruction tool for medical and other graduate level health professional students." FASEB Journal 26(Meeting Abstract Supplement): 530.539.

[Full-Text](#)

Department of Biomedical Sciences

Administration

Human anatomy laboratory remains to be one of the most challenging courses in medical school. Students are required to perform high quality dissections, even though most of them do not have previous experience and struggle with learning by merely reading a lab manual. To make this task less daunting we produced a series of anatomy dissection videos to visually and audibly teach students the landmarks to focus on and how to dissect. Videos are approximately ten minutes in duration and illustrate dissection techniques and important anatomical relationships. Student feedback of the videos was overwhelmingly positive with 68% increased satisfaction from a group of students utilizing the dissection videos versus a control group. Student comments include "I have greater confidence and understanding of the dissections" and "I couldn't understand what they described in the book, but the video helped it all make sense." Furthermore, dissection quality of the students viewing the videos was significantly better than the control group (p<0.01). We discuss the process of producing the videos and advocate the use of dissection videos to help guide students in human anatomy dissection.

Beitsch PD, Wilkinson JB, **Vicini FA**, Haffty B, Fine R, Whitworth P, Kuerer H, Zannis V and Lyden M (2012). "Tumor bed control with balloon-based accelerated partial breast irradiation: incidence of true recurrences versus elsewhere failures in the American Society of Breast Surgery MammoSite (R) registry trial." Annals of Surgical Oncology 19(10): 3165-3170.

[Full-Text](#)

Department of Internal Medicine

Randomized trials demonstrate that lumpectomy plus whole-breast irradiation (WBI) yields survival equivalent to mastectomy. Studies that use WBI, however, typically report higher tumor bed recurrence rates than elsewhere failures (EF) (historically considered new primary lesions). The rate of true recurrence (TR) versus EF was queried for a large patient cohort treated with accelerated partial breast irradiation (APBI). A total of 1,449 cases of early-stage breast cancer were treated on the American Society of Breast Surgeons MammoSite(A (R)) Registry Trial with lumpectomy plus balloon-based APBI (34 Gy, 10 BID fractions). A total of 1,255 cases (87 %) had invasive breast cancer, and 194 patients (13 %) had ductal carcinoma in situ. Rates of TR versus EF were calculated and compared to historical WBI controls. Median follow-up was 60 (range 0-109) months. Fifty patients (3.5 %) developed an ipsilateral breast tumor recurrence (IBTR). The 5-year actuarial rate of IBTR was 3.6 % (invasive breast cancer 3.6 %, ductal carcinoma in situ 3.4 %). Fourteen IBTR (1.1 %) were TR, while 36 (2.6 %) were EF. Estrogen receptor-negative status was associated with IBTR for invasive malignancies as well as for EF only ($p < 0.001$). Trends for increased rates of EF were noted for increased tumor size ($p = 0.067$) and extensive intraductal component ($p = 0.087$). No pathologic factors were explicitly associated with TR. IBTR after balloon-based APBI is low and similar to rates reported for WBI. In this data set, APBI had fewer tumor bed recurrences (presumably initial cancer recurrences) than EF (presumably new primary lesions). This suggests that balloon-based APBI has a tumor bed control rate that is at least equal to (and potentially higher than) WBI.

Berger A, **Hartrick C**, Edelsberg J, Sadosky A and Oster G (2012). "Economic costs of work and productivity losses in employees with osteoarthritis." Journal of Health and Productivity 6(1): 24.

[Full-Text](#)

Department of Biomedical Sciences

OBJECTIVE To examine the economic costs of work and productivity loss among workers with osteoarthritis (OA). **METHODS** Using a large US longitudinal database from a number of self-insured employers containing information on work loss, we identified all employed persons aged ≥ 18 years with ≥ 1 health care encounters for OA during calendar year (CY) 2007. Persons not enrolled for all of CY2007 were dropped. We examined total days and costs of work loss due to illness, including total paid claims for short-term disability and workers' compensation, and the total cost of absenteeism, estimated as hours of work loss due to illness (excluding short-term disability and workers' compensation) multiplied by mean hourly earnings of US workers in CY2007. We examined all workers with OA and subgroups thereof defined based on medication use (ie, opioids, nonsteroidal anti-inflammatory drugs [NSAIDs], injectable corticosteroids) and selected comorbidities. **RESULTS** We identified a total of 2399 persons with OA. Mean (SD) age was 53 (7) years; 62% were men. Study subjects averaged 39.2 (SD=61.2) days of work loss due to illness (ie, exclusive of recreation/ leave). The mean total cost of short-term disability, workers' compensation, and absenteeism combined was \$5002 among all OA patients, and ranged from \$7133 among those with long-term use of opioids to \$4719 among those who received injectable corticosteroids; it ranged from \$6247 among those with comorbid diabetes to \$4941 among those with cancer. **CONCLUSION** Economic costs of work and productivity loss are high among workers with OA, and vary in relation to medication use and comorbidities.

Billecke SS, D'Alecy LG and **Marcovitz PA** (2012). "Potential treatment influences and mechanisms related to asymmetric dimethylarginine control in heart failure." Journal of the American College of Cardiology 60(10): 948-949.

[Full-Text](#)

Department of Internal Medicine

Boyanton B and **Crisan D** (2012). Sample collection, processing, and storage for molecular genetic testing, in Kottke-Marchant K. and Davis B. (ed). Laboratory Hematology Practice: Wiley-Blackwell: 145-154.

[Request Form](#)

Department of Pathology

Boyanton BL, Jr., Sural P, Loomis CR, Pesta C, Gonzalez-Krellwitz L, **Robinson-Dunn B** and Riska P (2012). "Loop-mediated isothermal amplification compared to real-time PCR and enzyme immunoassay for toxigenic clostridium difficile detection." Journal of Clinical Microbiology 50(3): 640-645.

[Full-Text](#)

Department of Pathology

Clostridium difficile infection is the primary cause of health care-associated diarrhea. While most laboratories have been using rapid antigen tests for detecting C. difficile toxins, they have poor sensitivity; newer molecular methods offer rapid results with high test sensitivity and specificity. This study was designed to compare the performances of two molecular assays (Meridian illumigene and BD GeneOhm) and two antigen assays (Wampole Quik Chek Complete and TechLab Tox A/B II) to detect toxigenic C. difficile. Fecal specimens from hospitalized patients (n = 139) suspected of having C. difficile infection were tested by the four assays. Nine specimens were positive and 109 were negative by all four methods. After discrepant analysis by toxigenic culture (n = 21), the total numbers of stool specimens classified as positive and negative for toxigenic C. difficile were 21 (15%) and 118 (85%), respectively. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were as follows: GeneOhm (95.2%, 100%, 100%, and 99.2%), illumigene (95.2%, 96.6%, 83.3%, and 99.2%), Tox A/B II (52.4%, 97.5%, 78.6%, and 92.4%), and Quik Chek Complete (47.6%, 100%, 100%, and 91.9%). The illumigene assay performed comparably to the GeneOhm assay with a slight decrease in test specificity; the sensitivities of both far exceeded those of the antigen assays. The clinical characteristics of the concordant and discrepant study patients were similar, including stool consistency and frequency. In the era of rapid molecular-based tests for toxigenic C. difficile, toxin enzyme immunoassays (EIAs) should no longer be considered the standard of care.

Boyer A, **Amin M** and **Jafri S** (2012). "Small cell carcinoma of the urinary bladder: CT features and prediction of histopathology." American Journal of Roentgenology 198(5 Suppl): E621.

[Request Form](#)

Department of Pathology

Department of Diagnostic Radiology and Molecular Imaging

Brown OW (2012). "Legal implications of pushing the endovascular envelope." Journal of Vascular Surgery 56(1): 273-274.

[Request Form](#)

Department of Surgery

Endovascular technology continues to improve for the treatment of vascular disease. However, application of these technologies without first obtaining proper informed consent may result in medical malpractice litigation. Similarly, use of these technologies without proper government and/or hospital approval may result in both criminal and/or civil liability. Care must be taken when pushing the envelope of endovascular interventions.

Brush GS, Najor NA, Dombkowski AA, Cukovic D and **Sawarynski KE** (2012). "Yeast IME2 functions early in meiosis upstream of cell cycle-regulated SBF and MBF targets." PloS One 7(2): e31575.

[Full-Text](#)

Department of Biomedical Sciences

Background: In *Saccharomyces cerevisiae*, the G1 cyclin/cyclin-dependent kinase (CDK) complexes Cln1,-2,-3/Cdk1 promote S phase entry during the mitotic cell cycle but do not function during meiosis. It has been proposed that the meiosis-specific protein kinase Ime2, which is required for normal timing of pre-meiotic DNA replication, is equivalent to Cln1,-2/Cdk1. These two CDK complexes directly catalyze

phosphorylation of the B-type cyclin/CDK inhibitor Sic1 during the cell cycle to enable its destruction. As a result, Clb5,-6/Cdk1 become activated and facilitate initiation of DNA replication. While Ime2 is required for Sic1 destruction during meiosis, evidence now suggests that Ime2 does not directly catalyze Sic1 phosphorylation to target it for destabilization as Cln1,-2/Cdk1 do during the cell cycle.

Methodology/Principal Findings: We demonstrated that Sic1 is eventually degraded in meiotic cells lacking the IME2 gene (ime2 Delta), supporting an indirect role of Ime2 in Sic1 destruction. We further examined global RNA expression comparing wild type and ime2D cells. Analysis of these expression data has provided evidence that Ime2 is required early in meiosis for normal transcription of many genes that are also periodically expressed during late G1 of the cell cycle. Conclusions/Significance: Our results place Ime2 at a position in the early meiotic pathway that lies upstream of the position occupied by Cln1,-2/Cdk1 in the analogous cell cycle pathway. Thus, Ime2 may functionally resemble Cln3/Cdk1 in promoting S phase entry, or it could play a role even further upstream in the corresponding meiotic cascade.

Budge MD, **Moravek JE**, Zimel MN, Nolan EM and Wiater JM (2012). "Reverse total shoulder arthroplasty for the management of failed shoulder arthroplasty with proximal humeral bone loss: is allograft augmentation necessary?" Journal of Shoulder and Elbow Surgery 22(6): 739-744.

[Full-Text](#)

Department of Surgery

BACKGROUND: Patients undergoing revision shoulder arthroplasty frequently have deficient proximal humeral bone stock. Proximal humeral allograft has been recommended to augment reverse total shoulder arthroplasty (RTSA) to improve stability and function. This study reports the results of RTSA without proximal humeral allograft in patients with proximal humeral bone loss secondary to failed shoulder arthroplasty. MATERIALS AND METHODS: From 2005 to 2008, 251 patients were enrolled in a prospective RTSA cohort study. Significant humeral bone loss was demonstrated in 15 of 56 undergoing revision for failed arthroplasty. Average age was 67 years. Average bone loss measured 38.4 mm (range, 26-72 mm). Patients were followed up for a minimum of 2 years with American Shoulder and Elbow Surgeons (ASES), Subjective Shoulder Value (SSV), Constant Score (CS), and visual analog scale (VAS) pain scores, as well as self-reported satisfaction and radiographs. RESULTS: Patients demonstrated significant improvement in mean CS (23.0 to 44.2), ASES (38.2 to 68.3), ASES activities of daily living (7.0 to 15.9), SSV (19.2 to 75.8), and VAS pain (4.6 to 1.6) scores. Thirteen of 15 patients reported satisfaction (87%). Range of motion improved in forward flexion (38.3 degrees to 103.2 degrees) and external rotation (-0.5 degrees to 11.9 degrees). Radiographs demonstrated notching in 3 patients (20%), no humeral subsidence or loosening, and prosthetic fracture of 1 modular humeral stem. CONCLUSIONS: Use of RTSA for failed shoulder arthroplasty and deficient humeral bone stock provides a significant clinical benefit without the need for allograft augmentation. Monoblock humeral component use may diminish risk for prosthetic fracture.

Burks FN, Liu AB, Suh RS, Schuster TG, Bradford T, Moylan DA, Knapp PM, Murtagh DS, Dunn RL, Montie JE and Miller DC (2012). "Understanding the use of immediate intravesical chemotherapy for patients with bladder cancer." Journal of Urology 188(6): 2108-2113.

[Request Form](#)

Department of Urology

Purpose: Despite its established efficacy in reducing recurrence rates for patients with urothelial carcinoma, immediate intravesical chemotherapy is reportedly used infrequently. Accordingly, the Urological Surgery Quality Collaborative implemented a project aimed at understanding and improving the use of immediate intravesical chemotherapy. Materials and Methods: Surgeons in 5 Urological Surgery Quality Collaborative practices prospectively collected clinical and baseline intravesical chemotherapy use data for patients undergoing bladder biopsy or transurethral bladder tumor resection from September 2010 through January 2012. In the second phase of data collection (June 2011 through January 2012) treating surgeons also documented reasons for not administering intravesical chemotherapy. We defined patients with 1 to 2 clinical stage Ta/T1, completely resected, papillary tumor(s) as ideal candidates for treatment with immediate intravesical chemotherapy. For ideal and nonideal patients we examined baseline use of intravesical chemotherapy across Urological Surgery Quality Collaborative practices as well as reasons for not

administering therapy among ideal patients. Results: Among 1,931 patients 37.2% met criteria as ideal cases for intravesical chemotherapy administration. We observed significant variation in the use of intravesical chemotherapy across Urological Surgery Quality Collaborative practices for ideal (range 27% to 50%) and nonideal cases (9% to 24%) ($p < 0.001$). Reasons for not treating ideal candidates included lack of confirmation of malignancy (4, 2.8%), uncertainty regarding the benefits of intravesical chemotherapy (28, 19.6%) and logistic factors such as the unavailability of medication (34, 23.8%). Conclusions: Use of immediate intravesical chemotherapy by Urological Surgery Quality Collaborative practices is higher than reported elsewhere but still varies widely, even among ideal candidates. Efforts to optimize use will be aided by disseminating evidence supporting indications and benefits of intravesical chemotherapy, and by addressing local logistic factors that limit access to this evidence-based therapy. © 2012 American Urological Association Education and Research, Inc.

Burks FN, Salmon SA, Smith AC and Santucci RA (2012). "Urethroplasty: a geographic disparity in care." *Journal of Urology* 187(6): 2124-2127.

[Request Form](#)

Department of Urology

PURPOSE: Urethroplasty is the gold standard for urethral strictures but its geographic prevalence throughout the United States is unknown. We analyzed where and how often urethroplasty was being performed in the United States compared to other treatment modalities for urethral stricture. **MATERIALS AND METHODS:** De-identified case logs from the American Board of Urology were collected from certifying/recertifying urologists from 2004 to 2009. Results were categorized by ZIP codes to determine the geographic distribution. **RESULTS:** Case logs from 3,877 urologists (2,533 recertifying and 1,344 certifying) were reviewed including 1,836 urethroplasties, 13,080 urethrotomies and 19,564 urethral dilations. The proportion of urethroplasty varied widely among states (range 0% to 17%). The ratio of urethroplasty-to-urethrotomy/dilation also varied widely from state to state, but overall 1 urethroplasty was performed for every 17 urethrotomies or dilations performed. Certifying urologists were 3 times as likely to perform urethroplasty as recertifying urologists (12% vs 4%, respectively, $p < 0.05$). Urethroplasties were performed more commonly in states with residency programs (mean 5% vs 3%). Some states reported no urethroplasties during the observation period (Vermont, North Dakota, South Dakota, Maine and West Virginia). **CONCLUSIONS:** To our knowledge this is the first report on the geographic distribution of urethroplasty for urethral stricture disease. There are large variations in the rates of urethroplasty performed throughout the United States, indicating a disparity of care, especially for those regions in which few or no urethroplasties were reported. This disparity may decrease with time as younger certifying urologists are performing 3 times as many urethroplasties as older recertifying urologists.

Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen S-A, Crijns HJG, Damiano Jr RJ, Davies DW, DiMarco J, Edgerton J, Ellenbogen K, Ezekowitz MD, **Haines DE**, Haissaguerre M, Hindricks G, Iesaka Y, Jackman W, Jalife J, Jais P, Kalman J, Keane D, Kim Y-H, Kirchhof P, Klein G, Kottkamp H, Kumagai K, Lindsay BD, Mansour M, Marchlinski FE, McCarthy PM, Mont JL, Morady F, Nademanee K, Nakagawa H, Natale A, Nattel S, Packer DL, Pappone C, Prystowsky E, Raviele A, Reddy V, Ruskin JN, Shemin RJ, Tsao H-M and Wilber D (2012). "2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: Recommendations for Patient Selection, Procedural Techniques, Patient Management and Follow-up, Definitions, Endpoints, and Research Trial Design: A report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. Developed in partnership with the European Heart Rhythm Association (EHRA), a registered branch of the European Society of Cardiology (ESC) and the European Cardiac Arrhythmia Society (ECAS); and in collaboration with the American College of Cardiology (ACC), American Heart Association (AHA), the Asia Pacific Heart Rhythm Society (APHRS), and the Society of Thoracic Surgeons (STS). Endorsed by the governing bodies of the American College of Cardiology Foundation, the American Heart Association, the European Cardiac Arrhythmia Society, the European Heart Rhythm Association, the Society of Thoracic Surgeons, the Asia Pacific Heart Rhythm Society, and the Heart Rhythm Society." *Heart Rhythm* 9(4): 632-696.e621. *Europace*. 614(634) 528-606. *Journal of Interventional Cardiac Electrophysiology*. 633(632) 171-257.

[Full-Text](#)

Department of Internal Medicine

Campochiaro PA, Brown DM, Pearson A, Chen S, Boyer D, Ruiz-Moreno J, **Garretson B**, Gupta A, Hariprasad SM, Bailey C, Reichel E, Soubrane G, Kapik B, Billman K, Kane FE and Green K (2012). "Sustained delivery fluocinolone acetonide vitreous inserts provide benefit for at least 3 years in patients with diabetic macular edema." Ophthalmology 119(10): 2125-2132.

[Full-Text](#)

Department of Ophthalmology

Objective: To assess long-term efficacy and safety of intravitreal inserts releasing 0.2 µg/d (low dose) or 0.5 µg/d (high dose) fluocinolone acetonide (FAC) in patients with diabetic macular edema (DME). Design: Two randomized, sham injection-controlled, double-masked, multicenter clinical trials. Participants: Subjects with persistent DME despite <1 macular laser treatment were randomized 1:2:2 to sham injection (n = 185), low-dose insert (n = 375), or high-dose insert (n = 393). Methods: Subjects received study drug or sham injection and after 6 weeks were eligible for rescue laser. Based on retreatment criteria, additional study drug or sham injections could be given after 1 year. Main Outcome Measures: Percentage of patients with improvement of <15 letters from baseline. Secondary outcomes included other parameters of visual function and foveal thickness. Results: At month 36, the percentage of patients who gained <15 in letter score using the last observation carried forward method was 28.7% (low dose) and 27.8% (high dose) in the FAC insert groups compared with 18.9% (P = 0.018) in the sham group, and considering only those patients still in the trial at month 36, it was 33.0% (low dose) and 31.9% (high dose) compared with 21.4% in the sham group (P = 0.030). Preplanned subgroup analysis demonstrated a doubling of benefit compared with sham injections in patients who reported duration of DME <3 years at baseline; the percentage who gained <15 in letter score at month 36 was 34.0% (low dose; P<0.001) or 28.8% (high dose; P = 0.002) compared with 13.4% (sham). An improvement <2 steps in the Early Treatment Diabetic Retinopathy Study retinopathy scale occurred in 13.7% (low dose) and 10.1% (high dose) compared with 8.9% in the sham group. Almost all phakic patients in the FAC insert groups developed cataract, but their visual benefit after cataract surgery was similar to that in pseudophakic patients. The incidence of incisional glaucoma surgery at month 36 was 4.8% in the low-dose group and 8.1% in the high-dose insert group. Conclusions: In patients with DME FAC inserts provide substantial visual benefit for up to 3 years and would provide a valuable addition to the options available for patients with DME. Financial Disclosure(s): Proprietary or commercial disclosure may be found after the references. © 2012 American Academy of Ophthalmology.

Cappell M (2012). "The art of salary negotiation in academic medicine: lessons from a 32-year career."

Gastrointestinal Endoscopy 75(4): 857-860.

[Full-Text](#)

Department of Internal Medicine

Many physicians are insufficiently aware of, or skilled in, the negotiation process and find significant barriers to negotiate in academia. Salary negotiation is the process of reaching an agreement on what an organization will pay for one's skills, knowledge, and experience. Contrary to popular belief, this is not an adversarial process. It is in both the organization's and physician's best interest to come to a mutually beneficial agreement. In this month's Fellows' Corner, Dr. Mitchell Cappell shares with us the tips and tricks of efficient salary negotiation in academic medicine.

Cappell M (2012). "Famous endoscopy quotes." Gastroenterology Nursing 35(2): 129-132.

[Full-Text](#)

Department of Internal Medicine

These quotations, whether humorous or serious, provide insight into how gastroenterology nurses, gastroenterologists, and endoscopists feel about themselves as professionals, how other healthcare professionals perceive them, and their image in popular culture. Recognition of these aspects of gastroenterology nursing, gastroenterology, and endoscopy are important for self-improvement, correcting public misperceptions, and appreciating how patient misperceptions about gastroenterology nurses and gastroenterologists and patient attitudes toward endoscopy may present barriers that gastroenterology

professionals must overcome to improve patient care. These quotations also fulfill a need for witticisms during dry endoscopy lectures!

Cappell M (2012). Hepatic and gastrointestinal diseases, in Gabbe S. G. (ed). Obstetrics: Normal and Problem Pregnancies: Elsevier: 1014-1041.

[Full-Text](#)

Department of Internal Medicine

Cappell M and Lebowitz O (2012). Hereditary hemorrhagic telangiectasia, in Lebowitz M. G. (ed). Treatment of Skin Disease: Comprehensive Therapeutic Strategies. London: Saunders.

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Department of Internal Medicine

Cappell MS (2012). "Famous gastroenterology quotes." Gastroenterology Nursing 35(5): 357-364.

[Full-Text](#)

Department of Internal Medicine

Chancellor M and Boone T (2012). "Anticholinergics for overactive bladder therapy: central nervous system effects." CNS Neuroscience & Therapeutics 18(2): 167-174.

[Full-Text](#)

Department of Urology

The mainstay of pharmacological treatment of overactive bladder (OAB) is anticholinergic therapy using muscarinic receptor antagonists (tertiary or quaternary amines). Muscarinic receptors in the brain play an important role in cognitive function, and there is growing awareness that antimuscarinic OAB drugs may have adverse central nervous system (CNS) effects, ranging from headache to cognitive impairment and episodes of psychosis. This review discusses the physicochemical and pharmacokinetic properties of OAB antimuscarinics that affect their propensity to cause adverse CNS effects, as observed in phase III clinical trials and in specific investigations on cognitive function and sleep architecture. PubMed/MEDLINE was searched for OAB plus muscarinic antagonists or anticholinergic drug. Additional relevant literature was identified by examining the reference lists of papers identified through the search. Preclinical and clinical trials in adults were assessed, focusing on the OAB antimuscarinics approved in the United States. The bloodbrain barrier (BBB) plays a key role in protecting the CNS, but it is penetrable. The lipophilic tertiary amines, particularly oxybutynin, are more likely to cross the BBB than the hydrophilic quaternary amine trospium chloride, for which there are very few reports of adverse CNS effects. In fact, in 2008 the US product labels for oral oxybutynin were modified to include the potential for anticholinergic CNS events and a warning to monitor patients for adverse CNS effects. Even modest cognitive impairment in the elderly may negatively affect independence; therefore, selection of an antimuscarinic OAB drug with reduced potential for CNS effects is advisable.

Chancellor MB (2012). "Editorial comment from Dr Chancellor to periurethral injection of autologous adipose-derived regenerative cells for the treatment of male stress urinary incontinence: report of three initial cases." International Journal of Urology 19(7): 661.

[Full-Text](#)

Department of Urology

Chancellor MB (2012). "State-of-the-art lecture 2: clinical development of muscle stem cells for stress urinary incontinence treatment." International Journal of Urology 19(4): 383.

[Full-Text](#)

Department of Urology

The American Urological Association (AUA) and the Japanese Urological Association (JUA) have been working together to extend collaboration in the science and art of urology. On behalf of JUA, we are pleased to announce the 7th AUA/JUA International Affiliate Society Meeting at the 108th Annual Meeting of AUA

(19–23 May 2012, Atlanta, GA, USA). We are grateful for the support of AUA, with which this joint program was prepared and materialized. We would also like to express our sincere appreciation to all people concerned, including the moderators, lecturers and panelists of both societies. To stimulate better communication between the two societies, this year's joint program has more case discussions than previous ones, covering two topics each in oncology (renal cell carcinoma [RCC] and castration-resistant prostate cancer [CRPC]) and benign urology (overactive bladder [OAB] and urinary tract infection [UTI]). One symposium and two state-of-the-art lectures compose the framework of the program. We look forward to the participation of many members of both societies in this joint program. Last, we would like to thank Dr Sushil Lacy, AUA President; Dr Gopal Badlani, AUA Secretary General; and Dr Robert Flanigan, Program Coordinator, for their dedication to develop and deepen the mutual relationship between AUA and JUA.

Chancellor MB, Staskin DR, Kay GG, Sandage BW, Jr., Oefelein MG and Tsao JW (2012). "Blood-brain barrier permeation and efflux exclusion of anticholinergics used in the treatment of overactive bladder." *Drugs and Aging* 29(4): 259-273.

[Full-Text](#)

Department of Urology

Overactive bladder (OAB) is a common condition, particularly in the elderly. Anticholinergic agents are the mainstay of pharmacological treatment of OAB; however, many anticholinergics can cross the blood brain barrier (BBB) and may cause central nervous system (CNS) effects, including cognitive deficits, which can be especially detrimental in older patients. Many anticholinergics have the potential to cause adverse CNS effects due to muscarinic (M-1) receptor binding in the brain. Of note, permeability of the BBB increases with age and can also be affected by trauma, stress, and some diseases and medications. Passive crossing of a molecule across the BBB into the brain is dependent upon its physicochemical properties. Molecular characteristics that hinder passive BBB penetration include a large molecular size, positive or negative ionic charge at physiological pH, and a hydrophilic structure. Active transport across the BBB is dependent upon protein-mediated transporter systems, such as that of permeability-glycoprotein (P-gp), which occurs only for P-gp substrates, such as trospium chloride, darifenacin and fesoterodine. Reliance on active transport can be problematic since genetic polymorphisms of P-gp exist, and many commonly used drugs and even some foods are P-gp inhibitors or are substrates themselves and, due to competition, can reduce the amount of the drug that is actively transported out of the CNS. Therefore, for drugs that are preferred not to cross into the CNS, such as potent anticholinergics intended for the bladder, it is optimal to have minimal passive crossing of the BBB, although it may also be beneficial for the drug to be a substrate for an active efflux transport system. Anticholinergics demonstrate different propensities to cross the BBB. Darifenacin, fesoterodine and trospium chloride are substrates for P-gp and, therefore, are actively transported away from the brain. In addition, trospium chloride has not been detected in cerebrospinal fluid assays and does not appear to have significant CNS penetration. This article reviews the properties of anticholinergics that affect BBB penetration and active transport out of the CNS, discusses issues of increased BBB permeability in patients with OAB, and examines the clinical implications of BBB penetration on adverse events associated with anticholinergics.

Chen JJ, **Trosch RM**, Comella CL, Hall SB, Silay Y, Coleman CM, Chang SF and Marchese D (2012). "ANCHOR-CD (abobotulinumtoxin a neurotoxin: clinical and health economics outcomes registry in cervical dystonia): a multicenter, observational study of dysport in cervical dystonia: baseline data and cycle one outcomes data." *Pharmacotherapy* 32(10): E220-E221.

[Request Form](#)

Department of Internal Medicine

Chen PY, Shah C, Wilkinson J, Wallace M, Ye H, Fowler A, **Dekhne N**, **Benitez P**, **Brabbins DS** and **Grills IS** (2012). "Clinical efficacy of 2-versus 5-day accelerated partial breast irradiation delivered via balloon-based brachytherapy: results of a matched pair analysis." *International Journal of Radiation Oncology Biology Physics* 84(3): S86.

[Full-Text](#)

Department of Radiation Oncology

Department of Surgery

Limited data is available comparing clinical outcomes using alternative accelerated partial breast irradiation (APBI) schedules. The purpose of this analysis was to compare efficacy between a 2-day and 5-day schedule in women with early-stage breast cancer.

Chinnaiyan KM, Depetris AM, Al-Mallah M, Abidov A, Ananthasubramaniam K, **Gallagher MJ**, Girard S, Goraya TY, Kazerooni EA, **Patel S**, Peyser P, Poopat C, **Raff GL**, Saba S, Song T and Share D (2012). "Rationale, design, and goals of the advanced cardiovascular imaging consortium (ACIC): a Blue Cross Blue Shield of Michigan collaborative quality improvement project." *American Heart Journal* 163(3): 346-353.

[Full-Text](#)

Department of Internal Medicine

BACKGROUND: Coronary computed tomography angiography (CCTA) is an emerging noninvasive anatomical method for evaluation of patients with suspected coronary artery disease (CAD). Multicenter clinical registries are key to efforts to establish the role of CCTA in CAD diagnosis and management. The Advanced Cardiovascular Imaging Consortium (ACIC) is a statewide, multicenter collaborative quality initiative with the intent to establish quality and appropriate use of CCTA in Michigan. **METHODS:** The ACIC is sponsored by the Blue Cross Blue Shield of Michigan/Blue Care Network, and its 47 sites include imaging centers that offer CCTA and meet established structure and process standards for participation. Patients enrolled include those with suspected ischemia with or without known CAD, and individuals across the entire spectrum of CAD risk. Patient demographics, history, CCTA scan-related data and findings, and 90-day follow-up data are entered prospectively into a centralized database with strict validation tools and processes. Collaborative quality initiatives include radiation dose reduction and appropriate CCTA use by education and feedback to participating sites and referring physicians. **CONCLUSIONS:** Across a wide range of institutions, the ACIC permits evaluation of "real-world" utilization and effectiveness of CCTA and examines an alternative, nontraditional approach to utilization management wherein physicians and payers collaborate to address the growing problem of cardiac imaging overutilization.

Chinnaiyan KM, Peyser P, Goraya T, Ananthasubramaniam K, Gallagher M, Depetris A, **Boura JA**, Kazerooni E, Poopat C, Al-Mallah M, Saba S, **Patel S**, Girard S, Song T, Share D and Raff G (2012). "Impact of a continuous quality improvement initiative on appropriate use of coronary computed tomography angiography: results from a multicenter, statewide registry, the Advanced Cardiovascular Imaging Consortium." *Journal of the American College of Cardiology* 60(13): 1185-1191.

[Full-Text](#)

Department of Internal Medicine

OBJECTIVES: The purpose of the study was to determine the effectiveness of a collaborative educational, continuous quality improvement (CQI) initiative to increase appropriate use of coronary computed tomography angiography (CCTA). **BACKGROUND:** Potential overuse of CCTA has prompted multisociety appropriate use criteria (AUC) publications. **METHODS:** This prospective, observational study was conducted with pre-intervention (July 2007 to June 2008), intervention (July 2008 to June 2010), and follow-up (July 2010 to December 2010) periods during which patients were enrolled in the Advanced Cardiovascular Imaging Consortium (ACIC) at 47 Michigan hospitals. Continuous education was provided to referring physicians. The possibility of losing third-party payer coverage in the absence of a measurable change in AUC was emphasized. AUC was compared between the 3 periods. **RESULTS:** The study group included 25,387 patients. Compared with the pre-intervention period, there was a 23.4% increase in appropriate (61.3% to 80%, $p < 0.0001$), 60.3% decrease in inappropriate (14.6% to 5.8%, $p < 0.0001$), 40.8% decrease in uncertain (10.3% to 6.1%, $p < 0.0001$), and 41.7% decrease in unclassifiable (13.9% to 8.1%, $p < 0.0001$) scans during follow-up. Between pre-intervention and follow-up, change in CCTA referrals by provider specialty were cardiology (appropriate: 60.4% to 79.5%; inappropriate: 13% to 5.2%; $p < 0.0001$), internal medicine/family practice (appropriate: 51.1% to 70.4%; inappropriate: 20.2% to 12.5%; $p < 0.0001$), emergency medicine (appropriate: 83.6% to 91.6%; inappropriate: 9.1% to 0.6%; $p < 0.0001$), and other (appropriate: 61.1% to

83.2%; inappropriate: 18.6% to 5.9%; $p < 0.0001$). CONCLUSIONS: Application of a systematic CQI and emphasis on possible loss of coverage were associated with a significant improvement in the proportion of CCTA examinations meeting AUC across referring physician specialties.

Chinnaiyan KM, Raff GL and Ananthasubramaniam K (2012). "Coronary CT angiography after stress testing: An efficient use of resources? Implications of the Advanced Cardiovascular Imaging Consortium (ACIC) results." Journal of Nuclear Cardiology 19(4): 649-657.

[Request Form](#)

Department of Internal Medicine

Coronary CT angiography (CCTA) has matured to be a fast noninvasive imaging test in the evaluation of coronary artery disease (CAD). It has demonstrated excellent accuracy for defining the presence and the severity of luminal coronary artery stenoses and is probably the best noninvasive test to reliably exclude atherosclerotic coronary disease. Furthermore, accumulating CCTA data indicate that it can identify individuals at risk for all-cause mortality. It is also well known that despite the wealth of data regarding diagnostic and prognostic values of stress testing in CAD, up to 10% of stress imaging studies are considered inconclusive, leading to subsequent invasive coronary angiography for definitive diagnosis often with negative results. Moreover, recent data indicate that up to 30 % of patients undergoing angiography have no significant CAD despite a majority of them having had a prior stress test. Whether CCTA can serve as a cost-effective methodology to invasive angiography has been a source of active research. In this context, we will discuss the implications of the recently published data from the Advanced Cardiovascular Imaging Consortium registry looking at the use of CCTA after stress testing in Michigan. Copyright © 2012 American Society of Nuclear Cardiology.

Chinnaiyan KM, Raff GL, Goraya T, Ananthasubramaniam K, **Gallagher MJ**, Abidov A, **Boura JA**, Share D and Peyser PA (2012). "Coronary computed tomography angiography after stress testing: results from a multicenter, statewide registry, ACIC (Advanced Cardiovascular Imaging Consortium)." Journal of the American College of Cardiology 59(7): 688-695.

[Full-Text](#)

Department of Internal Medicine

Department of Biomedical Sciences

OBJECTIVES: This study was conducted to evaluate the correlation between stress test results and coronary computed tomography angiography (CCTA) findings and comparative diagnostic performance of the 2 modalities in patients undergoing invasive coronary angiography (ICA). BACKGROUND: Recent data suggest that only a third of patients undergoing ICA have obstructive coronary artery disease (CAD); accurate pre-ICA risk stratification is needed. METHODS: At 47 centers participating in the ACIC (Advanced Cardiovascular Imaging Consortium) in Michigan, patients without known CAD who were undergoing CCTA within 3 months of a stress test were studied. Demographics, risk factors, symptoms, and stress test results were correlated with obstructive CAD (>50% stenosis) on CCTA and ICA. RESULTS: Among 6,198 patients (age 56 +/- 12 years, 48% men), >50% stenosis was seen in 1,158 (18.7%) on CCTA. Independent predictors included male sex (odds ratio [OR]: 2.37, 95% confidence interval [CI]: 1.83 to 3.06), current smoking (OR: 2.23, 95% CI: 1.57 to 3.17), older age (OR per 10-year increment: 2.14, 95% CI: 1.89 to 2.41), hypertension (OR: 1.8, 95% CI: 1.37 to 2.34), and typical angina (OR: 1.48, 95% CI: 1.03 to 2.12). Stress test results were not predictive. Among patients undergoing ICA (n = 621), there was a strong correlation of ICA with CCTA findings (OR: 9.09, 95% CI: 5.57 to 14.8, $p < 0.001$), but not stress results (OR: 0.79, 95% CI: 0.56 to 1.11, $p = 0.17$). CONCLUSIONS: Stress test findings did not predict obstructive CAD on CCTA, observed in <20% of patients in this large study group. The strong association of CCTA with ICA suggests that it may serve as an effective "gatekeeper" to invasive testing in patients needing adjudication of stress test results. (Advanced Cardiovascular Imaging Consortium: A Collaborative Quality Improvement Project [ACIC]; NCT00640068).

Chinnaiyan KM and Voros S (2012). "Coronary CT angiography versus myocardial perfusion imaging: War or peace?" *Journal of Cardiovascular Computed Tomography* 6(4): 284-286.

[Full-Text](#)

Department of Internal Medicine

Chisti MM, Brahmanday GR, Muslimani AA, Yadav S, Rigo P, **Wong CYO, Jaiyesimi I** and **Huang J** (2012). "Risk stratification of follicular lymphomas using two independent prognostic factors: lymphoma cell size assessment by flow cytometry and FDG PET based metabolic activity." *Blood* 120(21): 5098.

[Full-Text](#)

Department of Internal Medicine

Department of Pathology

Follicular Lymphoma (FL) comprises of 20–30% of Non-Hodgkin's Lymphomas. It is the most common lymphoma with varied clinical aggressiveness, depending on morphological grading on histology. The prognosis of FL is heterogeneous. Therefore therapeutic options for FL are increasingly becoming more risk-adopted. Pathologically, FL has been graded into grade 1–2 (FL1–2) and grade 3 (FL3) by visual counting or estimating the absolute number of centroblasts in neoplastic follicles. Recent studies found that the average tumor cell size of FL is highly variable, but is consistently reproducible, achieved by an objective measurement using flow cytometry. A significant variation in metabolic activity has also been observed in FL studied by PET scan. The purpose of this study was to investigate a new risk stratification method for FL using a combined criterion of Flow cytometry based cell size of FL cells and metabolic activity based on FDG PET scan to further evaluate their prognostic values.

Chittick P, Russo V, **Sims M**, Oleszkowicz S, **Sawarynski K**, Powell K, Makin J, Darnell E, **Robinson-Dunn B**, Boyanton BL, Jr. and **Band J** (2012). "Pseudomonas aeruginosa respiratory tract infections associated with contaminated ultrasound gel used for transesophageal echocardiography-Michigan, December 2011-January 2012 (Reprinted from MWMR, vol 61, pg 262-264, 2012)." *JAMA* 307(21): 2248-2250.

[Full-Text](#)

Department of Internal Medicine

Department of Biomedical Sciences

Department of Pathology

Cho I, Chang HJ, Sung JM, Pencina MJ, Lin FY, Dunning AM, Achenbach S, Al-Mallah M, Berman DS, Budoff MJ, Callister TQ, Chow BJ, Delago A, Hadamitzky M, Hausleiter J, Maffei E, Cademartiri F, Kaufmann P, Shaw LJ, **Raff GL**, **Chinnaiyan KM**, Villines TC, Cheng V, Nasir K, Gomez M and Min JK (2012). "Coronary computed tomographic angiography and risk of all-cause mortality and nonfatal myocardial infarction in subjects without chest pain syndrome from the CONFIRM Registry (coronary CT angiography evaluation for clinical outcomes: an international multicenter registry)." *Circulation* 126(3): 304-313.

[Full-Text](#)

Department of Internal Medicine

BACKGROUND: The predictive value of coronary computed tomographic angiography (cCTA) in subjects without chest pain syndrome (CPS) has not been established. We investigated the prognostic value of coronary artery disease detection by cCTA and determined the incremental risk stratification benefit of cCTA findings compared with clinical risk factor scoring and coronary artery calcium scoring (CACS) for individuals without CPS. **METHODS AND RESULTS:** An open-label, 12-center, 6-country observational registry of 27 125 consecutive patients undergoing cCTA and CACS was queried, and 7590 individuals without CPS or history of coronary artery disease met the inclusion criteria. All-cause mortality and the composite of all-cause mortality and nonfatal myocardial infarction were measured. During a median follow-up of 24 months (interquartile range, 18-35 months), all-cause mortality occurred in 136 individuals. After risk adjustment, compared with individuals without evidence of coronary artery disease by cCTA, individuals with obstructive 2- and 3-vessel disease or left main coronary artery disease experienced higher rates of death and composite outcome ($P < 0.05$ for both). Both CACS and cCTA significantly improved the performance of standard risk factor prediction models for all-cause mortality and the composite outcome (likelihood ratio $P < 0.05$ for all),

but the incremental discriminatory value associated with their inclusion was more pronounced for the composite outcome and for CACS (C statistic for model with risk factors only was 0.71; for risk factors plus CACS, 0.75; for risk factors plus CACS plus cCTA, 0.77). The net reclassification improvement resulting from the addition of cCTA to a model based on standard risk factors and CACS was negligible. CONCLUSIONS: Although the prognosis for individuals without CPS is stratified by cCTA, the additional risk-predictive advantage by cCTA is not clinically meaningful compared with a risk model based on CACS. Therefore, at present, the application of cCTA for risk assessment of individuals without CPS should not be justified.

Chuang YC, Chung MS, Wang PW, Lee WC, Chen CD, Chang HW, Yang KD, **Chancellor MB** and Liu R (2012). "Albuminuria is an independent risk factor of erectile dysfunction in men with type 2 diabetes." Journal of Sexual Medicine 9(4): 1055-1064.

[Request Form](#)

Department of Urology

Introduction. Erectile dysfunction (ED) is a frequent comorbidity in men with diabetes and is frequently overlooked in routine clinical evaluation. Albuminuria, a marker of endothelial dysfunction, may link to ED. Aim. The study evaluated the association of albuminuria with risk factors of ED in men with type 2 diabetes. Methods. The diagnosis of ED was based on a self-administered questionnaire containing Sexual Health Inventory for Men. Urinary albumin excretion rate was determined by urine albumin-to-creatinine ratio (UACR) in spot urine. Main Outcome Measures. The clinical variables and diabetes-associated complications to risk of ED were evaluated. Results. Of 666 patients who received the questionnaire, 455 patients completed it. Among them, 82.0%, 28.1%, and 35.8% reported having ED, severe ED, and albuminuria, respectively. The UACR level was significantly higher in ED (0.20 +/- 0.83) and severe ED (0.34 +/- 1.18) groups compared with non-ED group (0.07 +/- 0.33). The presence of albuminuria adjusted for age and duration of diabetes was significantly associated with ED (OR = 2.76), and macroalbuminuria has stronger impact (OR = 4.49) than microalbuminuria (OR = 2.48). The other associated risk factors included hypertension, higher level of systolic blood pressure, lower level of serum hemoglobin, and estimated glomerular filtration rate. The presence of retinopathy, neuropathy, insulin therapy, using calcium channel blocker, and higher level of HbA1c further correlated with severe ED. Men with severe ED have higher prevalence of subnormal testosterone than the no ED patients. The high sensitivity C-reactive protein level, and the presence of metabolic syndrome were not risk factors. The 211 nonrespondents to the questionnaire had similar or worse risk profiles compared with the ED patients. Conclusion. Albuminuria is an important independent risk factor of ED in men with diabetes after adjustment of age and diabetes mellitus duration. Identification and control of albuminuria and other associated risk factors might play a role in the prevention or reversal of ED. Chuang Y-C, Chung M-S, Wang P-W, LeeW-C, Chen C-D, Chang H-W, Yang KD, Chancellor MB, and Liu RT. Albuminuria is an independent risk factor of erectile dysfunction in men with type 2 diabetes. *J Sex Med* 2012; 9: 1055-1064.

Chuang YC, Chung MS, Wang PW, Lee WC, Chen CD, Chang HW, Yang KD, **Chancellor MB** and Liu RT (2012). "Albuminuria is an Independent Risk Factor of Erectile Dysfunction in Men with Type 2 Diabetes." Journal of Sexual Medicine 9(4): 1055-1064.

[Request Form](#)

Department of Urology

Introduction. Erectile dysfunction (ED) is a frequent comorbidity in men with diabetes and is frequently overlooked in routine clinical evaluation. Albuminuria, a marker of endothelial dysfunction, may link to ED. Aim. The study evaluated the association of albuminuria with risk factors of ED in men with type 2 diabetes. Methods. The diagnosis of ED was based on a self-administered questionnaire containing Sexual Health Inventory for Men. Urinary albumin excretion rate was determined by urine albumin-to-creatinine ratio (UACR) in spot urine. Main Outcome Measures. The clinical variables and diabetes-associated complications to risk of ED were evaluated. Results. Of 666 patients who received the questionnaire, 455 patients completed it. Among them, 82.0%, 28.1%, and 35.8% reported having ED, severe ED, and albuminuria, respectively. The UACR level was significantly higher in ED (0.20±0.83) and severe ED (0.34±1.18) groups compared with non-ED group (0.07±0.33). The presence of albuminuria adjusted for age and duration of

diabetes was significantly associated with ED (OR=2.76), and macroalbuminuria has stronger impact (OR=4.49) than microalbuminuria (OR=2.48). The other associated risk factors included hypertension, higher level of systolic blood pressure, lower level of serum hemoglobin, and estimated glomerular filtration rate. The presence of retinopathy, neuropathy, insulin therapy, using calcium channel blocker, and higher level of HbA1c further correlated with severe ED. Men with severe ED have higher prevalence of subnormal testosterone than the no ED patients. The high sensitivity C-reactive protein level, and the presence of metabolic syndrome were not risk factors. The 211 nonrespondents to the questionnaire had similar or worse risk profiles compared with the ED patients. Conclusion. Albuminuria is an important independent risk factor of ED in men with diabetes after adjustment of age and diabetes mellitus duration. Identification and control of albuminuria and other associated risk factors might play a role in the prevention or reversal of ED. © 2011 International Society for Sexual Medicine.

