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Henry Ford Health System Publication List – January 2017

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health System personnel. Searches were conducted in PubMed, Embase, Web of Science, and Google Scholar during the beginning of February, and then imported into EndNote for formatting. There are 122 unique citations listed this month. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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Bone and Joint Center

Kim W, **Oravec D**, **Divine GW**, **Flynn MJ**, and **Yeni YN**. Effect of view, scan orientation and analysis volume on digital tomosynthesis (dts) based textural analysis of bone *Ann Biomed Eng* 2017;PMID: 28083858. Full Text

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Digital tomosynthesis (DTS) derived textural parameters of human vertebral cancellous bone have been previously correlated to the finite element (FE) stiffness and 3D microstructure. The objective of this study was to optimize scanning configuration and use of multiple image slices in the analysis, so that FE stiffness prediction using DTS could be maximized. Forty vertebrae (T6, T8, T11, and L3) from ten cadavers (63-90 years) were scanned using microCT to obtain trabecular bone volume fraction (BV/TV) and FE stiffness. The vertebrae were then scanned using DTS anteroposteriorly (AP) and laterally (LM) while aligned axially (0 degrees), transversely (90 degrees) or obliquely (23 degrees) to the superior-inferior axis of the vertebrae. From the serial DTS images, fractal dimension (FD), mean intercept length (MIL) and line fraction deviation (LFD) parameters were obtained from a 2D-single mid-stack location and 3D-multi-image stack. The DTS derived textural parameters were then correlated with FE stiffness using linear regression models within each scanning orientation. 3D-multi-image stack models obtained from Transverse-LM scanning orientation (90 degrees) were most explanatory regardless of accounting for the effects of BV/TV. Therefore, DTS scanning perpendicular to the axis of the spine in an LM view is the preferred configuration for prediction of vertebral cancellous bone stiffness.

Cardiology

Ahmed AM, Qureshi WT, O'Neal WT, Khalid F, and **Al-Mallah MH**. Incremental prognostic value of SPECT-MPI in chronic kidney disease: A reclassification analysis *J Nucl Cardiol* 2017;PMID: 28050863. Article Request Form

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BACKGROUND: Traditional cardiovascular (CV) risk factors have limited predictive value of CV mortality in patients with chronic kidney disease (CKD, creatinine clearance less than 60 mL/minute per 1.73 m2). The aim of this study was to evaluate incremental and independent prognostic value of single-photon emission computerized tomography-

myocardial perfusion imaging (SPECT-MPI) across continuum of renal function. METHODS: We retrospectively studied 11,518 (mean age, 65 +/- 12 years; 52% were men) patients referred for a clinical indication of SPECT-MPI between April 2004 and May 2009. Primary end point was composite of cardiac death and non-fatal myocardial infarction (CD/MI). We examined the relationship of total perfusion defect (TPD) and CD/MI in multiple Cox regression models for CV risk factors and GFR. The incremental predictive value of TPD was examined using Harrell's c-index, net reclassification index (NRI), and integrated discrimination index (IDI). RESULTS: Over a median follow-up of 5 years (25th to 75th percentiles, 3.0-6.5 years), 1,692 (14.5%) patients experienced CD/MI (740 MI and 1,182 CD). In a multivariable model adjusted for traditional CV risk factors and GFR, the presence of a perfusion defect was independently associated with increased risk of CD/MI (HR = 2.10; 95% CI 1.81, 2.43, p < .001). Using Cox regression, TPD improved the discriminatory ability beyond traditional CV risk factors and GFR [from AUC = 0.725, (95% CI 0.712-0.738) to 0.784, (95% CI 0.772-0.796), p < .0001]. Furthermore, TPD improves risk stratification of CKD patients over and above traditional CV risk factors and GFR [NRI = 14%, 95% CI (12%-16%, p < .001) and relative IDI = 60%, 95% CI (51%, 66%, p < .001)]. CONCLUSIONS: Across the spectrum of renal function, SPECT-MPI perfusion defects independently and incrementally reclassified patients for their risk of CD/MI, beyond traditional CV risk factors.

Cardiology

Aladin AI, Al Rifai M, Rasool SH, **Keteyian SJ**, **Brawner CA**, Blumenthal RS, Blaha MJ, **Al-Mallah MH**, and McEvoy JW. Relation of resting heart rate to incident atrial fibrillation (from the henry ford hospital exercise testing project) *Am J Cardiol* 2017; 119(2):262-267. PMID: 28126149. Full Text

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Autonomic nervous system (ANS) dysfunction plays a role in atrial fibrillation (AF) initiation. Cardiorespiratory fitness modulates ANS function and is inversely associated with resting heart rate (RHR) and risk of AF. Thus, we sought to study the association between RHR, as a surrogate for ANS function, and incident AF independent of exercise capacity (EC). We analyzed 51,436 subjects without previous AF who underwent a clinically indicated exercise stress test. Incident AF was ascertained through claims files. RHR was measured before stress testing, and EC was estimated by peak metabolic equivalents of task. We studied the association between RHR categories (<70, 70 to 85 [reference], and >85 beats/min) and incident AF using Cox models adjusted for risk factors and for EC. We tested for interaction between RHR and age, gender, smoking, and EC. Mean (SD) age was 53 (13) years, 53% were men, and 28% were black. Participants with RHR <70 beats/min were older, more likely to be men, have higher EC, and more likely to smoke but less likely to have diabetes and hypertension. Over a median of 5.5 years, RHR <70 beats/min was associated with 14% increased risk of AF (95 CI 6% to 25%) in fully adjusted models, whereas RHR >85 beats/min was not associated with AF risk after adjusting for EC. Results for RHR analyzed continuously and by quartile were similar. No interaction was seen. In conclusion, subjects with low RHR at all levels of EC are at increased risk of AF and may benefit from heart rhythm surveillance, particularly in the presence of other AF risk factors.

Cardiology

Basir MB, Schreiber TL, Grines CL, Dixon SR, Moses JW, Maini BS, **Khandelwal AK**, Ohman EM, and **O'Neill WW**. Effect of early initiation of mechanical circulatory support on survival in cardiogenic shock *Am J Cardiol* 2016;PMID: 28040188. Full Text

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The role and timing of percutaneous mechanical circulatory support (MCS) devices in the treatment of acute myocardial infarction complicated by cardiogenic shock (AMICS) are not well understood. We sought to evaluate patient characteristics and predictors of outcomes in patients presenting with AMICS supported with an axial flow percutaneous MCS device; 287 consecutive unselected patients enrolled in the catheter-based ventricular assist device registry presenting with AMICS who underwent percutaneous coronary intervention (PCI) were included in this analysis. All patients were supported with either the Impella 2.5 or Impella CP. Mean patient age was 66 +/- 12.5 years, 76% were men, and mean left ventricular ejection fraction was 25 +/- 12%. Before receiving MCS, 80% of patients required inotropes or vasopressors and 40% were supported with intra-aortic balloon pump; 9% of patients were under active cardiopulmonary resuscitation at the time of MCS implantation. Survival to discharge was 44%. In a multivariate analysis, early implantation of a MCS device before PCI (p = 0.04) and before requiring inotropes and vasopressors (p = 0.05) was associated with increased survival. Survival was 66% when MCS was initiated <1.25 hours from shock onset, 37% when initiated within 1.25 to 4.25 hours, and 26% when initiated after 4.25 hours (p = 0.017). Survival was 68%, 46%, 35%, 35%, and 26% for patients requiring 0, 1, 2, 3, and >/=4 inotropes before MCS support, respectively (p <0.001). In conclusion, MCS implantation early after shock onset, before initiation of inotropes or vasopressors and before PCI, is independently associated with improved survival in patients presenting with AMICS.

Cardiology

Karatasakis A, Danek BA, Karmpaliotis D, **Alaswad K**, Vo M, Carlino M, Patel MP, Rinfret S, and Brilakis ES. Approach to CTO intervention: Overview of techniques *Curr Treat Options Cardiovasc Med* 2017; 19(1):1. PMID: 28105600. Full Text

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OPINION STATEMENT: Successful percutaneous coronary intervention (PCI) of chronic total occlusions (CTOs) has been associated with significant clinical benefits, but remains technically demanding. Failure to cross the CTO with a guidewire is the most common cause of CTO PCI failure. CTO crossing can be achieved in the antegrade or retrograde direction and can be accomplished by maintaining true lumen position throughout or via subintimal dissection/reentry techniques. A procedural plan should be created prior to the procedure through careful angiographic review of four key parameters: (a) morphology of the proximal occlusion cap; (b) length of the occlusion; (c) quality of the distal vessel and presence of bifurcation at the distal cap; and (d) suitability of collateral circulation for retrograde crossing. Dual coronary injection is recommended in all cases with contralateral collaterals for detailed characterization of the lesion. If one approach fails to progress, a quick transition to the next approach is encouraged to maximize efficacy and efficiency. Procedural complications, including vessel perforation, may occur more frequently in CTO as compared with non-CTO PCI; hence, availability of necessary equipment and expertise in treating such complications are essential.

Cardiology

Kupsky DF, Ahmed AM, Sakr S, Qureshi WT, **Brawner CA**, Blaha MJ, **Ehrman JK**, **Keteyian SJ**, and **Al-Mallah MH**. Cardiorespiratory fitness and incident heart failure: The Henry Ford ExercIse Testing (FIT) Project *American Heart Journal* 2017; 185:35-42. PMID: Not yet assigned. Full Text

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Background Prior studies have demonstrated cardiorespiratory fitness (CRF) to be a strong marker of cardiovascular health. However, there are limited data investigating the association between CRF and risk of progression to heart failure (HF). The purpose of this study was to determine the relationship between CRF and incident HF. Methods We

included 66,329 patients (53.8% men, mean age 55 years) free of HF who underwent exercise treadmill stress testing at Henry Ford Health Systems between 1991 and 2009. Incident HF was determined using International Classification of Diseases, Ninth Revision codes from electronic medical records or administrative claim files. Cox proportional hazards models were performed to determine the association between CRF and incident HF. Results A total of 4,652 patients developed HF after a median follow-up duration of 6.8 (±3) years. Patients with incident HF were older (63 vs 54 years, P < .001) and had higher prevalence of known coronary artery disease (42.3% vs 11%, P < .001). Peak metabolic equivalents (METs) of task were 6.3 (±2.9) and 9.1 (±3) in the HF and non-HF groups, respectively. After adjustment for potential confounders, patients able to achieve ≥12 METs had an 81% lower risk of incident HF compared with those achieving <6 METs (hazard ratio 0.19 [95% CI 0.14-0.29], P for trend < .001). Each 1 MET achieved was associated with a 16% lower risk (hazard ratio 0.84 [95% CI 0.82-0.86], P < .001) of incident HF. Conclusions Our analysis demonstrates that higher level of fitness is associated with a lower incidence of HF independent of HF risk factors.

Cardiology

Lederman RJ, **Greenbaum AB**, Rogers T, Khan JM, Fusari M, and Chen MY. Anatomic suitability for transcaval access based on computed tomography *JACC Cardiovasc Interv* 2017; 10(1):1-10. PMID: 28057275. Full Text

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Transcaval access has been used successfully for over 200 transcatheter aortic valve replacements, large-bore percutaneous left ventricular assist devices, and thoracic endovascular aortic aneurysm repairs. This review teaches how to plan transcaval access and closure based on computed tomography. The main planning goals are to: 1) identify calcium-free crossing targets in the abdominal aorta along with optimal fluoroscopic projection angles and level with respect to lumbar vertebrae; 2) identify obstacles such as interposed bowel or pedunculated aortic atheroma; 3) plan covered stent bailout; and 4) identify jeopardized vascular branches such as renal arteries that might be obstructed by bailout covered stents if employed. The aorta and inferior vena cava are segmented (sculpted) using an image reconstruction workstation and crossing targets are highlighted. Important measurements such as aortic lumen diameter and target distance from renal arteries, aortoiliac bifurcation, and right femoral vein puncture site are reported to assist the operator. The proposed classification for transcaval feasibility has been revised, making some previously unfavorable candidates now feasible or favorable based on procedural success to date. Transcaval access allows percutaneous introduction of large devices into the aorta despite small or diseased iliofemoral arteries. By following these simplified procedures, both operators and imaging specialists can easily prepare comprehensive treatment plans.

Cardiology

Parsh J, Seth M, Green J, Sutton NR, Chetcuti S, Dixon S, Grossman PM, **Khandelwal A**, Dupree JM, and Gurm HS. Coronary artery perforations after contemporary percutaneous coronary interventions: Evaluation of incidence, risk factors, outcomes, and predictors of mortality *Catheter Cardiovasc Interv* 2017;PMID: 28145612. Full Text

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OBJECTIVES: We sought to evaluate the incidence, risk factors, in-hospital, and long-term outcomes and predictors of mortality of coronary artery perforations (CAP) in the contemporary percutaneous coronary intervention (PCI) era. BACKGROUND: CAP is a rare but serious complication of PCI associated with increased risk of morbidity and mortality. METHODS: We included 181,590 procedures performed across 47 hospitals in Michigan from January 1, 2010 to December 31, 2015. Endpoints evaluated included the incidence of CAP and its association with in-hospital outcomes. Logistic regression analysis was utilized to determine independent risk factors for CAP and to examine whether the effect of CAP on mortality varied by gender. RESULTS: CAP occurred in 625 (0.34%) patients. Independent predictors for CAP included older age, peripheral arterial disease, presence of left ventricular dysfunction or cardiomyopathy, lower body mass index, pre-PCI insertion of a mechanical ventricular support device, treatment of complex lesions (Type C), and treatment of chronic total occlusions, the latter of which was the strongest

predictor of perforation (adjusted odds ratio (OR) 7.01, P < 0.001). After adjusting for baseline risk, the incidence of adverse outcomes remained substantially greater in patients with a perforation, with an adjusted OR estimate of 5.00 for mortality (95% CI 3.42-7.31), 3.25 for acute kidney injury (95% CI 2.30-4.58), and 5.26 for transfusion (95% CI 4.03-6.87) (all P < 0.001). Perforation was associated with a higher mortality in women than men (interaction P value = 0.01). CONCLUSIONS: CAP is a rare complication but is associated with high morbidity and mortality especially in women. Further investigation is warranted to determine why women fare worse after CAP.

Cardiology

Singh V, Rodriguez AP, Bhatt P, Alfonso CE, Sakhuja R, Palacios IF, Inglessis-Azuaje I, Cohen MG, Elmariah S, and **O'Neill WW**. Ventricular septal defect complicating st-elevation myocardial infarctions: A call for action *Am J Med* 2017;PMID: 28065768. Full Text

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BACKGROUND: Ventricular septal defect is a lethal complication after an acute myocardial infarction which have become infrequent with the advent of reperfusion strategies however; they remain a major contributor to mortality. METHODS: We identified patients using the ICD-9CM procedure codes from the Nationwide Inpatient Sample between the years 2001 and 2013. A multivariate hierarchical logistic regression model was used to identify significant predictors of in-hospital mortality. RESULTS: We identified 3,373,206 ST-elevation myocardial infarctions, out of which 10,012 (0.3%) were complicated with ventricular septal defect s. Most of the patients (60%) were older than 65, male (55%), and white (63%). Inferior (49.7%) and anterior (41.1%) myocardial infarctions were more commonly implicated with the development of VSDs. The median (IQR) hospitalization length was 7 days (3.0-13.5). Only 7.65% of patients underwent some intervention with 7% surgical and 0.65% minimally invasive. Mechanical support devices were used in 36.5% of patients, with intra-aortic balloon pump (96%) being the most common. In-hospital mortality remained high at 30.5% (downward trending from 41.6% in 2001 to 23.3% in 2013). Age, cardiogenic shock, and in-hospital cardiac arrest were statistically significant predictors of in-hospital mortality. The utilization of corrective procedures significantly declined. The use of mechanical support devices and performing a corrective procedure were associated with higher mortality, length of stay and cost. CONCLUSION: Ventricular septal defects after acute myocardial infarctions remain associated with significantly high mortality rates. Highly specialized regional centers with individual expertise in the management of septal ruptures are required to improve outcomes of these patients.

Center for Athletic Medicine

Kruskall LJ, Manore MM, Eickhoff-Shemek JM, and **Ehrman JK**. DRAWING THE LINE Understanding the Scope of Practice Among Registered Dietitian Nutritionists and Exercise Professionals *Acsms Health & Fitness Journal* 2017; 21(1):23-32. PMID: Not assigned. Full Text

Center for Health Policy and Health Services Research

Yang JJ, **Williams LK**, and Buu A. Identifying pleiotropic genes in genome-wide association studies for multivariate phenotypes with mixed measurement scales *PLoS One* 2017; 12(1):e0169893. PMID: 28081206. Full Text

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We propose a multivariate genome-wide association test for mixed continuous, binary, and ordinal phenotypes. A latent response model is used to estimate the correlation between phenotypes with different measurement scales so that the empirical distribution of the Fisher's combination statistic under the null hypothesis is estimated efficiently. The simulation study shows that our proposed correlation estimation methods have high levels of accuracy. More importantly, our approach conservatively estimates the variance of the test statistic so that the type I error rate is

controlled. The simulation also shows that the proposed test maintains the power at the level very close to that of the ideal analysis based on known latent phenotypes while controlling the type I error. In contrast, conventional approaches-dichotomizing all observed phenotypes or treating them as continuous variables-could either reduce the power or employ a linear regression model unfit for the data. Furthermore, the statistical analysis on the database of the Study of Addiction: Genetics and Environment (SAGE) demonstrates that conducting a multivariate test on multiple phenotypes can increase the power of identifying markers that may not be, otherwise, chosen using marginal tests. The proposed method also offers a new approach to analyzing the Fagerstrom Test for Nicotine Dependence as multivariate phenotypes in genome-wide association studies.

Dermatology
Hao J, Lou Q, Wei Q, Mei S, Li L, **Mi QS**, Mei C, and Dong Z. MicroRNA-375 Is induced in cisplatin nephrotoxicity to repress hepatocyte nuclear factor 1-beta *J Biol Chem* 2017;PMID: 28119452. Full Text

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Nephrotoxicity is a major adverse effect of cisplatin-mediated chemotherapy in cancer patients. The pathogenesis of cisplatin-induced nephrotoxicity remains largely unclear, making it difficult to design effective renoprotective approaches. Here, we have examined the role of microRNAs (miRNAs) in cisplatin-induced nephrotoxicity. We show that cisplatin nephrotoxicity was not affected by overall depletion of both beneficial and detrimental miRNAs from kidney proximal tubular cells in mice in which the miRNA-generating enzyme Dicer had been conditionally knocked out. To identify miRNAs involved in cisplatin nephrotoxicity, we used microarray analysis to profile miRNA expression and identified 47 up- regulated microRNAs and 20 down-regulated microRNAs in kidney cortical tissues. One up-regulated miRNA was miR-375, whose expression was also induced in cisplatin-treated renal tubular cells. Interestingly, inhibition of miR-375 decreased cisplatin-induced apoptosis, suggesting that miR-375 is a cell-damaging or pro-apoptotic agent. Blockade of p53 or NF-kappaB attenuated cisplatin-induced miR-375 expression, supporting a role of p53 and NF-kappaB in miR-375 induction. We also identified hepatocyte nuclear factor 1 homeobox B (Hnf-1beta) as a key downstream target of miR-375. Of note, we further demonstrated that Hnf-1beta protected renal cells against cisplatin-induced apoptosis. Together, these results suggest that upon cisplatin exposure, p53 and NF-kappaB collaboratively induce miR-375 expression, which, in turn, represses Hnf-1beta activity, resulting in renal tubular cell apoptosis and nephrotoxicity.

Dermatology
Herzog SM, **Lim HW**, **Williams MS**, de Maddalena ID, Osterwalder U, and Surber C. Sun protection factor communication of sunscreen effectiveness: A web-based study of perception of effectiveness by dermatologists *JAMA Dermatol* 2017;PMID: 28146234. Full Text

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Dermatology
Maranda EL, **Sheinin R**, **Brys A**, **Rubin B**, and **Lim HW**. A case of eosinophilic fasciitis associated with pyoderma gangrenosum *J Eur Acad Dermatol Venereol* 2017;PMID: 28150344. Full Text

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Eosinophilic fasciitis (EF) is a rare, systemic inflammatory disease that is characterized by symmetrical swelling and scleroderma-like indurations of the distal extremities and trunk, often accompanied by pain and eosinophilia. Rarely, muscle degeneration may occur. Histologically, EF is marked by thickened, fibrotic fascia and fascial inflammation with lymphocytes and eosinophils.1,2 Herein, we present a previously unreported case of concurrent pyoderma

gangrenosum (PG) and biopsy-proven EF successfully treated with rituximab.

Dermatology
Porto DA, Wang SQ, and **Lim HW**. Counseling patients on photoprotection: What the dermatologist needs to know *JAMA Dermatol* 2017; 153(1):110. PMID: 28114519. Full Text

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Emergency Medicine
Coz Yataco A, **Jaehne AK**, and **Rivers EP**. Protocolized early sepsis care is not only helpful for patients: It prevents medical errors *Crit Care Med* 2017;PMID: 28098592. Full Text

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Emergency Medicine
Gingold DB, Pierre-Mathieu R, Cole B, Miller AC, and **Khaldun JS**. Impact of the Affordable Care Act Medicaid expansion on emergency department high utilizers with ambulatory care sensitive conditions: A cross-sectional study *Am J Emerg Med* 2017;PMID: 28110978. Full Text

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OBJECTIVES: The effect of the Affordable Care Act on emergency department (ED) high utilizers has not yet been thoroughly studied. We sought to determine the impact of changes in insurance eligibility following the 2014 Medicaid expansion on ED utilization for ambulatory care sensitive conditions (ACSC) by high ED utilizers in an urban safety net hospital. METHODS: High utilizers were defined as patients with >/=4 visits in the 6months before their most recent visit in the study period (July-December before and after Maryland's Medicaid expansion in January 2014). A differences-in-differences approach using logistic regression was used to investigate if differences between high and low utilizer cohorts changed from before and after the expansion. RESULTS: During the study period, 726 (4.1%) out of 17,795 unique patients in 2013 and 380 (2.4%) of 16,458 during the same period in 2014 were high utilizers (p-value <0.001). ACSC-associated visit predicted being a high utilizer in 2013 (OR 1.66 (95% CI [1.37, 2.01])) and 2014 (OR 1.65 (95% CI [1.27, 2.15])) but this was not different between years (OR ratio 0.99, 95% CI [0.72, 1.38], p-value 0.97). CONCLUSION: Although the proportion of high utilizers decreased significantly after Maryland's Medicaid expansion, ACSC-associated ED visits by high ED utilizers were unaffected.

Emergency Medicine
Manthey DE, Hartman ND, **Newmyer A**, Gunalda JC, Hiestand BC, and Askew KL. Trends in NRMP data from 2007-2014 for U.S. seniors matching into emergency medicine *West J Emerg Med* 2017; 18(1):105-109. PMID: 28116018. Full Text

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INTRODUCTION: Since 1978, the National Residency Matching Program (NRMP) has published data demonstrating characteristics of applicants who have matched into their preferred specialty in the NRMP main residency match. These data have been published approximately every two years. There is limited information about trends within these published data for students matching into emergency medicine (EM). Our objective was to investigate and describe trends in NRMP data to include the following: the ratio of applicants to available EM positions; United State Medical Licensing Examination (USMLE) Step 1 and Step 2 scores (compared to the national means); number of programs ranked; and Alpha Omega Alpha Honor Medical Society (AOA) membership among U.S. seniors matching

into EM. METHODS: This was a retrospective observational review of NRMP data published between 2007 and 2016. We analyzed the data using analysis of variance (ANOVA) or Kruskal-Wallis testing, and Fischer's exact or chi-squared testing, as appropriate to determine statistical significance. RESULTS: The ratio of applicants to available EM positions remained essentially stable from 2007 to 2014 but did increase slightly in 2016. We observed a net upward trend in overall Step 1 and Step 2 scores for EM applicants. However, this did not outpace the national trend increase in Step 1 and 2 scores overall. There was an increase in the mean number of programs ranked by EM applicants over the years studied from 7.8 (SD4.2) to 9.2 (SD5.0, p<0.001), driven predominantly by the cohort of U.S. students successful in the match. Among time intervals, there was a difference in the number of EM applicants with AOA membership (p=0.043) due to a drop in the number of AOA students in 2011. No sustained statistical trend in AOA membership was identified over the seven-year period studied. CONCLUSION: NRMP data demonstrate trends among EM applicants that are similar to national trends in other specialties for USMLE board scores, and a modest increase in number of programs ranked. AOA membership was largely stable. EM does not appear to have become more competitive relative to other specialties or previous years in these categories.

Emergency Medicine

Wilson SP, **Vohra T**, **Knych M**, **Goldberg J**, **Price C**, **Calo S**, **Mahan M**, and **Miller J**. Gonorrhea and chlamydia in the emergency department: Continued need for more focused treatment for men, women and pregnant women *Am J Emerg Med* 2017;PMID: 28073612. Full Text

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INTRODUCTION: Delay in current nucleic acid amplification testing for Neisseria gonorrhoeae and Chlamydia trachomatis has led to recommendations for presumptive treatment in patients with concern for infection and unreliable follow-up. In the urban setting, it is assumed that many patients have unreliable follow-up, therefore presumptive therapy is thought to be used frequently. We sought to measure the frequency of disease and accuracy of presumptive treatment for these infections. METHODS: This was an observational cohort study performed at an urban academic Level 1 trauma center ED with an annual census of 95,000 visits per year. Testing was performed using the APTIMA Unisex swab assay (Gen-Probe Incorporated, San Diego, CA). Presumptive therapy was defined as receiving treatment for both infections during the initial encounter without confirmation of diagnosis. RESULTS: A total of 1162 patients enrolled. Infection was present in 26% of men, 14% of all women and 11% of pregnant women. Despite high frequency of presumptive treatment, >4% of infected patients in each category went untreated. CONCLUSION: Inaccuracy of presumptive treatment was common for these sexually transmitted infections. There is an opportunity to improve diagnostic accuracy for treatment.

Endocrinology

Beck RW, Riddlesworth T, Ruedy K, Ahmann A, Bergenstal R, Haller S, Kollman C, **Kruger D**, McGill JB, Polonsky W, Toschi E, Wolpert H, and Price D. Effect of continuous glucose monitoring on glycemic control in adults with type 1 diabetes using insulin injections: The diamond randomized clinical trial *Jama* 2017; 317(4):371-378. PMID: 28118453. Full Text

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Importance: Previous clinical trials showing the benefit of continuous glucose monitoring (CGM) in the management of type 1 diabetes predominantly have included adults using insulin pumps, even though the majority of adults with type 1 diabetes administer insulin by injection. Objective: To determine the effectiveness of CGM in adults with type 1 diabetes treated with insulin injections. Design, Setting, and Participants: Randomized clinical trial conducted between October 2014 and May 2016 at 24 endocrinology practices in the United States that included 158 adults with type 1 diabetes who were using multiple daily insulin injections and had hemoglobin A1c (HbA1c) levels of 7.5% to 9.9%. Interventions: Random assignment 2:1 to CGM (n = 105) or usual care (control group; n = 53). Main Outcomes

and Measures: Primary outcome measure was the difference in change in central-laboratory-measured HbA1c level from baseline to 24 weeks. There were 18 secondary or exploratory end points, of which 15 are reported in this article, including duration of hypoglycemia at less than 70 mg/dL, measured with CGM for 7 days at 12 and 24 weeks. Results: Among the 158 randomized participants (mean age, 48 years [SD, 13]; 44% women; mean baseline HbA1c level, 8.6% [SD, 0.6%]; and median diabetes duration, 19 years [interquartile range, 10-31 years]), 155 (98%) completed the study. In the CGM group, 93% used CGM 6 d/wk or more in month 6. Mean HbA1c reduction from baseline was 1.1% at 12 weeks and 1.0% at 24 weeks in the CGM group and 0.5% and 0.4%, respectively, in the control group (repeated-measures model P < .001). At 24 weeks, the adjusted treatment-group difference in mean change in HbA1c level from baseline was -0.6% (95% CI, -0.8% to -0.3%; P < .001). Median duration of hypoglycemia at less than <70 mg/dL was 43 min/d (IQR, 27-69) in the CGM group vs 80 min/d (IQR, 36-111) in the control group (P = .002). Severe hypoglycemia events occurred in 2 participants in each group. Conclusions and Relevance: Among adults with type 1 diabetes who used multiple daily insulin injections, the use of CGM compared with usual care resulted in a greater decrease in HbA1c level during 24 weeks. Further research is needed to assess longer-term effectiveness, as well as clinical outcomes and adverse effects. Trial Registration: clinicaltrials.gov Identifier: NCT02282397.

Endocrinology

Strong J, **Kruger D**, and Novak L. Insulin glargine 300 units/mL: a guide for healthcare professionals involved in the management of diabetes *Curr Med Res Opin* 2017:1-19. PMID: 28132529. Article Request Form

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Insulin glargine 300 units/mL (Gla-300) is a formulation of insulin glargine that delivers the same number of insulin units in one-third of the injectable volume of insulin glargine 100 units/mL (Gla-100). Recently approved in the United States and in Europe for use in type 1 and type 2 diabetes, Gla-300 has a more constant and evenly distributed glucose-lowering effect compared with Gla-100, with a duration of action beyond 24 hours and lower within-day and between-day intra-individual variability in blood glucose levels. These benefits translate into predictable and sustained glucose control from a once-daily injection, with potential for fewer hypoglycemia episodes and less weight gain. Case studies are presented to highlight the potential clinical benefits and considerations associated with initiating treatment with Gla-300 in people with type 1 and type 2 diabetes.

Gastroenterology

Poordad F, Felizarta F, Asatryan A, Sulkowski MS, Reindollar RW, Landis CS, **Gordon SC**, Flamm SL, Fried MW, Bernstein DE, Lin CW, Liu R, Lovell SS, Ng TI, Kort J, and Mensa FJ. Glecaprevir and pibrentasvir for 12 weeks for hcv genotype 1 infection and prior direct-acting antiviral treatment *Hepatology* 2017;PMID: 28128852. Full Text

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Although direct-acting antiviral (DAA) therapies for chronic hepatitis C virus (HCV) infection have demonstrated high rates of sustained virologic response, virologic failure may still occur, potentially leading to the emergence of viral resistance, which can decrease the effectiveness of subsequent treatment. Treatment options for patients who failed previous DAA-containing regimens, particularly those with NS5A inhibitors, are limited, and remain an area of unmet medical need. This phase 2, open-label study (MAGELLAN-1) evaluated the efficacy and safety of glecaprevir (GLE) + pibrentasvir (PIB) +/- ribavirin (RBV) in HCV genotype 1-infected patients with prior virologic failure to HCV DAA-containing therapy. A total of 50 non-cirrhotic patients were randomized to three arms: 200 mg GLE + 80 mg PIB (Arm A), 300 mg GLE + 120 mg PIB with 800 mg once-daily RBV (Arm B), or 300 mg GLE + 120 mg PIB without RBV (Arm C). By intent-to-treat analysis, sustained virologic response at post-treatment week 12 (SVR12) was achieved in 100% (6/6, 95% CI 61 - 100), 95% (21/22, 95% CI 78 - 99), and 86% (19/22, 95% CI 67 - 95) of patients in Arms A, B, and C, respectively. Virologic failure occurred in no patients in Arm A, and 1 patient each in Arms B and

C (two patients lost to follow-up in Arm C). The majority of adverse events were mild in severity; no serious adverse events related to study drug and no relevant laboratory abnormalities in alanine aminotransferase, total bilirubin, or hemoglobin, were observed. CONCLUSION: The combination of GLE and PIB was highly efficacious and well-tolerated in patients with HCV GT1 infection and prior failure to DAA-containing therapy; RBV coadministration did not improve efficacy. This article is protected by copyright. All rights reserved.