Chuang YC, Chung MS, Wang PW, Lee WC, Chen CD, Chang HW, Yang KD, **Chancellor MB** and Liu RT (2012). "Risk of erectile dysfunction in type 2 diabetic men with albuminuria." Journal of Sexual Medicine 9(Suppl 2): 0P20.

[Request Form](#)

Department of Urology

Chuang YC, Huang CC, Smith C, Somogyi G, Kaufman J, Nirmal J, **Tyagi P** and **Chancellor M** (2012). "Effect of liposome encapsulation on the pharmacokinetics of tacrolimus after intravesical administration." Neurourology and Urodynamics 31(2): 233.

[Full-Text](#)

Department of Urology

Chuang YC, **Tyagi P**, Huang CC, **Chancellor MB** and Yoshimura N (2012). "Mechanisms and urodynamic effects of a potent and selective EP4 receptor antagonist, MF191, on cyclophosphamide and prostaglandin E(2) -induced bladder overactivity in rats." BJU International 110(10): 1558-1564.

[Full-Text](#)

Department of Urology

Study Type - Aetiology (case control) Level of Evidence 3b What's known on the subject? and What does the study add? Recent evidence has suggested that up-regulation of the prostaglandin E(2) (PGE(2)) receptor subtype 4 (EP4) receptor in the bladder is involved in bladder overactivity. The present study found that MF191, a selective EP4 receptor antagonist, may have effects on the bladder urothelium and inflammatory cells and suppress CYP- or PGE(2) -induced bladder overactivity. Systemic or intravesical MF191 administration for the treatment of overactive bladder may merit clinical study. OBJECTIVE: * To investigate the mechanisms and urodynamic effects of a potent and selective prostaglandin E(2) (PGE(2)) receptor subtype 4 (EP4) antagonist, MF191, on cyclophosphamide (CYP) or PGE(2) -induced bladder overactivity in rats. MATERIALS AND METHODS: * Experimental and control rats were injected with CYP (200 mg/kg i.p.) or saline on day 1. Continuous cystometrograms (CMGs) were performed on day 3. * In group 1, MF191 (vehicle 0.1 and 1 mg/kg) was given i.v. The bladder was then harvested for histology and immunohistochemistry. Some bladders were harvested for analysis of EP4 expression by Western blotting without a CMG study. * In group 2, MF191 (vehicle 10 nM, and 100 nM) was continuously infused into the bladder. * In group 3, bladder overactivity was induced by intravesical instillation of PGE(2) (200 uM) and vehicle or MF191 (1 mg/kg) was given i.v. RESULTS: * CYP induced bladder inflammation, overactivity and EP4 upregulation. The CYP effects were suppressed by MF191 (1 mg/kg i.v.; intercontraction interval [ICI]: 39.4% increase, and reduced inflammatory cells infiltration, and EP4 expression). * Intravesical instillation of MF191 (100 nM) suppressed CYP-induced bladder overactivity (ICI: 71.8% increase). * PGE(2) -induced bladder overactivity was suppressed by MF191 (ICI: 43.2% increase). * MF191 had no significant effects on other CMG variables or on control rats. CONCLUSIONS: * MF191 might affect the bladder urothelium and inflammatory cells and suppresses CYP- or PGE(2) -induced bladder overactivity. * Systemic or intravesical MF191 administration for the treatment of overactive bladder merits clinical study.

Clark CL, Berman AD, McHugh A, Roe EJ, Boura JA and Swor RA (2012). "Hospital process intervals, not EMS time intervals, are the most important predictors of rapid reperfusion in EMS Patients with ST-segment elevation myocardial infarction." Prehospital Emergency Care 16(1): 115-120.

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Department of Emergency Medicine

Department of Internal Medicine

Department of Biomedical Sciences

OBJECTIVE: To assess the relationship of emergency medical services (EMS) intervals and internal hospital intervals to the rapid reperfusion of patients with ST-segment elevation myocardial infarction (STEMI). **METHODS:** We performed a secondary analysis of a prospectively collected database of STEMI patients transported to a large academic community hospital between January 1, 2004, and December 31, 2009. EMS and hospital data intervals included EMS scene time, transport time, hospital arrival to myocardial infarction (MI) team activation (D2Page), page to catheterization laboratory arrival (P2Lab), and catheterization laboratory arrival to reperfusion (L2B). We used two outcomes: EMS scene arrival to reperfusion (S2B) ≤ 90 minutes and hospital arrival to reperfusion (D2B) ≤ 90 minutes. Means and proportions are reported. Pearson chi-square and multivariate regression were used for analysis. **RESULTS:** During the study period, we included 313 EMS-transported STEMI patients with 298 (95.2%) MI team activations. Of these STEMI patients, 295 (94.2%) were taken to the cardiac catheterization laboratory and 244 (78.0%) underwent percutaneous coronary intervention (PCI). For the patients who underwent PCI, 127 (52.5%) had prehospital EMS activation, 202 (82.8%) had D2B ≤ 90 minutes, and 72 (39%) had S2B ≤ 90 minutes. In a multivariate analysis, hospital processes EMS activation (OR 7.1, 95% CI 2.7, 18.4), Page to Lab [6.7, 95% CI 2.3, 19.2] and Lab arrival to Reperfusion [18.5, 95% CI 6.1, 55.6]) were the most important predictors of Scene to Balloon ≤ 90 minutes. EMS scene and transport intervals also had a modest association with rapid reperfusion (OR 0.85, 95% CI 0.78, 0.93 and OR 0.89, 95% CI 0.83, 0.95, respectively). In a secondary analysis, Hospital processes (Door to Page [OR 44.8, 95% CI 8.6, 234.4], Page 2 Lab [OR 5.4, 95% CI 1.9, 15.3], and Lab arrival to Reperfusion [OR 14.6 95% CI 2.5, 84.3]), but not EMS scene and transport intervals were the most important predictors D2B ≤ 90 minutes. **CONCLUSIONS:** In our study, hospital process intervals (EMS activation, door to page, page to laboratory, and laboratory to reperfusion) are key covariates of rapid reperfusion for EMS STEMI patients and should be used when assessing STEMI care.

Colen CB and Allcut E (2012). "Quality of life and outcomes in glioblastoma management." Neurosurgery Clinics of North America 23(3): 507-513.

[Request Form](#)

Department of Urology

This article explores the effects of modern treatment on the health-related quality of life in patients who suffer from glioblastoma multiforme.

Coley W, Rayavarapu S, Pandey GS, **Sabina RL**, Van der Meulen J. H. Ampong B, Wortmann RL, Rawat R and Nagaraju K (2012). "The molecular basis of skeletal muscle weakness in a mouse model of inflammatory myopathy." Arthritis & Rheumatism 64(11): 3750-3759.

[Full-Text](#)

Department of Biomedical Sciences

OBJECTIVE: It is generally believed that muscle weakness in patients with polymyositis and dermatomyositis is due to autoimmune and inflammatory processes. However, it has been observed that there is a poor correlation between the suppression of inflammation and a recovery of muscle function in these patients. This study was undertaken to examine whether nonimmune mechanisms also contribute to muscle weakness. In particular, it has been suggested that an acquired deficiency of AMP deaminase 1 (AMPD1) may be responsible for muscle weakness in myositis. **METHODS:** We performed comprehensive functional, behavioral, histologic, molecular, enzymatic, and metabolic assessments before and after the onset of inflammation in a class I major histocompatibility complex (MHC)-transgenic mouse model of autoimmune inflammatory myositis. **RESULTS:** Muscle weakness and metabolic disturbances were detectable in the mice

prior to the appearance of infiltrating mononuclear cells. Force contraction analysis of muscle function revealed that weakness was correlated with AMPD1 expression and was myositis specific. Decreasing AMPD1 expression resulted in decreased muscle strength in healthy mice. Fiber typing suggested that fast-twitch muscles were converted to slow-twitch muscles as myositis progressed, and microarray results indicated that AMPD1 and other purine nucleotide pathway genes were suppressed, along with genes essential to glycolysis. CONCLUSION: These data suggest that an AMPD1 deficiency is acquired prior to overt muscle inflammation and is responsible, at least in part, for the muscle weakness that occurs in the mouse model of myositis. AMPD1 is therefore a potential therapeutic target in myositis.

Corney SM, Dukatz T, Rosenblatt S, Harrison B, **Murray R**, Sakharova A and Balasubramaniam M (2012). "Comparison of insulin pump therapy (continuous subcutaneous insulin infusion) to alternative methods for perioperative glycemic management in patients with planned postoperative admissions." Journal of Diabetes Science and Technology 6(5): 1003-1015.

[Full-Text](#)

Department of Radiation Oncology

BACKGROUND: Patients with diabetes who use insulin pumps [continuous subcutaneous insulin infusion (CSII)] undergo surgeries that require postoperative hospital admission. There are no defined guidelines for CSII perioperative use. METHODS: This retrospective single-institution study identified type 1 and type 2 diabetes subjects by electronically searching 2005-2010 anesthesia preoperative assessments for "pump." Surgical cases (n = 92) were grouped according to intraoperative insulin delivery method: (a) CSII continuation of basal rate with/without correctional insulin bolus(es) (n = 53); (b) conversion to intravenous insulin infusion (n = 20); and (c) CSII suspension with/without correctional insulin bolus(es) (n = 19). These groups were compared on mean intraoperative blood glucose (BG) and category of most extreme intraoperative BG. RESULTS: Differences were found on baseline characteristics of diabetes duration (p = .010), anesthesia time (p = .011), proportions receiving general anesthesia (p = .013), and preoperative BG (p = .033). The conversion group had the longest diabetes duration and anesthesia time; it had a higher proportion of general anesthesia recipients and a higher mean preoperative BG than the continuation group. There was no significant difference in mean BG/surgical case between continuation (163.5 +/- 58.5 mg/dl), conversion (152.3 +/- 28.9 mg/dl), and suspension groups (188.3 +/- 44.9 mg/dl; p = .128). The suspension group experienced a greater percentage of cases (84.2%) with one or more intraoperative BG > 179 mg/dl than continuation (45.3%) and conversion (40%) groups Figure 1 groupings (p = .034). CONCLUSIONS: In this limited sample, preliminary findings are consistent with similar intraoperative glycemic control between CSII continuation and CSII conversion to intravenous insulin infusions. Continuous subcutaneous insulin infusion suspension had a greater rate of hyperglycemia. Preoperative differences between insulin delivery groups complicate interpretations of findings.

Cotrell A, Sayedian F, Huang M, **Smith M** and **Huang J** (2012). "Development and validation of a flow cytometry protocol for measuring tumor cell size of B-cell non-hodgkin lymphomas." Modern Pathology 25(Suppl 2): 331A.

[Full-Text](#)

Department of Pathology

DeJong AT (2012). "Clinical applications: cardiac rehabilitation: Underutilized care offering substantial benefits." ACSM's Health and Fitness Journal 16(2): 31-33.

[Full-Text](#)

Department of Biomedical Sciences

Cardiovascular disease is the number one cause of mortality in the U.S., attributing to approximately one of every six deaths. In addition, nearly one of every three individuals has been diagnosed with some form of cardiovascular disease. As recommended by numerous professional organizations, cardiac rehabilitation (CR) is an established component of preventive medical care after the diagnosis of coronary artery disease or an acute cardiac event (5,15,27,33). Although CR programs vary in size and scope, the core components include individualized exercise training, patient evaluation, medical surveillance, lifestyle modification, and psychosocial counseling.

Dekhne N, Shah C, Wilkinson JB, Mitchell C, Chen P, Margolis J and Vicini F (2012). "Axillary lymph node failure in patients treated with accelerated partial breast irradiation." *Cancer* 118(1): 38-43.

[Full-Text](#)

Department of Surgery

Department of Internal Medicine

Department of Radiation Oncology

BACKGROUND: Data on the risk of axillary failure (AF) after accelerated partial breast irradiation (APBI) are limited. In this study, the authors determined the rate of AF and regional lymph node failure (RNF) in patients who received various forms of APBI and identified factors that were associated with its occurrence.

METHODS: In total, 534 patients with early stage breast cancer were treated at William Beaumont Hospital with APBI, including 466 patients (87%) with invasive breast cancer and 68 patients (13%) with ductal carcinoma in situ. Clinical variables (patient age, tumor location), pathologic variables (tumor size, grade, estrogen receptor status, margin status, lymph node status), and treatment-related variables (receipt of hormone and systemic chemotherapy) were analyzed to determine which factors were associated with AF and RNF. The median length of follow-up was 63 months (range, 1-201 months). **RESULTS:** The 5-year actuarial AF rate was 0.19%. Three patients (0.56%) developed RNF (all patients initially had invasive breast cancer) with a 5-year actuarial rate of 0.37%. Two of the regional recurrences were in the supraclavicular fossa, and 1 was in the axilla. No variables were associated with AF. However, patient numbers were very small. The median survival after RNF was 0.8 years (range, 0.3-1.7 years), and 2 of the 3 patients died of disease. **CONCLUSIONS:** The rate of AF and RNF after APBI was low and appeared to be similar to the rate observed with whole-breast irradiation. No variables were associated with a higher rate of AF after APBI. *Cancer* 2012; 118: 38-43. (C) 2011 American Cancer Society.

Denby KS, Briones AJ, Bourne PA, Spaulding BO, Lu D, Fischer-Colbrie R, **Qu Z**, Wang HL and Xu H (2012). "IMP3, NESP55, TTF-1 and CDX2 serve as an immunohistochemical panel in the distinction among small-cell carcinoma, gastrointestinal carcinoid, and pancreatic endocrine tumor metastasized to the liver." *Applied Immunohistochemistry & Molecular Morphology* 20(6): 573-579.

[Full-Text](#)

Department of Pathology

Histopathologic distinction among small-cell carcinoma (SCC), pancreatic endocrine tumor (PET), and gastrointestinal carcinoids metastasized to the liver in needle core biopsies can be extremely challenging because of limited material, crush artifact, and lack of detailed clinical history. In this study, a total of 61 surgically resected or biopsied specimens, including 27 SCCs (lung, 17; colon, 1; gallbladder, 2; stomach, 1; and unknown primary, 6), 18 gastrointestinal carcinoid tumors (GICTs) (stomach, 2; small intestine, 14; colon, 2), and 16 PETs were immunohistochemically examined for the expression of IMP3, TTF-1, CDX2, and NESP55 to evaluate their diagnostic value. The results showed that 24 (89%) of 27 SCCs exhibited strong cytoplasmic staining for IMP3 in 60% to 100% of the tumor cells. Eighteen (67%) SCCs were strongly and diffusely positive for TTF-1. In the remaining 9 TTF-1-negative SCCs (including 4 extrapulmonary cases), 7 showed strong and diffuse IMP3 expression. All SCCs were negative for CDX2 except for 1 case of colonic origin that showed strong CDX2 immunoreactivity. All 16 metastatic PETs were positively stained for IMP3 with 12 cases (75%) showing a diffuse and moderate-to-strong staining pattern while they were negative for TTF-1. Six PETs exhibited moderate-to-strong positivity for CDX2 with nuclear staining in 5% to 40% of tumor cells, and 5 showed a varying degree of positivity for NESP55. Three (17%) of 18 metastatic GICTs showed moderate IMP3 staining in 50% to 90% of the tumor cells, whereas CDX2 was expressed in 17 (94%) cases with moderate-to-strong staining in 50% to 100% of tumor cells. No NESP55 immunoreactivity was detected in metastatic SCCs and GICTs. In conclusion, a panel of these 4 markers is useful in segregating among SCC, PET, and GICT to help determine the primary site of hepatic metastasis.

Desai TK, Bortman J, Al-Sibae R and Bonkovsky H (2012). "The role of iron in hepatitis C infection." Current Hepatitis Reports 11(1): 41-47.

[Full-Text](#)

Department of Internal Medicine

Iron overload of varying degrees is common among patients with chronic hepatitis C. The clinical significance of this iron overload is uncertain. Studies that have evaluated the effect of hepatic iron stores on the response to anti-viral treatment or on the natural history of chronic hepatitis C have found variable results depending on the technique used to measure hepatic iron stores and the degree of iron overload present among the study population. We have tried to comprehensively analyze the literature regarding the clinical interaction between iron overload and the natural history of chronic hepatitis C. The one clear relationship that emerges is that pre treatment serum ferritin inversely correlates with the odds of achieving sustained virological(SVR) response after combination interferon ribavirin treatment. We have also reviewed the limited literature that reports the effect of therapeutic phlebotomy to reverse iron overload among patients with chronic hepatitis C. A small meta-analysis of 6 prospective randomized trials and a subsequent seventh trial do suggest that phlebotomy to induce iron depletion enhances the likelihood of achieving (SVR) after anti-viral therapy. However, these studies are primarily in patients receiving interferon monotherapy, which is of course now obsolete. Finally, a few small studies suggest that therapeutic phlebotomy to induce iron depletion reduces liver transaminase levels and may improve histology, and perhaps even reduce the risk of hepato-cellular carcinoma. Prospective randomized controlled trials of phlebotomy among patients with advanced hepatitis C and iron overload are needed. © 2012 Springer Science+Business Media, LLC.

Desai TK, Krishnan K, Samala N, Singh J, Cluley J, Perla S and Howden CW (2012). "The incidence of oesophageal adenocarcinoma in non-dysplastic Barrett's oesophagus: a meta-analysis." Gut 61(7): 970-976.

[Request Form](#)

Department of Biomedical Sciences

INTRODUCTION: The risk of oesophageal adenocarcinoma (OAC) in non-dysplastic Barrett's oesophagus (BO) may have been overestimated. The objective was to estimate the incidence of OAC in patients with BO without dysplasia. **METHODS:** The authors searched MEDLINE and EMBASE from 1966 to 2011 and performed a bibliographic review of previous publications, excluding abstracts, non-peer-reviewed publications and those not published in English, for prospective or retrospective studies of the incidence of OAC in patients with BO. They excluded patients with any degree of dysplasia at baseline and those without documented intestinal metaplasia. Studies were independently reviewed by two individuals. 57 of 3450 studies were included. The authors extracted information on number of patients with BO, length of follow-up, incident cases of OAC, mean age of patients, country of origin, whether prospective or retrospective, mean length of BO segments and mortality from causes other than OAC. Study quality was assessed by the Ottawa Newcastle criteria. **RESULTS:** The 57 included studies comprised 11,434 patients and 58,547 patient-years of follow-up. The pooled annual incidence of OAC was 0.33% (95% CI 0.28% to 0.38%). Among 16 studies that provided appropriate information on mortality, there were 56 incident cases of OAC but 684 deaths from apparently unrelated causes. Among 16 studies that provided information on patients with short-segment BO, the annual incidence of OAC was only 0.19%. **CONCLUSIONS:** The incidence of OAC in non-dysplastic BO is around 1 per 300 patients per year. The incidence of OAC in short-segment BO is under 1 per 500 patients per year.

Dixon SR, Grines CL, Munir A, Madder RD, **Safian RD, Hanzel GS**, Pica MC and **Goldstein JA** (2012). "Analysis of target lesion length before coronary artery stenting using angiography and near-infrared spectroscopy versus angiography alone." American Journal of Cardiology 109(1): 60-66.

[Full-Text](#)

Department of Internal Medicine

Lipid core plaque (LCP) can extend beyond the angiographic margins of a target lesion, potentially resulting in incomplete lesion coverage. We sought to compare the target lesion length using near-infrared spectroscopy (NIRS) combined with conventional coronary angiography versus angiography alone. NIRS was

performed in 69 patients (75 lesions) undergoing native vessel percutaneous coronary intervention (LipiScan Coronary Imaging System). Chemograms were analyzed for the presence and location of LCP, either within or extending beyond, the angiographic margins of the target lesion. The target lesion length was measured by quantitative coronary angiography (QCA) and compared to the lesion length measured using QCA and NIRS. LCP was present in 50 target lesions (67%). In 42 lesions (84%), LCP was present only within the target lesion. In 8 lesions (16%) LCP extended beyond the angiographic margins of the lesion. Of these 8 lesions, 4 (8%) had LCP 5 mm from the angiographic margins. The mean distance that the LCP extended beyond the angiographic lesion margin was 7 +/- 4 mm (range 2 to 14). For these 8 lesions, the target lesion length with NIRS plus QCA was 28 +/- 10 mm versus 21 +/- 8 mm with QCA alone. In conclusion, patients undergoing coronary artery stenting could have LCP extending beyond the intended treatment margins as defined using QCA alone. This could have implications for stent length selection and optimal lesion coverage.

Dixon SR and **Safian RD** (2012). "The year in interventional cardiology." Journal of the American College of Cardiology 59(17): 1497-1508.

[Full-Text](#)

Department of Internal Medicine

We are delighted to provide readers of the Journal with this review of major scientific work published in the field of interventional cardiology in 2011, including late-breaking trials presented at the American College of Cardiology, Transcatheter Cardiovascular Therapeutics, European Society of Cardiology, and American Heart Association conferences. We hope that the paper will provide a broad overview for general cardiologists, as well as a framework for more detailed study for those interested in interventional cardiology.

Dohany L, Gustafson S, Ducaine W and **Zakalik D** (2012). "Psychological distress with direct-to-consumer genetic testing: a case report of an unexpected BRCA positive test result." Journal of Genetic Counseling 21(3): 399-401.

[Full-Text](#)

Department of Internal Medicine

We report a case of a client who discovered she had a BRCA mutation following direct-to-consumer (DTC) genetic testing in the absence of genetic counseling. After testing she presented for genetic counseling with anxiety, distress, and a deficit of knowledge about what the DTC genetic testing revealed. Genetic counseling helped alleviate distress while empowering the client to apply the results of testing to improve medical management. Despite recent studies demonstrating no negative psychological impact of DTC genetic testing on the consumer, this case illustrates that significant psychological distress and confusion can occur as a result of DTC genetic testing for highly penetrant single gene disorders. Pre- and post-test genetic counseling in conjunction with DTC genetic testing may alleviate consumers' distress and empower clients to proactively utilize their result information.

Donaldson PR (2012). "Does generalized joint hypermobility predict joint injury in sport? A review." Clinical Journal of Sport Medicine 22(1): 77-78.

[Full-Text](#)

Department of Orthopedic Surgery

Donaldson PR (2012). "Surgical versus nonsurgical treatment of acute Achilles tendon rupture: commentary." Clinical Journal of Sport Medicine 22(2): 169-170.

[Full-Text](#)

Department of Orthopedic Surgery

Dutchshen N, **Maerz T**, Rabban P, Haut RC, Button KD, **Baker KC** and Guettler J (2012). "The acute effect of bipolar radiofrequency energy thermal chondroplasty on intrinsic biomechanical properties and thickness of chondromalacic human articular cartilage." Journal of Biomechanical Engineering 134(8): 081007.

[Full-Text](#)

Department of Surgery

Radio frequency energy (RFE) thermal chondroplasty has been a widely-utilized method of cartilage debridement in the past. Little is known regarding its effect on tissue mechanics. This study investigated the acute biomechanical effects of bipolar RFE treatment on human chondromalacic cartilage. Articular cartilage specimens were extracted (n = 50) from femoral condyle samples of patients undergoing total knee arthroplasty. Chondromalacia was graded with the Outerbridge classification system. Tissue thicknesses were measured using a needle punch test. Specimens underwent pretreatment load-relaxation testing using a spherical indenter. Bipolar RFE treatment was applied for 45 s and the indentation protocol was repeated. Structural properties were derived from the force-time data. Mechanical properties were derived using a fibril-reinforced biphasic cartilage model. Statistics were performed using repeated measures ANOVA. Cartilage thickness decreased after RFE treatment from a mean of 2.61 mm to 2.20 mm in Grade II, II-III, and III specimens (P < 0.001 each). Peak force increased after RFE treatment from a mean of 3.91 N to 4.91 N in Grade II and III specimens (P = 0.002 and P = 0.003, respectively). Equilibrium force increased after RFE treatment from a mean of 0.236 N to 0.457 N (P < 0.001 each grade). Time constant decreased after RFE treatment from a mean of 0.392 to 0.234 (P < 0.001 for each grade). Matrix modulus increased in all specimens following RFE treatment from a mean 259.12 kPa to 523.36 kPa (P < 0.001 each grade). Collagen fibril modulus decreased in Grade II and II-III specimens from 60.50 MPa to 42.04 MPa (P < 0.001 and P = 0.005, respectively). Tissue permeability decreased in Grade II and III specimens from $2.04 \times 10^{-15} \text{ m}^4/\text{Ns}$ to $0.91 \times 10^{-15} \text{ m}^4/\text{Ns}$ (P < 0.001 and P = 0.009, respectively). RFE treatment decreased thickness, time constant, fibril modulus, permeability, but increased peak force, equilibrium force, and matrix modulus. While resistance to shear and tension could be compromised due to removal of the superficial layer and decreased fibril modulus, RFE treatment increases matrix modulus and decreases tissue permeability which may restore the load-bearing capacity of the cartilage.

Eadie JA, **Faia LJ**, Wong SC and **Trese MT** (2012). "Bilateral colobomas with avascular peripheral retina: Case report." Canadian Journal of Ophthalmology 47(5): e21-e22.

[Full-Text](#)

Department of Ophthalmology

Eadie JA, **Luo CK** and **Trese MT** (2012). "Novel clinical manifestation of congenital x-linked retinoschisis." Archives of Ophthalmology 130(2): 255-257.

[Full-Text](#)

Department of Ophthalmology

Eastwood JL, Sadler TD, Zeidler DL, Lewis A, Amiri L and Applebaum S (2012). "Contextualizing nature of science instruction in socioscientific issues." International Journal of Science Education 34(15): 2289-2315.

[Request Form](#)

Department of Biomedical Sciences

The purpose of this study was to investigate the effects of two learning contexts for explicit-reflective nature of science (NOS) instruction, socioscientific issues (SSI) driven and content driven, on student NOS conceptions. Four classes of 11th and 12th grade anatomy and physiology students participated. Two classes experienced a curricular sequence organized around SSI (the SSI group), and two classes experienced a content-based sequence (the Content group). An open-ended NOS questionnaire was administered to both groups at the beginning and end of the school year and analyzed to generate student profiles. Quantitative analyses were performed to compare pre-instruction NOS conceptions between groups as well as pre to post changes within groups and between groups. Both SSI and Content groups showed significant gains in most NOS themes, but between-group gains were not significantly different. Qualitative analysis of post-instruction responses, however, revealed that students in the SSI group tended to use examples to describe their views of the social/cultural NOS. The findings support SSI contexts as effective for promoting gains in students' NOS understanding and suggest that these contexts facilitate nuanced conceptions that should be further explored.

Eastwood JL and Schlegel WM (2012). "A comparative study for advancing understanding of interdisciplinary learning in STEM." FASEB Journal 26: 720.711.

[Request Form](#)

Department of Biomedical Sciences

Eckleberry-Hunt J and **Tucciarone J** (2012). "It's a new generation: teaching strategies for medical education." Society of General Internal Medicine Forum 35(9): 15.

[Full-Text](#)

Department of Family Medicine

Evonich RF, **Nori DM** and **Haines DE** (2012). "Efficacy of pulmonary vein isolation with a novel hot balloon ablation catheter." Journal of Interventional Cardiac Electrophysiology 34(1): 29-36.

[Full-Text](#)

Department of Internal Medicine

Due to the variable anatomy of the human pulmonary vein (PV), PV isolation for atrial fibrillation ablation is challenging. A novel hot balloon ablation catheter has been developed to improve ablation outcomes. The efficacy, histopathologic lesion characteristics, and thermodynamics of this technology were examined. Swine underwent left atrial (n = 24) and superior vena cava (SVC, n = 7) catheterization with a compliant balloon catheter filled with saline and contrast. After PV mapping and angiography, ablation was performed with radiofrequency energy heating of the balloon contents. Central balloon temperatures were varied from 60A degrees C to 90A degrees C, and durations of energy delivery were varied from 60 to 300 s. Endocardial and epicardial temperatures were recorded contiguous to the balloon during SVC ablations. Pathology was examined. With a mean of 1.4 +/- 0.9 ablations per PV at 70A degrees C, 93% were electrically isolated. Necropsy exam revealed extraostial lesions without charring. PVs ablated at temperatures a parts per thousand yen80A degrees C and durations a parts per thousand yen180 s were associated with a high rate of successful isolation with a single ablation. Higher-temperature lesions displayed greater histopathologic uniformity, but more marked fibrin deposition. Chronic lesions revealed granulation tissue and fibrosis. No thromboembolic events were observed and histopathology of the phrenic nerve and esophagus was normal in all specimens. The hot balloon ablation catheter appears to be a safe and effective tool for PV isolation. Higher temperatures and longer ablation durations are associated with a higher single ablation success rate.

Ferrari M, Harrison B, Rawashdeh O, Hammond R, Avery Y, Rawashdeh M, Sa'deh W and **Maddens ME** (2012). "Clinical feasibility trial of a motion detection system for fall prevention in hospitalized older adult patients." Geriatric Nursing 33(3): 177-183.

[Full-Text](#)

Department of Internal Medicine

The purpose of this pilot study was to test the feasibility of a wireless 5-sensor, motion detection system (5S-MDS) with hospitalized older adults. Interventions to prevent hospital-based falls in older adults are important to reduce morbidity, mortality, and health care costs. Wearable motion sensors, which track and wirelessly transmit body movements, may identify human movement patterns that immediately precede falls, thus allowing early prevention. Descriptive feasibility study in which 5 hospitalized older adults were recruited to wear the 5S-MDS for 4 hours. Measurement included assessment of participant acceptance, skin integrity, and sensor accuracy. All 5 participants (mean age, 90.2 years) agreed that sensors were acceptable and skin integrity was maintained. The sensor data accurately reflected the patient movements. The 5S-MDS was feasible for 4 hours' use with hospitalized older adults. It has potential as an early warning system for falls. © 2012 Mosby, Inc.

Ferrari M, Harrison B, Rawashdeh O, Rawashdeh M, **Hammond R** and **Maddens M** (2012). "A pilot study testing a fall prevention intervention for older adults determining the feasibility of a five-sensor motion detection system." Journal of Gerontological Nursing 38(1): 13-16.

[Full-Text](#)

Department of Surgery

Department of Internal Medicine

Interventions to prevent hospital-based falls in older adults are critically important to reduce morbidity, mortality, and health care costs. The purpose of this pilot study was to test the accuracy and acceptability of a wireless five-sensor motion detection system (5S-MDS) for detecting falls. Wearable motion sensors, which measure and integrate movement in space, may identify human movement patterns that immediately precede falls, thus allowing prevention. However, sensors must be accurate, and older adults must find wearable sensors acceptable. This descriptive feasibility study recruited 5 healthy older adults (mean age = 69.6) who wore the 5S-MDS while performing 35 movement scenarios. All participants agreed the sensors were acceptable, and skin integrity was maintained for all. The 5S-MDS accurately reflected the patients' movements and was found acceptable to the older adults; thus, the 5S-MDS has potential as an early warning system for falls.

Fitzgerald MP, Payne CK, Lukacz ES, Yang CC, **Peters KM**, Chai TC, Nickel JC, Hanno PM, Kreder KJ, Burks DA, Mayer R, Kotarinos R, Fortman C, Allen TM, Fraser L, Mason-Cover M, Furey C, Odabachian L, Sanfield A, Chu J, Huestis K, Tata GE, Dugan N, Sheth H, Bewyer K, Anaeme A, Newton K, Featherstone W, Halle-Podell R, Cen L, Landis JR, Propert KJ, Foster Jr HE, Kusek JW and Nyberg LM (2012). "Randomized multicenter clinical trial of myofascial physical therapy in women with interstitial cystitis/painful bladder syndrome and pelvic floor tenderness." *Journal of Urology* 187(6): 2113-2118.

[Request Form](#)

Department of Urology

Purpose: We determined the efficacy and safety of pelvic floor myofascial physical therapy compared to global therapeutic massage in women with newly symptomatic interstitial cystitis/painful bladder syndrome. **Materials and Methods:** A randomized controlled trial of 10 scheduled treatments of myofascial physical therapy vs global therapeutic massage was performed at 11 clinical centers in North America. We recruited women with interstitial cystitis/painful bladder syndrome with demonstrable pelvic floor tenderness on physical examination and a limitation of no more than 3 years' symptom duration. The primary outcome was the proportion of responders defined as moderately improved or markedly improved in overall symptoms compared to baseline on a 7-point global response assessment scale. Secondary outcomes included ratings for pain, urgency and frequency, the O'Leary-Sant IC Symptom and Problem Index, and reports of adverse events. We compared response rates between treatment arms using the exact conditional version of the Mantel-Haenszel test to control for clustering by clinical center. For secondary efficacy outcomes cross-sectional descriptive statistics and changes from baseline were calculated. **Results:** A total of 81 women randomized to the 2 treatment groups had similar symptoms at baseline. The global response assessment response rate was 26% in the global therapeutic massage group and 59% in the myofascial physical therapy group ($p = 0.0012$). Pain, urgency and frequency ratings, and O'Leary-Sant IC Symptom and Problem Index decreased in both groups during followup, and were not significantly different between the groups. Pain was the most common adverse event, occurring at similar rates in both groups. No serious adverse events were reported. **Conclusions:** A significantly higher proportion of women with interstitial cystitis/painful bladder syndrome responded to treatment with myofascial physical therapy than to global therapeutic massage. Myofascial physical therapy may be a beneficial therapy in women with this syndrome. © 2012 American Urological Association Education and Research, Inc.

Franklin BA (2012). "Multifactorial cardiac rehabilitation did not reduce mortality or morbidity after acute myocardial infarction (ACP Journal Club)." *Annals of Internal Medicine* 157(2): JC2-11.

[Full-Text](#)

Department of Internal Medicine

Question: In patients who have had a myocardial infarction (MI), what is the effect of multifactorial cardiac rehabilitation programs on mortality or morbidity? **Methods Design:** Randomized controlled trial (Rehabilitation After Myocardial Infarction Trial [RAMIT]). **Allocation:** Concealed.* **Blinding:** Blinded* (data collectors and {data analysts for initial analysis}†). **Follow-up period:** ≤ 9 years. **Setting:** 14 hospitals in England and Wales, UK. **Patients:** 1813 patients (mean age 64 y, 74% men) who were hospitalized with a

primary diagnosis of acute MI and discharged home within 28 days. Exclusion criteria included discharge to hospice or another hospital, previous cardiac rehabilitation, serious concurrent disease, physical frailty, mental confusion, and communication difficulty. Intervention: Multifactorial rehabilitation programs for ≥ 10 hours (n = 903) or usual care (n = 910). Rehabilitation programs comprised exercise training; education about the heart, heart disease, risk factors, and treatment; and recovery counseling and long-term secondary prevention advice. Programs were usually led by nurses with acute cardiac care experience, involved ≥ 1 other discipline (physician and/or cardiologist, exercise physiologist, dietician, pharmacist, psychologist, counselor, social worker, or health promotion specialist), were weekly or biweekly, and averaged 20 hours over 6 to 8 weeks. Outcomes: Mortality at 2 years. Secondary outcomes included mortality at 1 and 9 years, and cardiac outcomes, MI, hospitalization for heart disease, stroke, percutaneous transluminal coronary angioplasty, coronary artery bypass graft, health-related quality of life (Short Form-36) and psychological general well-being (Psychological General Well-Being [PGWB] scale) at 12 months. The trial had 80% power to detect a 20% difference in relative risk for mortality at 9 years. Patient follow-up: > 99% for vital status; 89% at 12 months (intention-to-treat analysis). Main results: Rehabilitation and usual care groups did not differ for mortality or other clinical outcomes (Table), or for any of the 8 health-related quality of life domains or the 3 domains of the PGWB scale (all $P > 0.05$). Conclusion: Multifactorial cardiac rehabilitation programs did not reduce mortality or morbidity after myocardial infarction. © 2012 American College of Physicians.

Franklin BA and Billecke S (2012). "Putting the benefits and risks of aerobic exercise in perspective." Current Sports Medicine Reports 11(4): 201-208.

[Full-Text](#)

Department of Internal Medicine

Although considerable epidemiologic and clinical evidence suggests that structured exercise, increased lifestyle activity, or both are cardioprotective, the absolute and relative risk of cardiovascular and musculoskeletal complications appear to increase transiently during vigorous physical activity. The estimated relative risk of exercise-related cardiac events ranges from 2.1 to 56 and is highest among habitually sedentary individuals with underlying cardiovascular disease who were performing unaccustomed vigorous physical exertion. Moreover, an estimated 7 million Americans receive medical attention for sports and recreation-related injuries each year. These risks, and their modulators, should be considered when endorsing strenuous leisure time or exercise interventions. If the current mantra "exercise is medicine" is embraced, underdosing and overdosing are possible. Thus, exercise may have a typical dose-response curve with a plateau in benefit or even adverse effects, in some individuals, at more extreme levels.

Fulton M and **Peters KM** (2012). "Neuromodulation for voiding dysfunction and fecal incontinence: a urology perspective." Urologic Clinics of North America 39(3): 405-412.

[Full-Text](#)

Department of Urology

Neuromodulation is an effective, minimally invasive technique for the management of urinary urgency and frequency, urgency incontinence, nonobstructive urinary retention, and fecal incontinence. This article reviews the physiology of neuromodulation, indications, implantation methods, and outcomes.

Furuta A, Suzuki Y, Honda M, Koike Y, Naruoka T, Asano K, **Chancellor M**, Egawa S and Yoshimura N (2012). "Time-dependent changes in bladder function and plantar sensitivity in a rat model of fibromyalgia syndrome induced by hydrochloric acid injection into the gluteus." BJU International 109(2): 306-310.

[Full-Text](#)

Department of Urology

OBJECTIVE: To examine the correlation between muscular pain and bladder hypersensitivity in order to clarify the pathogenesis of comorbidity of bladder pain syndrome/interstitial cystitis with other chronic pain conditions such as fibromyalgia syndrome (FMS). **MATERIALS AND METHODS:** Under isoflurane anaesthesia, 0.2 mL of hydrochloric acid (HCl) solution (pH 4.0) was injected into the bilateral gluteus muscles of female Sprague-Dawley rats to produce an FMS model, as the gluteus is one of the specific tender points in patients

with FMS. Control rats received saline injection (0.2 mL). The mechanical sensitivity of the plantar was evaluated using the mean number of bilateral hindlimb withdrawals in response to tactile stimulation with a 2.0-g von Frey filament at 1, 2 and 3 weeks after the HCl injection. In a separate rat group, cystometry was performed with the rats awake during saline infusion (0.06 mL/min) into the bladder before and after 1% lidocaine injection (0.2 mL) into the bilateral gluteus 1, 2 and 3 weeks after the HCl injection. RESULTS: The mean number of hindlimb withdrawals was significantly higher in FMS rats than in controls at 1 and 2 weeks. Using cystometry, we found that the intercontraction interval (ICI) and voided volume (VV) were significantly lower in FMS rats than in controls at 1 and 2 weeks. In addition, the voiding threshold pressure, ICI and VV were significantly higher after lidocaine injection in FMS rats, but not in controls, at 1 and 2 weeks. CONCLUSIONS: HCl injection (pH 4.0) into the gluteus can induce plantar hypersensitivity and urinary frequency for up to 2 weeks after the injection, suggesting that somatic (gluteus)-to-visceral (bladder) cross-sensitization might underlie bladder hypersensitivity in patients with FMS. Moreover, intervention at specific tender points outside the bladder could be effective in treating urinary frequency because lidocaine injection into the gluteus normalized bladder function in FMS rats for up to 2 weeks.

Gabel S and **Mulhem E** (2012). "How often can PPIs be successfully withdrawn from patients with GERD?" Evidence-Based Practice 15(11): 8-9.

[Request Form](#)

Department of Family Medicine

Gaynes R and **Band J** (2012). Epidemiology, pathogenesis, and microbiology of intravascular catheter infections, in Basow D. (ed). UpToDate: Wolters Kluwer Health.

[Full-Text](#)

Department of Internal Medicine

Gerszten PC, Kersh R, Sweeney RA, Sahgal A, Sheehan JP, Flickinger JC, **Fahim DK, Grills IS** and Guckenberger M (2012). "A multinational report on methods for institutional credentialing for spine radiosurgery." International Journal of Radiation Oncology Biology Physics 84(3 Suppl S): S286.

[Full-Text](#)

Department of Surgery

Department of Radiation Oncology

Radiosurgery (SRS) is a rapidly emerging treatment options for both malignant and benign spine tumors. Proper credentialing by physicians and medical physicists is important for the safe and effective adoption of spine SRS and may be associated with improved patient outcomes. This study was undertaken to provide a multi-national summary on methods for institutional credentialing for spine SRS.

Ghilezan M (2012). "Role of high dose rate brachytherapy in the treatment of prostate cancer." Cancer Radiotherapie 16(5-6): 418-422.

[Full-Text](#)

Department of Radiation Oncology

High dose rate (HDR) brachytherapy in intermediate and high-risk prostate cancer patients has started in the late eighties in Europe and the United States, as a boost combined with external beam radiation therapy, as an attractive method for dose escalation. The results of the first dose-escalation study performed at William Beaumont Hospital has established the safety and efficacy of this combined treatment approach. Likewise, this landmark study enabled a paradigm shift in the radiobiology of prostate cancer, demonstrating that the alpha/beta of prostate cancer was much lower than previously believed to be and therefore the sensitivity of this tumor model to higher-than-conventional doses per fraction led to a dramatic increase of hypofractionated treatment regimens, the object of significant clinical research efforts, currently under way. The excellent toxicity profile and clinical outcome of HDR boost combined treatment prompted investigators to expand HDR brachytherapy indications to low/intermediate prostate cancer patients as the sole treatment modality. The results, toxicity and a brief review of the literature for both HDR boost and HDR monotherapy will be presented.

Ghilezan M, Martinez A, Gustason G, Krauss D, Antonucci JV, Chen P, Fontanesi J, Wallace M, Ye H, Casey A, Sebastian E, Kim L and Limbacher A (2012). "High-dose-rate brachytherapy as monotherapy delivered in two fractions within one day for favorable/intermediate-risk prostate cancer: preliminary toxicity data." International Journal of Radiation Oncology, Biology, Physics 83(3): 927-932.

[Full-Text](#)

Department of Radiation Oncology

PURPOSE: To report the toxicity profile of high-dose-rate (HDR)-brachytherapy (BT) as monotherapy in a Human Investigation Committee-approved study consisting of a single implant and two fractions (12 Gy x 2) for a total dose of 24 Gy, delivered within 1 day. The dose was subsequently increased to 27 Gy (13.5 Gy x 2) delivered in 1 day. We report the acute and early chronic genitourinary and gastrointestinal toxicity. **METHODS AND MATERIALS:** A total of 173 patients were treated between December 2005 and July 2010. However, only the first 100 were part of the IRB-approved study and out of these, only 94 had a minimal follow-up of 6 months, representing the study population for this preliminary report. All patients had clinical Stage T2b or less (American Joint Committee on Cancer, 5th edition), Gleason score 6-7 (3+4), and prostate-specific antigen level of ≤ 12 ng/mL. Ultrasound-guided HDR-BT with real-time dosimetry was used. The prescription dose was 24 Gy for the first 50 patients and 27 Gy thereafter. The dosimetric goals and constraints were the same for the two dose groups. Toxicity was scored using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 3. The highest toxicity scores encountered at any point during follow-up are reported. **RESULTS:** The median follow-up was 17 months (range, 6-40.5). Most patients had Grade 0-1 acute toxicity. The Grade 2 acute genitourinary toxicity was mainly frequency/urgency (13%), dysuria (5%), hematuria, and dribbling/hesitancy (2%). None of the patients required a Foley catheter at any time; however, 8% of the patients experienced transient Grade 1 diarrhea. No other acute gastrointestinal toxicities were found. The most common chronic toxicity was Grade 2 urinary frequency/urgency in 16% of patients followed by dysuria in 4% of patients; 2 patients had Grade 2 rectal bleeding and 1 had Grade 4, requiring laser treatment. **CONCLUSIONS:** Favorable-risk prostate cancer patients treated with a single implant HDR-BT to 24-27 Gy in two fractions within 1 day have excellent tolerance with minimal acute and chronic toxicity. Longer follow-up is needed to confirm these encouraging early results.

Gillies C, Patel N, **Akervall J** and **Wilson G** (2012). "Majority voting genetic programming classifier." International Journal of Advanced Intelligence Paradigms 4(3-4): 241-255.

[Request Form](#)

Department of Biomedical Sciences

Department of Radiation Oncology

Glazier JJ and Dixon SR (2012). "Skin injury following prolonged fluoroscopy: early and late appearances." QJM 105(6): 571-573.

[Full-Text](#)

Department of Internal Medicine

Go JL, Rothman S, Prosper A, **Silbergleit R** and Lerner A (2012). "Spine infections." Neuroimaging Clinics of North America 22(4): 755-772.