Hematology / Oncology

Bendell JC, Javle M, Bekaii-Saab TS, Finn RS, Wainberg ZA, Laheru DA, Weekes CD, Tan BR, **Khan GN**, Zalupski MM, Infante JR, Jones S, Papadopoulos KP, Tolcher AW, Chavira RE, Christy-Bittel JL, Barrett E, and Patnaik A. A phase 1 dose-escalation and expansion study of binimetinib (MEK162), a potent and selective oral MEK1/2 inhibitor *Br J Cancer* 2017;PMID: 28152546. Full Text

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BACKGROUND: Binimetinib (MEK162; ARRY-438162) is a potent and selective oral MEK 1/2 inhibitor. This phase 1 study determined the maximum tolerated dose (MTD), safety, pharmacokinetic and pharmacodynamic profiles, and preliminary anti-tumour activity of binimetinib in patients with advanced solid tumours, with expansion cohorts of patients with biliary cancer or KRAS- or BRAF-mutant colorectal cancer. METHODS: Binimetinib was administered twice daily. Expansion cohorts were enroled after MTD determination following a 3+3 dose-escalation design. Pharmacokinetic properties were determined from plasma samples. Tumour samples were assessed for mutations in RAS, RAF, and other relevant genes. Pharmacodynamic properties were evaluated in serum and skin punch biopsy samples. RESULTS: Ninety-three patients received binimetinib (dose-escalation phase, 19; expansion, 74). The MTD was 60 mg twice daily, with dose-limiting adverse events (AEs) of dermatitis acneiform and chorioretinopathy. The dose for expansion patients was subsequently decreased to 45 mg twice daily because of the frequency of treatment-related ocular toxicity at the MTD. Common AEs across all dose levels included rash (81%), nausea (56%), vomiting (52%), diarrhoea (51%), peripheral oedema (46%), and fatigue (43%); most were grade 1/2. Dose-proportional increases in binimetinib exposure were observed and target inhibition was demonstrated in serum and skin punch biopsy samples. Three patients with biliary cancer had objective responses (one complete and two partial). CONCLUSIONS: Binimetinib demonstrated a manageable safety profile, target inhibition, and dose-proportional exposure. The 45 mg twice daily dose was identified as the recommended phase 2 dose. The three objective responses in biliary cancer patients are encouraging and support further evaluation in this population.British Journal of Cancer advance online publication, 2 February 2017; doi:10.1038/bjc.2017.10 www.bjcancer.com.

Hematology / Oncology

Eggly S, Hamel LM, Foster TS, Albrecht TL, **Chapman R**, Harper FW, Thompson H, Griggs JJ, Gonzalez R, Berry-Bobovski L, Tkatch R, Simon M, Shields A, Gadgeel S, Loutfi R, Ali H, Wollner I, and Penner LA. Randomized trial of a question prompt list to increase patient active participation during interactions with black patients and their oncologists *Patient Educ Couns* 2016;PMID: 28073615. Full Text

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OBJECTIVE: Communication during racially-discordant interactions is often of poor quality and may contribute to racial treatment disparities. We evaluated an intervention designed to increase patient active participation and other communication-related outcomes during interactions between Black patients and non-Black oncologists. METHODS: Participants were 18 non-Black medical oncologists and 114 Black patients at two cancer hospitals in Detroit, Michigan, USA. Before a clinic visit to discuss treatment, patients were randomly assigned to usual care or to one of two question prompt list (QPL) formats: booklet (QPL-Only), or booklet and communication coach (QPL-plus-Coach). Patient-oncologist interactions were video recorded. Patients reported perceptions of the intervention, oncologist communication, role in treatment decisions, and trust in the oncologist. Observers assessed interaction length, patient active participation, and oncologist communication. RESULTS: The intervention was viewed positively and did not increase interaction length. The QPL-only format increased patient active participation; the QPL-plus-Coach format decreased patient perceptions of oncologist communication. No other significant effects were found. CONCLUSION: This QPL booklet is acceptable and increases patient active participation in racially-discordant oncology interactions. Future research should investigate whether adding physician-focused interventions might improve other outcomes. PRACTICE IMPLICATIONS: This QPL booklet is acceptable and can improve patient active participation in racially-discordant oncology interactions.

Hospital Medicine

Barnes GD, **Kaatz S**, Lopez A, Gu X, Kozlowski J, **Krol GD**, and Froehlich JB. Discontinuation of warfarin therapy for patients with atrial fibrillation: The michigan anticoagulation quality improvement initiative experience *JAMA Cardiol* 2017;PMID: 28052153. Full Text

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Hospital Medicine

Kataruka A, Kong X, Haymart B, Kline-Rogers E, Almany S, Kozlowski J, **Krol GD**, **Kaatz S**, McNamara MW, Froehlich JB, and Barnes GD. SAMe-TT2R2 predicts quality of anticoagulation in patients with acute venous thromboembolism: The MAQI2 experience *Vasc Med* 2017:1358863x16682863. PMID: 28145152. Full Text

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A high SAMe-TT2R2 score predicted poor warfarin control and adverse events among atrial fibrillation patients. However, the SAMe-TT2R2 score has not been well validated in venous thromboembolism (VTE) patients. A cohort of 1943 warfarin-treated patients with acute VTE was analyzed to correlate the SAMe-TT2R2 score with time in therapeutic range (TTR) and clinical adverse events. A TTR <60% was more frequent among patients with a high (>2) versus low (0-1) SAMe-TT2R2 score (63.4% vs 52.3%, p<0.0001). A high SAMe-TT2R2 score (>2) correlated with increased overall adverse events (7.9 vs 4.5 overall adverse events/100 patient years, p=0.002), driven primarily by increased recurrent VTE rates (4.2 vs 1.5 recurrent VTE/100 patient years, p=0.0003). The SAMe-TT2R2 score had a modest predictive ability for international normalized ratio (INR) quality and adverse clinical events among warfarin-treated VTE patients. The utility of the SAMe-TT2R2 score to guide clinical decision-making remains to be investigated.

Hypertension and Vascular Research

Chen J, **Cui C**, **Yang X**, **Xu J**, **Venkat P**, **Zacharek A**, **Yu P**, and **Chopp M**. Mir-126 affects brain-heart interaction after cerebral ischemic stroke *Transl Stroke Res* 2017;PMID: 28101763. Article Request Form

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Cardiovascular diseases are approximately three times higher in patients with neurological deficits than in patients without neurological deficits. MicroRNA-126 (MiR-126) facilitates vascular remodeling and decreases fibrosis and is emerging as an important factor in the pathogenesis of cardiovascular diseases and cerebral stroke. In this study, we tested the hypothesis that decreased miR-126 after ischemic stroke may play an important role in regulating cardiac function. Wild-type (WT), specific conditional-knockout endothelial cell miR-126 (miR-126EC-/-), and miR-126 knockout control (miR-126fl/fl) mice were subjected to distal middle cerebral artery occlusion (dMCAo) (n = 10/group). Cardiac hemodynamics and function were measured using transthoracic Doppler echocardiography. Mice were sacrificed at 28 days after dMCAo. WT mice subjected to stroke exhibited significantly decreased cardiac ejection fraction and increased myocyte hypertrophy, fibrosis as well as increased heart inflammation, infiltrating macrophages, and oxidative stress compared to non-stroke animals. Stroke significantly decreased serum and heart miR-126 expression and increased miR-126 target genes, vascular cell adhesion protein-1, and monocyte chemotactic protein-1 gene, and protein expression in the heart compared to non-stroke mice. MiR-126EC-/- mice exhibited significantly decreased cardiac function and increased cardiomyocyte hypertrophy, fibrosis, and inflammatory factor expression after stroke compared to miR-126fl/fl stroke mice. Exosomes derived from endothelial cells of miR-126EC-/- (miR-126EC-/-EC-Exo) mice exhibited significantly decreased miR-126 expression than exosomes derived from miR-126fl/fl (miR-126fl/fl-EC-Exo) mice. Treatment of cardiomyocytes subjected to oxygen glucose deprivation with miR-126fl/fl-EC-Exo exhibited significantly decreased hypertrophy than with miR-126EC-/-EC-Exo treatment. Ischemic stroke directly induces cardiac dysfunction. Decreasing miR-126 expression may contribute to cardiac dysfunction after stroke in mice.

Hypertension and Vascular Research
Karuppagounder V, Arumugam S, Giridharan VV, Sreedhar R, Bose RJ, Vanama J, **Palaniyandi SS**, Konishi T, Watanabe K, and Thandavarayan RA. Tiny molecule, big power: Multi-target approach for curcumin in diabetic cardiomyopathy *Nutrition* 2017; 34:47-54. PMID: 28063511. Full Text

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Diabetic cardiomyopathy (DCM) is described as impaired cardiac diastolic and systolic functions. Diabetes mellitus (DM), a related cardiovascular disease, has become one of the major causes of death in DM patients. Mortality in these diseases is 2 to 3 times higher than in non-DM patients with cardiovascular disease. The progression of DCM and the cellular and molecular perturbations associated with the pathogenesis are complex and multifactorial. Although considerable progress has been achieved, the molecular etiologies of DCM remain poorly understood. There is an expanding need for natural antidiabetic medicines that do not cause the side effects of modern drugs. Curcumin, a pleiotropic molecule, from Curcuma longa, is known to possess numerous impacts such as scavenging free radical, antioxidant, antitumor, and antiinflammatory activities. The reports from preclinical and clinical findings revealed that curcumin can reverse insulin resistance, hyperglycemia, obesity, and obesity-related metabolic diseases. The current review provides an updated overview of the possible molecular mechanism of DCM and multitarget approach of curcumin in alleviating DCM and diabetic complication. Additionally, we mentioned the approaches that are currently being implemented to improve the bioavailability of this promising natural product in diabetes therapeutics.

Infectious Diseases

Arshad S, Huang V, **Hartman P**, **Perri MB**, **Moreno D**, and **Zervos MJ**. Ceftaroline fosamil monotherapy for methicillin-resistant Staphylococcus aureus bacteremia (MRSAB): A comparative clinical outcomes study *Int J Infect Dis* 2017;PMID: 28131729. Full Text

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OBJECTIVES: Vancomycin is the treatment of choice for methicillin-resistant Staphylococcus aureus (MRSA) bacteremia; however, it has been scrutinized due to failure in severe infections. Ceftaroline fosamil (CPT-F) is approved for MRSA acute bacterial skin and skin structure infection (ABSSSI) but not in bloodstream infections. We evaluated clinical outcomes of treatment with CPT-F in patients with MRSA bacteremia (MRSAB). METHODS: Patients diagnosed with MRSAB at Henry Ford Hospital in Detroit, MI due to isolates with vancomycin MIC>/=1.0mg/L, and susceptible in vitro to CPT-F were systematically reviewed retrospectively. CPT-F-treated patients were matched with vancomycin- and daptomycin-treated patients based on age (>/=65years), ICU status, and severity of illness. Outcomes evaluated included duration of hospitalization, duration of therapy, adverse events, relapse, hospital readmission, and death. RESULTS: 30 consecutive cases of MRSAB treated with CPT-F were identified from May 2011 - June 2013, and matched to 56 vancomycin and 46 daptomycin MRSAB patients. Primary sources of CPT-F-treated MRSAB cohort were endocarditis (n=7, 23%), skin/wound (n=9, 30%), and bone/joint (n=8, 27%). Origin of CPT-F-treated MRSAB was 43% community-acquired, 43% healthcare-associated, and 13% hospital-acquired. Mean hospital length of stay for CPT-F pts was 22 days. Overall 30-day mortality rate was observed in 13% (n=4) of CPT-F cases versus 24% (n=11) of daptomycin pts and 11% (n=6) in the vancomycin cohort (p=0.188). CONCLUSIONS: Ceftaroline fosamil demonstrated comparable clinical outcomes in MRSAB patients compared with the other agents, especially as salvage therapy.

Internal Medicine

Barnes GD, **Kaatz S**, Lopez A, Gu X, Kozlowski J, **Krol GD**, and Froehlich JB. Discontinuation of warfarin therapy for patients with atrial fibrillation: The michigan anticoagulation quality improvement initiative experience *JAMA Cardiol* 2017;PMID: 28052153. Full Text

Frankel Cardiovascular Center, University of Michigan Health System, Ann Arbor.
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Internal Medicine

Joshi S, and **Vanderhoek M**. SU-F-I-71: Fetal protection during fluoroscopy: To shield or not to shield? *Med Phys* 2016; 43(6):3403. PMID: 28047626. Abstract

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PURPOSE: Lead aprons are routinely used to shield the fetus from radiation during fluoroscopically guided interventions (FGI) involving pregnant patients. When placed in the primary beam, lead aprons often reduce image quality and increase fluoroscopic radiation output, which can adversely affect fetal dose. The purpose of this work is to identify an effective and practical method to reduce fetal dose without affecting image quality. METHODS: A pregnant patient equivalent abdominal phantom is set on the table along with an image quality test object (CIRS model 903) representing patient anatomy of interest. An ion chamber is positioned at the x-ray beam entrance to the phantom, which is used to estimate the relative fetal dose. For three protective methods, image quality and fetal dose measurements are compared to baseline (no protection):1. Lead apron shielding the entire abdomen2. Lead apron shielding part of the abdomen, including the fetus 3. Narrow collimation such that fetus is excluded from the primary beam RESULTS: With lead shielding the entire abdomen, the dose is reduced by 80% relative to baseline along with a drastic deterioration of image quality. With lead shielding only the fetus, the dose is reduced by 65% along with complete preservation of image quality, since the image quality test object is not shielded. However, narrow collimation results in 90% dose reduction and a slight improvement of image quality relative to baseline. CONCLUSION: The use of narrow collimation to protect the fetus during FGI is a simple and highly effective method that simultaneously reduces fetal dose and maintains sufficient image quality. Lead aprons are not as effective at fetal dose reduction, and if placed improperly, they can severely degrade image quality. Future work aims to investigate a wider variety of fluoroscopy systems to confirm these results across many different system geometries.

Internal Medicine
Kataruka A, Kong X, Haymart B, Kline-Rogers E, Almany S, Kozlowski J, **Krol GD**, **Kaatz S**, McNamara MW, Froehlich JB, and Barnes GD. SAMe-TT2R2 predicts quality of anticoagulation in patients with acute venous thromboembolism: The MAQI2 experience *Vasc Med* 2017:1358863x16682863. PMID: 28145152. Full Text

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A high SAMe-TT2R2 score predicted poor warfarin control and adverse events among atrial fibrillation patients. However, the SAMe-TT2R2 score has not been well validated in venous thromboembolism (VTE) patients. A cohort of 1943 warfarin-treated patients with acute VTE was analyzed to correlate the SAMe-TT2R2 score with time in therapeutic range (TTR) and clinical adverse events. A TTR <60% was more frequent among patients with a high (>2) versus low (0-1) SAMe-TT2R2 score (63.4% vs 52.3%, p<0.0001). A high SAMe-TT2R2 score (>2) correlated with increased overall adverse events (7.9 vs 4.5 overall adverse events/100 patient years, p=0.002), driven primarily by increased recurrent VTE rates (4.2 vs 1.5 recurrent VTE/100 patient years, p=0.0003). The SAMe-TT2R2 score had a modest predictive ability for international normalized ratio (INR) quality and adverse clinical events among warfarin-treated VTE patients. The utility of the SAMe-TT2R2 score to guide clinical decision-making remains to be investigated.

Internal Medicine
Maranda EL, **Sheinin R**, **Brys A**, **Rubin B**, and **Lim HW**. A case of eosinophilic fasciitis associated with pyoderma gangrenosum *J Eur Acad Dermatol Venereol* 2017;PMID: 28150344. Full Text

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Eosinophilic fasciitis (EF) is a rare, systemic inflammatory disease that is characterized by symmetrical swelling and scleroderma-like indurations of the distal extremities and trunk, often accompanied by pain and eosinophilia. Rarely, muscle degeneration may occur. Histologically, EF is marked by thickened, fibrotic fascia and fascial inflammation with lymphocytes and eosinophils.1,2 Herein, we present a previously unreported case of concurrent pyoderma gangrenosum (PG) and biopsy-proven EF successfully treated with rituximab.

Internal Medicine
Nakagawa P, **Masjoan-Juncos JX**, **Basha H**, **Janic B**, **Worou ME**, **Liao TD**, **Romero CA**, **Peterson EL**, and **Carretero OA**. Effects of N-acetyl-seryl-asparyl-lysyl-proline on blood pressure, renal damage, and mortality in systemic lupus erythematosus *Physiol Rep* 2017; 5(2)PMID: 28126732. Full Text

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Systemic lupus erythematosus (SLE) is an autoimmune disease with a high prevalence of hypertension. NZBWF1 (SLE-Hyp) mice develop hypertension that can be prevented by modulating T cells. The peptide N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) decreases renal damage and improves renal function in a model of SLE without hypertension (MRL/lpr). However, it is not known whether Ac-SDKP prevents hypertension in NZBWF1 mice. We hypothesized that in SLE-Hyp, Ac-SDKP prevents hypertension and renal damage by modulating T cells. Animals were divided into four groups: (1) control + vehicle, (2) control + Ac-SDKP, (3) SLE + vehicle, and (4) SLE + Ac-SDKP Systolic blood pressure (SBP), albuminuria, renal fibrosis, and T-cell phenotype were analyzed. SBP was higher in SLE compared to control mice and was not decreased by Ac-SDKP treatment. Half of SLE mice developed an acute and severe form of hypertension accompanied by albuminuria followed by death. Ac-SDKP delayed development of severe hypertension, albuminuria, and early mortality, but this delay did not reach statistical significance. Ac-SDKP prevented glomerulosclerosis, but not interstitial fibrosis in SLE-Hyp mice. SLE-Hyp mice

showed a decrease in helper and cytotoxic T cells as well as an increase in double negative lymphocytes and T helper 17 cells, but these cells were unaffected by Ac-SDKP In conclusion, Ac-SDKP prevents kidney damage, without affecting blood pressure in an SLE animal model. However, during the acute relapse of SLE, Ac-SDKP might also delay the manifestation of an acute and severe form of hypertension leading to early mortality. Ac-SDKP is a potential tool to treat renal damage in SLE-Hyp mice.

Internal Medicine

Yang JJ, **Williams LK**, and Buu A. Identifying pleiotropic genes in genome-wide association studies for multivariate phenotypes with mixed measurement scales *PLoS One* 2017; 12(1):e0169893. PMID: 28081206. Full Text

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We propose a multivariate genome-wide association test for mixed continuous, binary, and ordinal phenotypes. A latent response model is used to estimate the correlation between phenotypes with different measurement scales so that the empirical distribution of the Fisher's combination statistic under the null hypothesis is estimated efficiently. The simulation study shows that our proposed correlation estimation methods have high levels of accuracy. More importantly, our approach conservatively estimates the variance of the test statistic so that the type I error rate is controlled. The simulation also shows that the proposed test maintains the power at the level very close to that of the ideal analysis based on known latent phenotypes while controlling the type I error. In contrast, conventional approaches-dichotomizing all observed phenotypes or treating them as continuous variables-could either reduce the power or employ a linear regression model unfit for the data. Furthermore, the statistical analysis on the database of the Study of Addiction: Genetics and Environment (SAGE) demonstrates that conducting a multivariate test on multiple phenotypes can increase the power of identifying markers that may not be, otherwise, chosen using marginal tests. The proposed method also offers a new approach to analyzing the Fagerstrom Test for Nicotine Dependence as multivariate phenotypes in genome-wide association studies.

Medical Education

Awdish RL, **Buick D**, **Kokas M**, **Berlin H**, **Jackman C**, **Williamson C**, **Mendez MP**, and **Chasteen K**. A communications bundle to improve satisfaction for critically ill patients and their families: A prospective, cohort pilot study *J Pain Symptom Manage* 2016;PMID: 28042074. Full Text

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CONTEXT: Communication skills training with simulated patients is used by many academic centers, but how to translate skills learned in simulated settings to improve communication in real encounters has not been described. OBJECTIVE: We developed a communications bundle to facilitate skill transfer from simulation to real encounters and improve patient and/or family satisfaction with physician communication. We tested the feasibility of its use in our hospital's medical intensive care unit (MICU). METHODS: This prospective cohort 2-week feasibility study included patients admitted to the MICU with APACHE IV predicted mortality >30% and/or single organ failure. The communications bundle included simulation communication training for MICU physicians, scheduling a family meeting within 72 hours of MICU admission, standardized pre- and post-meeting team huddles with the aid of a mobile app to set an agenda, choose a communication goal, and get feedback, and documentation of meeting in the electronic medical record. The intervention group receiving the communications bundle was located in a geographically separate unit than the control group receiving standard of care from MICU physicians who had not received training in the communications bundle. Patient satisfaction surveys were given within 48 hours of the family meeting and scores compared between the two groups. We also compared trainee self-perceived communication preparation. RESULTS: The intervention group (N = 15) scored significantly higher on satisfaction than the control group (N = 16) (P = 0.018). Intervention group trainees reported improvement in self-perceived communication preparation. CONCLUSION: Use of the communications bundle proved feasible in the MICU and suggests association with improved patient satisfaction and trainee self-perception of communication preparedness.

Nephrology

Kumbar L, **Soi V**, **Adams E**, **Brown Deacon C**, **Zidan M**, and **Yee J**. Coronal mode ultrasound guided hemodialysis cannulation: A pilot randomized comparison with standard cannulation technique *Hemodial Int* 2017;PMID: 28067467. Full Text

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Background Infiltrations from cannulation result in significant morbidity including loss of hemodialysis (HD) vascular access (VA). Cannulation is dependent on personnel skill and VA characteristics. Surface marking of VA lacks real-time information and traditional ultrasound (US) devices are large, expensive, requiring skilled operators. Sonic Window(c) (Analogic Ultrasound, Peabody, MA, USA) is a coronal mode ultrasound device (CMUD) approved for VA cannulation. Methods Single center randomized, prospective pilot study comparing handheld US-guided cannulation of new arteriovenous fistula (AVF) to standard cannulation practices. Patients with end stage renal disease (ESRD) on in-center HD who had a new AVF cleared for cannulation and dialysis were enrolled. Patients with new AVF received either standard cannulation (control group) or image guidance using CMUD (study group) for 3 weeks. Ultrasound characteristics of VA, cannulation practices and complications end points were obtained. Results An infiltration rate of 9.7% was noted during the study. Slightly lower odds ratio (OR) of infiltration was observed in the study group (OR 0.94, 95% CI: 0.26-3.41, P value = 0.93). Study group yielded longer time for assessment (101.8 +/- 80.2 vs. 22.3 +/- 22.5 seconds, P = < 0.001), increased cannulation time (41.1 +/- 70.6 vs. 25.0 +/- 27.9 seconds, P = 0.04), and increased patient satisfaction (94.6% vs. 82%, P = 0.04) compared to control group. Number of cannulation attempts, needle size, arterial or venous needle insertion, and tourniquet usage between groups were not statistically different. Conclusion Handheld ultrasound is a safe and useful aid in cannulation of dialysis access.

Nephrology

Yee J. One isn't the loneliest of numbers: N-of-1 trials *Adv Chronic Kidney Dis* 2016; 23(6):341-342. PMID: 28115074. Full Text

Division of Nephrology and Hypertension, Department of Internal Medicine, Henry Ford Hospital, Detroit, MI.

Neurology

Bagher-Ebadian H, Dehkordi A, and **Ewing J**. SU-F-I-26: Maximum likelihood and nested model selection techniques for pharmacokinetic analysis of dynamic contrast enhanced mri in patients with glioblastoma tumors *Med Phys* 2016; 43(6):3392. PMID: 28048158. Abstract

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PURPOSE: This pilot study introduces a novel approach for estimation of pharmacokinetic parameters in dynamic contrast enhanced magnetic resonance imaging (DCE-MRI). In this study Maximum Likelihood (ML) and Nested Model Selection (NMS) techniques are combined to construct an approximately unbiased estimator for DCE-MRI data analysis. METHODS: DCE T1-weighted MRI using the contrast agent (CA) gadopentetate dimeglumine was performed on 20 patients with Glioblastoma tumor. ML Estimation (MLE) technique was recruited for optimizing 3 physiologically nested models constructed based on the extended Tofts model in the course of DCE-MRI experimental. The Log-Likelihood-Ratio (LLR) measures for three nested models were used to choose the best model explaining the variation of the experimental DCE-MRI data and to estimate its Pharmacokinetic (PK) parameters. The observed information matrix or the matrix of Log-Likelihood was used to estimate the variance and co-variance of the estimated PK parameters for each of selected models. RESULTS: The PK parameters along with the model choice maps estimated by the MLE and NMS are highly in agreement with the physiological condition of underlying pathology and the values for the permeability parameters of the brain reported by the literature. The low variance and covariance measures of the estimated PK parameters being reasonably in-range imply that the proposed estimator is robust for estimation of physiological parameters in DCE-MRI studies. CONCLUSION: This pilot study confirms that only three parameters of the standard model are sufficient to fit the most complicated time trace of CA concentration in DCE-T1 weighted studies for GBM tumors under the conditions of the experiment. This study is supported in part by Dykstra Family (F60570) and mentored grants (A10237).

Neurology

Bagher-Ebadian H, **Mohammadian Behbahani M**, and **Ewing J**. WE-FG-206-03: An adaptive model for pharmacokinetic nested model selection in dynamic contrast enhanced mri data analysis *Med Phys* 2016; 43(6):3831. PMID: 28048278. Abstract

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PURPOSE: This study introduces an adaptive Model Selection (MS) technique to perform Pharmacokinetic nested MS from the time trace of longitudinal relaxation rate change, DeltaR1 (R1 = 1/T1) in Dynamic Contrast Enhanced (DCE) MRI studies. METHODS: Three physiologically nested models derived from the standard Tofts model along with an averaged (over 30 patients) arterial input function were used to simulate a set of DeltaR1 profiles to describe possible physiological conditions of underlying tissue pathology: Model-1: the vascular compartment is filled with contrast agent (CA) with no outward leakage. Model-2: the vascular compartment is filled with CA with outward leakage but no evidence of back-flux. Model-3: the vascular compartment is filled with CA with both outward and backward-flux. Three different sets of simulated DeltaR1 profiles in presence of different signal-to-noise ratios (5, 10, 15, 30, 70, 100, and no noise) were used to train an Artificial Neural Network (ANN) for performing MS. A k-fold cross-validation method was used to validate and optimize the ANN architecture. The trained-ANN was also applied on the DCE-MRI data of 20 patients with Glioblastoma and results were compared to the models selected by the Log-Likelihood-Ratio (LLR) technique using Dice coefficient. RESULTS: The confusion matrix and the strong similarity (Dice coefficients of 0.87, 0.89 for Models 2 and 3) between the models selected by the trained ANN and the LLR method confirms that the performance of the adaptive NMS technique is superior to the LLR method. The ANN showed a strong sensitivity for selecting models with higher orders; thus less type-II errors (never misses any tissues with leaky vasculature (Models 2 and 3). CONCLUSION: The noise insensitivity, speed, and superiority of the ANN technique in choosing the best PK model would allow a less biased estimation of cerebrovascular permeability parameters in tumorous tissues. This work is supported in part by HFHS mentored Grant (A10237).

Neurology

Bagic AI, **Bowyer SM**, Kirsch HE, Funke ME, and Burgess RC. American Clinical MEG Society (ACMEGS) Position Statement #2: The value of magnetoencephalography (meg)/magnetic source imaging (msi) in noninvasive presurgical mapping of eloquent cortices of patients preparing for surgical interventions *J Clin Neurophysiol* 2017;PMID: 28059855. Full Text

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Neurology

Chen J, **Cui C**, **Yang X**, **Xu J**, **Venkat P**, **Zacharek A**, **Yu P**, and **Chopp M**. Mir-126 affects brain-heart interaction after cerebral ischemic stroke *Transl Stroke Res* 2017;PMID: 28101763. Article Request Form

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Cardiovascular diseases are approximately three times higher in patients with neurological deficits than in patients without neurological deficits. MicroRNA-126 (MiR-126) facilitates vascular remodeling and decreases fibrosis and is emerging as an important factor in the pathogenesis of cardiovascular diseases and cerebral stroke. In this study, we tested the hypothesis that decreased miR-126 after ischemic stroke may play an important role in regulating cardiac function. Wild-type (WT), specific conditional-knockout endothelial cell miR-126 (miR-126EC-/-), and miR-126 knockout control (miR-126fl/fl) mice were subjected to distal middle cerebral artery occlusion (dMCAo) (n = 10/group). Cardiac hemodynamics and function were measured using transthoracic Doppler echocardiography. Mice were sacrificed at 28 days after dMCAo. WT mice subjected to stroke exhibited significantly decreased cardiac ejection fraction and increased myocyte hypertrophy, fibrosis as well as increased heart inflammation, infiltrating macrophages, and oxidative stress compared to non-stroke animals. Stroke significantly decreased serum and heart miR-126 expression and increased miR-126 target genes, vascular cell adhesion protein-1, and monocyte

chemotactic protein-1 gene, and protein expression in the heart compared to non-stroke mice. MiR-126EC-/- mice exhibited significantly decreased cardiac function and increased cardiomyocyte hypertrophy, fibrosis, and inflammatory factor expression after stroke compared to miR-126fl/fl stroke mice. Exosomes derived from endothelial cells of miR-126EC-/- (miR-126EC-/-EC-Exo) mice exhibited significantly decreased miR-126 expression than exosomes derived from miR-126fl/fl (miR-126fl/fl-EC-Exo) mice. Treatment of cardiomyocytes subjected to oxygen glucose deprivation with miR-126fl/fl-EC-Exo exhibited significantly decreased hypertrophy than with miR-126EC-/-EC-Exo treatment. Ischemic stroke directly induces cardiac dysfunction. Decreasing miR-126 expression may contribute to cardiac dysfunction after stroke in mice.

Neurology
Ding G, **Chen J**, **Chopp M**, **Li L**, **Yan T**, **Davoodi-Bojd E**, **Li Q**, **Davarani SP**, and **Jiang Q**. White matter changes after stroke in type 2 diabetic rats measured by diffusion magnetic resonance imaging *J Cereb Blood Flow Metab* 2017; 37(1):241-251. PMID: 26685128. Full Text

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Diffusion-related magnetic resonance imaging parametric maps may be employed to characterize white matter of brain. We hypothesize that entropy of diffusion anisotropy may be most effective for detecting therapeutic effects of bone marrow stromal cell treatment of ischemia in type 2 diabetes mellitus rats. Type 2 diabetes mellitus was induced in adult male Wistar rats. These rats were then subjected to 2 h of middle cerebral artery occlusion, and received bone marrow stromal cell (5 x 106, n = 8) or an equal volume of saline (n = 8) via tail vein injection at three days after middle cerebral artery occlusion. Magnetic resonance imaging was performed on day one and then weekly for five weeks post middle cerebral artery occlusion. The diffusion metrics complementarily permitted characterization of axons and axonal myelination. All six magnetic resonance imaging diffusion metrics, confirmed by histological measures, demonstrated that bone marrow stromal cell treatment significantly ($p < 0.05$) improved magnetic resonance imaging diffusion indices of white matter in type 2 diabetes mellitus rats after middle cerebral artery occlusion compared with the saline-treated rats. Superior to the fractional anisotropy metric that provided measures related to organization of neuronal fiber bundles, the entropy metric can also identify microstructures and low-density axonal fibers of cerebral tissue after stroke in type 2 diabetes mellitus rats.

Neurology
Howell BN, and **Newman DS**. Dysfunction of central control of breathing in amyotrophic lateral sclerosis *Muscle Nerve* 2017;PMID: 28063152. Full Text

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Dysfunction in central control of breathing in some amyotrophic lateral sclerosis (ALS) patients is not adequately detected with standard evaluation for respiratory dysfunction. Nocturnal oximetry reveals periodic desaturations despite normal respiratory muscle movements. Continuous diaphragmatic electromyography has provided in vivo data consistent with impaired central control of diaphragm motor units. Current understanding of central control of breathing identifies the pre-Botzinger complex as the inspiratory rhythm generator. Animal models of pre-Botzinger complex neurodegeneration demonstrate rapid eye movement-related central sleep apneas progressing to loss of rapid eye movement sleep, also apparent in some ALS patients. Evidence supports the hypothesis that dysfunction in central control of breathing in some ALS patients may be related to pre-Botzinger complex degeneration. As the impact dysfunction of central control of breathing has on ALS becomes better defined the current standard of evaluating respiratory dysfunction in ALS patients may need updating. This article is protected by copyright. All rights reserved.

Neurology
Janic B, **Bhuiyan MP**, **Ewing JR**, and **Ali MM**. pH-Dependent cellular internalization of paramagnetic nanoparticle *ACS Sens* 2016; 1(8):975-978. PMID: 28066811. Full Text

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A hallmark of the tumor microenvironment in malignant tumor is extracellular acidosis, which can be exploited for targeted delivery of drugs and imaging agents. A pH sensitive paramagnetic nanoaparticle (NP) is developed by incorporating GdDOTA-4AmP MRI contrast agent and pHLIP (pH Low Insertion Peptide) into the surface of a G5-PAMAM dendrimer. pHLIP showed pH-selective insertion and folding into cell membranes, but only in acidic conditions. We demonstrated that pHLIP-conjugated Gd44-G5 paramagnetic nanoparticle binds and fuses with cellular membrane at low pH, but not at normal physiological pH, and that it promotes cellular uptake. Intracellular trafficking of NPs showed endosomal/lysosomal path ways.

Neurology

Jia J, Wei C, **Jia L**, Tang Y, Liang J, Zhou A, Li F, Shi L, and Doody RS. Efficacy and safety of donepezil in chinese patients with severe alzheimer's disease: A randomized controlled trial *J Alzheimers Dis* 2017;PMID: 28157100. Article Request Form

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BACKGROUND: Donepezil has been used worldwide for the treatment of severe Alzheimer's disease (AD). Whether it is also appropriate for severe AD in Chinese patients remains unknown. OBJECTIVE: To determine whether donepezil is effective and tolerable for Chinese patients with severe AD. METHODS: The present study was a 24-week, multicenter, double-blind, randomized, placebo-controlled, parallel-group study conducted at 38 investigational hospitals in China. Patients with severe AD were enrolled in this trail. Patients were randomly assigned in a 1:1 ratio to receive either donepezil or placebo (5 mg for 6 weeks and10 mg for the remaining 18 weeks). The efficacy for donepezil were evaluated by the SIB, the Clinician's Interview-Based Impression of Change-Plus caregiver input (CIBIC-plus) and the MMSE. Safety parameters were monitored throughout. RESULTS: A total of 313 patients included the donepezil (n = 157) and the placebo groups (n = 156). Donepezil group improved more in SIB scores (least squares [LS] mean difference: 4.8, 95% CI 1.56 to 8.08, p = 0.004) and CIBIC-plus scores (drug-placebo difference: -0.4, 95% CI -0.66 to 0.03, p = 0.04) than placebo groups at Week 24. The MMSE scores between drug and placebo groups did not differ significantly. Twenty-nine patients with serious adverse events (SAEs) were reported in donepezil (n = 11) and placebo groups (n = 18) (p = 0.08). Most SAEs were not considered drug-related. CONCLUSION: Donepezil for 24 weeks was more effective than placebo and showed good safety and tolerability in Chinese patients with severe AD. This study supports utility of the drug in severe stages of AD in the Chinese population.

Neurology

Jia L, **Wang L**, **Chopp M**, **Li C**, **Zhang Y**, **Szalad A**, and **Zhang ZG**. MiR-29c/PRKCI regulates axonal growth of dorsal root ganglia neurons under hyperglycemia *Mol Neurobiol* 2017;PMID: 28070856. Full Text

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Diabetes initially induces distal axonal damage of peripheral nerves, but molecular mechanisms that mediate axonal injury are not fully understood. MircoRNAs (miRNAs) regulate axonal growth. We found that diabetic db/db mice exhibited substantial upregulation of miR-29c in dorsal root ganglia (DRG) neurons, sciatic nerve, and foot pad tissues. Bioinformatic analysis revealed PRKCI, a gene that encodes a member of the protein kinase C (PKC) iota, as a putative target for miR-29c. Western blot analysis showed that diabetic mice exhibited a considerable reduction of PRKCI protein levels in sciatic nerve tissues and DRG neurons. Using dual-luciferase assay, we found that co-transfection of a plasmid containing miR-29c binding site at 3' UTR of PRKCI gene and miR-29c mimics effectively reduced luminescence activity, which was abolished when miR-29c seed sequences at 3' UTR of PRKCI gene were mutated. In vitro, high glucose substantially upregulated and reduced miR-29c and PRKCI protein levels, respectively, in DRG neurons, which were associated with significant reduction of axonal growth. Knockdown of endogenous miR-29c in DRG neurons by siRNAs overcame reduced PRKCI protein and axonal growth under high glucose condition. Moreover, knockdown of PRKCI in DRG neurons by siRNAs under regular glucose condition considerably inhibited axonal growth. Together, these findings suggest that miR-29c is a negative regulator of axonal growth of DRG neurons by targeting PRKCI under hyperglycemia.

Neurology
Wang HH, **Varelas PN**, Henderson GV, Wijdicks EF, and Greer DM. Improving uniformity in brain death determination policies over time *Neurology* 2017; 88(6):562-568. PMID: 28077490. Full Text

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OBJECTIVE: To demonstrate that progress has been made in unifying brain death determination guidelines in the last decade by directly comparing the policies of the US News and World Report's top 50 ranked neurologic institutions from 2006 and 2015. METHODS: We solicited official hospital guidelines in 2015 from these top 50 institutions, generated summary statistics of their criteria as benchmarked against the American Academy of Neurology Practice Parameters (AANPP) and the comparison 2006 cohort in 5 key categories, and statistically compared the 2 cohorts' compliance with the AANPP. RESULTS: From 2008 to 2015, hospital policies exhibited significant improvement ($p = 0.005$) in compliance with official guidelines, particularly with respect to criteria related to apnea testing ($p = 0.009$) and appropriate ancillary testing ($p = 0.0006$). However, variability remains in other portions of the policies, both those with specific recommendation from the AANPP (e.g., specifics for ancillary tests) and those without firm guidance (e.g., the level of involvement of neurologists, neurosurgeons, or physicians with education/training specific to brain death in the determination process). CONCLUSIONS: While the 2010 AANPP update seems to be concordant with progress in achieving greater uniformity in guidelines at the top 50 neurologic institutions, more needs to be done. Whether further interventions come as grassroots initiatives that leverage technological advances in promoting adoption of new guidelines or as top-down regulatory rulings to mandate speedier approval processes, this study shows that solely relying on voluntary updates to professional society guidelines is not enough.

Neurosurgery
Bilsky MH, Chang SD, Gerszten PC, and **Kalkanis S**. Introduction: Spinal radiosurgery *Neurosurg Focus* 2017; 42(1):E2. PMID: 28041322. Full Text

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Neurosurgery
Boyce-Fappiano D, **Elibe E**, **Schultz L**, Ryu S, **Siddiqui MS**, **Chetty I**, **Lee I**, **Rock J**, **Movsas B**, and **Siddiqui F**. Analysis of the factors contributing to vertebral compression fractures after spine stereotactic radiosurgery *Int J Radiat Oncol Biol Phys* 2017; 97(2):236-245. PMID: 28068232. Full Text

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PURPOSE: To determine our institutional vertebral compression fracture (VCF) rate after spine stereotactic radiosurgery (SRS) and determine contributory factors. METHODS AND MATERIALS: Retrospective analysis from 2001 to 2013 at a single institution was performed. With institutional review board approval, electronic medical records of 1905 vertebral bodies from 791 patients who were treated with SRS for the management of primary or metastatic spinal lesions were reviewed. A total of 448 patients (1070 vertebral bodies) with adequate follow-up imaging studies available were analyzed. Doses ranging from 10 Gy in 1 fraction to 60 Gy in 5 fractions were delivered. Computed tomography and magnetic resonance imaging were used to evaluate the primary endpoints of this study: development of a new VCF, progression of an existing VCF, and requirement of stabilization surgery after SRS. RESULTS: A total of 127 VCFs (11.9%; 95% confidence interval [CI] 9.5%-14.2%) in 97 patients were potentially SRS induced: 46 (36%) were de novo, 44 (35%) VCFs progressed, and 37 (29%) required stabilization surgery after SRS. Our rate for radiologic VCF development/progression (excluding patients who underwent surgery)

was 8.4%. Upon further exclusion of patients with hematologic malignancies the VCF rate was 7.6%. In the univariate analyses, females (hazard ratio [HR] 1.54, 95% CI 1.01-2.33, P=.04), prior VCF (HR 1.99, 95% CI 1.30-3.06, P=.001), primary hematologic malignancies (HR 2.68, 95% CI 1.68-4.28, P<.001), thoracic spine lesions (HR 1.46, 95% CI 1.02-2.10, P=.02), and lytic lesions had a significantly increased risk for VCF after SRS. On multivariate analyses, prior VCF and lesion type remained contributory. CONCLUSIONS: Single-fraction SRS doses of 16 to 18 Gy to the spine seem to be associated with a low rate of VCFs. To the best of our knowledge, this is the largest reported experience analyzing SRS-induced VCFs, with one of the lowest event rates reported.

Neurosurgery

Cava C, Colaprico A, Bertoli G, Graudenzi A, Silva TC, Olsen C, **Noushmehr H**, Bontempi G, Mauri G, and Castiglioni I. SpidermiR: An R/Bioconductor package for integrative analysis with miRNA data *Int J Mol Sci* 2017; 18(2)PMID: 28134831. Full Text

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Gene Regulatory Networks (GRNs) control many biological systems, but how such network coordination is shaped is still unknown. GRNs can be subdivided into basic connections that describe how the network members interact e.g., co-expression, physical interaction, co-localization, genetic influence, pathways, and shared protein domains. The important regulatory mechanisms of these networks involve miRNAs. We developed an R/Bioconductor package, namely SpidermiR, which offers an easy access to both GRNs and miRNAs to the end user, and integrates this information with differentially expressed genes obtained from The Cancer Genome Atlas. Specifically, SpidermiR allows the users to: (i) query and download GRNs and miRNAs from validated and predicted repositories; (ii) integrate miRNAs with GRNs in order to obtain miRNA-gene-gene and miRNA-protein-protein interactions, and to analyze miRNA GRNs in order to identify miRNA-gene communities; and (iii) graphically visualize the results of the analyses. These analyses can be performed through a single interface and without the need for any downloads. The full data sets are then rapidly integrated and processed locally.

Neurosurgery

Macki M, Uzosike A, Kerezoudis P, Bydon A, Bydon M, and Gokaslan ZL. Duration of indwelling drain following instrumented posterolateral fusion of the lumbar spine does not predict surgical site infection requiring reoperation *J Clin Neurosci* 2017;PMID: 28117258. Full Text

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The objective of this study was to determine the incidence and predictors of reoperation for surgical site infections (SSI) among patients whose lumbar, closed wound suction drains were removed in the inpatient setting prior to hospital discharge (pre-discharge cohort) versus after inpatient discharge during the first follow up visit (post-discharge cohort). All patients who were admitted for first-time, posterolateral decompression and fusion for degenerative lumbar spine disease were retrospectively reviewed at a single institution. In order to eliminate biases, neither the pre-discharge nor post-discharge cohorts experienced any intra-/postoperative sentinel events other than the primary outcome measure: reoperation for SSI. Of 209 patients in the pre-discharge (n=130) and post-discharge (n=79) cohorts, 15 patients required reoperation for SSI. Although time to drain discontinuation was significantly longer in the post-discharge (8.28days) than the pre-discharge (4.65days) cohorts ($p<0.001$), the incidences of reoperation for SSI did not significantly differ (6.33 vs 7.69%, respectively, $p=0.711$). In a multivariable regression, only smoking (OR=5.75, $p=0.007$) and depression (OR=4.11, $p=0.040$) predicted reoperation for SSI. Neither time to drain removal nor setting of drain removal was a predictor of reoperation for SSI. Although time to drain discontinuation was expectedly longer in the post-discharge versus pre-discharge cohorts, the incidences of reoperation for SSI did not significantly differ. Neither time to drain removal nor setting of drain removal predicted reoperation for SSI. These results suggest that patients may be safely discharged from the hospital with the surgical drain in place.

Obstetrics, Gynecology and Women's Health Services
Ghanem AI, **Khan NT**, **Mahan M**, **Ibrahim A**, **Buekers T**, and **Elshaikh MA**. The impact of lymphadenectomy on survival endpoints in women with early stage uterine endometrioid carcinoma: A matched analysis *Eur J Obstet Gynecol Reprod Biol* 2016; 210:225-230. PMID: 28068595. Full Text

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OBJECTIVES: The role of pelvic lymphadenectomy (LA) in women with stage I endometrial carcinoma (EC) is controversial. The objective of this study is to investigate the prognostic impact of LA on survival endpoints in matched cohorts of women with stage I EC solely of endometrioid histology. Survival endpoints included recurrence-free (RFS), disease-specific (DSS) and overall survival (OS). METHODS AND MATERIALS: Patients with FIGO stage I EC who underwent hysterectomy with LA as part of their surgical staging between 1/1990 and 6/2015 were matched to a similar group that underwent hysterectomy without lymphadenectomy (NLA), based on stage, grade and adjuvant management. Univariate and multivariate modeling with Cox regression analysis was carried out for predictors of survival endpoints. RESULTS: 870 women constituted the study cohort (435 in each group). Median number of dissected lymph node in the LA group was 9 (range, 5-75). There was no statistically significant difference between the two groups in regards to 5-year OS (87.2% for LA vs. 91.7% for NLA) ($p=0.36$), DSS 97.7% vs. 98% ($p=0.54$) and RFS (93.7% vs. 90% ($p=0.08$), respectively. Lymphadenectomy was not a predictor of any of the studied survival endpoints. On multivariate analysis for the entire cohort, older age, deep myometrial invasion and higher tumor grade were predictors of worse RFS. For DSS, higher tumor grade, lower uterine segment (LUS) involvement and FIGO stage IB were significant predictors of worse outcome. For OS, older age and LUS involvement were the only two independent predictors for shorter OS. CONCLUSIONS: After matching for FIGO stage, grade and adjuvant management, it appears that lymphadenectomy in women with stage I EC does not impact survival endpoints.

Obstetrics, Gynecology and Women's Health Services
Haley L, **Burmeister C**, **Buekers T**, and **Elshaikh MA**. Is older age a real adverse prognostic factor in women with early-stage endometrial carcinoma? A matched analysis *Int J Gynecol Cancer* 2017;PMID: 28060139. Full Text

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OBJECTIVES: The aim of this study was to evaluate if older age alone negatively impacts survival endpoints in women with early-stage uterine endometrioid carcinoma (EC), or its reported prognostic impact is due to an interaction with other well-known adverse factors using matched-analysis methodology. METHODS: We identified 1254 patients with International Federation of Gynecology and Obstetrics stage I-II EC who underwent hysterectomy

at our institution. We created 2 matched groups based on International Federation of Gynecology and Obstetrics stage, tumor grade, lymph node dissection status, and the type of adjuvant management. Recurrence-free (RFS), disease-specific (DSS) and overall survival (OS) were calculated. RESULTS: A total 297 women 70 years or older were matched with 297 women younger than 70 years. The 2 groups were well balanced except for age and higher body mass index in younger patients. There were no significant difference between older and younger patients in regard to 5-year RFS (85% vs 87%; P = 0.52) or DSS (93% for both groups with P = 0.77). Five-year OS was shorter in older patients (76% vs 88% with P < 0.001). On multivariate analysis for RFS and DSS, high tumor grade and the presence of lymphovascular space invasion (LVSI) were the only 2 predictors of shorter RFS and DSS (P = 0.01 and P = 0.02, and P = 0.01 and P = 0.01, respectively). Tumor grade and LVSI also were predictors of shorter OS. CONCLUSIONS: Our study suggests that when older patients with EC are matched with younger patients based on tumor stage, grade, and adjuvant management the prognostic impact of old age disappears. High tumor grade and LVSI remained as independent predictors of survival endpoints.

Obstetrics, Gynecology and Women's Health Services

Khalife T, and **Hanna RK**. The K-technique: A novel technique for laparoscopic apical suspension using barbed sutures *Female Pelvic Med Reconstr Surg* 2017;PMID: 28118169. Full Text

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OBJECTIVES: Hysterectomy is among the most common gynecologic procedures performed for women, second only to cesarean sections, and the proportion of it performed laparoscopically continues to increase. Addressing apical support at the time of the hysterectomy is crucial to minimizing the risk of posthysterectomy prolapse. Barriers to addressing apical support include the lack of experience in laparoscopic suturing and knot tying that require advanced skills and dexterity. The K-technique is a novel modification of the uterosacral ligament suspension procedure using the knot-less barbed suture technology, rendering suturing easier and quicker to perform. METHOD: The vaginal cuff epithelium is closed with 2 unidirectional barbed sutures that are started at the lateral fornices and ran until the midsection. The same sutures will then serially purchase the anterior and posterior vaginal endopelvic fascia and the midsegment of the uterosacral ligament. Two more passes are thrown through the same structures, yet farther laterally, back and forth. A video illustration of the procedure is attached. RESULTS: Eighteen patients underwent the procedure with no urinary tract injuries documented by cystoscopy and no postoperative morbidity documented during the 6-week postoperative follow-up period. Limited short- and long-term follow-up data are reassuring, but more will be needed to confirm the efficacy of barbed sutures in prolapse repair. CONCLUSIONS: The K-technique combines the conventional uterosacral ligament suspension concept with the ease, effectiveness, and safety of barbed sutures. The technique might aid the surgeon to add the apical vaginal support when indicated.

Obstetrics, Gynecology and Women's Health Services

Rossi EC, Kowalski LD, Scalici J, Cantrell L, Schuler K, **Hanna RK**, Method M, Ade M, Ivanova A, and Boggess JF. A comparison of sentinel lymph node biopsy to lymphadenectomy for endometrial cancer staging (FIRES trial): a multicentre, prospective, cohort study *Lancet Oncol* 2017;PMID: 28159465. Full Text

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BACKGROUND: Sentinel-lymph-node mapping has been advocated as an alternative staging technique for endometrial cancer. The aim of this study was to measure the sensitivity and negative predictive value of sentinel-lymph-node mapping compared with the gold standard of complete lymphadenectomy in detecting metastatic disease for endometrial cancer. METHODS: In the FIRES multicentre, prospective, cohort study patients with clinical stage 1 endometrial cancer of all histologies and grades undergoing robotic staging were eligible for study inclusion. Patients

received a standardised cervical injection of indocyanine green and sentinel-lymph-node mapping followed by pelvic lymphadenectomy with or without para-aortic lymphadenectomy. 18 surgeons from ten centres (tertiary academic and community non-academic) in the USA participated in the trial. Negative sentinel lymph nodes (by haematoxylin and eosin staining on sections) were ultra-staged with immunohistochemistry for cytokeratin. The primary endpoint, sensitivity of the sentinel-lymph-node-based detection of metastatic disease, was defined as the proportion of patients with node-positive disease with successful sentinel-lymph-node mapping who had metastatic disease correctly identified in the sentinel lymph node. Patients who had mapping of at least one sentinel lymph node were included in the primary analysis (per protocol). All patients who received study intervention (injection of dye), regardless of mapping result, were included as part of the assessment of mapping and in the safety analysis in an intention-to-treat manner. The trial was registered with ClinicalTrials.gov, number NCT01673022 and is completed and closed. FINDINGS: Between Aug 1, 2012, and Oct 20, 2015, 385 patients were enrolled. Sentinel-lymph-node mapping with complete pelvic lymphadenectomy was done in 340 patients and para-aortic lymphadenectomy was done in 196 (58%) of these patients. 293 (86%) patients had successful mapping of at least one sentinel lymph node. 41 (12%) patients had positive nodes, 36 of whom had at least one mapped sentinel lymph node. Nodal metastases were identified in the sentinel lymph nodes of 35 (97%) of these 36 patients, yielding a sensitivity to detect node-positive disease of 97.2% (95% CI 85.0-100), and a negative predictive value of 99.6% (97.9-100). The most common grade 3-4 adverse events or serious adverse events were postoperative neurological disorders (4 patients) and postoperative respiratory distress or failure (4 patients). 22 patients had serious adverse events, with one related to the study intervention: a ureteral injury incurred during sentinel-lymph-node dissection. INTERPRETATION: Sentinel lymph nodes identified with indocyanine green have a high degree of diagnostic accuracy in detecting endometrial cancer metastases and can safely replace lymphadenectomy in the staging of endometrial cancer. Sentinel lymph node biopsy will not identify metastases in 3% of patients with node-positive disease, but has the potential to expose fewer patients to the morbidity of a complete lymphadenectomy. FUNDING: Indiana University Health, Indiana University Health Simon Cancer Center, and the Indiana University Department of Obstetrics and Gynecology.

Orthopaedics

Baumer TG, **Davis L**, **Dischler J**, **Siegal DS**, **van Holsbeeck M**, **Moutzouros V**, and **Bey MJ**. Shear wave elastography of the supraspinatus muscle and tendon: Repeatability and preliminary findings *J Biomech* 2017;PMID: 28110933. Full Text

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Shear wave elastography (SWE) is a promising tool for estimating musculoskeletal tissue properties, but few studies have rigorously assessed its repeatability and sources of error. The objectives of this study were to assess: (1) the extent to which probe positioning error and human user error influence measurement accuracy, (2) intra-user, inter-user, and day-to-day repeatability, and (3) the extent to which active and passive conditions affect shear wave speed (SWS) repeatability. Probe positioning and human usage errors were assessed by acquiring SWE images from custom ultrasound phantoms. Intra- and inter-user repeatability were assessed by two users acquiring five trials of supraspinatus muscle and tendon SWE images from ten human subjects. To assess day-to-day repeatability, five of the subjects were tested a second time, approximately 24h later. Imaging of the phantoms indicated high inter-user repeatability, with intraclass correlation coefficient (ICC) values of 0.68-0.85, and RMS errors of no more than 4.1%. SWE imaging of the supraspinatus muscle and tendon had high repeatability, with intra- and inter-user ICC values of greater than 0.87 and 0.73, respectively. Day-to-day repeatability demonstrated ICC values greater than 0.33 for passive muscle, 0.48 for passive tendon, 0.65 for active muscle, and 0.94 for active tendon. This study indicates the technique has good to very good intra- and inter-user repeatability, and day-to-day repeatability is appreciably higher when SWE images are acquired under a low level of muscle activation. The findings from this study establish the feasibility and repeatability of SWE for acquiring data longitudinally in human subjects.

Orthopaedics

Baumer TG, **Dischler J**, **Mende V**, **Zauel R**, **van Holsbeeck M**, **Siegal DS**, **Divine G**, **Moutzouros V**, and **Bey MJ**. Effects of asymptomatic rotator cuff pathology on in vivo shoulder motion and clinical outcomes *J Shoulder Elbow Surg* 2017;PMID: 28131679. Full Text

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BACKGROUND: The incidence of asymptomatic rotator cuff tears has been reported to range from 15% to 39%, but the influence of asymptomatic rotator cuff pathology on shoulder function is not well understood. This study assessed the effects of asymptomatic rotator cuff pathology on shoulder kinematics, strength, and patient-reported outcomes. METHODS: A clinical ultrasound examination was performed in 46 asymptomatic volunteers (age: 60.3 +/- 7.5 years) with normal shoulder function to document the condition of their rotator cuff. The ultrasound imaging identified the participants as healthy (n = 14) or pathologic (n = 32). Shoulder motion was measured with a biplane x-ray imaging system, strength was assessed with a Biodex (Biodex Medical Systems, Inc., Shirley, NY, USA), and patient-reported outcomes were assessed using the Western Ontario Rotator Cuff Index and visual analog scale pain scores. RESULTS: Compared with healthy volunteers, those with rotator cuff pathology had significantly less abduction (P = .050) and elevation (P = .041) strength, their humerus was positioned more inferiorly on the glenoid (P = .018), and the glenohumeral contact path length was longer (P = .007). No significant differences were detected in the Western Ontario Rotator Cuff Index, visual analog scale, range of motion, or acromiohumeral distance. CONCLUSIONS: The differences observed between the healthy volunteers and those with asymptomatic rotator cuff pathology lend insight into the changes in joint mechanics, shoulder strength, and conventional clinical outcomes associated with the early stages of rotator cuff pathology. Furthermore, these findings suggest a plausible mechanical progression of kinematic and strength changes associated with the development of rotator cuff pathology.

Orthopaedics

Keller RA, Mehran N, **Marshall NE**, **Okoroha KR**, Khalil L, Tibone JE, and **Moutzouros V**. Major League pitching workload after primary ulnar collateral ligament reconstruction and risk for revision surgery *J Shoulder Elbow Surg* 2017; 26(2):288-294. PMID: 28104091. Full Text

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BACKGROUND: Literature has attempted to correlate pitching workload with risk of ulnar collateral ligament (UCL) injury; however, limited data are available in evaluating workload and its relationship with the need for revision reconstruction in Major League Baseball (MLB) pitchers. METHODS: We identified 29 MLB pitchers who underwent primary UCL reconstruction surgery and subsequently required revision reconstruction and compared them with 121 MLB pitchers who underwent primary reconstruction but did not later require revision surgery. Games pitched, pitch counts, and innings pitched were evaluated and compared for the seasons after returning from primary reconstruction and for the last season pitched before undergoing revision surgery. RESULTS: The difference in workload between pitchers who did and did not require revision reconstruction was not statistically significant in games pitched, innings pitched, and MLB-only pitch counts. The one significant difference in workload was in total pitch counts (combined MLB and minor league), with the pitchers who required revision surgery pitching less than those who did not (primary: 1413.6 pitches vs. revision: 959.0 pitches, P = .04). In addition, pitchers who required revision surgery underwent primary reconstruction at an early age (22.9 years vs. 27.3 years, P < .001) and had less MLB experience (1.5 years vs. 5.0 years, P < .001). CONCLUSIONS: There is no specific number of pitches, innings, or games that place a pitcher at an increase risk for injury after primary UCL reconstruction. However, correlations of risk may be younger age and less MLB experience at the time of the primary reconstruction.

Orthopaedics

Makhni EC, Meadows M, Hamamoto JT, Higgins JD, Romeo AA, and Verma NN. Patient reported outcomes measurement information system (promis) in the upper extremity: The future of outcomes reporting? *J Shoulder Elbow Surg* 2017; 26(2):352-357. PMID: 28104094. Full Text

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Patient reported outcomes (PROs) serve an integral role in clinical research by helping to determine the impact of clinical care as experienced by the patient. With recent initiatives in health care policy and pay for performance, outcome reporting is now recognized as a policy-driven requirement in addition to a clinical research tool. For

outcome measures to satisfy these regulatory requirements and provide value in understanding disease outcomes, they must be responsive and efficient. Recent research has uncovered certain concerns regarding traditional PROs in patients with upper extremity disability and injury. These include lack of consensus regarding selection of PROs for a given diagnoses, inconsistent techniques of administration of the same PROs, and the administrative burden to patients and providers of completing these forms. To address these limitations, emphasis has been placed on streamlining the outcomes reporting process, and, as a result, the National Institutes of Health (NIH) created the Patient Reported Outcomes Measurement Information System (PROMIS). PROMIS forms were created to comprehensively and efficiently measure outcomes across multiple disease states, including orthopedics. These tools exist in computer adaptive testing and short forms with the intention of more efficiently measuring outcomes compared with legacy PROs. The goals of this review are to highlight the main components of PROMIS reporting tools and identify recent use of the scores in the upper extremity literature. The review will also highlight the research and health policy potentials and limitations of implementing PROMIS into everyday orthopedic practice.

Orthopaedics

Radzak KN, **Putnam AM**, Tamura K, Hetzler RK, and Stickley CD. Asymmetry between lower limbs during rested and fatigued state running gait in healthy individuals *Gait Posture* 2017; 51:268-274. PMID: 27842295. Full Text

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Although normal gait is often considered symmetrical in healthy populations, differences between limbs during walking suggest that limbs may be used preferentially for braking or propulsion. The purpose of this study was to evaluate kinematic and kinetic variables, at both rested state and following a two-stage treadmill fatiguing run, for asymmetry between limbs. Kinematic (240Hz) and kinetic (960Hz) running data were collected bilaterally for 20 physically active individuals at both rested and fatigued states. Symmetry angles were calculated to quantify asymmetry magnitude at rested and fatigued states. Paired t-tests were used to evaluate differences between right and left limbs at rested and fatigued states, as well as rested and fatigued states symmetry angles. Variables that have been previously associated with the development of overuse injuries, such as knee internal rotation, knee stiffness, loading rate, and adduction free moment, were found to be significantly different between limbs at both rested and fatigued states. Significant differences in vertical stiffness were found, potentially indicating functional asymmetry during running. Symmetry angle was used to investigate changes in percentage of asymmetry at rested and fatigued states. Small (1-6%), but significant decreases in vertical stiffness, loading rate, and free moment symmetry angles indicate that these variables may become more symmetrical with fatigue. Knee internal rotation and knee stiffness became more asymmetrical with fatigue, increasing by 14% and 5.3%, respectively. The findings of the current study indicate that fatigue induced changes in gait may progress knee movement pattern asymmetry.