[Request Form](#)

Department of Diagnostic Radiology and Molecular Imaging

Spine Infections John L. Go, Stephen Rothman, Ashley Prosper, Richard Silbergleit, and Alexander Lerner Infections of the spine represent a rare but potentially debilitating and neurologically devastating condition for patients. Early diagnosis, imaging, and intervention may prevent some of the more critical complications that may ensue from this disease process, including alignment abnormalities, central canal compromise, nerve root impingement, vascular complications, and spinal cord injury. This article reviews the underlying pathophysiologic basis of infection, clinical manifestations, and imaging modalities used to diagnose infections of the spine and spinal cord.

Goldstein J (2012). Acute right ventricular infarction, in Chatterjee K. (ed). Cardiology : An Illustrated Textbook: Jaypee Brothers Publishers: 960-968.

[Request Form](#)

Department of Internal Medicine

Goldstein J, Madden S, Sum S, **Dixon S**, Madder R and Muller J (2012). Intravascular spectroscopy, in Eeckhout E. (ed). Percutaneous Interventional Cardiovascular Medicine: The PCR-EACPI Textbook. **1**: 665-680.

Department of Internal Medicine

Goldstein JA (2012). "Acute right ventricular infarction: insights for the interventional era." Current Problems in Cardiology 37(12): 533-557.

[Full-Text](#)

Department of Internal Medicine

Acute right ventricular infarction is associated with higher in-hospital morbidity and mortality related to life-threatening hemodynamic compromise and arrhythmias during acute occlusion and abruptly with reperfusion, complications which have implications for interventional management. Acute right coronary artery occlusion proximal to the right ventricular (RV) branches results in depressed RV systolic function, leading to diminished transpulmonary delivery of left ventricular preload and resulting in low-output hypotension. Under these conditions, RV pressure generation and output are dependent on left ventricular-septal contraction via paradoxical septal motion. With culprit lesions distal to the right atrial (RA) branches, augmented RA contractility enhances RV performance and cardiac output, whereas proximal occlusions induce RA ischemia, which exacerbates hemodynamic compromise. Hypotension may respond to volume resuscitation and restoration of a physiologic rhythm. Refractory cases usually respond to parenteral inotropes, though in some cases mechanical support is required. The right ventricle is relatively resistant to infarction and usually recovers even after prolonged occlusion. Acute percutaneous mechanical reperfusion enhances recovery of RV performance and improves the clinical course and survival of patients with right ventricular infarction. (Curr Probl Cardiol 2012;37:533-557.)

Goldstein JA (2012). "Periprocedural myocardial infarction: It's the plaque, not the stent." Catheterization and Cardiovascular Interventions 80(4): 531-532.

[Full-Text](#)

Department of Internal Medicine

Goldstein JA (2012). "Preventing distal embolization: Plaque composition is the matter." Catheterization and Cardiovascular Interventions 80(7): 1163-1164.

[Full-Text](#)

Department of Internal Medicine

Goldstein JA and Kern MJ (2012). "Percutaneous mechanical support for the failing right heart." Cardiology Clinics 30(2): 303-310.

[Full-Text](#)

Department of Internal Medicine

Right ventricular (RV) failure is an increasingly common clinical problem that may require mechanical support. In contrast to severe left ventricular failure, RV failure is typically more reversible. Therefore, application of shorter-term percutaneous support devices is potentially attractive. Current innovations promise greater availability of such percutaneous RV support devices. This article considers the available mechanical approaches to provide hemodynamic support to treat profound RV failure in the common clinical scenarios in which percutaneous mechanical RV support may be most beneficial.

Goldstein JA and Rich JD (2012). "Faces of right ventricular failure." Cardiology Clinics 30(2): xi.

[Full-Text](#)

Department of Internal Medicine

Goncalves LF, Bronsteen R and **Lee W** (2012). "Fetal heart: a 4-chamber view is not enough." Clinical Obstetrics and Gynecology 55(1): 266-280.

[Full-Text](#)

Department of Obstetrics and Gynecology

The majority of children born with congenital heart disease have no identifiable risk factors and, therefore, prenatal diagnosis relies on routine ultrasonographic screening. First proposed in 1985, the 4-chamber view is a component of the basic fetal cardiac examination. However, many life-threatening conditions (eg, transposition of the great arteries) can present with a normal 4-chamber view and may only be detected by systematic evaluation of the outflow tracts. Although this is a technically challenging skill, its mastery is a worthwhile goal of ultrasonography training, as it likely to improve the lives of at least some of the children affected by the most severe forms of congenital heart disease.

Gonçalves LF, Espinoza J and **Bronsteen R** (2012). "3D/4D fetal echocardiography." Applied Radiology 41(3): 31-43.

[Full-Text](#)

Department of Obstetrics and Gynecology

Granadier R (2012). Cavernous sinus syndrome/orbital apex syndrome, in Maguire J., Murchison A. and Jaeger E. (ed). Wills Eye Institute 5-Minute Ophthalmology Consult. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins: 134-135.

[Request Form](#)

Department of Ophthalmology

Greer K, **Swanberg S**, Hristova M, Switzer AT, Daniel D and Perdue SW (2012). "Beyond the web tutorial: development and implementation of an online, self-directed academic integrity course at Oakland University." Journal of Academic Librarianship 38(5): 251-258.

[Full-Text](#)

Medical Library

Intentional and unintentional plagiarism cases occur frequently and present unique pedagogical challenges for librarians, who often are deemed responsible for ensuring that undergraduates gain a solid understanding of academic integrity issues via information literacy instruction. This article describes the process by which faculty from the Oakland University Libraries and the Oakland University Writing Center developed an online, self-directed academic integrity course aimed at reducing plagiarism on campus. Prior to this course, the library offered a substantially shorter web-based plagiarism tutorial, which was used in course instruction and the Cite Right Program, the writing center's intervention for academic dishonesty. A recent assessment of this tool revealed that it no longer addressed the needs of the campus community. To address its gaps, the library and the writing center collaborated on more substantial content, which is detailed herein.

Grills IS, Hope AJ, Guckenberger M, **Kestin LL**, Werner-Wasik M, Yan D, Sonke JJ, Bissonnette JP, Wilbert J, Xiao Y and Belderbos J (2012). "A collaborative analysis of stereotactic lung radiotherapy outcomes for early-stage non-small-cell lung cancer using daily online cone-beam computed tomography image-guided radiotherapy." Journal of Thoracic Oncology 7(9): 1382-1393.

[Full-Text](#)

Department of Radiation Oncology

INTRODUCTION: We report lung stereotactic-body radiotherapy (SBRT) outcomes for a large pooled cohort treated using daily online cone-beam computed tomography. METHODS: Five hundred and five stage I-IIb (T1-3N0M0) non-small-cell lung cancer (NSCLC) cases underwent SBRT using cone-beam computed

tomography image guidance at five international institutions from 1998 to 2010. Median age was 74 years (range, 42-92) whereas median forced expiratory volume in 1 second/diffusing lung capacity for carbon monoxide were 1.4 liter (65%) and 10.8 ml/min/mmHg (53%). Of the 505 cases, 64% were biopsy proven and 87% medically inoperable. Staging was: IA 63%, IB 33%, IIA 2%, and recurrent 1%. Median max tumor dimension was 2.6 cm (range, 0.9-8.5). Median heterogeneously calculated volumetric prescription dose (PD) was 54 Gy (range, 20-64 Gy) in three fractions (range, 1-15) over 8 days (range, 1-27). Median biologically equivalent PD biological equivalent doses (BED10) was 132 Gy (range, 60-180). RESULTS: With a median follow-up of 1.6 years (range, 0.1-7.3), the 2-year Kaplan-Meier local control (LC), regional control, and distant metastasis (DM) rates were 94%, 89%, and 20%, respectively, whereas cause-specific and overall survival were 87% and 60% (78% operable, 58% inoperable, $p = 0.01$), respectively. Stage, gross-tumor volume size (≥ 2.7 cm) and PD(BED10) predicted local relapse (LR) and DM. LR was 15% for BED10 less than 105 Gy versus 4% for BED10 of 105 Gy or more ($p < 0.001$); DM was 31% versus 18% for BED10 less than 105 versus 105 Gy or more ($p = 0.01$). On multivariate analysis, PD(BED10) and elapsed days during radiotherapy predicted LR; gross-tumor volume size predicted DM. Grade 2 or higher pneumonitis, rib fracture, myositis, and dermatitis were 7%, 3%, 1%, and 2%, respectively. CONCLUSIONS: In the largest early-stage NSCLC SBRT data set to date, a high rate of local control was achieved, which was correlated with a PD(BED10) of 105 Gy or more. Failures were primarily distant, severe toxicities were rare, and overall survival was encouraging in operable patients.

Haines DE (2012). "Atrial fibrillation ablation in the real world." Journal of the American College of Cardiology 59(2): 150-152.

[Full-Text](#)

Department of Internal Medicine

Hajj Hussein I, Dali B, Atiyeh BS and Jurjus A (2012). "Rat model of burn wound healing: effect of botox." Journal of Biological Regulators & Homeostatic Agents 26(3): 389-400.

[Request Form](#)

Department of Biomedical Sciences

Animal models of burn play a crucial role in studying the mechanisms of burn wound progression and the factors that regulate various stages of healing. In this study, using a rat model, we assessed the effect of Botox in the healing process through parameters like transepidermal water loss (TEWL), histological alterations, transforming growth factor β (TGF- β 1) and tumor necrosis factor alpha (TNF- α). Fifty Sprague-Dawley rats were inflicted with 5 cm² second degree burn and divided into 2 groups; one group was injected intralesionally with Botox and the other with saline. Daily observation and transepidermal water loss measurement were performed. Biopsies were taken on days 0, 3, 8, 14, and 28 for histology and polymerase chain reaction, testing TGF- β and TNF- α . The results showed no significant difference in TEWL except for slightly better preservation of moisture with Botox. Histology revealed relatively better and faster regeneration with Botox, delayed lower grade inflammation, and increase in fibroblasts. TNF- α had an acute increase of 21-fold then tapered down while TGF- β levels increased on day 3 after TNF- α , peaked on day 8 and then started to decrease until complete healing. Botox improved the healing process and the cosmetic appearance of burn scar.

Hajj Hussein I, Freund JN, J-M R, Shams A, Yamine M, Leone A and Jurjus AR (2012). "Enteropathogenic E.coli sustains iodoacetamide –induced ulcerative colitis-like colitis in rats: modulation of IL-1B, IL-6, TNF-alpha, COX-2 and apoptosis." Journal of Biological Regulators & Homeostatic Agents 26(3): 515-526.

[Request Form](#)

Department of Biomedical Sciences

Pathogenic or non-pathogenic bacteria from flora may play a key role in inflammatory bowel disease (IBD) pathogenesis. However, a specific infectious agent causing IBD has not been identified. This study assessed the impact of enteropathogenic E. coli (EPEC) on the modulation of IL-1 β , IL-6, TNF- α , COX-2, BAX and Bcl-2 expression, in sustaining inflammation of a rat colitis model. Two hundred male Sprague-Dawley rats (4 groups) were inoculated weekly or bi-weekly for 70 days, with 1% methylcellulose (MC), (b) 6%

iodoacetamide (IA) in 1% MC, (c) 4x10⁸ CFU of EPEC, and (d) IA+EPEC. After a month, treatment was stopped in half of the animals in each group. IL-1 β , IL-6, TNF- α , COX-2, BAX and Bcl-2 expression were measured in colonic mucosa scrapings. IL-1 β , IL-6, TNF- α , and COX-2 were significantly increased in colonic mucosa of the IA+EPEC group and to a lesser but significant level in the IA group compared to controls, or EPEC alone, both in continued and discontinued treatment groups. Additionally, the BAX/Bcl-2 ratio decreased, indicating less apoptosis in the IA+EPEC group which exhibited more necrosis. These effects increased with experiment duration. This work provides new arguments favouring the role of bacteria in IBD pathogenesis.

Hall A, Qu G, Sethi IK and **Hartrick C** (2012). "Tensor-based temporal behavior analysis in pain medicine." Proceedings of the 11th IEEE International Conference on Machine Learning and Applications, ICMLA 2012, Boca Raton, FL. Vol. 1: 626.

[Full-Text](#)

Department of Biomedical Sciences

Hall LM and O'Lenic K (2012). "Treatment strategies to overcome end-of-dose failure with oral and transdermal opioids." Journal of Pharmacy Practice 25(5): 503-509.

[Full-Text](#)

Department of Biomedical Sciences

Extended-release oral and transdermal opioids are increasingly being used for the management of chronic pain. Although the dosing intervals for these products were established through controlled clinical trials, expanded use of extended-release and transdermal dosage forms has resulted in awareness that a significant number of patients with chronic pain experience loss of baseline pain control prior to the next scheduled dose. End-of-dose failure (EDF) is the term used to describe this type of pain manifestation. By recognizing potential causes of EDF, strategies may be developed to overcome its occurrence to improve patients' pain control.

Halpin C, Shi H, Reda D, Antonelli PJ, **Babu S**, Carey JP, Gantz BJ, Goebel JA, Hammerschlag PE, Harris JP, Isaacson B, Lee D, Linstrom CJ, Parnes LS, Slattery WH, Telian SA, Vrabec JT and Rauch S (2012). "Audiology in the sudden hearing loss clinical trial." Otology and Neurotology 33(6): 907-911.

[Full-Text](#)

Department of Surgery

Objective: To report the pretreatment and posttreatment population characteristics and the overall stability of the audiologic outcomes found during the Sudden Hearing Loss Clinical Trial (ClinicalTrials.gov: Identifier NCT00097448). Study Design: Multicenter, prospective randomized noninferiority trial of oral versus intratympanic (IT) steroid treatment of sudden sensorineural hearing loss (SSNHL). Setting: Fifteen academically based otology practices. Patients: Two hundred fifty patients with unilateral SSNHL presenting within 14 days of onset with 50 dBHL or greater pure tone average hearing threshold in the affected ear. Intervention: Either 60 mg/d oral prednisone for 14 days with a 5-day taper (121 patients) or 4 IT doses for 14 days of 40 mg/ml methylprednisolone (129 patients). Main Outcome Measure: Primary end point was change in hearing [dB PTA] at 2 months after treatment. Noninferiority was defined as less than 10 dB difference in hearing outcome between treatments. In this article, pretreatment and posttreatment hearing findings will be reported in detail. Results: A general (and stable) effect of treatment and a specific effect of greater improvement at low frequencies were found in both treatment groups. Conclusion: Hearing improvements are stable, and a significantly greater improvement occurs with lower frequency after either oral or IT steroid treatment of SSNHL. © 2012, Otology & Neurotology, Inc.

Hammond RL, Hanna K, Morgan C, Perakis P, Najafi N, **Long GW** and **Shanley CJ** (2012). "A wireless and battery-less miniature intracardiac pressure sensor: early implantation studies." ASAIO Journal 58(1): 83-87.

[Full-Text](#)

Department of Surgery

Permanently implantable hemodynamic monitors show great promise in providing personalized and cost-efficient care to heart failure patients by providing timely intracardiac pressure data under ambulatory conditions. The data may be used to titrate maintenance therapies and to monitor health status so that more intensive interventions can be planned and performed under optimal conditions. In this pilot study, we present the results of the implantation of a novel wireless, battery-less pressure sensor into the apex of the left ventricle of four dogs for a period of 8 weeks. All animals recovered to a normal state and did not show any clinical signs of cardiac insufficiency or any complications suggestive of thromboembolism. All sensors functioned throughout the implantation period and provided detailed waveforms of ventricular pressure. ASAIO Journal 2012; 58:83-87.

Hanna K, Seder CW, **Chengelis D**, McCullough PA and **Krause K** (2012). "Shorter circular staple is height associated with lower anastomotic stricture rate in laparoscopic gastric bypass." [Surgery for Obesity and Related Diseases](#) 8(2): 181-184.

[Request Form](#)

Department of Surgery

Background: Anastomotic stenosis, leak, and hemorrhage are common stapler-related complications of laparoscopic Roux-en-Y gastric bypass. In May 2007, we transitioned from a 25-mm diameter, 4.8-mm-height circular stapler to a 25-mm, 3.5-mm-height circular stapler. We hypothesized that the staple height would be associated with a decreased incidence of perioperative complications. Methods: The records of 360 consecutive patients who had undergone laparoscopic Roux-en-Y gastric bypass from May 1, 2006 to March 31, 2008 were retrospectively abstracted. The National Surgical Quality Improvement Project and Michigan Bariatric Surgery Collaborative databases were used to collect the patient demographics and track complications of laparoscopic Roux-en-Y gastric bypass. Data were collected on the rates of anastomotic stenosis requiring dilation of the gastrojejunostomy, anastomotic leak, hemorrhage requiring transfusion, and wound infection. Patients with a 4.8-mm staple height gastrojejunostomy were compared with those with a 3.5-mm staple height gastrojejunostomy for differences in complications. Results: The groups were similar with respect to age, gender, body mass index, hypertension, hyperlipidemia, diabetes, sleep apnea, and surgery duration. In the 4.8- and 3.5-mm staple height groups, 15% and 6.1% required gastrojejunal dilation, respectively (P = .01). A trend was seen toward a decrease in postoperative hemorrhage (5% versus 2.8%) with the shorter staple height. No anastomotic leaks occurred, and the incidence of wound infection (1.7% versus 2.2%) was similar between the 2 groups. Conclusion: In the present study, the use of a 25-mm, 3.5-mm staple height circular stapler was associated with a decreased rate of anastomotic stenosis. (*Surg Obes Relat Dis* 2012;8:181-184.) (c) 2012 American Society for Metabolic and Bariatric Surgery. All rights reserved.

Hartrick C (2012). "Noradrenergic reuptake inhibitors for the treatment of pain." [Expert Opinion on Investigational Drugs](#) 21(12): 1827-1834.

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Department of Biomedical Sciences

Introduction: Noradrenergic reuptake inhibitors can be effective analgesics, finding application in a wide variety of clinical pain settings. Due to a shift toward noradrenergic-mediated pain pathways following nerve injury, they are particularly well suited to the treatment of neuropathic pain. This phenotypic shift makes neuropathic pain difficult to control with opioids alone; some noradrenergic reuptake inhibitors have demonstrated synergy with opioids. Agents currently in early clinical trials are discussed and include both novel delivery of old drugs and the development of new drugs. Areas covered: This review was limited to noradrenergic reuptake inhibitors and analgesia. Literature search included the terms adrenergic, noradrenergic, reuptake, inhibitors, analgesia, NET, norepinephrine transporter, and pain using Medline, Google scholar, Web of Knowledge, www.clinicaltrials.gov, and Pharmaprojects (Informa UK Ltd. 2012). Expert opinion: Topical drug delivery and the use of combinations of agents both topically and systemically are under active investigation. The intrathecal delivery of noradrenergic reuptake inhibitors, allowing delivery directly to the central nervous system thus limiting systemic exposure, represents an exciting avenue of investigation. Gaps in current knowledge have complicated the development of prophylactic therapies for

susceptible individuals or preemptive intervention. Disease-modifying agents and selective inhibitors would facilitate these treatment strategies.

Hartrick C (2012). "TS48 Why formal pain medicine education and board certification matter." [Pain Practice](#) 12(S1): 14.
[Full-Text](#)

Department of Biomedical Sciences

Hartrick C, Gatchel R and Conroy S (2012). "Identification and management of pain medication abuse and misuse: current state and future directions." [Expert Review of Neurotherapeutics](#) 12(5): 601-610.

[Full-Text](#)

Department of Biomedical Sciences

Long-term opioid therapy poses a risk for abuse and misuse in some patients. Identifying which patients may potentially be at risk prior to initiation of therapy, and identifying patients in whom these problems develop during therapy, are significant challenges. Outcome prediction is impeded by the complexity of the problem, where considerable heterogeneity results from psychological and socioeconomic factors, as well as interindividual variation in biological pathways due to genetic and epigenetic factors. Screening tools designed to detect opioid misuse and urine drug testing are both used clinically; scant evidence currently exists to allow the formulation of an algorithm for judicious use of these tools. Moreover, these tools may not be addressing the underlying alterations in biological pathways that occur owing to the development of chronic pain or in response to chronic opioid administration. An evidence-based algorithmic approach to risk mitigation that can be applied in a cost-effective manner to guide therapy is urgently needed.

Hartrick CT (2012). "Capsaicin instillation for postoperative pain following total knee arthroplasty reply." [Clinical Drug Investigation](#) 32(2): 145.

[Request Form](#)

Department of Biomedical Sciences

Hartrick CT (2012). "Editorial note: in appreciation." [Pain Practice](#) 12(8): 674-674.

[Full-Text](#)

Department of Anesthesiology

Department of Biomedical Sciences

Hartrick CT (2012). "Noradrenergic reuptake inhibition in the treatment of pain." [Expert Opinion on Investigational Drugs](#) 21(12): 1827-1834.

[Request Form](#)

Department of Biomedical Sciences

Introduction: Noradrenergic reuptake inhibitors can be effective analgesics, finding application in a wide variety of clinical pain settings. Due to a shift toward noradrenergic-mediated pain pathways following nerve injury, they are particularly well suited to the treatment of neuropathic pain. This phenotypic shift makes neuropathic pain difficult to control with opioids alone; some noradrenergic reuptake inhibitors have demonstrated synergy with opioids. Agents currently in early clinical trials are discussed and include both novel delivery of old drugs and the development of new drugs. Areas covered: This review was limited to noradrenergic reuptake inhibitors and analgesia. Literature search included the terms adrenergic, noradrenergic, reuptake, inhibitors, analgesia, NET, norepinephrine transporter, and pain using Medline, Google scholar, Web of Knowledge, www.clinicaltrials.gov, and Pharmaprojects (Informa UK Ltd. 2012). Expert opinion: Topical drug delivery and the use of combinations of agents both topically and systemically are under active investigation. The intrathecal delivery of noradrenergic reuptake inhibitors, allowing delivery directly to the central nervous system thus limiting systemic exposure, represents an exciting avenue of investigation. Gaps in current knowledge have complicated the development of prophylactic therapies for susceptible individuals or preemptive intervention. Disease-modifying agents and selective inhibitors would facilitate these treatment strategies.

Hartrick CT, Gatchel RJ and **Conroy S** (2012). "Identification and management of pain medication abuse and misuse: current state and future directions." Expert Review of Neurotherapeutics 12(5): 601-610.

[Full-Text](#)

Department of Biomedical Sciences

Expert Rev. Neurother. 12(5), 601-610 (2012) Long-term opioid therapy poses a risk for abuse and misuse in some patients. Identifying which patients may potentially be at risk prior to initiation of therapy, and identifying patients in whom these problems develop during therapy, are significant challenges. Outcome prediction is impeded by the complexity of the problem, where considerable heterogeneity results from psychological and socioeconomic factors, as well as interindividual variation in biological pathways due to genetic and epigenetic factors. Screening tools designed to detect opioid misuse and urine drug testing are both used clinically; scant evidence currently exists to allow the formulation of an algorithm for judicious use of these tools. Moreover, these tools may not be addressing the underlying alterations in biological pathways that occur owing to the development of chronic pain or in response to chronic opioid administration. An evidence-based algorithmic approach to risk mitigation that can be applied in a cost-effective manner to guide therapy is urgently needed.

Hartrick CT and Rodriguez HJ (2012). "Tapentadol for pain: a treatment evaluation." Expert Opinion on Pharmacotherapy 13(2): 283-286.

[Request Form](#)

Department of Biomedical Sciences

Tapentadol is a newly approved novel analgesic drug with a dual mode of action: a mu-opioid agonist and an inhibitor of norepinephrine reuptake (MOR-NRI). Preclinical evidence supports a synergistic interaction between these two effects. It is the first opioid agonist to exhibit predominant norepinephrine reuptake inhibition with minimal serotonin effects. It is FDA approved for use in the US for moderate to severe pain in adults, available in the immediate release form for acute pain and as an extended-release formulation for chronic pain when continuous analgesia is required. Tapentadol has demonstrated reduced treatment-emergent opioid-related gastrointestinal adverse effects compared with pure opioid agonists. The synergistic mu-opioid and alpha(2)-adrenergic effects suggest the potential for particular utility in neuropathic pain states or other pain states associated with hyperalgesia.

Hartrick CT, Rozek RJ, **Conroy S**, Dobritt D and **Felten D** (2012). "Pain education: getting an early start." Pain Practice 12(8): 593-594.

[Full-Text](#)

Department of Anesthesiology

Department of Biomedical Sciences

Hartrick CT, **Tang Y-S**, **Siwek D**, Murray R, **Hunstad D** and **Smith G** (2012). "The effect of initial local anesthetic dose with continuous interscalene analgesia on postoperative pain and diaphragmatic function in patients undergoing arthroscopic shoulder surgery: a double-blind, randomized controlled trial." BMC Anesthesiology 12: 6.

[Full-Text](#)

Department of Biomedical Sciences

Background: Interscalene block (ISB) is commonly performed using 20-40 mL of local anesthetic. Spread to adjacent structures and consequent adverse effects including paralysis of the ipsilateral hemidiaphragm are frequent. Pain ratings, analgesic requirements, adverse events, satisfaction, function and diaphragmatic excursion were compared following interscalene block (ISB) with reduced initial bolus volumes. Methods: Subjects undergoing arthroscopic rotator cuff repair were randomized to receive 5, 10, or 20 mL ropivacaine 0.75% for ISB in a double-blind fashion (N = 36). Continuous infusion with ropivacaine 0.2% was maintained for 48 h. Pain and diaphragmatic excursion were assessed before block and in the recovery unit. Results: Pain ratings in the recovery room were generally less than 4 (0-10 NRS) for all treatment groups, but a statistically significant difference was noted between the 5 and 20 mL groups (NRS: 2.67 vs. 0.62 respectively; p = 0.04). Pain ratings and supplemental analgesic use were similar among the groups at 24 h, 48 h and 12 weeks.

There were no differences in the quality of block for surgical anesthesia. Dyspnea was significantly greater in the 20 mL group ($p = 0.041$). Subjects with dyspnea had significant diaphragmatic impairment more frequently (Relative risk: 2.5; 95% CI: 1.3-4.8; $p = 0.042$). Increased contralateral diaphragmatic motion was measured in 29 of the 36 subjects. Physical shoulder function at 12 weeks improved over baseline in all groups (baseline mean SST: 6.3, SEM: 0.6; 95% CI: 5.1-7.5; 12 week mean SST: 8.2, SEM: 0.46; 95% CI: 7.3-9.2; $p = 0.0035$). Conclusions: ISB provided reliable surgical analgesia with 5 mL, 10 mL or 20 mL ropivacaine (0.75%). The 20 mL volume was associated with increased complaints of dyspnea. The 5 mL volume was associated with statistically higher pain scores in the immediate postoperative period. Lower volumes resulted in a reduced incidence of dyspnea compared to 20 mL, however diaphragmatic impairment was not eliminated. Compensatory increases in contralateral diaphragmatic movement may explain tolerance for ipsilateral paresis.

Heise RL, Parekh A, Joyce EM, **Chancellor MB** and Sacks MS (2012). "Strain history and TGF-beta1 induce urinary bladder wall smooth muscle remodeling and elastogenesis." *Biomech Model Mechanobiology* 11(1-2): 131-145.

[Full-Text](#)

Department of Anesthesiology

Mechanical cues that trigger pathological remodeling in smooth muscle tissues remain largely unknown and are thought to be pivotal triggers for strain-induced remodeling. Thus, an understanding of the effects mechanical stimulation is important to elucidate underlying mechanisms of disease states and in the development of methods for smooth muscle tissue regeneration. For example, the urinary bladder wall (UBW) adaptation to spinal cord injury (SCI) includes extensive hypertrophy as well as increased collagen and elastin, all of which profoundly alter its mechanical response. In addition, the pro-fibrotic growth factor TGF-beta1 is upregulated in pathologies of other smooth muscle tissues and may contribute to pathological remodeling outcomes. In the present study, we utilized an ex vivo organ culture system to investigate the response of UBW tissue under various strain-based mechanical stimuli and exogenous TGF-beta1 to assess extracellular matrix (ECM) synthesis, mechanical responses, and bladder smooth muscle cell (BSMC) phenotype. Results indicated that a 0.5-Hz strain frequency triangular waveform stimulation at 15% strain resulted in fibrillar elastin production, collagen turnover, and a more compliant ECM. Further, this stretch regime induced changes in cell phenotype while the addition of TGF-beta1 altered this phenotype. This phenotypic shift was further confirmed by passive strip biomechanical testing, whereby the bladder groups treated with TGF-beta1 were more compliant than all other groups. TGF-beta1 increased soluble collagen production in the cultured bladders. Overall, the 0.5-Hz strain-induced remodeling caused increased compliance due to elastogenesis, similar to that seen in early SCI bladders. Thus, organ culture of bladder strips can be used as an experimental model to examine ECM remodeling and cellular phenotypic shift and potentially elucidate BMSCs ability to produce fibrillar elastin using mechanical stretch either alone or in combination with growth factors.

Herkowitz HN (2012). "Point of view commentary for SPINE 120131." *Spine* 38(1).

[Full-Text](#)

Department of Orthopedic Surgery

Hill M and **French T** (2012). "Using the GIR annual survey to identify trends and provide information for educational technology management (iCollaborative)." from <https://www.mededportal.org/icollaborative/resource/406>

[Full-Text](#)

Department of Biomedical Sciences

Department of Education Technology

The GIR Annual Survey provides a rich source of usable information. If you participate in completing the annual survey your school will receive access to the GIR IT reporting tool which provides school level information on areas such as IT organization, FTE, technology in use or planned for, and future plans. The tool currently includes data from 2009-2011, though 2008 data is also obtainable from the AAMC. The

analysis of data allows medical school management to assess trends, commonalities, and models essential in the educational technology decision-making process. *Presented at GIR 2012 Information Technology Poster Session

Hollander J and Dyche D (2012). Local anesthesia for minimally invasive treatment of the prostate in the office setting, (ed). Smith's Textbook of Endourology: Wiley-Blackwell: 1481-1489.

[Request Form](#)

Department of Urology

Holtrop P, Swails T, **Riggs T**, **De Witte D**, **Klarr J** and **Pryce C** (2012). "Resuscitation of infants born at 22 weeks gestation: a 20-year retrospective." Journal of Perinatology 33(3): 222-225.

[Request Form](#)

Department of Pediatrics

Objective: To compare the characteristics of infants born at 22 weeks gestational age (GA) who were resuscitated at birth with those of infants who were not resuscitated. Study Design: We reviewed records of all the infants with a GA of 22 0/7 through 22 6/7 weeks who were born alive at William Beaumont Hospital from 1990 through 2009. Deliveries were attended by a neonatologist if they were in the hospital at the time of delivery or requested by the obstetrician and otherwise were attended by a pediatric resident or neonatal nurse practitioner. Result: There were 85 infants born alive at 22 weeks GA during the study period. Thirty-six were intubated in the delivery room and defined as having been resuscitated. Two of them survived. On multivariate analysis, a higher birth weight (odds ratio 2.39 per 100 g increase, 95% confidence interval 1.21 to 4.73) and the presence of a neonatologist at delivery (odds ratio 6.72, 95% confidence interval 1.72 to 26.2) were each associated with an increased likelihood of resuscitation. Conclusion: Infants born at 22 weeks GA were more likely to be resuscitated if they were larger or if the delivery was attended by a neonatologist. We encourage neonatal groups to follow the recommendations of the American Academy of Pediatrics Committee on the Fetus and Newborn regarding initiation of resuscitation in these infants: inform parents that a good outcome is very unlikely and respect the parents' choice of whether resuscitation should be initiated. Journal of Perinatology advance online publication, 5 July 2012; doi:10.1038/jp.2012.88.

Honda M, Takenaka A, Inoue S, **Chancellor MB** and Yoshimura N (2012). "Sensory neurone-specific receptor-mediated regulation of micturition reflex in urethane-anaesthetized rats." BJU International 109(4): 628-633.

[Full-Text](#)

Department of Urology

OBJECTIVE To investigate the effect of sensory neurone-specific receptors (SNSRs) activation on the micturition reflex in rats. MATERIALS AND METHODS Continuous cystometrograms (CMGs, 0.04 mL/min) were performed in female Sprague-Dawley rats under urethane anaesthesia. After stable micturition cycles were established, a selective rat SNSR1 agonist, bovine adrenal medulla 8-22 (BAM8-22), was administered intravenously (i.v.) or intrathecally (i.t.) in normal rats or rats pretreated with capsaicin 4 days before the experiments. Micturition variables were recorded and compared before and after drug administration. RESULTS Administration (i.v.) of BAM8-22 (3-100 µg/kg) significantly increased intercontraction intervals in a dose-dependent fashion, but did not affect residual urine or baseline pressure at any doses tested. Administration (i.t.) of BAM8-22 (0.01-0.3 µg) also increased intercontraction intervals in a dose-dependent fashion, but did not affect residual urine or baseline pressure at any doses tested. These inhibitory effects of i.v. (30 µg/kg) or i.t. (0.3 µg) administration of BAM8-22 still occurred after capsaicin pretreatment. CONCLUSIONS These results indicate that in urethane-anaesthetized rats activation of SNSRs can inhibit the micturition reflex via pathways independent of capsaicin-sensitive C-fibres. Thus SNSRs could be a potential target for the treatment of bladder dysfunction, e.g. overactive bladder. © 2011 BJU INTERNATIONAL.

Honda M, Yoshimura N, Inoue S, Hinata N, **Chancellor MB** and Takenaka A (2012). "Inhibitory effect of somatostatin receptor subtype-4 agonist NNC 26-9100 on micturition reflex in rats." Urology 80(6): 1391.e1399-1391.e1313.

[Full-Text](#)

Department of Urology

Objective: To investigate the effects of activation of somatostatin subtype 4 (SST4) on the micturition reflex in rats. Methods: Continuous cystometrograms (0.04 mL/min infusion rate) were performed in female Sprague-Dawley rats (242-265 g) under urethane anesthesia. After stable micturition cycles were established, a selective SST4 receptor agonist, NNC 26-9100, was administered intravenously in normal rats or rats pretreated with capsaicin 4 days before the experiments. The micturition parameters were recorded and compared before and after drug administration. Results: Intravenous administration of NNC 26-9100 (10-300 µg/kg) significantly increased the intercontraction interval in a dose-dependent fashion. Intravenous administration of NNC 26-9100 (10-300 µg/kg) also significantly increased the pressure threshold in a dose-dependent fashion. No significant changes were seen in the baseline pressure, maximum voiding pressure, or postvoid residual urine volume. However, NNC 26-9100-induced increases in the intercontraction intervals and pressure threshold were not seen in rats with C-fiber desensitization induced by capsaicin pretreatment. Conclusion: These results indicate that in urethane-anesthetized rats, activation of the SST4 receptor can inhibit the micturition reflex by suppression of capsaicin-sensitive C-fiber afferent pathways. Thus, the SST4 receptor could be a potential target for the treatment of C-fiber afferent-mediated bladder dysfunction. © 2012 Elsevier Inc. All Rights Reserved.

Hong RS and **Kartush JM** (2012). "Acoustic neuroma neurophysiologic correlates: facial and recurrent laryngeal nerves before, during, and after surgery." *Otolaryngologic Clinics of North America* 45(2): 291-306.

[Full-Text](#)

Department of Surgery

This article focuses on the facial nerve with additional comments on the recurrent laryngeal nerve as a proxy for the lower cranial nerves. Methods, advantages and disadvantages, and techniques are listed. The article addresses the anatomy of the facial nerve, discusses neurophysiologic testing, the role of electroneurography in preoperative, intraoperative, and postoperative testing, and presents 7 steps to set up for and perform facial nerve monitoring. Details are provided on interpretation of testing, and the pitfalls of interpretation are discussed. Studies are reviewed presenting outcomes of testing. © 2012 Elsevier Inc.

Huang J, Chunta JL, Amin M, Lee DY, **Grills IS, Wong CY**, Yan D, **Marples B, Martinez AA** and **Wilson GD** (2012). "Detailed characterization of the early response of head-neck cancer xenografts to irradiation using (18)F-FDG-PET imaging." *International Journal of Radiation Oncology, Biology, Physics* 84(2): 485-491.

[Full-Text](#)

Department of Pathology

Department of Radiation Oncology

Department of Diagnostic Radiology and Molecular Imaging

PURPOSE: To investigate the metabolic information provided by (18)F-fluorodeoxyglucose-positron emission tomography (FDG-PET) during the early response of head-and-neck squamous cell carcinoma (HNSCC) xenografts to radiotherapy (RT). METHODS AND MATERIALS: Low-passage HNSCC cells (UT14) were injected into the rear flanks of female nu/nu mice to generate xenografts. After tumors grew to 400-500 mm³, they were treated with either 15 Gy in one fraction (n = 18) or sham RT (n = 12). At various time points after treatment, tumors were assessed with 2-h dynamic FDG-PET and immediately harvested for direct histological correlation. Different analytical parameters were used to process the dynamic PET data: kinetic index (Ki), standard uptake value (SUV), sensitivity factor (SF), and retention index (RI). Tumor growth was assessed using the specific growth rate (SGR) and correlated with PET parameters using the Pearson correlation coefficient (r). Receiver operating characteristic (ROC) and the area under the ROC curve (AUC) were used to test PET parameters for their ability to predict for radiation necrosis and radiation change. RESULTS: Tumor growth was arrested for the first 20 days after RT and recovered thereafter. Histologically, radiation change was observed in the peripheral regions of tumors between days 7 and 23 after RT, and radiation necrosis were observed in the central regions of tumors between days 7 and 40. Ki provided the best correlation with SGR (r = 0.51) and was the optimal parameter to predict for early radiation necrosis (AUC = 0.804, p = 0.07). SUV(30 min) was the strongest predictor for late radiation necrosis (AUC = 0.959, p = 0.004). Both RI(30-60min) and SF(12-70 min) were very accurate in predicting for radiation change (AUC =

0.891 and 0.875, $p = 0.009$ and 0.01 , respectively). CONCLUSIONS: Dynamic FDG-PET analysis (such as Ki or SF) may provide informative assessment of early radiation necrosis or radiation change of HNSCC xenografts after RT.

Huang J, Robertson JM, Ye H, Margolis J, Nadeau L and Yan D (2012). "Dose-volume analysis of predictors for gastrointestinal toxicity after concurrent full-dose gemcitabine and radiotherapy for locally advanced pancreatic adenocarcinoma." International Journal of Radiation Oncology, Biology, Physics 83(4): 1120-1125.

[Full-Text](#)

Department of Pathology

Department of Radiation Oncology

Department of Internal Medicine

PURPOSE: To identify dosimetric predictors for the development of gastrointestinal (GI) toxicity in patients with locally advanced pancreatic adenocarcinoma (LAPC) treated with concurrent full-dose gemcitabine and radiotherapy (GemRT). METHODS AND MATERIALS: From June 2002 to June 2009, 46 LAPC patients treated with definitive GemRT were retrospectively analyzed. The stomach and duodenum were retrospectively contoured separately to determine their dose-volume histogram (DVH) parameters. GI toxicity was defined as Grade 3 or higher GI toxicity. The follow-up time was calculated from the start of RT to the date of death or last contact. Univariate analysis (UVA) and multivariate analysis (MVA) using Kaplan-Meier and Cox regression models were performed to identify risk factors associated with GI toxicity. The receiver operating characteristic curve and the area under the receiver operating characteristic curve (AUC) were used to determine the best DVH parameter to predict for GI toxicity. RESULTS: Of the patients, 28 (61%) received concurrent gemcitabine alone, and 18 (39%) had concurrent gemcitabine with daily erlotinib. On UVA, only the V(20Gy) to V(35Gy) of duodenum were significantly associated with GI toxicity (all $p < 0.05$, respectively ($p = 0.03$). However, excluding the erlotinib group, the V(35Gy) is the best predictor (AUC = 0.725), and the 12-month GI toxicity rate was 0% vs. 41% for V(35Gy) 20%, respectively ($p = 0.04$). CONCLUSIONS: DVH parameters of duodenum may predict Grade 3 GI toxicity after GemRT for LAPC. Concurrent use of erlotinib during GemRT may increase GI toxicity.

Huang J, **Vicini FA**, Williams SG, Ye H, McGrath S, **Ghilezan M, Krauss D, Martinez AA** and **Kestin LL** (2012).

"Percentage of positive biopsy cores: a better risk stratification model for prostate cancer?" International Journal of Radiation Oncology Biology Physics 83(4): 1141-1148.

[Full-Text](#)

Department of Internal Medicine

Department of Radiation Oncology

Purpose: To assess the prognostic value of the percentage of positive biopsy cores (PPC) and perineural invasion in predicting the clinical outcomes after radiotherapy (RT) for prostate cancer and to explore the possibilities to improve on existing risk-stratification models. Methods and Materials: Between 1993 and 2004, 1,056 patients with clinical Stage T1c-T3N0M0 prostate cancer, who had four or more biopsy cores sampled and complete biopsy core data available, were treated with external beam RT, with or without a high-dose-rate brachytherapy boost at William Beaumont Hospital. The median follow-up was 7.6 years. Multivariate Cox regression analysis was performed with PPC, Gleason score, pretreatment prostate-specific antigen, T stage, PNI, radiation dose, androgen deprivation, age, prostate-specific antigen frequency, and follow-up duration. A new risk stratification (PPC classification) was empirically devised to incorporate PPC and replace the T stage. Results: On multivariate Cox regression analysis, the PPC was an independent predictor of distant metastasis, cause-specific survival, and overall survival (all $p < 0.05$ was associated with significantly greater distant metastasis (hazard ratio, 4.01; 95% confidence interval, 1.86-8.61), and its independent predictive value remained significant with or without androgen deprivation therapy (all $p < 0.05$ was associated with significantly greater distant metastasis (hazard ratio, 4.01; 95% confidence interval, 1.86-8.61), and its independent predictive value remained significant with or without androgen deprivation therapy (all $p < 0.05$) with National Comprehensive Cancer Network risk stratification demonstrated added prognostic value of distant metastasis for the intermediate-risk (hazard ratio, 5.44; 95% confidence interval, 1.78-16.6) and high-risk (hazard ratio, 4.39; 95% confidence interval, 1.70-11.3) groups, regardless of the use

of androgen deprivation and high-dose RT (all $p < .05$). The proposed PPC classification appears to provide improved stratification of the clinical outcomes relative to the National Comprehensive Cancer Network classification. Conclusions: The PPC is an independent and powerful predictor of clinical outcomes of prostate cancer after RT. A risk model replacing T stage with the PPC to reduce subjectivity demonstrated potentially improved stratification. (C) 2012 Elsevier Inc.

Huang JZ, Folbe MH, Richards SK and **Kolins MD** (2012). "Chronic lymphocytic leukemia with nuclear budding." European Journal of Haematology 88(1): 92.

[Full-Text](#)

Department of Pathology

Iacco A, Billimoria N and **Howells G** (2012). "Fatal disruption of a left atrial myxoma associated with trauma." Case Reports in Medicine 2012: 486309.

[Full-Text](#)

Department of Surgery

Cardiac myxomas are benign tumors composed of sparse stellate cells in an extensive mucoid stroma. The surface of these tumors is often friable and gelatinous. Their intracardiac location makes embolization a constant threat. We report a patient who had diffuse systemic embolization of a left atrial myxoma coincident with a low-velocity frontal motor vehicle crash.

Ionascu D, Yang K, Wilkinson JB, Yan D, **Grills IS** and Martin S (2012). "A differential treatment planning strategy for locally advanced non-small cell lung cancer to facilitate dual patient setup procedure for improved target coverage and normal tissue sparing." Journal of Thoracic Oncology 7(9): S233.

[Request Form](#)

Department of Radiation Oncology

Jackson A, **Maerz T**, Koueiter DM, Andreovich CJ, **Baker KC** and **Anderson K** (2012). "Strength of ulnar fixation in ulnar collateral ligament reconstruction: a biomechanical comparison of traditional bone tunnels to the tension-slide technique." Journal of Shoulder and Elbow Surgery 21(12): 1674-1679.

[Full-Text](#)

Department of Surgery

Department of Orthopaedic Surgery

BACKGROUND: Surgical reconstruction of the ulnar collateral ligament after rupture has evolved substantially since the original description. Reconstruction techniques vary significantly at the ulnar and humeral interface. The purpose of this study was to develop a model to isolate, test, and compare the ulnar fixation of the traditional bone tunnel technique and a new technique, the tension slide. **MATERIALS AND METHODS:** Six matched pairs of cadaveric arms were dissected to isolate the ulna. Pairs were randomized to the bone tunnel or tension-slide ulnar fixation technique, and consistent tendon grafts were used for each reconstruction. A specialized tendon clamp was used to grip the grafts. Specimens were preloaded with a valgus force to 1 Nm and tested to failure in torsion at 4.5 degrees /s. Statistical analysis was performed with 1-way analysis of variance with the Tukey post hoc test ($\alpha = .05$). **RESULTS:** The bone tunnel technique exhibited higher initial and total stiffness, as well as higher torsional torque at 10 degrees and 30 degrees of valgus angulation and at ultimate failure. The tension-slide technique exhibited significantly higher angular displacement at 3 Nm but not at ultimate failure. The bone tunnel technique exhibited higher work at 10 degrees and 30 degrees of valgus angulation. **CONCLUSION:** In this model, traditional bone tunnels performed superior to the tension-slide construction in terms of both strength and stiffness. Whether there is a kinematic benefit to the tension slide, which moves the ulnar fixation to within the native ulnar collateral ligament footprint, is yet to be determined. Further study is needed to assess the clinical benefit of a stronger ulnar fixation.