Otolaryngology – Head and Neck Surgery

Craig JR, Palmer JN, and Zhao K. Computational fluid dynamic modeling of nose-to-ceiling head positioning for sphenoid sinus irrigation *Int Forum Allergy Rhinol* 2017;PMID: 28092136. Article Request Form

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BACKGROUND: After sinus surgery, patients are commonly instructed to irrigate with saline irrigations with their heads over a sink and noses directed inferiorly (nose-to-floor). Although irrigations can penetrate the sinuses in this head position, no study has assessed whether sphenoid sinus penetration can be improved by irrigating with the nose directed superiorly (nose-to-ceiling). The purpose of this study was to use a validated computational fluid dynamics (CFD) model of sinus irrigations to assess the difference in sphenoid sinus delivery of irrigations after irrigating in a nose-to-floor vs nose-to-ceiling head position. METHODS: Bilateral maxillary antrostomies, total ethmoidectomies, wide sphenoidotomies, and a Draf III frontal sinusotomy were performed on a single fresh cadaver head. CFD models were created from postoperative computed tomography maxillofacial scans. CFD modeling software was used to simulate a 120-mL irrigation to the left nasal cavity with the following parameters: flow rate 30 mL/second, angle of irrigation 20 degrees to the nasal floor, and either nose-to-floor or nose-to-ceiling head positioning. RESULTS: In the postoperative CFD models, the sphenoid sinuses were completely penetrated by the irrigation while in a nose-to-ceiling head position. However, no sphenoid sinus penetration occurred in the nose-to-floor position. Other sinuses were similarly penetrated in both head positions, although the ipsilateral maxillary sinus was less penetrated in the nose-to-ceiling position. CONCLUSION: CFD modeling demonstrated that the nose-to-

ceiling head position was superior to the nose-to-floor position in delivering a 120-mL irrigation to the sphenoid sinuses.

Otolaryngology – Head and Neck Surgery
Kandinov A, **Smith M**, and **Ahsan SF**. Middle ear mass causing vertigo and facial nerve weakness *JAMA Otolaryngol Head Neck Surg* 2017;PMID: 28056134. Full Text

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Otolaryngology – Head and Neck Surgery
Komorowska-Timek E, **Turfe Z**, and Davis AT. Outcomes of prosthetic reconstruction of irradiated and nonirradiated breasts with fat grafting *Plast Reconstr Surg* 2017; 139(1):1e-9e. PMID: 28027220. Full Text

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BACKGROUND: Fat grafting may be beneficial in prosthetic reconstruction of irradiated tissues, but there is a paucity of data on the complication rates associated with this clinical scenario. METHODS: All consecutive patients who had undergone fat grafting and prosthetic reconstruction from 2010 to 2013 were enrolled. Variables obtained related to fat grafting and history of irradiation. Implant-related complications in relation to irradiation status were also noted. RESULTS: Eighty-five patients (age 49 +/- 10 years) underwent 117 fat grafting procedures. The mean follow-up was 2.6 +/- 0.7 years. Fat grafting was predominantly performed to correct soft-tissue deficiency [112 of 117 (95.7 percent)] or to alter skin after irradiation [five of 117 (4.3 percent)]. Thirty-two procedures (27.4 percent) were associated with a complication, with the most common being palpable fat necrosis (23.1 percent). Volume of transferred fat averaged 151.2 +/- 76.6 ml per breast. Fat grafting complications did not depend on donor site, technique of fat processing, volume of transferred fat, number of procedures, or irradiation. Implant-related complications were observed after 26 of 117 overall procedures (22.2 percent). No association between implant-related complications and irradiation was observed (OR, 1.3; 95 percent CI, 0.4 to 4.1; p = 0.63). Overall complications following fat grafting in nonirradiated [37 of 82 (45.1 percent)] and irradiated [16 of 35 (45.7 percent)] breasts were not statistically different (OR, 1.02; 95 percent CI, 0.41 to 2.57; p = 0.96). CONCLUSION: Similar outcomes of irradiated and nonirradiated prosthetic breast reconstruction can be achieved with additional fat grafting. CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, III.

Otolaryngology – Head and Neck Surgery
Yaremchuk K. USPSTF recommendation for obstructive sleep apnea screening in adults *JAMA Otolaryngol Head Neck Surg* 2017;PMID: 28118426. Full Text

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Palliative Care
Awdish RL, **Buick D**, **Kokas M**, **Berlin H**, **Jackman C**, **Williamson C**, **Mendez MP**, and **Chasteen K**. A communications bundle to improve satisfaction for critically ill patients and their families: A prospective, cohort pilot study *J Pain Symptom Manage* 2016;PMID: 28042074. Full Text

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CONTEXT: Communication skills training with simulated patients is used by many academic centers, but how to translate skills learned in simulated settings to improve communication in real encounters has not been described. OBJECTIVE: We developed a communications bundle to facilitate skill transfer from simulation to real encounters and improve patient and/or family satisfaction with physician communication. We tested the feasibility of its use in our hospital's medical intensive care unit (MICU). METHODS: This prospective cohort 2-week feasibility study included

patients admitted to the MICU with APACHE IV predicted mortality >30% and/or single organ failure. The communications bundle included simulation communication training for MICU physicians, scheduling a family meeting within 72 hours of MICU admission, standardized pre- and post-meeting team huddles with the aid of a mobile app to set an agenda, choose a communication goal, and get feedback, and documentation of meeting in the electronic medical record. The intervention group receiving the communications bundle was located in a geographically separate unit than the control group receiving standard of care from MICU physicians who had not received training in the communications bundle. Patient satisfaction surveys were given within 48 hours of the family meeting and scores compared between the two groups. We also compared trainee self-perceived communication preparation. RESULTS: The intervention group (N = 15) scored significantly higher on satisfaction than the control group (N = 16) (P = 0.018). Intervention group trainees reported improvement in self-perceived communication preparation. CONCLUSION: Use of the communications bundle proved feasible in the MICU and suggests association with improved patient satisfaction and trainee self-perception of communication preparedness.

Pathology

Cohen D, Allen TC, Balci S, Cagle PT, Teruya-Feldstein J, Fine SW, Gondim DD, Hunt JL, Jacob J, Jewett K, Jiang X, Kaplan KJ, Kulac I, Meunier R, Riddle ND, Rush PS, Stall J, Stuart LN, Terrano D, Uthman E, Wasco MJ, **Williamson SR**, Wu RI, and Gardner JM. #InSituPathologists: how the #USCAP2015 meeting went viral on Twitter and founded the social media movement for the United States and Canadian Academy of Pathology *Mod Pathol* 2017; 30(2):160-168. PMID: 28084341. Full Text

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Professional medical conferences over the past five years have seen an enormous increase in the use of Twitter in real-time, also known as "live-tweeting". At the United States and Canadian Academy of Pathology (USCAP) 2015 annual meeting, 24 attendees (the authors) volunteered to participate in a live-tweet group, the #InSituPathologists. This group, along with other attendees, kept the world updated via Twitter about the happenings at the annual meeting. There were 6,524 #USCAP2015 tweets made by 662 individual Twitter users; these generated 5,869,323 unique impressions (potential tweet-views) over a 13-day time span encompassing the dates of the annual meeting. Herein we document the successful implementation of the first official USCAP annual meeting live-tweet group, including the pros/cons of live-tweeting and other experiences of the original #InSituPathologists group members. No prior peer-reviewed publications to our knowledge have described in depth the use of an organized group to "live-tweet" a pathology meeting. We believe our group to be the first of its kind in the field of pathology.

Pathology

Flynt LK, **Veve MP**, **Samuel LP**, and **Tibbetts RJ**. Comparison of etest to broth microdilution for testing of susceptibility of pseudomonas aeruginosa to ceftolozane-tazobactam *J Clin Microbiol* 2017; 55(1):334-335. PMID: 27795348. Article Request Form

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Pathology
Go P, **Watson J**, **Lu Z**, **Carlin A**, and **Hammoud Z**. Robotic resection of a mediastinal parathyroid cyst *Gen Thorac Cardiovasc Surg* 2017; 65(1):52-55. PMID: 26353995. Full Text

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Mediastinal parathyroid cysts (PC) are rare, benign lesions, reported in fewer than 150 cases worldwide. Although most are asymptomatic and discovered incidentally on imaging, symptoms of dyspnea, dysphagia, hoarseness, palpitations, hypercalcemia, and innominate or jugular venous thrombosis have been reported. Sternotomy or thoracotomy has traditionally been the approach used to resect mediastinal PCs. We describe the first reported case of a robot-assisted resection of a mediastinal PC.

Pathology
Wang X, Lopez-Beltran A, Osunkoya AO, Wang M, Zhang S, Davidson DD, Emerson RE, **Williamson SR**, Tan PH, Kaimakliotis HZ, Baldridge LA, MacLennan GT, Montironi R, and Cheng L. TERT promoter mutation status in sarcomatoid urothelial carcinomas of the upper urinary tract *Future Oncol* 2017;PMID: 28052688.
Article Request Form

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AIM: To determine TERT promoter mutation status as well as the expression of PAX8, GATA3, p63, p40, p53 and uroplakin III in 17 patients with the upper urinary tract sarcomatoid urothelial carcinoma. METHODS & RESULTS: TERT C228T mutations were found in six of 17 cases (35%). p53 was expressed in 77% of these tumors. PAX8, GATA3, p40 and uroplakin III are less frequently expressed. Lymph node metastases were present in ten cases (59%). Eight patients (47%), including all three patients with TERT mutation, died of cancer within 2 years after surgery. CONCLUSION: Sarcomatoid carcinoma of the upper urinary tract is an aggressive tumor and the presence of TERT mutation may portend poor prognosis.

Pharmacy
Flynt LK, **Veve MP**, **Samuel LP**, and **Tibbetts RJ**. Comparison of etest to broth microdilution for testing of susceptibility of pseudomonas aeruginosa to ceftolozane-tazobactam *J Clin Microbiol* 2017; 55(1):334-335. PMID: 27795348. Article Request Form

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Pharmacy
Smith AL, Palmer V, Farhat N, **Kalus JS**, **Thavarajah K**, **Digiovine B**, and **Macdonald NC**. Hospital-based clinical pharmacy services to improve ambulatory management of chronic obstructive pulmonary disease *J Pharm Technol* 2017; 33(1):8-14. PMID: Not assigned. Full Text

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Background: No systematic evaluations of a comprehensive clinical pharmacy process measures currently exist to determine an optimal ambulatory care collaboration model for chronic obstructive pulmonary disease (COPD) patients. Objective: Describe the impact of a pharmacist-provided clinical COPD bundle on the management of COPD in a hospital-based ambulatory care clinic. Methods: This retrospective cohort analysis evaluated patients with COPD managed in an outpatient pulmonary clinic. The primary objective of this study was to assess the completion of 4 metrics known to improve the management of COPD: (1) medication therapy management, (2) quality measures including smoking cessation and vaccines, (3) patient adherence, and (4) patient education. The secondary objective was to evaluate the impact of the clinical COPD bundle on clinical and economic outcomes at 30 and 90 days post-initial visit. Results: A total of 138 patients were included in the study; 70 patients served as controls and 68 patients received the COPD bundle from the clinical pharmacist. No patients from the control group had all 4 metrics completed as documented, compared to 66 of the COPD bundle group (P <.0001). Additionally, a statistically significant difference was found in all 4 metrics when evaluated individually. Clinical pharmacy services reduced the number of phone call consults at 90 days (P =.04) but did not have a statistically significant impact on any additional pre-identified clinical outcomes. Conclusion: A pharmacist-driven clinical COPD bundle was associated with significant increases in the completion and documentation of 4 metrics known to improve the outpatient management of COPD.

Pharmacy

Tarantino MD, and **Pindolia VK**. Hemophilia management via data collection and reporting: Initial findings from the comprehensive care sustainability collaborative *J Manag Care Spec Pharm* 2017; 23(1):51-56. PMID: 28025929.
Full Text

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BACKGROUND: Despite being a rare disorder, hemophilia represents a significant driver of health care resource utilization and requires expert hematologic and multidisciplinary services to achieve optimal outcomes. Since their inception nearly 40 years ago, hemophilia treatment centers (HTCs) have served as centers of excellence in providing the intensive care and ancillary services necessary for this unique patient base; however, the full capabilities of these centers may be underused in the current framework of managed care, largely because of a lack of communication and information shared between payers and HTC stakeholders. PROGRAM DESCRIPTION: In an effort to enact tangible change toward improving the quality of care for bleeding disorders, the National Hemophilia Foundation developed an ongoing initiative among 18 leading clinicians and managed care decision makers called the Comprehensive Care Sustainability Collaborative (CCSC). The primary aim of the CCSC is to develop a framework for quality improvement pilot programs that can be replicated across the United States between payers and HTCs to facilitate cost-effective hemophilia management by integrating the HTC comprehensive care model. OBSERVATIONS: After CCSC committee members shared perspectives on care delivery, quality, and value, actionable data points were reviewed at length in order to develop meaningful metrics to facilitate information sharing between HTC and payer stakeholders. The following pragmatic measures will be reported by HTCs and payers via a series of pilot programs (reporting group is indicated in brackets): (a) patient classification by diagnosis (type, severity, and inhibitor status) [HTC]; (b) total cost of clotting factor [payer]; (c) prescribed factor dose/dispensed dose/patient weight (+/- range) [payer and HTC]; (d) emergency department visits/hospitalizations [payer and HTC]; (e) home infusion of clotting factor (%) [HTC]; (f) total cost per patient [payer]; and (g) patient contacts (e.g., clinic visits, follow-ups, telemedicine, and e-mail) [HTC]. IMPLICATIONS: Routine information sharing between HTCs and payer stakeholders is paramount to improving the quality and reducing the cost of hemophilia care, and the CCSC initiative provides a unique forum for such dialogue. Over the course of several consensus meetings, the CCSC has rigorously developed a set of quality improvement and cost management metrics. These metrics will be used in a first-of-its-kind series of pilot projects that are anticipated to forge innovative collaboration between payers and HTCs so as to improve outcomes in the management of bleeding disorders. DISCLOSURES: The preparation of this article was funded as part of the Comprehensive Care Sustainability Collaborative (CCSC) initiative, which is jointly sponsored by the National Hemophilia Foundation (NHF) and Impact Education, LLC, and supported via a charitable donation from Shire. Tarantino and Pindolia are members of the CCSC and were part of the NHF CCSC group that developed the metrics included in this article. Both authors received honorariums from the NHF for content development and expert review of the manuscript. Both authors contributed equally to the concept and design of this article and to analysis and manuscript preparation.

Pharmacy

Wong A, Erdman M, Hammond DA, Holt T, Holzhausen JM, **Horng M**, Huang LL, Jarvis J, Kram B, Kram S, Lesch C, Mercer J, Rech MA, Rivosecchi R, Stump B, Teevan C, and Day S. Major publications in the critical care pharmacotherapy literature in 2015 *Am J Health Syst Pharm* 2017;PMID: 28122702. Full Text

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PURPOSE: Recently published practice guidelines and research reports on pharmacotherapy in critical care patient populations are summarized. SUMMARY: The Critical Care Pharmacotherapy Literature Update (CCPLU) Group is composed of over 50 experienced critical care pharmacists who evaluate 31 peer-reviewed journals monthly to identify literature pertaining to pharmacotherapy in critical care populations. Articles are chosen for summarization in a monthly CCPLU Group publication on the basis of applicability and relevance to clinical practice and strength of study design. From January to December 2015, a total of 121 articles were summarized; of these, 3 articles presenting clinical practice guidelines and 12 articles presenting original research findings were objectively selected for inclusion in this review based on their potential to change or reinforce current evidence-based practice. The reviewed guidelines address the management of intracranial hemorrhage (ICH), adult advanced cardiac life support (ACLS) and post-cardiac arrest care, and the management of supraventricular tachycardia (SVT). The reviewed research reports address topics such as nutrition in critically ill adults, administration of beta-lactams for severe sepsis, anticoagulant selection in the context of continuous renal replacement therapy, early goal-directed therapy in septic shock, magnesium use for neuroprotection in acute stroke, and progesterone use in patients with traumatic brain injury. CONCLUSION: Important recent additions to the critical care pharmacy literature include updated joint clinical practice guidelines on the management of spontaneous ICH, ACLS, and SVT.

Public Health Sciences

Baumer TG, **Dischler J**, **Mende V**, **Zauel R**, **van Holsbeeck M**, **Siegal DS**, **Divine G**, **Moutzouros V**, and **Bey MJ**. Effects of asymptomatic rotator cuff pathology on in vivo shoulder motion and clinical outcomes *J Shoulder Elbow Surg* 2017;PMID: 28131679. Full Text

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BACKGROUND: The incidence of asymptomatic rotator cuff tears has been reported to range from 15% to 39%, but the influence of asymptomatic rotator cuff pathology on shoulder function is not well understood. This study assessed the effects of asymptomatic rotator cuff pathology on shoulder kinematics, strength, and patient-reported outcomes. METHODS: A clinical ultrasound examination was performed in 46 asymptomatic volunteers (age: 60.3 +/- 7.5 years) with normal shoulder function to document the condition of their rotator cuff. The ultrasound imaging identified the participants as healthy (n = 14) or pathologic (n = 32). Shoulder motion was measured with a biplane x-ray imaging system, strength was assessed with a Biodex (Biodex Medical Systems, Inc., Shirley, NY, USA), and patient-reported outcomes were assessed using the Western Ontario Rotator Cuff Index and visual analog scale pain scores. RESULTS: Compared with healthy volunteers, those with rotator cuff pathology had significantly less abduction (P = .050) and elevation (P = .041) strength, their humerus was positioned more inferiorly on the glenoid (P = .018), and the glenohumeral contact path length was longer (P = .007). No significant differences were detected in the Western Ontario Rotator Cuff Index, visual analog scale, range of motion, or acromiohumeral distance. CONCLUSIONS: The

differences observed between the healthy volunteers and those with asymptomatic rotator cuff pathology lend insight into the changes in joint mechanics, shoulder strength, and conventional clinical outcomes associated with the early stages of rotator cuff pathology. Furthermore, these findings suggest a plausible mechanical progression of kinematic and strength changes associated with the development of rotator cuff pathology.

Public Health Sciences

Ghanem AI, **Khan NT**, **Mahan M**, **Ibrahim A**, **Buekers T**, and **Elshaikh MA**. The impact of lymphadenectomy on survival endpoints in women with early stage uterine endometrioid carcinoma: A matched analysis *Eur J Obstet Gynecol Reprod Biol* 2016; 210:225-230. PMID: 28068595. Full Text

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OBJECTIVES: The role of pelvic lymphadenectomy (LA) in women with stage I endometrial carcinoma (EC) is controversial. The objective of this study is to investigate the prognostic impact of LA on survival endpoints in matched cohorts of women with stage I EC solely of endometrioid histology. Survival endpoints included recurrence-free (RFS), disease-specific (DSS) and overall survival (OS). METHODS AND MATERIALS: Patients with FIGO stage I EC who underwent hysterectomy with LA as part of their surgical staging between 1/1990 and 6/2015 were matched to a similar group that underwent hysterectomy without lymphadenectomy (NLA), based on stage, grade and adjuvant management. Univariate and multivariate modeling with Cox regression analysis was carried out for predictors of survival endpoints. RESULTS: 870 women constituted the study cohort (435 in each group). Median number of dissected lymph node in the LA group was 9 (range, 5-75). There was no statistically significant difference between the two groups in regards to 5-year OS (87.2% for LA vs. 91.7% for NLA) (p=0.36), DSS 97.7% vs. 98% (p=0.54) and RFS (93.7% vs. 90% (p=0.08), respectively. Lymphadenectomy was not a predictor of any of the studied survival endpoints. On multivariate analysis for the entire cohort, older age, deep myometrial invasion and higher tumor grade were predictors of worse RFS. For DSS, higher tumor grade, lower uterine segment (LUS) involvement and FIGO stage IB were significant predictors of worse outcome. For OS, older age and LUS involvement were the only two independent predictors for shorter OS. CONCLUSIONS: After matching for FIGO stage, grade and adjuvant management, it appears that lymphadenectomy in women with stage I EC does not impact survival endpoints.

Public Health Sciences

Haley L, **Burmeister C**, **Buekers T**, and **Elshaikh MA**. Is older age a real adverse prognostic factor in women with early-stage endometrial carcinoma? A matched analysis *Int J Gynecol Cancer* 2017;PMID: 28060139. Full Text

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OBJECTIVES: The aim of this study was to evaluate if older age alone negatively impacts survival endpoints in women with early-stage uterine endometrioid carcinoma (EC), or its reported prognostic impact is due to an interaction with other well-known adverse factors using matched-analysis methodology. METHODS: We identified 1254 patients with International Federation of Gynecology and Obstetrics stage I-II EC who underwent hysterectomy at our institution. We created 2 matched groups based on International Federation of Gynecology and Obstetrics stage, tumor grade, lymph node dissection status, and the type of adjuvant management. Recurrence-free (RFS), disease-specific (DSS) and overall survival (OS) were calculated. RESULTS: A total 297 women 70 years or older were matched with 297 women younger than 70 years. The 2 groups were well balanced except for age and higher body mass index in younger patients. There were no significant difference between older and younger patients in regard to 5-year RFS (85% vs 87%; P = 0.52) or DSS (93% for both groups with P = 0.77). Five-year OS was shorter in older patients (76% vs 88% with P < 0.001). On multivariate analysis for RFS and DSS, high tumor grade and the presence of lymphovascular space invasion (LVSI) were the only 2 predictors of shorter RFS and DSS (P = 0.01 and P = 0.02, and P = 0.01 and P = 0.01, respectively). Tumor grade and LVSI also were predictors of shorter OS. CONCLUSIONS: Our study suggests that when older patients with EC are matched with younger patients based on tumor stage, grade, and adjuvant management the prognostic impact of old age disappears. High tumor grade and LVSI remained as independent predictors of survival endpoints.

Public Health Sciences
Kim W, **Oravec D**, **Divine GW**, **Flynn MJ**, and **Yeni YN**. Effect of view, scan orientation and analysis volume on digital tomosynthesis (dts) based textural analysis of bone *Ann Biomed Eng* 2017;PMID: 28083858. Full Text

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Digital tomosynthesis (DTS) derived textural parameters of human vertebral cancellous bone have been previously correlated to the finite element (FE) stiffness and 3D microstructure. The objective of this study was to optimize scanning configuration and use of multiple image slices in the analysis, so that FE stiffness prediction using DTS could be maximized. Forty vertebrae (T6, T8, T11, and L3) from ten cadavers (63-90 years) were scanned using microCT to obtain trabecular bone volume fraction (BV/TV) and FE stiffness. The vertebrae were then scanned using DTS anteroposteriorly (AP) and laterally (LM) while aligned axially (0 degrees), transversely (90 degrees) or obliquely (23 degrees) to the superior-inferior axis of the vertebrae. From the serial DTS images, fractal dimension (FD), mean intercept length (MIL) and line fraction deviation (LFD) parameters were obtained from a 2D-single mid-stack location and 3D-multi-image stack. The DTS derived textural parameters were then correlated with FE stiffness using linear regression models within each scanning orientation. 3D-multi-image stack models obtained from Transverse-LM scanning orientation (90 degrees) were most explanatory regardless of accounting for the effects of BV/TV. Therefore, DTS scanning perpendicular to the axis of the spine in an LM view is the preferred configuration for prediction of vertebral cancellous bone stiffness.

Public Health Sciences
Mahmoudi F, **Poisson L**, **Bagher-Ebadian H**, **Nazem-Zadeh M**, and **Soltanian-Zadeh H**. SU-F-R-02: Imaging-genomics for predicting gbm molecular subclasses and survival *Med Phys* 2016; 43(6):3373. PMID: 28047590. Abstract

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PURPOSE: Glioblastoma (GBM) is the most common and fatal primary intracranial neoplasm. GBM is categorized into five sub-classes (classical, G-CIMP, mesenchymal, proneural and neural) that can only be determined by an invasive brain biopsy followed by RNA and DNA methylation profiling. The goal of this study is to develop imaging features extracted from conventional MRI scans and an ensemble-classification method as a potential noninvasive method to predict the five molecular sub-classes and 12-month survival status. METHODS: Tumors are segmented into 4 cardinal sub-volumes that are enhancing, non-enhancing, necrosis, and edema by BraTuma software and post-manual modification. After intensity normalization, mean, standard deviation, skewness, and kurtosis of voxel intensities and normalized volume of each of the 4 sub-volumes are calculated. The first four features are extracted from three different modalities (T1 pre & post contrast and T2 FLAIR) and the tumor texture is quantified. A feature selection phase (wrapper algorithm) is preceded the classification stage. Ensembles of binary classifiers with one versus rest strategy, along with a separate binary classifier are employed respectively for molecular classification and survival status. Two different binary classifiers are tested (SVM and K* IBL) and their confidences are used for tie-breaking technique. RESULTS: With the select combination of features of the MRI modalities, the ROC area and accuracy of the prediction are 0.750 and 95% for classical, 1.000 and 100% for G-CIMP, 0.719 and 85% for mesenchymal, 0.875 and 95% for neural, 0.922 and 95% for proneural, and 0.990 and 95% for survival status respectively. CONCLUSION: The study proposes a set of three-dimensional and rotation invariant imaging features that represent texture and volumetric characteristics of GBM tumors. The results show the select features are predictive for five molecular sub-classes and survival status in GBM. These results indicate the feasibility of obviating the biopsy for obtaining genomic information of tumor.

Public Health Sciences
Nakagawa P, **Masjoan-Juncos JX**, **Basha H**, **Janic B**, **Worou ME**, **Liao TD**, **Romero CA**, **Peterson EL**, and **Carretero OA**. Effects of N-acetyl-seryl-asparyl-lysyl-proline on blood pressure, renal damage, and mortality in systemic lupus erythematosus *Physiol Rep* 2017; 5(2)PMID: 28126732. Full Text

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Systemic lupus erythematosus (SLE) is an autoimmune disease with a high prevalence of hypertension. NZBWF1 (SLE-Hyp) mice develop hypertension that can be prevented by modulating T cells. The peptide N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) decreases renal damage and improves renal function in a model of SLE without hypertension (MRL/lpr). However, it is not known whether Ac-SDKP prevents hypertension in NZBWF1 mice. We hypothesized that in SLE-Hyp, Ac-SDKP prevents hypertension and renal damage by modulating T cells. Animals were divided into four groups: (1) control + vehicle, (2) control + Ac-SDKP, (3) SLE + vehicle, and (4) SLE + Ac-SDKP Systolic blood pressure (SBP), albuminuria, renal fibrosis, and T-cell phenotype were analyzed. SBP was higher in SLE compared to control mice and was not decreased by Ac-SDKP treatment. Half of SLE mice developed an acute and severe form of hypertension accompanied by albuminuria followed by death. Ac-SDKP delayed development of severe hypertension, albuminuria, and early mortality, but this delay did not reach statistical significance. Ac-SDKP prevented glomerulosclerosis, but not interstitial fibrosis in SLE-Hyp mice. SLE-Hyp mice showed a decrease in helper and cytotoxic T cells as well as an increase in double negative lymphocytes and T helper 17 cells, but these cells were unaffected by Ac-SDKP In conclusion, Ac-SDKP prevents kidney damage, without affecting blood pressure in an SLE animal model. However, during the acute relapse of SLE, Ac-SDKP might also delay the manifestation of an acute and severe form of hypertension leading to early mortality. Ac-SDKP is a potential tool to treat renal damage in SLE-Hyp mice.

Public Health Sciences

Wilson SP, **Vohra T**, **Knych M**, **Goldberg J**, **Price C**, **Calo S**, **Mahan M**, and **Miller J**. Gonorrhea and chlamydia in the emergency department: Continued need for more focused treatment for men, women and pregnant women *Am J Emerg Med* 2017;PMID: 28073612. Full Text

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INTRODUCTION: Delay in current nucleic acid amplification testing for Neisseria gonorrhoeae and Chlamydia trachomatis has led to recommendations for presumptive treatment in patients with concern for infection and unreliable follow-up. In the urban setting, it is assumed that many patients have unreliable follow-up, therefore presumptive therapy is thought to be used frequently. We sought to measure the frequency of disease and accuracy of presumptive treatment for these infections. METHODS: This was an observational cohort study performed at an urban academic Level 1 trauma center ED with an annual census of 95,000 visits per year. Testing was performed using the APTIMA Unisex swab assay (Gen-Probe Incorporated, San Diego, CA). Presumptive therapy was defined as receiving treatment for both infections during the initial encounter without confirmation of diagnosis. RESULTS: A total of 1162 patients enrolled. Infection was present in 26% of men, 14% of all women and 11% of pregnant women. Despite high frequency of presumptive treatment, >4% of infected patients in each category went untreated. CONCLUSION: Inaccuracy of presumptive treatment was common for these sexually transmitted infections. There is an opportunity to improve diagnostic accuracy for treatment.

Pulmonary

Awdish RL. A view from the edge - creating a culture of caring *N Engl J Med* 2017; 376(1):7-9. PMID: 28052225. Full Text

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Pulmonary

Awdish RL, **Buick D**, **Kokas M**, **Berlin H**, **Jackman C**, **Williamson C**, **Mendez MP**, and **Chasteen K**. A communications bundle to improve satisfaction for critically ill patients and their families: A prospective, cohort pilot study *J Pain Symptom Manage* 2016;PMID: 28042074. Full Text

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CONTEXT: Communication skills training with simulated patients is used by many academic centers, but how to translate skills learned in simulated settings to improve communication in real encounters has not been described. OBJECTIVE: We developed a communications bundle to facilitate skill transfer from simulation to real encounters and improve patient and/or family satisfaction with physician communication. We tested the feasibility of its use in our hospital's medical intensive care unit (MICU). METHODS: This prospective cohort 2-week feasibility study included patients admitted to the MICU with APACHE IV predicted mortality >30% and/or single organ failure. The communications bundle included simulation communication training for MICU physicians, scheduling a family meeting within 72 hours of MICU admission, standardized pre- and post-meeting team huddles with the aid of a mobile app to set an agenda, choose a communication goal, and get feedback, and documentation of meeting in the electronic medical record. The intervention group receiving the communications bundle was located in a geographically separate unit than the control group receiving standard of care from MICU physicians who had not received training in the communications bundle. Patient satisfaction surveys were given within 48 hours of the family meeting and scores compared between the two groups. We also compared trainee self-perceived communication preparation. RESULTS: The intervention group (N = 15) scored significantly higher on satisfaction than the control group (N = 16) (P = 0.018). Intervention group trainees reported improvement in self-perceived communication preparation. CONCLUSION: Use of the communications bundle proved feasible in the MICU and suggests association with improved patient satisfaction and trainee self-perception of communication preparedness.

Pulmonary

Mullon JJ, Burkart KM, Silvestri G, Hogarth DK, Almeida F, Berkowitz D, Eapen G, Feller-Kopman D, Fessler HE, Folch E, Gillespie C, Haas A, Islam S, Lamb C, Levine SM, Majid A, Maldonado F, Musani A, Piquette C, **Ray C**, Reddy C, Rickman O, **Simoff M**, Wahidi MM, and Lee H. Interventional pulmonology fellowship accreditation standards: Executive summary of the multi-society interventional pulmonology fellowship accreditation committee *Chest* 2017;PMID: 28132754. Full Text

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Interventional Pulmonology (IP) is a rapidly evolving subspecialty of pulmonary medicine. In the last ten years formal IP fellowships have increased substantially in number from just five to now over thirty. The vast majority of IP fellowship trainees are selected through the National Residency Matching Program, and validated in-service and certification exams for IP exist. Practice standards and training guidelines for IP fellowship programs have been published, however considerable variability in the environment, curriculum, and experience offered by the various fellowship programs still exists and there is currently no formal accreditation process in place to standardize IP fellowship training. Recognizing the need for more uniform training across the various fellowship programs, a multi-society accreditation committee was formed with the intent to establish common accreditation standards for all IP fellowship programs in the United States. This article provides a summary of those standards and can serve as an accreditation template for training programs and their offices of graduate medical education as they move through the accreditation process.

Pulmonary
Smith AL, Palmer V, Farhat N, **Kalus JS**, **Thavarajah K**, **Digiovine B**, and **Macdonald NC**. Hospital-based clinical pharmacy services to improve ambulatory management of chronic obstructive pulmonary disease *J Pharm Technol* 2017; 33(1):8-14. PMID: Not assigned. Full Text

A.L. Smith, Wayne State University, Detroit, United States

Background: No systematic evaluations of a comprehensive clinical pharmacy process measures currently exist to determine an optimal ambulatory care collaboration model for chronic obstructive pulmonary disease (COPD) patients. Objective: Describe the impact of a pharmacist-provided clinical COPD bundle on the management of COPD in a hospital-based ambulatory care clinic. Methods: This retrospective cohort analysis evaluated patients with COPD managed in an outpatient pulmonary clinic. The primary objective of this study was to assess the completion of 4 metrics known to improve the management of COPD: (1) medication therapy management, (2) quality measures including smoking cessation and vaccines, (3) patient adherence, and (4) patient education. The secondary objective was to evaluate the impact of the clinical COPD bundle on clinical and economic outcomes at 30 and 90 days post-initial visit. Results: A total of 138 patients were included in the study; 70 patients served as controls and 68 patients received the COPD bundle from the clinical pharmacist. No patients from the control group had all 4 metrics completed as documented, compared to 66 of the COPD bundle group (P <.0001). Additionally, a statistically significant difference was found in all 4 metrics when evaluated individually. Clinical pharmacy services reduced the number of phone call consults at 90 days (P =.04) but did not have a statistically significant impact on any additional pre-identified clinical outcomes. Conclusion: A pharmacist-driven clinical COPD bundle was associated with significant increases in the completion and documentation of 4 metrics known to improve the outpatient management of COPD.

Radiation Oncology
Bagher-Ebadian H, **Chetty I**, **Liu C**, **Movsas B**, and **Siddiqui F**. SU-F-R-38: Impact of smoothing and noise on robustness of cbct textural features for prediction of response to radiotherapy treatment of head and neck cancers *Med Phys* 2016; 43(6):3381. PMID: 28046928. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To examine the impact of image smoothing and noise on the robustness of textural information extracted from CBCT images for prediction of radiotherapy response for patients with head/neck (H/N) cancers. METHODS: CBCT image datasets for 14 patients with H/N cancer treated with radiation (70 Gy in 35 fractions) were investigated. A deformable registration algorithm was used to fuse planning CT's to CBCT's. Tumor volume was automatically segmented on each CBCT image dataset. Local control at 1-year was used to classify 8 patients as responders (R), and 6 as non-responders (NR). A smoothing filter [2D Adaptive Weiner (2DAW) with 3 different windows (psi=3, 5, and 7)], and two noise models (Poisson and Gaussian, SNR=25) were implemented, and independently applied to CBCT images. Twenty-two textural features, describing the spatial arrangement of voxel intensities calculated from gray-level co-occurrence matrices, were extracted for all tumor volumes. RESULTS: Relative to CBCT images without smoothing, none of 22 textural features extracted showed any significant differences when smoothing was applied (using the 2DAW with filtering parameters of psi=3 and 5), in the responder and non-responder groups. When smoothing, 2DAW with psi=7 was applied, one textural feature, Information Measure of Correlation, was significantly different relative to no smoothing. Only 4 features (Energy, Entropy, Homogeneity, and Maximum-Probability) were found to be statistically different between the R and NR groups (Table 1). These features remained statistically significant discriminators for R and NR groups in presence of noise and smoothing. CONCLUSION: This preliminary work suggests that textural classifiers for response prediction, extracted from H&N CBCT images, are robust to low-power noise and low-pass filtering. While other types of filters will alter the spatial frequencies differently, these results are promising. The current study is subject to Type II errors. A much larger cohort of patients is needed to confirm these results. This work was supported in part by a grant from Varian Medical Systems (Palo Alto, CA).

Radiation Oncology
Bagher-Ebadian H, Dehkordi A, and **Ewing J**. SU-F-I-26: Maximum likelihood and nested model selection techniques for pharmacokinetic analysis of dynamic contrast enhanced mri in patients with glioblastoma tumors *Med Phys* 2016; 43(6):3392. PMID: 28048158. Abstract

Henry Ford Health System, Detroit, MI.
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Henry Ford Hospital, Detroit, MI.

PURPOSE: This pilot study introduces a novel approach for estimation of pharmacokinetic parameters in dynamic contrast enhanced magnetic resonance imaging (DCE-MRI). In this study Maximum Likelihood (ML) and Nested Model Selection (NMS) techniques are combined to construct an approximately unbiased estimator for DCE-MRI data analysis. METHODS: DCE T1-weighted MRI using the contrast agent (CA) gadopentetate dimeglumine was performed on 20 patients with Glioblastoma tumor. ML Estimation (MLE) technique was recruited for optimizing 3 physiologically nested models constructed based on the extended Tofts model in the course of DCE-MRI experimental. The Log-Likelihood-Ratio (LLR) measures for three nested models were used to choose the best model explaining the variation of the experimental DCE-MRI data and to estimate its Pharmacokinetic (PK) parameters. The observed information matrix or the matrix of Log-Likelihood was used to estimate the variance and co-variance of the estimated PK parameters for each of selected models. RESULTS: The PK parameters along with the model choice maps estimated by the MLE and NMS are highly in agreement with the physiological condition of underlying pathology and the values for the permeability parameters of the brain reported by the literature. The low variance and covariance measures of the estimated PK parameters being reasonably in-range imply that the proposed estimator is robust for estimation of physiological parameters in DCE-MRI studies. CONCLUSION: This pilot study confirms that only three parameters of the standard model are sufficient to fit the most complicated time trace of CA concentration in DCE-T1 weighted studies for GBM tumors under the conditions of the experiment. This study is supported in part by Dykstra Family (F60570) and mentored grants (A10237).

Radiation Oncology

Bagher-Ebadian H, **Mohammadian Behbahani M**, and **Ewing J**. WE-FG-206-03: An adaptive model for pharmacokinetic nested model selection in dynamic contrast enhanced mri data analysis *Med Phys* 2016; 43(6):3831. PMID: 28048278. Abstract

Henry Ford Health System, Detroit, MI, Amir-Kabir University of Technology, Tehran, Iran.

PURPOSE: This study introduces an adaptive Model Selection (MS) technique to perform Pharmacokinetic nested MS from the time trace of longitudinal relaxation rate change, DeltaR1 (R1 = 1/T1) in Dynamic Contrast Enhanced (DCE) MRI studies. METHODS: Three physiologically nested models derived from the standard Tofts model along with an averaged (over 30 patients) arterial input function were used to simulate a set of DeltaR1 profiles to describe possible physiological conditions of underlying tissue pathology: Model-1: the vascular compartment is filled with contrast agent (CA) with no outward leakage. Model-2: the vascular compartment is filled with CA with outward leakage but no evidence of back-flux. Model-3: the vascular compartment is filled with CA with both outward and backward-flux. Three different sets of simulated DeltaR1 profiles in presence of different signal-to-noise ratios (5, 10, 15, 30, 70, 100, and no noise) were used to train an Artificial Neural Network (ANN) for performing MS. A k-fold cross-validation method was used to validate and optimize the ANN architecture. The trained-ANN was also applied on the DCE-MRI data of 20 patients with Glioblastoma and results were compared to the models selected by the Log-Likelihood-Ratio (LLR) technique using Dice coefficient. RESULTS: The confusion matrix and the strong similarity (Dice coefficients of 0.87, 0.89 for Models 2 and 3) between the models selected by the trained ANN and the LLR method confirms that the performance of the adaptive NMS technique is superior to the LLR method. The ANN showed a strong sensitivity for selecting models with higher orders; thus less type-II errors (never misses any tissues with leaky vasculature (Models 2 and 3). CONCLUSION: The noise insensitivity, speed, and superiority of the ANN technique in choosing the best PK model would allow a less biased estimation of cerebrovascular permeability parameters in tumorous tissues. This work is supported in part by HFHS mentored Grant (A10237).

Radiation Oncology

Boyce-Fappiano D, **Elibe E**, **Schultz L**, Ryu S, **Siddiqui MS**, **Chetty I**, **Lee I**, **Rock J**, **Movsas B**, and **Siddiqui F**. Analysis of the factors contributing to vertebral compression fractures after spine stereotactic radiosurgery *Int J Radiat Oncol Biol Phys* 2017; 97(2):236-245. PMID: 28068232. Full Text

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PURPOSE: To determine our institutional vertebral compression fracture (VCF) rate after spine stereotactic radiosurgery (SRS) and determine contributory factors. METHODS AND MATERIALS: Retrospective analysis from 2001 to 2013 at a single institution was performed. With institutional review board approval, electronic medical records of 1905 vertebral bodies from 791 patients who were treated with SRS for the management of primary or metastatic spinal lesions were reviewed. A total of 448 patients (1070 vertebral bodies) with adequate follow-up

imaging studies available were analyzed. Doses ranging from 10 Gy in 1 fraction to 60 Gy in 5 fractions were delivered. Computed tomography and magnetic resonance imaging were used to evaluate the primary endpoints of this study: development of a new VCF, progression of an existing VCF, and requirement of stabilization surgery after SRS. RESULTS: A total of 127 VCFs (11.9%; 95% confidence interval [CI] 9.5%-14.2%) in 97 patients were potentially SRS induced: 46 (36%) were de novo, 44 (35%) VCFs progressed, and 37 (29%) required stabilization surgery after SRS. Our rate for radiologic VCF development/progression (excluding patients who underwent surgery) was 8.4%. Upon further exclusion of patients with hematologic malignancies the VCF rate was 7.6%. In the univariate analyses, females (hazard ratio [HR] 1.54, 95% CI 1.01-2.33, P=.04), prior VCF (HR 1.99, 95% CI 1.30-3.06, P=.001), primary hematologic malignancies (HR 2.68, 95% CI 1.68-4.28, P<.001), thoracic spine lesions (HR 1.46, 95% CI 1.02-2.10, P=.02), and lytic lesions had a significantly increased risk for VCF after SRS. On multivariate analyses, prior VCF and lesion type remained contributory. CONCLUSIONS: Single-fraction SRS doses of 16 to 18 Gy to the spine seem to be associated with a low rate of VCFs. To the best of our knowledge, this is the largest reported experience analyzing SRS-induced VCFs, with one of the lowest event rates reported.

Radiation Oncology

Chetvertkov M, **Siddiqui F**, **Chetty I**, **Kumarasiri A**, **Liu C**, and **Gordon J**. SU-F-R-41: Regularized pca can model treatment-related changes in head and neck patients using daily cbcts *Med Phys* 2016; 43(6):3382. PMID: 28046748. Abstract

Wayne State University, Detroit, MI.
Henry Ford Health System, Detroit, MI.

PURPOSE: To use daily cone beam CTs (CBCTs) to develop regularized principal component analysis (PCA) models of anatomical changes in head and neck (H&N) patients, to guide replanning decisions in adaptive radiation therapy (ART). METHODS: Known deformations were applied to planning CT (pCT) images of 10 H&N patients to model several different systematic anatomical changes. A Pinnacle plugin was used to interpolate systematic changes over 35 fractions, generating a set of 35 synthetic CTs for each patient. Deformation vector fields (DVFs) were acquired between the pCT and synthetic CTs and random fraction-to-fraction changes were superimposed on the DVFs. Standard non-regularized and regularized patient-specific PCA models were built using the DVFs. The ability of PCA to extract the known deformations was quantified. PCA models were also generated from clinical CBCTs, for which the deformations and DVFs were not known. It was hypothesized that resulting eigenvectors/eigenfunctions with largest eigenvalues represent the major anatomical deformations during the course of treatment. RESULTS: As demonstrated with quantitative results in the supporting document regularized PCA is more successful than standard PCA at capturing systematic changes early in the treatment. Regularized PCA is able to detect smaller systematic changes against the background of random fraction-to-fraction changes. To be successful at guiding ART, regularized PCA should be coupled with models of when anatomical changes occur: early, late or throughout the treatment course. CONCLUSION: The leading eigenvector/eigenfunction from the both PCA approaches can tentatively be identified as a major systematic change during radiotherapy course when systematic changes are large enough with respect to random fraction-to-fraction changes. In all cases the regularized PCA approach appears to be more reliable at capturing systematic changes, enabling dosimetric consequences to be projected once trends are established early in the treatment course. This work is supported in part by a grant from Varian Medical Systems, Palo Alto, CA.

Radiation Oncology

Devpura S, **Li H**, **Liu C**, **Fraser C**, **Ajlouni M**, **Movsas B**, and **Chetty I**. SU-D-204-07: Retrospective correlation of dose accuracy with regions of local failure for early stage lung cancer patients treated with stereotactic body radiotherapy *Med Phys* 2016; 43(6):3333. PMID: 28048314. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To correlate dose distributions computed using six algorithms for recurrent early stage non-small cell lung cancer (NSCLC) patients treated with stereotactic body radiotherapy (SBRT), with outcome (local failure). METHODS: Of 270 NSCLC patients treated with 12Gyx4, 20 were found to have local recurrence prior to the 2-year time point. These patients were originally planned with 1-D pencil beam (1-D PB) algorithm. 4D imaging was performed to manage tumor motion. Regions of local failures were determined from follow-up PET-CT scans. Follow-up CT images were rigidly fused to the planning CT (pCT), and recurrent tumor volumes (Vrecur) were mapped to the pCT. Dose was recomputed, retrospectively, using five algorithms: 3-D PB, collapsed cone convolution (CCC), anisotropic analytical algorithm (AAA), AcurosXB, and Monte Carlo (MC). Tumor control probability (TCP) was computed using the Marsden model (1,2). Patterns of failure were classified as central, in-field, marginal, and distant for Vrecur >/=95% of prescribed dose, 95-80%, 80-20%, and </=20%, respectively (3). RESULTS: Average PTV D95

(dose covering 95% of the PTV) for 3-D PB, CCC, AAA, AcurosXB, and MC relative to 1-D PB were 95.3+/-2.1%, 84.1+/-7.5%, 84.9+/-5.7%, 86.3+/-6.0%, and 85.1+/-7.0%, respectively. TCP values for 1-D PB, 3-D PB, CCC, AAA, AcurosXB, and MC were 98.5+/-1.2%, 95.7+/-3.0, 79.6+/-16.1%, 79.7+/-16.5%, 81.1+/-17.5%, and 78.1+/-20%, respectively. Patterns of local failures were similar for 1-D and 3D PB plans, which predicted that the majority of failures occur in centraldistal regions, with only approximately 15% occurring distantly. However, with convolution/superposition and MC type algorithms, the majority of failures (65%) were predicted to be distant, consistent with the literature. CONCLUSION: Based on MC and convolution/superposition type algorithms, average PTV D95 and TCP were approximately 15% lower than the planned 1-D PB dose calculation. Patterns of failure results suggest that MC and convolution/superposition type algorithms predict different outcomes for patterns of failure relative to PB algorithms. Work supported in part by Varian Medical Systems, Palo Alto, CA.

Radiation Oncology

Dumas M, and **Wen N**. SU-F-T-578: Characterization of vidar dosimetrypro advantage red scanner with application to sbrt and srs qa *Med Phys* 2016; 43(6):3596. PMID: 28047018. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To use Gafchromic EBT3 film to quantify key dosimetric characteristics of the Vidar DosimetryPro Advantage RED film scanner for use in SBRT/SRS QA, by analyzing scanner uniformity and dose sensitivity. METHOD: Gafchromic EBT3 film was used in this study. Films were irradiated using 6MV FFF and 10MV FFF beams from a Varian Edge linear accelerator, with setup of 100cm SAD at depth 5 cm. Nine doses were delivered per film, with calibration dose ranges of 1-10 Gy and 3-24 Gy for 6MV FFF, and 3-27 Gy for 10MV FFF. Films were scanned with the long side of the film parallel to the detector array. Dose calibration curves were fitted to a 3rd degree polynomial. The derivative of a calibration curve was taken to determine the scanner's sensitivity per dose delivered (OD/Gy). Scanner non-uniformity was calculated in 2 dimensions by taking the mean of standard deviation in each row and column. Absolute dose SRS/SBRT Gamma analyses were performed with passing criteria of 3% and 1mm DTA. For comparison, Gamma analyses were also performed using an Epson Expression 10000 XL. RESULTS: Uniformity for the Vidar scanner was 0.37% +/- 0.03% in the perpendicular to scan direction and 0.67% +/- 0.05% in the parallel to scan direction, with an overall uniformity of 0.52% +/- 0.03%. Epson red channel uniformity was 0.85% +/- 0.05% and 0.88% +/- 0.08% for the green channel. The Vidar average dose sensitivity from 1-10 Gy was 0.112 OD/Gy and 0.061 OD/Gy for 3-24 Gy. SBRT/SRS Gamma pass rates were 97.8 +/- 1.4 for Vidar and 97.5 +/- 1.4 for Epson. CONCLUSION: The Vidar scanner has 41% less non-uniformity compared to Epson XL10000 green channel. The dose sensitivity is 2-3 time greater for the Vidar scanner compared to the Epson in the SRS/SBRT dose range of 5-24 Gy.

Radiation Oncology

Gardner S, **Doemer A**, **Miller B**, **Wen N**, and **Chetty I**. SU-G-BRC-07: Evaluation of AAA focal spot size for srs planning using end-to-end dosimetric data *Med Phys* 2016; 43(6):3628. PMID: 28048385. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To use end-to-end dosimetric measurements with Gafchromic film to evaluate the effects of focal spot size parameter for small-field dose calculations using AAA for SRS lesions. METHODS: A total of 13 plans, corresponding to 7 patients previously treated with cranial SRS, were analyzed in this study (target volume range:[0.67cc,13.9cc]). The plans included DCA delivery (4 plans total) and VMAT delivery (9 plans total). All plans were mapped to a solid water phantom (15 cm thickness; isocenter and film plane at 7.5 depth). Dose calculation was performed with AAA v.11 (1.0mm grid size); three focal spot size settings were tested: 0mm, 0.5mm, and 1.5mm. For each plan, three calculated doses (corresponding to each focal spot size setting) were compared to measured film dose using quantitative methods [Gamma Analysis(1%,1mm,10% threshold criteria)] and qualitative methods (visual dose profile comparison). Film calibration and analysis were performed using in-house calibration methods and software package. RESULTS: Gamma(1%,1mm) analysis passing rate results [mean(st.dev){%}] were as follows. For DCA plans: 98.74(0.54)-[0mm Focal Spot Size]; 98.24(1.26)-[0.5mm Focal Spot Size]; 95.42(2.29)-[1.5mm Focal Spot Size]. For VMAT plans: 98.75(0.54)-[0mm Focal Spot Size]; 98.89(0.73)-[0.5mm Focal Spot Size]; 97.43(1.30)-[1.5mm Focal Spot Size]. The majority of failing points (Gamma value>1.0) were found to be within the high dose region for all Focal Spot Size calculation models. Visual inspection of the dose profile, showed that the 1.5mm Focal Spot size calculation exhibited blurring in the high dose region (defined as >85% of the peak dose), resulting in a more gradual shoulder of the dose profile relative to measurements. CONCLUSION: The dose calculation accuracy of DCA and VMAT plans is paramount for SRS treatment planning. Our results indicate similar behavior of the AAA model with focal spot sizes of 0mm and 0.5mm, while 1.5mm focal spot size tends to result in blurring of the high dose region. Henry Ford Health System has research agreements with Varian and Philips.

Radiation Oncology

Ghanem AI, **Khan NT**, **Mahan M**, **Ibrahim A**, **Buekers T**, and **Elshaikh MA**. The impact of lymphadenectomy on survival endpoints in women with early stage uterine endometrioid carcinoma: A matched analysis *Eur J Obstet Gynecol Reprod Biol* 2016; 210:225-230. PMID: 28068595. Full Text

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OBJECTIVES: The role of pelvic lymphadenectomy (LA) in women with stage I endometrial carcinoma (EC) is controversial. The objective of this study is to investigate the prognostic impact of LA on survival endpoints in matched cohorts of women with stage I EC solely of endometrioid histology. Survival endpoints included recurrence-free (RFS), disease-specific (DSS) and overall survival (OS). METHODS AND MATERIALS: Patients with FIGO stage I EC who underwent hysterectomy with LA as part of their surgical staging between 1/1990 and 6/2015 were matched to a similar group that underwent hysterectomy without lymphadenectomy (NLA), based on stage, grade and adjuvant management. Univariate and multivariate modeling with Cox regression analysis was carried out for predictors of survival endpoints. RESULTS: 870 women constituted the study cohort (435 in each group). Median number of dissected lymph node in the LA group was 9 (range, 5-75). There was no statistically significant difference between the two groups in regards to 5-year OS (87.2% for LA vs. 91.7% for NLA) (p=0.36), DSS 97.7% vs. 98% (p=0.54) and RFS (93.7% vs. 90% (p=0.08), respectively. Lymphadenectomy was not a predictor of any of the studied survival endpoints. On multivariate analysis for the entire cohort, older age, deep myometrial invasion and higher tumor grade were predictors of worse RFS. For DSS, higher tumor grade, lower uterine segment (LUS) involvement and FIGO stage IB were significant predictors of worse outcome. For OS, older age and LUS involvement were the only two independent predictors for shorter OS. CONCLUSIONS: After matching for FIGO stage, grade and adjuvant management, it appears that lymphadenectomy in women with stage I EC does not impact survival endpoints.

Radiation Oncology

Glide-Hurst C, **Zheng W**, Stehning C, Weiss S, and Renisch S. SU-G-JeP2-10: On the need for a dynamic model for patient-specific distortion corrections for mr-only pelvis treatment planning *Med Phys* 2016; 43(6):3661. PMID: 28048910. Abstract

Henry Ford Health System, Detroit, MI.
Philips Research Laboratories, Hamburg, Germany.

PURPOSE: Patient-specific distortions, particularly near tissue/air interfaces, require assessment and possible corrections for MRI-only radiation treatment planning (RTP). However, patients are dynamic due to changes in physiological status and motion during imaging sessions. This work investigated the need for dynamic patient-specific distortion corrections to support pelvis MR-only RTP. METHODS: The pelvises of healthy volunteers were imaged at 1.0T, 1.5T, and 3.0T. Patient-specific distortion field maps were generated using a dual-echo gradient-recalled echo (GRE) sequence with B0 field maps obtained from the phase difference between the two echoes acquired at two timepoints: empty and full bladders. To quantify changes arising from respiratory state, end-inhalation and end-expiration data were acquired. Distortion map differences were computed between the empty/full bladder and inhalation/expiration to characterize local changes. The normalized frequency distortion distributions in T2-weighted TSE images were characterized, particularly for simulated prostate planning target volumes (PTVs). RESULTS: Changes in rectal and bowel air location were observed, likely due to changes in bladder filling. Within the PTVs, displacement differences (mean +/- stdev, range) were -0.02 +/- 0.02 mm (-0.13 to 0.07 mm) for 1.0T, -0.1 +/- 0.2 mm (-0.92 to 0.74 mm) for 1.5T, and -0.20 +/- 0.03 mm (-0.61 to 0.38 mm) for 3.0T. Local changes of approximately 1 mm at the prostate-rectal interface were observed for an extreme case at 1.5T. For end-inhale and end-exhale scans at 3.0T, 99% of the voxels had Deltax differences within +/-0.25mm, thus the displacement differences due to respiratory state appear negligible in the pelvis. CONCLUSION: Our work suggests that transient bowel/rectal gas due to bladder filling may yield non-negligible patient-specific distortion differences near the prostate/rectal interface, whereas respiration had minimal effect. A temporal patient model for patient-specific distortion corrections may be advantageous for MR-only RTP, although further investigations in larger cohorts are needed to fully characterize distortion magnitude. The submitting institution has research agreements with Philips Healthcare. Research sponsored by a Henry Ford Health System Internal Mentored Grant.

Radiation Oncology

Haley L, **Burmeister C**, **Buekers T**, and **Elshaikh MA**. Is older age a real adverse prognostic factor in women with early-stage endometrial carcinoma? A matched analysis *Int J Gynecol Cancer* 2017;PMID: 28060139. Full Text

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OBJECTIVES: The aim of this study was to evaluate if older age alone negatively impacts survival endpoints in women with early-stage uterine endometrioid carcinoma (EC), or its reported prognostic impact is due to an interaction with other well-known adverse factors using matched-analysis methodology. METHODS: We identified 1254 patients with International Federation of Gynecology and Obstetrics stage I-II EC who underwent hysterectomy at our institution. We created 2 matched groups based on International Federation of Gynecology and Obstetrics stage, tumor grade, lymph node dissection status, and the type of adjuvant management. Recurrence-free (RFS), disease-specific (DSS) and overall survival (OS) were calculated. RESULTS: A total 297 women 70 years or older were matched with 297 women younger than 70 years. The 2 groups were well balanced except for age and higher body mass index in younger patients. There were no significant difference between older and younger patients in regard to 5-year RFS (85% vs 87%; P = 0.52) or DSS (93% for both groups with P = 0.77). Five-year OS was shorter in older patients (76% vs 88% with P < 0.001). On multivariate analysis for RFS and DSS, high tumor grade and the presence of lymphovascular space invasion (LVSI) were the only 2 predictors of shorter RFS and DSS (P = 0.01 and P = 0.02, and P = 0.01 and P = 0.01, respectively). Tumor grade and LVSI also were predictors of shorter OS. CONCLUSIONS: Our study suggests that when older patients with EC are matched with younger patients based on tumor stage, grade, and adjuvant management the prognostic impact of old age disappears. High tumor grade and LVSI remained as independent predictors of survival endpoints.

Radiation Oncology

Huang Y, **Gardner S**, **Liu C**, **Zhao B**, **Wen N**, **Brown S**, and **Chetty I**. SU-F-J-11: Radiobiologically optimized patient localization during prostate external beam localization *Med Phys* 2016; 43(6):3408. PMID: 28046819. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To present a novel positioning strategy which optimizes radiation delivery with radiobiological response knowledge, and to evaluate its application during prostate external beam radiotherapy. METHODS: Ten patients with low or intermediate risk prostate cancer were evaluated retrospectively in this IRB-approved study. For each patient, a VMAT plan was generated on the planning CT (PCT) to deliver 78 Gy in 39 fractions with PTV = prostate + 7 mm margin, except for 5mm in the posterior direction. Five representative pretreatment CBCT images were selected for each patient, and prostate, rectum, and bladder were delineated on all CBCT images. Each CBCT was auto-registered to the corresponding PCT. Starting from this auto-matched position (AM-position), a search for optimal treatment position was performed utilizing a score function based on radiobiological and dosimetric indices (D98_DTV, NTCP_rectum, and NTCP_bladder) for the daily target volume (DTV), rectum, and bladder. DTV was defined as prostate + 4 mm margin to account for intra-fraction motion as well as contouring variability on CBCT. We termed the optimal treatment position the radiobiologically optimized couch shift position (ROCS-position). RESULTS: The indices, averaged over the 10 patients' treatment plans, were (mean+/-SD): 77.7+/-0.2 Gy (D98_PTV), 12.3+/-2.7% (NTCP_rectum), and 53.2+/-11.2% (NTCP_bladder). The corresponding values calculated on all 50 CBCT images at the AM-positions were 72.9+/-11.3 Gy (D98_DTV), 15.8+/-6.4% (NTCP_rectum), and 53.0+/-21.1% (NTCP_bladder), respectively. In comparison, calculated on CBCT at the ROCS-positions, the indices were 77.0+/-2.1 Gy (D98_DTV), 12.1+/-5.7% (NTCP_rectum), and 60.7+/-16.4% (NTCP_bladder). Compared to autoregistration, ROCS-optimization recovered dose coverage to target volume and lowered the risk to rectum. Moreover, NTCPrectum for one patient remained high after ROCS-optimization and therefore could potentially benefit from adaptive planning. CONCLUSION: These encouraging results illustrate the potential utility of applying radiobiologically optimized correction for online image-guided radiotherapy of prostate patients.

Radiation Oncology

Jain M, **Gamage NH**, Alsulami M, Shankar A, Achyut BR, Angara K, Rashid MH, Iskander A, Borin TF, Wenbo Z, Ara R, **Ali MM**, Lebedyeva I, **Chwang WB**, Guo A, **Bagher-Ebadian H**, and Arbab AS. Intravenous formulation of het0016 decreased human glioblastoma growth and implicated survival benefit in rat xenograft models *Sci Rep* 2017; 7:41809. PMID: 28139732. Full Text

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Glioblastoma (GBM) is a hypervascular primary brain tumor with poor prognosis. HET0016 is a selective CYP450 inhibitor, which has been shown to inhibit angiogenesis and tumor growth. Therefore, to explore novel treatments, we have generated an improved intravenous (IV) formulation of HET0016 with HPssCD and tested in animal models of human and syngeneic GBM. Administration of a single IV dose resulted in 7-fold higher levels of HET0016 in plasma and 3.6-fold higher levels in tumor at 60 min than that in IP route. IV treatment with HPssCD-HET0016 decreased tumor growth, and altered vascular kinetics in early and late treatment groups ($p < 0.05$). Similar growth inhibition was observed in syngeneic GL261 GBM ($p < 0.05$). Survival studies using patient derived xenografts of GBM811, showed prolonged survival to 26 weeks in animals treated with focal radiation, in combination with HET0016 and TMZ ($p < 0.05$). We observed reduced expression of markers of cell proliferation (Ki-67), decreased neovascularization (laminin and alphaSMA), in addition to inflammation and angiogenesis markers in the treatment group ($p < 0.05$). Our results indicate that HPssCD-HET0016 is effective in inhibiting tumor growth through decreasing proliferation, and neovascularization. Furthermore, HPssCD-HET0016 significantly prolonged survival in PDX GBM811 model.

Radiation Oncology

Janic B, **Bhuiyan MP**, **Ewing JR**, and **Ali MM**. pH-Dependent cellular internalization of paramagnetic nanoparticle *ACS Sens* 2016; 1(8):975-978. PMID: 28066811. Full Text

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A hallmark of the tumor microenvironment in malignant tumor is extracellular acidosis, which can be exploited for targeted delivery of drugs and imaging agents. A pH sensitive paramagnetic nanoaparticle (NP) is developed by incorporating GdDOTA-4AmP MRI contrast agent and pHLIP (pH Low Insertion Peptide) into the surface of a G5-PAMAM dendrimer. pHLIP showed pH-selective insertion and folding into cell membranes, but only in acidic conditions. We demonstrated that pHLIP-conjugated Gd44-G5 paramagnetic nanoparticle binds and fuses with cellular membrane at low pH, but not at normal physiological pH, and that it promotes cellular uptake. Intracellular trafficking of NPs showed endosomal/lysosomal path ways.