Jing X, **Wey E** and Michael CW (2012). "Diagnostic value of fine needle aspirates processed by ThinPrep(R) for the assessment of axillary lymph node status in patients with invasive carcinoma of the breast." Cytopathology. ePub Ahead of Print.

[Full-Text](#)

Department of Pathology

X. Jing, E. Wey and C. W. Michael Diagnostic value of fine needle aspirates processed by ThinPrep(R) for the assessment of axillary lymph node status in patients with invasive carcinoma of the breast Objective: To evaluate the utility of ThinPrep(R) as an optional specimen processing method for the detection of axillary lymph node metastasis of invasive breast carcinoma. Methods: A computer SNOMED search from the file at our institution between January 2003 and August 2011 retrieved a total of 209 fine needle aspiration (FNA) specimens of axillary lymph nodes prepared by ThinPrep and followed by axillary lymph node biopsy and/or dissection. Original cytological diagnoses and corresponding histological diagnoses were documented. Using the histological diagnoses as the gold standard, the diagnostic parameters including sensitivity, specificity, positive (PPV) and negative predictive values (NPV) and diagnostic accuracy were calculated. Both cytology and histology slides from cyto-histologically discrepant cases were reviewed. Results: Out of a total of 209 specimens, 193 (92%) had adequate diagnostic material while the remaining 16 specimens (8%) were inadequate for cytological assessment. The diagnostic specimens included 168 invasive ductal carcinomas (IDC), 15 invasive lobular carcinomas (ILC) and 10 mixed carcinomas (IDC and ILC). Excluding 19 cases with malignant cells on FNA in which no residual tumour was found in fibrotic lymph nodes after neoadjuvant therapy (cytology and histology confirmed on review) ThinPrep detected nodal metastasis with an overall sensitivity of 77.5%, specificity of 100%, PPV of 100% and NPV of 53.7%. Diagnostic accuracy was 82.2%. There was no difference in Bloom-Richardson grade or the number or size of metastases between tumours with true-positive and false-negative cytology. Sampling error was the sole factor contributing to cyto-histological discrepancy. Conclusions: ThinPrep is a good alternative to the conventional smear for cytological assessment of axillary lymph node status in patients with invasive breast carcinoma, particularly when specimens are collected at remote sites or when cytologists are not available for assistance during FNA.

Johnson M, Mangona VS, Yan D, Shaitelman SF, **Kestin LL**, Wloch JB, Martin SK, Ye H, Kreofsky C and **Grills IS** (2012). "Survival and toxicity after standard dose 3-D conformal radiation therapy or high-dose intensity modulated radiation therapy for locally advanced non-small cell lung cancer." International Journal of Radiation Oncology Biology Physics 84(3): S607.

[Request Form](#)

Department of Biomedical Sciences

Department of Radiation Oncology

Jolepalem P, Grigore C and **Palka JC** (2012). "Scintigraphic evaluation of a suspected cavernous hemangioma." Journal of Nuclear Medicine Technology 40(4): 290-292.

[Request Form](#)

Department of Diagnostic Radiology and Molecular Imaging

Jung D (2012). "An integrated module on acute wound care." Annals of Emergency Medicine 60(4 Suppl S): S160.

[Full-Text](#)

Department of Emergency Medicine

Jurjus A and **Hajj Hussein I** (2012). The Mediterranean: cradle of medicine and anatomy, (ed). The Arte Medendi: Plumelia: 27.

[Request Form](#)

Department of Biomedical Sciences

Jurjus A, **Hajj Hussein I**, Khatib A, Dali Balta N, Shaalan T, Watfa W and Atiyeh B (2012). "Modulation of TNF- α and TGF- β 1 in Botox treated rats with burn wounds." American Association of Immunologists 188(Meeting Abstract Suppl): 62.62.

[Full-Text](#)

Department of Biomedical Sciences

Abstract Many attempts have been made to improve wound healing using growth factors and a large array of medications. This study reexamined the effect of Botox on second degree burn wound in rats. Histological alterations and temporal evolution of two cytokines TGF β 1, and TNF- α were assessed in presence and absence of Botox. Fifty adult Sprague Dawley rats were used; one group was injected 10 units of Botox into wound. Daily observation and transepidermal water loss were assessed. Punch biopsies were taken on days 0, 3, 8, 14 and 28 for RNA extraction and PCR, and for routine light microscopy. Botox treated rats showed a delayed inflammation, necrosis, and earlier crust detachment compared to controls. On day 14, a better and smoother epithelialization was noted in the Botox groups. Finally, by day 28, the wound surface area was smaller and the quality of the skin was better with more fibroblasts in the regenerated dermis of Botox group, which expressed 2-4 times more TGF β 1. It peaked on days 3 and 8 and then decreased to almost half the control group by day 28. On the other hand, the TNF- α peaked immediately after burn to almost 20 times the control, then decreased between 2.72 to 5.5 times during the rest of the experiment very much like TGF β 1, or lower. Botox could possibly play an alleviating role and have a positive effect on burn wound healing.

Jurjus AR, **Hajj Hussein I** and Eid A (2012). "Health tourism quality in Lebanon: the first world health service at a third world cost." 16th International Conference on ISO & TQM & 8th Cooperation & Competition Conference, Linnaeus University, Vaxjo, Sweden: 1.

[Full-Text](#)

Department of Biomedical Sciences

Jurjus AR, **Hajj Hussein I** and Gerges AA (2012). Knowledge, attitude, behavior, and practice of the UNIFIL peacekeepers on human immunodeficiency virus, (ed). Sexually Transmitted Infections: INTECH: 219.

[Full-Text](#)

Department of Biomedical Sciences

Jury RP, Thibodeau BJ, Fortier LE, Geddes TJ, Ahmed S, Pruetz BL, Farinola MA and **Wilson GD** (2012). "Gene expression changes associated with the progression of intraductal papillary mucinous neoplasms." Pancreas 41(4): 611-618.

[Full-Text](#)

Department of Surgery

Department of Radiation Oncology

OBJECTIVES: The diagnosis of high-grade intraductal papillary mucinous neoplasm (IPMN) is difficult to distinguish from low-grade IPMN. The aim of this study was to identify potential markers for the discrimination of high-grade and invasive (HgInv) IPMN from low- and moderate-grade dysplasia IPMN. METHODS: Laser capture microdissection was used to isolate distinct foci of low-grade, moderate-grade, high-grade, and invasive IPMN from paraffin-embedded archival tissue from 14 patients who underwent resection for IPMN. Most samples included multiple grades in the same specimen. Affymetrix Human Exon microarrays were used to compare low- and moderate-grade dysplasia IPMN with HgInv IPMN. RESULTS: Sixty-two genes were identified as showing significant changes in expression ($P \leq 0.05$ and a 2-fold cutoff), including up-regulation of 41 in HgInv IPMN. Changes in gene expression are associated with biological processes related to malignant behavior including cell motion, cell proliferation, response to hypoxia, and epithelial-to-mesenchymal transition. In addition, altered signaling in several transforming growth factor beta-related pathways was exhibited in the progression of IPMN to malignancy. CONCLUSIONS: This study identifies a set of genes associated with the progression of IPMN to malignancy. These genes are potential markers that could be used to identify IPMN requiring surgical resection.

Kandil E, Noureldine SI, **Koffron A**, Yao L, Saggi B and Buell JF (2012). "Outcomes of laparoscopic and open resection for neuroendocrine liver metastases." Surgery 152(6): 1225-1231.

[Full-Text](#)

Department of Surgery

Background. We sought to compare the outcomes in patients with hepatic carcinoid tumor metastases treated with open versus laparoscopic liver resection. Methods. A retrospective analysis of our liver surgery database was performed. All patients who underwent liver resection for hepatic carcinoid tumor metastases were included. Patients were divided into 2 groups depending on the surgical approach. Patients with concomitant primary and metastatic liver lesions underwent open resection. Results. Thirty-six patients underwent resection over a 10-year period (21 open and 15 laparoscopic). Both groups were similar in terms of gender, body mass index, tumor size, incidence of carcinoid syndrome, and extent of resection ($P > .05$). The laparoscopic group had less mean operative time (2.7 vs 5.4 hours), less mean blood loss (158.3 vs 538.9 mL), and a shorter hospital stay (3.2 vs 7.5 days; $P < .05$ for all). Complications were similar in both groups (20% vs 33%; $P = .21$). Two laparoscopic cases required conversion. The 3-year disease-free survival for the laparoscopic group was 73.3% compared to 47.6% for the open group ($P = .2$). Conclusion. To our knowledge, this is the first reported study comparing laparoscopic versus open liver resection in the treatment of liver metastases from carcinoid tumors. Our series confirms that selective cases can safely be managed laparoscopically, (Surgery 2012;152:1225-31.)

Kaplan L, Kurdziel M, Baker KC and Verner J (2012). "Characterization of daptomycin-loaded antibiotic cement." Orthopedics 35(4): e503-e509.

[Request Form](#)

Department of Orthopedic Surgery

Department of Surgery

Antibiotics are commonly mixed with polymethylmethacrylate (PMMA) cement to suppress severe periprosthetic infections associated with total joint arthroplasty. The relationship between antibiotic concentration and the resulting elution kinetics remains unclear. The purpose of this study was to characterize the release of daptomycin from PMMA cement and the subsequent effects on mechanical properties. Varying concentrations of daptomycin and tobramycin were vacuum mixed in commercially available PMMA and subjected to an in vitro elution period. High-performance liquid chromatography was used to quantify the concentration of the amount of daptomycin eluted at predetermined time points. Samples were subjected to compressive loading to analyze the effect of antibiotic concentration on cement mechanical properties. Daptomycin elution increased when initial tobramycin concentration was increased. Furthermore, the addition of antibiotics increased the compressive strength of the cement in the postelution period. The binary addition of tobramycin with daptomycin antibiotics modifies the elution and mechanical properties of PMMA bone cement. Based on the findings of our study, 2 g of daptomycin and 3.6 g of tobramycin per 40-g packet of cement should be used to promote daptomycin elution without sacrificing PMMA mechanical properties.

Katz AW, Chawla S, **Qu Z**, Kashyap R, Milano MT and Hezel AF (2012). "Stereotactic hypofractionated radiation therapy as a bridge to transplantation for hepatocellular carcinoma: Clinical outcome and pathological correlation."

International Journal of Radiation Oncology Biology Physics 83(3): 895-900.

[Full-Text](#)

Department of Pathology

Purpose: We sought to determine efficacy, safety, and outcome of stereotactic hypofractionated radiation therapy (SHORT) as a suitable bridging therapy for patients awaiting liver transplantation (LT) for hepatocellular carcinoma (HCC). We also examined histological response to radiation in the resected or explanted livers. Methods and Materials: Between August 2007 and January 2009, 18 patients with 21 lesions received SHORT. A median total dose of 50 Gy was delivered in 10 fractions. Three patients underwent either chemoembolization ($n = 1$) or radiofrequency ablation ($n = 2$) prior to SHORT. Radiographic response was based on computed tomography evaluation at 3 months after SHORT. Histological response as a percentage

of tumor necrosis was assessed by a quantitative morphometric method. Results: Six of 18 patients were delisted because of progression (n = 3) or other causes (n = 3). Twelve patients successfully underwent major hepatic resection (n = 1) or LT (n = 11) at a median follow-up of 6.3 months (range, 0.6-11.6 months) after completion of SHORT. No patient developed gastrointestinal toxicity Grade ≥ 3 or radiation-induced liver disease. Ten patients with 11 lesions were evaluable for pathological response. Two lesions had 100% necrosis, three lesions had $\geq 50\%$ necrosis, four lesions had $\leq 50\%$ necrosis, and two lesions had no necrosis. All patients were alive after LT and/or major hepatic resection at a median follow-up of 19.6 months. Conclusions: SHORT is an effective bridging therapy for patients awaiting LT for HCC. It provides excellent in-field control with minimal side effects, helps to downsize or stabilize tumors prior to LT, and achieves good pathological response. © 2012 Elsevier Inc. All rights reserved.

Kersten AD, Fabing M, Ensminger S, Demetropoulos CK, Cooper R, **Baker KC** and **Anderson K** (2012). "Suture capsulorrhaphy versus capsulolabral advancement for shoulder instability." Arthroscopy-the Journal of Arthroscopic and Related Surgery 28(10): 1344-1351.

[Full-Text](#)

Department of Surgery

Department of Orthopaedic Surgery

Purpose: The purpose of this study was to test the strength of a suture capsulorrhaphy repair versus a capsulolabral repair with knotless suture anchors in a cadaveric model with anteroinferior shoulder instability. Methods: Fourteen cadaveric shoulders were tested with either a suture capsulorrhaphy to the intact labrum or a capsulolabral advancement using a knotless suture anchor into the glenoid. Specimens were translated with the shoulder in an abducted, externally rotated position to failure. Results: The capsulolabral advancement showed a significantly higher load to failure than did the suture capsulorrhaphy group (P = .030). Conclusions: Capsulolabral advancement with suture anchors may offer greater initial strength when compared with a suture capsulorrhaphy. In the setting of shoulder instability without evidence of a labral tear, the capsulolabral advancement technique may be considered biomechanically superior. Clinical Relevance: In the setting of shoulder instability due to capsular insufficiency, the capsulolabral advancement may be considered biomechanically superior to a traditional suture capsulorrhaphy.

Kim J, Jarboe MD, Arnold MA, DiPietro MA, **Bloom DA** and Teitelbaum DH (2012). "Biliary duplication cyst with heterotopic gastric mucosa resulting in obstruction of the biliary system: a case report." Journal of Pediatric Surgery 47(6): E5-E8.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Biliary tract duplication cysts with heterotopic gastric mucosa are rare congenital anomalies, with our case representing only the fourth reported case in the literature. An 8-year-old girl with several months of abdominal pain was found to have a complex cystic mass communicating with the biliary system via the common hepatic duct. Intraoperatively, inflammation caused by the cystic mass was found to have resulted in a Mirizzi-like syndrome, with a nearly complete obstruction at the confluence of the left and right hepatic ducts. Histopathologic examination of the biliary mass revealed it to be a duplication cyst lined by heterotopic gastric mucosa with secondary ulceration and fibrosis. Biliary duplication cysts are a rare but important process that should be considered in a child with a mass in the portal triad and biliary obstruction. (C) 2012 Elsevier Inc. All rights reserved.

Kim J, **Xu X** and **Zhang T** (2012). "A novel dual source array tetrahedron beam computed tomography (TBCT) system for image guided radiotherapy." Medical Physics 39(6): 3855.

[Full-Text](#)

Department of Radiation Oncology

Kircher ML and **Kartush JM** (2012). "Pitfalls in intraoperative nerve monitoring during vestibular schwannoma surgery." Neurosurgical Focus 33(3): Article Number E5.

[Request Form](#)

Department of Surgery

Despite the widespread acceptance of intraoperative neurophysiological monitoring in skull base surgery over the last 2 decades, surgeon training in the technical and interpretive aspects of nerve monitoring has been conspicuously lacking. Inadequate fundamental knowledge of neurophysiological monitoring may lead to misinterpretations and an inability to troubleshoot system errors. Some surgeons perform both the technical and interpretive aspects of monitoring themselves while others enjoin coworkers (surgical residents, nurses, anesthesiologists, or a separate monitoring service) to perform the technical portion. Regardless, the surgeon must have a thorough understanding to avoid potential medical and legal pitfalls because poor monitoring is worse than no monitoring. A structured curriculum and protocol in both the technical and interpretive aspects of monitoring is recommended for all personnel involved in the monitoring process. This paper details the technical, interpretive, and surgical correlates necessary for optimal intraoperative nerve monitoring during vestibular schwannoma surgery with an emphasis on electromyographic monitoring for facial and recurrent laryngeal nerves. Just as the American Society of Anesthesiologists' 1986 'Standards for Basic Anesthetic Monitoring' became a useful tool for both patients and anesthesiologists, impending guidelines in intraoperative neurophysiological monitoring should likewise become an important instrument for optimizing intraoperative neurophysiological monitoring.

Kitta T, **Chancellor MB**, De Groat WC, Kuno S, Nonomura K and Yoshimura N (2012). "Suppression of bladder overactivity by adenosine A2A receptor antagonist in a rat model of Parkinson disease." Journal of Urology 187(5): 1890-1897.

[Request Form](#)

Department of Urology

Purpose: Overactive bladder is highly prevalent among patients with Parkinson disease. Adenosine is an important neurotransmitter in the central nervous system but it is not fully clarified how adenosine receptors regulate the micturition reflex. Thus, we examined the effect of an adenosine A2A receptor antagonist on the micturition reflex in a rat model of Parkinson disease. Materials and Methods: In a rat model of Parkinson disease induced by 6-hydroxydopamine (Tocris Bioscience, Ellisville, Missouri) injection we examined the effects of the adenosine A2A receptor antagonist ZM241385, the dopamine D1 receptor agonist SKF38393 and the dopamine D2 receptor agonist quinpirole on bladder activity. Results: Intravenous administration of ZM241385 increased the intercontraction interval in a dose dependent manner in rats with Parkinson disease and sham operated rats but the inhibitory effect was greater in the Parkinson disease group. Intrathecal and intracerebroventricular administration of ZM241385 increased the intercontraction interval in each group. However, in rats with Parkinson disease the inhibitory effects induced by intracerebroventricular administration of ZM241385 were greater than in sham operated rats. Intravenous administration of SKF38393 increased the intercontraction interval in rats with Parkinson disease and subsequent administration of ZM further increased the intercontraction interval. However, SKF38393 did not increase the intercontraction interval after ZM241385 application. Also, ZM241385 increased the intercontraction interval without being affected by pre-administration or post-administration of quinpirole, which decreased the intercontraction interval. Conclusions: Results indicate that the adenosine A2A receptor mediated excitatory mechanism is enhanced at a supraspinal site to induce bladder overactivity and A2A receptor inhibition effectively suppresses bladder overactivity in rats with Parkinson disease. Thus, adenosine A2A receptor antagonists could be useful for bladder dysfunction in Parkinson disease cases. © 2012 American Urological Association Education and Research, Inc.

Kolacki C and **Rocco V** (2012). "The combined vaginal contraceptive ring, nuvaring, and cerebral venous sinus thrombosis: a case report and review of the literature." Journal of Emergency Medicine 42(4): 413-416.

[Full-Text](#)

Department of Emergency Medicine

BACKGROUND: Combined oral contraceptives are known to confer a risk of venous thromboembolism, including cerebral venous sinus thrombosis (CVST), to otherwise healthy women. NuvaRing (Organon USA, Inc., Roseland, NJ) is a contraceptive vaginal ring that delivers 120 mug of etonogestrel and 15 mug of ethinyl estradiol per day. Its use has been associated with rare venous thromboembolic events, but few cases of CVST associated with NuvaRing have been reported. OBJECTIVE: To describe a case that illustrates the increased risk of CVST associated with use of NuvaRing. We describe the case of a NuvaRing user who presented to our emergency department with a headache, who was diagnosed with CVST. CONCLUSION: Evidence suggests that NuvaRing has at least as much prothrombotic potential as combined oral contraceptives. Thus, emergency physicians should suspect serious venous thromboembolic events, including CVST, deep venous thrombosis, and pulmonary embolism, in NuvaRing users in the proper clinical setting.

Krauss DJ, Amin M, Stone B, Ye H, Hayek S, Brabbins DS and **Gustafson GS** (2012). "Neuroendocrine differentiation in gleason score 7-10 prostate adenocarcinoma treated with primary radiation therapy: a new prognostic variable to be considered." International Journal of Radiation Oncology Biology Physics 84(3 Suppl S): S59.

[Full-Text](#)

Department of Radiation Oncology

Department of Pathology

Kupelian V, Rosen RC, Roehrborn CG, **Tyagi P, Chancellor MB** and McKinlay JB (2012). "Association of overactive bladder and C-reactive protein levels. results from the Boston Area Community Health (BACH) survey." BJU International 110(3): 401-407.

[Full-Text](#)

Department of Radiation Oncology

Department of Urology

OBJECTIVE To investigate the association between overactive bladder (OAB) and C-reactive protein (CRP) in a population-based sample of men and women. SUBJECTS AND METHODS Epidemiological survey of urological symptoms among men and women aged 30-79 years. A multi-stage stratified cluster design was used to randomly sample 5503 adults from the city of Boston. Analyses were conducted on 1898 men and 1854 women with available CRP levels. The International Continence Society defines OAB as 'Urgency with or without urge incontinence, usually with frequency and nocturia.' OAB was defined as: (1) urgency, (2) urgency with frequency, and (3) urgency with frequency and nocturia. Odds ratios (OR) and 95% confidence intervals (95% CI) of the CRP and OAB association were estimated using logistic regression. RESULTS Prevalence of OAB increased with CRP levels in both men and women. In men, adjusted ORs (95% CI) per log(10) (CRP) levels were 1.90 (1.26-2.86) with OAB defined as urgency, 1.65 (1.06-2.58) with OAB defined as urgency and frequency, and 1.92 (1.13-3.28) with OAB defined as urgency, frequency and nocturia. The association was more modest in women with ORs (95% CI) of 1.53 (1.07-2.18) for OAB as defined urgency, 1.51 (1.02-2.23) for OAB defined as urgency and frequency, and 1.34 (0.85-2.12) for OAB defined as urgency, frequency and nocturia. CONCLUSIONS Results show a consistent association of increasing CRP levels and OAB among both men and women. These results support our hypothesis for the role of inflammation in the development of OAB and a possible role for anti-inflammatory agents in its treatment.

LaBan MM (2012). "Re: electrodiagnosis in cancer treatment and rehabilitation." American Journal of Physical Medicine and Rehabilitation 91(3): 278.

[Full-Text](#)

Department of Physical Medicine and Rehabilitation

LampI M, **Lee W**, Koo W, Frongillo EA, Barker DJP and Romero R (2012). "Ethnic differences in the accumulation of fat and lean mass in late gestation." American Journal of Human Biology 24(5): 640-647.

[Full-Text](#)

Department of Obstetrics and Gynecology

Objectives: Lower birth weight within the normal range predicts adult chronic diseases, but the same birth weight in different ethnic groups may reflect different patterns of tissue development. Neonatal body composition was investigated among non-Hispanic Caucasians and African Americans, taking advantage of variability in gestational duration to understand growth during late gestation. Methods: Air displacement plethysmography assessed fat and lean body mass among 220 non-Hispanic Caucasian and 93 non-Hispanic African American neonates. The two ethnic groups were compared using linear regression. Results: At 36 weeks of gestation, the average lean mass of Caucasian neonates was 2,515 g vs. that of 2,319 g of African American neonates (difference, $P = 0.02$). The corresponding figures for fat mass were 231 and 278 g, respectively (difference, $P = 0.24$). At 41 weeks, the Caucasians were 319 g heavier in lean body mass ($P < 0.001$) but were also 123 g heavier in fat mass ($P = 0.001$). The slopes for lean mass vs. gestational week were similar, but the slope of fat mass was 5.8 times greater ($P = 0.009$) for Caucasian (41.0 g/week) than for African American neonates (7.0 g/week). Conclusions: By 36 weeks of gestation, the African American fetus developed similar fat mass and less lean mass compared with the Caucasian fetus. Thereafter, changes in lean mass among the African American fetus with increasing gestational age at birth were similar to the Caucasian fetus, but fat accumulated more slowly. We hypothesize that different ethnic fetal growth strategies involving body composition may contribute to ethnic health disparities in later life. *Am. J. Hum. Biol.* 2012. (c) 2012 Wiley Periodicals, Inc.

Lang ES, Spaite DW, Oliver ZJ, Gotschall CS, **Swor RA**, Dawson DE and Hunt RC (2012). "A national model for developing, implementing, and evaluating evidence-based guidelines for prehospital care." *Academic Emergency Medicine* 19(2): 201-209.

[Full-Text](#)

Department of Emergency Medicine

In 2007, the Institute of Medicines (IOMs) Committee on the Future of Emergency Care recommended that a multidisciplinary panel establish a model for developing evidence-based protocols for the treatment of emergency medical systems (EMS) patients. In response, the National EMS Advisory Council (NEMSAC) and the Federal Interagency Committee on EMS (FICEMS) convened a panel of multidisciplinary experts to review current strategies for developing evidence-based guidelines (EBGs) and to propose a model for developing such guidelines for the prehospital milieu. This paper describes the eight-step model endorsed by FICEMS, NEMSAC, and a panel of EMS and evidence-based medicine experts. According to the model, prehospital EBG development would begin with the input of evidence from various external sources. Potential EBG topics would be suggested following a preliminary evidentiary review; those topics with sufficient extant foundational evidence would be selected for development. Next, the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology would be used to determine a quality-of-evidence rating and a strength of recommendation related to the patient care guidelines. More specific, contextualized patient care protocols would then be generated and disseminated to the EMS community. After educating EMS professionals using targeted teaching materials, the protocols would be implemented in local EMS systems. Finally, effectiveness and uptake would be measured with integrated quality improvement and outcomes monitoring systems. The constituencies and experts involved in the model development process concluded that the use of such transparent, objective, and scientifically rigorous guidelines could significantly increase the quality of EMS care in the future.

LaRouere M, Bojrab D, Naumann I and Hong R (2012). Classification and pathophysiology of temporal bone fractures: General considerations, in Mathog R., Carron M. and Shibuya T. (ed). *Mathog's Atlas of Craniofacial Trauma*: Wolters Kluwer Health: 533-535.

[Request Form](#)

Department of Surgery

LaRouere M, Bojrab D, Naumann I and Hong R (2012). Decompression and repair of facial nerve, in Mathog R., Carron M. and Shibuya T. (ed). *Mathog's Atlas of Craniofacial Trauma*: Wolters Kluwer Health: 537-542.

[Request Form](#)

Department of Surgery

LaRouere M, Bojrab D, Naumann I and Hong R (2012). Repair of tympanic membrane perforation, in Mathog R., Carron M. and Shibuya T. (ed). Mathog's Atlas of Craniofacial Trauma: Wolters Kluwer Health: 543-549.

[Request Form](#)

Department of Surgery

LaRouere M, Bojrab D, Naumann I and Hong R (2012). Treatment of canalithiasis with a plugging of the posterior semicircular canal, in Mathog R., Carron M. and Shibuya T. (ed). Mathog's Atlas of Craniofacial Trauma: Wolters Kluwer Health: 550-554.

[Request Form](#)

Department of Surgery

Lee W, Riggs T, Koo W, Deter RL, Yeo L and Romero R (2012). "The relationship of newborn adiposity to fetal growth outcome based on birth weight or the modified neonatal growth assessment score." Journal of Maternal-Fetal & Neonatal Medicine 25(10): 1933-1940.

[Request Form](#)

Department of Obstetrics and Gynecology

Department of Pediatrics

Objectives: (1) Develop reference ranges of neonatal adiposity using air displacement plethysmography. (2) Use new reference ranges for neonatal adiposity to compare two different methods of evaluating neonatal nutritional status. Methods: Three hundred and twenty-four normal neonates (35-41 weeks post-menstrual age) had body fat (%BF) and total fat mass (FM, g) measured using air displacement plethysmography shortly after delivery. Results were stratified for 92 of these neonates with corresponding fetal biometry using two methods for classifying nutritional status: (1) population-based weight percentiles; and (2) a modified neonatal growth assessment score (m(3)NGAS(51)). Results: At the 50th percentile, %BF varied from 7.7% (35 weeks) to 11.8% (41 weeks), while the corresponding 50th percentiles for total FM were 186-436 g. Among the subset of 92 neonates, no significant differences in adiposity were found between small for gestational age (SGA), appropriate for gestational age (AGA), and large for gestational age (LGA) groups using population-based weight standards. Classification of the same neonates using m(3)NGAS(51) showed significant differences in mean %BF between corresponding groups. Conclusions: Population-based weight criteria for neonatal nutritional status can lead to misclassifications on the basis of adiposity. A neonatal growth assessment score, that considers the growth potential of several anatomic parameters, appears to more effectively classify under- and over-nourished newborns.

Leone A, Rappa F, Campanella C, Guranotta C, **Hajj Hussein I**, Cappello F and Jurjus A (2012). "Human dental pulp cell apoptosis: immunohistochemical study after applying orthodontic traction." Journal of Biological Regulators and Homeostatic Agents 26(4): 713-720.

[Request Form](#)

Department of Biomedical Sciences

The aim of this study was to compare human dental pulp stress and programmed cell death after 3 and 6 months of orthodontic treatments by assessing the degree of apoptosis and related proteins. Human dental pulps were collected from twenty young patients orthodontically treated by Straight Wire technique. Samples were fixed, paraffin-embedded and processed for histology and immunohistochemistry using anti-heat shock protein 60 kDa (Hsp60), -caspase 3, -caspase 9, and -PCNA antibodies, as well as TUNEL reactions. Moreover, we performed immunoprecipitation for Hsp60 and caspase 3, and for Hsp60 and caspase 9, from paraffin extracted tissues. Increased levels of both caspases and Hsp60 occurred in 6-months treated samples; at the same time, we found increased levels of proliferating cell nuclear antigen and terminal deoxynucleotidyl transferase dUTP nick end labeling positive cells. Immunoprecipitation showed that Hsp60 forms a complex with both Pro-caspase 3 and Caspase 3, and this may accelerate Pro-caspase 3 activation, especially in the 6-months treated group. On the contrary, no complex between Hsp60 and Pro-caspase 9 was detected. The orthodontic tractions may be a cause of stress, apoptosis and proliferation in pulp tissue. These results suggest the need of further studies about the effects of long term orthodontic treatments on the dental pulp.

Leone A, Uzzo ML, Rappa F, **Hajj Hussein I**, Gerbino A, Spatola GF and Jurjus A (2012). "Immunohistochemical expression of apoptotic factors, Cytokines, and Metalloproteinase-9 in periapical and epithelialized gingival lesions." *Folia Histochemica et Cytobiologica* 50(4): 497-503.

[Full-Text](#)

Department of Biomedical Sciences

The aim of the study was to assess the involvement of apoptotic factors, cytokeratins and metalloproteinase-9 in the histogenesis of both Epithelialized Gingival Lesions (EGL) and Periapical Lesions (PAL). 55 consecutive patients, 30 with PAL and 25 with EGL, were selected for the study after clinical and radiological examinations. The PAL patients had severe periapical lesions and tooth decay with exposure of the pulp chamber. All PAL and EGL biopsies were surgically extracted, fixed in 10% buffered formalin, and processed for routine light microscopy. Ten biopsies of each category were processed for immunohistochemistry (IHC). Serial paraffin sections were stained by IHC with appropriate antibodies to detect cytokeratins (CKs) 1, 5, 8, 10 and 14, caspase-3 and -9, metalloproteinase-9, and for PCNA and TUNEL assays. Both PAL and EGL showed a high expression of the cytokeratin 1, 5 and 8 with higher expression in EGL. Moreover, CK10 was markedly less intense expressed in EGL compared to PAL, while CK14 was almost three times stronger expressed in EGL. The expression of caspase-3 and -9 was stronger in PAL compared to EGL, however, the difference was only significant for caspase-9. In PAL apoptosis detected by TUNNEL method and the expression of MMP-9 were higher than in EGL, whereas PCNA was significantly more expressed in EGL. The results clearly suggest that both lesions have exclusively an epithelial origin and that epithelial proliferation was correlated with the degree of apoptosis in both entities. PAL and EGL presented mostly similar cytokeratin expression except for CK10 and CK14, though with marked differences in the distribution and intensity of IHC reactions. Finally, the degradation of extracellular matrix in both lesions could be partially attributed to the strong presence of MMP-9.

Lerman R, Jarski R, Rea H, Gellish R and **Vicini F** (2012). "Improving symptoms and quality of life of female cancer survivors: a randomized controlled study." *Annals of Surgical Oncology* 19(2): 373-378.

[Full-Text](#)

Department of Internal Medicine

Surgeons, along with the Centers for Disease Control and Prevention, emphasize the importance of managing symptoms and improving the quality of life of cancer survivors. A 2008 meta-analysis of mindfulness-based stress reduction (MBSR) concluded that this technique might improve patients' adjustment to their disease. However, randomized controlled trials using standardized measures for evaluating MBSR are limited. The primary objective of this study was to evaluate, using valid and reliable measures, the effects of a unique, interactive, 8-week cancer recovery and wellness program on symptoms and quality of life of female cancer survivors. Sixty-eight female cancer patients were randomized into either an intervention or waitlisted control group. Patients were evaluated using the Symptoms Checklist (SCL-90-R), the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ-30), and the Symptoms of Stress Inventory (SOSI). Of the participants, 70.6% were breast cancer survivors. Mean age was 57.5 years (treatment group) and 56.4 years (control group). Between-group demographic differences were not significant ($P > 0.6$). The treatment group improved significantly on the EORTC QLQ-30 ($P = 0.005$), on six of the eight SOSI subscales (P a parts per thousand currency sign 0.049), and on both SCL-90-R subscales (P a parts per thousand currency sign 0.023), while the control group did not improve on any of these measures ($P > 0.2$). The MBSR-based cancer recovery and wellness intervention improved the symptoms and quality of life of this largely breast cancer survivor population across a variety of cancer symptoms and quality-of-life measures.

Lerner A and Beqaj S (2012). "Abortive lytic Epstein-Barr virus replication in tonsil-B lymphocytes in infectious mononucleosis and a subset of the chronic fatigue syndrome." *Virus Adaptation and Treatment* 4(1): 85-91.

[Request Form](#)

Department of Internal Medicine

A systematic 2001–2007 review of 142 chronic fatigue syndrome (CFS) patients identified 106 CFS patients with elevated serum IgG antibodies to the herpesviruses Epstein–Barr virus (EBV), cytomegalovirus, or human herpesvirus (HHV) 6 in single or multiple infections, with no other co-infections detected. We named these 106 patients group-A CFS. Eighty-six of these 106 group-A CFS patients (81%) had elevated EBV early antibody, early antigen (diffuse), serum titers. A small group of six patients in the group-A EBV subset of CFS, additionally, had repetitive elevated-serum titers of antibody to the early lytic replication-encoded proteins, EBV dUTPase, and EBV DNA polymerase. The presence of these serum antibodies to EBV dUTPase and EBV DNA polymerase indicated EBV abortive lytic replication in these 6 CFS patients. None of 20 random control people (age- and sex-matched, with blood drawn at a commercial laboratory) had elevated serum titers of antibody to EBV dUTPase or EBV DNA polymerase ($P < 0.01$). This finding needs verification in a larger group of EBV CFS subset patients, but if corroborated, it may represent a molecular marker for diagnosing the EBV subset of CFS. We review evidence that EBV abortive lytic replication with unassembled viral proteins in the blood may be the same in infectious mononucleosis (IM) and a subset of CFS. EBV-abortive lytic replication in tonsil plasma cells is dominant in IM. No complete lytic virion is in the blood of IM or CFS patients. Complications of CFS and IM include cardiomyopathy and encephalopathy. Circulating abortive lytic-encoded EBV proteins (eg, EBV dUTPase, EBV DNA polymerase, and others) may be common to IM and CFS. The intensity and duration of the circulating EBV-encoded proteins might differentiate the IM and EBV subsets of CFS. Abortive lytic replication may be a pathogenic mechanism for EBV disease. EBV (HHV4) is a gamma herpesvirus composed of dsDNA about 170 Kb in length. For this discussion, there are early genes (including expressions of encoded proteins EBV dUTPase, DNA polymerase, and nuclear proteins) and late genes (including expressions of capsid and membrane proteins). Abortive infection infers incomplete virion expressions of either early or late proteins, but the virion is incomplete. The lytic virus infers a complete virion. The pathologic consequences of EBV abortive replication are currently being investigated by authors.

Lerner AM, Ariza ME, Williams M, Jason L, Beqaj S, Fitzgerald JT, Lemeshow S and Glaser R (2012). "Antibody to epstein-barr virus deoxyuridine triphosphate nucleotidohydrolase and deoxyribonucleotide polymerase in a chronic fatigue syndrome Subset." *PloS One* 7(11): e47891.

[Full-Text](#)

Department of Internal Medicine

Background: A defined diagnostic panel differentiated patients who had been diagnosed with chronic fatigue syndrome (CFS), based upon Fukuda/Carruthers criteria. This diagnostic panel identified an Epstein-Barr virus (EBV) subset of patients (6), excluding for the first time other similar "clinical" conditions such as cytomegalovirus (CMV), human herpesvirus 6 (HHV6), babesiosis, ehrlichiosis, borreliosis, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and adult rheumatic fever, which may be mistakenly called CFS. CFS patients were treated with valacyclovir (14.3 mg/kg q6h) for ≥ 12 months. Each patient improved, based upon the Functional Activity Appraisal: Energy Index Score Healthcare Worker Assessment (EIPS), which is a validated (FSS-9), item scale with high degree of internal consistency measured by Cronbach's alpha. Methods: Antibody to EBV viral capsid antigen (VCA) IgM, EBV Diffuse Early Antigen EA(D), and neutralizing antibodies against EBV-encoded DNA polymerase and EBV-encoded dUTPase were assayed serially approximately every three months for 13-16 months from sera obtained from patients with CFS (6) and from sera obtained from twenty patients who had no history of CFS. Results: Antibodies to EBV EA(D) and neutralizing antibodies against the encoded-proteins EBV DNA polymerase and deoxyuridine triphosphate nucleotidohydrolase (dUTPase) were present in the EBV subset CFS patients. Of the sera samples obtained from patients with CFS 93.9% were positive for EA(D), while 31.6% of the control patients were positive for EBV EA(D). Serum samples were positive for neutralizing antibodies against the EBV-encoded dUTPase (23/52; 44.2%) and DNA polymerase (41/52; 78.8%) in EBV subset CFS patients, but negative in sera of controls. Conclusions: There is prolonged elevated antibody level against the encoded proteins EBV dUTPase and EBV DNA polymerase in a subset of CFS patients, suggesting that this antibody panel could be used to identify these patients, if these preliminary findings are corroborated by studies with a larger number of EBV subset CFS patients.

Lever JF, Servat JJ, **Nesi-Eloff F** and **Nesi FA** (2012). "Trichoadenoma of an eyelid in an adult mimicking sebaceous cell carcinoma." Ophthalmic Plastic and Reconstructive Surgery 28(4): e101-e102.

[Full-Text](#)

Department of Ophthalmology

The purpose of this report is to detail the clinical and histologic findings of a rare trichoadenoma of the eyelid. A 63-year-old male with a recurrent left lower eyelid lesion underwent a shave biopsy with inconclusive results until referred to an oculoplastic surgeon. The patient presented with a lesion suspicious for sebaceous cell carcinoma of the eyelid. An excisional biopsy was performed, and the specimen was sent for permanent section histologic analysis. The results revealed the lesion to be a trichoadenoma of the eyelid. The remaining lesion was excised, and the lower eyelid was reconstructed.

Levine RA, **Wasvary H** and **Kadro O** (2012). "Endoprosthesis management of refractory ileocolonic anastomotic strictures after resection for Crohn's disease: report of nine-year follow-up and review of the literature." Inflammatory Bowel Diseases 18(3): 506-512.

[Full-Text](#)

Department of Surgery

BACKGROUND: The role of endoluminal stenting in benign obstruction, especially for Crohn's disease (CD), is controversial, with limited data and widely disparate outcomes. The purpose of this study was to determine the long-term efficacy and safety of this technology in the treatment of fibrostenotic CD and to review the existing literature on this topic. **METHODS:** We undertook a retrospective review of all patients undergoing endoluminal stenting for CD strictures at our institution from 2001 to 2010. Outcome measures included technical success, clinical improvement, duration of stent and luminal patency, and need for re-intervention. **RESULTS:** Five patients underwent this procedure with a 100% rate of technical and an 80% rate of clinical success. Mean follow-up was 28 months (range 3 weeks to 109 months) and mean long-term luminal patency was 34.8 months (range 4.5-109 months). There was one complication involving reobstruction which required surgical intervention and no mortalities. **CONCLUSIONS:** Endoluminal stenting of CD strictures is a safe and effective alternative to surgery which can provide lasting benefit in select patients. Further studies are necessary to clarify the full impact of this technology on long-term management of this complex disease.

Lisak RP, Benjamins JA, Nedelkoska L, Barger JL, **Ragheb S**, Fan B, Ouamara N, Johnson TA, Rajasekharan S and Bar-Or A (2012). "Secretory products of multiple sclerosis B cells are cytotoxic to oligodendroglia in vitro." Journal of Neuroimmunology 246(1-2): 85-95.

[Full-Text](#)

Department of Biomedical Sciences

B cells are important in the pathogenesis of multiple sclerosis (MS) and some of the effects are not dependent on maturation of B cells into immunoglobulin (Ig) producing plasmablasts and plasma cells. B cells present antigen, activate T cells, and are involved in immunoregulation and cytokine secretion. To determine if B cells from MS patients secrete products that have deleterious effects on glial cells not mediated by Ig, and to compare effects with secretory products of normal controls (NC), we isolated B cells from 7 patients with relapsing remitting MS (RRMS) and 4 NC. B cells were cultured alone or after stimulation with CD40 ligand (CD40L), CD40L + cross-linking of the B cell antigen receptor (xBCR) and CD40L + xBCR + stimulation of toll like receptor 9 (TLR9). Supernatants were harvested and incubated with mixed central nervous system (CNS) neonatal rat glial cells. Supernatants from unstimulated NC B cells induced on average death of 7% (range 0-24%) of differentiated oligodendrocytes (OL); in contrast, supernatants from unstimulated B cells from RRMS patients induced death of 57% (range 35-74%) of OL. Supernatants of stimulated B cells from NC did not increase the minimal OL death whereas stimulation of B cells from RRMS had variable results compared to unstimulated B cells. Supernatants from both NC and RRMS induced microglial enlargement and loss of normal resting bipolar morphology. OL death did not correlate with levels of tumor necrosis alpha (TNF-alpha), lymphotoxin alpha (LT-alpha), interleukin 6 (IL-6), IL-10, transforming growth factor beta 1 (TGF-beta 1) or any combination or ratio of these cytokines. Analysis of 26 supernatants from NC and RRMS patients failed to detect IgM. There were very low levels of IgG in 8 of the 26

supernatants, and no correlation between of OL death and presence or absence of IgG. Sera used in both the B cell and glial cell cultures were heated, which inactivates complement. The effects of B cell supernatants on OL could be direct and/or indirect involving either microglia and/or astrocytes. The identity of the toxic factor(s) is as yet unknown. Thus we have demonstrated that B cells from patients with RRMS but not NC secrete one or more factors toxic to OL. It is possible that such factors produced by peripheral blood B cells when within the CNS could contribute to demyelination in MS patients. (C) 2012 Elsevier B.V. All rights reserved.

Lisak RP and **Ragheb S** (2012). "The role of B cell-activating factor in autoimmune myasthenia gravis." Annals of the New York Academy of Sciences 1274(1): 60-67.

[Full-Text](#)

Department of Biomedical Sciences

B cell-activating factor (BAFF) is important in the development and maturation of B cells and their progeny-plasma blasts and plasma cells. There is increasing evidence that BAFF is involved in the pathogenesis of several autoimmune diseases including myasthenia gravis. Increased expression of BAFF and receptors for BAFF have been demonstrated in thymus of patients with myasthenia gravis, and an increase in serum levels of BAFF have been reported in patients with myasthenia gravis. While the exact role of BAFF in the pathogenesis of myasthenia gravis is not clear, BAFF and its receptors may provide potential targets for therapy in patients with myasthenia gravis.

Liu RT, Chung MS, Chuang YC, Lee JJ, Lee WC, Chang HW, Yang KD and **Chancellor MB** (2012). "The presence of overactive bladder wet increased the risk and severity of erectile dysfunction in men with type 2 diabetes." Journal of Sexual Medicine 9(7): 1913-1922.

[Full-Text](#)

Department of Urology

Introduction. Diabetes is a common risk factor for overactive bladder (OAB) syndrome and erectile dysfunction (ED). Aim. The study evaluated the risk factors of OAB and association of OAB and ED in type 2 diabetic men. Methods. The diagnosis of ED and OAB was based on a self-administered questionnaire containing Sexual Health Inventory for Men (SHIM) and OAB symptom score (OABSS, 0-15, indicating increasing severity of symptoms), respectively. Main Outcome Measures. The clinical variables and diabetes-associated complications, including ED, which are risk factors for OAB, were evaluated. Results. Of 453 consecutive subjects attending outpatient diabetic clinic with a mean age of 60.6 years, 25.4%, 10.2%, 81.9%, and 28.3% reported having OAB, OAB wet, ED, and severe ED, respectively. The OABSS is inversely associated with SHIM (correlation coefficient 0.275). The patients with OAB have significantly lower SHIM score, testosterone level, and serum albumin level, have more proportion of severe ED, were older, and have longer duration of diabetes mellitus (DM). After adjustment for age and duration of DM, the presence of severe ED was associated with OAB (odds ratio [OR] = 1.58), and severe ED (OR = 2.36), SHIM score (OR = 0.92), and serum albumin level (OR = 0.24) were risk factors for OAB wet (patients with urgency incontinence, once a week or more). The OR of ED in patients with OAB or OAB wet compared with no OAB was 1.82, and 3.61, respectively. Among the OAB components, urgency incontinence has the strongest impact on ED (OR = 4.06), followed by nocturia, urgency, and frequency. About 15.1% (N = 68) without OAB and ED are younger and have shorter DM duration, lower systolic BP, and higher serum albumin level after multivariate analysis compared with patients with OAB or ED. Conclusion. The presence of severe ED was significantly associated with OAB, especially OAB wet. The presence of OAB wet increased the risk and severity of ED. Liu R-T, Chung M-S, Chuang Y-C, Lee J-J, Lee W-C, Chang H-W, Yang KD, and Chancellor MB. The presence of overactive bladder wet increased the risk and severity of erectile dysfunction in men with type 2 diabetes. *J Sex Med* 2012;9:1930-1939.