Radiation Oncology

Joshi S, and **Vanderhoek M**. SU-F-I-71: Fetal protection during fluoroscopy: To shield or not to shield? *Med Phys* 2016; 43(6):3403. PMID: 28047626. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: Lead aprons are routinely used to shield the fetus from radiation during fluoroscopically guided interventions (FGI) involving pregnant patients. When placed in the primary beam, lead aprons often reduce image quality and increase fluoroscopic radiation output, which can adversely affect fetal dose. The purpose of this work is to identify an effective and practical method to reduce fetal dose without affecting image quality. METHODS: A pregnant patient equivalent abdominal phantom is set on the table along with an image quality test object (CIRS model 903) representing patient anatomy of interest. An ion chamber is positioned at the x-ray beam entrance to the phantom, which is used to estimate the relative fetal dose. For three protective methods, image quality and fetal dose measurements are compared to baseline (no protection):1. Lead apron shielding the entire abdomen2. Lead apron shielding part of the abdomen, including the fetus 3. Narrow collimation such that fetus is excluded from the primary beam RESULTS: With lead shielding the entire abdomen, the dose is reduced by 80% relative to baseline along with a drastic deterioration of image quality. With lead shielding only the fetus, the dose is reduced by 65% along with complete preservation of image quality, since the image quality test object is not shielded. However, narrow collimation results in 90% dose reduction and a slight improvement of image quality relative to baseline. CONCLUSION: The use of narrow collimation to protect the fetus during FGI is a simple and highly effective method that simultaneously reduces fetal dose and maintains sufficient image quality. Lead aprons are not as effective at fetal dose reduction, and if placed improperly, they can severely degrade image quality. Future work aims to investigate a wider variety of fluoroscopy systems to confirm these results across many different system geometries.

Radiation Oncology

Kim G, Muir B, Culberson W, Davis S, **Huang Y**, Lee S, Lowenstein J, Sarfehnia A, Tolani N, and Siebers J. TU-D-201-03: Results of a survey on the implementation of the tg-51 protocol and associated addendum on reference dosimetry of external beams *Med Phys* 2016; 43(6):3743. PMID: 28047408. Abstract

University of California, San Diego, La Jolla, CA.
National Research Council, Ottawa, AB.
University of Wisconsin Madison, Madison, WI.
McGill University Health Center, Montreal, QC.
Henry Ford Health System, West Bloomfield, MI.
University of Maryland School of Medicine, Columbia, MD.
UT MD Anderson Cancer Center, Houston, TX.
Sunnybrook Health Science Center, Toronto, ON.
Michael E. DeBakey VA Medical Center, Sugarland, AA.
University of Virginia Health System, Charlottesville, VA.

PURPOSE: The working group on the review and extension of the TG-51 protocol (WGTG51) collected data from American Association of Physicists in Medicine (AAPM) members with respect to their current TG-51 and associated addendum usage in the interest of considering future protocol addenda and guidance on reference dosimetry best practices. This study reports an overview of this survey on dosimetry of external beams. METHODS: Fourteen survey questions were developed by WGTG51 and released in November 2015. The questions collected information on reference dosimetry, beam quality specification, and ancillary calibration equipment. RESULTS: Of the 190 submissions completed worldwide (U.S. 70%), 83% were AAPM members. Of the respondents, 33.5% implemented the TG-51 addendum, with the maximum calibration difference for any photon beam, with respect to the original TG-51 protocol, being <1% for 97.4% of responses. One major finding is that 81.8% of respondents used the same cylindrical ionization chamber for photon and electron dosimetry, implying that many clinics are foregoing the use of parallel-plate chambers. Other evidence suggests equivalent dosimetric results can be obtained with both cylindrical and parallel-plate chambers in electron beams. This, combined with users comfort with cylindrical chambers for electrons will likely impact recommendations put forward in an upcoming electron beam addendum to the TG-51 protocol. Data collected on ancillary equipment showed 58.2% (45.0%) of the thermometers (barometers) in use for beam calibration had NIST traceable calibration certificates, but 48.4% (42.7%) were never recalibrated. CONCLUSION: This survey provides a snapshot of TG-51 external beam reference dosimetry practice in radiotherapy centers. Findings demonstrate the rapid take-up of the TG-51 photon beam addendum and raise issues for the WGTG51 to focus on going forward, including guidelines on ancillary equipment and the choice of chamber for electron beam dosimetry.

Radiation Oncology

Kim J, **Myers E**, **Forbes M**, **Chetty I**, and **Glide-Hurst C**. SU-G-IeP2-07: Investigation of 3d-printed phantoms for synthetic ct benchmarking in an mr-only workflow *Med Phys* 2016; 43(6):3657. PMID: 28046242. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: As we move toward MR-only treatment planning, a need exists to develop multi-modality phantoms to benchmark synthetic CT (synCT) generation. We evaluated candidate materials for CT/MR compatible 3D printed phantoms to support MR-only planning. METHODS: Overall, 14 different 3D printing molding thermoplastic and UV photopolymer products were evaluated. Product samples (5.35 cm diameter disks) were obtained of urethane and silicone products of varying durometer: ClearFlex (50 and 95), Task 12, Smooth-Cast (45D, 60-61D), ReoFlex (20 through 60), VytaFlex 10, Flex Foam-iT! 17 urethane products as well as DragonSkin 10 and SORTA-Clear 18 silicone rubbers. Standard clinical sequences (T1-weighted FFE, T2-weighted TSE, and balanced turbo field echo) were acquired on a 1.0T open bore MR-simulator. An ultra-short echo-Dixon sequence (TE1= 0.144s) was obtained to identify bone materials for our synCT pipeline. Irregular objects and organs were segmented from CT images and 3D printed using ABS and UV photopolymers. CT images were acquired and compared to MR. RESULTS: ClearFlex, Task, Smooth-Cast, and Flex Foam-iT! products could not be visualized for any MR sequence. No urethane products were visible using T2-weighted images. VytaFlex 10 (CT range: -2 to 18HU) and Reoflex 20, 30, and 40 (CT range: -35 to -3HU) provided appreciable signal in both T1 and bTFE signals, while ReoFlex 50 and 60 (CT ranges: 8 to 35HU) provided distinguishable signal only in UTE images, thus rendering these materials as possible bone surrogate candidates. Silicone rubbers (DragonSkin 10 (CT range: 185 to 218HU) and SORTA-Clear 18 (CT range: 201 to 224HU)) were visible for all MR sequences used in our synCT pipeline. Irregular objects yielded appreciable signal in MR images with close congruence to CT. CONCLUSION: Several candidate materials, including bone surrogates, were identified for 3D printed phantoms. Future work includes characterizing MR relaxation properties

and performance at other field strengths. The submitting institution has research agreements with Philips Healthcare. Research sponsored by a Henry Ford Health System Internal Mentored Grant.

Radiation Oncology
Kumarasiri A, **Liu C**, **Brown S**, **Glide-Hurst C**, **Elshaikh M**, **Chetty I**, and **Movsas B**. WE-AB-207B-09: Margin reduction for planning target volume (ptv) in patients with localized prostate cancer: Impact on delivered dose and quality of life *Med Phys* 2016; 43(6):3806. PMID: 28047756. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To estimate the delivered (cumulative) dose to targets and organs at risk for localized prostate cancer patients treated with reduced PTV margins and to evaluate preliminary patient reported quality-of-life (QOL). METHODS: Under an IRB-approved protocol, 20 prostate cancer patients (including 11 control patients) were treated with reduced planning margins (5 mm uniform with 4 mm at prostate/rectum interface). Control patients had standard margin (10/6 mm)-based treatments. A parameter-optimized Elastix algorithm along with energy-mass mapping was used to deform and resample dose of the day onto the planning CT for each fraction to estimate the delivered dose over all fractions. QOL data were collected via Expanded Prostate cancer Index Composite (EPIC-26) questionnaires at time points pre-treatment, post-treatment, and at 2, 6, 12, 18 month follow-ups. Standardized QOL scores [range: 0-100] were determined and baseline-corrected by subtracting pre-treatment QOL data. Mean QOL differences between the margin reduced group and control group (QOLmr-QOLcontrol) were calculated for first 18 months. RESULTS: The difference between the cumulative mean dose (Dmean) and the planned mean dose (+/-SD) for PTV, prostate, bladder, and rectum were -2.2+/-1.0, 0.3+/-0.5, -0.7+/-2.6, and -2.1+/-1.3 Gy respectively for the margin-reduced group, and -0.8+/-2.0, 0.9+/-1.4, - 0.7+/-3.1 and -1.0+/-2.4 Gy for the control group. Difference between the two groups was statistically insignificant (p=0.1). Standardized and baseline corrected QOLmr-QOLcontrol for EPIC domains categorized as "Urinary Incontinence", "Urinary Irritative/Obstructive", "Bowel", "Sexual", and "Hormonal" were 0.6, 12.1, 9.1, 13.3, and -0.9 for the 18 months following radiation therapy (higher values better). Delivered dose to rectum showed a weak correlation to "Bowel" domain (Pearson's coefficient -0.24, $p<0.001$), while bladder dose did not correlate to Urinary Incontinence/Irritative/Obstructive QOL domains. CONCLUSION: The margin-reduced group exhibited clinically meaningful improvement of QOL without compromising the PTV dose. A larger number of patients and greater follow-up is needed to draw unequivocal conclusions. This work was supported in part by a research grant from Varian Medical Systems, Palo Alto, CA.

Radiation Oncology
Li H, **Zhong H**, **Qin Y**, **Snyder K**, **Chetty I**, and **Wen N**. SU-F-T-555: Accurate stereotactic cone tmrs converted from pdds scanned with ray trace *Med Phys* 2016; 43(6):3591. PMID: 28047603. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To investigate whether the accuracy of TMRs for stereotactic cones converted from PDDs scanned with Ray Trace can be improved, when compared against the TMRs converted from the traditional PDDs. METHODS: Ray Trace measurement in Sun Nuclear 3D Scanner is for accurate scan of small field PDDs. The system detects the center of field at two depths, for example, at 3 and 20 cm in our study, and then performs scan along the line passing the two centers. With both Ray Trace and the traditional method, PDDs for conical cones of 4, 5, 7.5, 10, 12.5, 15, and 17.5 mm diameter (jaws set to 5x5 cm) were obtained for 6X FFF and 10X FFF energies on a Varian Edge linac, using Edge detectors. The formalism of converting PDD to TMR given in Khan's book (4th Edition, p.161) was applied. Sp values at dmax were obtained by measuring cone Scp and Sc. Continuous direct measurement of TMR by filling/draining water to/from the tank and spot measurement by moving the tank and detector were also performed with the same equipment, using 100 cm SDD. RESULTS: For 6XFFF energy and all the cones, TMRs converted from Ray Trace were very close to the continuous and spot measurement, while TMRs converted from traditional PDDs had larger deviation. Along the central axis beyond dmax, 1.7% of TMR data points calculated from Ray Trace had more 3% deviation from measurement, with maximal deviation of 5.2%. Whereas, 34% of TMR points calculated from traditional PDDs had more than 3% deviation, with maximum of 5.7%. In this initial study, Ray Trace scans for 10XFFF beam were noisy, further measurement is warranted. CONCLUSION: The Ray Trace could improve the accuracy of PDDs measurement and the calculated TMRs for stereotactic cones, which was within 3% of the measured TMRs.

Radiation Oncology

Liu C, **Chetty I**, **Mao W**, **Kumarasiri A**, **Zhong H**, **Brown S**, and **Siddiqui F**. SU-F-J-68: Deformable dose accumulation for voxel-based dose tracking of ptv cold spots for adaptive radiotherapy of the head and neck *Med Phys* 2016; 43(6):3421-3422. PMID: 28047440. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To utilize deformable dose accumulation (DDA) to determine how cold spots within the PTV change over the course of fractionated head and neck (H&N) radiotherapy. METHODS: Voxel-based dose was tracked using a DDA platform. The DDA process consisted of B-spline-based deformable image registration (DIR) and dose accumulation between planning CT's and daily cone-beam CT's for 10 H&N cancer patients. Cold spots within the PTV (regions receiving less than the prescription, 70 Gy) were contoured on the cumulative dose distribution. These cold spots were mapped to each fraction, starting from the first fraction to determine how they changed. Spatial correlation between cold spot regions over each fraction, relative to the last fraction, was computed using the Jaccard index Jk (Mk,N), where N is the cold spot within the PTV at the end of the treatment, and Mk the same region for fraction k. RESULTS: Figure 1 shows good spatial correlation between cold spots, and highlights expansion of the cold spot region over the course of treatment, as a result of setup uncertainties, and anatomical changes. Figure 2 shows a plot of Jk versus fraction number k averaged over 10 patients. This confirms the good spatial correlation between cold spots over the course of treatment. On average, Jk reaches approximately 90% at fraction 22, suggesting that possible intervention (e.g. reoptimization) may mitigate the cold spot region. The cold spot, D99, averaged over 10 patients corresponded to a dose of approximately 65 Gy, relative to the prescription dose of 70 Gy. CONCLUSION: DDA-based tracking provides spatial dose information, which can be used to monitor dose in different regions of the treatment plan, thereby enabling appropriate mid-treatment interventions. This work is supported in part by Varian Medical Systems, Palo Alto, CA.

Radiation Oncology

Liu M, **Wen N**, **Beyer C**, **Siddiqui F**, **Chetty I**, and **Zhao B**. SU-F-T-506: Development and commissioning of the effective and efficient grid therapy using high dose rate flattening filter free beam and multileaf collimator *Med Phys* 2016; 43(6):3579-3580. PMID: 28048441. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: Treating bulky tumors with grid therapy (GT) has demonstrated high response rates. Long delivery time (approximately 15min), with consequent increased risk of intrafraction motion, is a major disadvantage of conventional MLC-based GT (MLC-GT). The goal of this study was to develop and commission a MLC-GT technique with similar dosimetric characteristics, but more efficient delivery. METHODS: Grid plan was designed with 10X-FFF (2400MU/min) beam and MLC in a commercial treatment planning system (TPS). Grid size was 1cm by 1cm and grid-to-grid distance was 2cm. Field-in-field technique was used to flatten the dose profile at depth of 10cm. Prescription was 15Gy at 1.5cm depth. Doses were verified at depths of 1.5cm, 5cm and 10cm. Point dose was measured with a plastic scintillator detector (PSD) while the planar dose was measured with calibrated Gafchromic EBT3 films in a 20cm think, 30cmx30cm solid water phantom. The measured doses were compared to the doses calculated in the treatment planning system. Percent depth dose (PDD) within the grid was also measured using EBT3 film. Five clinical cases were planned to compare beam-on time. RESULTS: The valley-to-peak dose ratio at the 3 depths was approximately 10-15%, which is very similar to published result. The average point dose difference between the PSD measurements and TPS calculation is 2.1+/-0.6%. Film dosimetry revealed good agreement between the delivered and calculated dose. The average gamma passing rates at the 3 depths were 95% (3%, 1mm). The average percent difference between the measured PDD and calculated PDD was 2.1% within the depth of 20cm. The phantom plan delivery time was 3.6 min. Average beam-on time was reduced by 66.1+/-5.6% for the 5 clinical cases. CONCLUSION: An effective and efficient GT technique was developed and commissioned for the treatment of bulky tumors using FFF beam combined with MLC and automation. The Department of Radiation Oncology at Henry Ford Health System receives research support from Varian Medical Systems and Philips Health Care.

Radiation Oncology

Mahmoudi F, **Poisson L**, **Bagher-Ebadian H**, **Nazem-Zadeh M**, and **Soltanian-Zadeh H**. SU-F-R-02: Imaging-genomics for predicting gbm molecular subclasses and survival *Med Phys* 2016; 43(6):3373. PMID: 28047590. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: Glioblastoma (GBM) is the most common and fatal primary intracranial neoplasm. GBM is categorized into five sub-classes (classical, G-CIMP, mesenchymal, proneural and neural) that can only be determined by an invasive brain biopsy followed by RNA and DNA methylation profiling. The goal of this study is to develop imaging features extracted from conventional MRI scans and an ensemble-classification method as a potential noninvasive method to predict the five molecular sub-classes and 12-month survival status. METHODS: Tumors are segmented into 4 cardinal sub-volumes that are enhancing, non-enhancing, necrosis, and edema by BraTuma software and post-manual modification. After intensity normalization, mean, standard deviation, skewness, and kurtosis of voxel intensities and normalized volume of each of the 4 sub-volumes are calculated. The first four features are extracted from three different modalities (T1 pre & post contrast and T2 FLAIR) and the tumor texture is quantified. A feature selection phase (wrapper algorithm) is preceded the classification stage. Ensembles of binary classifiers with one versus rest strategy, along with a separate binary classifier are employed respectively for molecular classification and survival status. Two different binary classifiers are tested (SVM and K* IBL) and their confidences are used for tie-breaking technique. RESULTS: With the select combination of features of the MRI modalities, the ROC area and accuracy of the prediction are 0.750 and 95% for classical, 1.000 and 100% for G-CIMP, 0.719 and 85% for mesenchymal, 0.875 and 95% for neural, 0.922 and 95% for proneural, and 0.990 and 95% for survival status respectively. CONCLUSION: The study proposes a set of three-dimensional and rotation invariant imaging features that represent texture and volumetric characteristics of GBM tumors. The results show the select features are predictive for five molecular sub-classes and survival status in GBM. These results indicate the feasibility of obviating the biopsy for obtaining genomic information of tumor.

Radiation Oncology

Mao W, **Liu C**, **Zhong H**, Rozario T, Lu W, Gu X, Yan Y, Jia X, Sumer B, and Schwartz D. SU-C-202-05: Pilot study of online treatment evaluation and adaptive re-planning for laryngeal sbrt *Med Phys* 2016; 43(6):3323-3324. PMID: 28047110. Abstract

The University of Texas Southwestern Medical Ctr, Dallas, TX.
Henry Ford Health System, Detroit, MI.

PURPOSE: We have instigated a phase I trial of 5-fraction stereotactic body radiotherapy (SBRT) for advanced-stage laryngeal cancer. We conducted this pilot dosimetric study to confirm the potential utility of online adaptive re-planning to preserve treatment quality. METHODS: Ten cases of larynx cancer were evaluated. Baseline and daily SBRT treatment plans were generated per trial protocol. Daily volumetric images were acquired prior to every fraction of treatment. Reference simulation CT images were deformably registered to daily volumetric images using Eclipse. Planning contours were then deformably propagated to daily images. Reference SBRT plans were directly copied to calculate delivered dose distributions on deformed reference CT images. In-house software platform has been developed to calculate cumulative dose over a course of treatment in four steps: 1) deforming delivered dose grid to reference CT images using deformation information exported from Eclipse; 2) generating tetrahedrons using deformed dose grid as vertices; 3) resampling dose to a high resolution within every tetrahedron; 4) calculating dose-volume histograms. Our inhouse software was benchmarked with a commercial software, Mirada. RESULTS: In all ten cases including 49 fractions of treatments, delivered daily doses were completely evaluated and treatment could be re-planned within 10 minutes. Prescription dose coverage of PTV was less than intended in 53% of fractions of treatment (mean: 94%, range: 84%-98%) while minimum coverage of CTV and GTV was 94% and 97%, respectively. Maximum bystander point dose limits to arytenoids, parotids, and spinal cord remained respected in all cases, although variances in carotid artery doses were observed in a minority of cases. CONCLUSION: Although GTV and CTV coverage is preserved by in-room 3D image guidance of larynx SBRT, PTV coverage can vary significantly from intended plans. Online adaptive treatment evaluation and re-planning is potentially necessary and our procedure is clinically applicable to fully preserve treatment quality. This project is supported by CPRIT Individual Investigator Research Award RP150386.

Radiation Oncology

Mao W, and Wang G. TU-H-BRA-05: A system design for integration of an interior mri and a linear accelerator *Med Phys* 2016; 43(6):3769. PMID: 28047265. Abstract

UT Southwestern Medical Center, Dallas, TX.
Henry Ford Hospital, Detroit, MI.
Rensselaer Polytechnic Instit., Troy, NY.

PURPOSE: MRI is a highly desirable modality to guide radiation therapy but it is difficult to combine a conventional MRI scanner directly with a linear accelerator (linac). An interior MRI (iMRI) concept has been proposed to acquire MRI images within a small field of view only covering targets and immediate surrounding tissues. The objective of this

project is to design an interior MRI system to work with a linac using a magnet to provide a field around 0.2T in a cube of 20cm per side, and perform image reconstruction with a slightly inhomogeneous static magnetic fields. METHODS: All the results are simulated using a commercially available software package, FARADY. In our design, a ring structure holds the iMRI system and also imbeds a linac treatment head. The ring is synchronized to the linac gantry rotation. Half of the ring is made of steel and becomes a magnetic flux return path (yoke) so that a strong magnetic field will be limited inside the iron circuit and fringe fields will be very weak. In order to increase the static magnetic field homogeneity, special steel magnet boots or tips were simulated. Three curved boots were designed based on two-dimensional curves: arc, parabola and hyperbola. RESULTS: Different boot surfaces modify magnetic field distributions differently. With the same pair of neodymium-iron-boron (NdFeB) magnets, the magnetic induction at the centers are 0.217T, 0.201T, 0.204T, and 0.212T for flat, arc, parabola and hyperbola boots, respectively. The hyperbola boots lead to the most homogeneous results, the static magnetic field deviations are within 0.5% in a cube of 20cm, and can be further improved using shimming techniques. CONCLUSION: This study supports the concept of an iMRI design. Successful development of iMRI will provide crucial information for tumor delineation in radiation therapy.

Radiation Oncology

Mayyas E, **Vance S**, **Brown S**, **Liu J**, **Kim J**, **Zhen S**, **Devpura S**, **Ajlouni M**, **Salim S**, **Chetty I**, and **Movsas B**. WE-AB-207B-12: Prospective study of the relationship between dose-volume clinical toxicity and patient reported outcomes in lung cancer patients treated with SBRT *Med Phys* 2016; 43(6):3806-3807. PMID: 28048506. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To determine in a prospective study, the correlation between radiation dose/volume, clinical toxicities and patient-reported, quality of life (QOL) resulting from lung SBRT. METHODS: For 106 non-small cell lung cancer (NSCLC) patients receiving SBRT (12 Gy x 4), symptoms including cough, dyspnea, fatigue and pneumonitis were measured at baseline (before treatment), after treatment and 3, 6, and 12 months post-treatment. Toxicity was graded from zero to five. Dosimetric parameters such as the MLD, D10%, D20%, and lung subvolumes (V10 and V20) were obtained from the treatment plan. Dosimetric parameters and number of patients demonstrating toxicity >/= grade 2 were tabulated. Linear regression analysis was used to calculate correlations between MLD and D10, D20, V10 and V20. RESULTS: The percentages of patients with > grade 2 pneumonitis, fatigue, cough, and dyspnea over 3 to 12 months increased from 0.0% to 3.5%, 3.2% to 10.5%, 4.3% to 8.3%, and 10.8% to 18.8%, respectively. Computed dose indices D10%, D20% were 7.9+/-4.8 Gy and 3.0+/-2.3 Gy, respectively. MLD ranged from 0.34 Gy up to 9.9 Gy with overall average 3.0+/-1.7 Gy. The averages of the subvolumes V10 and V20 were respectively 8.9+/-5.3% and 3.0+/-2.4%. The linear regression analysis showed that V10 and D10 demonstrated the strongest correlation to MLD; R2= 0.92 and 0.87, respectively. V20, and D20 were also strongly correlated with MLD; R2 = 0.81 and 0.84 respectively. A correlation was also found to exist between MLD > 2 Gy and >/= grade 2 cough and dyspnea. Subvolume values for 2Gy MLD were 5.3% for V10 and 2% for V20. CONCLUSION: Dosimetric indices: MLD >/= 2Gy, D10 >/= 5Gy and V10 >/= 5% of the total lung volume were predictive of > grade 2 cough and dyspnea QOL data. The QOL results are a novel component of this work. acknowledgement of the Varian grant support.

Radiation Oncology

McLaughlin PW, Liss AL, Nguyen PL, Assimos DG, D'Amico AV, Gottschalk AR, Gustafson GS, Keole SR, Liauw SL, Lloyd S, **Movsas B**, Prestidge BR, Showalter TN, Taira AV, Vapiwala N, and Davis BJ. ACR appropriateness criteria(r) locally advanced, high-risk prostate cancer *Am J Clin Oncol* 2017; 40(1):1-10. PMID: 28059930. Full Text

*University of Michigan, Novi parallelWilliam Beaumont Hospital, Troy daggerdaggerHenry Ford Health System, Detroit, MI daggerDana-Farber Cancer Institute/Brigham and Women's Hospital, American Society of Clinical Oncology, Boston, MA double daggerUniversity of Alabama School of Medicine, Birmingham, AL, American Urological Association section signUniversity of California San Francisco, San Francisco parallel parallelMills Peninsula Hospital, San Mateo, CA paragraph signMayo Clinic, Scottsdale, AZ #The University of Chicago Medical Center, Chicago, IL **Huntsman Cancer Hospital, Salt Lake City, UT double daggerdouble daggerBon Secours Cancer Institute, Norfolk section sign section signUniversity of Virginia, Charlottesville, VA paragraph sign paragraph signUniversity of Pennsylvania, Philadelphia, PA ##Mayo Clinic, Rochester, MN.

PURPOSE: To present the most updated American College of Radiology consensus guidelines formed from an expert panel on treatment of locally advanced, high-risk prostate cancer METHODS:: The American College of Radiology Appropriateness Criteria are evidence-based guidelines for specific clinical conditions that are reviewed annually by a multidisciplinary expert panel. The guideline development and revision include an extensive analysis of current medical literature from peer-reviewed journals and the application of well-established methodologies (RAND/UCLA Appropriateness Method and Grading of Recommendations Assessment, Development, and

Evaluation or GRADE) to rate the appropriateness of imaging and treatment procedures for specific clinical scenarios. In those instances where evidence is lacking or equivocal, expert opinion may supplement the available evidence to recommend imaging or treatment. RESULTS: The panel summarized the most recent and relevant literature on the topic and voted on 4 clinical variants illustrating the appropriate management of locally advanced, high-risk cancer. Numerical rating and commentary reflecting the panel consensus was given for each treatment approach in each variant. CONCLUSIONS: Aggressive local approaches including surgery followed by adjuvant XRT, beam combined with androgen deprivation therapy, and beam combined with brachytherapy have resulted in unpresented success in locally advanced, high-risk prostate cancer. By combining most recent medical literature and expert opinion, this guideline can aid clinicians in the appropriate integration of available therapeutic modalities.

Radiation Oncology
Morris ED, Klahr P, and **Glide-Hurst C**. MO-DE-207A-12: Toward patient-specific 4dct reconstruction using adaptive velocity binning *Med Phys* 2016; 43(6):3703. PMID: 28047399. Abstract

Henry Ford Health System, Detroit, MI.
Wayne State University, Detroit, MI.
Philips Healthcare, Cleveland, Ohio.

PURPOSE: While 4DCT provides organ/tumor motion information, it often samples data over 10-20 breathing cycles. For patients presenting with compromised pulmonary function, breathing patterns can change over the acquisition time, potentially leading to tumor delineation discrepancies. This work introduces a novel adaptive velocity-modulated binning (AVB) 4DCT algorithm that modulates the reconstruction based on the respiratory waveform, yielding a patient-specific 4DCT solution. METHODS: AVB was implemented in a research reconstruction configuration. After filtering the respiratory waveform, the algorithm examines neighboring data to a phase reconstruction point and the temporal gate is widened until the difference between the reconstruction point and waveform exceeds a threshold value-defined as percent difference between maximum/minimum waveform amplitude. The algorithm only impacts reconstruction if the gate width exceeds a set minimum temporal width required for accurate reconstruction. A sensitivity experiment of threshold values (0.5, 1, 5, 10, and 12%) was conducted to examine the interplay between threshold, signal to noise ratio (SNR), and image sharpness for phantom and several patient 4DCT cases using ten-phase reconstructions. Individual phase reconstructions were examined. Subtraction images and regions of interest were compared to quantify changes in SNR. RESULTS: AVB increased signal in reconstructed 4DCT slices for respiratory waveforms that met the prescribed criteria. For the end-exhale phases, where the respiratory velocity is low, patient data revealed a threshold of 0.5% demonstrated increased SNR in the AVB reconstructions. For intermediate breathing phases, threshold values were required to be >10% to notice appreciable changes in CT intensity with AVB. AVB reconstructions exhibited appreciably higher SNR and reduced noise in regions of interest that were photon deprived such as the liver. CONCLUSION: We demonstrated that patient-specific velocity-based 4DCT reconstruction is feasible. Image noise was reduced with AVB, suggesting potential applications for low-dose acquisitions and to improve 4DCT reconstruction for irregular breathing patients. The submitting institution holds research agreements with Philips Healthcare.

Radiation Oncology
Morris ED, Klahr P, and **Glide-Hurst C**. MO-DE-207A-03: Characterization of potential gains in a novel exponential 4dct reconstruction algorithm *Med Phys* 2016; 43(6):3700. PMID: 28046714. Abstract

Henry Ford Health System, Detroit, MI.
Wayne State University, Detroit, MI.
Philips Healthcare, Cleveland, OH.

PURPOSE: To sample the breathing cycle and obtain accurate target volumes, 4DCT requires the entire field of view (FOV) to be illuminated during one breathing period. However, interplay effects between internal motion and couch pitch may adversely impact the temporal resolution, thereby blurring object edges. This work performs a characterization of exponential 4DCT reconstruction to highlight potential gains over standard cos2 weighted reconstruction algorithm. METHODS: A respiratory motion platform translated several objects in the superior-inferior direction at varied breathing rates (8-20 breaths/minute) and couch pitches (0.06-0.1 A.U.) to evaluate the interplay between parameters. Ten-phase 4DCTs were acquired (0.5s rotation) and data were reconstructed with cos2 and exponential weighting factors. To isolate a metric to quantify temporal resolution (i.e. remove couch interplay effects), a small object was translated in the anterior-posterior direction. Full-width half maximum (FWHM) intensity distributions were quantified between reconstruction algorithms and a static case. 4DCT sinogram data for fifteen lung and abdomen patients were retrospectively reconstructed using cos2 and exponential weighting factors. Image subtractions were generated to elucidate intensity and boundary differences. RESULTS: After taking the static object

size into account, the FWHM of exponential weighting was 1.5+/-1.2 mm (range: 0.1-4.1) as compared to the FWHM of cos2 3.4+/-2.4 mm (range: 0.3-8.0). This translated to estimated improvements in temporal resolution of 33.5+/-48.2 ms (range: 0.03-170.9). Slower breathing periods, faster couch pitches, and intermediate 4DCT phases where velocity is highest showed a tendency to have the largest improvements in temporal resolution with exponential reconstruction. For patient cases, coronal views showed less blurring at object boundaries and local intensity differences near moving features. CONCLUSION: Exponential weighted 4DCT offers potential for improving temporal resolution in 4DCT, thus improving the image sharpness near the boundaries. Understanding the potential implications on delineation ability is an important next step of this work. The submitting institution holds research agreements with Philips Healthcare.

Radiation Oncology
Price RG, **Kim J**, **Zheng W**, **Chetty IJ**, and **Glide-Hurst C**. SU-G-JeP2-08: Image-guided radiation therapy using synthetic cts in brain cancer *Med Phys* 2016; 43(6):3661. PMID: 28048467. Abstract

Wayne State School of Medicine, Detroit, MI.
Henry Ford Health System, Detroit, MI.

PURPOSE: Synthetic-CTs(synCTs) are essential for MR-only treatment planning. However, the performance of synCT for IGRT must be carefully assessed. This work evaluated the accuracy of synCT and synCT-generated DRRs and determined their performance for IGRT in brain cancer radiation therapy. METHODS: MR-SIM and CT-SIM images were acquired of a novel anthropomorphic phantom and a cohort of 12 patients. SynCTs were generated by combining an ultra-short echo time (UTE) sequence with other MRI datasets using voxel-based weighted summation. For the phantom, DRRs from synCT and CT were compared via bounding box and landmark analysis. Planar (MV/KV) and volumetric (CBCT) IGRT performance were evaluated across several platforms. In patients, retrospective analysis was conducted to register CBCTs (n=34) to synCTs and CTs using automated rigid registration in the treatment planning system using whole brain and local registration techniques. A semi-automatic registration program was developed and validated to rigidly register planar MV/KV images (n=37) to synCT and CT DRRs. Registration reproducibility was assessed and margin differences were characterized using the van Herk formalism. RESULTS: Bounding box and landmark analysis of phantom synCT DRRs were within 1mm of CT DRRs. Absolute 2D/2D registration shift differences ranged from 0.0-0.7mm for phantom DRRs on all treatment platforms and 0.0-0.4mm for volumetric registrations. For patient planar registrations, mean shift differences were 0.4+/-0.5mm (range: -0.6-1.6mm), 0.0+/-0.5mm, (range: -0.9-1.2mm), and 0.1+/-0.3mm (range: -0.7-0.6mm) for the superior-inferior(S-I), left-right(L-R), and anterior-posterior(A-P) axes, respectively. Mean shift differences in volumetric registrations were 0.6+/-0.4mm (range: -0.2-1.6mm), 0.2+/-0.4mm (range: -0.3-1.2mm), and 0.2+/-0.3mm (range: -0.2-1.2mm) for S-I, L-R, and A-P axes, respectively. CT-SIM and synCT derived margins were within 0.3mm. CONCLUSION: DRRs generated via synCT agreed well with CT-SIM. Planar and volumetric registrations to synCT-derived targets were comparable to CT. This validation is the next step toward clinical implementation of MR-only planning for the brain. The submitting institution has research agreements with Philips Healthcare. Research sponsored by a Henry Ford Health System Internal Mentored Grant.

Radiation Oncology
Price RG, **Knight RA**, Hwang K, Bayram E, and **Glide-Hurst C**. TU-AB-BRA-05: Optimization of a novel large field of view distortion phantom for mr-only treatment planning *Med Phys* 2016; 43(6):3734. PMID: 28046653. Abstract

Wayne State School of Medicine, Detroit, MI.
Henry Ford Health System, Detroit, MI.
University of Texas MD Anderson Cancer Center, Houston, TX.
GE Healthcare, Houston, TX.

PURPOSE: MR-only treatment planning requires images of high geometric fidelity, particularly for large fields of view (FOV). However, the availability of large FOV distortion phantoms with accompanying analysis software is currently limited to in-house solutions. This work sought to optimize the design of a modular distortion phantom that can accommodate several bore configurations and implement distortion corrections. METHODS: 1.0T MR and CT images were acquired of twelve urethane foam samples of various densities and strengths. Samples were precision machined to accommodate 6 mm diameter paintballs used as landmarks and signal-to-noise ratio was calculated. Final material candidates were selected by balancing strength, machinability, weight, and cost. Bore sizes and minimum aperture width resulting from couch position were tabulated from the literature for 13 systems across 4 vendors. Bore geometry and couch position were simulated in MATLAB to generate machine-specific models to optimize the phantom build. Previously developed software for distortion characterization (control point detection, polynomial fitting, and correction map generation) was modified for several magnet geometries and integrated into

Slicer, a widely available image analysis toolkit. RESULTS: All foam samples provided sufficient image contrast with paintball landmarks. Urethane foam with a compressive strength of approximately 1000psi and density of 20lb/ft3 was chosen for its accurate machinability and relatively light weight. A modular phantom design was optimized to accommodate all magnet geometries with the following parameters: 15 foam plates, 55x55x37.5cm, 5,082 landmarks, and 66 lbs. To accommodate wide bore magnets (>70 cm), an extended build spanned 55x55x50cm over 20 plates with 7,497 landmarks and weighing 97lbs. Distortion characterization software was implemented as an external module into Slicer's plugin framework. CONCLUSION: We optimized the design and implementation of a modular, extendable distortion phantom to support an MR-only workflow and MR-IGRT. The phantom will be useful for future multi-institution collaborations and cross-validation studies. The submitting institution has research agreements with Philips Healthcare. Research sponsored by a Henry Ford Health System Internal Mentored Grant. Technical support and initial distortion phantom design was provided by GE Healthcare.

Radiation Oncology

Qin Y, and **Chetty I**. SU-F-T-543: The impact of density overrides in imrt and vmat planning for lung cancer patients treated sbrt *Med Phys* 2016; 43(6):3588. PMID: 28046460. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To evaluate the dosimetric impact of target volume overrides on the quality of IMRT and VMAT lung, SBRT treatment plans. METHODS: Ninety one patients previously treated with lung SBRT at our institution were retrospectively studied. IMRT and VMAT plans were created on 5 image sets for each patient: free breathing scans(FB), average scans(AVE), average scan with internal target volume overridden to tumor density(ITVoverride), average scan with planning target volume overridden(PTVoverride), and a hybrid method where the internal target volume was set to tumor density and the set-up margin was set to an intermediate density between lung and tumor(HBoverride). All plans were optimized with the same constraints as the original clinical plan AVE. Dose fractionation scheme included 12Gyx4, 10Gyx4, 8Gyx4, 12Gyx3, and 9Gyx5. EQD2 was computed for various target metrics (mean, D1%, D99%) and normal lung metrics (V5Gy, V20Gy, mean lung dose). Plan quality was investigated via conformity index (CI) and gradient index (GI). RESULTS: The ITVoverride plans achieved the highest mean target EQD2(0.38+/-0.69Gy over AVE) and the highest D1% hotspot(0.73+/-1.17Gy over AVE) in comparison to all other plans. PTVoverride and HBoverride also demonstrated higher mean target EQD2 than AVE, but lower hotspots. Compared to AVE, PTVoverride and HBoverride resulted in lower coldspots of -9.95+/-3.78Gy and -9.91+/-3.68Gy respectively. All override plans achieved lower lung metrics than the AVE plans, with the largest reductions in PTVoverride (-0.31+/-0.30Gy for V20Gy, -0.44+/-0.44Gy for V5Gy, -0.23+/-0.18Gy for mean lung dose). Comparing FB (largest CI,GI) to PTVoverride (smallest CI,GI), CI and GI improved from 1.05 to 1.00, and 4.81 to 4.48 respectively. The differences in these metrics did not correlate with tumor motion or target volume. CONCLUSION: Despite the improvements in CI and GI, density overrides in target volumes for 91 lung SBRT patients showed limited dosimetric advantages over clinical plans on the average CT.

Radiation Oncology

Qin Y, **Gardner S**, **Huang Y**, **Kim J**, **Wen N**, and **Chetty I**. SU-G-TeP2-08: Evaluation of plastic scintillator detector for small field stereotactic patient-specific quality assurance *Med Phys* 2016; 43(6):3664. PMID: 28047648. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To evaluate the performance of a commercial plastic scintillator detector (PSD) for small-field stereotactic patient-specific quality assurance using flattening-filter-free (FFF) beams. METHODS: A total of ten spherical targets (volume range:[0.03cc-2cc]) were planned using Dynamic Conformal Arc(DCA-10 plans) and Volumetric Modulated Arc Therapy(VMAT-10 plans) techniques in Eclipse(AAA v.11, 1mm dose calculation grid size). Additionally, 15 previously-treated cranial and spine SRS plans were evaluated (6 DCA, 9 VMAT, volume range:[0.04cc-119.02cc]). All measurements were acquired using Varian Edge equipped with HDMLC. Three detectors were used: PinPoint ion chamber (PTW;active volume 0.015cc), Exradin W1 PSD (Standard Imaging;active volume 0.002cc), and Gafchromic EBT3 film (Ashland). PinPoint and PSD were positioned perpendicular to beam axis in a Lucy phantom (Standard Imaging). Films were placed at isocenter in solid water. Calibration films were delivered for absolute dose analysis. RESULTS: For large spherical targets(>1.5cc) with DCA, all detectors agreed within 1% of AAA calculations. As target volume decreased, PSD measured higher doses than AAA (maximum difference: 3.3% at 0.03cc target), while PinPoint chamber measured lower doses (maximum difference:-3.8% at 0.03cc target). Inter-detector differences between pinpoint and PSD increased with decreasing target size; differences>5% were observed for targets<0.09cc. Similar trends for inter-detector behavior were observed for clinical plans. For target sizes<0.08cc, PSD measured>5% higher dose than PinPoint chamber (maximum difference: 9.25% at 0.04cc target). Film demonstrated agreement of -0.19+/-1.47% with PSD for all spherical targets, and agreement within -0.98+/-2.25% for all 15 clinical

targets. Unlike DCA, VMAT plans did not show improved AAA-to-detector agreements for large targets. CONCLUSION: For all targets, the PSD measurements agreed with film within 1.0%, on average. For small volume targets (<0.10cc), PSD agreed with film but measured significantly higher doses (>5%) compared with the pin point ion chamber. The plastic scintillator detector appears to be suitable for accurate measurements of small SRS targets.

Radiation Oncology
Rozario T, Chiu T, Lu W, Chen M, Yan Y, Bereg S, and **Mao W**. TH-AB-202-01: Daily lung tumor motion characterization on epids using a markerless tiling model *Med Phys* 2016; 43(6):3856. PMID: 28047157. Abstract

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PURPOSE: Tracking lung tumor motion in real time allows for target dose escalation while simultaneously reducing dose to sensitive structures, thus increasing local control without increasing toxicity. We present a novel intra-fractional markerless lung tumor tracking algorithm using MV treatment beam images acquired during treatment delivery. Strong signals superimposed on the tumor significantly reduced the soft tissue resolution; while different imaging modalities involved introduce global imaging discrepancies. This reduced the comparison accuracies. A simple yet elegant Tiling algorithm is reported to overcome the aforementioned issues. METHODS: MV treatment beam images were acquired continuously in beam's eye view (BEV) by an electronic portal imaging device (EPID) during treatment and analyzed to obtain tumor positions on every frame. Every frame of the MV image was simulated by a composite of two components with separate digitally reconstructed radiographs (DRRs): all non-moving structures and the tumor. This Titling algorithm divides the global composite DRR and the corresponding MV projection into sub-images called tiles. Rigid registration is performed independently on tile-pairs in order to improve local soft tissue resolution. This enables the composite DRR to be transformed accurately to match the MV projection and attain a high correlation value through a pixel-based linear transformation. The highest cumulative correlation for all tile-pairs achieved over a user-defined search range indicates the 2-D coordinates of the tumor location on the MV projection. RESULTS: This algorithm was successfully applied to cine-mode BEV images acquired during two SBRT plans delivered five times with different motion patterns to each of two phantoms. Approximately 15000 beam's eye view images were analyzed and tumor locations were successfully identified on every projection with a maximum/average error of 1.8 mm / 1.0 mm. CONCLUSION: Despite the presence of strong anatomical signal overlapping with tumor images, this markerless detection algorithm accurately tracks intrafractional lung tumor motions. This project is partially supported by an Elekta research grant.

Radiation Oncology
Santoso A, **Song K**, **Qin Y**, **Gardner S**, **Liu C**, **Cattaneo R**, **Chetty I**, **Movsas B**, **Aljouni M**, and **Wen N**. SU-F-J-38: Dose rates and preliminary evaluation of contouring similarity metrics using 4d cone beam ct *Med Phys* 2016; 43(6):3414. PMID: 28048111. Abstract

Wayne State University School of Medicine, Detroit, Michigan.
Henry Ford Health System, Detroit, MI.

PURPOSE: 4D imaging modalities require detailed characterization for clinical optimization. The On-Board Imager mounted on the linear accelerator was used to investigate dose rates in a tissue mimicking phantom using 4D-CBCT and assess variability of contouring similarity metrics between 4D-CT and 4D-CBCT retrospective reconstructions. METHODS: A 125 kVp thoracic protocol was used. A phantom placed on a motion platform simulated a patient's breathing cycle. An ion chamber was affixed inside the phantom's tissue mimicking cavities (i.e. bone, lung, and soft tissue). A sinusoidal motion waveform was executed with a five second period and superior-inferior motion. Dose rates were measured at six ion chamber positions. A preliminary workflow for contouring similarity between 4D-CT and 4D-CBCT was established using a single lung SBRT patient's historical data. Average intensity projection (Ave-IP) and maximum intensity projection (MIP) reconstructions generated offline were compared between the 4D modalities. Similarity metrics included Dice similarity coefficient (DSC), Hausdorff distance, and center of mass (COM) deviation. Two isolated lesions were evaluated in the patient's scans: one located in the right lower lobe (ITVRLL) and one located in the left lower lobe (ITVLLL). RESULTS: Dose rates ranged from 2.30 (lung) to 5.18 (bone) E-3 cGy/mAs. For fixed acquisition parameters, cumulative dose is inversely proportional to gantry speed. For ITVRLL, DSC were 0.70 and 0.68, Hausdorff distances were 6.11 and 5.69 mm, and COM deviations were 1.24 and 4.77 mm, for Ave-IP and MIP respectively. For ITVLLL, DSC were 0.64 and 0.75, Hausdorff distances were 10.74 and 8.00 mm, and COM deviations were 7.55 and 4.3 mm, for Ave-IP and MIP respectively. CONCLUSION: While the dosimetric output of 4D-CBCT is low, characterization is necessary to assure clinical optimization. A basic

workflow for comparison of simulation and treatment 4D image-based contours was established. This work was partially supported by a Research Scholar Grant (RSG-15-137-01-CCE) from the American Cancer Society.

Radiation Oncology

Sharifi H, Zhang H, Jin JY, Kong FM, **Chetty IJ**, and **Zhong H**. TU-AB-202-07: A novel method for registration of mid-treatment pet/ct images under conditions of tumor regression for patients with locally advanced lung cancers *Med Phys* 2016; 43(6):3738. PMID: 28047401. Abstract

Department of Radiation Oncology, Henry Ford Health System, Detroit, MI.
Department of Physics, Oakland University, Rochester, MI.
Department of Radiation Oncology, GRU Cancer Center, Augusta GA.

PURPOSE: In PET-guided adaptive radiotherapy (RT), changes in the metabolic activity at individual voxels cannot be derived until the duringtreatment CT images are appropriately registered to pre-treatment CT images. However, deformable image registration (DIR) usually does not preserve tumor volume. This may induce errors when comparing to the target. The aim of this study was to develop a DIR-integrated mechanical modeling technique to track radiation-induced metabolic changes on PET images. METHODS: Three patients with non-small cell lung cancer (NSCLC) were treated with adaptive radiotherapy under RTOG 1106. Two PET/CT image sets were acquired 2 weeks before RT and 18 fractions after the start of treatment. DIR was performed to register the during-RT CT to the pre-RT CT using a B-spline algorithm and the resultant displacements in the region of tumor were remodeled using a hybrid finite element method (FEM). Gross tumor volume (GTV) was delineated on the during-RT PET/CT image sets and deformed using the 3D deformation vector fields generated by the CT-based registrations. Metabolic tumor volume (MTV) was calculated using the pre- and during-RT image set. The quality of the PET mapping was evaluated based on the constancy of the mapped MTV and landmark comparison. RESULTS: The B-spline-based registrations changed MTVs by 7.3%, 4.6% and -5.9% for the 3 patients and the correspondent changes for the hybrid FEM method -2.9%, 1% and 6.3%, respectively. Landmark comparisons were used to evaluate the Rigid, B-Spline, and hybrid FEM registrations with the mean errors of 10.1 +/- 1.6 mm, 4.4 +/- 0.4 mm, and 3.6 +/- 0.4 mm for three patients. The hybrid FEM method outperforms the B-Spline-only registration for patients with tumor regression CONCLUSION: The hybrid FEM modeling technique improves the B-Spline registrations in tumor regions. This technique may help compare metabolic activities between two PET/CT images with regressing tumors. The author gratefully acknowledges the financial support from the National Institutes of Health Grant.

Radiation Oncology

Wen N, **Lu S**, **Qin Y**, **Huang Y**, **Zhao B**, **Liu C**, and **Chetty I**. SU-F-T-566: Absolute film dosimetry for stereotactic radiosurgery and stereotactic body radiotherapy quality assurance using gafchromic ebt3 films *Med Phys* 2016; 43(6):3593. PMID: 28047636. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To evaluate the dosimetric uncertainty associated with Gafchromic (EBT3) films and establish an absolute dosimetry protocol for Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiotherapy (SBRT). METHODS: EBT3 films were irradiated at each of seven different dose levels between 1 and 15 Gy with open fields, and standard deviations of dose maps were calculated at each color channel for evaluation. A scanner non-uniform response correction map was built by registering and comparing film doses to the reference diode array-based dose map delivered with the same doses. To determine the temporal dependence of EBT3 films, the average correction factors of different dose levels as a function of time were evaluated up to four days after irradiation. An integrated film dosimetry protocol was developed for dose calibration, calibration curve fitting, dose mapping, and profile/gamma analysis. Patient specific quality assurance (PSQA) was performed for 93 SRS/SBRT treatment plans. RESULTS: The scanner response varied within 1% for the field sizes less than 5 x 5 cm2 , and up to 5% for the field sizes of 10 x 10 cm2 . The scanner correction method was able to remove visually evident, irregular detector responses found for larger field sizes. The dose response of the film changed rapidly (approximately 10%) in the first two hours and plateaued afterwards, approximately 3% change between 2 and 24 hours. The mean uncertainties (mean of the standard deviations) were <0.5% over the dose range 1 approximately 15Gy for all color channels for the OD response curves. The percentage of points passing the 3%/1mm gamma criteria based on absolute dose analysis, averaged over all tests, was 95.0 +/- 4.2. CONCLUSION: We have developed an absolute film dose dosimetry protocol using EBT3 films. The overall uncertainty has been established to be approximately 1% for SRS and SBRT PSQA. The work was supported by a Research Scholar Grant, RSG-15-137-01-CCE from the American Cancer Society.

Radiation Oncology

Wen N, **Snyder K**, Scheib S, **Qin Y**, **Li H**, and **Chetty I**. SU-F-J-177: A novel image analysis technique (center pixel method) to quantify end-to-end tests *Med Phys* 2016; 43(6):3448-3449. PMID: 28046890. Abstract

Henry Ford Health System, Detroit, MI.
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Henry Ford Health System, Detroit, Michigan.

PURPOSE: To implement a novel image analysis technique, "center pixel method", to quantify end-to-end tests accuracy of a frameless, image guided stereotactic radiosurgery system. METHODS: The localization accuracy was determined by delivering radiation to an end-to-end prototype phantom. The phantom was scanned with 0.8 mm slice thickness. The treatment isocenter was placed at the center of the phantom. In the treatment room, CBCT images of the phantom (kVp=77, mAs=1022, slice thickness 1 mm) were acquired to register to the reference CT images. 6D couch correction were applied based on the registration results. Electronic Portal Imaging Device (EPID)-based Winston Lutz (WL) tests were performed to quantify the errors of the targeting accuracy of the system at 15 combinations of gantry, collimator and couch positions. The images were analyzed using two different methods. a) The classic method. The deviation was calculated by measuring the radial distance between the center of the central BB and the full width at half maximum of the radiation field. b) The center pixel method. Since the imager projection offset from the treatment isocenter was known from the IsoCal calibration, the deviation was determined between the center of the BB and the central pixel of the imager panel. RESULTS: Using the automatic registration method to localize the phantom and the classic method of measuring the deviation of the BB center, the mean and standard deviation of the radial distance was 0.44 +/- 0.25, 0.47 +/- 0.26, and 0.43 +/- 0.13 mm for the jaw, MLC and cone defined field sizes respectively. When the center pixel method was used, the mean and standard deviation was 0.32 +/- 0.18, 0.32 +/- 0.17, and 0.32 +/- 0.19 mm respectively. CONCLUSION: Our results demonstrated that the center pixel method accurately analyzes the WL images to evaluate the targeting accuracy of the radiosurgery system. The work was supported by a Research Scholar Grant, RSG-15-137-01-CCE from the American Cancer Society.

Radiation Oncology

Wu Q, **Devpura S**, **Feghali K**, **Liu C**, **Ajlouni M**, **Movsas B**, and **Chetty I**. WE-AB-207B-05: Correlation of normal lung density changes with dose after stereotactic body radiotherapy (sbrt) for early stage lung cancer *Med Phys* 2016; 43(6):3805. PMID: 28048563. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: To investigate correlation of normal lung CT density changes with dose accuracy and outcome after SBRT for patients with early stage lung cancer. METHODS: Dose distributions for patients originally planned and treated using a 1-D pencil beam-based (PB-1D) dose algorithm were retrospectively recomputed using algorithms: 3-D pencil beam (PB-3D), and model-based METHODS: AAA, Acuros XB (AXB), and Monte Carlo (MC). Prescription dose was 12 Gy x 4 fractions. Planning CT images were rigidly registered to the followup CT datasets at 6-9 months after treatment. Corresponding dose distributions were mapped from the planning to followup CT images. Following the method of Palma et al .(1-2), Hounsfield Unit (HU) changes in lung density in individual, 5 Gy, dose bins from 5-45 Gy were assessed in the peri-tumor region, defined as a uniform, 3 cm expansion around the ITV(1). RESULTS: There is a 10-15% displacement of the high dose region (40-45 Gy) with the model-based algorithms, relative to the PB method, due to the electron scattering of dose away from the tumor into normal lung tissue (Fig.1). Consequently, the high-dose lung region falls within the 40-45 Gy dose range, causing an increase in HU change in this region, as predicted by model-based algorithms (Fig.2). The patient with the highest HU change (approximately 110) had mild radiation pneumonitis, and the patient with HU change of approximately 80-90 had shortness of breath. No evidence of pneumonitis was observed for the 3 patients with smaller CT density changes (<50 HU). Changes in CT densities, and dose-response correlation, as computed with model-based algorithms, are in excellent agreement with the findings of Palma et al. (1-2). CONCLUSION: Dose computed with PB (1D or 3D) algorithms was poorly correlated with clinically relevant CT density changes, as opposed to model-based algorithms. A larger cohort of patients is needed to confirm these results. This work was supported in part by a grant from Varian Medical Systems, Palo Alto, CA.

Radiation Oncology
Xu H, **Chetty I**, and **Wen N**. SU-D-BRA-03: Analysis of systematic errors with 2d/3d image registration for target localization and treatment delivery in stereotactic radiosurgery *Med Phys* 2016; 43(6):3339-3340. PMID: 28047080. Abstract

Wayne State University, Detroit, MI.
Henry Ford Health System, Detroit, MI.

PURPOSE: Determine systematic deviations between 2D/3D and 3D/3D image registrations with six degrees of freedom (6DOF) for various imaging modalities and registration algorithms on the Varian Edge Linac. METHODS: The 6DOF systematic errors were assessed by comparing automated 2D/3D (kV/MV vs. CT) with 3D/3D (CBCT vs. CT) image registrations from different imaging pairs, CT slice thicknesses, couch angles, similarity measures, etc., using a Rando head and a pelvic phantom. The 2D/3D image registration accuracy was evaluated at different treatment sites (intra-cranial and extra-cranial) by statistically analyzing 2D/3D pre-treatment verification against 3D/3D localization of 192 Stereotactic Radiosurgery/Stereotactic Body Radiation Therapy treatment fractions for 88 patients. RESULTS: The systematic errors of 2D/3D image registration using kV-kV, MV-kV and MV-MV image pairs using 0.8 mm slice thickness CT images were within 0.3 mm and 0.3 degrees for translations and rotations with a 95% confidence interval (CI). No significant difference between 2D/3D and 3D/3D image registrations (P>0.05) was observed for target localization at various CT slice thicknesses ranging from 0.8 to 3 mm. Couch angles (30, 45, 60 degree) did not impact the accuracy of 2D/3D image registration. Using pattern intensity with content image filtering was recommended for 2D/3D image registration to achieve the best accuracy. For the patient study, translational error was within 2 mm and rotational error was within 0.6 degrees in terms of 95% CI for 2D/3D image registration. For intra-cranial sites, means and std. deviations of translational errors were -0.2+/-0.7, 0.04+/-0.5, 0.1+/-0.4 mm for LNG, LAT, VRT directions, respectively. For extra-cranial sites, means and std. deviations of translational errors were - 0.04+/-1, 0.2+/-1, 0.1+/-1 mm for LNG, LAT, VRT directions, respectively. 2D/3D image registration uncertainties for intra-cranial and extra-cranial sites were comparable. CONCLUSION: The Varian Edge radiosurgery 6DOF-based system, can perform 2D/3D image registration with high accuracy for target localization in image-guided stereotactic radiosurgery. The work was supported by a Research Scholar Grant, RSG-15-137-01-CCE from the American Cancer Society.

Radiation Oncology
Zhong H, **Siddiqui S**, **Movsas B**, and **Chetty I**. Evaluation of adaptive treatment planning for patients with non-small cell lung cancer *Phys Med Biol* 2017;PMID: 28072395. Article Request Form

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The purpose of this study was to develop metrics to evaluate uncertainties in deformable dose accumulation (DDA) for patients with non-small cell lung cancer (NSCLC). Initial treatment plans (primary) and cone-beam CT (CBCT) images were retrospectively processed for seven NSCLC patients, who showed significant tumor regression during the course of treatment. Each plan was developed with IMRT for 2 Gy33 fractions. A B-spline-based DIR algorithm was used to register weekly CBCT images to a reference image acquired at fraction 21 and the resultant displacement vector fields (DVFs) were then modified using a finite element method (FEM). The doses were calculated on each of these CBCT images and mapped to the reference image using a tri-linear dose interpolation method, based on the B-spline and FEM-generated DVFs. For iso-prescription adaptive plans (relative to initial plans), mean lung dose (MLD) was reduced, on average from 17.3 Gy (initial plan) to 15.2, 14.5 and 14.8 Gy for the plans adapted using the rigid, B-Spline and FEM-based registrations. Similarly, for iso-toxic adaptive plans (considering MLD relative to initial plans) using the rigid, B-Spline and FEM-based registrations, the average doses were 69.96.8, 65.75.1 and 67.25.6 Gy in the initial volume (PTV1), and 81.525.8, 77.721.6, and 78.922.5 Gy in the residual volume (PTV21), respectively. Tumor volume reduction was correlated with dose escalation (for isotoxic plans, correlation coefficient=0.92), and with MLD reduction (for iso-fractional plans, correlation coefficient=0.85). For the case of the iso-toxic dose escalation, plans adapted with the B-Spline and FEM DVFs differed from the primary plan adapted with rigid registration by 2.81.0 Gy and 1.80.9 Gy in PTV1, and the mean difference between doses accumulated using the B-spline and FEM DVFs was 1.10.6 Gy. As a dose mapping-induced energy change, energy defect in the tumor volume was 20.813.4% and 4.52.4% for the B-spline and FEM-based dose accumulations, respectively. The energy defect of the B-Spline-based dose accumulation is significant in the tumor volume and highly correlated to the difference between the B-Spline and FEM-accumulated doses with their correlation coefficient equal to 0.79. Adaptive planning helps escalate target dose and spare normal tissue for patients with NSCLC, but

deformable dose accumulation may have a significant loss of energy in regressed tumor volumes when using image intensity-based DIR algorithms. The metric of energy defect is a useful tool for evaluation of adaptive planning accuracy for lung cancer patients.

Radiation Oncology
Zhong H, **Siddiqui S**, **Zhao B**, **Li H**, **Barton K**, **Siddiqui F**, **Movsas B**, and **Chetty I**. SU-F-R-49: A novel kinetic model for prediction of tumor local control for patients with lung cancer *Med Phys* 2016; 43(6):3384. PMID: 28048749. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: Modeling tumor control probability (TCP) can help optimize treatment plans for better treatment outcomes. This study sought to quantify the radiobiological parameters of the TCP model for patients with lung cancer. METHODS: A two-compartment kinetic model was developed to model tumor regression for five NSCLC patients. The model has three parameters: cell survival fraction, dead-cell-resolving time and tumor doubling time. The last one was extended to a function of tumor volume. Each of these patients was treated with 2 Gyx33 fractions. Daily CBCT images were acquired during the course of treatment. Gross tumor volume (GTV) was delineated on each of these CBCT images, and the visible tumor volumes were fitted to the kinetic model to optimize the parameters, where the Jacobian of this model was constrained by daily tumor volumetric changes. RESULTS: Among the five patients, three had tumor recurrence: 455, 520 and 590 days after the completion of treatment. Recurrent tumor volumes were, respectively, 28.9, 13.7 and 4.8 cm3, measured at distant locations. With the assumption of cell density = 108 cells/cm3, tumor doubling times required for circulating tumor cells to progress to the recurrent volumes are 16.1, 19.2 and 23.1 days. By fitting the kinetic model with 33 measured tumor volumes, the average cell survival fraction for the five patients is 0.5+/-0.21, and tumor doubling times are in the range of 10 approximately 35 days, comparable to the doubling time derived from tumor recurrence data. The doubling times modeled from invisible cells are different from the median (357 days) or mean (166 days) of the doubling time measured directly from visible tumor volumes. CONCLUSION: A kinetic model has been developed to simulate the process of tumor progressing from invisible cells to visible tumor volumes. This model may be useful for TCP prediction for patients with locally advanced lung cancer.

Radiology
Bakalyar D. SU-F-I-39: In search of infinity: Finding the limiting dose for an infinite ct scan on a cylinder of finite length *Med Phys* 2016; 43(6):3395. PMID: 28046880. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: The ICRU/TG200 phantom is a cylinder of polyethylene, 30 cm in diameter and 60 cm long. The dose h(L) in the central plane of the phantom resulting from a scan of length L increases asymptotically with increasing L to a limiting value Deq. However, even after scanning the entire length of this phantom, it is clear that the resultant dose h(60 cm) is still somewhat below the limiting value. The known behavior of h(L) provides a means for estimating the true limit. METHODS: h(L) approaches its limiting but unknown value Deq exponentially. By estimating Deq as Deq* and plotting Deq* - h(L) as a function of L on a semi-log scale, a straight line will result only if Deq* = Deq. If not, there will be significant curvature at the end of the plotted data. Adjusting Deq* by trial-and-error or by an iterative scheme will, if done correctly, accurately determine Deq. RESULTS: The log of Deq* - h(L) was plotted as a function of L using Microsoft Excel. The coefficient of determination (R-squared) was displayed and Deq* was adjusted until R-squared equaled 1. Alternatively, iteration using the Solver tool in Excel can automatically find the best estimate of Deq. The resultant values for Deq was were an increase of around 1.5% above h(60 cm) for the center and 0.8% at the periphery. CONCLUSION: The experiments show that a 60 cm phantom is long enough for the central dose to be within a couple of percentage points of what would be achieved with an infinite phantom. Though this small underestimation of Deq is of little consequence for dose estimates, an accurate determination of Deq allows for a better parameterization of continuous functions representing h(L).