Louwers LM, Bortman J, **Koffron A, Stecevic V, Cohn S** and **Raofi V** (2012). "Noncirrhotic portal hypertension due to nodular regenerative hyperplasia treated with surgical portacaval shunt." Case Reports in Medicine 2012: 965304.

[Full-Text](#)

Department of Surgery

Department of Internal Medicine

Nodular regenerative hyperplasia (NRH) is an uncommon condition, but an important cause of noncirrhotic intrahepatic portal hypertension (NCIPH), characterized by micronodules of regenerative hepatocytes throughout the liver without intervening fibrous septae. Herein, we present a case of a thirty-seven-year-old female with systemic lupus erythematosus (SLE) who was discovered to have significant esophageal varices on endoscopy for dyspepsia. Her labs revealed a slight elevation in the alkaline phosphatase and mild thrombocytopenia. Abdominal MRI revealed seven focal hepatic masses, splenomegaly, no ascites, and a patent portal vein. Ultrasound-guided core biopsy was reported as focal nodular hyperplasia. However, her varices persisted despite treatment with beta-blockers and four additional upper endoscopies with banding. She was subsequently referred for a surgical opinion. At that time, given her history of SLE, azathioprine use, and portal hypertension, suspicion for NRH was raised. Given her normal synthetic function and lack of parenchymal liver disease, the patient was offered surgical shunting. During shunt surgery, a liver wedge biopsy was also performed and this confirmed NRH. An upper endoscopy six weeks after shunting verified complete resolution of varices. Currently, fifteen months after surgery duplex ultrasonography demonstrates shunt patency and the patient is without recurrence of her portal hypertension.

Madder RD, Smith JL, **Dixon SR** and **Goldstein JA** (2012). "Composition of target lesions by near-infrared spectroscopy in patients with acute coronary syndrome versus stable angina." *Circulation: Cardiovascular Interventions* 5(1): 55-61.

[Full-Text](#)

Department of Internal Medicine

Background-Whereas acute coronary syndromes (ACS) typically develop from the rupture of lipid core plaque (LCP), lesions causing stable angina are believed to be composed of fibrocalcific plaque. In this study, intracoronary near-infrared spectroscopy (NIRS) was used to determine the frequency of LCP at target and remote sites in patients with ACS versus those with stable angina. Methods and Results-The study was performed in patients having ≥ 1 target lesion identified by invasive angiography who also underwent NIRS before intervention. LCP was defined as a 2-mm segment on the NIRS block chemogram having a strong positive reading indicated by a bright-yellow color. Patients with ACS and those with stable angina were compared for the frequency of LCP at target and remote sites. Among 60 patients (46.7% with ACS) undergoing invasive angiography and NIRS, 68 target lesions were identified. Although target lesions in patients with ACS were more frequently composed of LCP than targets in patients with stable angina (84.4% versus 52.8%, $P=0.004$), approximately one half of target lesions in patients with stable angina contained LCP. LCPs anatomically remote from the target lesion were frequent in patients with ACS and less common in patients with stable angina (73.3% versus 17.6%, $P=0.002$). Conclusions-Target lesions responsible for ACS were frequently composed of LCP; in addition, LCPs often were found in remote, nontarget areas. Both target and remote LCPs were more common in patients with ACS than in those with stable angina. Approximately one half of target lesions in stable patients were also composed of LCP. © 2012 American Heart Association, Inc.

Maini B, Naidu SS, Mulukutla S, Kleiman N, Schreiber T, Wohns D, **Dixon S**, Rihal C, Dave R and O'Neill W (2012). "Real-world use of the Impella 2.5 circulatory support system in complex high-risk percutaneous coronary intervention: The USpella Registry." *Catheterization and Cardiovascular Interventions* 80(5): 717-725.

[Full-Text](#)

Department of Internal Medicine

Objectives: We report on the real-world, multicenter experience of the Impella 2.5 circulatory support system during high-risk PCI, a subset of the larger USpella Registry. Background: Standard of care for most patients with compromised ventricular function with multivessel or high-risk coronary lesions has been coronary artery bypass grafting. In poor operative candidates, high-risk PCI is increasingly considered, despite an increased risk for periprocedural hemodynamic compromise. Methods: 175 consecutive patients who underwent high-risk PCI with prophylactic support of the Impella 2.5 were evaluated. The primary safety endpoint was the incidence of major adverse cardiac events (MACE) at 30 days. Secondary endpoints

included safety and efficacy related to the device and patient outcomes, including survival at 12 months. Results: Overall angiographic revascularization was successful in 99% of patients and in 90% of those with multivessel revascularization, resulting in a reduction of the mean SYNTAX score post-PCI from 36 ± 15 to 18 ± 15 ($P < 0.0001$) and an improvement of the ejection fraction (from $31 \pm 15\%$ to $36 \pm 14\%$, $P < 0.0001$). In 51% of patients, the functional status improved by one or more NYHA class ($P < 0.001$). At 30-day follow-up, the rate of MACE was 8%, and survival was 96%, 91%, and 88% at 30 days, 6 months, and 12 months, respectively. Conclusions: The use of Impella 2.5 in high-risk PCI appeared feasible and safe in the real-world setting. The utilization of the Impella 2.5 was successful, resulting in favorable short- and midterm angiographic, procedural and clinical outcomes. © 2012 Wiley Periodicals, Inc. Copyright © 2012 Wiley Periodicals, Inc.

Maisels M and Newman T (2012). Epidemiology of neonatal jaundice, in Stevenson D., Maisels M. and Watchko J. (ed). Care of the Jaundiced Neonate. New York, NY: McGraw-Hill: 97-113.

[Request Form](#)

Department of Pediatrics

Maisels M and Newman T (2012). Prevention, screening and postnatal management of neonatal hyperbilirubinemia, in Stevenson D., Maisels M. and Watchko J. (ed). Care of the Jaundiced Neonate. New York: McGraw-Hill: 175-194.

[Request Form](#)

Department of Pediatrics

Maisels M and Stevenson D (2012). Phototherapy and other treatments, in Stevenson D., Maisels M. and Watchko J. (ed). Care of the Jaundiced Neonate. New York: McGraw-Hill: 195-227.

[Request Form](#)

Department of Pediatrics

Maisels M and Watchko J (2012). Neonatal hyperbilirubinemia, in Fanaroff A. and Fanaroff J. (ed). Care of the High-Risk Neonate. Philadelphia: WB Saunders Company: 310-345.

[Request Form](#)

Department of Pediatrics

Maisels M and Watchko J (2012). Treatment of hyperbilirubinemia, in Buonocore G., Bracci R. and Weindling M. (ed). Neonatology: A Practical Approach to Neonatal Management: Springer-Verlag: 629-640.

[Full-Text](#)

Department of Pediatrics

Maisels MJ (2012). "Neonatal transcutaneous bilirubin measurements: an opportunity to enhance laboratory utilization and improve patient care." Clinical Chemistry 58(10): 1395-1396.

[Full-Text](#)

Department of Pediatrics

Maisels MJ (2012). "Noninvasive measurements of bilirubin." Pediatrics 129(4): 779-781.

[Full-Text](#)

Department of Pediatrics

Maisels MJ, Watchko JF, Bhutani VK and Stevenson DK (2012). "An approach to the management of hyperbilirubinemia in the preterm infant less than 35 weeks of gestation." Journal of Perinatology 32(9): 660-664.

[Request Form](#)

Department of Pediatrics

We provide an approach to the use of phototherapy and exchange transfusion in the management of hyperbilirubinemia in preterm infants of <35 weeks of gestation. Because there are limited data for evidence-based recommendations, these recommendations are, of necessity, consensus-based. The recommended treatment levels are based on operational thresholds for bilirubin levels and represent those

levels beyond which it is assumed that treatment will likely do more good than harm. Long-term follow-up of a large population will be needed to evaluate whether or not these recommendations should be modified.

Maisels MJ and Yang H (2012). "Tin-mesoporphyrin in the treatment of refractory hyperbilirubinemia due to Rh incompatibility." Journal of Perinatology 32(11): 899-900.

[Request Form](#)

Department of Pediatrics

We describe the use of tin-mesoporphyrin (SnMP) in the treatment of an infant with Rh hemolytic disease. The infant's hyperbilirubinemia responded to phototherapy but every time the phototherapy was discontinued, the serum bilirubin rebounded and repeat phototherapy was necessary. A single intramuscular dose of SnMP on day 18 eliminated the need for further phototherapy and allowed us to discharge this infant. Journal of Perinatology (2012) 32, 899-900; doi:10.1038/jp.2012.45

Maksoud R, Jambart S, Oueidat D, **Hajj Husein I** and Jurjus A (2012). "Therapeutic effect of estrogen in experimental colitis." International Journal of Experimental and Clinical Anatomy 6(Suppl): S61.

[Full-Text](#)

Department of Biomedical Sciences

Mangona V, **Kestin L**, Yan D, Stone B, Gustafson B, **Wong C-Y**, **Ionascu D** and **Grills I** (2012). "Can 18FDG-PET predict local failure after Stereotactic Body Radiotherapy (SBRT) for Non-Small Cell Lung Cancer (NSCLC)? an analysis of PET Kinetics." American Journal of Clinical Oncology-Cancer Clinical Trials 35(2): 187.

[Full-Text](#)

Department of Radiation Oncology

Department of Diagnostic Radiology and Molecular Imaging

Mangona VS, **Kestin LL**, **Wong CO**, McGee MC, Hung B, Lurie M, Yan D and **Grills IS** (2012). "SUV kinetics of weekly (18)FDG-PET during radiation therapy predict eventual outcome in locally-advanced Non-small Cell Lung Cancer (NSCLC)." International Journal of Radiation Oncology Biology Physics 84(3 Suppl S): S103-S104.

[Full-Text](#)

Department of Radiation Oncology

Department of Diagnostic Radiology and Molecular Imaging

Manohar VA, **Levin RN**, Karadolian SS, Usmani A, Timmis RM, Dery ME and **Dixon SR** (2012). "The impact of intra-aortic balloon pump weaning protocols on in-hospital clinical outcomes." Journal of Interventional Cardiology 25(2): 140-146.

[Full-Text](#)

Department of Internal Medicine

BACKGROUND: Current literature recommends weaning intra-aortic balloon pump (IABP) support prior to discontinuation. To date, no studies have compared various weaning strategies for safety or efficacy. This study was designed to evaluate the impact of weaning on in-hospital clinical outcomes. **METHODS:** From 5/1/07 through 5/1/09 429 patients receiving IABP therapy were retrospectively identified using CPT1 billing codes. The study population and clinical outcomes analysis were stratified by use of weaning protocols versus immediate discontinuation of the IABP. In a subset analysis the patients receiving weaning protocols prior to IABP discontinuation were stratified for further analysis of clinical outcomes by whether they had received 1:3 ratio counterpulsation during their wean or whether they only received 1:2 counterpulsation prior to IABP discontinuation. These groups were analyzed for differences in primary and secondary end-points. **RESULTS:** Of the 429 patients identified, 344 (80.2%) were weaned prior to IABP discontinuation and 85 (19.8%) of the patients had their IABP abruptly discontinued. Patients not weaned had a lower heart rate after IABP discontinuation than those weaned, but no difference in systolic and mean blood pressure or urine output. There was no significant difference in mortality. Weaning was associated with a nonsignificant trend toward increased length of stay. **CONCLUSIONS:** This study suggests that weaning protocols offer no hemodynamic benefits or improvement in in-hospital mortality rates. Weaning is associated with trend

toward increased length of stay. We conclude that weaning offers no advantage over direct device removal and would advocate that balloon pumps be directly withdrawn when counterpulsation is terminated.

Matsumoto Y, Miyazato M, Yokoyama H, Kita M, Hirao Y, **Chancellor MB** and Yoshimura N (2012). "Role of M2 and M3 muscarinic acetylcholine receptor subtypes in activation of bladder afferent pathways in spinal cord injured rats." *Urology* 79(5): 1184.e1115-1120.

[Full-Text](#)

Department of Urology

OBJECTIVE: To evaluate the role of M2 and M3 muscarinic acetylcholine receptor (mAChR) subtypes in the activation of bladder afferent pathways in rats with chronic spinal cord injury (SCI). **METHODS:** Adult female Sprague-Dawley rats were spinalized at the T9 level. Continuous cystometry was performed under awake conditions 2 or 4 weeks after SCI. The effects of intravesical administration of an mAChR agonist (oxotremorine-methiodide), a nonselective antagonist (atropine), an M2-selective antagonist (methoctramine), and an M3-selective antagonist (darifenacin) were examined. After cystometry, the bladder was removed and separated into the mucosa and detrusor, and the M2 and M3 mAChR mRNA expression in the mucosa was determined using real-time quantitative polymerase chain reaction. **RESULTS:** At 2 and 4 weeks after SCI, intravesical administration of a nonselective mAChR agonist (25 µM oxotremorine-methiodide) increased the area under the curve of nonvoiding contractions, although the intercontraction interval of voiding contractions and maximal voiding pressure did not change. This effect was blocked by atropine and methoctramine (10 µM) but not by darifenacin (50 µM). However, mAChR antagonists alone (10-50 µM) had no effect on cystometric parameters. M2 mAChR mRNA expression was increased in the mucosa of SCI rats compared with that in normal rats. **CONCLUSION:** Our results suggest that the M2 mAChR subtype plays an important role in bladder afferent activation that enhances detrusor overactivity in SCI rats. However, because mAChR antagonists alone did not affect any cystometric parameters, the muscarinic mechanism controlling bladder afferent activity might not be involved in the emergence of detrusor overactivity in SCI.

McCullough PA, Williams FJ, Stivers DN, **Cannon L, Dixon S**, Alexander P, Runyan D and David S (2012). "Neutrophil gelatinase-associated lipocalin: a novel marker of contrast nephropathy risk." *American Journal of Nephrology* 35(6): 509-514.

[Request Form](#)

Department of Internal Medicine

BACKGROUND: Neutrophil gelatinase-associated lipocalin (NGAL, siderocalin) is a protein secreted by the kidney in the setting of acute kidney injury in an attempt to regulate and bind the release of catalytic iron from injured cells. We sought to evaluate the relationships between baseline NGAL, renal filtration function, and the degree of injury reflected by further increases in NGAL. **METHODS:** This study was a prospective, blinded assessment of blood samples taken from patients with estimated glomerular filtration rate (eGFR) 25% or ≥ 0.5 mg/dl. Multivariate regression revealed that baseline NGAL ($p < 0.001$) and not eGFR ($p = 0.95$) was independently associated with the NGAL value at 48 h. **CONCLUSIONS:** Baseline NGAL is strongly correlated with eGFR in patients with reduced renal filtration function undergoing coronary angiography. The magnitude of rise in NGAL is positively associated with the baseline value and is analogous to the time course of Cr in blood after contrast exposure. NGAL and not eGFR is an independent predictor of changes in the post-procedure NGAL. A baseline NGAL level is necessary for the interpretation of NGAL levels in the evaluation of acute kidney injury.

McGuire KJ, Harrast J, **Herkowitz H** and Weinstein JN (2012). "Geographic variation in the surgical treatment of degenerative cervical disc disease: American Board of Orthopedic Surgery Quality Improvement Initiative; Part II candidates." *Spine* 37(1): 57-66.

[Full-Text](#)

Department of Orthopedic Surgery

Study Design: Retrospective case series. Objective: To examine and document the change in rates and the geographic variation in procedure type and utilization of plating by orthopedic surgeons for anterior cervical discectomy-fusion. Summary of Background: Age- and sex-adjusted rates of cervical spine surgery have not increased, but the rate of cervical spinal fusion has, accounting for 41% of all fusion procedures in 2004. Methods: Records were selected from the American Board of Orthopedic Surgeons part II examination from 1999 to 2008. Current Procedural Terminology (CPT) and International Classification of Diseases, 9th Revision, Clinical Modification (ICDM-9-CM) codes were used to determine utilization of structural allograft, autograft/interbody devices, and anterior cervical plating over time and within geographic region. Main outcome measures were physician workforce, and rates and variation of procedure types. Results: From 1999 to 2008, the number of self-declared orthopedic spine surgeon candidates increased 24%. Over this period, the annual number of discectomies with fusions for degenerative cervical disc disease increased by 67%, whereas the number of such operations per surgeon operating on at least 1 such case increased 48% ($P = 0.018$). Interbody device (0%-31%; $P < 0.0001$), anterior cervical plating (39%-79%; $P < 0.0001$), and allograft (14%-59%; $P < 0.0001$) use increased, whereas autograft use decreased (86%-10%; $P < 0.0001$). The Southwest and Southeast were more likely than the Midwest to use interbody devices (OR: 2.42 and 1.66, respectively). The Southwest and Northeast were more likely than the Midwest to use autograft (OR: 1.55 and 1.49). The Southwest, Northeast, and Southeast were less likely to use allograft than the Midwest (OR: 0.408, 0.742, and 0.770). The Northeast was less likely and the Southeast more likely than the Midwest to utilize anterior cervical plating (OR: 0.67 and 1.33). Surgical complications were more often associated with autograft compared with allograft (OR: 1.61). Conclusion: From 1999 to 2008, the number of orthopedic surgeon candidates performing spine surgery has increased. These surgeons are performing more fusions and utilizing more structural allografts, interbody devices, and/or anterior cervical plates. Regional variations also remain in the types of constructs utilized.

McLennan GP, Khourdaji I, Killinger KA, **Boura JA** and **Peters KM** (2012). "Apremilast in the treatment of chronic prostatitis/chronic pelvic pain syndrome: a pilot study." LUTS: Lower Urinary Tract Symptoms 4(3): 140-143.

[Request Form](#)

Department of Biomedical Sciences

Department of Urology

Objective: Chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS) is a disease with an uncertain cause and limited effective treatments. Apremilast (Celgene Corporation, Summit, NJ, USA) is a selective phosphodiesterase type 4 (PDE4) inhibitor that modulates the immune system. An open-label, one-arm, pilot study was conducted to explore its potential for improving CP/CPPS symptoms. Methods: Males ≥ 18 years of age were treated with 20 mg oral apremilast twice daily for up to 12 weeks. Outcomes were measured with Global Response Assessment (GRA), pain visual analog scale (VAS), Chronic Prostatitis Symptom Index (CPSI), Pittsburgh Sleep Quality Index (PSQI), SF-12 mental (MCS) and physical (PCS) health-related quality of life subscales, and voiding diaries. Repeated measures and paired t-tests evaluated changes from baseline to end of treatment, and at a final visit 4 weeks off the drug. Results: Seventeen men (94% Caucasian; mean age 48.2 ± 10 years) were treated (mean 115.8 ± 56.1 doses). Mean VAS (3.4 ± 2.0 vs 1.8 ± 1.7 ; $P = 0.0011$), PSQI (9.4 ± 4.4 vs 7.4 ± 4.2 ; $P = 0.037$) and CPSI (26.1 ± 5.0 vs 17.2 ± 8.3 ; $P = 0.0016$) scores improved from baseline to end of treatment. Incontinence episodes per day improved slightly ($P = 0.042$). When only those completing at least 8 weeks of treatment were examined ($n = 9$), significant changes in CPSI, VAS, and PSQI were still observed. At the final visit, 8/9 (88.9%) men also reported some improvement in pain related to sex. Side-effects were generally mild and well tolerated. Conclusion: These results suggest that apremilast may improve CP/CPPS symptoms with only mild side-effects. However, placebo controlled studies are necessary to determine efficacy. © 2012 Wiley Publishing Asia Pty Ltd.

Mi M (2012). "Evidence based medicine teaching in undergraduate medical education: A literature review." Evidence Based Library and Information Practice 7(3 A): 98-120.

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Medical Library

Mi M, Moseley JL and Green ML (2012). "An instrument to characterize the environment for residents' evidence-based medicine learning and practice." Family Medicine 44(2): 98-104.

[Full-Text](#)

Medical Library

BACKGROUND AND OBJECTIVES: Many residency programs offer training in evidence-based medicine (EBM). However, these curricula often fail to achieve optimal learning outcomes, perhaps because they neglect various contextual factors in the learning environment. We developed and validated an instrument to characterize the environment for EBM learning and practice in residency programs. METHODS: An EBM Environment Scale was developed following scale development principles. A survey was administered to residents across six programs in primary care specialties at four medical centers. Internal consistency reliability was analyzed with Cronbach's coefficient alpha. Validity was assessed by comparing predetermined subscales with the survey's internal structure as assessed via factor analysis. Scores were also compared for subgroups based on residency program affiliation and residency characteristics. RESULTS: Out of 262 eligible residents, 124 completed the survey (response rate 47%). The overall mean score was 3.89 (standard deviation=0.56). The initial reliability analysis of the 48-item scale had a high reliability coefficient (Cronbach alpha=.94). Factor analysis and further item analysis resulted in a shorter 36-item scale with a satisfactory reliability coefficient (Cronbach alpha=.86). Scores were higher for residents with prior EBM training in medical school (4.14 versus 3.62) and in residency (4.25 versus 3.69). CONCLUSIONS: If further testing confirms its properties, the EBM Environment Scale may be used to understand the influence of the learning environment on the effectiveness of EBM training. Additionally, it may detect changes in the EBM learning environment in response to programmatic or institutional interventions.

Mi M, Stefaniak J and Solomonson W (2012). "Application of web 2.0 technologies in enhancing teaching and learning in medical education." from <http://www.mededportal.org/publication/9290>

[Full-Text](#)

Medical Library

Department of Biomedical Sciences

Micale M and Mohamed A (2012). Molecular cytogenetic (FISH) analysis of hematolymphoid disorders, in Kottke-Marchant K. (ed). Laboratory Hematology Practice: Wiley-Blackwell: 181-198.

[Request Form](#)

Department of Pathology

Miles M and **Doshi D** (2012). Vocal cord dysfunction, in Anbar R. (ed). Functional Respiratory Disorders: Humana Press: 105.

[Full-Text](#)

Department of Pediatrics

Miller WM, Spring TJ, Zalesin KC, Kaeding KR, Janosz KEN, McCullough PA and **Franklin BA** (2012). "Lower than predicted resting metabolic rate is associated with severely impaired cardiorespiratory fitness in obese individuals." Obesity 20(3): 505-511.

[Full-Text](#)

Department of Internal Medicine

Department of Biomedical Sciences

Obese individuals have reduced cardiorespiratory fitness as compared with leaner counterparts. Regular exercise maintains or increases fitness and lean body mass. Lean body mass, in turn, has a direct impact on resting metabolic rate (RMR). Given these relationships, we sought to evaluate the association between RMR and cardiorespiratory fitness in obese individuals. We evaluated 64 obese individuals (78% female) with direct assessment of RMR and cardiorespiratory fitness via breath-by-breath measurement of oxygen consumption and carbon dioxide production at rest and during exercise. The mean age and BMI were 47.4 +/- 12.2 years and 47.2 +/- 9.2 kg/m², respectively. The majority of subjects, 69%, had a measured RMR above that predicted by the Harris-Benedict equation. Compared with the higher RMR group, those with a

lower than predicted RMR had increased BMI, with values of 52.9 vs. 44.7 kg/m², P = 0.001, respectively. Analysis of those demonstrating significant effort during cardiopulmonary exercise testing (peak respiratory exchange ratio \geq 1.10) revealed a significantly higher peak oxygen uptake (VO₂ peak) in the higher RMR group (17.3 +/- 3.5 ml/min/kg) compared with the lower RMR group (13.6 +/- 1.9 ml/min/kg), P = 0.003. In summary, a lower than predicted RMR was associated with a severely reduced VO₂ peak and a higher BMI in this cohort. These data suggest that morbid obesity may be a vicious cycle of increasing BMI, reduced cardiorespiratory fitness, muscle deconditioning, and lower RMR. Collectively, these responses may, over time, exacerbate the imbalance between energy intake and expenditure, resulting in progressive increases in body weight and fat stores.

Min JK, Berman DS, Dunning A, Achenbach S, Al-Mallah M, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, Cheng V, **Chinnaiyan K**, Chow BJW, Cury R, Delago A, Feuchtner G, Hadamitzky M, Hausleiter J, Kaufmann P, Karlsberg RP, Kim YJ, Leipsic J, Lin FY, Maffei E, Plank F, **Raff G**, Villines T, Labounty TM and Shaw LJ (2012). "All-cause mortality benefit of coronary revascularization vs. medical therapy in patients without known coronary artery disease undergoing coronary computed tomographic angiography: Results from CONFIRM (COronary CT Angiography EvaluationN for Clinical Outcomes: An International Multicenter Registry)." *European Heart Journal* 33(24): 3088-3097.

[Full-Text](#)

Department of Internal Medicine

Aims To date, the therapeutic benefit of revascularization vs. medical therapy for stable individuals undergoing invasive coronary angiography (ICA) based upon coronary computed tomographic angiography (CCTA) findings has not been examined. **Methods and results** We examined 15 223 patients without known coronary artery disease (CAD) undergoing CCTA from eight sites and six countries who were followed for median 2.1 years (interquartile range 1.4-3.3 years) for an endpoint of all-cause mortality. Obstructive CAD by CCTA was defined as a \geq 50% luminal diameter stenosis in a major coronary artery. Patients were categorized as having high-risk CAD vs. non-high-risk CAD, with the former including patients with at least obstructive two-vessel CAD with proximal left anterior descending artery involvement, three-vessel CAD, and left main CAD. Death occurred in 185 (1.2%) patients. Patients were categorized into two treatment groups: revascularization (n = 1103; 2.2% mortality) and medical therapy (n = 14 120, 1.1% mortality). To account for non-randomized referral to revascularization, we created a propensity score developed by logistic regression to identify variables that influenced the decision to refer to revascularization. Within this model (C index 0.92, $\chi^2 = 1248$, P < 0.0001), obstructive CAD was the most influential factor for referral, followed by an interaction of obstructive CAD with pre-test likelihood of CAD (P = 0.0344). Within CCTA CAD groups, rates of revascularization increased from 3.8% for non-high-risk CAD to 51.2% high-risk CAD. In multivariable models, when compared with medical therapy, revascularization was associated with a survival advantage for patients with high-risk CAD [hazards ratio (HR) 0.38, 95% confidence interval 0.18-0.83], with no difference in survival for patients with non-high-risk CAD (HR 3.24, 95% CI 0.76-13.89) (P-value for interaction = 0.03). **Conclusion** In an intermediate-term follow-up, coronary revascularization is associated with a survival benefit in patients with high-risk CAD by CCTA, with no apparent benefit of revascularization in patients with lesser forms of CAD. © 2012 The Author.

Min JK, Dunning A, Lin FY, Achenbach S, Al-Mallah M, Budoff MJ, Cademartiri F, Callister TQ, Chang H-J, Cheng V, **Chinnaiyan K**, Chow BJW, Delago A, Hadamitzky M, Hausleiter J, Kaufmann P, Maffei E, **Raff G**, Shaw LJ, Villines T and Berman DS (2012). "Reply." *Journal of the American College of Cardiology* 59(7): 701-701.

[Full-Text](#)

Department of Internal Medicine

Previous population studies have demonstrated significant improvement in risk stratification by CACS beyond clinical risk factors, and CACS is now considered reasonable for asymptomatic adults at 10% to 20% 10-year risk of events (2-3). In contrast, CCTA has generally been used for symptomatic individuals for detection or exclusion of coronary stenosis, and current American College of Cardiology Foundation Appropriate Use Criteria are in keeping with this practice (4). CCTA is safe, with significant improvements in technology now allowing performance with radiation doses similar to CACS (5). To date, the differential prognostic utility of CCTA stenosis and CACS has been inadequately explored.

Mishulin A, Lever JF, Porter W, Servat JJ, **Gladstone G** and **Black E** (2012). "Aggressive glabellar angiomyxoma with orbital extension." Orbit 31(5): 361-363.

[Request Form](#)

Department of Ophthalmology

Mohammed N, **Kestin L**, **Grills I**, Shah C, Glide-Hurst C, Yan D and **Ionascu D** (2012). "Comparison of IGRT registration strategies for optimal coverage of primary lung tumors and involved nodes based on multiple four-dimensional CT scans obtained throughout the radiotherapy course." International Journal of Radiation Oncology, Biology, Physics 82(4): 1541-1548.

[Full-Text](#)

Department of Radiation Oncology

PURPOSE: To investigate the impact of primary tumor and involved lymph node (LN) geometry (centroid, shape, volume) on internal target volume (ITV) throughout treatment for locally advanced non-small cell lung cancer using weekly four-dimensional computed tomography (4DCT). METHODS AND MATERIALS: Eleven patients with advanced non-small cell lung cancer were treated using image-guided radiotherapy with acquisition of weekly 10-Phase 4DCTs (n = 51). Initial ITV was based on planning 4DCT. Master-ITV incorporated target geometry across the entire treatment (all 4DCTs). Geographic miss was defined as the % Master-ITV positioned outside of the initial planning ITV after registration is complete. Registration strategies considered were bony (B), primary tumor soft tissue alone (T), and registration based on primary tumor and involved LNs (T_LN). RESULTS: The % geographic miss for the primary tumor, mediastinal, and hilar lymph nodes based on each registration strategy were (1) B: 30%, 30%, 30%; (2) T: 21%, 40%, 36%; and (3) T_LN: 26%, 26%, 27%. Mean geographic expansions to encompass 100% of the primary tumor and involved LNs were 1.2 +/- 0.7 cm and 0.8 +/- 0.3 cm, respectively, for B and T_LN. Primary and involved LN expansions were 0.7 +/- 0.5 cm and 1.1 +/- 0.5 cm for T. CONCLUSION: T is best for solitary targets. When treatments include primary tumor and LNs, B and T_LN provide more comprehensive geographic coverage. We have identified high % geographic miss when considering multiple registration strategies. The dosimetric implications are the subject of future study.

Mulhem E, **Amin M**, **Copeland J**, Sharma J and Hunter S (2012). "Type-specific human papillomavirus DNA detected in atypical glandular cell pap tests." Acta Cytologica 56(2): 155-159.

[Request Form](#)

Department of Family Medicine

Department of Pathology

Objectives: To evaluate the presence of type-specific human papillomavirus (HPV) DNA in atypical glandular cells (AGCs) from cervical liquid-based cytology and to report the relationship between HPV types and cervical histological abnormalities. Study Design: We used a nested multiplex polymerase chain reaction assay to test AGC Papanicolaou (Pap) tests for the presence of 14 high-risk (HR) HPV types. Results: HR HPV types were detected in 33 of 161 AGC Pap tests (20.3%). Types 16 and/or 18 were detected in 13 samples (8%). Eight other HPV types were detected in 1-4 samples each. HPV-associated disease was diagnosed in 8 AGC cases (8%) with available histology results. The sensitivity and specificity of the HR HPV test were 87.5 and 90%, respectively, and the negative predictive value (NPV) was 99%. For a test that can isolate HPV types 16 and 18, the sensitivity and specificity were 62.5 and 100%, respectively, the positive predictive value (PPV) was 100% and the NPV was 97%. Conclusion: HPV 16 and 18 were the most common types detected in AGC Paps. We found high specificity, PPV and NPV with a test that can isolate these 2 HPV types. These results indicate a possible role for type-specific HPV testing in the management of AGC Pap tests. Copyright (C) 2012 S. Karger AG, Basel

Muslimani A, Chisti MM, **Blenc AM**, **Boxwala I**, **Micale MA** and **Jaiyesimi I** (2012). "Langerhans/dendritic cell sarcoma arising from hairy cell leukemia: a rare phenomenon." Annals of Hematology 91(9): 1485.

[Full-Text](#)

Department of Pathology

Department of Internal Medicine

Muslimani A, Rifai A, Chisti MMM, **Margolis J, Nadeau L, Jaiyesimi I** and **Huang J** (2012). "Late clearance of Circulating Leukemic Blasts (CBs) during Induction Therapy (IT) is a predictive of refractory adult Acute Myeloid Leukemia (AML)." Blood 120(21): 4319.

[Request Form](#)

Department of Internal Medicine

Department of Pathology

Background: CBs are highly variable at diagnosis and during the course of IT in AML patients. Assessing response to IT carries a huge implication on the prognosis of individual patient with AML. Our study investigates whether late clearance of CBs during IT using standard cytarabine + anthracycline regimen is associated with refractory phenotype.

Nagar S, Iacco A, **Riggs T, Kestenberg W** and **Keidan R** (2012). "An analysis of fine needle aspiration versus core needle biopsy in clinically palpable breast lesions: a report on the predictive values and a cost comparison." American Journal of Surgery 204(2): 193-198.

[Full-Text](#)

Department of Pediatrics

Department of Surgery

BACKGROUND: Although fine-needle aspiration (FNA) is an established tool in the biopsy of breast masses, there has been a trend toward using core-needle biopsy (CNB). The aim of this study was to determine whether FNA has comparable predictive value with CNB and whether FNA is more cost effective. METHODS: A retrospective review was conducted on 162 patients who underwent either FNA or CNB of palpable breast lesions and had histologic confirmation with surgical biopsy in calendar year 2005. RESULTS: There were no false-positives or false-negatives in either group. The sensitivity, specificity, and positive predictive value for FNA were 89%, 98%, and 94%, respectively. CNB had sensitivity, specificity, and positive predictive value of 100%, 90%, and 93%, respectively. The cost to perform FNA was \$166.34, compared with \$477.92 for CNB. CONCLUSIONS: FNA and CNB had comparable predictive value, with FNA being more cost effective.

Nagar S, Reid D, **Czako P, Long G** and **Shanley C** (2012). "Outcomes analysis of intraoperative adjuncts during minimally invasive parathyroidectomy for primary hyperparathyroidism." American Journal of Surgery 203(2): 177-181.

[Full-Text](#)

Department of Surgery

BACKGROUND: The aim of this study was to determine whether minimally invasive radioguided parathyroidectomy (MIRP) and intraoperative parathyroid hormone-guided parathyroidectomy (ioPTH) have equivalent intermediate-term outcomes in primary hyperparathyroidism (PHPT). METHODS: A retrospective study of 244 patients who underwent parathyroidectomy for PHPT in a 25-month time period was conducted. Patients who either underwent MIRP- or ioPTH-guided parathyroidectomies were included. The primary outcome was persistent disease. Conversion to bilateral exploration, complications, and multigland disease (MGD) were secondary outcomes. RESULTS: There was 1 MIRP patient and no ioPTH patients who had persistent disease. The ioPTH group had more conversions to a bilateral exploration (bilateral neck exploration [BNE]) (3.7% vs 13%, $P = .024$). In the MIRP group, no patients were found to have MGD. In the ioPTH group, 7 patients with double adenomas and 6 patients with MGD were found (0 vs 13, $P = .0028$). CONCLUSIONS: ioPTH facilitates successful minimally invasive parathyroidectomy (MIP) when compared with MIRP and provides cure rates similar to BNE.

Nakazato R, Gransar H, Berman DS, Cheng VY, Lin FY, Achenbach S, Al-Mallah M, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, Cury RC, **Chinnaiyan K**, Chow BJW, Delago A, Hadamitzky M, Hausleiter J, Kaufmann P, Maffei E, **Raff G**, Shaw LJ, Villines TC, Dunning A, Feuchtner G, Kim YJ, Leipsic J and Min JK (2012). "Statins use and coronary artery plaque composition: Results from the International Multicenter CONFIRM Registry." Atherosclerosis 225(1): 148-153.

[Full-Text](#)

Department of Internal Medicine

Objective: The effect of statins on coronary artery plaque features beyond stenosis severity is not known. Coronary CT angiography (CCTA) is a novel non-invasive method that permits direct visualization of coronary atherosclerotic features, including plaque composition. We evaluated the association of statin use to coronary plaque composition type in patients without known coronary artery disease (CAD) undergoing CCTA. Methods: From consecutive individuals, we identified 6673 individuals (2413 on statin therapy and 4260 not on statin therapy) with no known CAD and available statin use status. We studied the relationship between statin use and the presence and extent of specific plaque composition types, which was graded as non-calcified (NCP), mixed (MP), or calcified (CP) plaque. Results: The mean age was 59 ± 11 (55% male). Compared to the individuals not taking statins, those taking statins had higher prevalence of risk factors and obstructive CAD. In multivariable analyses, statin use was associated with increased the presence of MP [odds ratio (OR) 1.46, 95% confidence interval (CI) 1.27-1.68], $p < 0.001$ and CP (OR 1.54, 95% CI 1.36-1.74, $p < 0.001$), but not NCP (OR 1.11, 95% CI 0.96-1.29, $p = 0.1$). Further, in multivariable analyses, statin use was associated with increasing numbers of coronary segments possessing MP (OR 1.52, 95% CI 1.34-1.73, $p < 0.001$) and CP (OR 1.52, 95% CI 1.36-1.70, $p < 0.001$), but not coronary segments with NCP (OR 1.09, 95% CI 0.94-1.25, $p = 0.2$). Conclusion: Statin use is associated with an increased prevalence and extent of coronary plaques possessing calcium. The longitudinal effect of statins on coronary plaque composition warrants further investigation. © 2012 Elsevier Ireland Ltd.

Nickel JC, Partin AW, Nirmal J, **Chancellor MB**, Loeb S, Brawer MK, Assimos D and Shapiro E (2012). "Best of the 2012 AUA Annual Meeting: Highlights From the 2012 American Urological Association Meeting, May 19-23, 2012, Atlanta, GA." Reviews Urology 14(3-4): 90-103.

[Full-Text](#)

Department of Urology

Nirmal J, **Chancellor M**, Tyagi V, Qu X, Kuo H-C, Lin H-T, Chuang Y-C and **Tyagi P** (2012). "Association of inflammaging (inflammation plus aging) with higher prevalence of OAB in elderly population." Neurourology and Urodynamics 31(2): 247.

[Full-Text](#)

Department of Urology

Nirmal J, Chuang Y-C, **Tyagi P** and **Chancellor MB** (2012). "Intravesical therapy for lower urinary tract symptoms." Urological Science (previously Journal of Taiwan Urological Association) 23(3): 70-77.

[Request Form](#)

Department of Urology

Intravesical (local) therapy for diseases emanating from the bladder is similar to the commonplace management of ocular diseases using eyedrops. The existing intravesical therapy involves administering dosage forms directly into the bladder (through a catheter). This mode of treatment is routine in the bladder cancer by instillation of bacillus Calmette–Guérin to provoke the body's own natural defenses against invasion by proliferating cancer cells in the bladder. Although convenient, the conventional routes of administration for treating diseases such as interstitial cystitis/painful bladder syndrome (IC/PBS) and overactive bladder (OAB) are less acceptable to patients owing to side effects, which may further exacerbate the disease symptoms. Intravesical therapy has demonstrated varying degrees of efficacy and safety in treating IC/PBS and OAB. In recent years, intravesical delivery of biotechnological products including neurotoxins using a liposome platform demonstrated immense promise for lower urinary tract symptoms. This review considers the current status of intravesical therapy in lower urinary tract diseases with special attention to novel drug-delivery systems.

Nirmal J, Dang L, **Tyagi P** and **Chancellor M** (2012). "Transmission electron microscopy ultrastructural study of liposome drug delivery uptake by urothelium." Neurourology and Urodynamics 31(2): 237.

[Full-Text](#)

Department of Urology

Nojkov B, Signori C, Konda A and Fontana RJ (2012). "Lenalidomide-associated hepatotoxicity - a case report and literature review." Anticancer Research 32(9): 4117-4119.

[Request Form](#)

Department of Internal Medicine

Background: Lenalidomide is an immunomodulatory drug frequently used for treatment of patients with multiple myeloma and myelodysplastic syndromes. This report presents a rare case of lenalidomide-associated hepatotoxicity and reviews the available literature. Case Report: A 67-year-old male with multiple myeloma was hospitalized with nausea, vomiting and jaundice, while treated with a second three-week course of lenalidomide. The patient was found to have acutely elevated bilirubin, alkaline phosphatase, AST and ALT. He also had acute on chronic renal function impairment. Serology for viral hepatitis, abdominal ultrasound, magnetic resonance cholangiopancreatography and hepatobiliary scan revealed no abnormalities. Lenalidomide was stopped, resulting in subsequent (8 days) clinical improvement and normalization of the liver abnormalities. The RUCAM causality assessment score was 8, consistent with probable lenalidomide-associated hepatotoxicity. Literature review revealed four other published cases of lenalidomide-associated hepatotoxicity with clinical presentation varying between cholestatic-, hepatocellular- or mixed-pattern of liver injury. All patients had clinical and laboratory improvement soon after lenalidomide discontinuation. Renal function impairment was present in 3 of the 5 reported cases. The exact mechanism of lenalidomide-associated liver injury remains unclear as only 2 patients had liver biopsies without specific findings. Conclusion: Physicians should be aware of the potential for lenalidomide-associated hepato toxicity, particularly in patients with underlying renal insufficiency.

Ogunyemi TO, Siadat MR, Arslanturk S, Killinger KA and **Diokno AC** (2012). "Novel application of statistical methods to identify new urinary incontinence risk factors." Advances in Urology 2012: 276501.

[Request Form](#)

Department of Urology

Longitudinal data for studying urinary incontinence (UI) risk factors are rare. Data from one study, the hallmark Medical, Epidemiological, and Social Aspects of Aging (MESA), have been analyzed in the past; however, repeated measures analyses that are crucial for analyzing longitudinal data have not been applied. We tested a novel application of statistical methods to identify UI risk factors in older women. MESA data were collected at baseline and yearly from a sample of 1955 men and women in the community. Only women responding to the 762 baseline and 559 follow-up questions at one year in each respective survey were examined. To test their utility in mining large data sets, and as a preliminary step to creating a predictive index for developing UI, logistic regression, generalized estimating equations (GEEs), and proportional hazard regression (PHREG) methods were used on the existing MESA data. The GEE and PHREG combination identified 15 significant risk factors associated with developing UI out of which six of them, namely, urinary frequency, urgency, any urine loss, urine loss after emptying, subject's anticipation, and doctor's proactivity, are found most highly significant by both methods. These six factors are potential candidates for constructing a future UI predictive index. © 2012 Theophilus O. Ogunyemi et al.

Ohri N, Werner-Wasik M, **Grills IS**, Belderbos J, Hope A, Yan D, **Kestin LL**, Guckenberger M, Sonke JJ, Bissonnette JP and Xiao Y (2012). "Modeling local control after hypofractionated stereotactic body radiation therapy for stage I non-small cell lung cancer: A report from the Elekta Collaborative Lung Research Group." International Journal of Radiation Oncology Biology Physics 84(3): e379-e384.

[Full-Text](#)

Department of Radiation Oncology

Purpose: Hypofractionated stereotactic body radiation therapy (SBRT) has emerged as an effective treatment option for early-stage non-small cell lung cancer (NSCLC). Using data collected by the Elekta Lung Research Group, we generated a tumor control probability (TCP) model that predicts 2-year local control after SBRT as a function of biologically effective dose (BED) and tumor size. Methods and Materials: We formulated our TCP model as follows: $TCP = e^{[BED10 - c * L - TCD50]/k} \div (1 + e^{[BED10 - c * L - TCD50]/k})$, where BED10 is the biologically effective SBRT dose, c is a constant, L is the maximal tumor diameter, and TCD50 and k are

parameters that define the shape of the TCP curve. Least-squares optimization with a bootstrap resampling approach was used to identify the values of c , TCD50, and k that provided the best fit with observed actuarial 2-year local control rates. Results: Data from 504 NSCLC tumors treated with a variety of SBRT schedules were available. The mean follow-up time was 18.4 months, and 26 local recurrences were observed. The optimal values for c , TCD50, and k were 10 Gy/cm, 0 Gy, and 31 Gy, respectively. Thus, size-adjusted BED (sBED) may be defined as BED minus 10 times the tumor diameter (in centimeters). Our TCP model indicates that sBED values of 44 Gy, 69 Gy, and 93 Gy provide 80%, 90%, and 95% chances of tumor control at 2 years, respectively. When patients were grouped by sBED, the model accurately characterized the relationship between sBED and actuarial 2-year local control ($r=0.847$, $P=.008$). Conclusion: We have developed a TCP model that predicts 2-year local control rate after hypofractionated SBRT for early-stage NSCLC as a function of biologically effective dose and tumor diameter. Further testing of this model with additional datasets is warranted. © 2012 Elsevier Inc.

Oleszkowicz SC, **Chittick P**, Russo V, Keller P, **Sims M** and **Band J** (2012). "Infections associated with use of ultrasound transmission gel: proposed guidelines to minimize risk." Infection Control and Hospital Epidemiology 33(12): 1235-1237.

[Full-Text](#)

Department of Internal Medicine

O'Neill WW, Kleiman NS, Moses J, Henriques JPS, **Dixon S**, Massaro J, Palacios I, Maini B, Mulukutla S, Džavík V, Popma J, Douglas PS and Ohman M (2012). "A prospective, randomized clinical trial of hemodynamic support with impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: The PROTECT II study." Circulation 126(14): 1717-1727.