Radiology
Bakalyar D, Feng W, and McKenney S. SU-G-206-06: Analytic dose function for ct scans in infinite cylinders as a function of scan length and cylinder radius *Med Phys* 2016; 43(6):3640. PMID: 28046900. Abstract

Henry Ford Health System, Detroit, MI.
New York Presbyterian Hospital, Tenafly, NJ.
Children's National Medical Center, Washington, DC.

PURPOSE: The radiation dose absorbed at a particular radius rho within the central plane of a long cylinder following a CT scan is a function of the length of the scan L and the cylinder radius R along with kVp and cylinder composition. An analytic function was created that that not only expresses these dependencies but is integrable in closed form over the area of the central plane. This feature facilitates explicit calculation of the planar average dose. The "approach to equilibrium" h(L) discussed in the TG111 report is seamlessly included in this function. METHODS: For a cylindrically symmetric radiation field, Monte Carlo calculations were performed to compute the dose distribution to long polyethylene cylinders for scans of varying L for cylinders ranging in radius from 5 to 20 cm. The function was developed from the resultant Monte Carlo data. In addition, the function was successfully fit to data taken from measurements on the 30 cm diameter ICRU/TG200 phantom using a real-time dosimeter. RESULTS: Symmetry and continuity dictate a local extremum at the center which is a minimum for the larger sizes. There are competing effects as the beam penetrates the cylinder from the outside: attenuation, resulting in a decrease; scatter, abruptly increasing at the circumference. This competition may result in an absolute maximum between the center and outer edge leading to a "gull wing" shape for the radial dependence. For the smallest cylinders, scatter may dominate to the extent that there is an absolute maximum at the center. CONCLUSION: An integrable, analytic function has been developed that provides the radial dependency of dose for the central plane of a scan of length L for cylinders of varying diameter. Equivalently, we have developed h(L,R,rho).

Radiology

Baumer TG, **Davis L**, **Dischler J**, **Siegal DS**, **van Holsbeeck M**, **Moutzouros V**, and **Bey MJ**. Shear wave elastography of the supraspinatus muscle and tendon: Repeatability and preliminary findings *J Biomech* 2017;PMID: 28110933.
Full Text

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Shear wave elastography (SWE) is a promising tool for estimating musculoskeletal tissue properties, but few studies have rigorously assessed its repeatability and sources of error. The objectives of this study were to assess: (1) the extent to which probe positioning error and human user error influence measurement accuracy, (2) intra-user, inter-user, and day-to-day repeatability, and (3) the extent to which active and passive conditions affect shear wave speed (SWS) repeatability. Probe positioning and human usage errors were assessed by acquiring SWE images from custom ultrasound phantoms. Intra- and inter-user repeatability were assessed by two users acquiring five trials of supraspinatus muscle and tendon SWE images from ten human subjects. To assess day-to-day repeatability, five of the subjects were tested a second time, approximately 24h later. Imaging of the phantoms indicated high inter-user repeatability, with intraclass correlation coefficient (ICC) values of 0.68-0.85, and RMS errors of no more than 4.1%. SWE imaging of the supraspinatus muscle and tendon had high repeatability, with intra- and inter-user ICC values of greater than 0.87 and 0.73, respectively. Day-to-day repeatability demonstrated ICC values greater than 0.33 for passive muscle, 0.48 for passive tendon, 0.65 for active muscle, and 0.94 for active tendon. This study indicates the technique has good to very good intra- and inter-user repeatability, and day-to-day repeatability is appreciably higher when SWE images are acquired under a low level of muscle activation. The findings from this study establish the feasibility and repeatability of SWE for acquiring data longitudinally in human subjects.

Radiology

Baumer TG, **Dischler J**, **Mende V**, **Zauel R**, **van Holsbeeck M**, **Siegal DS**, **Divine G**, **Moutzouros V**, and **Bey MJ**. Effects of asymptomatic rotator cuff pathology on in vivo shoulder motion and clinical outcomes *J Shoulder Elbow Surg* 2017;PMID: 28131679. Full Text

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BACKGROUND: The incidence of asymptomatic rotator cuff tears has been reported to range from 15% to 39%, but the influence of asymptomatic rotator cuff pathology on shoulder function is not well understood. This study assessed the effects of asymptomatic rotator cuff pathology on shoulder kinematics, strength, and patient-reported outcomes.

METHODS: A clinical ultrasound examination was performed in 46 asymptomatic volunteers (age: 60.3 +/- 7.5 years) with normal shoulder function to document the condition of their rotator cuff. The ultrasound imaging identified the participants as healthy (n = 14) or pathologic (n = 32). Shoulder motion was measured with a biplane x-ray imaging system, strength was assessed with a Biodex (Biodex Medical Systems, Inc., Shirley, NY, USA), and patient-reported outcomes were assessed using the Western Ontario Rotator Cuff Index and visual analog scale pain scores. RESULTS: Compared with healthy volunteers, those with rotator cuff pathology had significantly less abduction (P = .050) and elevation (P = .041) strength, their humerus was positioned more inferiorly on the glenoid (P = .018), and the glenohumeral contact path length was longer (P = .007). No significant differences were detected in the Western Ontario Rotator Cuff Index, visual analog scale, range of motion, or acromiohumeral distance. CONCLUSIONS: The differences observed between the healthy volunteers and those with asymptomatic rotator cuff pathology lend insight into the changes in joint mechanics, shoulder strength, and conventional clinical outcomes associated with the early stages of rotator cuff pathology. Furthermore, these findings suggest a plausible mechanical progression of kinematic and strength changes associated with the development of rotator cuff pathology.

Radiology

Bevins N. MO-F-204-00: Preparing for the ABR diagnostic and nuclear medical physics exams *Med Phys* 2016; 43(6):3708. PMID: 28048871. Abstract

Henry Ford Health System, Detroit, MI.

Adequate, efficient preparation for the ABR Diagnostic and Nuclear Medical Physics exams is key to successfully obtain ABR certification. Each part of the ABR exam presents its own challenges: Part I: Determine the scope of basic medical physics study material, efficiently review this material, and solve related written questions/problems. Part II: Understand imaging principles, modalities, and systems, including image acquisition, processing, and display. Understand the relationship between imaging techniques, image quality, patient dose and safety, and solve related written questions/problems. Part III: Gain crucial, practical, clinical medical physics experience. Effectively communicate and explain the practice, performance, and significance of all aspects of clinical medical physics. All parts of the ABR exam require specific skill sets and preparation: mastery of basic physics and imaging principles; written problem solving often involving rapid calculation; responding clearly and succinctly to oral questions about the practice, methods, and significance of clinical medical physics. This symposium focuses on the preparation necessary for each part of the ABR exam. Although there is some overlap, the nuclear exam covers a different body of knowledge than the diagnostic exam. A separate speaker will address those unique aspects of the nuclear exam, and how preparing for a second specialty differs from the first. Medical physicists who recently completed each ABR exam portion will share their experiences, insights, and preparation methods to help attendees best prepare for the challenges of each part of the ABR exam. In accordance with ABR exam security policy, no recalls or exam questions will be discussed. LEARNING OBJECTIVES: 1. How to prepare for Part 1 of the ABR exam by determining the scope of basic medical physics study material and related problem solving/calculations 2. How to prepare for Part 2 of the ABR exam by understanding diagnostic and/or nuclear imaging physics, systems, dosimetry, safety and related problem solving/calculations 3. How to prepare for Part 3 of the ABR exam by effectively communicating the practice, methods, and significance of clinical diagnostic and/or nuclear medical physics.

Radiology

Flynn M. TU-D-206-00: Body tomosynthesis *Med Phys* 2016; 43(6):3748. PMID: 28048053. Abstract

Henry Ford Health System, Detroit, MI.

The current use of tomosynthesis for musculo-skeletal, abdominal, and thoracic imaging will be considered in four sections: A. Current Practice (M. Bath) : The presently available systems for body tomosynthesis will be reviewed and the current diagnostic applications described. B. Image Features and artifacts (M. FLynn): The consequence of a limited angle linear acquisition scan on image features and artifacts will be explained. C. Radiation Dose (J. Sabol): The organ dose associated with common tomosynthesis protocols will be reported and compared to the dose for radiographic and computed tomography procedures. D. Acceptance testing and Quality Assurance (K. Jones): Recommended medical physics acceptance test will be described and appriate programs for quality assurance discussed. LEARNING OBJECTIVES: 1. Learn how body tomosynthesis is currently being used in diagnostic radiology. 2. Understand how scan acquisitions can be designed to optimize image content and minimize artifacts. 3. Learn to radiation dose associated with common protocols. 4. Understand how to best evaluate a newly purchased tomosynthesis system. J. Sabol, Presenter is an employee of GE Healthcare.

Radiology
Flynn M. TU-FG-206-01: Standards support for color in medical imaging *Med Phys* 2016; 43(6):3760. PMID: 28047330. Abstract

Henry Ford Health System.

The field of imaging informatics is a subfield of biomedical informatics that combines medical physics with computer, clinical, and cognitive sciences. In this session jointly sponsored with the Society of Imaging Informatics in Medicine, we will provide an overview of the field starting with the highly applied role of information technology working with imaging modalities to research areas in computer vision, annotation markup, and semantic ontologies that can leverage machine encoded reasoning systems. We will highlight new technologies that are beneficial to medical physicists conducting research as well as translating research into clinical practice. Define the field of imaging informatics as it relates to medical physics Discuss DICOM interoperability standards and the certification for imaging informatics professional. Highlight research areas in imaging informatics.

Radiology
Flynn M. TU-D-206-02: Body tomosynthesis image features and artifacts *Med Phys* 2016; 43(6):3748. PMID: 28046727. Abstract

Henry Ford Health System.

The current use of tomosynthesis for musculo-skeletal, abdominal, and thoracic imaging will be considered in four sections: A. Current Practice (M. Bath) : The presently available systems for body tomosynthesis will be reviewed and the current diagnostic applications described. B. Image Features and artifacts (M. FLynn): The consequence of a limited angle linear acquisition scan on image features and artifacts will be explained. C. Radiation Dose (J. Sabol): The organ dose associated with common tomosynthesis protocols will be reported and compared to the dose for radiographic and computed tomography procedures. D. Acceptance testing and Quality Assurance (K. Jones): Recommended medical physics acceptance test will be described and appriate programs for quality assurance discussed. LEARNING OBJECTIVES: 1. Learn how body tomosynthesis is currently being used in diagnostic radiology. 2. Understand how scan acquisitions can be designed to optimize image content and minimize artifacts. 3. Learn to radiation dose associated with common protocols. 4. Understand how to best evaluate a newly purchased tomosynthesis system. J. Sabol, Presenter is an employee of GE Healthcare.

Radiology
Jones A, Dave J, Fisher R, Hulme K, Rill L, Zamora D, Woodward A, Brady S, MacDougall R, Goldman L, **Lang S**, **Peck D**, Apgar B, Shepard S, Uzenoff R, and Willis C. TU-FG-209-08: Distribution of the deviation index (di) in digital radiography practices across the United States *Med Phys* 2016; 43(6):3762. PMID: 28048011. Abstract

UT MD Anderson Cancer Center, Houston, TX.
Thomas Jefferson University, Philadelphia, PA.
The Cleveland Clinic, Cleveland, OH.
The Cleveland Clinic, Beachwood, OH.
University Florida, Jacksonville Beach, FL.
University of Washington, Seattle, WA.
The University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.
St. Jude Children's Research Hospital, Memphis, TN.
Children's Hospital, Boston, MA.
Hartford Hospital, Hartford, CT.
Henry Ford Health System, Detroit, MI.
AGFA HealthCare, Greenville, SC.
FUJIFILM Medical Systems U.S.A., Inc., Weston, CT.
University of Texas MD Anderson Cancer Center, Bellaire, TX.

PURPOSE: To characterize the distribution of the deviation index (DI) in digital radiography practices across the United States. METHODS: DI data was obtained from 10 collaborating institutions in the United States between 2012 and 2015. Each institution complied with the requirements of the Institutional Review Board at their site. DI data from radiographs of the body parts chest, abdomen, pelvis and extremity were analyzed for anteroposterior, posteroanterior, lateral, and decubitus views. The DI data was analyzed both in aggregate and stratified by exposure control method, image receptor technology, patient age, and participating site for each body part and view. The number of exposures with DI falling within previously published control limits for DI and descriptive statistics were

calculated. RESULTS: DI data from 505,930 radiographic exposures was analyzed. The number of exposures with DI falling within published control limits for DI varied from 10 to 20% for adult patients and 10 to 23% for pediatric patients for different body parts and views. Mean DI values averaged over other parameters for radiographs of the abdomen, chest, pelvis, and extremities ranged from 0.3 to 1.0, -0.6 to 0.5, 0.8, and -0.9 to 0.5 for the different adult views and ranged from -1.6 to -0.1, -0.3 to 0.5, -0.1, -0.2 to 1.4 for the different pediatric views, respectively (DI data was solicited only for anteroposterior view of pelvis). Standard deviation values of DI from individual sites ranged from 1.3 to 3.6 and 1.3 to 3.0 for the different adult and pediatric views, respectively. Also of interest was that target exposure indicators varied by up to a factor of 6 between sites for certain body parts and views. CONCLUSION: Previously published DI control limits do not reflect the state of clinical practice in digital radiography. Mean DI and target exposure indicators are targets for quality improvement efforts in radiography.

Radiology
Kimpe T, Green P, Revie C, and **Flynn M**. SU-F-I-60: ICC MIWG Displays: Final recommendations for visualization of medical content on color display systems *Med Phys* 2016; 43(6):3400. PMID: 28047596. Abstract

Barco NV, Kortrijk, Belgium.
International Color Consortium, Reston, VA, USA.
FFEI ltd, Hemel Hempstead, Hertfordshire, UK.
Henry Ford Health System, Detroit, MI.

PURPOSE: Use of color images in medical imaging has increased significantly the last few years. There is no agreement yet on what is an appropriate visualization framework for color medical images. This lack of standardization results into large variability of color appearance and makes consistency and quality assurance a challenge. The ICC Medical-Imaging-Working-Group (MIWG) has defined recommendations for visualization of medical content on color display systems, whereby DICOM GSDF images, pseudo color images and color accurate images can all be presented effectively on the same display. METHODS: The MIWG characterized a wide range of color display systems (consumer, professional and medical), and collected representative greyscale and color medical images. Simulations and bench testing was done to quantitatively compare the performance of various architectures and imaging pipelines in an ICC framework context. This allowed making recommendations on imaging pipeline architectures, and defining minimum requirements to guarantee minimum performance levels. RESULTS: The ICC framework specification supports many possible architectures, profile types and pipeline characteristics. Numerous experiments have been performed to understand the effects related to choice of System design choices such as architecture, profile type (matrix, LUT, device, ...) and pipeline specifications (eg. bit depth, LUT size). The impact of inaccurate estimation of display luminance/contrast/tone rendering curve has also been studied. Specific recommendations have been made related to system configuration, ICC framework/CMM, and calibration process. CONCLUSION: There is a need to standardize how medical color images need to be visualized. The ICC Medical Imaging Working Group has defined recommendations for visualization of medical content on color display systems. It has been shown that it is possible to achieve accurate greyscale, pseudo color and absolute color visualization of medical images by means of the ICC framework, at least when appropriate choices are made related to profile specification, imaging pipeline and calibration procedure. Tom Kimpe, employee Barco NV.

Radiology
Singh V, McKenney S, Sunde P, Feng W, and Bakalyar D. SU-F-I-05: Dose symmetry for ctdi equivalent measurements with limited angle cbct *Med Phys* 2016; 43(6):3387. PMID: 28047451. Abstract

Henry Ford Hospital, Detroit, MI.
Children's National Medical Center, Washington, DC.
Radcal, Inc, Monrovia, AA.
New York Presbyterian Hospital, Tenafly, NJ.
Henry Ford Health System, Detroit, MI.

PURPOSE: CTDI measurements, useful for characterizing the x-ray output for multi-detector CT (MDCT), require a 360 degrees rotation of the gantry; this presents a problem for cone beam CT (CBCT) due to its limited angular rotation. The purpose of this work is to demonstrate a methodology for overcoming this limited angular rotation so that CTDI measurements can also be made on CBCT systems making it possible to compare the radiation output from both types of system with a common metric. METHODS: The symmetry of the CTDI phantom allows a 360 degrees CTDI measurement to be replaced with two 180 degrees measurements. A pencil chamber with a real-time digitizer was placed at the center of the head phantom (16 cm, PMMA) and the resulting exposure measurement from a 180 degrees acquisition was doubled. A pair of edge measurements, each obtained with the gantry passing through the same 180 arc, was obtained with the pencil chamber at opposite edges of the diameter of the phantom and then

summed. The method was demonstrated on a clinical CT scanner (Philips, Brilliance6) and then implemented on an interventional system (Siemens, Axiom Artis). RESULTS: The equivalent CTDI measurement agreed with the conventional CTDI measurement within 8%. The discrepancy in the two measurements is largely attributed to uncertainties in cropping the waveform to a 180 degrees acquisition. (Note: Because of the reduced fan angle in the CBCT, CTDI is not directly comparable to MDCT values when a 32 cm phantom is used.) CONCLUSION: The symmetry-based CTDI measurement is an equivalent measurement to the conventional CTDI measurement when the fan angle is large enough to encompass the phantom diameter. This allows a familiar metric of radiation output to be employed on systems with a limited angular rotation.

Radiology
Spain JA, **Rheinboldt M**, **Parrish D**, and **Rinker E**. Morel-lavallee injuries: A multimodality approach to imaging characteristics *Acad Radiol* 2017; 24(2):220-225. PMID: 28087046. Full Text

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Morel-Lavallee lesions are relatively rare closed degloving injuries caused by a shearing force resulting in separation of the dermis and the hypodermis from the subjacent deeper fascia. Although most commonly encountered lateral to the greater trochanter, these injuries may occur throughout the body in a variety of locations. Separation of the hypodermal tissue planes results in a complex serosanguinous fluid collection with areas of internal fat necrosis. The imaging appearance is variable and nonspecific, potentially mimicking superficial hemorrhagic bursitis, or cystic or necrotic primary soft tissue neoplasms. If not treated in the acute or early subacute setting, these collections are at risk of superinfection, overlying tissue necrosis, and continued expansion. In this article, we will review the pathophysiology, cross-sectional imaging features, and differential diagnostic considerations of Morel-Lavallee lesions as well as discuss management and treatment options.

Radiology
Spain JA, **Shaikh S**, and **Sandberg SA**. Sonographic findings and diagnostic pitfalls in evaluation for uterine rupture in a case of fetal demise and prior cesarean delivery of unknown type *Ultrasound Q* 2017;PMID: 28081020. Full Text

From the Department of Radiology, Henry Ford Hospital, Detroit, MI.

A 38-week pregnant patient with history of cesarean delivery was admitted to the hospital for induction of labor after diagnosis of fetal demise. When the clinical picture became concerning for uterine scar dehiscence, an ultrasound was ordered. After targeted ultrasound of the lower uterine segment, the sonographer initially reported thin but intact lower uterine segment and normal positioning of the fetus. By keeping a high level of suspicion, the radiologist analyzed the images submitted and found other clues suggesting possible dehiscence or rupture. Additional images were then obtained, ultimately demonstrating uterine rupture with fetus external to uterus.

Radiology
Vanderhoek M, and **Bevins N**. MO-DE-BRA-04: Hands-on fluoroscopy safety training with real-time patient and staff dosimetry *Med Phys* 2016; 43(6):3698-3699. PMID: 28048751. Abstract

Henry Ford Health System, Detroit, MI.

PURPOSE: Fluoroscopically guided interventions (FGI) are routinely performed across many different hospital departments. However, many involved staff members have minimal training regarding safe and optimal use of fluoroscopy systems. We developed and taught a hands-on fluoroscopy safety class incorporating real-time patient and staff dosimetry in order to promote safer and more optimal use of fluoroscopy during FGI. METHODS: The hands-on fluoroscopy safety class is taught in an FGI suite, unique to each department. A patient equivalent phantom is set on the patient table with an ion chamber positioned at the x-ray beam entrance to the phantom. This provides a surrogate measure of patient entrance dose. Multiple solid state dosimeters (RaySafe i2 dosimetry systemTM) are deployed at different distances from the phantom (0.1, 1, 3 meters), which provide surrogate measures of staff dose. Instructors direct participating clinical staff to operate the fluoroscopy system as they view live fluoroscopic images, patient entrance dose, and staff doses in real-time. During class, instructors work with clinical staff to investigate how patient entrance dose, staff doses, and image quality are affected by different parameters, including pulse rate, magnification, collimation, beam angulation, imaging mode, system geometry, distance, and shielding. RESULTS: Real-time dose visualization enables clinical staff to directly see and learn how to optimize their use of their own fluoroscopy system to minimize patient and staff dose, yet maintain sufficient image quality for FGI. As a direct result

of the class, multiple hospital departments have implemented changes to their imaging protocols, including reduction of the default fluoroscopy pulse rate and increased use of collimation and lower dose fluoroscopy modes. CONCLUSION: Hands-on fluoroscopy safety training substantially benefits from real-time patient and staff dosimetry incorporated into the class. Real-time dose display helps clinical staff visualize, internalize, and ultimately utilize the safety techniques learned during the training. RaySafe/Unfors/Fluke lent us a portable version of their RaySafe i2 Dosimetry System for 6 months.

Surgery
Go P, **Watson J**, **Lu Z**, **Carlin A**, and **Hammoud Z**. Robotic resection of a mediastinal parathyroid cyst *Gen Thorac Cardiovasc Surg* 2017; 65(1):52-55. PMID: 26353995. Full Text

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Mediastinal parathyroid cysts (PC) are rare, benign lesions, reported in fewer than 150 cases worldwide. Although most are asymptomatic and discovered incidentally on imaging, symptoms of dyspnea, dysphagia, hoarseness, palpitations, hypercalcemia, and innominate or jugular venous thrombosis have been reported. Sternotomy or thoracotomy has traditionally been the approach used to resect mediastinal PCs. We describe the first reported case of a robot-assisted resection of a mediastinal PC.

Surgery
Shimunov S, and **Baidoun F**. Denture molding causing small bowel obstruction: Case study *Surgery* 2017;PMID: 28111045. Full Text

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Surgery
Steinbeisser M, **McCracken J**, and **Kharbutli B**. Laparoscopic sleeve gastrectomy: Preoperative weight loss and other factors as predictors of postoperative success *Obes Surg* 2017;PMID: 28050788. Full Text

Department of Surgery, Henry Ford Wyandotte Hospital, 2333 Biddle Ave, Wyandotte, MI, 48192, USA.
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BACKGROUND: Correlation between weight loss before bariatric surgery and postoperative success has been discussed and investigated. It also has been a requirement for some surgeons and insurance companies. OBJECTIVE: The aim of this study is to address whether weight loss before sleeve gastrectomy is a predictor of postoperative success in terms of excess body weight lost (EBWL). SETTING: Study was performed at a community teaching hospital in Michigan. METHODS: We examined data from 204 patients who underwent laparoscopic sleeve gastrectomy between August 2011 and January 2015. Data was collected retrospectively including demographics, comorbidities, body mass index (BMI), percentage of EBW lost prior to surgery, percentage of EBW lost, and change in BMI at 3 months (191, 93.6%), 6 months (164, 80.4%), and 12 months (134, 65.7%). RESULTS: When examining postoperative mean percentage of EBW lost and change in BMI, we found that the group who lost >5% of their EBW before surgery had a statistically significant more weight loss than those who lost <5%. CONCLUSIONS: There was a statistically significant differences in adjusted postoperative mean percentage EBWL and change in BMI between those who preoperatively lost >5% of their EBW and those who lost <5% favoring those who lost >5%, but both groups still achieved similar postoperative weight loss success at 1 year. Increasing preoperative BMI resulted in decreasing postoperative percentage EBWL.

Urology
Abaza R, Eun DD, Gallucci M, Gill IS, **Menon M**, Mottrie A, and Shabsigh A. Robotic surgery for renal cell carcinoma with vena caval tumor thrombus *European Urology Focus* 2017;PMID: Not assigned. Full Text

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Context: Robotic surgery has significantly advanced the minimally-invasive management of kidney tumors with extension into the inferior vena cava requiring caval cross-clamping and tumor thrombectomy. Additional techniques have recently been developed to continue the evolution of this complex procedure and extend its indications. Objective: To review the current state of the art as regards robotic nephrectomy with inferior vena cava thrombectomy (RNIT). Evidence acquisition: A systematic review of the Medline database was performed. All literature available through October 2016 was included. Evidence synthesis: RNIT has been successfully adopted at select centers, but the number of patients reported to date remains limited. Modifications in clamping and tumor thrombus management have been described allowing for multiple options in surgical technique. Early perioperative outcomes appear favorable in comparison with traditional, open surgery, but further experience is needed. Conclusions: Feasibility and reproducibility of RNIT has been demonstrated, but longer-term outcomes and larger patient numbers are necessary before the role of this procedure is established. Patient summary: Kidney cancers invading the largest vein in the body, the vena cava, require complex surgery for removal. Traditionally this has required a large incision, but newer techniques with robotic surgery that continue to evolve have allowed for a minimally-invasive approach. Robotic surgery allows a completely minimally-invasive technique for tumor thrombectomy even for selected patients with relatively extensive thrombi. Such techniques have now been reproduced by several groups. Discrimination of ideal candidates and larger experiences will be necessary before widespread adoption and acceptance.

Urology

Chakravarthi BV, Goswami MT, Pathi SS, Dodson M, Chandrashekar DS, Agarwal S, Nepal S, Hodigere Balasubramanya SA, Siddiqui J, Lonigro RJ, Chinnaiyan AM, Kunju LP, **Palanisamy N**, and **Varambally S**. Expression and role of paics, a de novo purine biosynthetic gene in prostate cancer *Prostate* 2017; 77(1):10-21. PMID: 27550065. Full Text

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Department of Pathology, University of Michigan, Ann Arbor, Michigan.
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Comprehensive Cancer Center, University of Michigan Medical School, Ann Arbor, Michigan.
Department of Urology, University of Michigan, Ann Arbor, Michigan.
Howard Hughes Medical Institute, University of Michigan Medical School, Ann Arbor, Michigan.

BACKGROUND: Our goal was to investigate de novo purine biosynthetic gene PAICS expression and evaluate its role in prostate cancer progression. METHODS: Next-generation sequencing, qRTPCR and immunoblot analysis revealed an elevated expression of a de novo purine biosynthetic gene, Phosphoribosylaminoimidazole Carboxylase, Phosphoribosylaminoimidazole Succinocarboxamide Synthetase (PAICS) in a progressive manner in prostate cancer. Functional analyses were performed using prostate cancer cell lines- DU145, PC3, LnCaP, and VCaP. The oncogenic properties of PAICS were studied both by transient and stable knockdown strategies, in vivo chicken chorioallantoic membrane (CAM) and murine xenograft models. Effect of BET bromodomain inhibitor JQ1 on the expression level of PAICS was also studied. RESULTS: Molecular staging of prostate cancer is important factor in effective diagnosis, prognosis and therapy. In this study, we identified a de novo purine biosynthetic gene; PAICS is overexpressed in PCa and its expression correlated with disease aggressiveness. Through several in vitro and in vivo functional studies, we show that PAICS is necessary for proliferation and invasion in prostate cancer cells. We identified JQ1, a BET bromodomain inhibitor previously implicated in regulating MYC expression and demonstrated role in prostate cancer, abrogates PAICS expression in several prostate cancer cells. Furthermore, we observe loss of MYC occupancy on PAICS promoter in presence of JQ1. CONCLUSIONS: Here, we report that evaluation of PAICS in prostate cancer progression and its role in prostate cancer cell proliferation and invasion and suggest it as a valid therapeutic target. We suggest JQ1, a BET-domain inhibitor, as possible therapeutic option in targeting PAICS in prostate cancer. Prostate 77:10-21, 2017. (c) 2016 Wiley Periodicals, Inc.

Urology

Nocera L, Karabon P, and **Abdollah F**. 10-Year Outcomes in Localized Prostate Cancer *N Engl J Med* 2017; 376(2):178-179. PMID: 28079331. Full Text

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Urology

Seisen T, Briganti A, Blanchard P, and **Abdollah F**. Salvage radiation therapy for biochemical recurrence after radical prostatectomy: Is earlier always better? *J Clin Oncol* 2017:Jco2016706879. PMID: 28135149. Full Text

Thomas Seisen, Henry Ford Health System, Detroit, MI; Alberto Briganti, Istituti di Ricovero e Cura a Carattere Scientifico (IRCCS) Ospedale San Raffaele; and Vita-Salute San Raffaele University, Milan, Italy; Pierre Blanchard, Institut Gustave Roussy, Villejuif, France; and Firas Abdollah, Henry Ford Health System, Detroit, MI.

Urology

Swearingen R, **Sood A**, Madi R, Klaassen Z, Badani K, **Elder JS**, Wood K, Hemal A, and Ghani KR. Zero-fragment nephrolithotomy: A multi-center evaluation of robotic pyelolithotomy and nephrolithotomy for treating renal stones *Eur Urol* 2016;PMID: 28085668. Full Text

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BACKGROUND: Robotic pyelolithotomy (RPL) and robotic nephrolithotomy (RNL) may be utilized for treating kidney stones as an alternative to percutaneous nephrolithotomy or flexible ureteroscopy. OBJECTIVE: To describe the techniques of RPL and RNL, and present multi-center outcome data for patients undergoing these procedures. DESIGN, SETTING, AND PARTICIPANTS: This study was a retrospective analysis of 27 patients undergoing RPL and RNL at five tertiary academic institutions between 2008 and 2014. SURGICAL PROCEDURE: RPL and RNL without use of renal ischemia. MEASUREMENTS: We assessed stone clearance by visual assessment and postoperative imaging. We also examined other factors, including complications (Clavien grade), estimated blood loss, operative time, and length of stay. RESULTS AND LIMITATIONS: Twenty-seven patients underwent 28 procedures for a mean renal stone size of 2.74cm (standard deviation: 1.4, range: 0.8-5.8). The mean stone volume was 10.2cm3. RPL accounted for 26 of these procedures. RNL was performed in one patient, while another underwent combined RPL-RNL. Indications included failed previous endourological management (13), staghorn calculi (five), gas containing stone (one), calyceal diverticulum (one), complex urinary tract reconstruction (two), and patient preference (four). The mean patient age was 35.6 yr and mean body mass index was 25.5kg/m2. Mean operative time/console times were 182min and 128min, respectively. The mean estimated blood loss was 38ml. The mean length of stay was 1.7 d. There was no significant change in preoperative and postoperative serum creatinine levels. The overall complication rate was 18.5% (Clavien 1=3.7%; 2=7.4%; 3b=7.4%). The complete stone-free rate was 96%. CONCLUSIONS: RPL and RNL are safe and reasonable options for removing renal stones in select patients. In particular, RPL allows the removal of stones without transgressing the parenchyma, reducing potential bleeding and nephron loss. PATIENT SUMMARY: The robotic approach allows for complete removal of the renal stone without fragmentation, thereby maximizing chances for complete stone clearance in one procedure.