[Full-Text](#)

Department of Internal Medicine

BACKGROUND- Although coronary artery bypass grafting is generally preferred in symptomatic patients with severe, complex multivessel, or left main disease, some patients present with clinical features that make coronary artery bypass grafting clinically unattractive. Percutaneous coronary intervention with hemodynamic support may be feasible for these patients. Currently, there is no systematic comparative evaluation of hemodynamic support devices for this indication. **METHODS AND RESULTS-** We randomly assigned 452 symptomatic patients with complex 3-vessel disease or unprotected left main coronary artery disease and severely depressed left ventricular function to intra-aortic balloon pump (IABP) ($n=226$) or Impella 2.5 ($n=226$) support during nonemergent high-risk percutaneous coronary intervention. The primary end point was the 30-day incidence of major adverse events. A 90-day follow-up was required, as well, by protocol. Impella 2.5 provided superior hemodynamic support in comparison with IABP, with maximal decrease in cardiac power output from baseline of -0.04 ± 0.24 W in comparison with -0.14 ± 0.27 W for IABP ($P=0.001$). The primary end point (30-day major adverse events) was not statistically different between groups: 35.1% for Impella 2.5 versus 40.1% for IABP, $P=0.227$ in the intent-to-treat population and 34.3% versus 42.2%, $P=0.092$ in the per protocol population. At 90 days, a strong trend toward decreased major adverse events was observed in Impella 2.5-supported patients in comparison with IABP: 40.6% versus 49.3%, $P=0.066$ in the intent-to-treat population and 40.0% versus 51.0%, $P=0.023$ in the per protocol population, respectively. **CONCLUSIONS-** The 30-day incidence of major adverse events was not different for patients with IABP or Impella 2.5 hemodynamic support. However, trends for improved outcomes were observed for Impella 2.5-supported patients at 90 days. © 2012 American Heart Association, Inc.

Otaki Y, Arsanjani R, Gransar H, Cheng VY, Dey D, Labounty T, Lin FY, Achenbach S, Al-Mallah M, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, **Chinnaiyan K**, Chow BJW, Delago A, Hadamitzky M, Hausleiter J, Kaufmann P, Maffei E, **Raff G**, Shaw LJ, Villines TC, Dunning A, Cury RC, Feuchtner G, Kim YJ, Leipsic J, Berman DS and Min JK (2012). "What have we learned from CONFIRM? Prognostic implications from a prospective multicenter international observational cohort study of consecutive patients undergoing coronary computed tomographic angiography." Journal of Nuclear Cardiology 19(4): 787-795.

[Request Form](#)

Department of Internal Medicine

Coronary computed tomographic angiography (CCTA) employing CT scanners of 64-detector rows or greater represents a novel non-invasive method for detection of coronary artery disease (CAD), providing excellent diagnostic information when compared to invasive angiography. In addition to its high diagnostic performance, prior studies have shown that CCTA can provide important prognostic information, although these prior studies have been generally limited to small cohorts at single centers. The Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter registry, or CONFIRM, is a large, prospective, multinational, dynamic observational cohort study of patients undergoing CCTA. This registry currently represents more than 32,000 consecutive adults suspected of having CAD who underwent ≥ 64 -detector row CCTA at 12 centers in 6 countries between 2005 and 2009. Based on its large sample size and adequate statistical power, the data derived from CONFIRM registry have and will continue to provide key answers to many important topics regarding CCTA. Based on its multisite international national design, the results derived from CONFIRM should be considered as more generalizable than prior smaller single-center studies. This article summarizes the current status of several studies from CONFIRM registry. Copyright © 2012 American Society of Nuclear Cardiology.

Oueidat M, Jurjus A and **Hajj Hussein I** (2012). "OP-216 Forensic medicine in Lebanon: an update." International Journal of Legal Medicine 126(Suppl 1): S116.

[Full-Text](#)

Department of Biomedical Sciences

Park DK, Thomas AO, St Clair S and Bawa M (2012). "Percutaneous lumbar and thoracic pedicle screws: a trauma experience." Journal of spinal disorders & techniques. ePub Ahead of Print.

[Full-Text](#)

Department of Orthopedic Surgery

DESIGN:: Retrospective case study. OBJECTIVE:: Percutaneous pedicle screw (PPS) techniques do not allow direct visualization and may lead to erroneous screw placement. A technique utilizing only fluoroscopy is described. Verification of its accuracy and morphometric validation are presented. BACKGROUND:: Minimally invasive spine surgical techniques, particularly PPS placement, have been growing in popularity. The purported benefits of minimally invasive spine surgical stated may be even more advantageous in the trauma setting. METHODS:: Jamshidi needles were docked in the typical starting position verified with posterior-anterior image. Jamshidi needle (20 mm) was advanced ensuring that the tip remained lateral to the medial pedicle wall. A Kirschner (K-wire) was placed through the needle. Once all the K-wires were placed, a lateral image was taken confirming the correct trajectory and that the wire passed the posterior vertebral body wall. Patients with PPS fixation were retrospectively studied with postoperative computed tomography to verify screw accuracy. Screw grade was assessed as grade I when completely within the pedicle, II 4 mm outside the pedicle. Morphometrically, 40 thoracic and lumbar computed tomography scans of patients (grade II breach. The morphometric study demonstrated the pedicle length to range from 14.4 to 22.1 mm. The shortest was in the upper thoracic and the longest at L1-L2. CONCLUSIONS:: The morphometric study demonstrates if a K-wire is placed 20 mm into the bone and remains lateral to the medial pedicle wall and the tip just engages the vertebral body, the screw trajectory is safe particularly in the lower thoracic and upper lumbar spine. A smaller distance may be utilized in the upper thoracic. Breach rates are similar to other reports using other techniques; none were clinically significant. The advantage of this technique is the use of only PA fluoroscopy for placing all the wires percutaneously.

Park SS, Yan D, McGrath S, Dilworth JT, **Liang J**, Ye H, **Krauss DJ**, **Martinez AA** and **Kestin LL** (2012). "Adaptive image-guided radiotherapy (IGRT) eliminates the risk of biochemical failure caused by the bias of rectal distension in prostate cancer treatment planning: clinical evidence." International Journal of Radiation Oncology, Biology, Physics 83(3): 947-952.

[Full-Text](#)

Department of Radiation Oncology

PURPOSE: Rectal distension has been shown to decrease the probability of biochemical control. Adaptive image-guided radiotherapy (IGRT) corrects for target position and volume variations, reducing the risk of biochemical failure while yielding acceptable rates of gastrointestinal (GI)/genitourinary (GU) toxicities. METHODS AND MATERIALS: Between 1998 and 2006, 962 patients were treated with computed tomography (CT)-based offline adaptive IGRT. Patients were stratified into low (n = 400) vs. intermediate/high (n = 562) National Comprehensive Cancer Network (NCCN) risk groups. Target motion was assessed with daily CT during the first week. Electronic portal imaging device (EPID) was used to measure daily setup error. Patient-specific confidence-limited planning target volumes (cl-PTV) were then constructed, reducing the standard PTV and compensating for geometric variation of the target and setup errors. Rectal volume (RV), cross-sectional area (CSA), and rectal volume from the seminal vesicles to the inferior prostate (SVP) were assessed on the planning CT. The impact of these volumetric parameters on 5-year biochemical control (BC) and chronic Grades ≥ 2 and 3 GU and GI toxicity were examined. RESULTS: Median follow-up was 5.5 years. Median minimum dose covering cl-PTV was 75.6 Gy. Median values for RV, CSA, and SVP were 82.8 cm³, 5.6 cm², and 53.3 cm³, respectively. The 5-year BC was 89% for the entire group: 96% for low risk and 83% for intermediate/high risk ($p \geq 2$ and 3 GI toxicities were 21.2% and 2.9%, respectively. Respective values for GU toxicities were 15.5% and 4.3%. No differences in GI or GU toxicities were noted when patients were stratified by RV. CONCLUSIONS: Incorporation of adaptive IGRT reduces the risk of geometric miss and results in excellent biochemical control that is independent of rectal volume/distension while maintaining very low rates of chronic GI toxicity.

Patel VC, **Park DK** and **Herkowitz HN** (2012). "Lateral transposas fusion: indications and outcomes." [ScientificWorldJournal](#) 2012: 893608.

[Full-Text](#)

Department of Orthopedic Surgery

Spinal fusion historically has been used extensively, and, recently, the lateral transposas approach to the thoracic and lumbar spine has become an increasingly common method to achieve fusion. Recent literature on this approach has elucidated its advantage over more traditional anterior and posterior approaches, which include a smaller tissue dissection, potentially lower blood loss, no need for an access surgeon, and a shorter hospital stay. Indications for the procedure have now expanded to include degenerative disc disease, spinal stenosis, degenerative scoliosis, nonunion, trauma, infection, and low-grade spondylolisthesis. Lateral interbody fusion has a similar if not lower rate of complications compared to traditional anterior and posterior approaches to interbody fusion. However, lateral interbody fusion has unique complications that include transient neurologic symptoms, motor deficits, and neural injuries that range from 1 to 60% in the literature. Additional studies are required to further evaluate and monitor the short- and long-term safety, efficacy, outcomes, and complications of lateral transposas procedures.

Pentlak PA, Schuch-Miller D, **Hammond R**, Streetman R, Veenstra M, Pridmore D and **Robbins J** (2012). "A simulator module for percutaneous tracheostomy." [Journal of the American College of Surgeons](#) 215(3 Suppl S): S117.

[Full-Text](#)

Department of Surgery

Perakis PG, Yunus T, **Long G**, Cheema ZF, **Hammond R** and **Shanley CJ** (2012). "Platelet function after cessation of chronic clopidogrel therapy." [American Surgeon](#) 78(1): 51-56.

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Department of Surgery

Surgeons increasingly encounter patients on clopidogrel therapy who are preparing to undergo surgery. The goal of this study was to examine the change in platelet function after the common clinical scenario of discontinuing chronic clopidogrel therapy in those patients preparing to undergo an elective surgery, and the time course of platelet function recovery after clopidogrel discontinuation. Patients on clopidogrel therapy scheduled for an elective surgical procedure had their platelet function tested using a VerifyNow P2Y12 device (Accumetrics, San Diego, CA). Platelet inhibition was evaluated at baseline before clopidogrel discontinuation, and subsequently studied every other day in the week before their scheduled procedure.

Mean platelet inhibition was 32.1 per cent on Day 0 (before clopidogrel discontinuation), decreasing to 3.7 per cent on Day 4. Platelet inhibition decreased significantly after discontinuation of clopidogrel in a time-dependent manner ($P = 0.011$), although a considerable interindividual variability of P2Y12 reaction units values was observed over the study period. Patients on concomitant proton pump inhibitors and clopidogrel demonstrated a decreased effect of clopidogrel. In conclusion, individual platelet function monitoring may assist the surgeon in perioperative decision-making in patients receiving clopidogrel therapy preparing to undergo elective surgery.

Perez-Cruet MJ, Welsh RJ, Hussain NS, Begun EM, Lin J and Park P (2012). "Use of the da vinci minimally invasive robotic system for resection of a complicated paraspinal schwannoma with thoracic extension." *Neurosurgery* 71(1 Suppl Operative): 209-214.

[Full-Text](#)

Department of Neurosurgery

Department of Surgery

BACKGROUND:: and Importance: Applications of robotics to minimally invasive spine (MIS) surgery have produced several benefits while sparing patients the morbidity of traditional open surgery. MIS surgery offers the advantages of less pain and less blood loss along with quicker recovery and shorter hospital stays. The da Vinci robotic surgical system has recently been adapted to neurosurgical applications. This article details a posterior approach using a tubular retraction system in conjunction with an anterior approach using the da Vinci robot to completely remove large spinal schwannomas with intra-thoracic extension. This technique is an example of a novel application of existing technology, initially developed for other applications. **CLINICAL PRESENTATION::** Two patients with large thoracic schwannomas extending into the chest cavity are reviewed. We present images and video of the combined minimally invasive approach used to completely remove the lesions without complications. **CONCLUSION::** This report describes a novel neurosurgical application of an existing minimally invasive robotic surgical system.

Peters KM (2012). "Interstitial cystitis-is it time to look beyond the bladder?" *Journal of Urology* 187(2): 381-382.

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Department of Urology

Peters KM (2012). "Sacral neuromodulation is an effective treatment for interstitial cystitis/bladder pain syndrome." *Journal of Urology* 188(6): 2043-2044.

[Request Form](#)

Department of Urology

Peters KM (2012). "Sacral neuromodulation is an effective treatment for interstitial cystitis/bladder pain syndrome: pro." *Journal of Urology* 188(6): 2043-2044.

[Request Form](#)

Department of Urology

Peters KM, Hasenau DL, Anthony M, Kaufman J and Killinger KA (2012). "Novel therapy with intravesical liposomes for ulcerative interstitial cystitis/painful bladder syndrome." *LUTS: Lower Urinary Tract Symptoms* 4(1): 51-53.

[Request Form](#)

Department of Urology

Objectives: A Federal Drug Administration-approved, compassionate-use, investigational new drug single-subject trial was conducted to evaluate the safety and clinical outcomes of intravesical instillation of liposomes in a woman with ulcerative interstitial cystitis/painful bladder syndrome (IC/PBS). **Methods:** After obtaining informed consent, the 48-year-old woman, diagnosed with ulcerative IC/PBS, received four weekly instillations of intravesical liposomes. Subsequently she was evaluated for 8 weeks post bladder instillation. **Results:** No side effects or adverse events were reported during the 12 week study period. Voids per day decreased from a baseline of 18 voids per 24 h to 11.3 voids per 24 h at week 3, and 12.6 voids per 24 h at 8 weeks after final instillation. Urgency score also decreased from a pre-instillation mean of 1.75 (out of 10) to

1.07 8 weeks after the final instillation. Bladder ulcers noted by cystoscopy at baseline were absent at the 8 weeks post-treatment and no evidence of bladder inflammation was noted. Conclusion: Intravesical liposome instillation is minimally invasive and presents an appealing new treatment for IC/PBS. Prospective trials are needed to assess intravesical liposomes for IC/PBS. © 2011 Blackwell Publishing Asia Pty Ltd.

Pieper DR (2012). "The endoscopic approach to vestibular schwannomas and posterolateral skull base pathology." *Otolaryngologic Clinics of North America* 45(2): 439-454.

[Full-Text](#)

Department of Neurosurgery

This article provides an overview of the technical considerations of endoscopy of the posterolateral skull base and cerebellopontine angle (CPA). Specific areas of focus are on the instrumentation requirements for neuroendoscopy of the CPA; the learning curve associated with this technique; and a complete description of the surgical techniques necessary to perform the procedure, along with outcomes and results. The article provides a general overview of the endoscopic approach to the CPA. For a variety of pathologies, the emphasis is on performing this technique for acoustic tumors and hearing preservation. Insights as to how the author's practice evolved in its use of neuroendoscopic procedures are provided.

Pifer MA, Kibuule LK, **Maerz T**, Studzinski DM, **Baker KC** and **Herkowitz HN** (2012). "In vitro response of human chondrocytes to a combination of growth factors and a proteinase inhibitor." *Orthopedics* 35(1): 35-42.

[Full-Text](#)

Department of Surgery

Department of Orthopaedic Surgery

Degenerative disk disease is an accelerating cascade of tissue degeneration in the intervertebral disk. A harsh catabolic environment perpetuates the degeneration of the intervertebral disk. Tissue engineering-based techniques offer effective treatment to slow the progression of degenerative disk disease and regenerate intervertebral disk tissue. The purpose of this study was to assess the efficacy of a regenerative therapy for degenerative disk disease by treating human chondrocytes with anabolic growth factors and a proteinase inhibitor. The use of both proved effective in upregulating important extracellular matrix markers of human chondrocytes. These successful in vitro results have implications for the regeneration of the intervertebral disk.

Qu G, Wu H, **Hartrick C** and Niu J (2012). "Local analgesia adverse effects prediction using multi-label classification." *Neurocomputing* 92: 18-27.

[Full-Text](#)

Department of Biomedical Sciences

It is desirable to determine minimal effective initial local anesthetic bolus required to provide satisfactory analgesia following surgery. A way to predict potential adverse effects based on the type of anesthetic and initial bolus amount administered would be a significant contribution to personalized medicine. In this work, we propose new methods for multi-label classification to predict adverse effects in order to help doctors make appropriate treatment decisions. In this endeavor, the Pair-Dependency Multi-Label Bayesian Classifier (PDMLBC) and Complete-Dependency Multi-Label Bayesian Classifier (CDMLBC) models are proposed as classifiers that take into account the impact of features on the dependency between labels. We evaluated the proposed models on 36 patients who had recently received arthroscopic shoulder surgery. The experimental results show that the CDMLBC model outperforms other existing methods in multi-label classification.

Rao S, Swartz A, Obeid L, Rao S, **Joyce B**, Whitehouse S, Horst M, Butler J, Kinnen R, Shepard A and Rubinfeld I (2012). "e-Portfolio competency metadata: pilot study for a call to action." *Journal of Medical Systems* 36(2): 457-462.

[Full-Text](#)

Department of Biomedical Sciences

The six competency domains required by the Accreditation Council for Graduate Medical Education (ACGME) have led to a proliferation of measurement tools, assessment methods, and all forms of data from paper to electronic. The need exists to develop a standardized electronic (e)-portfolio to provide the aggregate data to improve education and patient care. This process requires a sound methodology using XML metadata to allow portability of e-portfolio data. We surveyed publicly available metadata and developed an e-portfolio system for the Henry Ford Hospital General Surgery Residency Program. Based on our implementation of e-portfolios for 70 physicians, we call upon the ACGME, the Residency Review Committees, and the American Board of Medical Specialties to establish a method to formalize and develop a standard for residency competency metadata. Using an approach similar to that of our study can streamline data and lead to improved medical education and ultimately better patient care.

Rawashdeh O, Sa'Deh W, Rawashdeh M, Qu G, Ferrari M, Harrison B, **Hammond R** and **Maddens M** (2012). "Development of a low-cost fall intervention system for hospitalized dementia patients." Proceedings of the 2012 IEEE International Conference on Electro/Information Technology: Page 1.

[Full-Text](#)

Department of Surgery

Department of Internal Medicine

Reimund J-M, Tavernier M, Viennot S, **Haji Hussein I**, Dupont B, Justum A-M, Jurjus AR, Freund J-N and Lechevrel M (2012). Ulcerative colitis associated colorectal cancer prevention by 5 aminosalicylates: current status and perspective, (ed). Ulcerative colitis 2: INTECH: 149.

[Full-Text](#)

Department of Biomedical Sciences

Robertson JM, Margolis JH, Jury RP, Balaraman S, Cotant MB, Ballouz S, Boxwala IG, Jaiyesimi IA, Nadeau L, Hardy-Carlson M, Marvin KS, Wallace M and Ye H (2012). "Phase I study of conformal radiotherapy and concurrent full-dose gemcitabine with erlotinib for unresected pancreatic cancer." International Journal of Radiation Oncology, Biology, Physics 82(2): e187-e192.

[Full-Text](#)

Department of Radiation Oncology

Department of Internal Medicine

Department of Surgery

PURPOSE: To determine the recommended dose of radiotherapy when combined with full-dose gemcitabine and erlotinib for unresected pancreas cancer. METHODS AND MATERIALS: Patients with unresected pancreatic cancer (Zubrod performance status 0-2) were eligible for the present study. Gemcitabine was given weekly for 7 weeks (1,000 mg/m²) with erlotinib daily for 8 weeks (100 mg). A final toxicity assessment was performed in Week 9. Radiotherapy (starting at 30 Gy in 2-Gy fractions, 5 d/wk) was given to the gross tumor plus a 1-cm margin starting with the first dose of gemcitabine. A standard 3 plus 3 dose escalation (an additional 4 Gy within 2 days for each dose level) was used, except for the starting dose level, which was scheduled to contain 6 patients. In general, Grade 3 or greater gastrointestinal toxicity was considered a dose-limiting toxicity, except for Grade 3 anorexia or Grade 3 fatigue alone. RESULTS: A total of 20 patients were treated (10 men and 10 women). Nausea, vomiting, and infection were significantly associated with the radiation dose (p = .01, p = .03, and p = .03, respectively). Of the 20 patients, 5 did not complete treatment and were not evaluable for dose-escalation purposes (3 who developed progressive disease during treatment and 2 who electively discontinued it). Dose-limiting toxicity occurred in none of 6 patients at 30 Gy, 2 of 6 at 34 Gy, and 1 of 3 patients at 38 Gy. CONCLUSION: The results of the present study have indicated that the recommended Phase II dose is 30 Gy in 15 fractions.

Rodenbaugh D, Lujan H and DiCarlo S (2012). "Learning by doing: construction and manipulation of a skeletal muscle model during lecture." Advances in Physiology Education 36(4): 302-306.

[Full-Text](#)

Department of Biomedical Sciences

Active learning, "learning by doing," enhances student performance on examinations and improves student retention of course content. Active learning also provides inquiry-based, collaborative, and problem-solving activities that promote curiosity, skepticism, objectivity, and the use of scientific reasoning. To incorporate active learning into our undergraduate anatomy and physiology course of 70 nursing students, students constructed working physical models of skeletal muscle during the scheduled class time. Our goals were to actively engage students in the process of building and testing their own mental models from the information they were acquiring. During the process, the focus was on the student acquiring knowledge, thinking about the information, testing assumptions, solving problems, and appreciating the joy, excitement, and love for learning. We conclude that the construction of physical models during class is a valuable educational experience.

Rodriguez DJ, Afzal A, Evonich R and **Haines DE** (2012). "The prevalence of methicillin resistant organisms among pacemaker and defibrillator implant recipients." *American Journal of Cardiovascular Disease* 2(2): 116-122.

[Full-Text](#)

Department of Internal Medicine

INTRODUCTION: Pacemaker and defibrillator infections are an uncommon, but catastrophic complication of device implantation. The present study examined the prevalence of device-related infections, the patterns of antibiotic resistance, and the presence of methicillin resistant staphylococcus aureus (MRSA) nares colonization in device implant recipients. **METHODS:** Two protocols were employed using a retrospective and a prospective analysis. A retrospective chart review of 218 patients with suspected device infection from 1/2000 to 1/2011 was performed. Demographics, infection rates, and patterns of antibiotic resistance were compared. The prospective analysis enrolled one hundred eighty two patients undergoing device implantations or generator replacements. The nares were swabbed and analyzed for the presence of staphylococcus aureus, and tested for methicillin sensitivity. **RESULTS:** Over a period of ten years, 12,771 device implants/generator changes/system revisions were performed, with an infection rate of 1.2%. Methicillin resistance (MR) was identified in 98/218 (44.9%) of patients. Those with MR infection had more diabetes and cardiomyopathy. There was no significant increase in methicillin resistance over time ($p=0.30$). Our prospective analysis included 110 men. A total of 32 patients (17.6%) had positive cultures for SA: 6.6% with MRSA. Patients positive for MRSA nares colonization had a statistically significant greater length of hospital stay 8.5 days (mean) versus 4.4 days ($P=0.049$). **CONCLUSIONS:** Methicillin resistant organisms appear to be emerging and persistent pathogens in device implants. The screening of MRSA colonization may identify new populations at risk. Further studies and analysis are needed to determine the cost effectiveness of a screening protocol.

Rosenblatt SI, Dukatz T, Jahn R, **Ramsdell C**, **Sakharova A**, Henry M, Arndt-Mutz M, Miller V, Rogers K and Balasubramaniam M (2012). "Insulin glargine dosing before next-day surgery: comparing three strategies." *Journal of Clinical Anesthesia* 24(8): 610-617.

[Full-Text](#)

Department of Internal Medicine

Department of Anesthesiology

Study Objective: To evaluate three evening insulin glargine dosing strategies for achievement of target (100-179 mg/dL; 5.5 - 9.8 mmol/L) and widened (80-249 mg/dL; 4.4 - 13.7 mmol/L) preoperative fasting blood glucose (FBG) ranges on the day of surgery. **Design:** Prospective, randomized, open trial. **Setting:** Preoperative units at two sites of a suburban hospital system. **Patients:** 401 adult, ASA physical status 3 and 4 patients with type 1 and type 2 diabetes, undergoing elective noncardiac surgery. **Interventions:** Patients were divided into two groups according to absence of daily rapid-acting/short-acting insulin (insulin glargine-only group) or presence of daily rapid-acting/short-acting insulin (insulin glargine plus bolus group). Subjects were then randomized to three evening insulin glargine dosing strategies: (a) take 80% of usual dose, (b) call physician for dose, or (c) refer to dosing table, based on self-reported usual FBG and insulin regimen. In the prehospital setting, patients administered the instructed insulin glargine dose on the evening before surgery. **Measurements:** Venous blood glucose values were recorded in the preoperative holding area on the day of surgery. **Main Results:** No significant differences in target preoperative FBG

achievement were detected among strategies in the insulin glargine-only group (n = 174) or the insulin glargine plus bolus group (n = 227). In widened preoperative FBG achievement, no significant difference was noted among strategies in the insulin glargine-only group. In the insulin glargine plus bolus group, fewer subjects following the dosing table had FBG > 249 mg/dL (> 13.7 mmol/L; P = 0.031). Conclusions: Target preoperative FBG achievement was similar among strategies in both insulin glargine groups. An insulin glargine adjustment strategy based on usual glycemic control may better prevent severe preoperative hyperglycemia in patients receiving basal/bolus regimens. (c) 2012 Elsevier Inc. All rights reserved.

Rosenson RS, Brewer HB, Jr., Davidson WS, Fayad ZA, Fuster V, **Goldstein J**, Hellerstein M, Jiang X-C, Phillips MC, Rader DJ, Remaley AT, Rothblat GH, Tall AR and Yvan-Charvet L (2012). "Cholesterol efflux and atheroprotection advancing the concept of reverse cholesterol transport." Circulation 125(15): 1905-1919.

[Full-Text](#)

Department of Internal Medicine

Safian RD (2012). "Bioresorbable vascular scaffolds: the shape of things to come?" Catheterization and Cardiovascular Interventions 79(2): 229-230.

[Full-Text](#)

Department of Internal Medicine

Safian RD (2012). "Carotid artery stenting payment, politics, and equipose." Journal of the American College of Cardiology 59(15): 1390-1391.

[Full-Text](#)

Department of Internal Medicine

Safian RD (2012). "Carotid stenting and proximal embolic protection: has the "game changer" changed the game?" Catheterization and Cardiovascular Interventions 80(7): 1079-1080.

[Full-Text](#)

Department of Internal Medicine

Safian RD (2012). "The inferior epigastric artery: the innocent bystander of femoral catheterization." Catheterization and Cardiovascular Interventions 79(4): 638-639.

[Full-Text](#)

Department of Internal Medicine

Safian RD (2012). "Subintimal space: the final frontier?" Catheterization and Cardiovascular Interventions 80(5): 814-815.

[Full-Text](#)

Department of Internal Medicine

Safian RD (2012). "Treatment of aortoiliac chronic total occlusions: Guidelines and reality." Catheterization and Cardiovascular Interventions 80(4): 655-656.

[Full-Text](#)

Department of Internal Medicine

Safian RD (2012). "Vascular surgeons and carotid revascularization: what's theirs is theirs, and what's ours is theirs." Catheterization and Cardiovascular Interventions 80(2): 335-336.

[Full-Text](#)

Department of Internal Medicine

Sag AA, **Silbergleit R**, **Olson RE**, **Wilson J** and **Krishnan A** (2012). "T1 hyperintense disc in alkaptonuria." Spine 37(21): E1361-E1363.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Department of Neurosurgery

Department of Pathology

STUDY DESIGN.: Case report. OBJECTIVE.: To report a rare case of alkaptonuria presenting as a T1-hyperintense disc herniation. SUMMARY OF BACKGROUND DATA.: A 46-year-old man without previous diagnosis of alkaptonuria underwent evaluation for progressive back pain revealing a T1-hyperintense disc herniation at the L3-L4 level. Discectomy recovered a blackened disc that was pathologically confirmed to be nucleus pulposus with alkaptonuric involvement. The differential diagnosis of a T1-hyperintense, T2-hypointense disc on magnetic resonance imaging is discussed, with emphasis on the pathophysiology of alkaptonuria. METHODS.: A single patient is reported. RESULTS.: Pathologically proven patient presentation with radiological and pathological images. CONCLUSION.: We report a rare case of alkaptonuria presenting as a T1-hyperintense disc herniation.

Sammon JD, Trinh QD, Sukumar S, Diaz M, Simone A, **Kaul S** and Menon M (2012). "Long-term follow-up of patients undergoing percutaneous suprapubic tube drainage after robot-assisted radical prostatectomy (RARP)." [BJU International](#) 110(4): 580-585.

[Full-Text](#)

Department of Urology

Objectives To evaluate the long-term safety and functional outcomes of patients undergoing percutaneous suprapubic tube (PST) drainage after robot-assisted radical prostatectomy (RARP). Patients and Methods Between January 2008 and October 2009, 339 patients undergoing RARP by one surgeon experienced in RA surgery (M.M.) had postoperative bladder drainage with PST and a minimum of 1-year follow-up for urinary function. Functional outcomes were obtained via patient-administered questionnaire. Complications were captured by exhaustive review of multiple datasets, including our prospective prostate cancer database, claims data, as well as electronic medical and institutional morbidity and mortality records. Results Urinary function assessed by patient-administered questionnaire was analysed at a mean (sd) follow-up of 11.5 (1.7) months; after RARP with PST placement, 293 patients (86.4%) had total urinary control and only nine (2.7%) required >1 pad/day. In all, 86 patients (25.4%) never wore a pad; the median time to 0-1 pad/day was 2 weeks (interquartile range [IQR] 0,6); median time to total control was 6 weeks (IQR 1,22). The mean (sd) follow-up for complications was 23.7 (6.1) months. In all, 15 patients (4.4%) had a procedure-specific complication, of which 13 were minor (Clavien Class I/II 3.8%); one patient had a bladder neck contracture. In all, 16 patients (4.7%) required Foley placement after RARP for gross haematuria (two patients), urinary retention (three), tube malfunction (four) or need for prolonged Foley catheterization (seven). ConclusionS PST placement after RARP is safe and efficacious on long-term follow-up. Splinting of the urethrovesical anastomosis is not a critical step of RP if a watertight anastomosis and excellent mucosal apposition are achieved. © 2011 THE AUTHORS. BJU INTERNATIONAL © 2011 BJU INTERNATIONAL.

Sanders W, **Fringer R** and **Swor R** (2012). "Management of an extremely premature infant in the out-of-hospital environment." [Prehospital Emergency Care](#) 16(2): 303-307.

[Request Form](#)

Department of Emergency Medicine

The rate of premature infant mortality has decreased over the last several decades, with an accompanying decrease in the gestational age of premature infants who survive to hospital discharge. Emergency medical services (EMS) providers are sometimes called to provide prehospital care for infants born at the edge of viability. Such extremely premature infants (EPIs) present medical and ethical challenges. In this case report, we describe an infant born at 24 weeks into a toilet by a mother who thought she had miscarried. The EMS providers evaluated the infant as nonviable and placed him in a plastic bag for transport to a local emergency department (ED). The ED staff found the infant to have a bradycardic rhythm, initiated resuscitation, and admitted him to the neonatal intensive care unit. The infant died seven days later. We review the literature for recommendations in resuscitation of EPIs and discuss the ethics regarding their management in the prehospital setting.

Sangal RB (2012). "Evaluating sleepiness-related daytime function by querying wakefulness inability and fatigue: Sleepiness-Wakefulness Inability and Fatigue Test (SWIFT)." Journal of Clinical Sleep Medicine 8(6): 701-711.

[Full-Text](#)

Department of Family Medicine

Study Objectives: Routine assessment of daytime function in Sleep Medicine has focused on "tendency to fall asleep" in soporific circumstances, to the exclusion of "wakefulness inability" or inability to maintain wakefulness, and fatigue/tiredness/lack of energy. The objective was to establish reliability and discriminant validity of a test for wakefulness inability and fatigue, and to test its superiority against the criterion standard for evaluation of sleepiness—the Epworth Sleepiness Scale (ESS). Methods: A 12-item self-administered instrument, the Sleepiness- Wakefulness Inability and Fatigue Test (SWIFT), was developed and administered, with ESS, to 256 adults \geq 18 years of age (44 retook the tests a month later); consecutive patients with symptoms of sleep disorders including 286 with obstructive sleep apnea ([OSA], apnea-hypopnea index \geq 5/h sleep on polysomnography [PSG]), 49 evaluated with PSG and multiple sleep latency test for narcolepsy and 137 OSA patients treated with continuous positive airway pressure (CPAP). Results: SWIFT had internal consistency 0.87 and retest intraclass coefficient 0.82. Factor analysis revealed 2 factors-general wakefulness inability and fatigue (GWIF) and driving wakefulness inability and fatigue (DWIF). Normal subjects differed from patients in ESS, SWIFT, GWIF, and DWIF. SWIFT and GWIF (but not DWIF) had higher area under ROC curve, Youden's index, and better positive and negative likelihood ratios than ESS. ESS, SWIFT, GWIF, and DWIF improved with CPAP. Improvements in SWIFT, GWIF, and DWIF (but not ESS) were significantly correlated with CPAP compliance. Conclusions: SWIFT is reliable and valid. SWIFT and its factor GWIF have a discriminant ability superior to that of the ESS. Keywords: Sleepiness, wakefulness inability, fatigue, obstructive sleep apnea, Epworth Sleepiness Scale

Sawyer KN, Shah P, Qu L, Clark C and Swor RA (2012). "Comparison of 30-day adverse events following triple rule out versus chest CT with subsequent provocative testing for evaluation of chest pain in the emergency department." Annals of Emergency Medicine 60(4 Suppl S): S8.

[Full-Text](#)

Department of Emergency Medicine

Schmeltz LR and Ferrise C (2012). "Glycemic management in the inpatient setting." Hospital Practice 40(2): 44-45.

[Request Form](#)

Department of Internal Medicine

Hyperglycemia occurs frequently in hospitalized patients and affects patient outcomes, including mortality, inpatient complications, hospital length of stay, and overall hospital costs. Various degrees of glycemic control have been studied and consensus statements from the American Diabetes Association/American Association of Clinical Endocrinologists and The Endocrine Society recommend a target blood glucose range of 140 to 180 mg/dL in most hospitalized patients. Insulin is the preferred modality for treating all hospitalized patients with hyperglycemia, as it is adaptable to changing patient physiology over the course of hospitalization. Critically ill patients should receive intravenous insulin infusion, and all noncritically ill patients with hyperglycemia (individuals with and without diabetes) should be managed using a subcutaneous insulin algorithm with basal, nutritional, and correctional dose components. Hypoglycemia remains a limiting factor to achieving optimal glycemic targets. Similar to hyperglycemia, hypoglycemia is an independent risk factor for poor outcomes in hospitalized patients. Improvement in glycemic control throughout the hospital includes efforts from all health care providers. Institutions can encourage safe insulin use by using insulin algorithms, preprinted order sets, and hypoglycemia protocols, as well as by supporting patient and health care provider education.

Schwartz J, Robinson-Dunn B, Makin J and Boyanton BL, Jr. (2012). "Evaluation of the BD MAX GBS assay to detect streptococcus group B in LIM broth-enriched antepartum vaginal-rectal specimens." Diagnostic Microbiology and Infectious Disease 73(1): 97-98.

[Full-Text](#)

Department of Biomedical Sciences

Department of Pathology

The BD MAX CBS real-time polymerase chain reaction assay was evaluated concomitantly with Centers for Disease Control and Prevention-endorsed culture methods to detect Streptococcus group B from LIM broth-enriched antepartum vaginal-rectal specimens. The sensitivity of both methods exceeded 98%. (C) 2012 Elsevier Inc. All rights reserved.

Schwartz J, Sims M, Movva K, Sawarynski K, Makin J, Powell K, Singh S, **Robinson-Dunn B** and Boyanton BL (2012). "Molecular typing links probiotic supplement use as the source of bacteremia and endocarditis." Journal of Molecular Diagnostics 14(6): 668-669.

[Full-Text](#)

Department of Pathology

Schwartz JD, Amin MB and **Zhang PL** (2012). "Immunohistochemical profile of stem/progenitor cell marker C133 in variants of renal tumors." Modern Pathology 25(Suppl 1): 240A.

[Full-Text](#)

Department of Biomedical Sciences

Department of Pathology

Sengupta DK and **Herkowitz HN** (2012). "Pedicule screw-based posterior dynamic stabilization: literature review." Advances in Orthopedics 2012: 424268.

[Full-Text](#)

Department of Orthopedic Surgery

Posterior dynamic stabilization (PDS) indicates motion preservation devices that are aimed for surgical treatment of activity related mechanical low back pain. A large number of such devices have been introduced during the last 2 decades, without biomechanical design rationale, or clinical evidence of efficacy to address back pain. Implant failure is the commonest complication, which has resulted in withdrawal of some of the PDS devices from the market. In this paper the authors presented the current understanding of clinical instability of lumbar motions segment, proposed a classification, and described the clinical experience of the pedicle screw-based posterior dynamic stabilization devices.

Servat JJ and **Black EH** (2012). "A comparison of surgical outcomes with the use of 2 different biodegradable multipoint fixation devices for endoscopic forehead elevation." Ophthalmic Plastic and Reconstructive Surgery 28(6): 401-404.

[Full-Text](#)

Department of Ophthalmology

Purpose: To assess the efficacy and rates of inflammatory cyst formation with the use of 2 different biodegradable multipoint fixation devices, Endotine versus Ultratine, for endoscopic forehead elevation. Methods: The charts of 138 patients who underwent endoscopic forehead elevation by the same surgeon (E.H.B.) were reviewed retrospectively. Data regarding patient demographics, type of biodegradable fixation device, loss of fixation in the immediate and late postoperative period, inflammatory cyst formation of the fixation device, additional complications, and reoperation status were collected from the charts. Patients implanted with Endotine and Ultratine were compared postoperatively for early and late loss of elevation (efficacy), inflammatory cyst formation, additional complications, and reoperation rates. Results: Of the 276 fixation devices implanted (117 Endotine and 159 Ultratine), 11 inflammatory cysts were found, all of them in the Ultratine group ($p = 0.0037$). Four patients required reoperation due to early loss of fixation. Three of these cases were in the Endotine group, and 1 case was observed in the Ultratine group ($p = 0.18$). A total of 4 patients had late loss of fixation, all of them in the Ultratine group ($p = 0.08$). Scalp hypoesthesia and/or dysesthesia beyond the sixth postoperative month were observed in 3.62% of the cases. Postsurgical neuralgia was observed in 2.17%, and focal alopecia was seen in 1.44%. Conclusions: The presence of

inflammatory cysts with the implantation of the Ultratine device is statistically higher than with Endotine. No statistical significant difference was found in either early or late fixation loss between the 2 groups. (*Ophthal Plast Reconstr Surg* 2012;28:401-404)

Servat JJ, **Black EH** and **Gladstone GJ** (2012). "A solution to the Jones tube continuous positive airway pressure (CPAP) dilemma?" *Ophthalmic Plastic and Reconstructive Surgery* 28(6): e151-e152.

[Full-Text](#)

Department of Ophthalmology

A 49-year-old woman, who had previously undergone bilateral Jones tube placement, began nasal continuous positive airway pressure for obstructive sleep apnea. The patient's use of continuous positive airway pressure was limited by intolerance of the transfer of air through the Jones tube to her ocular surface resulting in irritation and discomfort. A change from nasal continuous positive airway pressure to a full face mask, including both Jones tubes in the pressure circuit, resolved the problem.

Shah C, Berry S, **Dekhne N**, Lanni T, Lowry H and **Vicini F** (2012). "Implementation and outcomes of a multidisciplinary high-risk breast cancer program: the William Beaumont Hospital experience." *Clinical Breast Cancer* 12(3): 215-218.

[Full-Text](#)

Department of Surgery

Department of Internal Medicine

Limited data are available on the implementation of a high-risk assessment program in the construct of a community clinical oncology program. The development of a high-risk breast cancer screening program at our institution identified 15%-20% of patients screened as high risk, with limited increases in structural or personnel requirements. Identification of patients as high risk could potentially improve outcomes by allowing for individualized prevention strategies and more appropriate high-risk surveillance. Purpose: The implementation of a program that incorporates a risk assessment questionnaire (RAQ) to identify high-risk patients in a community-based health system was evaluated. Materials and Methods: Women with no history of breast cancer or ductal carcinoma in situ who were undergoing annual screening mammography were offered an RAQ. Cases determined to be high risk (Gail lifetime risk $\geq 20\%$ or as indicated through personal and/or family history) were offered referral to our High-risk Breast Cancer Program. A retrospective data review was conducted on completed questionnaires. Results: A total of 5878 women underwent evaluation with the RAQ between September 2009 and August 2010. The mean age of the cohort was 55 years old, with 84.9% (4990) of participants being white, and 6.8% (400) African American. In the entire population, 45.7% (2446) had at least 1 first-degree relative with breast cancer (BC), and 923 (17.2%) women were found to be high risk by the Gail model. Beyond the Gail model, 53 (0.9%) women had undergone prior chest radiation, 34 (0.6%) had a male relative with BC, 200 (3.4%), had 3 or more relatives with BC on one side of their family, 308 (5.2%) had a relative with breast and ovarian cancer on one side of the family, and 105 (1.8%) noted 2 relatives with BC with onset under age 50 years on the same side of the family. Conclusions: Our experience indicates that the identification of women at high risk for BC can be easily incorporated into an annual screening mammography visit. Identification of these patients as high risk can allow for individualized, more-appropriate surveillance and prevention.

Shah C, **Ghilezan M**, Arthur D, Wilkinson JB, Keisch M, **Chen P** and **Vicini FA** (2012). "Initial clinical experience with multilumen brachytherapy catheters for accelerated partial breast irradiation." *Brachytherapy* 11(5): 369-373.

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Department of Radiation Oncology

Department of Internal Medicine

PURPOSE: To review the initial experience of three institutions using multilumen catheters to deliver accelerated partial breast irradiation (APBI) and evaluate dosimetric improvements. METHODS AND MATERIALS: Patients were eligible for this analysis if they met criteria for accelerated partial breast irradiation at their respective institution and were not enrolled on the national Phase III trial. Minimum guidelines for treatment planning from the National Surgical Adjuvant Breast and Bowel Project B-39/Radiation Therapy

Oncology Group 0413 protocol were followed. Toxicities were coded using common toxicity criteria version 3.0 criteria. RESULTS: Sixty-two patients were analyzed as part of this study. Median skin spacing was 11 mm with a median skin dose of 86.9% (% of prescription dose [PD]). Median rib dose was 76.1% of the PD (range, 4.3-155.7%). The V-90, V-95, and V-100 of the PD for the planning target volume evaluation was 95.4%, 95.2%, and 80.3%, respectively. Seven patients had both skin and rib spacing <7 mm, with the median skin dose and rib dose being 113.4% and 130.9% of the PD. For these cases, the median V-90, V-95, and V-100 of the PD was 99.2%, 94.3%, and 81.1%, respectively, whereas the median V-150 and V-200 were 22.5 cc and 7.4 cc. Overall, Grade I and II radiation dermatitis were noted in 41.9% and 6.5% of patients. CONCLUSION: The multilumen device led to improvements in target coverage and normal structure doses compared with traditionally accepted guidelines. Similar toxicities were seen compared with single-lumen devices, even in patients with skin and rib spacing <7 mm. (C) 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Shah C, **Grills IS, Kestin LL**, McGrath S, Ye H, Martin SK and Yan D (2012). "Intrafraction variation of mean tumor position during image-guided hypofractionated stereotactic body radiotherapy for lung cancer." [International Journal of Radiation Oncology, Biology, Physics](#) 82(5): 1636-1641.

[Full-Text](#)

Department of Radiation Oncology

PURPOSE: Prolonged delivery times during daily cone-beam computed tomography (CBCT)-guided lung stereotactic body radiotherapy (SBRT) introduce concerns regarding intrafraction variation (IFV) of the mean target position (MTP). The purpose of this study was to evaluate the magnitude of the IFV-MTP and to assess target margins required to compensate for IFV and postonline CBCT correction residuals. Patient, treatment, and tumor characteristics were analyzed with respect to their impact on IFV-MTP. METHODS AND MATERIALS: A total of 126 patients with 140 tumors underwent 659 fractions of lung SBRT. Dose prescribed was 48 or 60 Gy in 12 Gy fractions. Translational target position correction of the MTP was performed via onboard CBCT. IFV-MTP was measured as the difference in MTP between the postcorrection CBCT and the posttreatment CBCT excluding residual error. RESULTS: IFV-MTP was 0.2 +/- 1.8 mm, 0.1 +/- 1.9 mm, and 0.01 +/- 1.5 mm in the craniocaudal, anteroposterior, and mediolateral dimensions and the IFV-MTP vector was 2.3 +/- 2.1 mm. Treatment time and excursion were found to be significant predictors of IFV-MTP. An IFV-MTP vector greater than 2 and 5 mm was seen in 40.8% and 7.2% of fractions, respectively. IFV-MTP greater than 2 mm was seen in heavier patients with larger excursions and longer treatment times. Significant differences in IFV-MTP were seen between immobilization devices. The stereotactic frame immobilization device was found to be significantly less likely to have an IFV-MTP vector greater than 2 mm compared with the alpha cradle, BodyFIX, and hybrid immobilization devices. CONCLUSIONS: Treatment time and respiratory excursion are significantly associated with IFV-MTP. Significant differences in IFV-MTP were found between immobilization devices. Target margins for IFV-MTP plus post-correction residuals are dependent on immobilization device with 5-mm uniform margins being acceptable for the frame immobilization device.

Shah C, Jones PM, Wallace M, **Kestin LL, Ghilezan M**, Fakhouri M, **Jaiyesimi I**, Ye H, **Martinez A** and **Vicini F** (2012). "Differences in disease presentation, treatment outcomes, and toxicities in african american patients treated with radiation therapy for prostate cancer." [American Journal of Clinical Oncology-Cancer Clinical Trials](#) 35(6): 566-571.

[Full-Text](#)

Department of Radiation Oncology

Department of Internal Medicine

Objectives: We analyzed differences in disease presentation, outcomes, and toxicities between African American (AA) and White (W) men treated with definitive radiation therapy for their prostate cancer. Methods: Three thousand one hundred eighty cases of prostate cancer treated with various radiation modalities at a single institution were reviewed. The cohort consisted of 92% W patients and 8% AA patients. Clinical and pathologic characteristics at presentation, treatment outcomes, and related toxicities were analyzed between the 2 groups. The median follow-up was 6.6 years (0.6 to 22.4 y). Results: At presentation, AA men were younger (P = 7 (47.9% vs. 39.2%, P = 0.006). No difference in the 5 or 10-year rates of

biochemical failure, disease-free survival, or distant metastases were noted. Although there was a trend for improved 10-year overall survival for AA men (65.3% vs. 57.4%, $P = 0.06$), cause-specific survival was significantly improved at 10 years (98.6% vs. 90.6%, $P = 0.002$). Similar findings were seen when controlling for radiation therapy dose, the use of hormonal therapy, and modality of radiation therapy used. Overall, genitourinary/gastrointestinal toxicities were similar regardless of the modality used. Conclusions: Despite differences in presenting characteristics, AA men did not have inferior clinical outcomes but rather improved cause-specific survival when treated with standard of care radiation therapy. Regardless of the treatment modality used, toxicities between AA and W men were comparable.

Shah C, Lanni T, Wilkinson JB, Jawad M, Wobb J, **Berry S**, Wallace M, **Chen P** and **Grills IS** (2012). "Cost-effectiveness of 3-dimensional conformal radiotherapy and applicator-based brachytherapy in the delivery of accelerated partial breast irradiation." *American Journal of Clinical Oncology*. ePub Ahead of Print.

[Full-Text](#)

Department of Obstetrics and Gynecology

Department of Radiation Oncology

PURPOSE:: To compare reimbursement and cost efficacy between accelerated partial breast irradiation (APBI) techniques. **MATERIALS/METHODS::** Four hundred fifty-three patients were treated with APBI using either 3-dimensional conformal radiotherapy (3D-CRT, $n=207$) or balloon-based brachytherapy (BB) [single-lumen (SL, $n=161$) and multilumen (ML, $n=85$)] between March 2000 and October 2011. To evaluate cost-effectiveness, reimbursement by treatment technique was calculated based on 2011 Medicare schedules. Facility costs were generated by technique based on ICD-9 codes. Incremental cost effectiveness ratios (ICER), which compares cost with clinical outcomes, were calculated according to the difference in reimbursement to the criteria being evaluated. **RESULTS::** With a median follow-up of 3.6 years, the 5-year rate of local recurrence was 1.9% for all patients (3D-CRT, 0%; BB, 4.1%; $P=0.23$). When pooled, BB patients had a significant improvement in excellent/good cosmesis (91.6% vs. 80.0%; $P=0.03$). Rates of combined grade 2 or higher dermatitis, hyper/hypopigmentation, pain, or fibrosis per technique were 62%, 28%, and 34% for 3D-CRT, SL, and ML patients, respectively ($P=0.26$). The ICER per percent improved cosmesis for SL/ML was \$519/\$850 based on reimbursement and \$301/\$643 based on cost compared with 3D-CRT. **CONCLUSIONS::** On the basis of ICER, brachytherapy for APBI is a cost-effective option with regard to cosmesis and toxicity. This economic analysis suggests the increased cost of applicator-based brachytherapy may be justified in appropriately selected patients.

Shah C, Lanni TB, Jr., **Ghilezan MI**, **Gustafson GS**, Marvin KS, Ye H, **Vicini FA** and **Martinez AA** (2012). "Brachytherapy provides comparable outcomes and improved cost-effectiveness in the treatment of low/intermediate prostate cancer." *Brachytherapy* 11(6): 441-445.

[Request Form](#)

Department of Radiation Oncology

Department of Internal Medicine

PURPOSE: To evaluate the cost-effectiveness and outcomes of low-dose-rate (LDR) and high-dose-rate (HDR) brachytherapy compared with intensity-modulated radiation therapy (IMRT) in patients with low/intermediate risk of prostate cancer. **METHODS AND MATERIALS:** One thousand three hundred twenty-eight patients with low or intermediate risk of prostate cancer were treated with LDR ($n = 207$), HDR with four fractions ($n = 252$), or IMRT ($n = 869$) between January 1992 and December 2008. LDR patients were treated with palladium seeds to a median dose of 120 Gy, whereas HDR patients were treated to a median dose 38.0 Gy (four fractions). IMRT patients received 42-44 fractions with a median dose of 75.6 Gy. Clinical outcomes were compared, including biochemical failure, cause-specific survival, and overall survival. **RESULTS:** Overall, no differences in 5-year biochemical control (BC) or cause-specific survival were noted among treatment modalities. The calculated reimbursement for LDR brachytherapy, HDR brachytherapy with four fractions, and IMRT was \$9,938; \$17,514; and \$29,356, respectively. HDR and LDR brachytherapy were statistically less costly to Medicare and the institution than IMRT ($p<0.001$), and LDR brachytherapy was less costly than HDR brachytherapy ($p = 0.01$ and $p<0.001$). Incremental cost-effectiveness ratios for cost to Medicare for BC with IMRT were \$4045 and \$2754 per percent of BC for LDR and HDR brachytherapy,

respectively. Incremental cost-effectiveness ratio using institutional cost comparing IMRT with LDR and HDR brachytherapy was \$4962 and \$4824 per 1% improvement in BC. CONCLUSIONS: In this study of patients with low and intermediate risk of prostate cancer, comparable outcomes at 5 years were noted between modalities with increased costs associated with IMRT. (C) 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Shah C, McGee M, Wilkinson JB, Berry S, **Grills I**, Wallace M, Mitchell C and **Vicini F** (2012). "Clinical outcomes using accelerated partial breast irradiation in patients with ductal carcinoma in situ." Clinical Breast Cancer 12(4): 259-263.

[Full-Text](#)

Department of Radiation Oncology

Department of Internal Medicine

Limited data are available on outcomes after accelerated partial breast irradiation (APBI) in women with ductal carcinoma in situ (DCIS). The results of this analysis demonstrate excellent clinical outcomes with a 5-year local recurrence rate of 1.4%, cause-specific survival of 100%, and overall survival (OS) of 94%. Compared with a prospective trial examining excision alone, rates of local recurrence were reduced with APBI in patients with similar pathologic characteristics. Background: Limited data exist on the use of accelerated partial breast irradiation (APBI) in patients with ductal carcinoma in situ (DCIS). The purpose of this analysis was to evaluate clinical outcomes after APBI in patients with DCIS. Patients and Methods: Between December 2002 and December 2010, 99 patients with DCIS underwent APBI as part of their breast-conserving therapy (BCT). Partial breast irradiation techniques included interstitial brachytherapy, balloon-based brachytherapy, and 3-dimensional conformal radiotherapy (3D-CRT). Clinical outcomes including local recurrence, regional recurrence, disease-free survival (DFS), cause-specific survival, and overall survival (OS) were analyzed. Results: Mean follow up was 3.0 years, with a mean patient age of 61.8 years. At 5 years, the rates of local recurrence and regional recurrence were 1.4% and 0%, respectively. Overall survival was 94%, whereas cause-specific survival was 100%. No difference was noted in local control for each treatment technique. When comparing rates using the Eastern Cooperative Oncology Group (ECOG) E-5194 trial groupings, the rate of local recurrence in our cohort was 2.0% for patients with grade I/II disease < 2.5 cm and 0% for grade III < 1.0 cm, representing a 50% and 100% decrease, respectively, in local recurrence compared with excision alone. Conclusions: Patients with DCIS treated with APBI had excellent clinical outcomes regardless of the APBI technique used. Until the publication of prospective phase III trials, these data confirm previous reports highlighting the efficacy of APBI in the treatment of noninvasive carcinoma of the breast.

Shah C, **Vicini F**, Keisch M, Kuerer H, Beitsch P, Haffty B and Lyden M (2012). "Outcome after ipsilateral breast tumor recurrence in patients who receive accelerated partial breast irradiation." Cancer 118(17): 4126-4131.

[Full-Text](#)

Department of Internal Medicine

BACKGROUND: The objective of this study was to examine clinical outcomes and patterns of failure in patients with early stage breast cancer who developed an ipsilateral breast tumor recurrence (IBTR) after breast-conserving therapy (BCT) using accelerated partial breast irradiation (APBI). METHODS: In total, 1440 patients (1449 tumors) with early stage breast cancer who underwent BCT were treated with the MammoSite device to deliver APBI (34 Gray [Gy] in 3.4-Gy fractions). One thousand two hundred fifty-five patients (87%) had invasive breast cancer (IBC) (median tumor size, 10 mm), and 194 patients (13%) had ductal carcinoma in situ (DCIS) (median tumor size, 8 mm). The median follow-up was 60 months. RESULTS: Fifty patients (3.5%) developed an IBTR for a 5-year actuarial rate of 3.61% (3.65% for IBC and 3.36% for DCIS). It was determined that 36 recurrences (72%) represented new primary cancers, and 14 recurrences (28%) represented recurrences of the index lesion. Of the 32 recurrences with known histology, 78% were IBC, and 22% were DCIS. After IBTR, 28 of 38 patients (74%) underwent salvage mastectomy, and 9 of 38 patients (26%) had a second attempt at BCT. Adjuvant therapies included tamoxifen in 8 patients (16%) and systemic chemotherapy in 6 patients (12%). The 3-year rates of disease-free survival, cause-specific survival, and overall survival after IBTR were 58.7%, 92.1%, and 80.5%, respectively. CONCLUSIONS: With 5 years of

follow-up, APBI produced clinical outcomes and patterns of failure comparable to those achieved with whole breast irradiation. Patients who developed an IBTR after APBI had excellent 3-year survival outcomes after salvage treatments. Cancer 2012. (c) 2012 American Cancer Society.

Shah C, Wilkinson JB, Baschnagel A, **Ghilezan M, Riutta J, Dekhne N, Balaraman S**, Mitchell C, Wallace M and **Vicini F** (2012). "Factors associated with the development of breast cancer-related lymphedema after whole-breast irradiation." International Journal of Radiation Oncology Biology Physics 83(4): 1095-1100.

[Full-Text](#)

Department of Radiation Oncology

Department of Physical Medicine and Rehabilitation

Department of Surgery

Department of Internal Medicine

Purpose: To determine the rates of breast cancer-related lymphedema (BCRL) in patients undergoing whole-breast irradiation as part of breast-conserving therapy (BCT) and to identify clinical, pathologic, and treatment factors associated with its development. Methods and Materials: A total of 1,861 patients with breast cancer were treated at William Beaumont Hospital with whole-breast irradiation as part of their BCT from January 1980 to February 2006, with 1,497 patients available for analysis. Determination of BCRL was based on clinical assessment. Differences in clinical, pathologic, and treatment characteristics between patients with BCRL and those without BCRL were evaluated, and the actuarial rates of BCRL by regional irradiation technique were determined. Results: The actuarial rate of any BCRL was 7.4% for the entire cohort and 9.9%, 14.7%, and 8.3% for patients receiving a supraclavicular field, posterior axillary boost, and internal mammary irradiation, respectively. BCRL was more likely to develop in patients with advanced nodal status (11.4% vs. 6.3%, $p = 0.001$), those who had a greater number of lymph nodes removed (14 nodes) (9.5% vs. 6.0%, $p = 0.01$), those who had extracapsular extension (13.4% vs. 6.9%, $p = 0.009$), those with Grade II/III disease (10.8% vs. 2.9%, $p < 0.001$), and those who received adjuvant chemotherapy (10.5% vs. 6.7%, $p = 0.02$). Regional irradiation showed small increases in the rates of BCRL ($p =$ not significant). Conclusions: These results suggest that clinically detectable BCRL will develop after traditional BCT in up to 10% of patients. High-risk subgroups include patients with advanced nodal status, those with more nodes removed, and those who receive chemotherapy, with patients receiving regional irradiation showing a trend toward increased rates. (C) 2012 Elsevier Inc.

Shah C, Wilkinson JB, Lyden M, Beitsch P and **Vicini FA** (2012). "Predictors of local recurrence following accelerated partial breast irradiation: a pooled analysis." International Journal of Radiation Oncology Biology Physics 82(5): E825-E830.

[Full-Text](#)

Department of Internal Medicine

Purpose: To analyze a pooled set of nearly 2,000 patients treated on the American Society of Breast Surgeons (ASBS) Mammosite Registry Trial and at William Beaumont Hospital (WBH) to identify factors associated with local recurrence following accelerated partial breast irradiation (APBI). Methods and Materials: A total of 1,961 women underwent partial breast irradiation between April 1993 and November 2010 as part of the ASBS Registry Trial or at WBH. Rates of ipsilateral breast tumor recurrence (IBTR), regional recurrence (RR), distant metastases (DM), disease-free survival (DFS), cause-specific survival (CSS), and overall survival (OS) were analyzed for each group and for the pooled cohort. Clinical, pathologic, and treatment-related variables were analyzed including age, tumor stage/size, estrogen receptor status, surgical margins, and lymph node status to determine their association with IBTR. Results: The two groups were similar, but WBH patients were more frequently node positive, had positive margins, and were less likely to be within the American Society for Radiation Oncology-unsuitable group. At 5 years, the rates of IBTR, RR, DM, DFS, CSS, and OS for the pooled group of patients were 2.9%, 0.5%, 2.4%, 89.1%, 98.5%, and 91.8%, respectively. The 5-year rate of true recurrence/marginal miss was 0.8%. Univariate analysis of IBTR found that negative estrogen receptor status (odds ratio [OR], 2.83, 95% confidence interval 1.55 -5.13, $p = 0.0007$) was the only factor significantly associated with IBTR, while a trend was seen for age less than 50 (OR 1.80, 95% confidence interval 0.90-3.58, $p = 0.10$). Conclusions: Excellent 5-year outcomes were seen following APBI in over 1,900 patients. Estrogen

receptor negativity was the only factor associated with IBTR, while a trend for age less than 50 was noted. Significant differences in factors associated with IBTR were noted between cohorts, suggesting that factors driving IBTR may be predicated based on the risk stratification of the patients being treated. (C) 2012 Elsevier Inc.

Shah C, Wilkinson JB, Lyden M, Mbah A, Keisch M, Beitsch P and **Vicini FA** (2012). "Comparison of survival and regional failure between accelerated partial breast irradiation and whole breast irradiation." Brachytherapy 11(4): 311-315.

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Department of Internal Medicine

PURPOSE: To compare rates of regional recurrence (RR) and overall survival (OS) between a pooled set of 1400 patients treated on the American Society of Breast Surgeons MammoSite (Hologic, Inc., Bedford, MA) Registry Trial to a cohort of 3600 patients treated with whole breast irradiation (WBI). **METHODS AND MATERIALS:** A total of 1440 women underwent accelerated partial breast irradiation (APBI) between 2002 and 2004 as part of the American Society of Breast Surgeons Registry Trial and a total of 3593 patients who received WBI were evaluated from the Surveillance Epidemiology and End Results database with treatment received between 1980 and 2009. A matched-pair analysis was performed based on age, receipt of hormonal therapy, chemotherapy, nodal status, and tumor size (1051 patients per arm). Rates of RR and OS were then analyzed for each group. **RESULTS:** After the match, no differences in patient characteristics were noted when tumor size was evaluated as a continuous variable. Rates of RR and OS were similar between the WBI and APBI groups. A Cox regression model found no difference between WBI and APBI with regard to RR; however, OS was improved in the APBI cohort (hazard ratio 0.008, $p < 0.0001$). **CONCLUSIONS:** With one of the largest patient populations to date comparing WBI and APBI, no difference in RR or OS was noted between WBI and APBI treatment. Until the publication of prospective Phase III trials, these data support the continued use of APBI on protocol and off protocol in appropriately selected patients. (C) 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Shah C, Wilkinson JB, Shaitelman S, **Grills IS, Chen PY, Dekhne N, Jaiyesimi I**, Wallace M, Mitchell CK and **Vicini FA** (2012). "Impact of lymph node status on clinical outcomes after accelerated partial breast irradiation." International Journal of Radiation Oncology Biology Physics 82(3): E409-E414.

[Full-Text](#)

Department of Radiation Oncology

Department of Surgery

Department of Internal Medicine

Purpose: To compare outcomes after accelerated partial breast irradiation (APBI) between node-negative and node-positive patients. **Methods and Materials:** A total of 534 patients with early-stage breast cancer received APBI including 39 node-positive (N+) cases. Clinical, pathologic, and treatment-related factors were compared between node-negative (Ne) and N+ cohorts. Local recurrence (LR), regional recurrence (RR), axillary failure (AF), distant metastases (DM), disease-free survival (DFS), causespecific survival (CSS), and overall survival (OS) were analyzed. **Results:** N+ patients were younger ($p = 0.04$), had larger tumors ($p < 0.001$), and were more likely to receive chemotherapy ($p < 0.001$). Mean follow-up was 7.8 years for N+ patients and 6.3 years for Ne patients ($p = 0.06$). No differences were seen in 5-year actuarial rates of LR (2.2% vs. 2.6%, $p = 0.86$), AF (0% vs. 0%, $p = 0.69$), DFS (90.0% vs. 88.0%, $p = 0.79$), or OS (91.0 vs. 84.0%, $p = 0.65$) between the two groups, whereas higher rates of RR (0% vs. 6.1%, $p < 0.001$) and DM (2.2% vs. 8.9%, $p = 0.005$) were noted in N+ patients. A trend for improved CSS ($p = 0.06$), was seen in Ne patients. Age, tumor size, receptor status, T-stage, chemotherapy, APBI technique, and nodal status ($p = 0.86$) were not associated with LR, while a trend for an association with LR was noted with close/positive margins, ($p = 0.07$), and failure to receive adjuvant hormonal therapy ($p = 0.06$). **Conclusions:** No differences were seen in the rates of LR or AF between N- and N+ patients after APBI. These results support the continued enrollment of node-positive patients in Phase III trials evaluating the efficacy of APBI including the National Surgical Adjuvant Breast and Bowel Project-B39/Radiation Therapy Oncology Group 0413. (C) 2012 Elsevier Inc.

Shah C, Wobb J, **Grills I**, Wallace M, Mitchell C and **Vicini FA** (2012). "Use of intensity modulated radiation therapy to reduce acute and chronic toxicities of breast cancer patients treated with traditional and accelerated whole breast irradiation." Practical Radiation Oncology 2(4): e45-e51.

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Department of Radiation Oncology

Department of Internal Medicine

Purpose: The purpose of this analysis was to examine the impact of applying intensity modulated radiation therapy (IMRT) on toxicity with traditional and accelerated whole breast irradiation (AWBI). **Methods and Materials:** A total of 335 patients with stage 0-IIb breast cancer were treated with either a conventional wedge technique (S-WBI, n = 87), IMRT (I-WBI, n = 93), or AWBI with IMRT (I-AWBI, n = 155). S-WBI and I-WBI patients received a median dose of 45 Gy to the breast with a median 16-Gy tumor bed boost for a cumulative median dose of 61 Gy. I-AWBI patients received a median dose of 42.56 Gy via an accelerated IMRT plan, without a boost. Acute and chronic toxicities were assessed using Common Toxicity Criteria v.3.0. **Results:** Median follow-up was 11.0, 9.1, and 1.1 years for S-WBI, I-WBI, and I-AWBI patients, respectively. When comparing patients of all breast sizes, I-WBI showed decreased incidences of grade 2+ acute radiation dermatitis and induration compared with I-AWBI (1% vs 23%, $P < .001$ /0% vs 5%; $P = .05$) and S-WBI (1% vs 12%, $P = .007$ /0% vs 6%; $P = .02$). I-WBI also had lower rates of chronic edema compared with S-WBI patients (3% vs 13%, $P = .03$). In larger breasted patients, I-WBI was associated with reduced acute toxicities compared with S-WBI with regard to grade 2 + dermatitis and edema (0% vs 19%, $P = .02$ /7% vs 24%, $P = .06$). No differences were seen between I-WBI and I-AWBI with IMRT techniques with the exception of increased acute radiation dermatitis in I-AWBI patients (0% vs 38%, $P < .001$). **Conclusions:** This analysis confirms previous data which have demonstrated that RT with IMRT is associated with reduced toxicities compared with conventional techniques. In larger breasted women, with the exception of acute skin reactions, I-AWBI showed comparable rates of toxicities compared with I-WBI. These data support the use of IMRT to expand the role of AWBI and the currently accruing Radiation Therapy Oncology Group 1005 trial. © 2012 American Society for Radiation Oncology.

Shaitelman SF, **Vicini FA**, **Grills IS**, **Martinez AA**, Yan D and Kim LH (2012). "Differences in effective target volume between various techniques of accelerated partial breast irradiation." International Journal of Radiation Oncology, Biology, Physics 82(1): 30-36.

[Full-Text](#)

Department of Internal Medicine

Department of Radiation Oncology

PURPOSE: Different cavity expansions are used to define the clinical target volume (CTV) for accelerated partial breast irradiation (APBI) delivered via balloon brachytherapy (1 cm) vs. three-dimensional conformal radiotherapy (3D-CRT) (1.5 cm). Previous studies have argued that the CTVs generated by these different margins are effectively equivalent. In this study, we use deformable registration to assess the effective CTV treated by balloon brachytherapy on clinically representative 3D-CRT planning images. **METHODS AND MATERIALS:** Ten patients previously treated with the MammoSite were studied. Each patient had two computed tomography (CT) scans, one acquired before and one after balloon implantation. In-house deformable registration software was used to deform the MammoSite CTV onto the balloonless CT set. The deformed CTV was validated using anatomical landmarks common to both CT scans. **RESULTS:** The effective CTV treated by the MammoSite was on average 7% +/- 10% larger and 38% +/- 4% smaller than 3D-CRT CTVs created using uniform expansions of 1 and 1.5 cm, respectively. The average effective CTV margin was 1.0 cm, the same as the actual MammoSite CTV margin. However, the effective CTV margin was nonuniform and could range from 5 to 15 mm in any given direction. Effective margins <1 cm were attributable to poor cavity-balloon conformance. Balloon size relative to the cavity did not significantly correlate with the effective margin. **CONCLUSION:** In this study, the 1.0-cm MammoSite CTV margin treated an effective volume that was significantly smaller than the 3D-CRT CTV based on a 1.5-cm margin.

Shannon FL, Fazzalari FL, Theurer PF, Bell GF, Sutcliffe KM and Prager RL (2012). "A method to evaluate cardiac surgery mortality: phase of care mortality analysis." Annals of Thoracic Surgery 93(1): 36-43; discussion 43.

[Request Form](#)

Department of Surgery

BACKGROUND: This is a study of a method of mortality review, adopted by the Michigan Society of Thoracic and Cardiovascular Surgeons, to enhance understanding of mortality and potentially avoidable deaths after cardiac surgery, utilizing a voluntary statewide database. **METHODS:** A system to categorize mortality was developed utilizing a phase of care mortality analysis approach as well as providing criteria to classify mortality as potentially "avoidable." For each mortality, the operating surgeon categorized a cardiac surgery mortality trigger into 1 of 5 time frames: preoperative, intraoperative, intensive care unit (ICU), postoperative floor, and discharge. **RESULTS:** A total of 53,674 adult cardiac operations were performed from January 1, 2006 to June 30, 2010 with a crude mortality of 3.5% (1,905 of 53,674). Of the mortalities analyzed, 35% (618 of 1,780) were preoperative, 25% (451 of 1,780) were ICU, 19% (333 of 1,780) were intraoperative, 11% (198 of 1,780) were floor, and 10% (180 of 1,780) were discharge phase. "Avoidable" mortality triggers occurred in 53% (174 of 333) of the intraoperative, 41% (253 of 618) and (184 of 451) of the preoperative and ICU phases, 42% (83 of 198) of the floor, and 19% (35 of 180) of the discharge phase. Overall potentially avoidable mortality was 41% (729 of 1780). Thirty-six percent (644 of 1,780) of the mortalities were coronary artery bypass grafting patients and 29% (188 of 644) of these were in the preoperative phase, with a mean predicted risk of 16%. **CONCLUSIONS:** This analysis identifies the occurrence of potentially avoidable mortalities in the 4 hospital phases of care, with the largest absolute number of avoidable mortalities occurring in the preoperative phase. A focus on these phases of care provides significant opportunity for quality improvement initiatives. Utilizing phase of care mortality analysis stimulates surgeons and hospitals to develop and refine mortality reviews and provides a structured statewide platform for discussion, education, quality improvement, and enhanced outcomes.

Shaw LJ, Hausleiter J, Achenbach S, Al-Mallah M, Berman DS, Budoff MJ, Cademartiri F, Callister TQ, Chang HJ, Kim YJ, Cheng VY, Chow BJ, Cury RC, Delago AJ, Dunning AL, Feuchtner GM, Hadamitzky M, Karlsberg RP, Kaufmann PA, Leipsic J, Lin FY, **Chinnaiyan KM**, Maffei E, **Raff GL**, Villines TC, Labounty T, Gomez MJ and Min JK (2012). "Coronary computed tomographic angiography as a gatekeeper to invasive diagnostic and surgical procedures: results from the multicenter CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: an International Multicenter) registry." Journal of the American College of Cardiology 60(20): 2103-2114.

[Full-Text](#)

Department of Internal Medicine

OBJECTIVES: This study sought to examine patterns of follow-up invasive coronary angiography (ICA) and revascularization (REV) after coronary computed tomography angiography (CCTA). **BACKGROUND:** CCTA is a noninvasive test that permits direct visualization of the extent and severity of coronary artery disease (CAD). Post-CCTA patterns of follow-up ICA and REV are incompletely defined. **METHODS:** We examined 15,207 intermediate likelihood patients from 8 sites in 6 countries; these patients were without known CAD, underwent CCTA, and were followed up for 2.3 +/- 1.2 years for all-cause mortality. Coronary artery stenosis was judged as obstructive when $\geq 50\%$ stenosis was present. A multivariable logistic regression was used to estimate ICA use. A Cox proportional hazards model was used to estimate all-cause mortality. **RESULTS:** During follow-up, ICA rates for patients with no CAD to mild CAD according to CCTA were low (2.5% and 8.3%), with similarly low rates of REV (0.3% and 2.5%). Most ICA procedures (79%) occurred ≤ 3 months of CCTA. Obstructive CAD was associated with higher rates of ICA and REV for 1-vessel (44.3% and 28.0%), 2-vessel (53.3% and 43.6%), and 3-vessel (69.4% and 66.8%) CAD, respectively. For patients with $< 50\%$ stenosis, early ICA rates were elevated; over the entirety of follow-up, predictors of ICA were mild left main, mild proximal CAD, respectively, or higher coronary calcium scores. In patients with $< 50\%$ stenosis, the relative hazard for death was 2.2 ($p = 0.011$) for ICA versus no ICA. Conversely, for patients with CAD, the relative hazard for death was 0.61 for ICA versus no ICA ($p = 0.047$). **CONCLUSIONS:** These findings support the concept that CCTA may be used effectively as a gatekeeper to ICA.

Silbergleit AK, Lewitt P, Junn F, Schultz LR, Collins D, Beardsley T, Hubert M, **Trosch R** and Schwalb JM (2012). "Comparison of dysphagia before and after deep brain stimulation in Parkinson's disease." Movement Disorders 27(14): 1763-1768.

[Full-Text](#)

Department of Internal Medicine

Although dysphagia is a common problem for many Parkinson's disease (PD) patients, the effect of deep brain stimulation (DBS) on swallowing is unclear. Fourteen subjects with advanced PD underwent videofluorographic swallowing studies prior to bilateral DBS of the subthalamic nucleus (STN) and at 3 and 12 months postprocedure. They were tested under several stimulation and medication conditions. Subjects completed the Dysphagia Handicap Index at each time. There was a strong trend toward improved swallowing response for solid intake in the medication-free condition with the stimulator on compared with the stimulator off ($P = .0107$). Also, there was a trend toward improved oral preparation of thin liquids ($P = .0368$) in the medication-free condition when the stimulator was on versus off 12 months later. The remaining swallowing parameters showed no change or worsening of swallowing function regardless of stimulator or medication status. Results of the Dysphagia Handicap Index revealed significant improvement in subject self-perception of swallowing 3 and 12 months following the procedure compared with baseline on the functional subscale ($P = .020$ and $P = .010$, respectively), the emotional subscale ($P = .013$ and $P = .003$, respectively), and the total score ($P = .025$ and $P = .003$, respectively). These data suggest that bilateral STN-DBS does not substantively impair swallowing in PD. In addition, it may improve motor sequencing of the oropharyngeal swallow for solid consistencies (which are known to provide increased sensory feedback to assist motor planning of the oropharyngeal swallow). Subjects with advanced PD who are undergoing DBS may perceive significant improvement in swallowing ability despite the lack of objective improvements in swallowing function. © 2012 Movement Disorder Society.

Silberstein EB, Alavi A, **Balon HR**, Clarke SE, Divgi C, Gelfand MJ, Goldsmith SJ, Jadvar H, Marcus CS, Martin WH, Parker JA, Royal HD, Sarkar SD, Stabin M and Waxman AD (2012). "The SNMMI practice guideline for therapy of thyroid disease with ^{131}I 3.0." Journal of Nuclear Medicine 53(10): 1633-1651.

[Full-Text](#)

Department of Internal Medicine

Sirls LT, Tennstedt S, Lukacz E, Rickey L, Kraus SR, Markland AD, Kenton K, Moalli P, Hsu Y, Huang L and Stoddard AM (2012). "Condition-specific quality of life 24 months after retropubic and transobturator sling surgery for stress urinary incontinence." Female Pelvic Medicine & Reconstructive Surgery 18(5): 291-295.

[Full-Text](#)

Department of Urology

AIMS: To compare quality of life (QoL) and factors associated with QoL change after retropubic (RMUS) and transobturator midurethral slings (TMUS) using the Incontinence Impact Questionnaire (IIQ) and the International Consultation on Incontinence Questionnaire (ICIQ). **METHODS:** Five hundred ninety-seven women in a multicenter randomized trial of RMUS versus TMUS were examined. The IIQ and the ICIQ were obtained at baseline and at 12 and 24 months. Repeated-measures analysis of variance tested for differences by treatment group over time. Multivariable analysis identified factors associated with QoL change at 12 months postoperative, controlling for treatment group and baseline QoL. **RESULTS:** Improvement in IIQ was associated with the following: treatment success, younger age, improvement in stress urinary incontinence (SUI) symptom severity, and bother (all $P < 0.05$). Improvement in ICIQ was associated with treatment success, younger age, improvement in SUI symptom severity and bother, lower body mass index, and no reoperation (all $P < 0.05$). Improvement of the IIQ was stable over time ($P = 0.35$) for both treatment groups ($P = 0.66$), whereas the ICIQ showed a small but clinically insignificant decline ($P = 0.03$) in both treatment groups ($P = 0.51$). **CONCLUSIONS:** Postoperative QoL was improved after RMUS and TMUS. Measures of QoL functioned similarly, although more surgically modifiable urinary incontinence factors predicted improvement with the IIQ.

Slocum NK, Grossman PM, Moscucci M, Smith DE, Aronow HD, **Dixon SR**, Share D and Gurm HS (2012). "The changing definition of contrast-induced nephropathy and its clinical implications: Insights from the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2)." [American Heart Journal](#) 163(5): 829-834.

[Full-Text](#)

Department of Internal Medicine

Background: The traditional definition of contrast-induced nephropathy (CIN) has been an absolute rise of serum creatinine (Cr) of ≥ 0.5 mg/dL, although most recent clinical trials have included a $\geq 25\%$ increase from baseline Cr. The clinical implication of this definition change remains unknown. Methods and Results: We compared the association of the two definitions with risk of death or need for dialysis among 58,957 patients undergoing percutaneous coronary intervention in 2007 to 2008 in a large collaborative registry. Patients with a preexisting history of renal failure requiring dialysis were excluded. Contrast-induced nephropathy as defined by a rise in Cr ≥ 0.5 mg/dL (CIN Traditional) developed in 1,601, whereas CIN defined either as Cr ≥ 0.5 mg/dL or $\geq 25\%$ increase in baseline Cr (CIN New) developed in 4,308 patients. Patients meeting the definition of CIN New but not CIN Traditional were classified as CIN Incremental (n = 2,707). Compared with CIN New, CIN Traditional was more commonly seen in patients with abnormal renal function, which was more likely to develop in patients with normal renal function at baseline. Compared with CIN Incremental, patients meeting the definition of CIN Traditional were more likely to die (16.7% vs 1.7%) and require in-hospital dialysis (9.8% vs 0%). Conclusions: Our data suggest that the traditional definition of CIN (a rise in Cr of ≥ 0.5 mg/dL) in patients undergoing PCI is superior to $\geq 25\%$ increase in Cr at identifying patients at greater risk for adverse renal and cardiac events. © 2012 Mosby, Inc.

Smorgick Y, Settecerri JJ, Baker KC, Herkowitz HN, Fischgrund JS and Zaltz I (2012). "Spinal cord position in adolescent idiopathic scoliosis." [Journal of Pediatric Orthopedics](#) 32(5): 500-503.

[Full-Text](#)

Department of Surgery

Department of Orthopaedic Surgery

BACKGROUND: The use of thoracic pedicle screws in deformity surgery provides a stable fixation system. The concept of acceptably positioned screws includes a worrisome subset of screws that perforate the medial pedicle cortex and may result in some compromise of the spinal canal. A significant higher incidence of cortical wall penetration on the concave side compared with the convex was previously found. Although several authors assumed that the spinal cord hugs the concave pedicles when the spinal deformity is scoliosis, the position of spinal cord in adolescent idiopathic scoliosis (AIS) has not been studied in depth. METHODS: We reviewed 45 patients who were candidate for operative treatment for AIS between August 2007 and October 2010 at our institution. Posteroanterior and lateral 3-ft standing preoperative radiographs of the spine were reviewed to determine: Cobb angle of the thoracic curves, apex vertebra of the curves, and end vertebrae of the curves. Magnetic resonance images were retrospectively reviewed. The lateral cord space (LCS) ratio, which reflects the relative position of the spinal cord in the spinal canal, was calculated for each level with a thoracic curve. RESULTS: The average LCS for thoracic curves of >50 degrees was 2.123. The average LCS for thoracic curves of <50 degrees was 1.551 (P=0.002). The LCS for the apex vertebra was 1.699. The LCS for the upper end vertebra and lower end vertebra were 1.212, 1.225, respectively (P<0.001). There was a statistically significant difference between right thoracic curves and left thoracic curve regarding the LCS. In right thoracic curve the LCS was 1.487 (1.487+0.45) while in left thoracic curve it was 0.761 (0.761+0.17) meaning that in both curves the spinal cord moved to the concave side of the curve. CONCLUSIONS: Our study confirms that spinal cord in AIS tend to follow the appearance of the curve with its being tethered on the concave side. The spinal cord is close to the pedicle around the apex area.

Smouha E and **Bojrab D** (2012). [Cholesteatoma](#). New York, Thieme Medical Publishers.

[Full-Text](#)

Department of Internal Medicine

Smythe MA, Koerber JM, Mehta TP, **Forsyth LL**, Conger E, Corbets LR and Mattson JC (2012). "Assessing the impact of a heparin-induced thrombocytopenia protocol on patient management, outcomes and cost." [Thrombosis and Haemostasis](#) 108(5): 992-998.

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Department of Biomedical Sciences

Establishing the diagnosis of heparin induced thrombocytopenia (HIT) is challenging as laboratory tests for HIT vary in specificity and availability. As HIT suspicion far exceeds confirmation of diagnosis, overtreatment is an emerging concern. This pilot study evaluated the impact of a HIT Recognition and Management Protocol on direct thrombin inhibitor (DTI) prescribing, outcomes, and cost. The primary endpoint was DTI cessation within 12 hours of receipt of negative HIT serology. An observational cohort study using a pre-post design was performed. Sixty-one patients were in the pre-period (before implementation) and 46 in the post-period (after implementation). DTI therapy was discontinued within 12 hours of negative serology in 19.4% of pre-period patients compared to 40% of post-period patients, $p=.058$. DTI therapy was discontinued within 24 hours of receipt of a negative PF4/heparin ELISA more often in the post-period ; 7/23 (30.4%) pre-period patients versus 16/26 (61.5%) post-period patients, $p <0.05$. Protocol implementation resulted in a significant improvement in timely initiation of DTI therapy (within 12 hours of HIT antibody testing) in those with a moderate to high suspicion of HIT; 8/31 (25.8%) of pre-period patients versus 24/31 (77.4%) of post-period patients, $p <0.0001$. Thrombotic events occurred in significantly more patients in the pre-period as compared to the post-period; 21/61 (34.4%) versus 6/46 (13%), respectively, $p = 0.01$. Major bleeding was reduced by 6.6 % after protocol implementation. The projected annual cost savings from decreased inappropriate DTI use was over \$450,000. Protocol implementation had a positive impact on DTI prescribing, outcomes and cost.

Smythe MA, Mehta TP, Koerber JM, **Forsyth LL**, **Sykes E**, Corbets LR, Melendy SM and **Parikh R** (2012). "Development and implementation of a comprehensive heparin-induced thrombocytopenia recognition and management protocol." [American Journal of Health-System Pharmacy : AJHP](#) 69(3): 241-248.

[Full-Text](#)

Department of Biomedical Sciences

Department of Pathology

Department of Internal Medicine

PURPOSE: A quality initiative to improve the management of heparin-induced thrombocytopenia (HIT) at an academic medical center, including the development of guidelines on the use of direct thrombin inhibitors (DTIs), is described. SUMMARY: In keeping with the Joint Commission's National Patient Safety Goal (NPSG) for anticoagulant therapy (goal 03.05.01), a multidisciplinary working group conducted a needs assessment to identify areas for improvement in the center's HIT management practices, particularly the use of DTI therapy (an issue not specifically addressed by NPSG 03.05.01). The resulting action steps included (1) the implementation of a detailed protocol for the recognition and management of HIT, as well as guidelines on the use of the DTIs argatroban and lepirudin, (2) more efficient use and optimized documentation of initial and confirmatory tests in the electronic medical record (EMR), and (3) the education of pharmacists, nurses, and physicians on the use of the HIT protocol, with initial and ongoing case-based competency testing of pharmacy staff. Early postimplementation experience indicated that the protocol and associated activities have resulted in improved DTI prescribing and dosing, HIT documentation, and patient education practices while expanding pharmacists' involvement in ensuring optimal, cost-effective management of patients with HIT. CONCLUSION: In one institution, an HIT working group extended the scope of NPSG 03.05.01 to include the parenteral DTIs. The implementation of the HIT protocol has resulted in greater compliance with appropriate DTI dosing and improved EMR documentation of HIT.

Staskin DR, **Peters KM**, MacDiarmid S, Shore N and De Groat WC (2012). "Percutaneous tibial nerve stimulation: A clinically and cost effective addition to the overactive bladder algorithm of care." [Current Urology Reports](#) 13(5): 327-334.

[Full-Text](#)

Department of Urology

Last Updated: Dec 11, 2013

Overactive bladder affects millions of adults, with profound personal and economic costs. Although antimuscarinic drugs can cause a reduction in voiding symptoms, the effect is modest, and many patients are intolerant of the side effects, or do not experience sufficient relief. For these patients, the modulation of bladder reflex pathways via percutaneous tibial nerve stimulation (PTNS) or via implanted sacral nerve stimulation (SNS) has been acknowledged as a logical next step in the algorithm of care. This review examines the mechanism of action, the relative benefits, adverse effects, and costs of percutaneous nerve stimulation compared to other treatment modalities. © The Author(s) 2012. This article is published with open access at Springerlink.com.

Stefaniak J, Baaki J and Blake AM (2012). "An examination of the decision-making process used by organizational leaders during the great recession." *Performance Improvement Quarterly* 24(4): 81-102.

[Full-Text](#)

Department of Medical Education

This exploratory qualitative study examines the decision-making processes that organizational leaders used during the recent economic crisis. Specifically, it analyzes whether leaders used a discovery process ("thinking first") or an idea-imposition process ("seeing first") to make decisions. In addition, the study examines whether leaders chose ready-made solutions or developed custom solutions in response to the decisions that they made. Contrary to the results that were anticipated based on the decision-making literature, research revealed that a majority of organizational leaders used an idea-imposition process during the economic crisis, and leaders were evenly divided between ready-made and custom solutions. © 2012 International Society for Performance Improvement.

Stefaniak J, Wunderlich T, Szura J, Beres J and Joyce B (2012). "Use of a facilitated debriefing to enhance reflective practice during a partners in care home visit (iCollaborative)." from

<https://www.mededportal.org/icollaborative/resource/588>

[Full-Text](#)

Department of Medical Education

Department of Biomedical Sciences

The Partners in Care longitudinal program was designed for first-year medical (M1) and second-year nursing students (N2) to work together on a home visit with an older adult in the community. Afterwards, a facilitated debriefing exercise was conducted, aimed at fostering self-reflection and deepening students' appreciation of interprofessional teamwork. This facilitated debriefing, coupled with reflective writing, provided an opportunity for students to reflect upon observations made during their visit with older adults and the implications that homecare could have on their medical career.

Stevenson D, **Maisels M** and Watchko J, Eds. (2012). *Care of the Jaundiced Neonate*. New York, McGraw Hill.

[Request Form](#)

Department of Pediatrics

Sylvester P, **Gould D** and Lee L (2012). "The cranial nerves and foramina: a visual recall device." from

<https://www.mededportal.org/publication/9244>

[Full-Text](#)

Department of Biomedical Sciences

The cogent, PDF file containing 27 slides of the diagram- and image-based learning resource on cranial nerves and skull foramina was created for use by faculty members, students and residents in the medicine and allied health fields as a concise, yet comprehensive review. Cranial nerve anatomy is a traditionally complicated subject, commonly requiring visual aids in addition to gross dissection, students often have a difficult time mastering the content. Furthermore, there is a limited amount of ancillary resources with images and/or diagrams to help students learn the material with efficiency. To that end, we have developed a diagram- and image-based 'recall device', a resource for learning the anatomy of the cranial nerves and

associated skull foramina. Students and instructors can utilize the resource to teach and learn about cranial nerve orientation and their relationship to the ventral surface of the brain and to the skull floor and foramina. Instructors are recommended to use the resource as formal or informal course content to provide a concise overview of cranial nerve anatomy. The resource is also an ideal ancillary learning and review tool that may be used outside of class at any time and any place. Additionally, all original images and diagrams provided in the PDF file may be adapted for use in a variety of educational settings to increase discussion, instructional efficiency and to foster a comprehensive review.

Szela J and Band J (2012). Infections associated with peritoneal dialysis, in Mayhall G. (ed). Hospital Epidemiology and Infection Control: Lippincott Williams & Wilkins: 957-966.

[Request Form](#)

Department of Internal Medicine

Tawil G, Akl FA, Dagher MF, Karam W, **Hajj Hussein I**, Leone A and Jurjus AR (2012). "Prevalence of IL-1B +3954 and IL-1A-889 polymorphism in the Lebanese population and its association with the severity of adult chronic periodontitis." Journal of Biological Regulators & Homoestatic Agents 26(4): 597-606.

[Request Form](#)

Department of Biomedical Sciences

Pro-inflammatory cytokines, i.e., IL-1 mediate the inflammatory response and are genetically regulated in periodontal diseases. Strong association was found between the composite genotype allele 2 of IL-1 β +3954 and IL-1 α -889 and severe chronic periodontitis. The aim of this study is to determine the prevalence of IL-1 β +3954 and IL-1 α -889 polymorphism in a group of Lebanese individuals of homogeneous ethnicity and the possible association between genotype positive individuals and the severity of periodontal disease. One hundred and fifty-seven patients aged 53.29 \pm 13.13 years participated in the study. Subjects were classified as follows: 1) healthy subjects with no attachment loss >1mm and no clinical signs of gingival or periodontal inflammation; 2) diseased subjects with mild periodontitis (less than 15% of global periodontal bone loss); 3) subjects with moderate periodontitis (less than 4 interproximal sites with bone loss = or >50% and mean bone loss between 15 and 30%); 4) subjects with severe periodontitis (more than 7 interproximal sites with >50% bone loss and mean bone loss >35%). Blood samples were taken and analyzed for polymorphism in the IL-1 α gene at position +4845 and in the IL-1 β gene at position +3953. Statistical analysis was performed using chi-square test, Fisher Exact test, and ANOVA followed by Bonferroni multiple comparisons. The prevalence of genotype-positive subjects was 52.3% in the healthy control group and 42 % in the diseased group. Positive genotype heterozygous of allele 1 and 2 for IL-1 β +3954 and IL-1 α -889 did not represent in this study a major risk for chronic periodontitis (p=0.590). Only subjects homozygous for allele2 of the IL-1 β +3954 and IL-1 α -889 were significantly more at risk for severe periodontitis with OR of 51.42.

Thurber CA and **Walton EA** (2012). "Homesickness and adjustment in university students." Journal of American College Health 60(5): 415-419.

[Full-Text](#)

Department of Pediatrics

The transition to college or university can be an exciting new experience for many young adults. For some, intense homesickness can make this move difficult, even unsustainable. Homesickness—defined as the distress or impairment caused by an actual or anticipated separation from home—carries the unique hallmark of preoccupying thoughts of home and attachment objects. Sufferers typically report depression and anxiety, withdrawn behavior, and difficulty focusing on topics unrelated to home. For domestic and international university students, intense homesickness is particularly problematic. It can exacerbate preexisting mood and anxiety disorders, precipitate new mental and physical health problems, and sometimes lead to withdrawal from school. New research, consolidated here for the first time, points to promising prevention and treatment strategies for homesick students, the result of which can be a healthy, gratifying, and productive educational experience.

Tonlaar N, Wilkinson JB, **Brabbins DS**, Dilworth JT, Ye H, Wallace M, **Grills I**, Yan D, **Gustafson G** and **Krauss DJ** (2012). "Image guided adaptive radiation therapy for prostate cancer: toxicity comparison for 3D conformal versus intensity modulated beams." International Journal of Radiation Oncology Biology Physics 84(3 Suppl S): S398-S399.
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Department of Radiation Oncology
Department of Internal Medicine

Traylor K, Gonzalez-Krellwitz L and **Balon H** (2012). "13-Year-old boy with a 3-day history of melena." Journal of Nuclear Medicine Technology 40(2): 119-121.

[Full-Text](#)

Department of Diagnostic Radiology and Molecular Imaging

Trese MT and Kashani AH (2012). "Advances in the diagnosis, management and pathophysiology of capillary nonperfusion." Expert Review of Ophthalmology 7(3): 281-292.

[Full-Text](#)

Department of Ophthalmology

'Capillary dropout or 'nonperfusion describes both an anatomic condition and an angiographic appearance in many retinal diseases. In this review, we will discuss several illustrative pediatric and adult retinal vascular diseases including retinopathy of prematurity, familial exudative vitreoretinopathy, diabetic retinopathy and retinal vein occlusions with capillary nonperfusion. Enhanced retinal imaging techniques have demonstrated that capillary nonperfusion is more common in vascular diseases than previously assumed. A large body of experimental evidence in animal models has started to elucidate the underlying pathophysiology of this process. In addition, it has become clear in hereditary and congenital diseases that genetic mutations involving Wnt signaling are integral to retinal vascular development and disease. Defects in the Wnt signaling pathway seem to be related to abnormalities in retinal vascular formation and/or angiomaintenance. Abnormalities in either of these processes may lead to capillary nonperfusion. We review clinical features of capillary nonperfusion and discuss the evolving management of this entity based on novel imaging modalities and molecular mediators. © 2012 Expert Reviews Ltd.

Trivax JE and McCullough PA (2012). "Phidippides cardiomyopathy: a review and case illustration." Clinical Cardiology 35(2): 69-73.

[Full-Text](#)

Department of Internal Medicine

Phidippides was a Greek messenger who experienced sudden death after running more than 175 miles in two days. In today's world, marathon running and other endurance sports are becoming more popular and raising concern about sudden deaths at these events. Once etiologies such as hypertrophic cardiomyopathy, anomalous coronary arteries, and coronary atherosclerosis have been excluded, there is now an additional consideration termed Phidippides cardiomyopathy. Because endurance sports call for a sustained increase in cardiac output for several hours, the heart is put into a state of volume overload. It has been shown that approximately one-third of marathon runners experience dilation of the right atrium and ventricle, have elevations of cardiac troponin and natriuretic peptides, and in a smaller fraction later develop small patches of cardiac fibrosis that are the likely substrate for ventricular tachyarrhythmias and sudden death. Cardiac magnetic resonance imaging is emerging as the diagnostic test of choice for this condition. This review and case report summarizes the key features of this newly appreciated disorder.

Tyagi P, Killinger K, Tyagi V, Nirmal J, **Chancellor M** and **Peters KM** (2012). "Urinary chemokines as noninvasive predictors of ulcerative interstitial cystitis." Journal of Urology 187(6): 2243-2248.

[Request Form](#)

Department of Urology

Purpose: Based on basic research findings an increase in chemokines and cytokines (CXCL-1 and 10, nerve growth factor and interleukin-6) is considered responsible for inflammation and afferent sensitization. In this

cross-sectional study we tested the hypothesis that select chemokines are increased in the urine of patients with ulcerative and nonulcerative interstitial cystitis/painful bladder syndrome. Materials and Methods: Midstream urinary specimens were collected from 10 patients with ulcerative and nonulcerative interstitial cystitis/painful bladder syndrome, respectively, and from 10 asymptomatic controls. Urinary levels of 7 cytokines were measured by a human cytokine/chemokine assay. Nerve growth factor was measured by enzyme-linked immunosorbent assay. Results: Urinary levels of most chemokines/cytokines were tenfold to 100-fold lower in asymptomatic controls vs patients with ulcerative and nonulcerative interstitial cystitis/painful bladder syndrome. Univariate comparison of 8 tested proteins in the ulcerative vs nonulcerative groups revealed a significant fivefold to twentyfold increase in CXCL-10 and 1, interleukin-6 and nerve growth factor (ANOVA $p < 0.001$). Conclusions: Differential expression of chemokines in ulcerative and nonulcerative subtypes of interstitial cystitis/painful bladder syndrome suggests differences in paracrine signaling between the 2 entities. © 2012 American Urological Association Education and Research, Inc.

Tyagi S and **Cappell M** (2012). Large bowel disorders, in McKean S. C. (ed). Principles and Practice of Hospital Medicine: McGraw-Hill: 1335-1351.

[Full-Text](#)

Department of Urology

Department of Internal Medicine

Updegraff A, **Bestul D** and **Doshi D** (2012). "Experience with carboplatin desensitization: a case series." Journal of Allergy and Clinical Immunology 129(2 Suppl S): AB71.

[Full-Text](#)

Department of Biomedical Sciences

Department of Pediatrics

Van Zundert J, Patijn J, **Hartrick C**, Lataster A, Huygen F, Mekhail N and van Kleef M, Eds. (2012). Evidence-based Interventional Pain Practice: According to Clinical Diagnoses. London, Wiley-Blackwell.

[Request Form](#)

Department of Anesthesiology

Chronic pain has been subject to multiple international initiatives through the World Health Organization. Interventional Pain Medicine, use of minimally invasive techniques to relieve pain, is the best approach when simpler measures such as physical therapy or medications fail. However, these procedures can be associated with significant risk and expense. Establishing uniformity in diagnostic criteria and procedural performance can reduce both morbidity and unnecessary procedures, and hence healthcare expenditures.

Vance S, Martin S, Wloch J, **Grills I** and Yan D (2012). "Evaluation of breathing excursion variability in lung cancer patients during conventional and hypofractionated radiation therapy." International Journal of Radiation Oncology Biology Physics 84(3 Suppl S): S729.

[Full-Text](#)

Department of Radiation Oncology

Vance S, Ye H, Baschnagel A, Mangona V, Yan D and **Grills I** (2012). "Clinical outcomes and toxicity after stereotactic body radiotherapy (SBRT) with or without adjuvant chemotherapy for stage I non-small cell lung cancer (NSCLC)." Journal of Thoracic Oncology 7(9 Suppl 4): S292-S293.

[Full-Text](#)

Department of Radiation Oncology

Vaupel ZM, **Baker KC**, **Kurdziel MD** and **Wiater JM** (2012). "Wear simulation of reverse total shoulder arthroplasty systems: effect of glenosphere design." Journal of Shoulder and Elbow Surgery 21(10): 1422-1429.

[Full-Text](#)

Department of Orthopedic Surgery

Department of Surgery

BACKGROUND: Although early results with reverse total shoulder arthroplasty (rTSA) have been promising, concern exists about the high reported rates of scapular notching and the potential for catastrophic failure of glenoid component fixation. Generation of polyethylene wear debris may also contribute to notching and osteolysis of the scapula. A testing model for polyethylene wear is currently unavailable for reverse shoulder prostheses. The goal of this study was to develop a testing protocol using a commercially available hip simulator. Component design may also influence the generation of polyethylene debris. It is hypothesized that increased polyethylene wear occurs in glenospheres with holes in the articulating surface. **MATERIALS AND METHODS:** Custom fixtures were fabricated to simulate both glenohumeral abduction and flexion on a 12-station hip wear simulator. Loading profiles for both abduction and flexion were alternated every 250,000 cycles for a total of 5 million cycles. Gravimetric analysis of humeral cups throughout the test was used to characterize wear. Lubricant fluid was collected throughout the test and digested for polyethylene particle analysis. **RESULTS:** Comparisons of volumetric wear rates and total volume loss between glenospheres with and without holes and between flexion and abduction loading profiles showed similar results. Particle analysis displayed fibrillar particles with an equivalent circle diameter of 0.3 +/- .1 μm and an aspect ratio of 2.5 +/- 1.4. **CONCLUSIONS:** This study represents the first wear simulation and particle characterization of reverse shoulder systems. No significant difference in wear was reported between glenospheres with and without holes.

Verma N and Sherwood F (2012). "Low saturated fat diet is effective in trigeminal neuralgia." *Neurology* 78(Meeting Abstracts 1): P03.237.

[Request Form](#)

Department of Internal Medicine

Vicini F, Shah C, Lyden M and Whitworth P (2012). "Bioelectrical impedance for detecting and monitoring patients for the development of upper limb lymphedema in the clinic." *Clinical Breast Cancer* 12(2): 133-137.

[Full-Text](#)

Department of Internal Medicine

Limited data are available on new diagnostic modalities in breast cancer-related lymphedema. Analysis of the implementation of bioimpedance spectroscopy to detect breast cancer-related lymphedema in the community oncology setting demonstrated its feasibility and simplicity. Further, in 64 patients, analysis within 90 days of surgery demonstrated that bioelectrical impedance had the ability to detect differences based on surgical and axillary procedure, which potentially allows for subclinical diagnosis. **Background:** Single-frequency bioelectrical impedance (BI) has been used to measure extracellular fluid in the upper limbs. The purpose of the study was to evaluate BI's ability to detect and monitor upper limb changes in based upon the extent of various treatments and to assess its practicality. **Methods:** Patients with newly diagnosed breast cancer were evaluated at baseline and after procedures that could potentially affect fluid accumulation in the arm and signal the possible development of early lymphedema. The magnitude of the change in lymphedema index ratios (LIR) from these procedures was evaluated to determine the sensitivity of BI. **Results:** A total of 64 patients were evaluated. Although no difference in LIRs was noted by the extent of surgical procedure (lumpectomy 2.1 vs. mastectomy 1.1; $P = .49$), a trend was noted for increased LIRs with more aggressive axillary staging when sentinel lymph node was compared with axillary lymph node dissection (1.3 vs. 3.4; $P = .08$). A trend for an increased LIR with more aggressive local therapy also was noted when using a cutoff of less than 4 lymph nodes sampled compared with 4 or more nodes sampled (1.2 vs. 2.6; $P = .09$). **Conclusions:** In this limited analysis, L-Dex readings paralleled the extent of surgical interventions and suggest that they can be used to monitor patients for the early onset of edema. Further studies are needed to help validate the extent, degree, and chronologic time frame of these changes to help define recommendations for closer monitoring of patients and possible early intervention.

Vicini FA, Keisch M, Shah C, Goyal S, Khan AJ, Beitsch PD, Lyden M and Haffty BG (2012). "Factors associated with optimal long-term cosmetic results in patients treated with accelerated partial breast irradiation using balloon-based brachytherapy." *International Journal of Radiation Oncology Biology Physics* 83(2): 512-518.

[Full-Text](#)

Department of Internal Medicine

Purpose: To evaluate factors associated with optimal cosmetic results at 72 months for early-stage breast cancer patients treated with Mammosite balloon-based accelerated partial breast irradiation (APBI). Methods and Materials: A total of 1,440 patients (1,449 cases) with early-stage breast cancer undergoing breast-conserving therapy were treated with balloon-based brachytherapy to deliver APBI (34 Gy in 3.4-Gy fractions). Cosmetic outcome was evaluated at each follow-up visit and dichotomized as excellent/good (E/G) or fair/poor (F/P). Follow-up was evaluated at 36 and 72 months to establish long-term cosmesis, stability of cosmesis, and factors associated with optimal results. Results: The percentage of evaluable patients with excellent/good (E/G) cosmetic results at 36 months and more than 72 months were 93.3%(n=708/759) and 90.4%(n=235/260). Factors associated with optimal cosmetic results at 72 months included: larger skin spacing (p=0.04) and T1 tumors (p=0.02). Using multiple regression analysis, the only factors predictive of worse cosmetic outcome at 72 months were smaller skin spacing (odds ratio [OR], 0.89; confidence interval [CI], 0.80-0.99) and tumors greater than 2 cm (OR, 4.96, CI, 1.53-16.07). In all, 227 patients had both a 36-month and a 72-month cosmetic evaluation. The number of patients with E/G cosmetic results decreased only slightly from 93.4% at 3 years to 90.8% (p=0.13) at 6 years, respectively. Conclusions: APBI delivered with balloon-based brachytherapy produced E/G cosmetic results in 90.4% of cases at 6 years. Larger tumors (T2) and smaller skin spacing were found to be the two most important independent predictors of cosmesis. (C) 2012 Elsevier Inc.

Vicini FA, Shah C, Wallace M, Jones P, Dykes V, Tull J, Akhtar A, Ballouz S, Boxwala I, Douglas-Nikitin V, Rivers A, Clark R, Jaiyesimi I and Fakhouri M (2012). "Strategies for reducing cancer incidence and mortality in African American and Arab American and Chaldean communities in the Detroit metropolitan area." [American Journal of Clinical Oncology](#) 35(4): 316-321.

[Full-Text](#)

Department of Internal Medicine

Department of Pathology

Department of Surgery

OBJECTIVES: We studied the feasibility of implementing a community-based participatory process (CBPP) that addressed cancer education, prevention, and screening in 2 ethnic minority populations by evaluating the improvement in rates of cancer screening compared with historical benchmarks. **METHODS:** From 2003 to 2009, 2281 community members participated in CBPPs conducted by the Beaumont Cancer Institute in cooperation with the Arab American and Chaldean (AAC) Council, the National Cancer Institute, and the American Cancer Society. The study population consisted of 1067 individuals who completed a postcancer forum survey: 642 from the African American (AA) and 425 from the AAC forums. Data were collected on participants' screening history and participation in subsequent screening tests after the previous year's CBPP. **RESULTS:** Following attendance of at least one cancer forum the previous year, 329 (30.8%) of the 1067 participant respondents underwent some type of cancer screening, 32% in the AA forums and 28.9% in the AAC forums. Compared with published controls, the CBPPs led to a 38.6% increase in mammographic screening and a 28.7% increase in prostate-specific antigen screening; the AA cohort had 39.7% and 28.4% increases whereas the AAC cohort had 36.3% and 28.9% increases in mammographic and prostate-specific antigen screening, respectively. **CONCLUSIONS:** The results of this study suggest that implementing CBPPs are feasible in underscreened ethnic minority populations. Further studies need to be performed to determine the absolute benefit of CBPPs compared with baseline levels of screening within these ethnic minority populations.

Visco AG, Brubaker L, Richter HE, Nygaard I, Paraiso MFR, Menefee SA, Schaffer J, Lowder J, Khandwala S, **Sirls L, Spino C, Nolen TL, Wallace D, Meikle SF and Pelvic Floor Disorders N (2012).** "Anticholinergic therapy vs. onabotulinumtoxinA for urgency urinary incontinence." [New England Journal of Medicine](#) 367(19): 1803-1813.

[Full-Text](#)

Department of Urology

Background Anticholinergic medications and onabotulinumtoxinA are used to treat urgency urinary incontinence, but data directly comparing the two types of therapy are needed. Methods We performed a

double-blind, double-placebo-controlled, randomized trial involving women with idiopathic urgency urinary incontinence who had five or more episodes of urgency urinary incontinence per 3-day period, as recorded in a diary. For a 6-month period, participants were randomly assigned to daily oral anticholinergic medication (solifenacin, 5 mg initially, with possible escalation to 10 mg and, if necessary, subsequent switch to trospium XR, 60 mg) plus one intradetrusor injection of saline or one intradetrusor injection of 100 U of onabotulinumtoxinA plus daily oral placebo. The primary outcome was the reduction from baseline in mean episodes of urgency urinary incontinence per day over the 6-month period, as recorded in 3-day diaries submitted monthly. Secondary outcomes included complete resolution of urgency urinary incontinence, quality of life, use of catheters, and adverse events. Results Of 249 women who underwent randomization, 247 were treated, and 241 had data available for the primary outcome analyses. The mean reduction in episodes of urgency urinary incontinence per day over the course of 6 months, from a baseline average of 5.0 per day, was 3.4 in the anticholinergic group and 3.3 in the onabotulinumtoxinA group (P = 0.81). Complete resolution of urgency urinary incontinence was reported by 13% and 27% of the women, respectively (P = 0.003). Quality of life improved in both groups, without significant between-group differences. The anticholinergic group had a higher rate of dry mouth (46% vs. 31%, P = 0.02) but lower rates of catheter use at 2 months (0% vs. 5%, P = 0.01) and urinary tract infections (13% vs. 33%, P<0.001). Conclusions Oral anticholinergic therapy and onabotulinumtoxinA by injection were associated with similar reductions in the frequency of daily episodes of urgency urinary incontinence. The group receiving onabotulinumtoxinA was less likely to have dry mouth and more likely to have complete resolution of urgency urinary incontinence but had higher rates of transient urinary retention and urinary tract infections. (Funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institutes of Health Office of Research on Women's Health; ClinicalTrials.gov number, NCT01166438.)

Viscusi ER, Frenkl TL, **Hartrick CT**, Rawal N, Kehlet H, Papanicolaou D, Gammaitoni A, Ko AT, Morgan LM, Mehta A, Curtis SP and Peloso PM (2012). "Perioperative use of etoricoxib reduces pain and opioid side-effects after total abdominal hysterectomy: a double-blind, randomized, placebo-controlled phase III study." Current Medical Research and Opinion 28(8): 1323-1335.

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Department of Biomedical Sciences

Objective: To evaluate the effects of two different doses of etoricoxib delivered perioperatively compared with placebo and standard pain management on pain at rest, pain with mobilization, and use of additional morphine/opioids postoperatively. Research design and methods: In this double-blind, placebo-controlled, randomized clinical trial, we evaluated postoperative pain following total abdominal hysterectomy over 5 days in patients receiving placebo or etoricoxib administered 90 min prior to surgery and continuing postoperatively. Patients were randomly assigned to receive either placebo (n = 144), etoricoxib 90 mg/day (n = 142), or etoricoxib 120 mg/day (n = 144). Average Pain Intensity at Rest over days 1-3 (0- to 10-point numerical rating scale [NRS]) was the primary efficacy endpoint. Secondary endpoints included Average Pain Intensity upon Sitting, Standing, and Walking over days 1-3 (0- to 10-point NRS) as well as Average Total Daily Dose of Morphine over days 1-3. Clinical trial registration: This trial is registered on www.clinicaltrials.gov (NCT00788710). Results: The least squares (LS) means (95% CI) for the primary endpoint were 3.26 (2.96, 3.55); 2.46 (2.16, 2.76); and 2.40 (2.11, 2.69) for placebo, etoricoxib 90 mg, and etoricoxib 120 mg, respectively, significantly different for both etoricoxib doses versus placebo (p<0.001). Patients on etoricoxib 90 mg and 120 mg required similar to 30% less morphine per day than those on placebo (p<0.001), which led to more rapid bowel recovery in the active treatment groups by similar to 10 hours vs. placebo. A greater proportion of patients on etoricoxib (10-30% greater than placebo) achieved mild levels of pain with movement, defined as pain <= 3/10. Limitations: A key limitation for this study was that movement-evoked pain measurements were not designated as primary endpoints. Conclusion: In patients undergoing total abdominal hysterectomy, etoricoxib 90 mg and 120 mg dosed preoperatively and then continued postoperatively significantly reduces both resting and movement-related pain, as well as reduced opioid (morphine) consumption that led to more rapid bowel recovery.

Washburn B, **Dekhne N** and Meininger M (2012). "Feasibility of nipple-sparing mastectomy: one community hospital's experience." Annals of Surgical Oncology 19(Sup 2): 114-115.

[Full-Text](#)

Department of Surgery

Watanabe T and **Chancellor MB** (2012). "Pelvic surgeons caught in the meshes of the law." Reviews in Urology 14(1-2): 35-36.

[Full-Text](#)

Department of Urology

Wilkinson JB, Cuttino LW, Julian TB, Arthur DW and **Vicini FA** (2012). "Limited-field and whole-breast hypofractionated radiotherapy: additional considerations." Oncology-New York 26(9): 838-839.

[Full-Text](#)

Department of Internal Medicine

With the publication of mature experiences using accelerated partial breast irradiation (APBI) and accelerated whole breast irradiation (AWBI), the use of shortened courses of radiotherapy has become increasingly popular. Dr. Mouw and Dr. Harris describe the potential benefits associated with accelerated treatment, but they also discourage widespread application of these techniques in the absence of long-term randomized data. We agree that controversy will exist until such data are available, and present several points to supplement the discussion of this important topic.

Wilkinson JB, **Grills IS**, Mangona VS, Fowler A, Wallace MF, Mitchell CK, Robertson JR and **Ionascu D** (2012). "Volumetric analysis of FDG-PET uptake after local recurrence following stereotactic body radiation therapy for early-stage non-small cell lung cancer." International Journal of Radiation Oncology Biology Physics 84(3 Suppl S): S103.

[Full-Text](#)

Department of Radiation Oncology

Wilkinson JB, Mangona VS, **Ionascu D**, Fowler A, Wallace MF, Mitchell CK and **Grills IS** (2012). "Predictors of local recurrence after stereotactic body radiation therapy for early-stage non-small cell lung cancer." International Journal of Radiation Oncology Biology Physics 84(3 Suppl S): S611.

[Full-Text](#)

Department of Radiation Oncology

Wilkinson JB, **Martinez A**, Yan D, Shah C, **Kestin L**, **Krauss D**, **Ghilezan M**, Wallace M, **Vicini F** and **Brabbins D** (2012). "Impact of dose-escalation using non-adaptive and adaptive radiotherapy for treatment of prostate cancer." American Journal of Clinical Oncology-Cancer Clinical Trials 35(2): 189.

[Full-Text](#)

Department of Radiation Oncology

Dose escalation in the treatment of prostate cancer increases biochemical control, prevents distant metastasis, and improves prostate cancer-related survival. We review our long-term outcomes using dose-escalated radiotherapy in the treatment of prostate cancer.

Wilkinson JB, **Martinez AA**, **Chen PY**, Ghilezan MI, Wallace MF, **Grills IS**, Shah CS, Mitchell CK, Sebastian E, Limbacher AS, **Benitez PR**, **Brown EA** and **Vicini FA** (2012). "Four-year results using balloon-based brachytherapy to deliver accelerated partial breast irradiation with a 2-day dose fractionation schedule." Brachytherapy 11(2): 97-104.

[Full-Text](#)

Department of Radiation Oncology

Department of Pathology

Department of Surgery

PURPOSE: We present 4-year results from a Phase I/II trial using balloon-based brachytherapy to deliver accelerated partial breast irradiation in 2 days. **MATERIALS/METHODS:** Forty-five patients received breast-conserving surgery followed by adjuvant radiation therapy using a balloon-based brachytherapy applicator delivering 2800 cGy in four fractions over 2 days. Outcomes analyzed include toxicities scored using the NCI Common Toxicity Criteria v3.0 scale, ipsilateral breast tumor recurrence, regional nodal failure, distant metastasis, disease-free survival, cause-specific survival, and overall survival. **RESULTS:** Median age was 66 years (range, 48-83 years) and median tumor size was 0.6 cm (range, 0.2-2.3 cm). Five percent of patients were node positive (n = 2), whereas 73% was estrogen receptor positive (n = 33). Median followup was 3.7 years (2.4-7.0 years) with greater than 2 years of followup for all patients. Only Grades 1 and 2 chronic toxicities were noted with fat necrosis (18%) and asymptomatic seromas (42%) being the most common toxicities. Seven percent of patients developed ipsilateral rib fractures (n = 3), although this was not statistically associated with maximum rib dose (p = 0.31). Ninety-eight percent of patients had a good or excellent radiation-related cosmetic outcome at the time of last followup. There were no ipsilateral breast tumor recurrences or regional nodal failures; however, 2 patients developed distant metastases. Four-year actuarial disease-free survival, cause-specific survival, and overall survival were 96%, 100%, and 93%, respectively. **CONCLUSIONS:** Treatment of early-stage breast cancer patients with breast-conserving therapy using a 2-day radiation dose schedule resulted in acceptable chronic toxicity and similar clinical outcomes as standard 5-day fractionation. (C) 2012 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Wilkinson JB, Shah C, Baschnagel A, Mitchell C, Limbacher A, Sebastian E, Wallace M, Ye H, **Benitez P** and **Vicini F** (2012). "Multi-lumen vs. single-lumen accelerated partial breast irradiation: a matched-pair dosimetric analysis." *American Journal of Clinical Oncology-Cancer Clinical Trials* 35(2): 193-194.

[Full-Text](#)

Department of Surgery

Department of Internal Medicine

Department of Radiation Oncology

To evaluate dosimetry of accelerated partial breast irradiation (APBI) in women with similar requirements of planning target volume (PTV) modification and skin spacing using single and multilumen (ML) applicator-based brachytherapy.

Wilkinson JB, **Vicini FA**, Shah C, Shaitelman S, Jawad MS, Ye H, **Kestin LL**, Goldstein NS, **Martinez AA**, **Benitez P** and **Chen PY** (2012). "Twenty-year outcomes after breast-conserving surgery and definitive radiotherapy for mammographically detected ductal carcinoma in situ." *Annals of Surgical Oncology* 19(12): 3785-3791.

[Full-Text](#)

Department of Internal Medicine

Department of Radiation Oncology

Department of Surgery

Department of Pathology

Management of mammographically detected ductal carcinoma in situ (DCIS) at a single institution was reviewed to determine long-term clinical outcomes after treatment with breast-conserving therapy (BCT). Data from all patient-cases with DCIS who received BCT between 1980 and 1993 were reviewed. Patient demographics and pathologic factors were analyzed for their effect on outcomes, including ipsilateral breast tumor recurrence (IBTR) and survival. BCT included breast-conserving surgery followed by external-beam radiotherapy to the whole breast, with 86 % of patients receiving a lumpectomy cavity boost. The median dose to the whole breast was 50 Gy and 60.4 Gy to the lumpectomy cavity. A total of 129 cases were evaluated; the median follow-up was 19.3 years. Twenty-one patients developed an ipsilateral breast tumor recurrence (IBTR), 76.2 % of which were invasive (n = 16). Fourteen recurrences (66 %) were within the same breast quadrant (true recurrence), while an additional 7 cases developed an IBTR elsewhere in the breast. True recurrences were more prevalent in women < 45 years of age (20 %/24 % vs. 5.1 %/8 %) at 10 and 20 years (p = 0.02). The 5-, 10-, 15-, and 20-year actuarial rates of IBTR for this cohort were 8.7, 10.4, 12.1, and

16.3 % (IBTR), while overall survival at 5, 10, and 20 years was 97.6, 96.8, and 96.8 %, respectively. Mammographically detected DCIS remains a clinically distinct subset of noninvasive breast cancer. With 20 year follow-up, local control and overall survival are excellent after BCT.

Williams GA (2012). "Ciliary neurotrophic factor for geographic atrophy and retinal degenerations." Ophthalmologica 228(Suppl 1): 28-30.

[Request Form](#)

Department of Ophthalmology

Williams GA (2012). "Health care reform 2012: Significant changes are expected in coming years." Retina Today(APRIL): 20.

[Request Form](#)

Department of Ophthalmology

Williams GA (2012). "Two-year CATT results." Ophthalmologica 228(Suppl 1): 42-43.

[Request Form](#)

Department of Ophthalmology

Wills S, Ravipati A, **Venuturumilli P**, Kresge C, Folkerd E, Dowsett M, Hayes DF and Decker DA (2012). "Effects of vaginal estrogens on serum estradiol levels in postmenopausal breast cancer survivors and women at risk of breast cancer taking an aromatase inhibitor or a selective estrogen receptor modulator." Journal of Oncology Practice 8(3): 144-149.

[Full-Text](#)

Department of Internal Medicine

BACKGROUND: Intravaginal estradiols (VE) have been proposed as safe alternatives to systemic estrogen therapy in breast cancer survivors. PATIENTS AND METHODS: Postmenopausal women with estrogen receptor-positive breast cancer or at high risk for breast cancer (n = 24) who were taking an aromatase inhibitor (AI) or a selective estrogen receptor modulator (SERM) and VE for \geq 90 days for atrophic vaginitis and 24 controls taking AI only participated in the study. Serum samples were drawn from VE ring patients before insertion and 30 and 60 days postinsertion, from VE tablet patients the morning before insertion and approximately 12 hours postinsertion, and once from controls. Samples were assayed for E2 concentrations by using highly sensitive radioimmunoassay after ether extraction. RESULTS: Mean E2 levels in controls were 3.72 pmol/L (range, < 3.0-7.7 pmol/L); mean E2 levels preinsertion and 12 weeks postinsertion in the VE ring patients were significantly greater than controls ($P < .001$ for each comparison). Mean preinsertion E2 levels in patients using VE tablets were not significantly different than those of controls ($P = .48$), and postinsertion levels were 76 pmol/L higher than preinsertion ($P < .001$). CONCLUSION: VE treatment increased E2 levels. Preinsertion levels for patients receiving VE tablets were not elevated compared with those of controls, suggesting that E2 elevations with this preparation may not be continuously sustained. We conclude that VE treatment, regardless of type, results in elevated circulating E2 levels in this population and should be used with caution.

Wilson GD, Geddes TJ, Pruetz BL, Thibodeau BJ, Murawka A, Colar JM, McCullough PA and **Trivax JE** (2012).

"SELDI-TOF-MS serum profiling reveals predictors of cardiac MRI changes in marathon runners." International Journal of Proteomics 2012: 679301.

[Full-Text](#)

Department of Radiation Oncology

Department of Internal Medicine

Purpose. To utilize proteomics to discover proteins associated with significant cardiac magnetic resonance imaging (MRI) changes in marathon runners. Methods. Serum from 25 runners was analyzed by surface enhanced laser desorption ionization time-of-flight mass spectrometry (SELDI-TOF-MS). Proteomic profiles were compared in serum samples obtained prior to the race, at the finish line and within 7 hours after race to identify dynamic proteins correlated with cardiac MRI changes. Results. 693 protein/peptide clusters were

identified using two ProteinChip surface chemistries and, of these, 116 were significantly different between the three time points. We identified 7 different patterns of protein expression change within the runners and 5 prerace protein peaks, 16 finish-line protein levels, and 15 postrace proteins which were correlated with significant postrace cardiac MRI changes. Conclusions. This study has identified baseline levels of proteins which may be predictive of risk of significant cardiac damage following a marathon race. Preliminary identification of the significant proteins suggested the involvement of cytokines and other proteins involved in stress and inflammatory response.

Wolfe JD (2012). "Meaningful use of her: meaningful use must be demonstrated to earn medicare incentive payments." Retina Today(MARCH 2012): 20.

[Request Form](#)

Department of Ophthalmology

Wong SC, Neuwelt MD and **Trese MT** (2012). "Delayed closure of paediatric macular hole in Coats' disease." Acta Ophthalmologica 90(4): e326-e327.

[Full-Text](#)

Department of Ophthalmology

Wood FO, Leonowicz NA, Vanhecke TE, **Dixon SR** and **Grines CL** (2012). "Mortality in patients with ST-segment elevation myocardial infarction who do not undergo reperfusion." American Journal of Cardiology 110(4): 509-514.

[Full-Text](#)

Department of Internal Medicine

Reperfusion therapy reduces mortality in patients presenting with ST-segment elevation myocardial infarctions (STEMI). However, some patients may not receive thrombolytic therapy or undergo primary percutaneous coronary intervention. The decision making and clinical outcomes of these patients have not been well described. In this study, 139 patients were identified from a total of 1,126 patients with STEMI who did not undergo reperfusion therapy at a high-volume percutaneous coronary intervention center from October 2006 to March 2011. Clinical data, reasons for no reperfusion, management, and mortality were obtained by chart review. The mean age was 80 +/- 13 years (61% women, 31% diabetic, and 37% known coronary artery disease). Of the 139 patients, 72 (52%) presented with primary diagnoses other than STEMI, and 39 (28%) developed STEMI >24 hours after admission. The most common reasons for no reperfusion were advanced age, co-morbid conditions, acute or chronic kidney injury, delayed presentation, advance directives precluding reperfusion, patient preference, and dementia. Eighty-four patients (60%) had >= 3 reasons for no reperfusion. Factors associated with hospital mortality were cardiogenic shock, intubation, and advance directives prohibiting reperfusion after physician consultation. In hospital and 1-year mortality were 53% and 69%, respectively. In conclusion, at a high-volume percutaneous coronary intervention center, most patients presenting with STEMI underwent immediate catheterization. The decision for no reperfusion was multifactorial, with advanced age reported as the most common factor. Outcomes were poor in this population, and fewer than half of these patients survived to hospital discharge.

Yee V and **Lauter C** (2012). "C1-INH: test use evaluation on in-patient adults." Journal of Allergy and Clinical Immunology 129(2 Suppl S): AB107.

[Full-Text](#)

Department of Internal Medicine

Yeh S, Fahle G, Forooghian F, **Faia LJ**, Weichel ED, Stout JT, Flaxel CJ, Lauer AK, Sen HN and Nussenblatt RB (2012). "Polymerase chain reaction-based ganciclovir resistance testing of ocular fluids for cytomegalovirus retinitis." Archives of Ophthalmology 130(1): 113-115.

[Full-Text](#)

Department of Ophthalmology

Yokoyama T, **Chancellor MB**, Oguma K, Yamamoto Y, Suzuki T, Kumon H and Nagai A (2012). "Botulinum toxin type A for the treatment of lower urinary tract disorders." International Journal of Urology 19(3): 202-215.

[Full-Text](#)

Department of Urology

Many papers report the clinical success of botulinum toxin A as a method of management of various bladder dysfunctions. The rationale was that botulinum toxin A was able to block the presynaptic release of acetylcholine from the parasympathetic efferent nerve. The efficacy might result not only from an inhibitory effect on detrusor muscle, but also some effects might be mediated by altering the afferent nerve input. This systematic literature review discusses the efficacy and safety of botulinum toxin A therapy for idiopathic detrusor overactivity, neurogenic detrusor overactivity, interstitial cystitis/painful bladder syndrome and benign prostatic hyperplasia. The information was gathered from a PubMed literature research for abstracts from recent urological meetings. Injection of botulinum toxin A appears to have a positive therapeutic effect in multiple urological conditions, such as refractory idiopathic detrusor overactivity, neurogenic detrusor overactivity, interstitial cystitis/painful bladder syndrome and benign prostatic hyperplasia. Because the United States Food and Drug Administration has approved botulinum toxin A (Botox) for injection for the treatment of urinary incontinence as a result of neurogenic detrusor overactivity (e.g. spinal cord injury, multiple sclerosis) in adults who have an inadequate response to or are intolerant of an ant cholinergic medication, the use of botulinum toxin A will spread and be a more familiar therapy in the urological arena. However, further robust evidence should be awaited. We will discuss the current use of this agent within the urological field.

Zaltz I (2012). "The biomechanical case for labral debridement." Clinical Orthopaedics and Related Research 470(12): 3398-3405.

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Department of Orthopedic Surgery

BACKGROUND: Labral repair is increasingly performed in conjunction with open and arthroscopic surgical procedures used to treat patients with mechanically related hip pain. The current rationale for labral repair is based on restoring the suction-seal function and clinical reports suggesting improved clinical outcome scores when acetabular rim trimming is accompanied by labral repair. However, it is unclear whether available scientific evidence supports routine labral repair. **QUESTIONS/PURPOSES:** The questions raised in this review were: (1) does labral repair restore normal histologic structure, tissue permeability, hip hydrodynamics, load transfer, and in vivo kinematics; and (2) does labral repair favorably alter the natural course of femoroacetabular impingement (FAI) treatment or age-related degeneration of the acetabular labrum? **METHODS:** An electronic literature search for the keywords acetabular labrum was performed. Three hundred fifty-five abstracts were reviewed and 52 selected for full-text review that described information concerning pertinent aspects of labral formation, development, degeneration, biomechanics, and clinical results of labral repair or resection. **RESULTS:** Several clinical studies support labral repair when performed in conjunction with acetabular rim trimming. Little data support or refute the use of routine labral repair for all patients with symptomatic labral damage associated with FAI. It is not known whether or how labral repair affects the natural course of FAI. **CONCLUSIONS:** Based on the current understanding of labral degenerative changes associated with mechanical hip abnormalities, the low biologic likelihood of restoring normal tissue characteristics, and mechanical data suggesting minimal consequence from small labral resections, routine labral repair over labral debridement is not supported.

Zaltz I, Hosalkar H and Wenger D (2012). "What's new in pediatric orthopaedic surgery." Journal of Bone and Joint Surgery American Volume 94(4): 375-381.

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Department of Orthopedic Surgery

Zaltz I and Leunig M (2012). "Parafoveal chondral defects associated with femoroacetabular impingement." Clinical Orthopaedics and Related Research 470(12): 3383-3389.

[Full-Text](#)

BACKGROUND: Cam-type, pincer, and mixed femoroacetabular impingement (FAI) are accepted causes of labral and acetabular rim injury; however, the abnormal contact stresses associated with motion may damage other areas of the hip. Although cartilage damage to the femoral head has been reported previously in athletes, FAI-associated focal parafoveal chondral defects differ from previously reported lesions and represent a rare manifestation of the complex pathomechanics associated with FAI. **QUESTIONS/PURPOSES:** We describe the clinical, radiographic, and surgical characteristics of a rare focal anterolateral parafoveal femoral chondral defect associated with FAI. **METHODS:** We retrospectively reviewed 10 patients with symptomatic FAI diagnosed with this unique focal defect confirmed at the time of surgical dislocation. Patients presented with hip pain, clinical findings of FAI, and, frequently, with an identifiable lesion on MRI arthrography. The minimum clinical followup was 12 months (mean, 29 months; range, 12-72 months). **RESULTS:** The consistent characteristics of these lesions associated with FAI differ from previously reported femoral chondral damage reported after hip dislocation or lateral impact in that there was no discrete injury such as a fall or dislocation/subluxation, no associated traumatic femoral lesion, and all were localized to the posterosuperior femoral head. Eight of 10 were diagnosed preoperatively using MR arthrography. **CONCLUSIONS:** Despite radiographic similarities to findings of osteoarthritis and osteonecrosis, these FAI-associated femoral chondral defects were amenable to surgical reconstruction using first- or second-generation cartilage repair techniques during surgical treatment of impingement. The etiology of these lesions may be related to complex intraarticular forces generated by FAI-associated transient hip subluxation or forceful nonconcentric motion. **LEVEL OF EVIDENCE:** Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

Zammit G, Huang H, **Sangal RB** and Versavel M (2012). "A randomized, placebo-controlled, double-blind, fixed-dose study of the efficacy and safety of eszopiclone in children (6 to 11 Years) and adolescents (12 to 17 years) with attention-deficit/hyperactivity disorder (ADHD)-associated insomnia." *Sleep* 35(Suppl S): A354-A355.

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Department of Family Medicine

Zhang B, Tzartos JS, Belimezi M, **Ragheb S**, Bealmear B, Lewis RA, Xiong W-C, Lisak RP, Tzartos SJ and Mei L (2012). "Autoantibodies to lipoprotein-related protein 4 in patients with double-seronegative myasthenia gravis." *Archives of Neurology* 69(4): 445-451.

[Full-Text](#)

Department of Biomedical Sciences

Objectives: To determine whether patients with myasthenia gravis (MG) have serum antibodies to lipoprotein-related protein 4 (LRP4), a newly identified receptor for agrin that is essential for neuromuscular junction formation, and to establish whether such antibodies contribute to MG pathogenesis. **Design:** Serum samples from patients with MG with known status of serum antibodies to the acetylcholine receptor (AChR) and muscle-specific kinase (MuSK) and serum samples from control subjects (healthy individuals and individuals with other diseases) were tested for antibodies to LRP4. Serum samples with such antibodies were tested to determine whether they had the ability to inhibit 2 different functions of LRP4 at the neuromuscular junction. **Setting:** Serum samples were collected at the Hellenic Pasteur Institute and Wayne State University. Samples were tested for LRP4 autoantibodies at Georgia Health Sciences University. Other immunoreactivities of the samples were tested at the Hellenic Pasteur Institute, Athens, Greece, or processed through University Laboratories of the Detroit Medical Center, Michigan. **Patients:** The study included 217 patients with MG, 76 patients with other neurologic or psychiatric diseases, and 45 healthy control subjects. **Results:** Anti-LRP4 antibodies were detected in 11 of 120 patients with MG without detectable anti-AChR or anti-MuSK antibodies (double seronegative) and in 1 of 36 patients without anti-AChR antibodies but with anti-MuSK antibodies, but they were not detected in any of the 61 patients with anti-AChR antibodies. No healthy control subjects and only 2 of the 76 control patients with neurologic disease had anti-LRP4 antibodies. Serum samples from patients with MG with anti-LRP4 antibodies were able to inhibit the LRP4-agrin interaction and/or alter AChR clustering in muscle cells. **Conclusions:** Anti-LRP4 antibodies were detected in the serum of approximately 9.2% of patients with double-seronegative MG. This frequency is

intermediate compared with 2 recent studies showing anti-LRP4 antibodies in 2% and 50% of patients with double-seronegative MG from different geographic locations. Together, these observations indicate that LRP4 is another autoantigen in patients with MG, and anti-LRP4 auto-antibodies may be pathogenic through different immunopathogenic processes.

Ziegler MA, Catto JA, Riggs TW, Gates ER, Grodsky MB and **Wasvary HJ** (2012). "Risk factors for anastomotic leak and mortality in diabetic patients undergoing colectomy: Analysis from a statewide surgical quality collaborative." Archives of Surgery 147(7): 600-605.

[Full-Text](#)

Department of Surgery

Objectives: To determine the risk factors in diabetic patients that are associated with increased postcolectomy mortality and anastomotic leak. **Design:** A prospectively acquired statewide database of patients who underwent colectomy was reviewed. Primary risk factors were diabetes mellitus, hyperglycemia (glucose level ≥ 140 mg/dL), steroid use, and emergency surgery. Categorical analysis, univariate logistic regression, and multivariate regression were used to evaluate the effects of these risk factors on outcomes. **Setting:** Participating hospitals within the Michigan Surgical Quality Collaborative. **Patients:** Database review of patients from hospitals within the Michigan Surgical Quality Collaborative. **Main Outcome Measures:** Anastomotic leak and 30-day mortality rate. **Results:** Of 5123 patients, 153 (3.0%) had leaks and 153 (3.0%) died. Preoperative hyperglycemia occurred in 15.6% of patients, only 54% of whom were known to have diabetes. Multivariate analysis showed that the risk of leak for patients with and without diabetes increased only by preoperative steroid use ($P < .05$). Mortality among diabetic patients was associated with emergency surgery ($P < .01$) and anastomotic leak ($P < .05$); it was not associated with hyperglycemia. Mortality among nondiabetic patients was associated with hyperglycemia ($P < .005$). The presence of an anastomotic leak was associated with increased mortality among diabetic patients (26.3% vs 4.5%; $P < .001$) compared with nondiabetic patients (6.0% vs 2.5%; $P < .05$). **Conclusions:** The presence of diabetes did not have an effect on the presence of an anastomotic leak, but diabetic patients who had a leak had more than a 4-fold higher mortality compared with nondiabetic patients. Preoperative steroid use led to increased rates of anastomotic leak in diabetic patients. Mortality was associated with hyperglycemia for nondiabetic patients only. Improved screening may identify high-risk patients who would benefit from perioperative intervention.

Zimmerman MK, **Kumar V**, **Maine GN** and **Sykes E** (2012). "Discrepant intact parathyroid hormone result by immunoassay." Clinica Chimica Acta 413(1-2): 344-345.

[Full-Text](#)

Department of Pathology

Zimny MH, **Walters BL** and **Bahl A** (2012). "Bedside ultrasound for hip dislocations." Journal of Emergency Medicine 43(6): 1063-1065.

[Full-Text](#)

Department of Emergency Medicine

BACKGROUND: Bedside ultrasound in the emergency department is being used with increasing frequency and for an increasing scope of conditions. **OBJECTIVES:** Demonstrate the use of bedside ultrasound as an adjunct for diagnosis of hip dislocation. **CASE REPORT:** A traumatic anterior hip dislocation was diagnosed with bedside ultrasound after an initial normal plain radiograph. **CONCLUSION:** Although the current standard of care for diagnosis of hip dislocation is plain radiographs, this case demonstrates that bedside ultrasound may be used as a diagnostic adjunct in this time-sensitive and potentially catastrophic diagnosis.